AMR Surveillance Best Practices

Five-day hybrid lecture series **9–15 October 2024**



Speaker: Dr Geetanjali Kapoor, Acting Head and Researcher, One Health Trust (formerly CDDEP)

Host: Professor Ben Cooper, Professor of Epidemiology, Nuffield Department of Medicine











Housekeeping

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Panel and agenda

Host: Professor Ben Cooper and Facilitator: Barney McManigal

Visiting fellow: Dr Geetanjali Kapoor - Acting Head and Researcher, One Health Trust (formerly CDDEP), India

Schedule

Day 1. Wed, Oct 9, 10:00-11:00 - Large Scale Surveillance for Antimicrobial Resistance:
Overview & 11:00-13:00 - AMR Series: Laboratory methods and definitions
Day 2. Thu, Oct 10, 11:00-13:30 - AMR Series: Surveillance in Human Health I
Day 3. Fri, Oct 11, 10:00-13:00 - AMR Series: Surveillance in Human Health II
Day 4. Mon, Oct 14, 9:00-12:00 - AMR Series: Surveillance Reports, Challenges, and Mitigation
Day 5. Tue, Oct 15, 10:00-13:00 - AMR Series: Conclusion and Open Discussion

Registered for the lecture series as of 09/10 AM - Thank you!



ACKNOWLEDGEMENT

Hamied Foundation UK-INDIA AMR Fellowship Yusuf and Farida Hamied Foundation The Academy of Medical Sciences Office of the Chief Medical Officer (CMO) for England

Professor Ben Cooper Dr Christiane Dolecek Dr Barney McManigal Isabela Cabrera Lalinde Sophie Patten Nuffield Department of Medicine, University of Oxford

The Global Health Network, University of Oxford

Dr John Stelling

One Health Trust

AGENDA

Date	Short title	Subtopics	Room	Time
Oct 9, 2024 Wednesday	Large Scale Surv	BDI LG 1	10.00 - 11.00	
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Day 1/5, Session 1: Large Scale Surveillance for Antimicrobial Resistance: Overview

Dr Geetanjali Kapoor

Acting Head and Researcher, One Health Trust (formerly CDDEP)

ANTIMICROBIAL RESISTANCE (AMR) STAKEHOLDERS

- UK Department of Health & Social Care, PHE, Fleming Fund, GRAM
- US Centers for Disease Control and Prevention & National Institutes
 of Health
- European Medicines Agency & Food and Drug Administration
- Multilaterals and international organizations FAO, OIE, WHO, UNEP, OECD...and more
- G20 (Argentina, Australia, Brazil, Canada, China, France, Germany, India, Indonesia, Italy, Japan, South Korea, Mexico, Russia, Saudi Arabia, South Africa, Turkey, United Kingdom and United States, plus the European Union)
- G7 (Canada, France, Germany, Italy, Japan, United Kingdom, and United States)
- Governments and academia
- Funders, Donors, Foundations, Nonprofits
- GAVI, MSF, FIND, BARDA, GARDP, OHT/CDDEP, REACT, ...and more ...
- GLASS Global Antimicrobial Resistance Surveillance System, JPIAMR Joint Programming Initiative on Antimicrobial Resistance, Surveillance platforms
- Pharmaceutical companies; R&D
- Citizens & advocacy groups
- and more...

ANTIMICROBIALS | FIRST ONES

- Quinine extraction (1600s; isolated in 1820) | Pierre Pelletier and Joseph Caventou | School of Pharmacy, Paris
- Penicillin discovery (1928) | Alexander Fleming |St. Mary's Hospital, London |Nobel Prize in 1945\
- Nystatin discovery (1949) | Elizabeth Hazen and Rachel Fuller Brown | Laboratories, New York State Department of Health
- Idoxuridine synthesis (1958) | William Prusoff at Yale University, CT

AMR | ACCELERATORS

Conducive environment for microbe and antimicrobial interactions

More microbes

- weak infection control
- poor sanitation
- low vaccine coverage

More antimicrobials

- weak stewardship
- regulations
- disposal practices

Environmental

wastewater management in human dwellings, animal farms and agriculture

& more

AMR DEVELOPMENT | TIMELINES SINCE 1940s

ANTIBIOTICS INTRODUCED





Ref: Antibiotic Resistance Threats in the United States, 2013 The discovery and development of Penicillin 1928-1945. Royal Society of Chemistry & American chemical Society. 1999.

WHAT IS THE AMR BURDEN? IS IT EASY TO QUANTIFY?

WHAT IS THE AMR BURDEN?

