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Genomics to address antimicrobial resistance

Surveillance, Prevention and Control

Antimicrobial Resistance Division

World Health Organization

Accelerating the Use of Pathogen Genomics and Metagenomics in Public Health Workshop

22 July 2024

Genomics and whole genome sequencing (WGS) open new horizons in understanding and addressing resistance

PHENOTYPIC assessment of resistance
- Clinical assessment (e.g., malaria)
- Susceptibility testing in the laboratory

MOLLECULAR aspects of resistance

Amplification of known resistance genes

Whole genome sequencing

+

Databases of genetic variations that correlate with phenotypes

GCTCTTG
GCTTTAA
GTTATAA
GTTGTAA
↓
GYTNTWR

INTERPRETATION for decision making and R&D at the individual, local, national and global level

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Molecular techniques to address resistance in HTM

Malaria: Early stage

- Therapeutic efficacy studies (TES)
- Artemisinin combinations work in sequence
- Lack of documented links between mutations and failure of key treatments
- Molecular surveillance can't be used yet for treatment policy but helps understanding parasite evolution

HIV: Technical reference

- Viral suppression prevents resistance: Monitoring is key
- Gene sequencing for detection of drug resistance if no viral suppression
- NGS to detect drug resistance mutations in target genes
- HIV drug resistance surveys

TB: Prime time for WGS

- PCR for routine detection of resistance before treatment
- NGS for comprehensive detection of MDR and XDR TB
- WGS to identify additional genes associated with resistance
- Use of primary specimens

NGS: Next Generation Sequencing

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Emerging applications of WGS for surveillance of emergence and spread of AMR

- More pathogens, more complexity
- Use cases at global, regional and national levels
- Opportunity of post COVID-19 infrastructure

1. Surveillance of **emergence** and prevalence at all levels

2. Investigation of **spread** (clusters investigations)

3: **Research:**
Evolution, molecular mechanisms, diagnosis

GLASS
Whole-genome sequencing for surveillance of antimicrobial resistance

Global Antimicrobial Resistance and Use Surveillance System (GLASS)

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World Health Organization. GLASS whole-genome sequencing for surveillance of antimicrobial resistance. Geneva: World Health Organization; 2020.

Aiming for impact of the work on genomics in AMR

Inputs

- Human resources
- SOPs, guidelines and standards for WGS
- High quality standardized WGS data
- High quality standardized AST data
- Standardized epidemiological metadata
- Central data repository

Activities

- Surveillance system
- Quality Assurance procedures
- Capacity building
- Analysis and interpretation
- Data integration
- Incorporation into GLASS centralized repository
- Reporting and communication
- Data sharing

Outputs

- Validated WGS data
- AMR reports with WGS and AST data
- Molecular AMR mechanisms identified
- AMR trends
- Ggeographical spread
- Comparison of genomes from different sites
- Evaluation of impact of interventions

Outcomes

- Enhanced surveillance and data sharing
- Control of dissemination
- Improved response to outbreaks
- Informed decision making
- Policy development

Impact

- Reduced AMR
- Reduced mortality
- New diagnostics
- New antimicrobial drugs

National commitment is key

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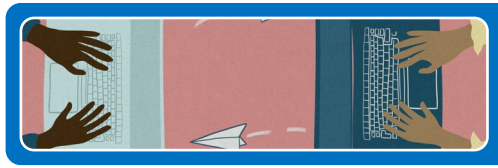
WHO global genomic surveillance strategy: Designed for epidemic and pandemic, fully applicable to AMR

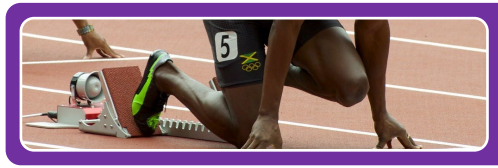
Access to tools to improve representativity

Strengthen workforce for speed, scale and quality

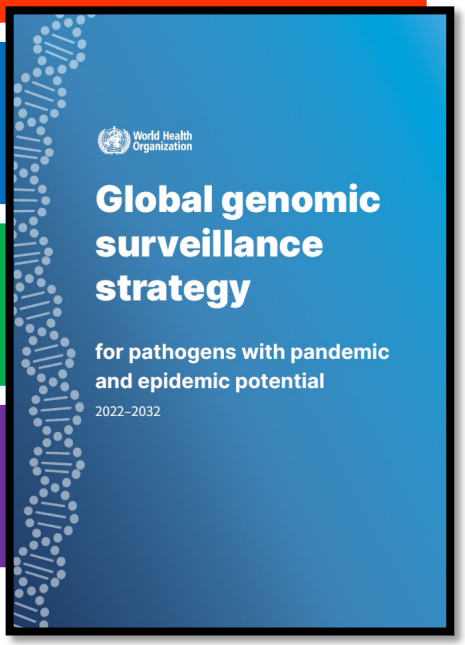


Data sharing for action

Connectivity for value add



Readiness posture for emergencies



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Way forward: Bridge genomics for programmes and for emergency preparedness to maintain a readiness posture

- **Diversified innovation portfolio:**
  - From applications ready for routine use to those coming up
- **Mutual benefit and health system resilience:**
  - Strengthen health system, improve preparedness and respond to AMR
- **Sustainability:** Integration in health strategies and plans for efficiency
- **Financing:** Opportunities to access existing funding streams
- **What's get measured get done:** Metrics to measure progress

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Thank you

PAHO REGIONAL STRATEGY FOR MOLECULAR SURVEILLANCE

CAPACITY- BUILDING

- Regional workshops (Barbados: real-time PCR for carbapenemase detection for CARICOM MS, TTO: phenotypic detection for CARICOM MS,)
- On-site trainings: ex. horizontal collaboration between Caribbean countries and Argentina.
- ReLAVRA+ workshop with 200+ participants

COUNTRY- SPECIFIC PROJECTS

- Support to 7 South American countries for the implementation of pilot projects for integrated AMR surveillance across human, veterinary health, agriculture and food production and the environment.
- Accompanying Costa Rica, Guatemala and Paraguay in data analysis, interpretation and publication of WGS findings from outbreak investigation and specific studies.

NETWORK INTEGRATION

- PAHO hosted the global meeting of WHO CC on AMR surveillance in 2023, including a special session on molecular surveillance.
- Improving national coordination on molecular surv. and use of resources: launch of PAHO Genomic Surveillance Regional Networks (PAHOGen) to integrate: PulseNet that monitors foodborne pathogens, ReLAVRA+, RELDA the Network of Arbovirus Laboratories of the Americas (now ViGenDA for genomic surveillance network for dengue virus and other arboviruses) and the Regional Genomic Surveillance Network for Respiratory Viruses (RESVIGEN).