Perspectives of transforming the surveillance from conventional methodologies to WGS in EU and Africa

Experiences from EURGEN-RefLabCap, FWD-AMR-RefLabCap, GenEpi-BioTrain and SeqAfrica projects

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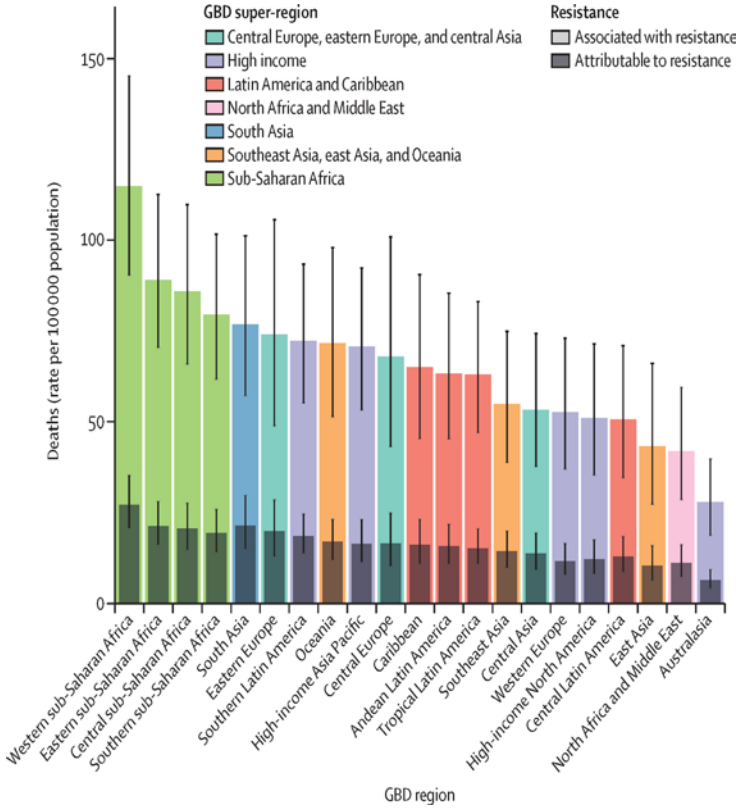
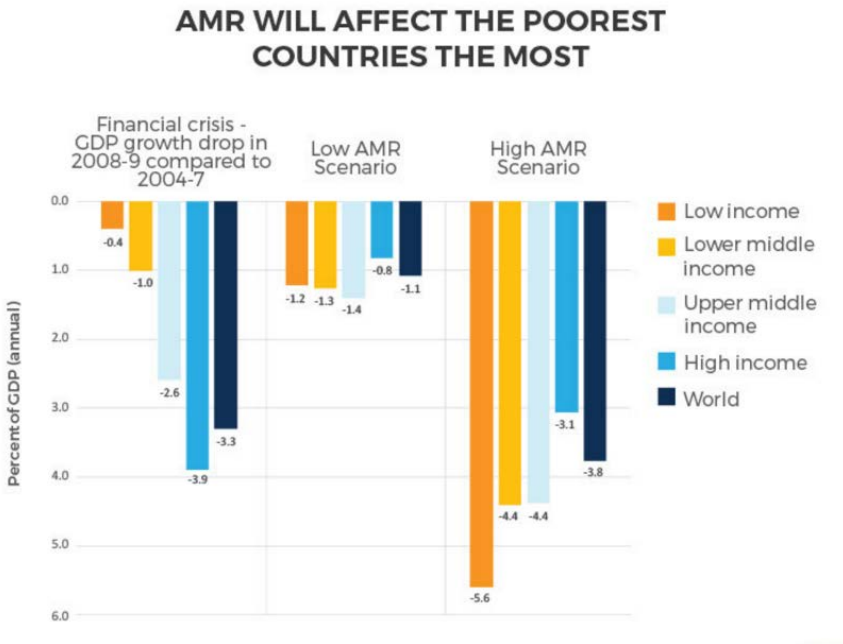
- The EURGEN-RefLabCap, FWD-AMR-RefLabCap and GenEpi-BioTrain projects are carried out in reply to a Call For Tender from the European Commission to provide services to the European Commission and to Member States

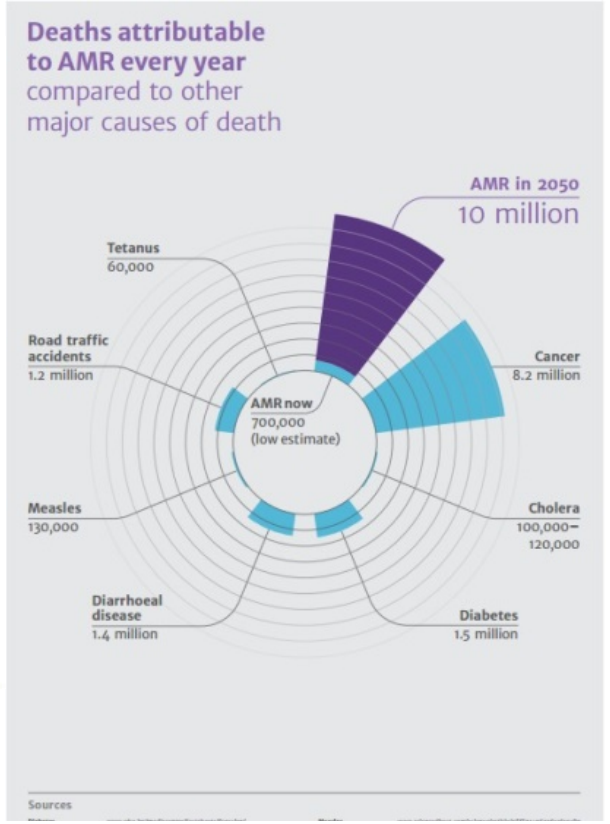
No lack of evidence – lack of action and harmonization

- Humans and animals are exposed more than ever to the emerging threat of antimicrobial resistant (AMR) bacterial pathogens.



