ANTIMICROBIAL RESISTANCE (AMR) COMMUNITY OF PRACTICE (CoP)

Addressing Antimicrobial Resistance (AMR) through surveillance in low and middle income African countries and South African situation

Olga Perovic,

A/Prof Olga Perovic, University of Witwatersrand

Director, AMR Division at WITS Health Consortium

Head, WHO Collaborating Centre for AMR

Honorary Pathologist

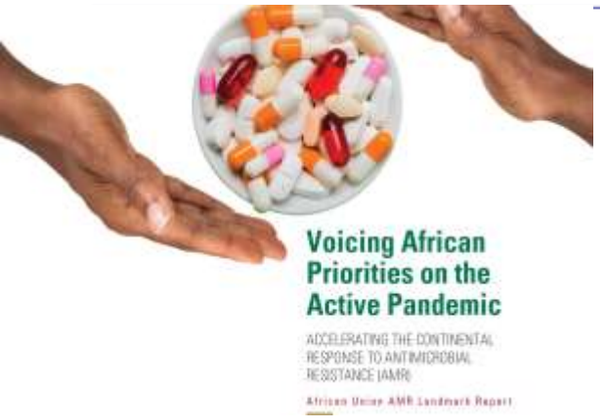
Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses (CHARM)

6th September 2024

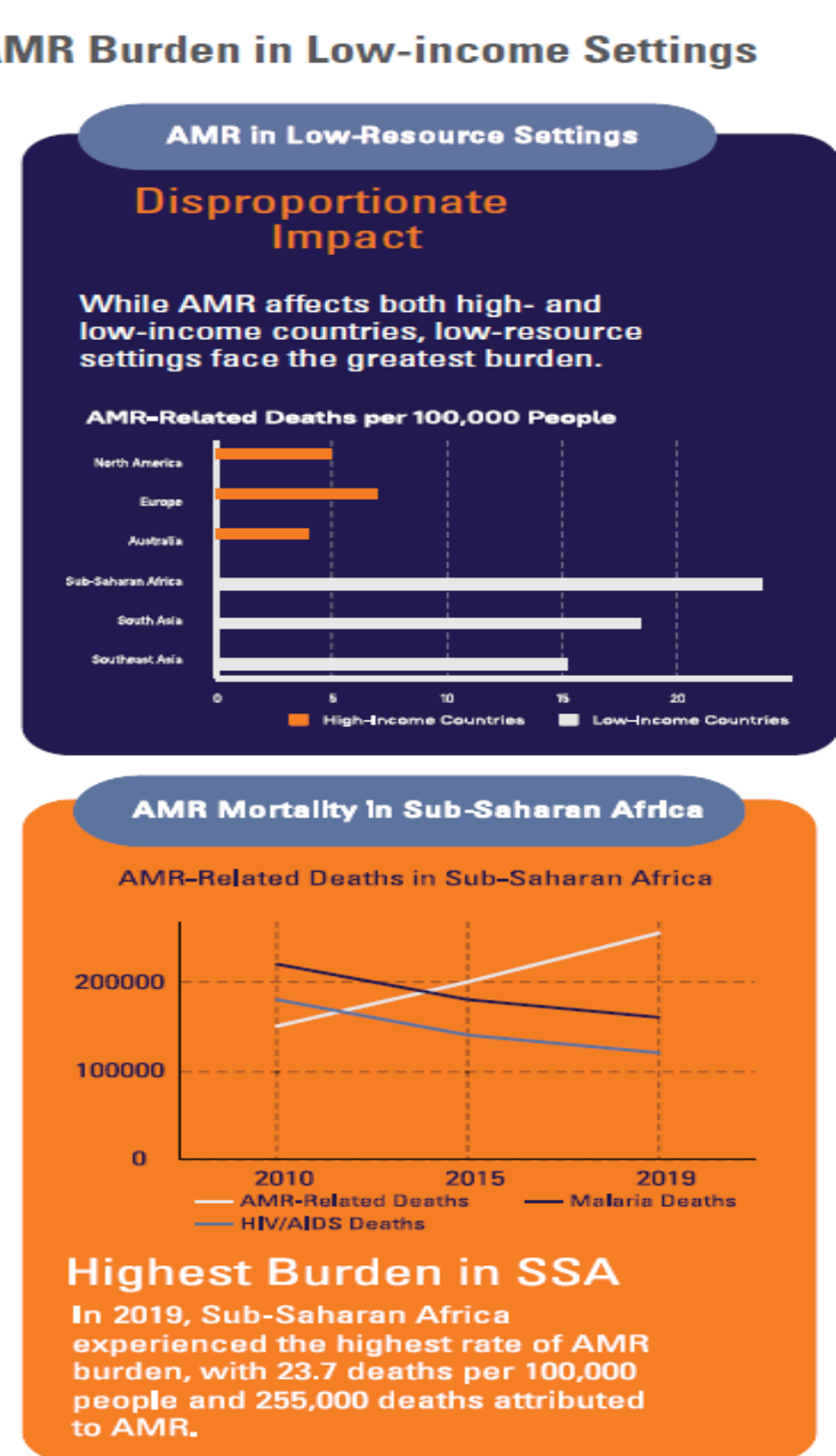
Outline for AMR in LMIC

- Current situation on AMR
- Regional and global perspective on AMR surveillance
- Case study, South Africa
- Addressing importance of surveillance for AMR

Voice of Africa priorities, landmark report



- African countries face challenges, including a lack of access to clean and safe water, poor Water, Sanitation, and Hygiene (WASH) programs, inadequate infection prevention measures, and suboptimal vaccinations for preventable diseases.
  - Africa views a significant burden of infectious diseases, approximately 95% of malaria deaths, 70% of people living with HIV, and 25% of TB deaths globally. In 2019, AMR was linked to approximately 55,000 deaths from HIV, 30,000 from malaria, and 255,000 overall.
  - AMR affects both high- and low-income countries (LMIC's), the Global Research on Antimicrobial Resistance (GRAM) study identified the highest burden in low-resource settings, with infectious diseases and weak health systems.



Africa Landmark Report Progress Since Implementation of GAP

While most countries in the region have developed and prioritized National Action Plans (NAPs) to tackle AMR, the overall response remains inadequate given the magnitude of the threat to human, animal, environmental, aquatic, and plant health.

Policy and Governance

Weakness in the governance structures and lack of legal mandate to involve other ministries for planning and commitments

Surveillance Systems

African countries enrollment to GLASS is better than submission of data due to limitation in laboratory systems

Capacity Building

Efforts by funding organization to strengthen laboratory capacities for AMR detection is progressing.

Reduce the incidence of infection by effective IPC and increase vaccination coverage

Only 13% of A countries have IPC/WASH programs in line with WHO guidelines and 20% of children do not receive essential vaccines.

Access to diagnostics

Access to essential diagnostics and continues to be a significant challenges

Strengthened collaborations

AU member states have increasingly formed strategic bilateral partnership with governmental agencies, however some inconsistencies exist.

Optimal use of antimicrobial agents

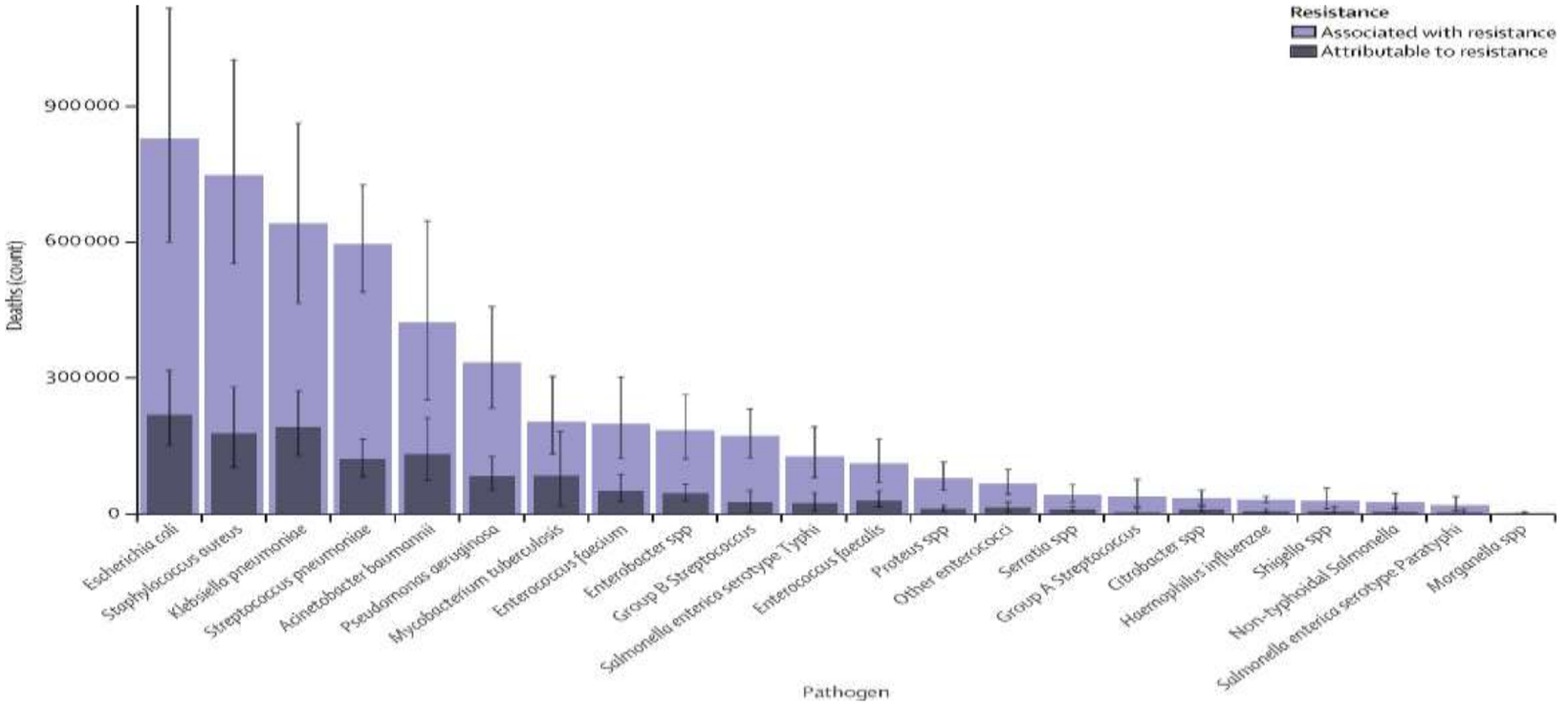
Despite efforts, significant challenges persists, particularly in regulation antibiotic use in agriculture.

Development of economic case for sustainable investments

It is essential to develop innovative financing mechanisms, which is still in the process

GRAM study

Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis
ESKAPE pathogens with resistance were responsible for 929 000 deaths

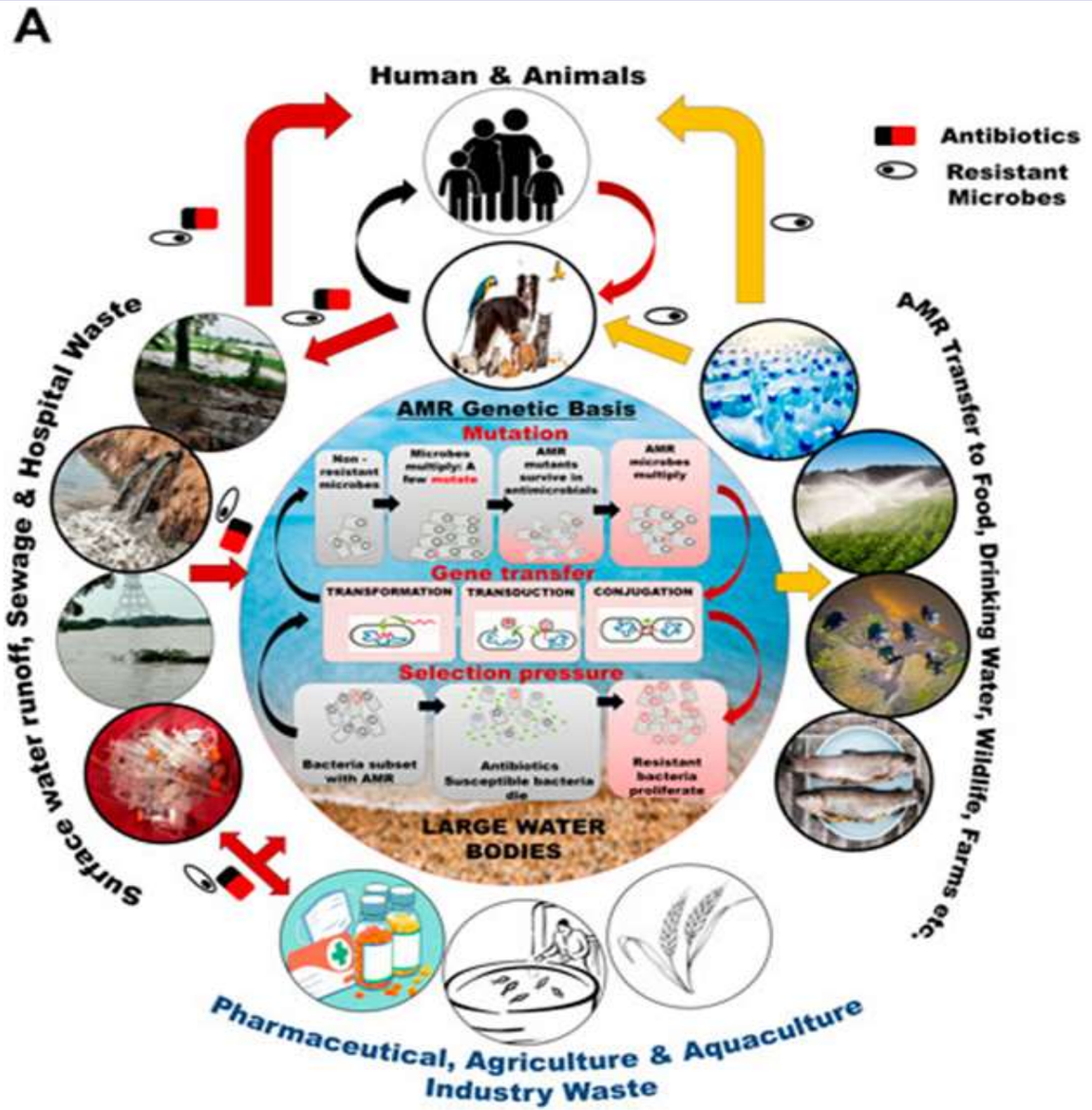


Professor Otto Cars quote:

"The GRAM study suggested that we start saying "bacterial AMR" when we talk about antibiotic resistance, which from a scientific view is not a particularly logical term. But it is my hope that we can start calling things by their right name now that we indeed have good data on both burden and economic impact of ABR. I think this is a good starting point for developing a more engaging narrative for the problem".