The Lancet 2022 399629-655DOI: (10.1016/S0140-6736(21)02724-0)





World Bank Group, March 2017, Drug-resistant Infections – A threat to our economic future/

Review on AMR, Dec. 2014

Global situation of antimicrobial resistance

"**Antimicrobial resistance is a crisis** that must be managed with the **outmost urgency**…..

….**Antimicrobial resistance threatens the very core of modern medicine** and the sustainability of an effective, global public health response to the enduring threat from infectious diseases…

…**Without harmonized and immediate action on a global scale, the world is heading towards a post-antibiotic era in which common infections could once again kill**"

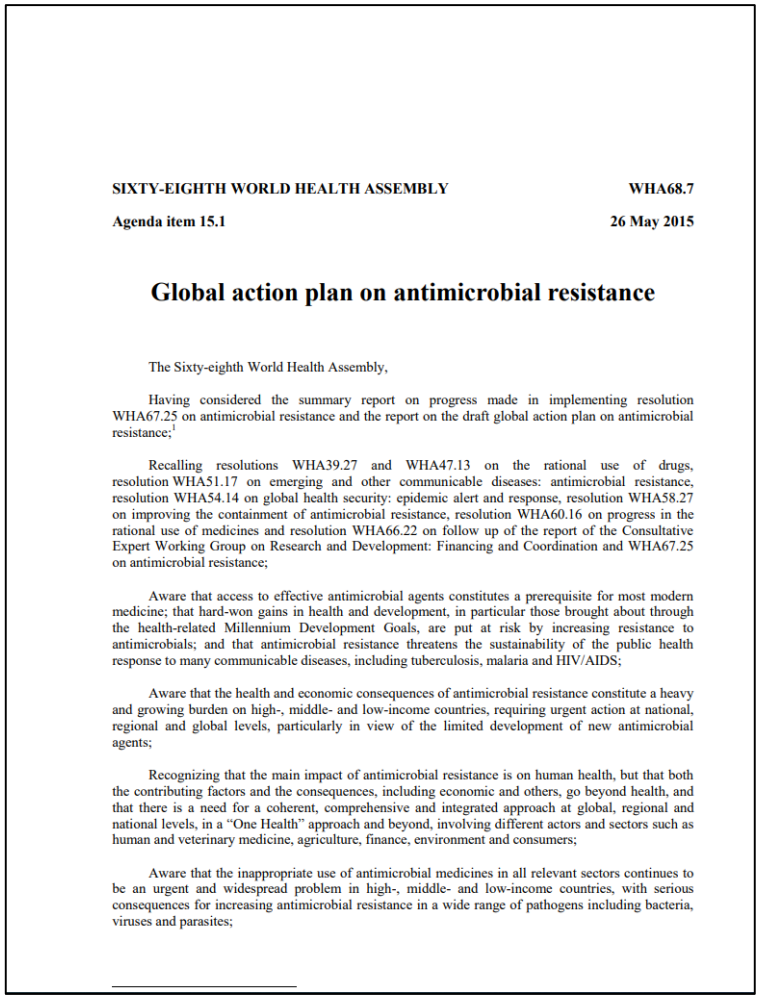
Dr Margaret Chan

Director-General (former DG)

World Health Organization

Harmonized and immediate action on a global scale

Recognizing that the main impact of antimicrobial resistance is on human health, but that both the contributing factors and the consequences, including economic and others, go beyond health, and that there is **a need for a coherent, comprehensive and integrated approach at global, regional and national levels, in a "One Health" approach** and beyond, involving different actors and sectors such as human and veterinary medicine, agriculture, finance, environment and consumers



SIXTY-EIGHTH WORLD HEALTH ASSEMBLY WHA68.7

Agenda item 15.1 26 May 2015

Global action plan on antimicrobial resistance

The Sixty-eighth World Health Assembly,

Having considered the summary report on progress made in implementing resolution WHA67.25 on antimicrobial resistance and the report on the draft global action plan on antimicrobial resistance;[1]

Recalling resolutions WHA39.27 and WHA47.13 on the rational use of drugs, resolution WHA51.17 on emerging and other communicable diseases: antimicrobial resistance, resolution WHA54.14 on global health security: epidemic alert and response, resolution WHA58.27 on improving the containment of antimicrobial resistance, resolution WHA60.16 on progress in the rational use of medicines and resolution WHA66.22 on follow up of the report of the Consultative Expert Working Group on Research and Development: Financing and Coordination and WHA67.25 on antimicrobial resistance;

Aware that access to effective antimicrobial agents constitutes a prerequisite for most modern medicine; that hard-won gains in health and development, in particular those brought about through the health-related Millennium Development Goals, are put at risk by increasing resistance to antimicrobials; and that antimicrobial resistance threatens the sustainability of the public health response to many communicable diseases, including tuberculosis, malaria and HIV/AIDS;

Aware that the health and economic consequences of antimicrobial resistance constitute a heavy and growing burden on high-, middle- and low-income countries, requiring urgent action at national, regional and global levels, particularly in view of the limited development of new antimicrobial agents;

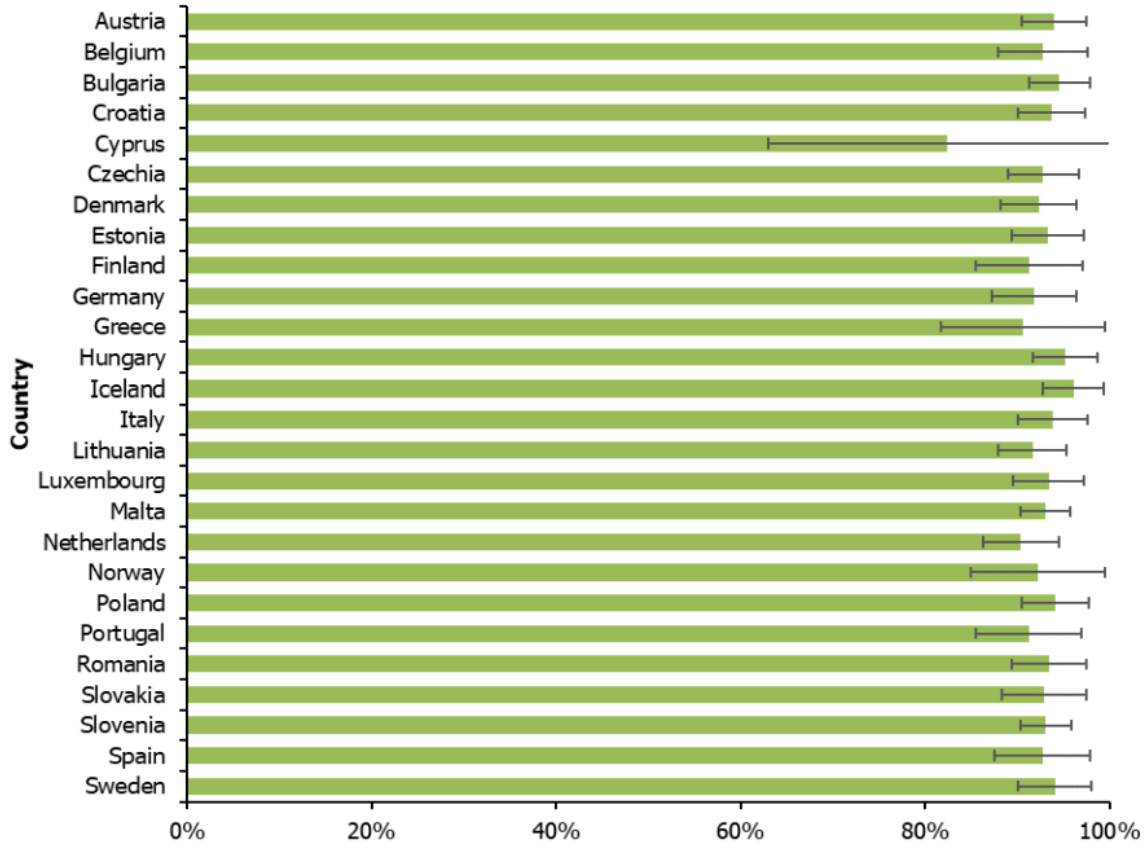
Recognizing that the main impact of antimicrobial resistance is on human health, but that both the contributing factors and the consequences, including economic and others, go beyond health, and that there is a need for a coherent, comprehensive and integrated approach at global, regional and national levels, in a "One Health" approach and beyond, involving different actors and sectors such as human and veterinary medicine, agriculture, finance, environment and consumers;

Aware that the inappropriate use of antimicrobial medicines in all relevant sectors continues to be an urgent and widespread problem in high-, middle- and low-income countries, with serious consequences for increasing antimicrobial resistance in a wide range of pathogens including bacteria, viruses and parasites;

Surveillance systems in place in EU and (Africa)

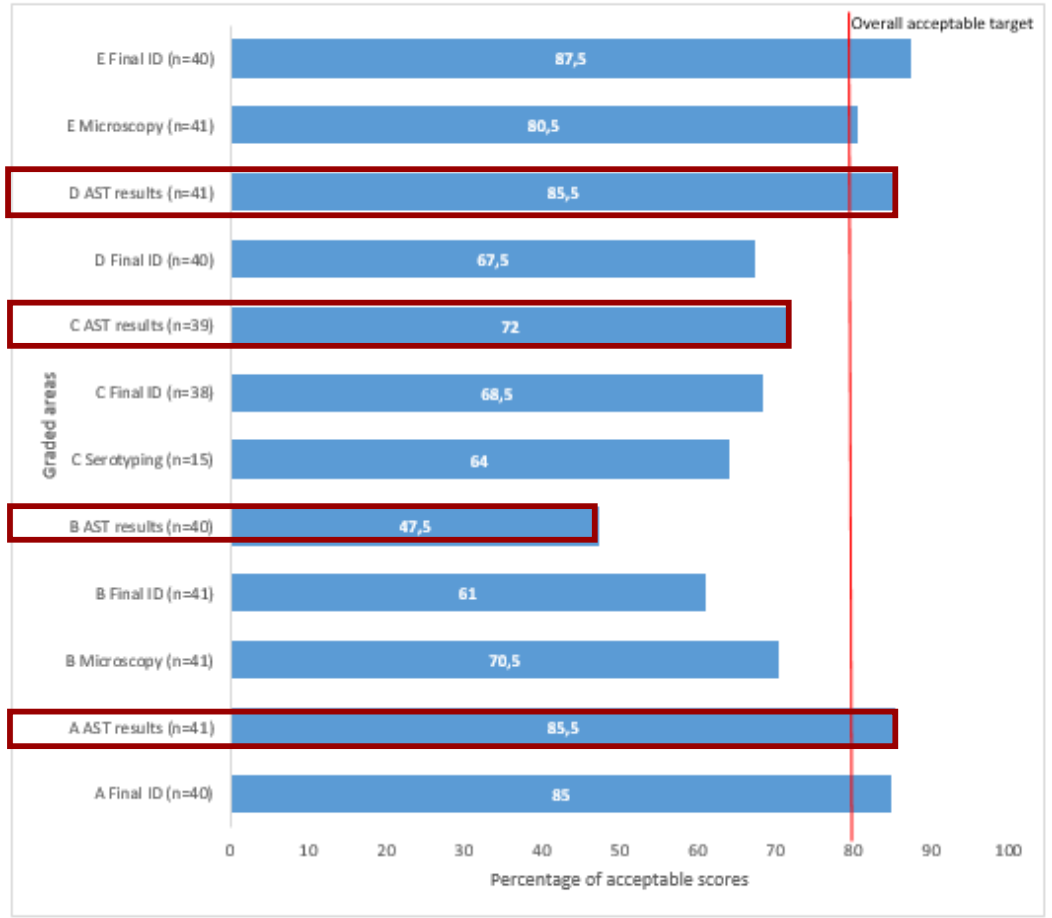
Conventional AST around for decades – still an issue with quality