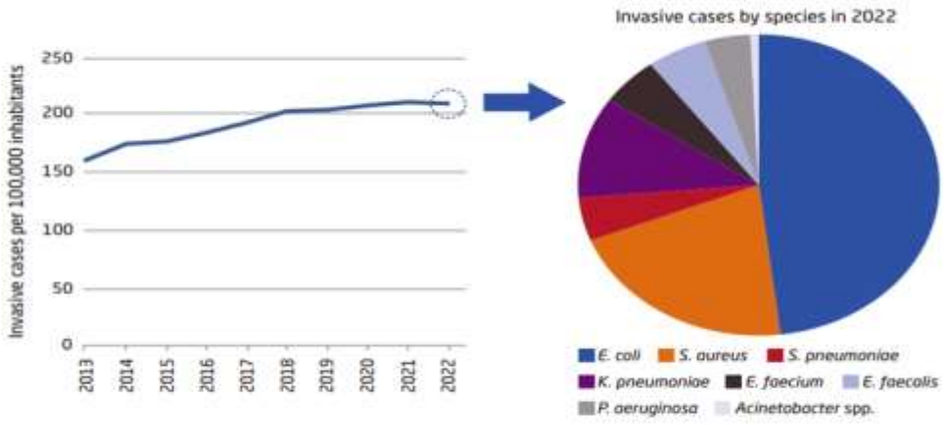
ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

One Health approach



DANMAP report

Figure 6.1 Number of monitored invasive cases, Denmark, 2013-2022



Resistance in monitored bacterial species in Denmark

Resistance in *E. coli* has remained below the 10% percentile for most antimicrobials for the past decade with particularly decreasing trends for resistance to ciprofloxacin, cephalosporins and gentamicin and increasing trends for resistance to piperacillin-tazobactam. However, increases in resistance towards multiple antibiotics were observed from 2021 to 2022. For *K. pneumoniae* similar trends were observed, the decreases in resistance to cephalosporins, fluoroquinolones and gentamicin being

Table 6.1 Resistance (%) in *E. coli* and *K. pneumoniae* from urine and blood cultures, 2022

	E. coli		*K. pneumoniae*	
	Urines from praxis	Invasive	Urines from praxis	Invasive
Ampicillin	35	43	100	100
Mecillinam	4.3	8.8	7.9	8.7
Trimethoprim	20	-	12.3	-
Amoxicillin/clavulanic acid	-	34.4	-	14
Piperacillin-tazobactam	-	6.3	-	9.2
Cefuroxim	-	9.9	-	7.7
3rd gen. cephalosporins	4.8	6.2	3.4	4.8
Ciprofloxacin	6.9	11	5.1	7.4
Carbapenem	-	0.0	-	0.4

DTU STATENS SERUM INSTITUT

SUMMARY DANMAP 2022

Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark

Figure 2.3 Total antimicrobial consumption of active compounds (kg) by animal species and humans, Denmark, 2013-2022

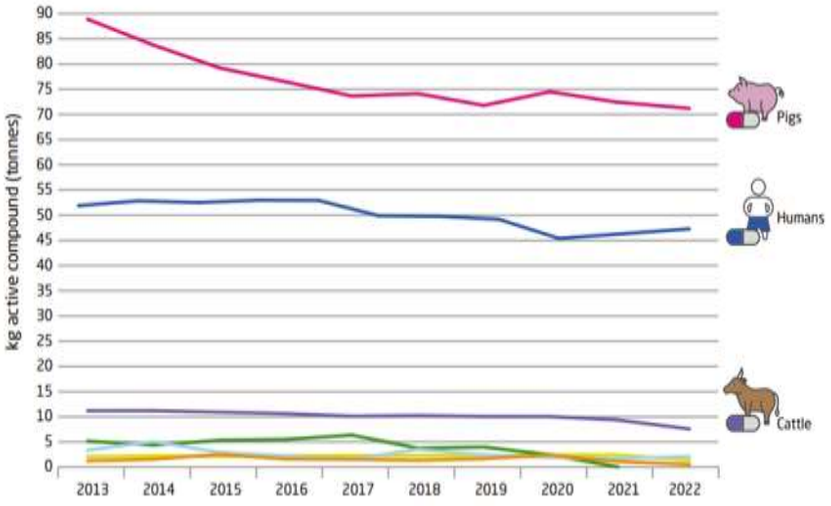
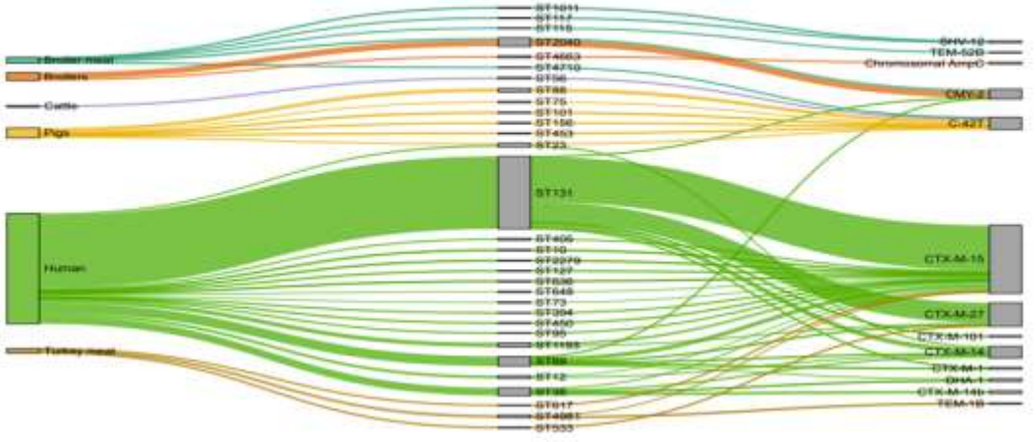


Figure 8.1 A Sankey diagram showing the source, MLST and ESBL/AmpC gene of the included isolates. Flows of a minimum of five are shown



SLM
SOCIETY FOR LABORATORY MEDICINE

Global AMR surveillance projects

Ongoing projects include:

- Investigating the burden of antimicrobial resistance in neonates from developing countries The Burden of Antibiotic Resistance in Neonates from Developing Societies (BERNARDS);
  - 6,300 children under 1 month old die every day
  - 1 in 4 of the estimated 4 million newborn deaths every year are due to neonatal sepsis
  - LMICs bear the burden of 99% of neonatal mortality worldwide
- Comparing the burden of AMR and treatment failure in low-middle and high income countries (BALANCE)
  - By enhancing and supporting the scientific capacity of hospitals in LMICs to capture high-quality clinical and laboratory data by addressing data imbalance.
- Investigating the role of arthropods (flies and insects) on AMR spread (AVIAR).
  - Multinational dataset:
    - Determine the prevalence of AMR bacteria carried by flies
    - Analyse AMR data in the context of antibiotic availability and usage in hospitals
    - Generate a spatio-temporal database
    - Model the prediction of numbers of AMR bacteria by flies in hospital settings

BERNARDS project

ARTICLES
https://doi.org/10.1038/s41564-021-00870-7
nature microbiology

OPEN

Characterization of antimicrobial-resistant Gram-negative bacteria that cause neonatal sepsis in seven low- and middle-income countries

Kirsty Sands[1,2,25], Maria J. Carvalho[1,3,25], Edward Portal[1], Kathryn Thomson[1], Calie Dyer[1,4], Chinenye Akpulu[1,5,6], Robert Andrews[1], Ana Ferreira[1], David Gillespie[4], Thomas Hender[1], Kerenza Hood[4], Jordan Mathias[1], Rebecca Milton[1,4], Maria Nieto[1], Khadijeh Taiyari[4], Grace J. Chan[7,8,9], Delayehu Bekele[9,10], Semaria Solomon[11], Sulagna Basu[12], Pinaki Chattopadhyay[13], Suchandra Mukherjee[13], Kenneth Iregbu[5], Fatima Modibbo[5,6], Stella Uwaezuoke[14], Rabaab Zahra[15], Haider Shirazi[16], Adil Muhammad[15], Jean-Baptiste Mazarati[17], Aniceth Rucogoza[17], Lucie Gaju[17], Shaheen Mehtar[18,19], Andre N. H. Bulabula[19,20], Andrew Whitelaw[21,22], BARNARDS Group[23,*] and Timothy R. Walsh[1,24]

Antimicrobial resistance in neonatal sepsis is rising, yet mechanisms of resistance that often spread between species via mobile genetic elements, ultimately limiting treatments in low- and middle-income countries (LMICs), are poorly characterized. The Burden of Antibiotic Resistance in Neonates from Developing Societies (BARNARDS) network was initiated to characterize the cause and burden of antimicrobial resistance in neonatal sepsis for seven LMICs in Africa and South Asia. A total of 36,285 neonates were enrolled in the BARNARDS study between November 2015 and December 2017, of whom 2,483 were diagnosed with culture-confirmed sepsis. *Klebsiella pneumoniae* ($n = 258$) was the main cause of neonatal sepsis, with *Serratia marcescens* ($n = 151$), *Klebsiella michiganensis* ($n = 117$), *Escherichia coli* ($n = 75$) and *Enterobacter cloacae* complex ($n = 57$) also detected. We present whole-genome sequencing, antimicrobial susceptibility and clinical data for 916 out of 1,038 neonatal sepsis isolates (97 isolates were not recovered from initial isolation at local sites). Enterobacterales (*K. pneumoniae*, *E. coli* and *E. cloacae*) harboured multiple cephalosporin and carbapenem resistance genes. All isolated pathogens were resistant to multiple antibiotic classes, including those used to treat neonatal sepsis. Intraspecies diversity of *K. pneumoniae* and *E. coli* indicated that multiple antibiotic-resistant lineages cause neonatal sepsis. Our results will underpin research towards better treatments for neonatal sepsis in LMICs.

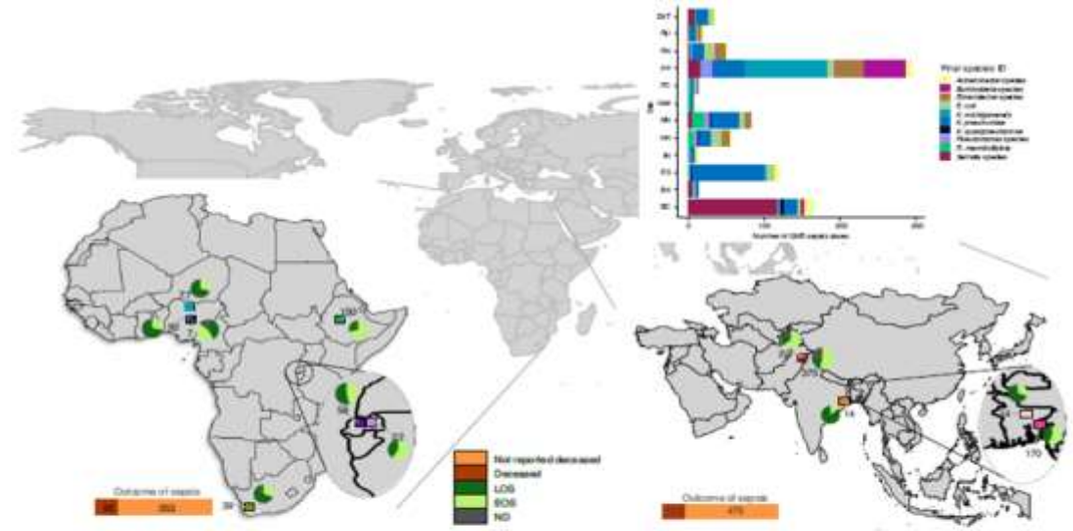


Fig. 2 | World map showing the BARNARDS study clinical site locations. The study sites are indicated by coloured squares. The African sites were located in Ethiopia (ES (green)), Nigeria (NK (cyan), NN (light blue) and NW (dark blue)), Rwanda (RK (dark purple) and RU (light purple)) and South Africa (ZAT; olive). The Asian sites were located in Bangladesh (BC (dark pink) and BK (light pink)), India (IN (orange)) and Pakistan (PC (peach) and PP (burgundy)). The numbers next to each clinical site location represent the total number of GNB identified. Inset: the stacked bar graph shows the distribution of the top ten GNB species recovered from blood cultures at the local sites. The onset of neonatal sepsis (EOS, LOS or ND) for GNB per clinical site is represented as a pie chart. The outcome of neonatal sepsis is shown for each continent.

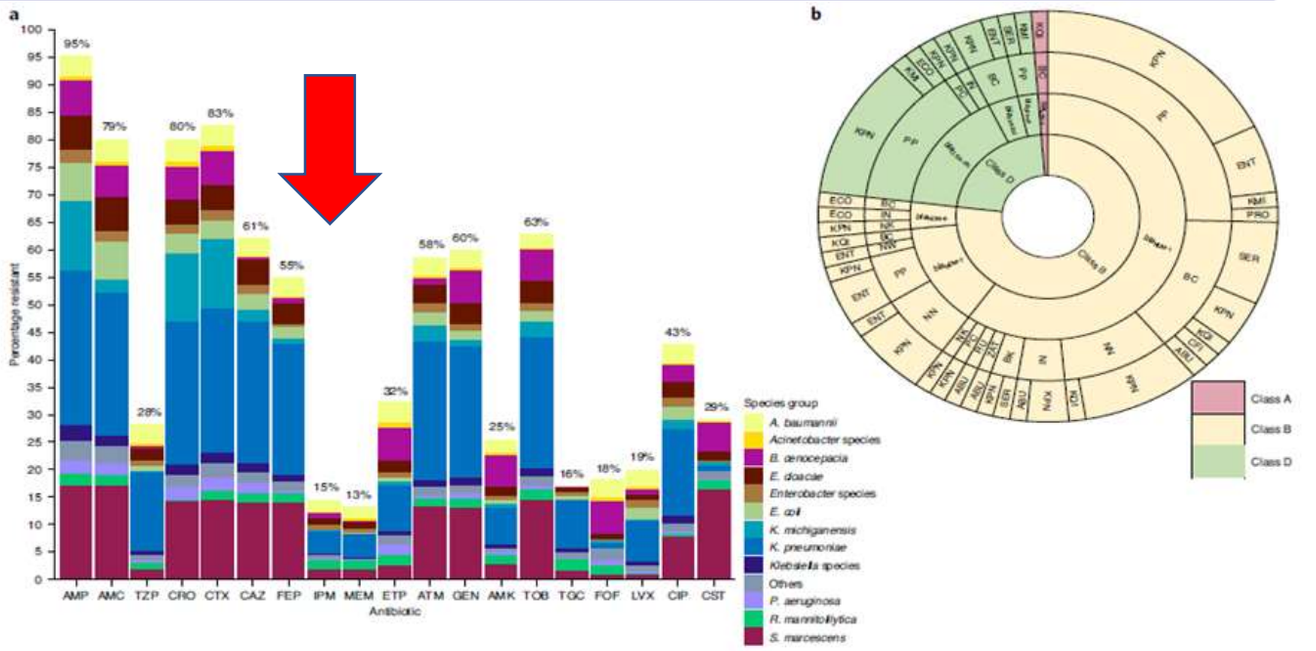


Fig. 3 | AMR of neonatal sepsis-causing pathogens. a, Percentages of antimicrobial-resistant aetiological agents of neonatal sepsis, coloured according to bacterial species/group ($n = 885$ isolates of GNB). The MICs of the antibiotics were determined by agar dilution and the results were interpreted according to EUCAST guidelines and documents[20,21]. AMC, amoxicillin/clavulanate; AMK, amikacin; AMP, ampicillin; ATM, aztreonam; CAZ, ceftazidime; CIP, ciprofloxacin; CRO, ceftriaxone; CST, colistin; CTX, cefotaxime; ETP, ertapenem; FEP, cefepime; FOF, fosfomycin; GEN, gentamicin; IPM, imipenem; LVX, levofloxacin; MEM, meropenem; TGC, tigecycline; TOB, tobramycin; TZP, piperacillin/tazobactam. **b**, Sunburst diagram detailing the class A (red), B (yellow) and D (green) carbapenemase resistance genes detected. The second ring from the centre shows the carbapenemase genes identified. The distributions across species and clinical sites are shown in the outer rings. ABU, *Acinetobacter baumannii*; CFI, *Citrobacter freundii*; ECO, *Escherichia coli*; ENT, *Enterobacter cloacae* complex; KMI, *Klebsiella michiganensis*; KPN, *Klebsiella pneumoniae*; KQI, *Klebsiella quasipneumoniae*; PRO, *Providencia rettgeri*; SER, *Serratia marcescens*.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

BALANCE project

Contents lists available at ScienceDirect

Journal of Infection and Public Health

journal homepage: http://www.elsevier.com/locate/jiph

Review

Menace of antimicrobial resistance in LMICs: Current surveillance practices and control measures to tackle hostility☆

Ayush Sharma[a,1], Akanksha Singh[a,1], Mukhtar Ahmad Dar[a], Rimple Jeet Kaur[b], Jaykaran Charan[b], Katia Iskandar[c,d,e], Mainul Haque[f], Krishna Murti[a], V. Ravichandiran[a,g], Sameer Dhingra[a,*]

[a] Department of Pharmacy Practice, National Institute of Pharmaceutical Education and Research (NIPER), Hajipur, Bihar, India
[b] Department of Pharmacology, All India Institute of Medical Sciences, Jodhpur, Rajasthan, India
[c] Lebanese University, School of Pharmacy, Beirut, Lebanon
[d] INSPECT-LB: Institute National de Sante Publique, Epidemiologie Clinique et Toxicologie, Beirut, Lebanon
[e] Universite Paul Sabatier UT3, INSERM, UMR1295, Toulouse, France
[f] The Unit of Pharmacology, Faculty of Medicine and Defence Health, Universiti Pertahanan Nasional Malaysia (National Defence University of Malaysia), Kem Perdana Sungai Besi, Kuala Lumpur, Malaysia
[g] Department of Natural Products, National Institute of Pharmaceutical Education and Research, Kolkata, West Bengal, India

ARTICLE INFO

Article history:
Received 3 September 2021
Received in revised form 8 December 2021
Accepted 9 December 2021

Keywords:
Antimicrobials
Antibiotics
Low- and middle-income countries
Transmission
Infectious diseases
Resistance
Surveillance
Survey
Control strategies
Antimicrobial stewardship

ABSTRACT

Antimicrobial Resistance (AMR) is significant challenge humanity faces today, with many patients losing their lives every year due to AMR. It is more widespread and has shown a higher prevalence in low- and middle-income countries (LMICs) due to lack of awareness and other associated reasons. WHO has suggested some crucial guidelines and specific strategies such as antimicrobial stewardship programs taken at the institutional level to combat AMR. Creating awareness at the grassroots level can help to reduce the AMR and promote safe and effective use of antimicrobials. Control strategies in curbing AMR also comprise hygiene and sanitation as microbes travel from contaminated surroundings to the human body surface. As resistance to multiple drugs increases, vaccines can play a significant role in curbing the menace of AMR. This article summarizes the current surveillance practices and applied control measures to tackle the hostility in these countries with particular reference to the role of antimicrobial stewardship programs and the responsibilities of regulatory authorities in managing the situation.