Figure 2. Mean concordance ± std (%) of the reported AST interpretations with the expected results for all six strains, by participating EU/EEA country, 2021 EARS-Net EQA exercise



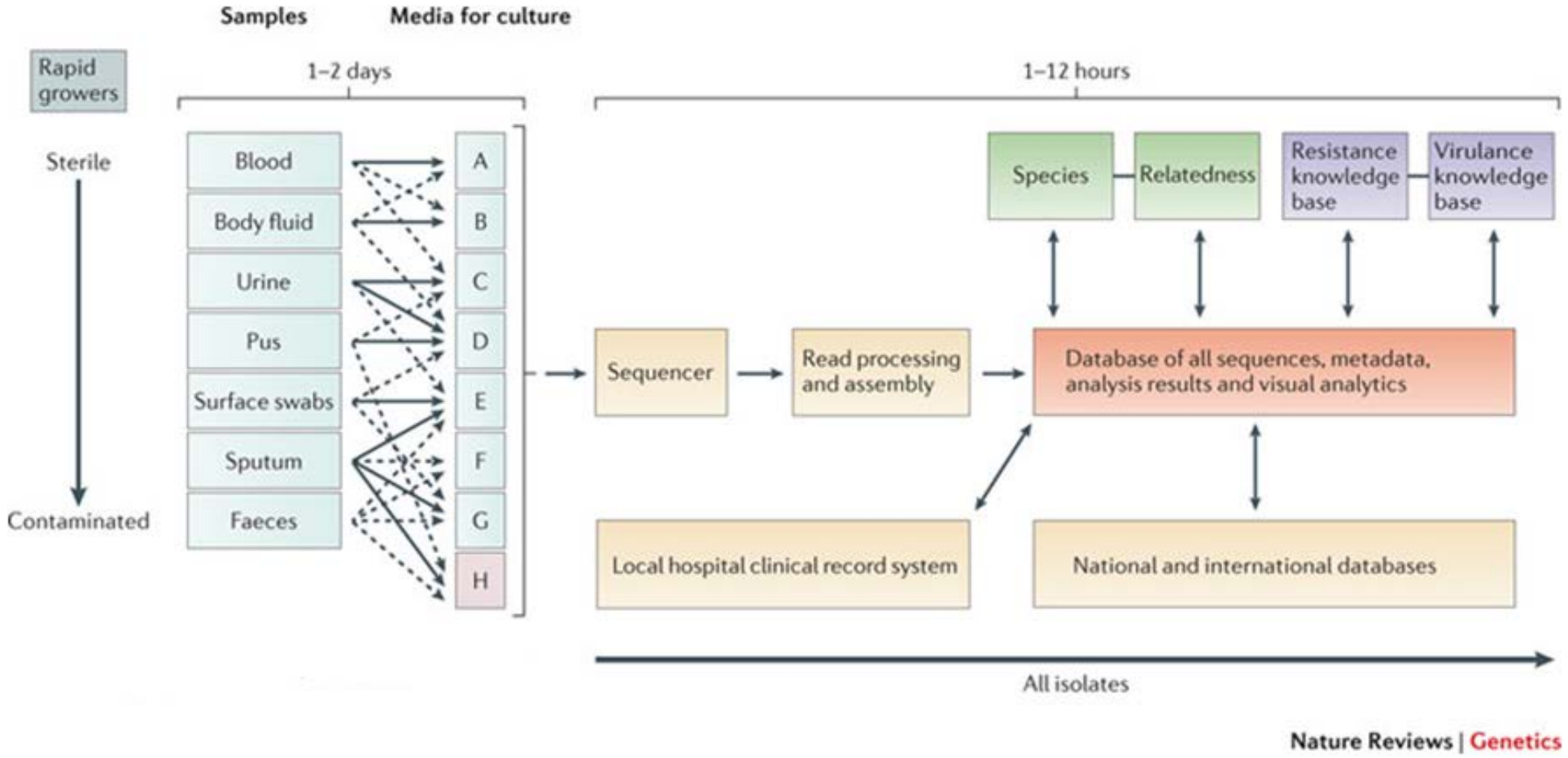
European Centre for Disease Prevention and Control. External quality assessment (EQA) of the performance of laboratories participating in the European Antimicrobial Resistance Surveillance Network (EARSNet), 2021. Stockholm: ECDC; 2022

Figure 10 shows the overall acceptable results for all graded areas in Cycle 2.