Open access Protocol

BMJ Open

Bacteremia Antibiotic Length Actually Needed for Clinical Effectiveness (BALANCE) randomised clinical trial: study protocol

Nick Daneman ,[1] Asgar H Rishu,[2] Ruxandra L Pinto,[3] Yaseen M Arabi,[4] Deborah J Cook,[5] Richard Hall,[6] Shay McGuinness,[7] John Muscedere,[8] Rachael Parke,[9] Steven Reynolds,[10] Benjamin Rogers,[11] Yahya Shehabi,[12] Robert A Fowler,[13] On behalf of the Canadian Critical Care Trials Group

The BALANCE trial (balance.ccctg.ca) is currently being conducted across a geographically and clinically diverse spectrum of ICUs and hospitals in Canada (currently 36 sites), Australia (6 sites), New Zealand (10 sites), the USA (2 sites), Saudi Arabia (2 sites) and Israel (1 site).

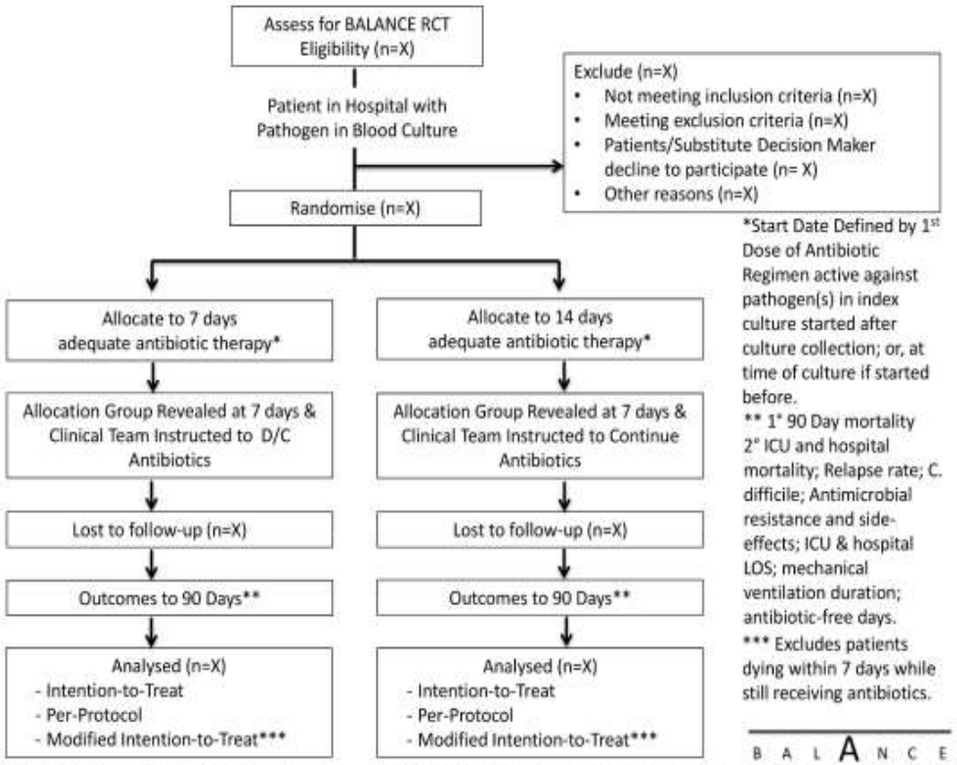
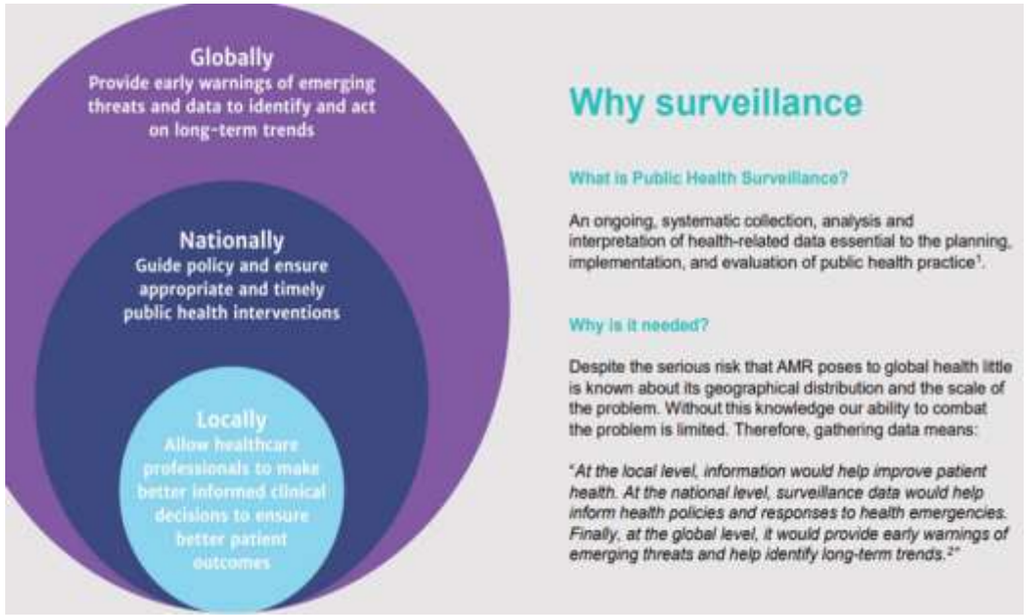


Figure 1 BALANCE RCT intervention flow diagram. BALANCE, Bacteremia Antibiotic Length Actually Needed for Clinical Effectiveness; *C. difficile*, *Clostridium difficile*; D/C, discontinue; ICU, intensive care unit; LOS, length of stay; RCT, randomised clinical trial.

Fleming Fund approach to surveillance



Why surveillance

What is Public Health Surveillance?

An ongoing, systematic collection, analysis and interpretation of health-related data essential to the planning, implementation, and evaluation of public health practice[1].

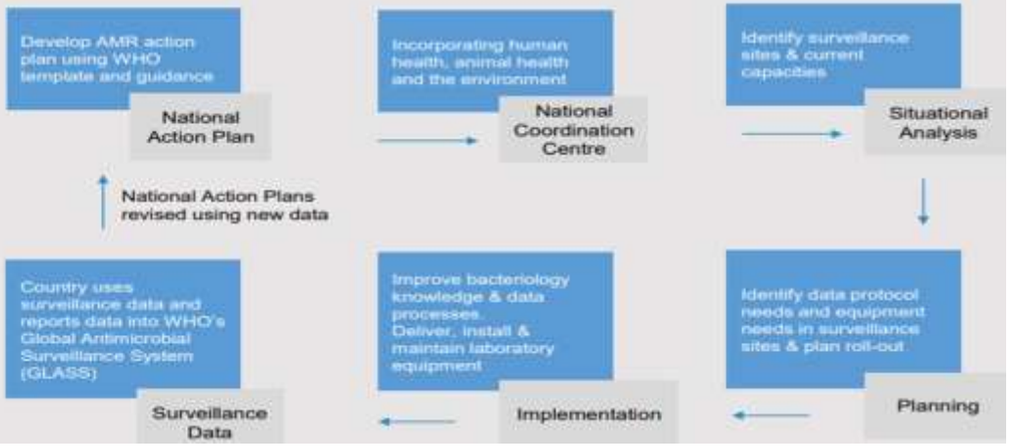
Why is it needed?

Despite the serious risk that AMR poses to global health little is known about its geographical distribution and the scale of the problem. Without this knowledge our ability to combat the problem is limited. Therefore, gathering data means:

"At the local level, information would help improve patient health. At the national level, surveillance data would help inform health policies and responses to health emergencies. Finally, at the global level, it would provide early warnings of emerging threats and help identify long-term trends.[2]"

Our Surveillance Approach

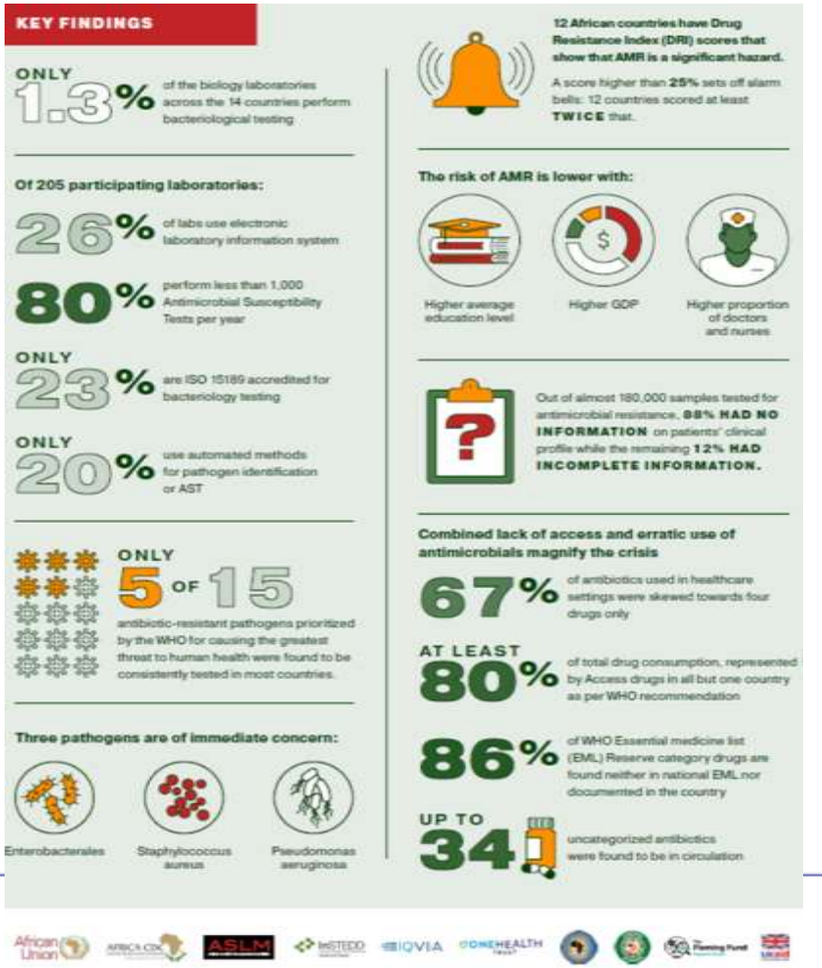
We use these steps to support and invest in One Health surveillance systems around the world. Our grantees build partnerships with country governments working through national coordinating centres and supporting national action plans.



ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

MAAP

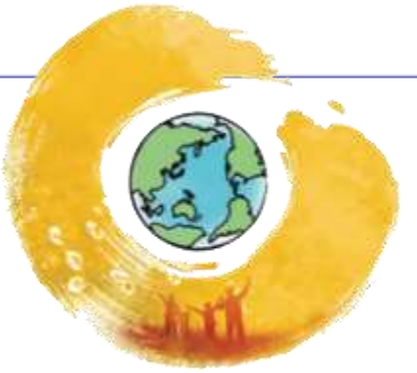
Most laboratories across Africa are not ready for AMR testing.
Only 1.3% of the 50,000 medical laboratories forming the laboratory networks of the 14 participating Member States conduct bacteriology testing.
Only a fraction can handle the scientific processes needed to evaluate AMR.
In eight of the 14 countries, more than half of the population is out of reach of any bacteriology laboratory.



ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

GHSA

Global Health Security Agenda
A partnership against global health threats-network of 70 countries



Global Health Security Agenda

AMR objectives

- Support the Global Action Plan on AMR and the associated work of the Tripartite Plus on AMR through information sharing and building capacity to assist Action Package members in realizing and implementing their associated commitments.

Laboratory system objectives

- Monitor and accelerate the activities and implementation of the Strategic Roadmap on National Laboratory System Strengthening.

Surveillance objectives

- Strengthen surveillance systems to detect events of significance for public health (animal, human, environment) and health security.
- Improve communication and collaboration across sectors and between national, regional and global levels regarding surveillance of public health significance.
- Improve country and regional capacity to analyse and link data from different sectors through establishing real-time surveillance systems, including electronic reporting systems.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

Africa activities

African Union

AFRICA CDC FRAMEWORK FOR ANTIMICROBIAL RESISTANCE, 2018-2023

Workforce and Implementing Homegrown Solutions for Enhanced Surveillance

Africa CDC established the Anti-Microbial Resistance Surveillance Network (AMRSNET).
AMRSNET is a network of public health institutions and leaders from human and animal sectors who collaborate to measure, prevent, and mitigate harms from AMR.

ReAct

Access to antibiotics – production & procurement

Do we want sustainable access to effective antibiotics? If so – it is time to act.

WHO AFRO-Regional perspective on AMR: Development and Implementation of AMR National Action Plans

To build effectively and address AMR in Africa:

- Investments for interventions with high impact, low complexity, low level of resources that build resilient systems and surveillance

EAST, CENTRAL AND SOUTHERN AFRICA HEALTH COMMUNITY
Fostering Regional cooperation for Better Health

The landscape of Africa mandates region-specific approaches for the implementation of National Antimicrobial Stewardship programs and the deployment of AMR surveillance systems.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

Research on AMR in Africa

International Journal of Infectious Diseases 143 (2024) 107035

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Carriage of antimicrobial-resistant *Enterobacterales* among pregnant women and newborns in Amhara, Ethiopia

Getnet Amsalu[1,2,a], Christine Tedijanto Wen[3,a], Olga Perovic[4,5], Addisalem Gebru[1,2,6], Bezawit M. Hunegnaw[2,7], Fisseha Tadesse[6], Marshagne Smith[4], Addisalem Fikre[1,2], Delayehu Bekele[8,10], Lisanu Taddesse[2], Grace J. Chan[9,10,*]

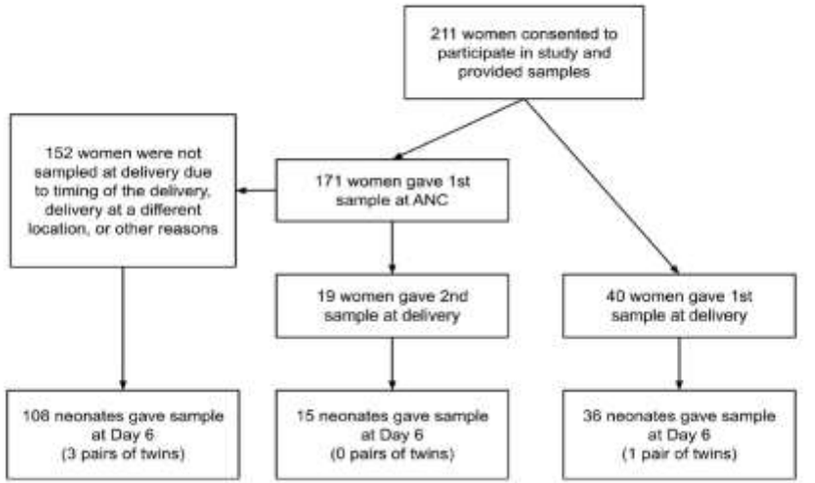
[1] Birhan HDSS, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
[2] HaSET Maternal and Child Health Research Program, Addis Ababa, Ethiopia
[3] Surgo Health, Washington, DC, USA
[4] Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses, National Institute for Communicable Diseases, a division of the National Health Laboratory Service, Johannesburg, South Africa
[5] Department of Clinical Microbiology and Infectious Diseases, University of Witwatersrand, Johannesburg, South Africa
[6] Department of Obstetrics and Gynecology, Debre Birhan Hospital, Debre Birhan, Ethiopia
[7] Department of Pediatrics and Child Health, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
[8] Department of Obstetrics and Gynecology, St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia
[9] Department of Pediatrics, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA
[10] Department of Epidemiology, Harvard T.H. Chan School of Public Health, Boston, MA, USA

Carriage prevalence of ESBL-producing organisms and CRE among mothers and neonates by time point and sampling site.

Sample type	Time point	Sample size	ESBL % (95% CI)	CRE % (95% CI)
Maternal samples				
Unique women, any sample type	Any	211	22.3 (16.8, 28.5)	0.9 (0.1, 3.4)
Rectal	ANC	171	19.9 (14.2, 26.7)	0 (0, 2.1)
Vaginal	ANC	171	0.6 (0.01, 3.2)	0 (0, 2.1)
Rectal	Labor/delivery	59	22.0 (12.3, 34.7)	3.4 (0.4, 11.7)
Vaginal	Labor/delivery	59	0 (0, 6.1)	0 (0, 6.1)
Neonatal samples				
Unique children, any sample type	Day 6	159	24.5 (18.1, 32.0)	2.5 (0.7, 6.3)
Perirectal	Day 6	73	24.7 (15.3, 36.1)	2.7 (0.3, 9.5)
Stool	Day 6	86	24.4 (15.8, 34.9)	2.3 (0.3, 8.1)

ANC, antenatal care; CRE, carbapenem-resistant *Enterobacterales*; ESBL, extended-spectrum-beta-lactamase.