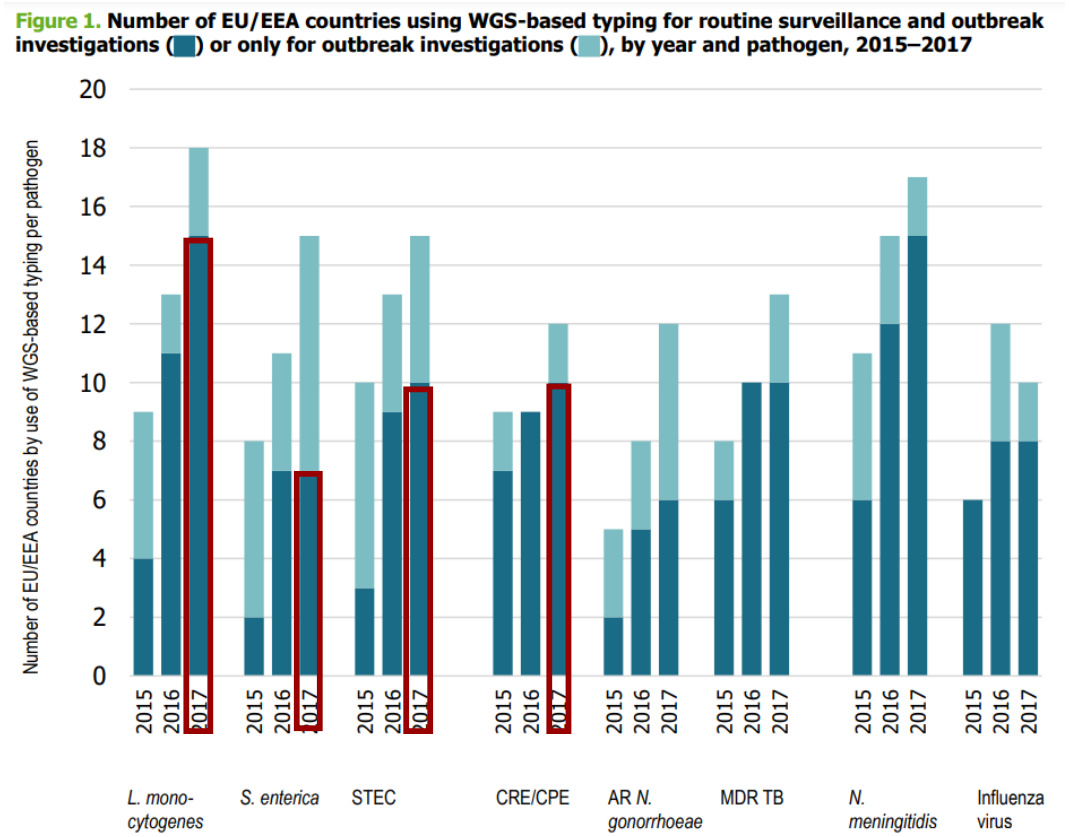


Fleming Fund EQAfrica 2022 - Cycle 2 - Summary report for Southern region

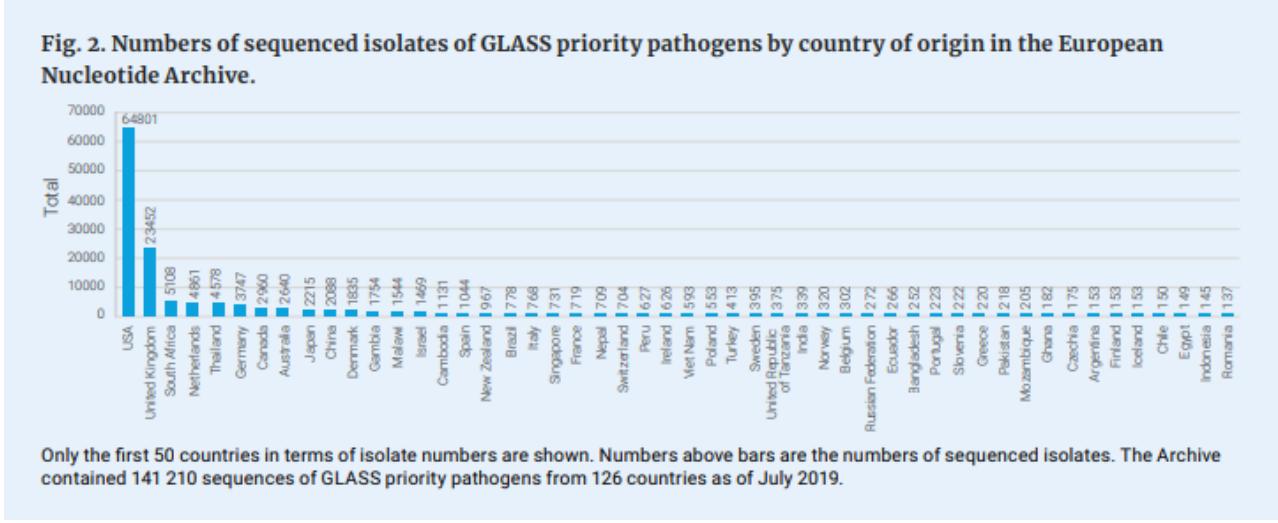
Paradigm shift in surveillance – “going genomics”
Not as easy as illustrated – lots of barriers



Public Health and Food/Animal Health - a decade behind academia



European Centre for Disease Prevention and Control. ECDC strategic framework for the integration of molecular and genomic typing into European surveillance and multi-country outbreak investigations – 2019–2021. Stockholm: ECDC; 2019.



GLASS whole-genome sequencing for surveillance of antimicrobial resistance. Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO.