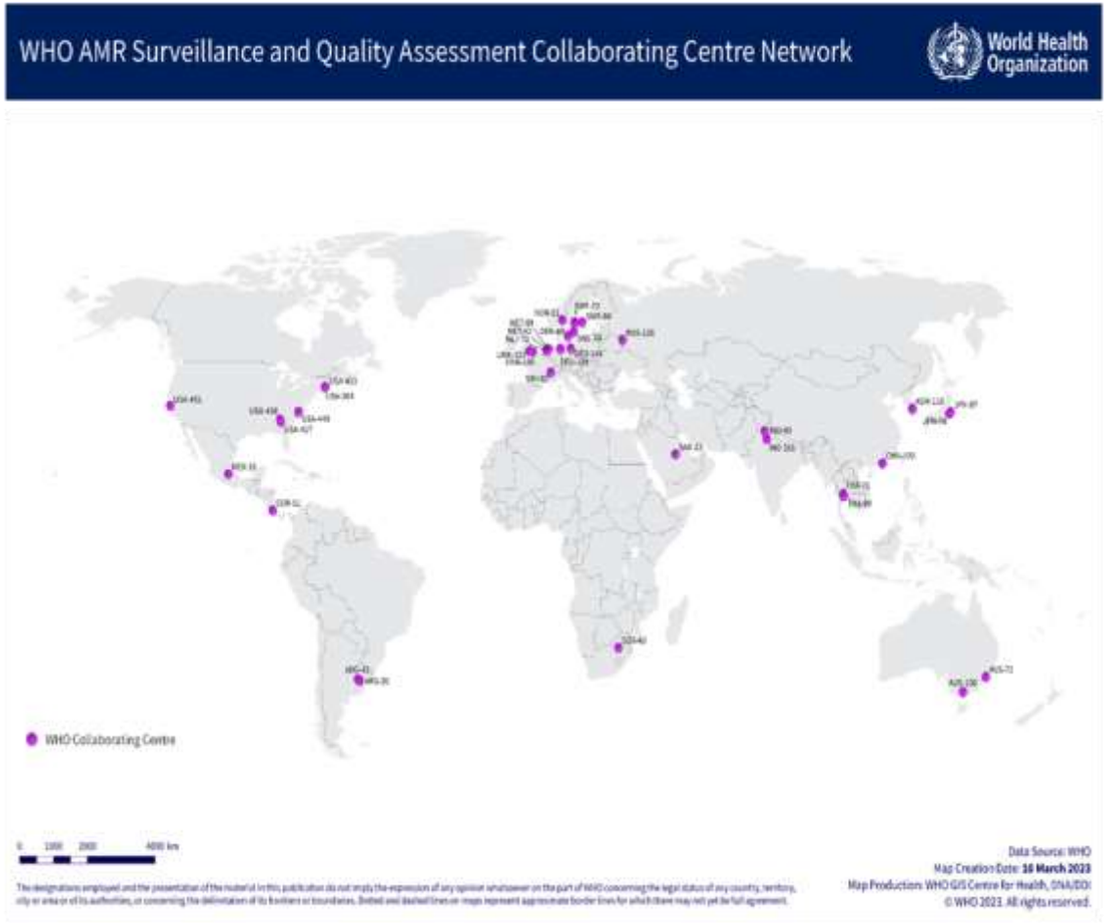
In a rural area of Amhara, Ethiopia, maternal and neonatal carriage of ESBL-producing organisms was around 25%, and carriage of CRE and GBS were very rare. Neonates whose mothers tested positive for ESBL-producing organisms at late-term antenatal care or labor/delivery were roughly twice as likely to test positive in the first week after birth. Based on our findings, future carriage monitoring was recommended.



22.3% of women were positive for ESBL-producing organisms and 0.9 were positive for CRE.

WHO AMR surveillance

The WHO AMR Surveillance and Quality Assessment Collaborating Centres Network



South Africa/SOA-43: WHO Collaborating Centre for Antimicrobial Resistance

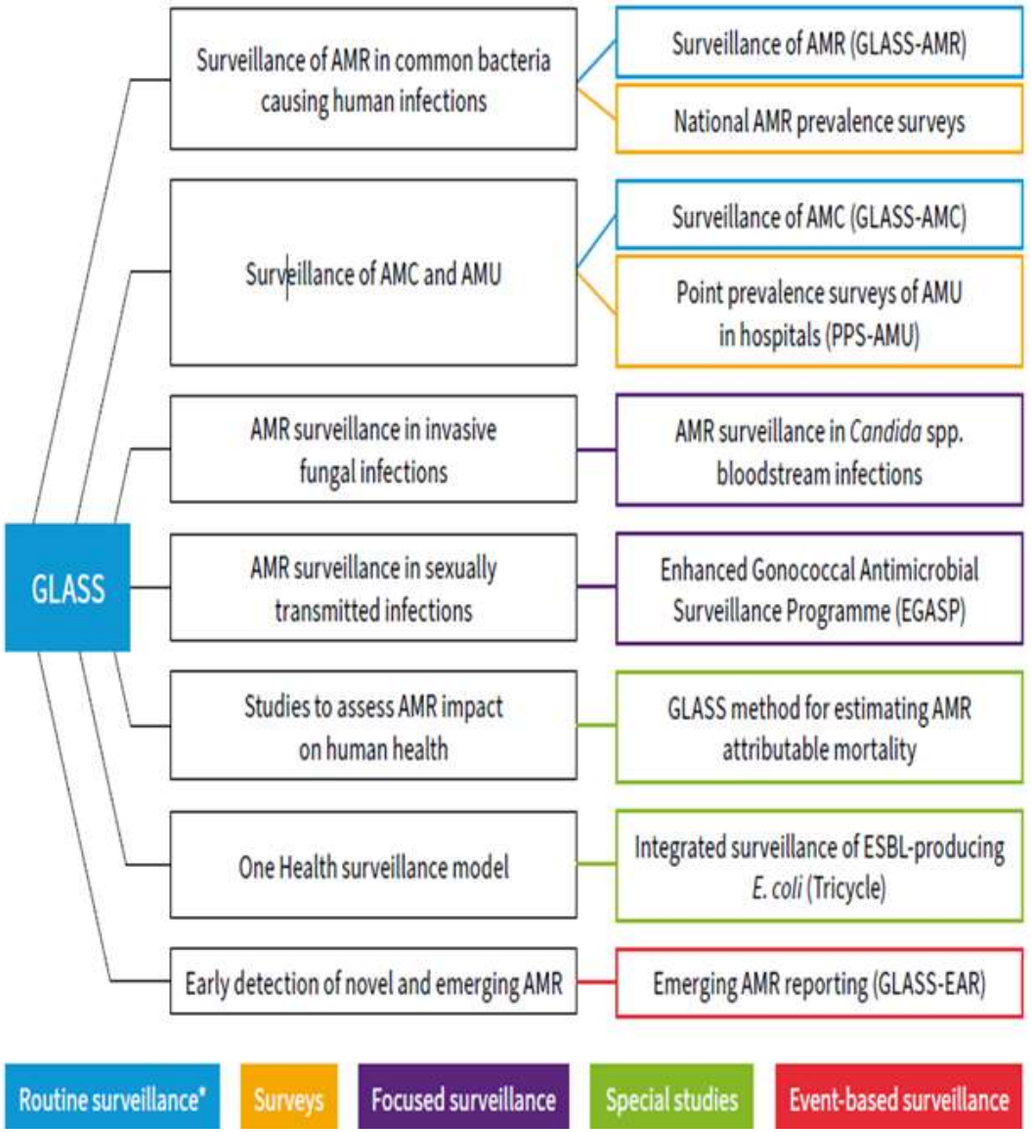
Contact: Prof Olga Perovic

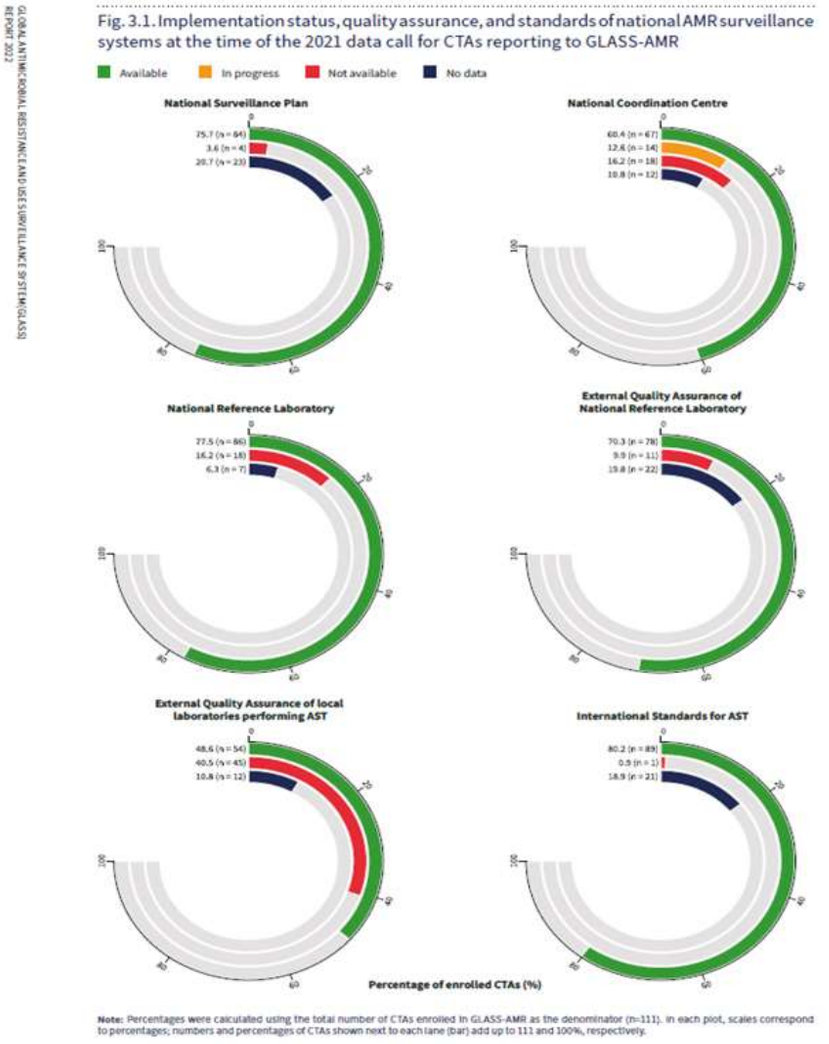
The CC supports with strengthening surveillance, addressing One Health responses, using available tools for assessing infection prevention and control in healthcare facilities and providing professional education. The CC supports the Network by leading work on the provision of technical assistance for developing functional and integrated laboratory quality systems and providing training in AMR detection and surveillance for GLASS organisms. The CC supports WHO in development of guidelines, manuals, and other tools for GLASS-related activities.

Institution: Antimicrobial Resistance Laboratory and Culture Collection, Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses (CHARM) at National Institute for Communicable Diseases, Johannesburg, South Africa

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

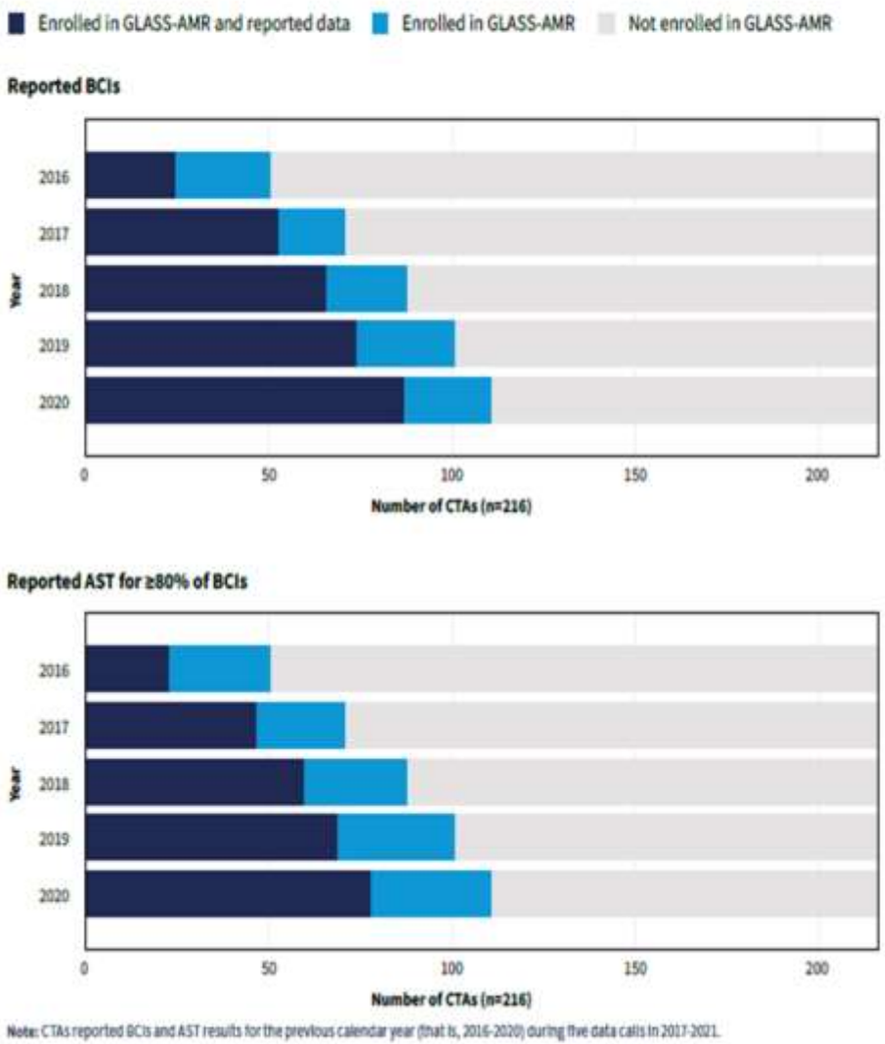
GLASS program





GLASS data

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.

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

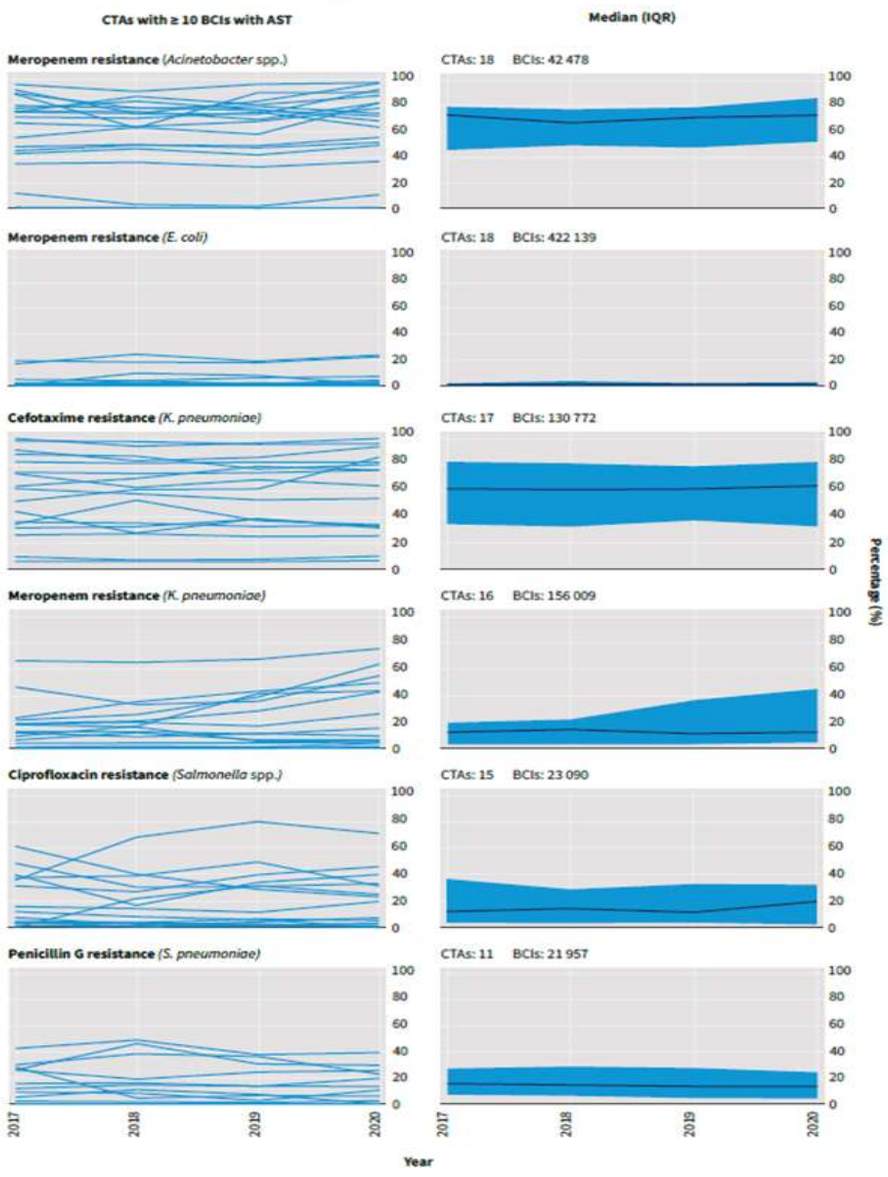
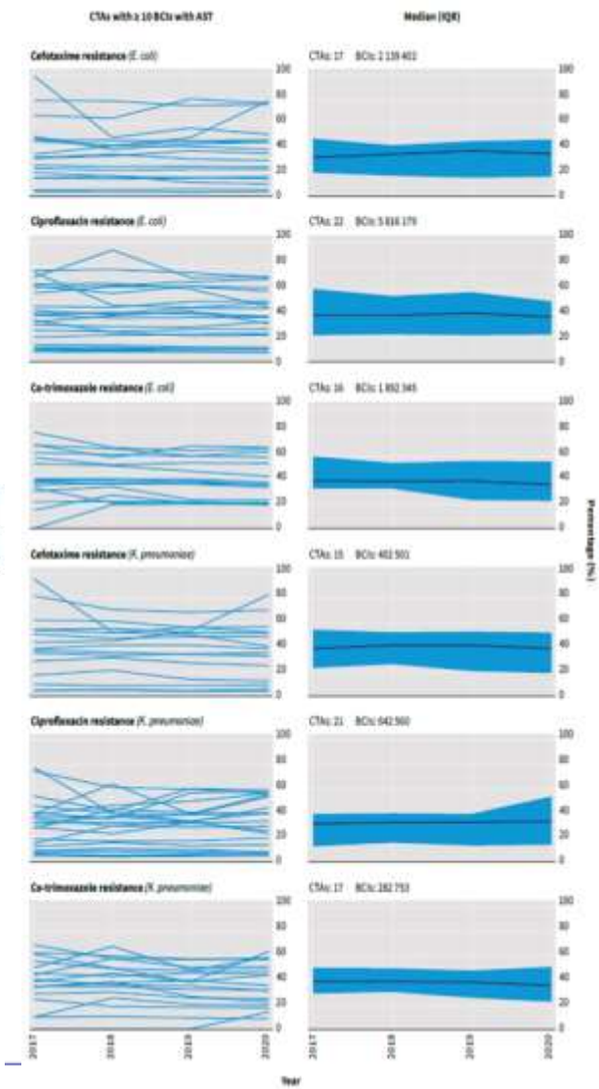
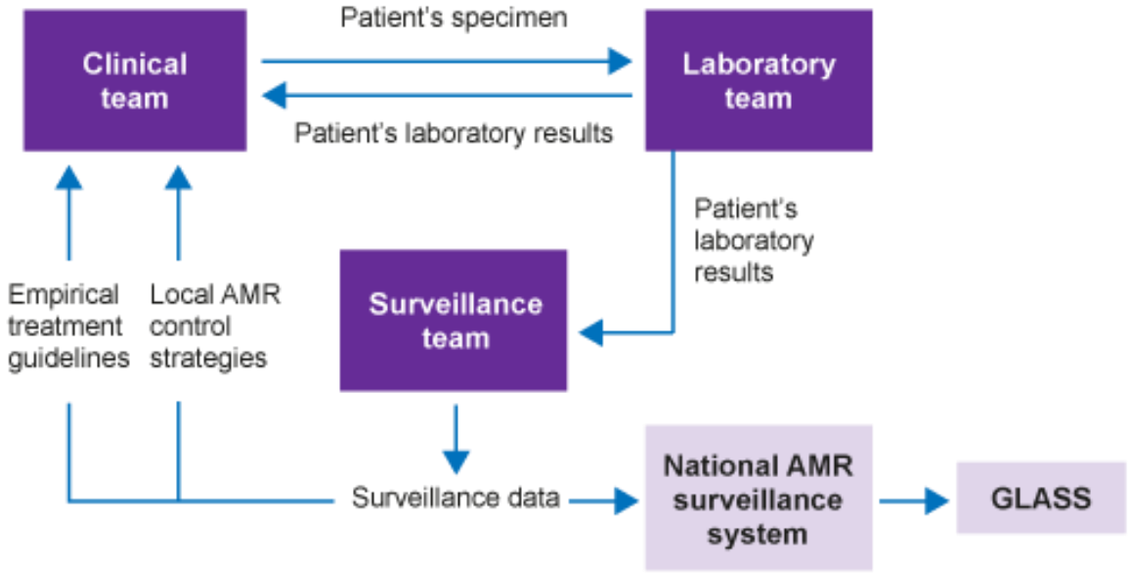


Fig. 3.8e. Percentage resistance to selected antimicrobials in CTAs reporting ≥10 urinary tract BCIs infections with AST results annually (2017-2020)



ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

Laboratory capacity



The implementation of QMS in clinical bacteriology in hospital settings will ultimately boost a culture of quality to all sectors of healthcare in low-resource settings.

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Review

Implementation of quality management for clinical bacteriology in low-resource settings

B. Barbé [1, *], C.P. Yansouni [2], D. Affolabi [3], J. Jacobs [1, 4]

[1] Institute of Tropical Medicine, Antwerp, Belgium
[2] JD MacLean Centre for Tropical Diseases, McGill University Health Centre, Montreal, Canada
[3] Clinical Microbiology, University Hospital Hubert Koutoukou Maga, Cotonou, Benin
[4] Department of Microbiology and Immunology, KU Leuven, Leuven, Belgium

Fig. 2. Map of sub-Saharan Africa showing countries with medical laboratories that have been accredited to internationally recognized standards by April 2017. Numbers below countries' names refer to number of accredited laboratories in that country.

New diagnostics to guide AMS

International Journal of Antimicrobial Agents
Available online 21 August 2024, 107300
In Press, Journal Pre-proof What's this?

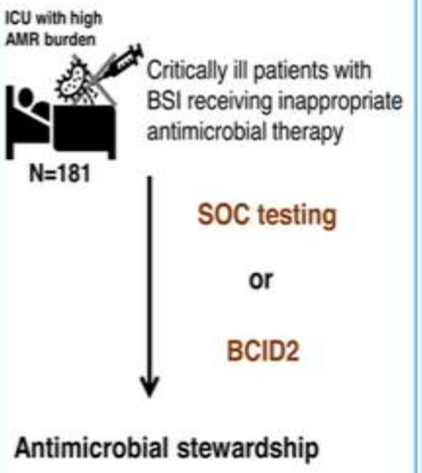
Reduced mortality with antimicrobial stewardship guided by BioFire FilmArray Blood Culture Identification 2 panel in critically ill patients with bloodstream infection: a retrospective propensity score-matched study

How-Yang Tseng [a †], Chieh-Lung Chen [a †], Wei-Cheng Chen [a b c d], Yu-Chu Kuo [a], Shinn-Jye Liang [c]
Chih-Yen Tu [a b], Yu-Chao Lin [a b] ✉, Po-Ren Hsueh [e f g] ✉

BCID2-guided antimicrobial stewardship was associated with a notable reduction in time to pathogen identification and time to implement appropriate antimicrobial therapy.

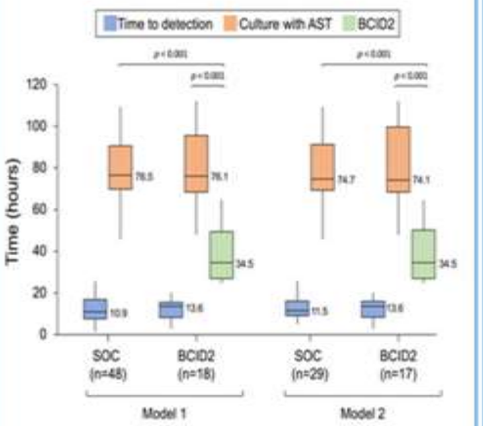
BioFire® FilmArray® Blood Culture Identification 2 Panel-guided antimicrobial stewardship improved mortality in patients with bloodstream infections receiving inappropriate antimicrobial therapy in the ICU

Study flow

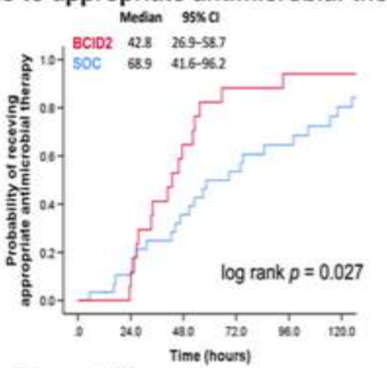


Results

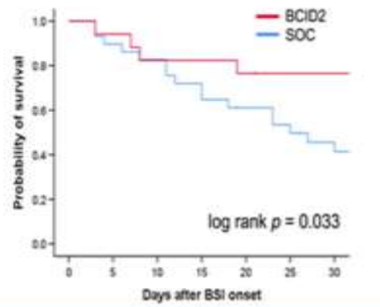
Time to pathogen identification



Time to appropriate antimicrobial therapy



Day-28 mortality



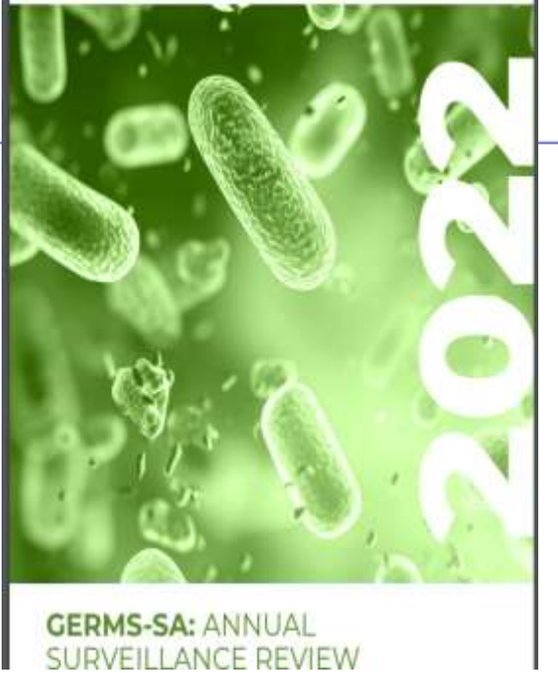
Conclusions

BCID2-guided antimicrobial stewardship was associated with shorter time to pathogen identification and appropriate antimicrobial therapy, as well as lower day-28 mortality in critically ill patients with BSIs facing an increased AMR burden and receiving inappropriate antimicrobial therapy.

AMR, antimicrobial resistance; BCID2, BioFire FilmArray Blood Culture Identification Panel 2; BSI, bloodstream infection; ICU, intensive care unit; SOC, standard of care; PSM, propensity score

National surveillance for AMR at NICD

There are 260 laboratories in public sector and approximately over 50 microbiology laboratory participated in the surveillance programme



Diseases under surveillance

GERMS SOUTH AFRICA

Provides laboratory-based surveillance platform for NICD Centres

AIDS-related OIs
- Cryptococcosis
- Salmonellosis
- TB (rifampicin resistant)

Epidemic-prone diseases
- Meningococcal disease
- Cholera
- Shigellosis
- Typhoid fever
- Diarrhoeagenic *E. coli* disease

Vaccine-preventable diseases
- *Haemophilus influenzae* disease
- Invasive pneumococcal disease
- Rotavirus

Hospital infections
- Candidaemia
- *Staphylococcus* bacteraemia
- Other ESKAPE organisms
- CREs

AMR surveillance at Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses (CHARM) at NICD

Laboratory based antimicrobial surveillance (LARS) since 2010 at GERMS

- Selection of sentinel sites (population-based surveillance was not feasible)
- National reference laboratory: confirm AST, detect unusual resistance and outbreak, implement national laboratory standards
- Laboratories networking

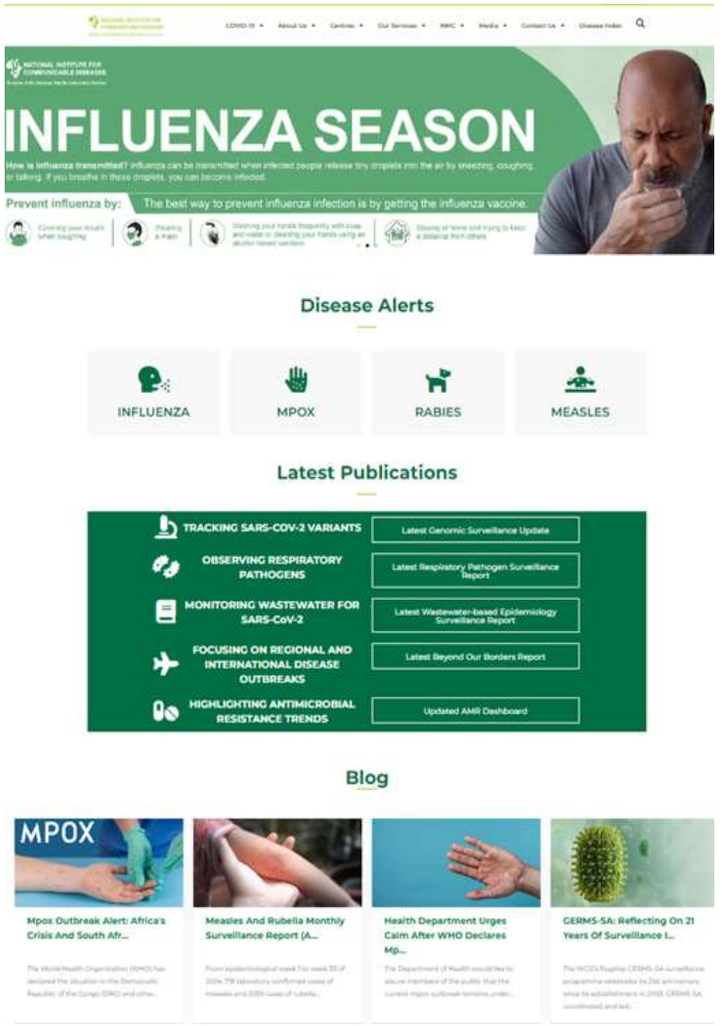
Electronic surveillance since 2013

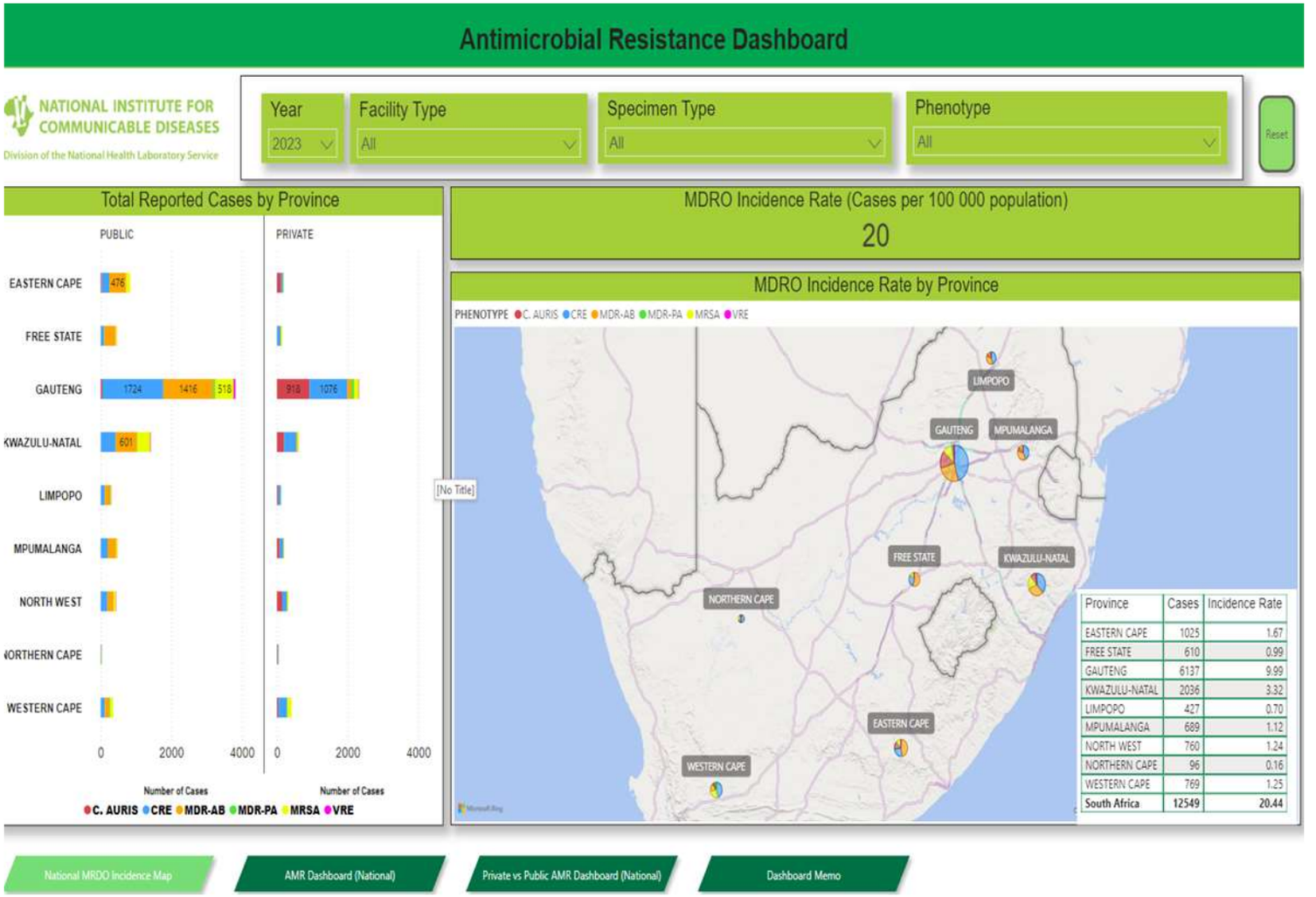
- Collection of national data from LIS according case definition exclusion and inclusion criteria and defining denominator data-SDW
- Notifiable Medical Condition (NMC) system throughout surveillance data warehouse (SDW) on monthly bases for MDROs.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