EU and Africa at the same level building WGS capacity for Public Health surveillance

3rd stage
”Train & Practice”

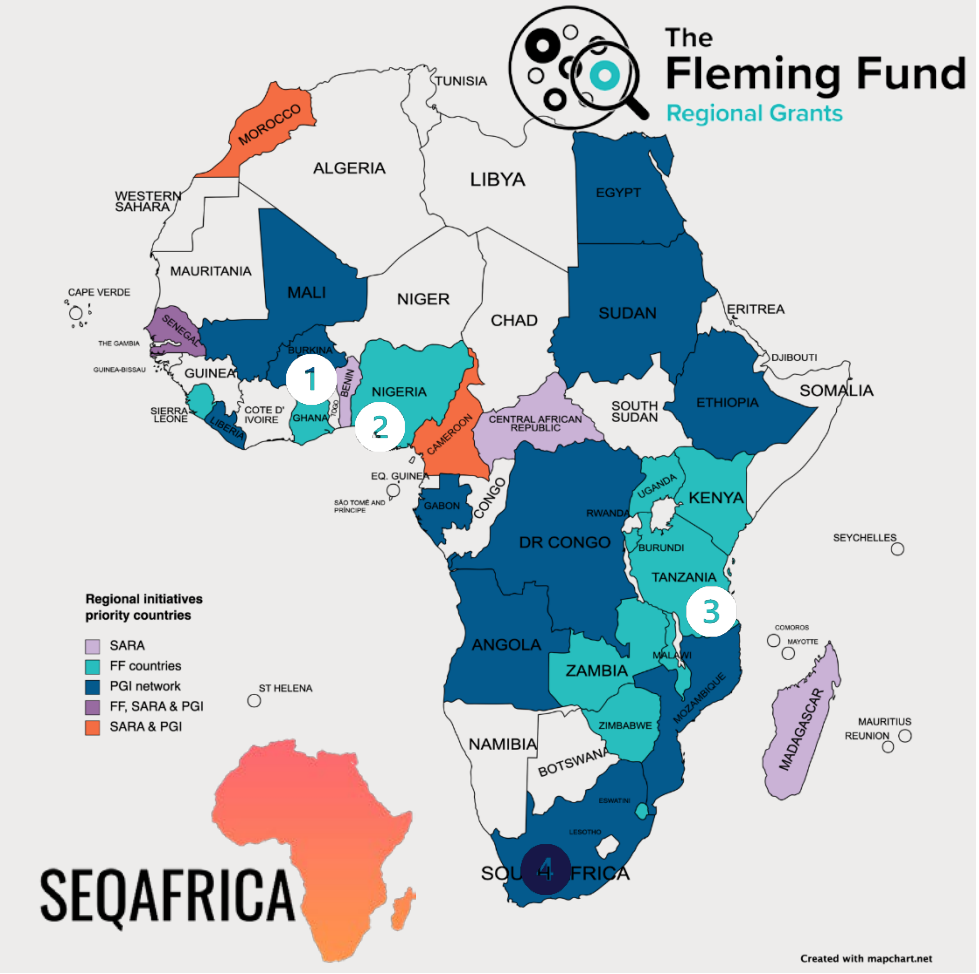
GenEpi-BioTrain

2nd stage
”Buidling capacity”

RefLabCap

FWD AMR· RefLabCap

1st stage
”Instrumentation”



EURGEN-RefLabCap / FWD-AMR-RefLabCap project goals and objectives

- In a period of 4 years support will be provided to a range of training, external quality assessment (EQA) schemes and networking activities to improve public health reference laboratory functioning through improved laboratory functioning at local, regional and national levels in all countries participating in the EU health programme

- The general objective is to enhance the validity and accuracy of surveillance data reported at EU level in compliance with the new EU AMR case definitions in order to inform concerted actions against AMR at EU level and enable better detection and control of cross border threats to human health from AMR

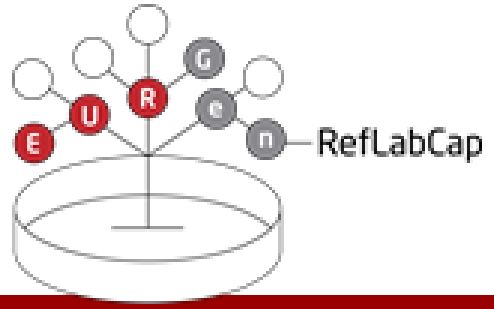
Funded by the European Union

EURGEN-RefLabCap / FWD-AMR-RefLabCap project purposes

EURGEN-RefLabCap

- Provision of EU networking and support for public health reference laboratory functions for antimicrobial resistance in **priority healthcare associated infections**

- To **strengthen coordination, support and capacity** in public health national microbiology reference laboratory functions for antimicrobial resistance in priority healthcare associated infections



FWD-AMR-RefLabCap

- Provision of EU networking and support for public health reference laboratory functions for antimicrobial resistance in **Salmonella and Campylobacter in human samples**

- To **strengthen coordination, support and capacity** in public health national microbiology reference laboratory functions for antimicrobial resistance (AMR).

FWD AMR· RefLabCap

Funded by the European Union

Projects objective

- The specific objective is to support the operation of public health reference laboratory networks by providing capacity-building activities including training, quality assurance, country visits and other tasks described in more details below, as well as validated AMR detection tools to national reference laboratories in compliance with the new EU AMR case definitions.

EURGEN-RefLabCap

- Address antimicrobial-resistant pathogens whose predominant modes of transmission are healthcare-associated
  - Carbapenem-resistant *Enterobacterales* (CRE) and colistin-resistant-CRE (CCRE)

FWD-AMR-RefLabCap

- In specifically for AMR in *Salmonella* species and *Campylobacter* species in human samples.