AMR surveillance data

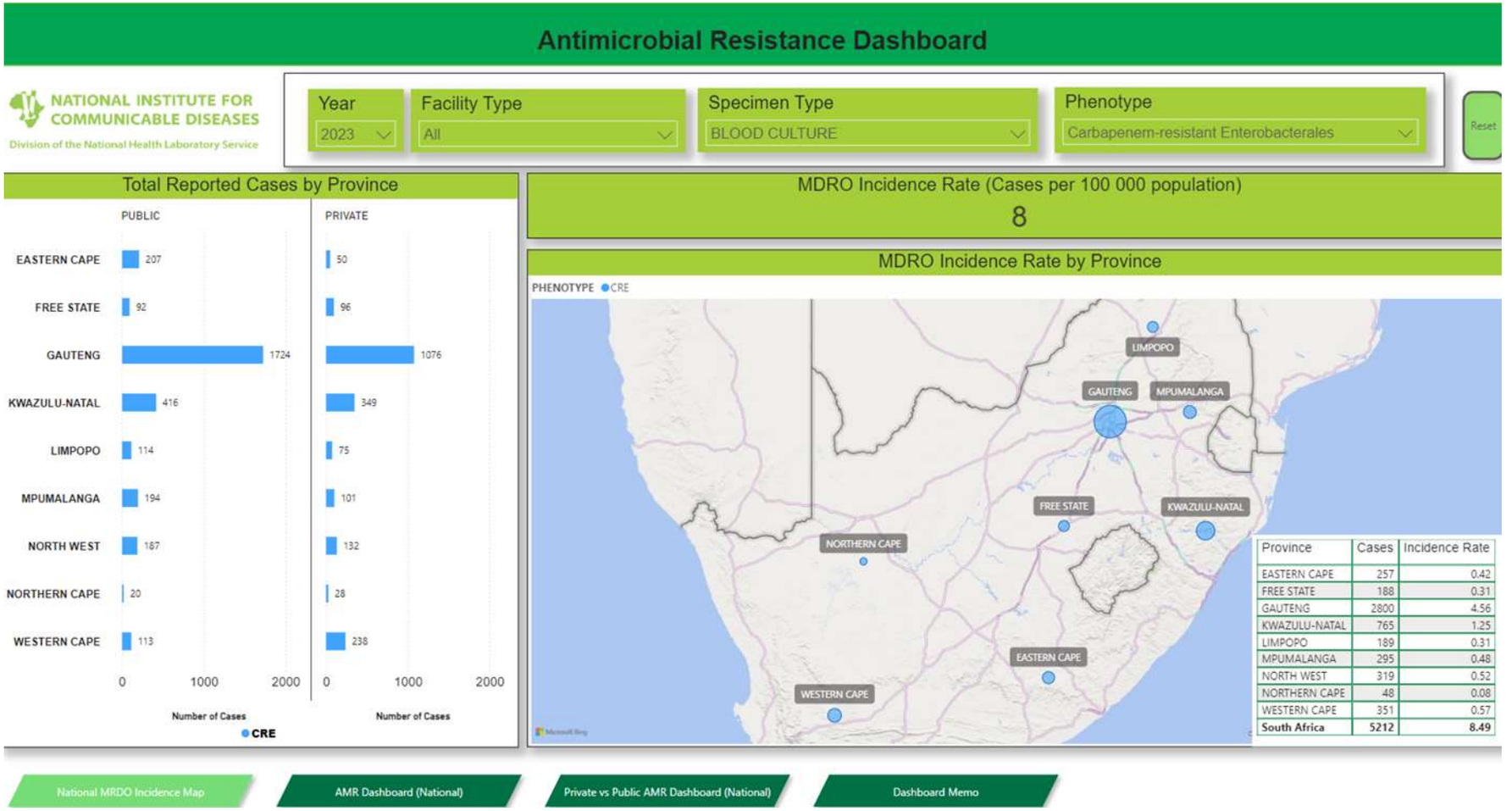
Access to information on AMR at the country level





National AMR data

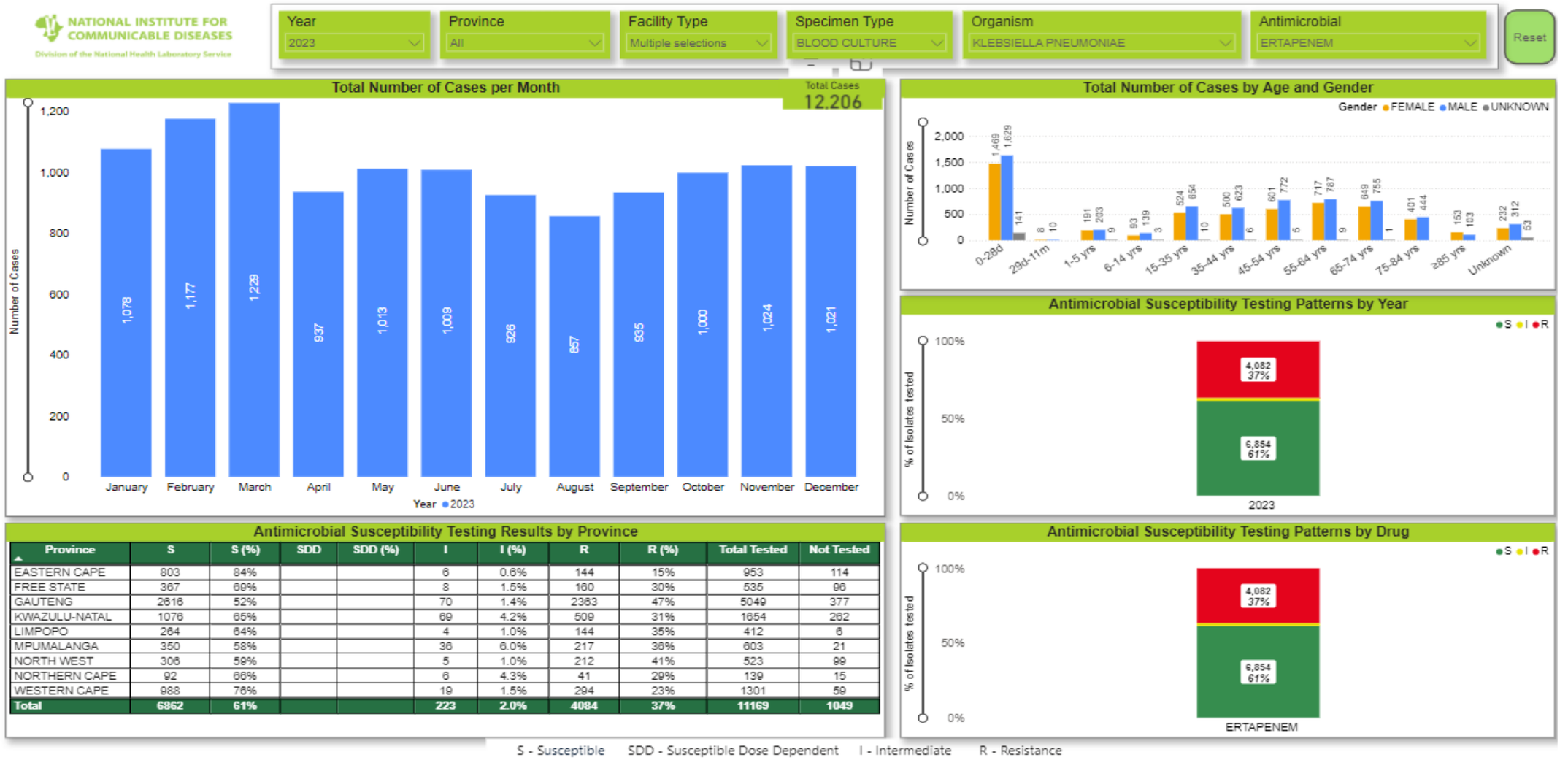
Incidence of CREs per province



Blood culture data

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

Blood culture AMR data



ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

Comparison public vs. private data

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

Public vs. private

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

Year	Quarter	Province	Specimen Type	Organism	Antimicrobial
Multiple selections	All	All	BLOOD CULTURE	Multiple selections	ERTAPENEM

Reset

Public - Antimicrobial Susceptibility Testing Results by Province

PROVINCE_NAME	S	S (%)	SDD	SDD (%)	I	I (%)	R	R (%)	Total Tested	Not Tested
EASTERN CAPE	1644	85%			13	0.7%	288	15%	1945	174
FREE STATE	816	85%			9	0.9%	137	14%	962	307
GAUTENG	5247	59%			156	1.7%	3518	39%	8921	1065
ERTAPENEM	5247	59%			156	1.7%	3518	39%	8921	1065
KWAZULU-NATAL	2274	78%			232	8.0%	394	14%	2900	622
LIMPOPO	692	82%			13	1.5%	135	16%	840	25
MPUMALANGA	737	62%			95	8.0%	357	30%	1189	53
NORTH WEST	563	76%			8	1.1%	166	23%	737	348
NORTHERN CAPE	127	79%					34	21%	161	8
WESTERN CAPE	1580	87%			13	0.7%	230	13%	1823	161
Total	13680	70%			539	2.8%	5259	27%	19478	2763

Private - Antimicrobial Susceptibility Testing Results by Province

PROVINCE_NAME	S	S (%)	SDD	SDD (%)	I	I (%)	R	R (%)	Total Test...	Not Tested
EASTERN CAPE	778	75%			27	2.7%	181	18%	986	59
FREE STATE	403	68%			17	2.9%	175	29%	595	21
GAUTENG	2897	50%			13	0.2%	2932	50%	5842	35
ERTAPENEM	2897	50%			13	0.2%	2932	50%	5842	35
KWAZULU-NATAL	548	48%			11	0.6%	1009	51%	1968	11
LIMPOPO	220	56%			1	0.3%	172	44%	393	1
MPUMALANGA	302	53%			1	0.2%	272	47%	575	1
NORTH WEST	389	53%			5	0.7%	340	46%	734	7
NORTHERN CAPE	143	68%			22	10.5%	44	21%	209	33
WESTERN CAPE	1410	64%			25	1.1%	781	35%	2216	18
Total	7490	55%			122	0.9%	5906	44%	13518	186

S - Susceptible SDD - Susceptible Dose Dependent I - Intermediate R - Resistance

Private vs Public AMR Dashboard (National) Dashboard Memo Antimicrobial Susceptibility Testing Patterns by Year

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

AST specific organisms and antibiotic

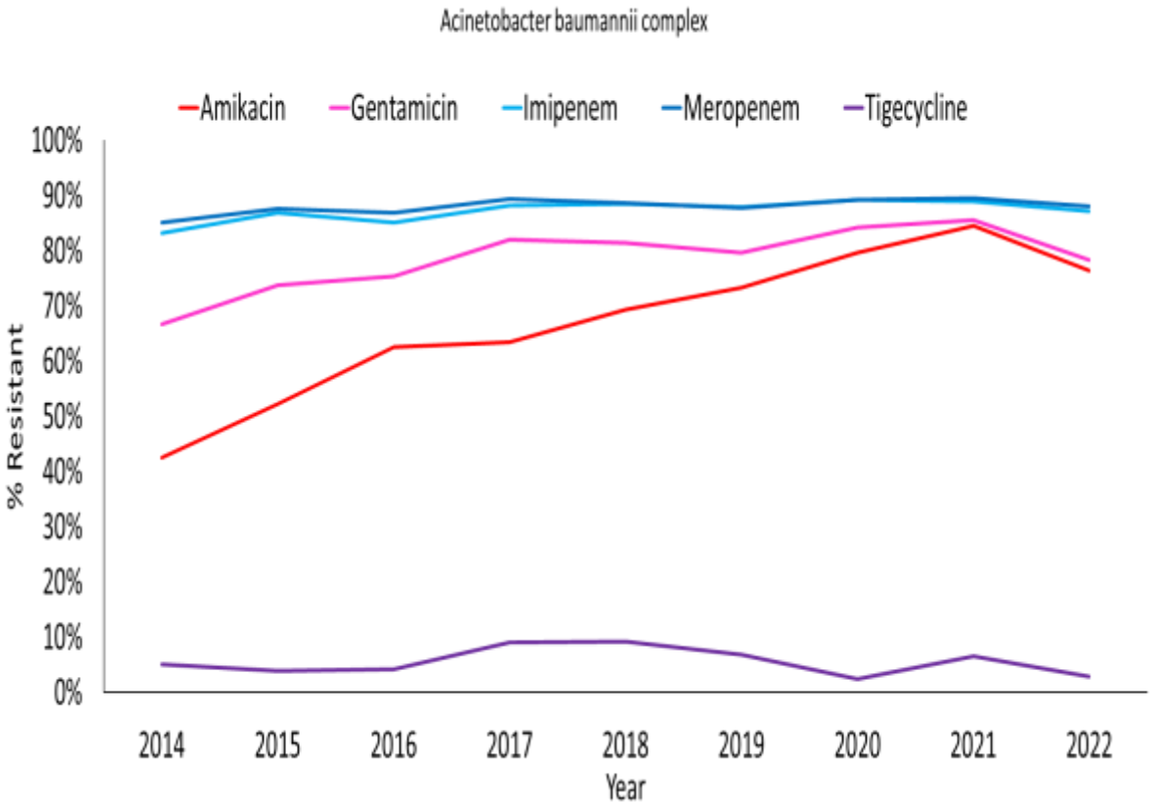
ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

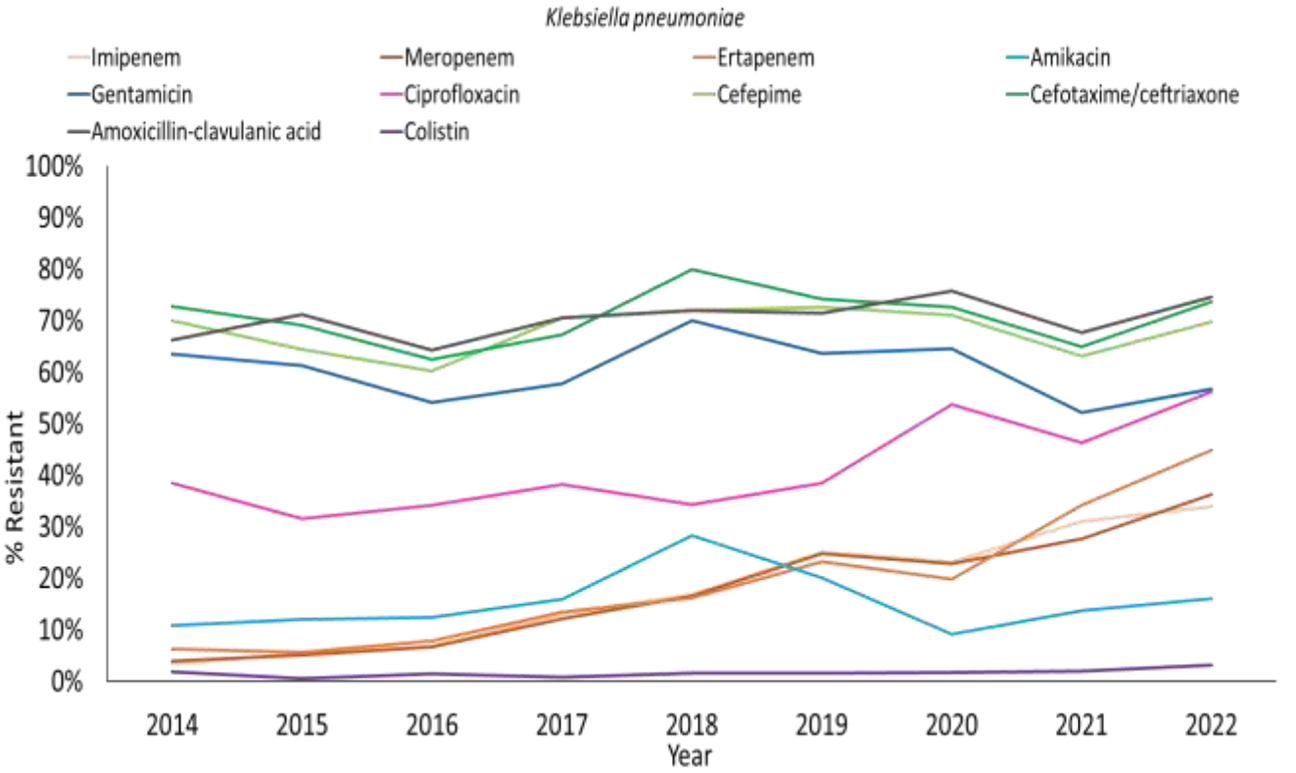
S. aureus trend

Province	S	S (%)	SDD	SDD (%)	I	I (%)	R	R (%)	Total Tested	Not Tested
EASTERN CAPE	4524	84%	1	0%			844	16%	5369	388
FREE STATE	1709	82%			1	0.0%	376	18%	2086	271
GAUTENG	14280	84%					2638	16%	16918	1577
KWAZULU-NATAL	6437	76%			1	0.0%	2004	24%	8442	672
LIMPOPO	1295	90%					138	10%	1433	29
MPUMALANGA	1640	87%			1	0.1%	245	13%	1886	118
NORTH WEST	1321	78%					380	22%	1701	174
NORTHERN CAPE	613	83%					130	17%	743	41
WESTERN CAPE	7470	87%					1094	13%	8564	510
Total	**39289**	**83%**	**1**	**0%**	**3**	**0.0%**	**7849**	**17%**	**47142**	**3780**

AMR trend

From one province a description of AMR trends can build a basis for guidance on appropriate antimicrobial use by healthcare workers.





Baby GERMS study

Culture-confirmed neonatal bloodstream infections and meningitis in South Africa, 2014–19: a cross-sectional study

Rudzani C Mashau, Susan T Meiring, Angela Dramowski, Rindidzani E Magobo, Vanessa C Quan, Olga Perovic, Anne von Gottberg, Cheryl Cohen, Sithembiso Velaphi, Erika van Schalkwyk, Nelesh P Govender, for Baby GERMS-SA*

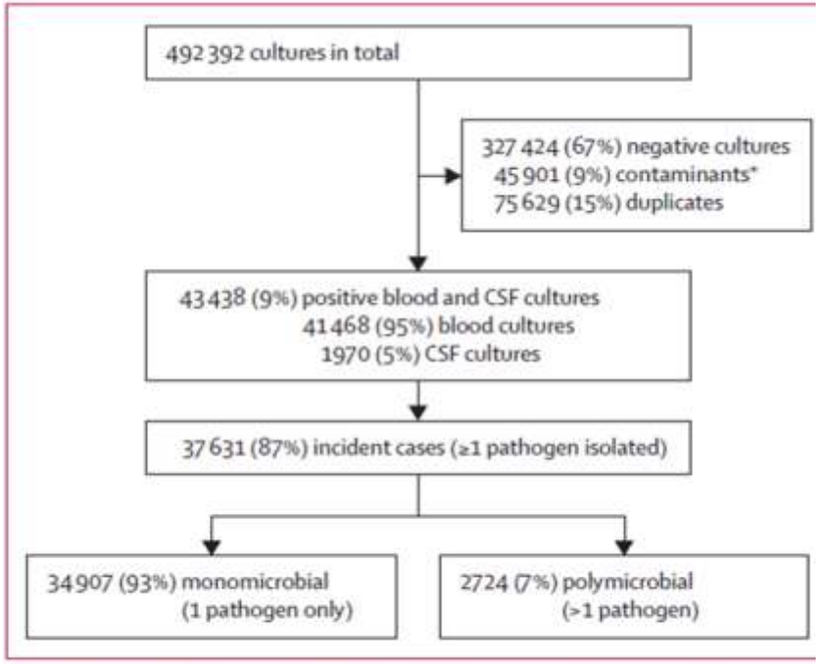


Figure 1: Flow diagram showing the selection of incident neonatal cases of bloodstream infection or meningitis from diagnostic pathology records stored in a national surveillance data warehouse

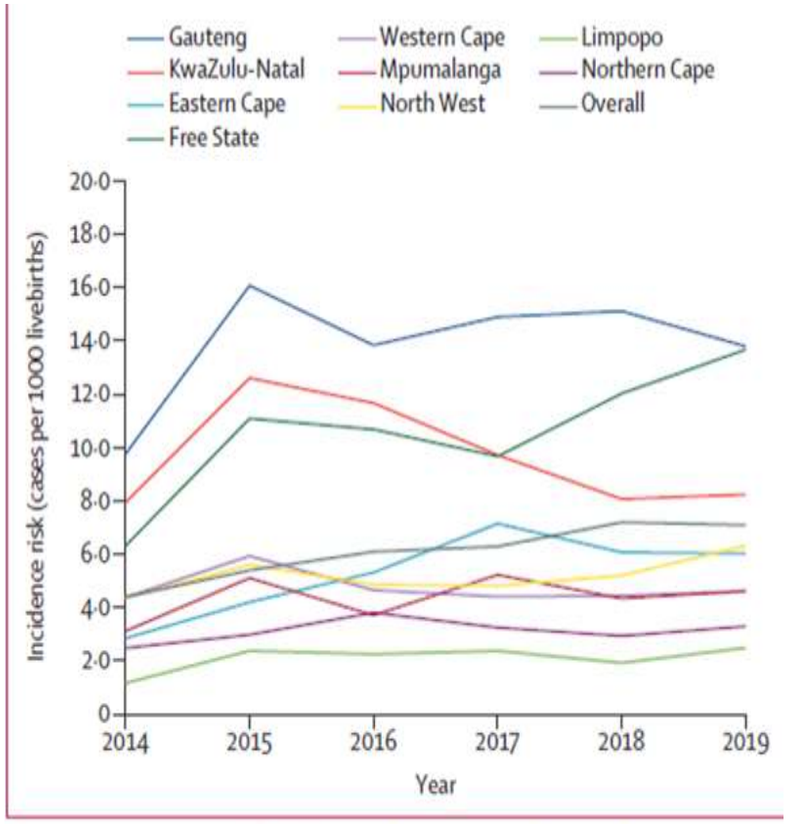


Figure 2: Incidence risk of culture-confirmed bloodstream infection or meningitis among neonates by province (cases per 1000 livebirths)

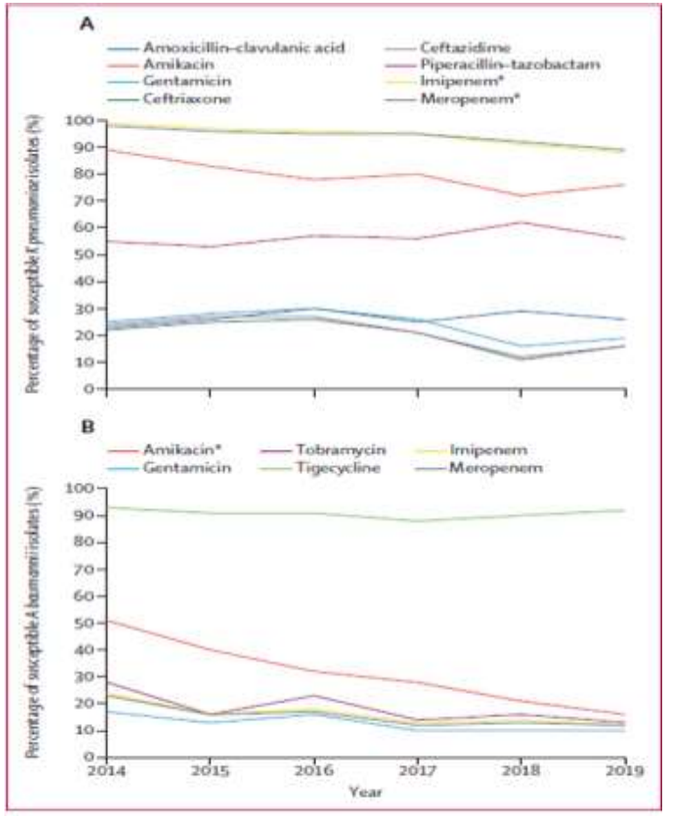


Figure 3: Antimicrobial susceptibility of *Klebsiella pneumoniae* and *Acinetobacter baumannii* isolates among neonates with culture-confirmed bloodstream infection or meningitis
(A) *Klebsiella pneumoniae*. (B) *Acinetobacter baumannii*. *p<0·05.

This is the first national population-level analysis of invasive neonatal infections in the South African public health sector. Although analysis was limited to culture-confirmed infections, it was found a high and rising incidence risk of neonatal BSI and meningitis, a predominance of infections caused by *K pneumoniae*, a varying pathogen distribution at different levels of health care, and reduced susceptibility of Gram-negative bacteria to most agents.

CRE surveillance publications

European Journal of Clinical Microbiology & Infectious Diseases
https://doi.org/10.1007/s10096-020-03845-4

ORIGINAL ARTICLE

Carbapenem-resistant Enterobacteriaceae in patients with bacteraemia at tertiary hospitals in South Africa, 2015 to 2018

O. Perovic[1,2] · H. Ismail[1] · V. Quan[1] · C. Bamford[3] · T. Nana[2,4] · V. Chibabhai[2,4] · P. Bhola[5,6] · P. Ramjathan K. Swe Swe-Han[5,6] · J. Wadula[2,8] · A. Whitelaw[9,10] · M. Smith[1] · Nontombi Mbelle[11] · A. Singh-Moodley[1,2] · for GERMS-SA

Received: 11 October 2019 / Accepted: 9 February 2020

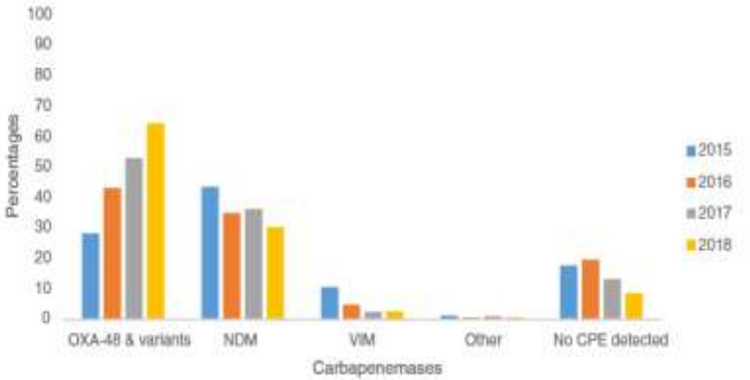


Fig. 3 Flow diagram illustrating the breakdown of carbapenem-resistant Enterobacteriaceae cases and isolates in South Africa for the surveillance period from July 2015 to December 2018

SAMJ RESEARCH

Carbapenem-resistant Enterobacterales in patients with bacteraemia at tertiary academic hospitals in South Africa, 2019 - 2020: An update

M Lowe,[1] PhD; L Shuping,[1] MPH; O Perovic,[1,2] MMed (Microbiol), FC Path (SA)

[1] Centre for Healthcare-associated Infections, Antimicrobial Resistance and Mycoses, National Institute for Communicable Diseases, National Health Laboratory Service, Johannesburg, South Africa
[2] Department of Clinical Microbiology and Infectious Diseases, School of Pathology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

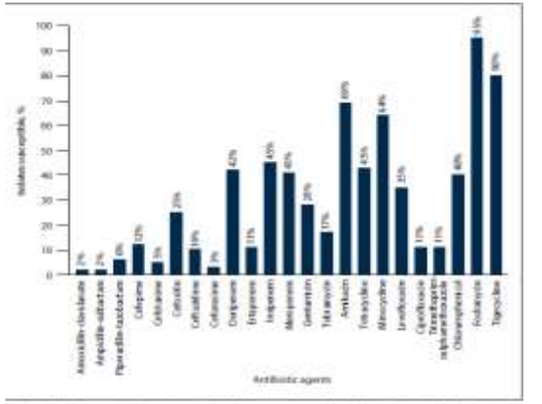


Fig. 5 Antibiotic susceptibility patterns of carbapenem-resistant Enterobacterales isolated from patients with bloodstream infections at the GERMS-SA sentinel surveillance sites, 2019 - 2020. The total percentages of tested isolates that were susceptible are indicated above the bars.

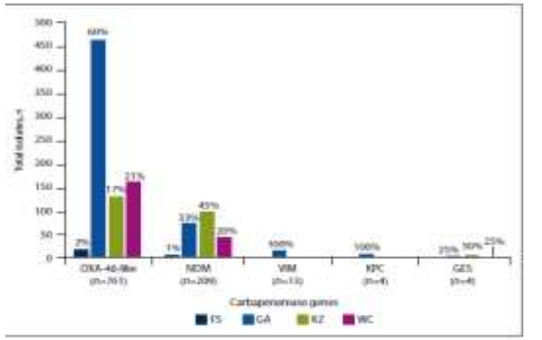


Fig. 6 Carbapenemase genes detected in carbapenem-resistant Enterobacterales from patients with bloodstream infections at the GERMS-SA sentinel surveillance sites, 2019 - 2020. Total percentages of genes detected are indicated above the bars. (FS = Free State; GA = Gauteng; KZ = KwaZulu-Natal; WC = Western Cape; OXA-48-like = carbapenem-hydrolysing oxacillinase-48; NDM = New Delhi metallo-β-lactamase; VIM = Verona integron-encoded metallo-β-lactamase; KPC = Klebsiella pneumoniae carbapenemase; GES = Guiana extended-spectrum β-lactamase.)

The study findings show overall consistent epidemiology of CRE bloodstream infections with slight changes that may become prominent over time. *K. pneumoniae* harboring the blaOXA-48-like gene remains the most prevalent organism among patients with CRE bacteremia in SA's public academic hospitals.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

Acinetobacter baumannii complex (ABC) GERMS SA surveillance

PLOS ONE

RESEARCH ARTICLE

Acinetobacter baumannii complex, national laboratory-based surveillance in South Africa, 2017 to 2019

Olga Perovic[1,2]*, Adrian Duse[2], Vindana Chibabhai[2,3], Marianne Black[2,3], Mohamed Said[1,4], Elizabeth Prentice[5], Jeannette Wadula[2,7], Yesholata Mahabeer[8,9], K. Swe Swe Han[8,9], Ruth Mogokotleng[1], Wilhelmina Strasheim[1], Michelle Lowe[1], Sabelle Jallow[1,2], Husna Ismail[1], for GERMS-SA[¶]

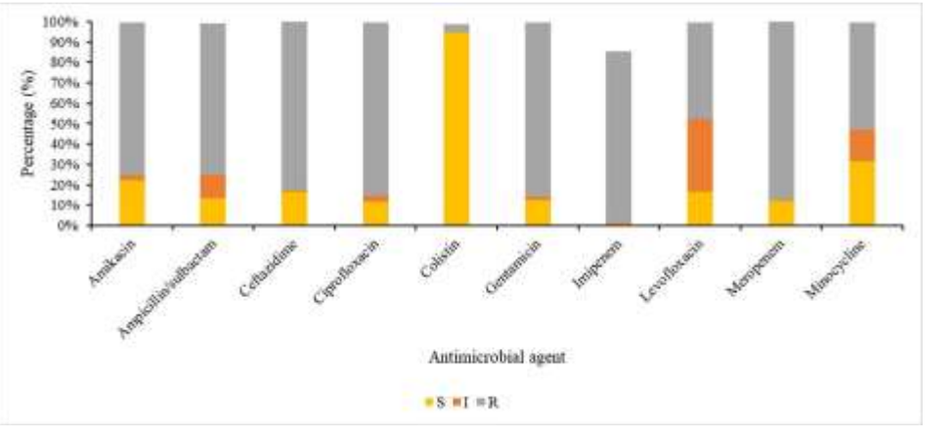
1 Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses, National Institute for Communicable Diseases, Johannesburg, South Africa, 2 Division of Clinical Microbiology and Infectious Diseases, Faculty of Health Science, School of Pathology of the University of the Witwatersrand and the National Health Laboratory Service (NHLS), Johannesburg, South Africa, 3 National Health Laboratory Service, Charlotte Maxeke Johannesburg Academic Hospital, Microbiology laboratory, Johannesburg, South Africa, 4 Department of Medical Microbiology, University of Pretoria, Pretoria, South Africa, 5 National Health Laboratory Services, Tshwane Academic Division, Pretoria, South Africa, 6 Department of Medical Microbiology University of Cape Town and the National Health Laboratory Services, Groote Schuur Hospital, Cape Town, South Africa, 7 Chris Hani Baragwanath Academic Hospital, Soweto, South Africa, 8 Department of Medical Microbiology, National Health Laboratory Service, Inkosi Albert Luthuli Central Hospital, Durban, South Africa, 9 School of Laboratory Medicine and Medical Sciences, Nelson R. Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa

¶ Membership of the GERMS-SA is listed in the Acknowledgments.

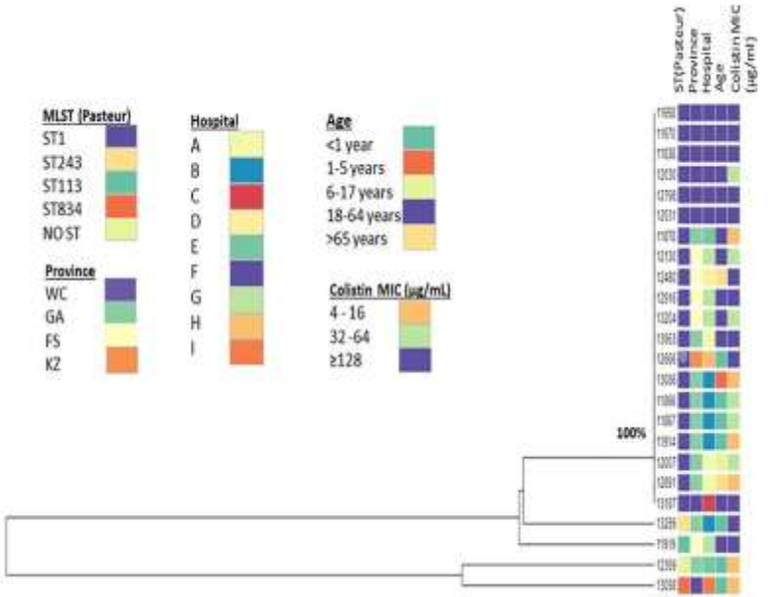
Check for updates

OPEN ACCESS

Citation: Perovic O, Duse A, Chibabhai V, Black M, Said M, Prentice E, et al. (2022) *Acinetobacter*



Antimicrobial susceptibility patterns of Acinetobacter baumannii complex (ABC) bloodstream isolates from South Africa from 1 April 2017 to 30 September 2019, n = 2033. Susceptible (S), Intermediate (I) and resistant (R).