Funded by the European Union

EURGEN-RefLabCap / FWD-AMR-RefLabCap project tasks

EURGEN-RefLabCap

- **Capacity building activities** provided to national reference laboratories (NRLs) for public health for the specified organisms **to improve NRLs' functions for AMR**
- **Strengthening the role of NRLs** for public health **to build capacities in regional and local laboratories** in the health systems of their countries
- **Modernisation of diagnostic and molecular typing** tests used in health systems for the specified organisms using whole genome sequencing (WGS)

FWD-AMR-RefLabCap

- **Capacity building activities** provided to national public health reference laboratories (NRLs) **to improve their functions for AMR in Salmonella and Campylobacter from human samples**.
- Local and regional laboratory capacity building activities. These activities focus on strengthening the role of NRLs for public health **to build capacities in regional and local laboratories** in their countries.
- **Modernisation of diagnostic and molecular typing** tests used in health systems for the specified organisms using whole genome sequencing (WGS)

Funded by the European Union

Fleming Fund regional grant SEQAFRICA phase II main activities

- Continue data generation, WGS & bioinformatics services
- Continue training
- Professional and leadership development
- Preparations for “Phase over” to other regional based initiative, i.e. sustainability
- Expand SEQAFRICA network with sentinel sites surveillence

Expansion of SEQAFRICA network with sentinel sites

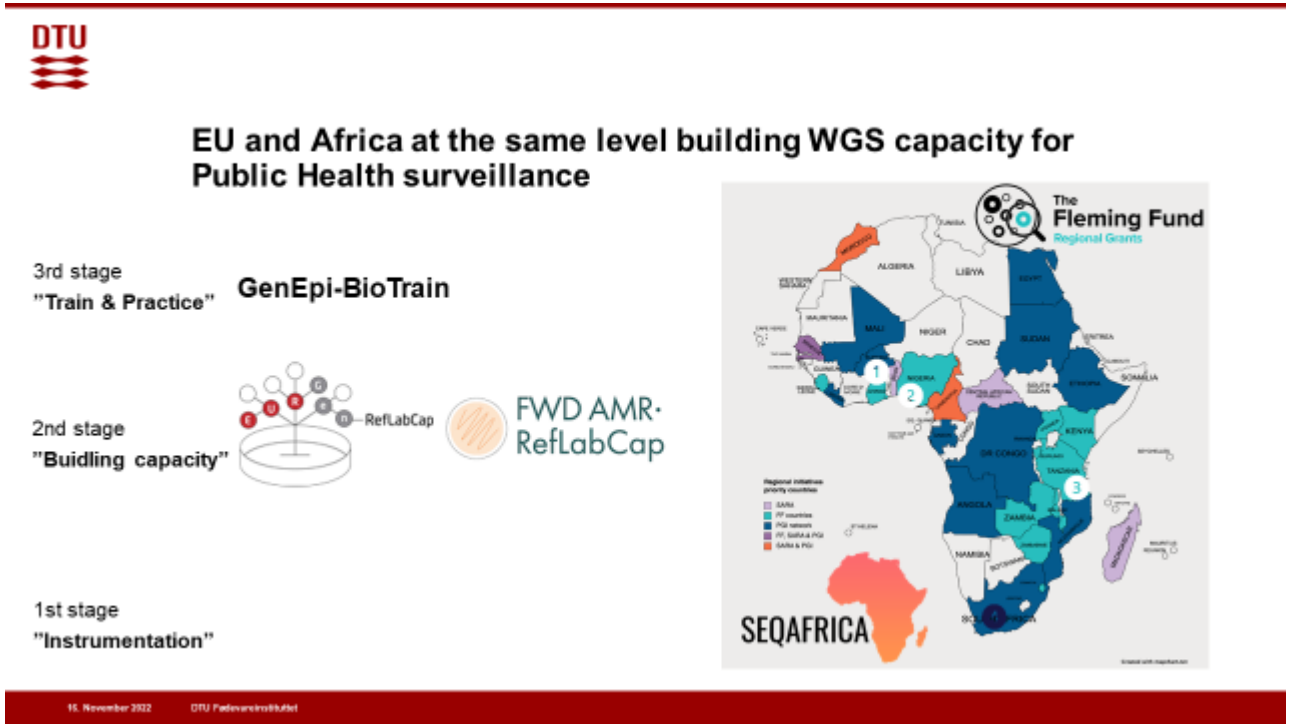
- Pathogen focus
  - In the beginning allow sites to WGS what they want to encourage and inspire use
  - Eventually focus on a limited number of pathogens/syndromes

- Selection of sentinel sites (up to 10 for year 1)
  - Expand nationally
  - Expand to other countries (FF countries, PGI & SARA sites)

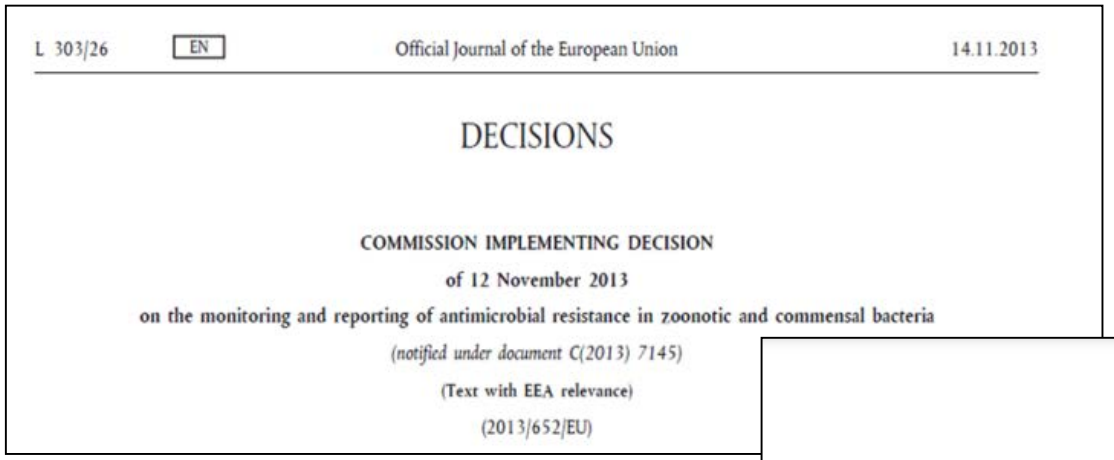
- Training
  - In-person, and remote supported by developed SOPs (written and videos)
  - Trained at the regional sites

Leverage activities from GenEpi-BioTrain to SEQAFRICA

- Face-to-face workshops “Bridging the gaps in bioinformatics”
- Face-to-face workshops “Interdisciplinary genomic epidemiology and public health bioinformatics”
- Exchange visits for bioinformaticians
- Face-to-face trainings on genomic epidemiology and/or public health bioinformatics
- Virtual trainings on genomic epidemiology and/or public health bioinformatics



EU AMR surveillance system in food and animals in place; Are we loosing the momentum?