Phylogenetic comparison of colistin-resistant *Acinetobacter baumannii* bloodstream isolates from South Africa from 1 April 2017 to 30 September 2019, n = 24.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

One Health surveillance research

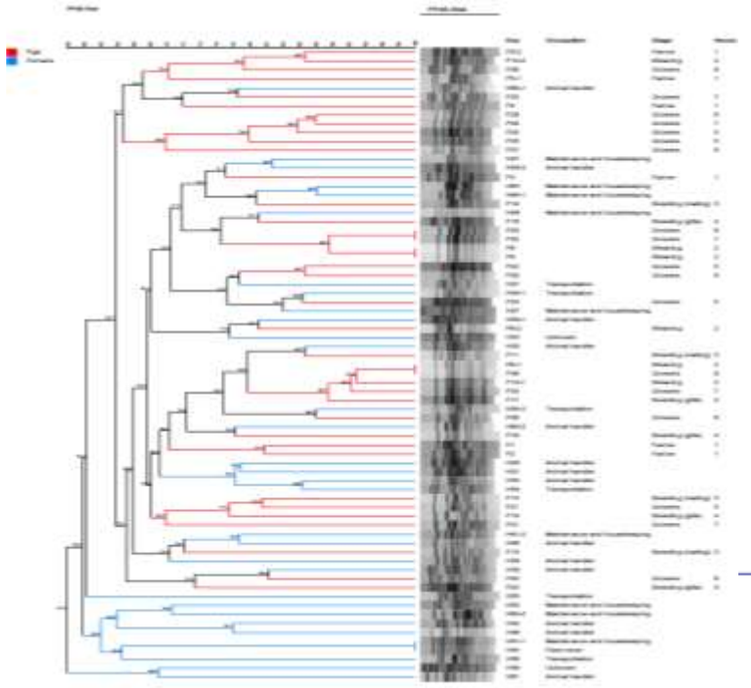
antibiotics MDPI

Article

Whole-Genome Sequencing of Human and Porcine *Escherichia coli* Isolates on a Commercial Pig Farm in South Africa

Wilhelmina Strasheim [1,2,*], Michelle Lowe [1,3], Anthony M. Smith [4,5], Eric M. C. Etter [2,6,7] and Olga Perovic [1,3,*]

1 Centre for Healthcare-Associated Infections, Antimicrobial Resistance and Mycoses, National Institute for Communicable Diseases (NICD), a Division of the National Health Laboratory Service (NHLS), Johannesburg 2192, South Africa
2 Department of Production Animal Studies, Faculty of Veterinary Science, University of Pretoria, Pretoria 0110, South Africa
3 Department of Clinical Microbiology and Infectious Diseases, School of Pathology, Faculty of Health Sciences University of Witwatersrand, Johannesburg 2193, South Africa
4 Centre for Enteric Diseases, National Institute for Communicable Diseases (NICD), a Division of the National Health Laboratory Service (NHLS), Johannesburg 2192, South Africa; anthonys@nicd.ac.za
5 Department of Medical Microbiology, School of Medicine, Faculty of Health Sciences, University of Pretoria Pretoria 0084, South Africa
6 CIRAD, UMR Animal, Santé, Territoires, Risque et Ecosystèmes (ASTRE), 97170 Petit-Bourg, France
7 ASTRE, University of Montpellier, CIRAD, INRAE, 34398 Montpellier, France
* Correspondence: wilhelminas@nicd.ac.za (W.S.); olgap@nicd.ac.za (O.P.)



Integrated ecosystem of the transfer and spread of antimicrobial resistance illustrates the critical importance of a One Health approach to the problem

We are conducting a collaborative "One Health" analysis on antimicrobial resistance in commercial meat production in South Africa to investigate the occurrence of antimicrobial resistance and relatedness among human and porcine isolates in a commercial farm.

Farm setting

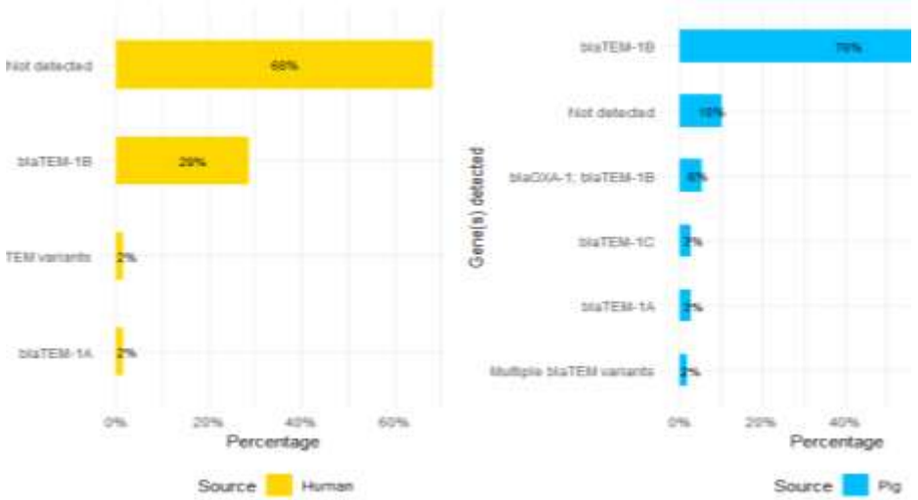
- Located in North-West province
- Consist of two production sites, with 25 production houses in total, managed by the same farmer
- In-operation since 1954 and employees 75 workers full-time
- Sow population of 1 415, closed production system
- Sows are impregnated through artificial insemination
- Most antimicrobials were used (89.4%) for lactation, weaning and gestation

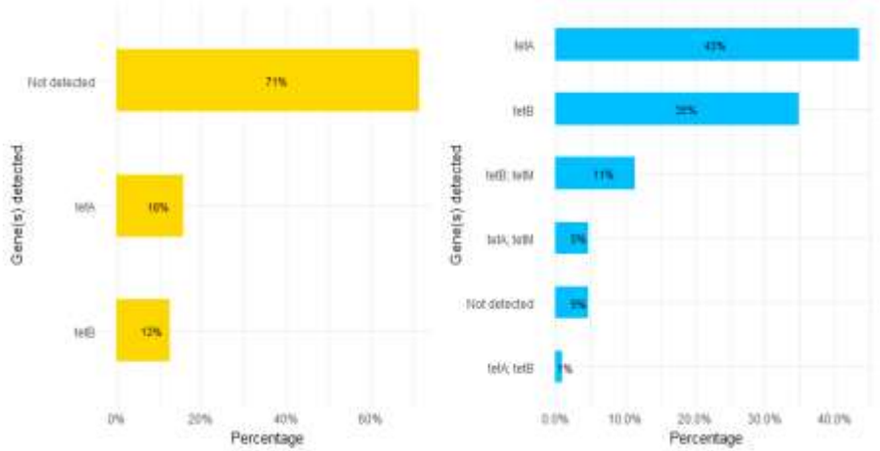
The majority of human and porcine *E. coli* isolates were non-pathogenic in this study, but different pathovars, namely EAEC, EPEC, ETEC, ExPEC and STEC, were detected at low frequencies. Enteroaggregative *E. coli* was only detected in humans, whereas EPEC, ETEC and STEC were predominantly isolated from pigs.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

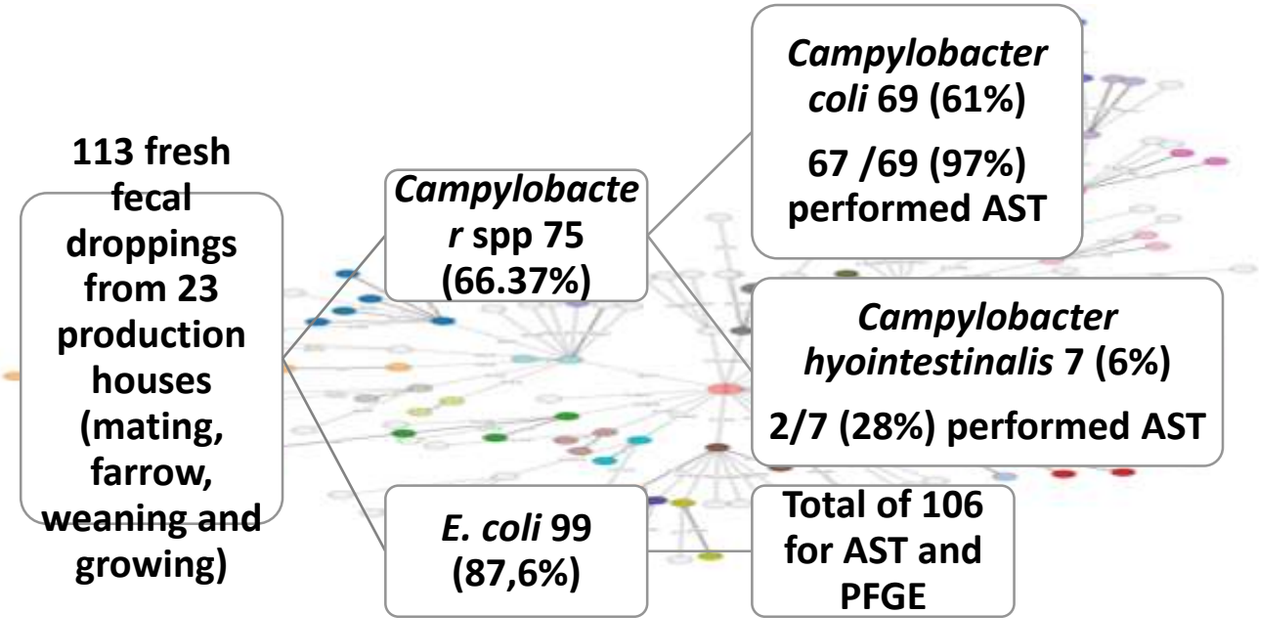
Continue

Antibiotic resistance genes: distribution of β-lactam resistance genes and tetracycline in *E. coli*





In human, resistance were observed for trimethoprim/sulfamethoxazole (40%, 25/63), ampicillin (32%, 20/63), tetracycline (30%, 19/63) and chloramphenicol (5%, 3/63)
Among porcine *E. coli* 94% (100/106) were resistant to ampicillin and tetracycline resistance (95%, 101/106).



WGS and metagenomics of retail meat

antibiotics

MDPI

Article

Bacterial and Genetic Features of Raw Retail Pork Meat: Integrative Analysis of Antibiotic Susceptibility, Whole-Genome Sequencing, and Metagenomics

Michelle Lowe [1,2], Wilhelmina Strasheim [1], Wai Yin Chan [3,4] and Olga Perovic [1,2,*]

[1] Centre for Healthcare Association Infections, Antimicrobial Resistance and Mycoses, National Institute for Communicable Diseases, a Division of the National Health Laboratory Service, Johannesburg 2192, South Africa; michelle.lowe@wits.ac.za (M.L.); wilhelminas@nicd.ac.za (W.S.)
[2] Department of Clinical Microbiology and Infectious Diseases, School of Pathology, University of Witwatersrand, Johannesburg 2193, South Africa
[3] Sequencing Core Facility, National Institute for Communicable Diseases, a Division of the National Health Laboratory Service, Johannesburg 2192, South Africa
[4] Department of Biochemistry, Genetics and Microbiology, Forestry and Agricultural Biotechnology Institute University of Pretoria, Pretoria 0002, South Africa
* Correspondence: olgap@nicd.ac.za; Tel.: +27-(0)113866278

The isolated *E. coli* and *E. faecalis* exhibited minimal phenotypic resistance, with WGS revealing the presence of tetracycline resistance genes. Both the isolated bacteria and meat samples harbored tetracycline resistance genes and the antibiotic residue concentrations were within acceptable limits for human consumption. In the metagenomic context, most identified bacteria were of food/meat spoilage and environmental origin.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

Surveillance for AMR important roles

Robust surveillance systems to monitor the prevalence and patterns of antimicrobial resistance in local and regional healthcare settings and global level.
Utilize advanced diagnostic tools to rapidly identify resistant organisms.

Roles:

- Antimicrobial Stewardship:
  - Develop and implement antimicrobial stewardship programs to optimize the use of antimicrobials, ensuring they are prescribed only when necessary and used appropriately. Educate healthcare professionals about the principles of antimicrobial stewardship.
- Infection Prevention and Control:
  - Emphasize strict infection prevention and control measures to prevent the transmission of resistant organisms within healthcare settings.
  - Implement hand hygiene, isolation precautions, and other measures to reduce the spread of infections.
- Treatment Guidelines:
  - Develop and regularly update evidence-based treatment guidelines that consider local resistance patterns.
    - Use combination therapy or alternative agents when necessary to overcome resistance.
- Diagnostic Advances:
  - Invest in research and development of new diagnostic technologies for rapid identification of resistant organisms and determination of their susceptibility profiles.

Roles

- Collaboration and Communication:
  - Between healthcare facilities, public health agencies, and researchers to share information on antimicrobial resistance and best practices.
  - Communicate effectively with patients, healthcare providers, and the community about the risks and challenges of antimicrobial resistance.
- Research and Development:
  - Support research efforts to discover and develop new antimicrobial agents with novel mechanisms of action.
  - Encourage the development of alternative therapies (phage therapy or immunotherapies).
- Global Coordination:
  - Participate in international efforts to address antimicrobial resistance, as it is a global health concern.
- Patient Education:
  - Educate patients about the appropriate use of antimicrobials, the importance of completing prescribed courses, and the potential risks associated with misuse.
- Regulatory Measures:
  - Implement and enforce regulations to control the use of antimicrobials in agriculture, aquaculture, and veterinary medicine to reduce the development of resistance.

Time for UNGA

High-level Meeting on Antimicrobial Resistance (AMR)

The High-level Meeting on Antimicrobial Resistance (AMR) presents an opportunity for countries and stakeholders to renew efforts and accelerate progress in combating the growing threat of AMR. This meeting will serve as the foundation for executing policies and ensuring accountability for strengthening health systems against AMR. Building on the momentum of previous declarations and commitments, participants will focus on enhancing international cooperation, promoting the responsible use of antimicrobials, and advancing the development of new treatments to safeguard global health.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

UNGA High Level meeting

Early and rolling GLG suggestions for consideration for UNGA HLM 2024

- **Financing:** Global financing instrument and domestic resource allocation mechanism to implement sector-specific and multisectoral NAPs **and novel investment approaches for R&D** of new antimicrobials (particularly antibiotics), vaccines, diagnostics, waste management tools, and safe and effective alternatives to antimicrobials, and to ensure equitable access to them.
- **Accountable governance:** Effective and functional multisectoral governance with formal and accountable global and national structures to implement AMR response across sectors.
- **Surveillance for action:** Strong sector specific and integrated AMR/U surveillance systems and enhanced information sharing for action in all sectors.
- **Transformed systems:** Effective and transformed human health, agri-food and animal health systems so use of antimicrobials is reduced.
- **Environment:** AMR addressed as part of biodiversity and climate solutions.
- **AMR and pandemic preparedness and response (PPR):** Strong link between AMR and PPR and effective implementation of the WHO pandemic accord (provided it is finalized and includes adequate provisions on AMR).
- **Targets:** Evidence- and outcome-oriented targets for actions that can drive change across sectors.

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

Remarks

- Continuous improvement of surveillance programs and strengthening evidence.
- Integrated AMR surveillance from human, animal and environmental sectors.
- Designing information system to optimize and sustain One Health surveillance.
- Quantification of antimicrobial usage to determine the selective pressure and determine the association between antibiotic use and resistance.
- Engaging laboratories for public health relevant surveillance for AMR.
- Share surveillance data towards guidelines and policies of public health importance.

ANTIMICROBIAL RESISTANCE (AMR) COMMUNITY OF PRACTICE (CoP)

THANK YOU

NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
Division of the National Health Laboratory Service

UNIVERSITY OF THE WITWATERSRAND JOHANNESBURG

ASLM
AFRICAN SOCIETY FOR LABORATORY MEDICINE

ETHIOPIA:
Joseph Tito Street,
Nega City Mall, Suite 800
P.O. Box 5487, Kirkos Subcity,
Kebele 08, Addis Ababa,
Tel: (+251) 11 557 1021
Fax: (+251) 11 557 1030

SOUTH AFRICA:
The Pivot, Block E, Third floor,
Montecasino Boulevard,
Fourways, 2055 - Gauteng,
Tel: (+27) 108 808 592

www.aslm.org