L 303/26 EN Official Journal of the European Union 14.11.2013

DECISIONS

COMMISSION IMPLEMENTING DECISION

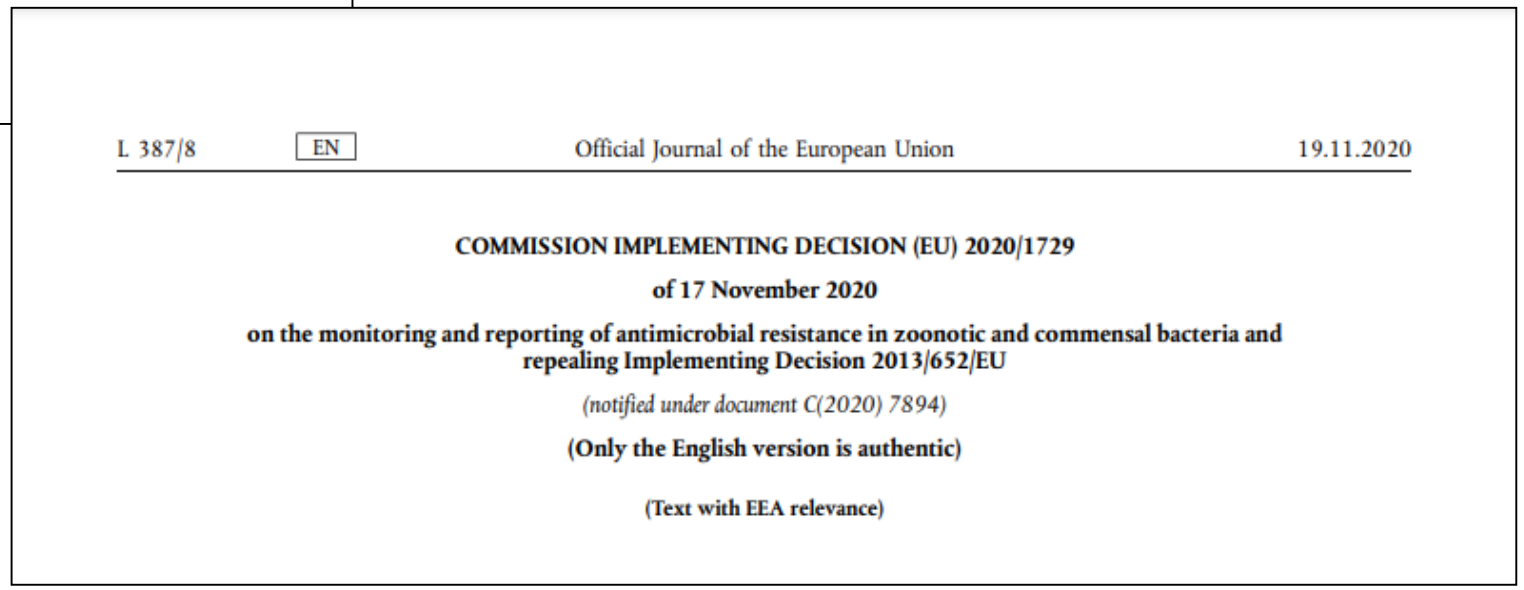
of 12 November 2013

on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria

(notified under document C(2013) 7145)

(Text with EEA relevance)

(2013/652/EU)



L 387/8 EN Official Journal of the European Union 19.11.2020

COMMISSION IMPLEMENTING DECISION (EU) 2020/1729

of 17 November 2020

on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria and repealing Implementing Decision 2013/652/EU

(notified under document C(2020) 7894)

(Only the English version is authentic)

(Text with EEA relevance)

Main challenges and barriers

- Training
  - Bioinformatics needs to know what software to use and basic programming
  - Microbiologists and epidemiologists needs to know how to analyse genomic data e.g. “when to trust a tree” etc.

- Procurement of instruments and reagents
  - Why do scientists in Africa have to pay more?

- Lack of closer engagement with the ministries
  - Why do the NRLs not receive the needed resources – lack of country buy-in

- High turnover of staff (especially bioinformaticists)
  - Employees quit due to higher saleries abroad or in the private industry

- Ensuring NRLs have funds to procure reagents, maintain staff contracts etc. to operate

Future perspectives

- Sequencing seems to be a realistic alternative to conventional phenotypic susceptibility methods for surveillance of AMR
  - Assessed and proven by research
  - Considerable large added value
  - The transition should be prioritized by governments and supranational organization
    - Limited by country buy-in

- The ”Silver Bullet” theory of AMR vaccines might by an intermediate cure but will not solve the problem – we need to have prudent usage

- Metagenomics might be a promising technology but ”we need to walk before we run” – long from being “standard procedure” in none-academia settings

- We need to address the monopoly by major companies and the barriers for procurements
  - Currently, the surveillance of AMR is limited by procurement and technical support

Thank you for your attention

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