HUMANISTIC & FINANCIAL

AMR infections	AMR attributed deaths	AMR associated deaths	Year	Scope	Source
-	0.7 M*	-	2014	Global	Lord Jim O'Neill
-	1.3 M**	4.9 M	2019	Global	Lancet report
2.8 M	35,000	-	-	USA	CDC AR threat report 2019

*Including HIV, TB, malaria; rise to 10M/year by 2050, if no action taken **Bacterial AMR (TB included)

	AMR's impact by 2050							
Decline in global livestock output	Decline in global exports	Decline in GDP	Decline in global economy	Rise in healthcare expenses	Rise in extreme global poverty	Source		
11 %	1.1-3.8%	1.1-3.8%	-	\$0.33-1.2 trillion	24 million people	World Bank		
-	-	-	100 trillion	-	-	Lord Jim O'Neill		

REAL WORLD CHALLENGES IN AMR QUANTIFICATION

Service delivery

Health workforce

Information

Medical products, vaccines and technology

Financing

Leadership and governance

WHO's Health System Building Blocks

Reliable estimates of the true AMR burden are scarce

Break See you in shortly.

01:00:00

Day 1/5, Session 2: AMR Series: Laboratory methods and definitions

Dr Geetanjali Kapoor

Acting Head and Researcher, One Health Trust (formerly CDDEP)

HOW TO DETECT AMR? HOW TO DEFINE MDR, XDR, AND PDR?

HOW TO DETECT AMR?

Phenotypic (Culture-Based)

Disk diffusion

Broth microdilution, gradient tests, breakpoint tests, agar dilution (bacterial isolates vs series of antimicrobials)

Automated systems (Phoenix, Vitek 2, Microscan, etc)

HOW TO DETECT AMR?

Genotypic (Detection of antibiotic resistance genes)

Microarrays & Hybridization

PCR/ Nucleic Acid Amplification Technology (NAAT)

Next-Generation Sequencing (NGS)- whole/metagenome

Mass Spectrometry-Based Methods (MALDI-TOF MS (Matrix-Assisted Laser Desorption/Ionization Time-of-Flight MS))

Bioinformatics Approach; Biosensors and Nanotechnology

Emerging Technologies-CRISPR (clustered repetitive interspaced short palindromic repeats); Machine Learning and Predictive Analytics

HOW TO DEFINE MDR, XDR, AND PDR?

CDC & ECDC 2011

- MDR: acquired non-susceptibility to at least one agent in three or more antimicrobial categories
- XDR: non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (bacterial isolates remain susceptible to only one or two categories)
- PDR: non-susceptibility to all agents in all antimicrobial categories

	Categ	gory 1	Ca	it 2	Ca	t 3	Cat	X-2	Cat	: X-1	Ca	t X
	Agent 1	Ag 2	Ag 1	Ag 2	Ag 1	Ag 2	Ag 1	Ag 2	Ag 1	Ag 2	Ag 1	Ag 2
MDR	R		R		R							
XDR	R		R		R		R					
PDR	R	R	R	R	R	R	R	R	R	R	R	R

GUIDANCE & DECLARATIONS



World Health Organization

Political Declaration of the High-level Meeting on Antimicrobial Resistance

SURVEILLANCE PLATFORMS

- Global Antimicrobial Resistance and Use Surveillance System (GLASS)
- Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR)
- EARS-Net (European Antimicrobial Resistance Surveillance Network)
- ReLAVRA (Latin American Network for Antimicrobial Resistance Surveillance)
- Industry-funded surveillance platforms

See you tomorrow. 11:00 London, same link.











Day 2/5: AMR Series: Surveillance in Human Health I

Dr Geetanjali Kapoor

Acting Head and Researcher, One Health Trust (formerly CDDEP)

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Day 2

SUBTOPICS

AMR Series: Surveillance in human health I – 1.5 hours

 As part of her lecture series on AMR surveillance best practices, Geetanjali will discuss AMR surveillance in human health, covering stakeholder engagements, mapping laboratory networks, site selection and data transfer agreements.

Discussion, Q&A – 1 hour

AMR SURVEILLANCE | STEPS



AMR SURVEILLANCE | TEAM FORMULATION



- Assemble a **diverse team** with clearly defined roles and responsibilities for each member
- A team leader should be appointed to provide direction, make critical decisions, and maintain focus on project goals
- Open communication is essential for leveraging the **strengths of each member**, fostering collaboration, and ensuring all voices are heard
- Roles and responsibilities should be flexible, adapting as needed to address evolving project demands, challenges, or changing circumstances
- Adaptability ensures the team remains responsive and effective throughout the project lifecycle

AMR SURVEILLANCE | PROBLEM STATEMENT & OBJECTIVES



Problem statement: To clarify the issue's importance and establish why it must be addressed, providing clear direction for the project

Key objectives

- Measurable, actionable targets that align with the problem statement
- Guide allocating resources, time, and funding toward the project's priority areas

Surveillance studies can be based on analysing existing data or designed as prospective studies to gather new information over time

AMR SURVEILLANCE | STAKEHOLDER ENGAGEMENTS



- Ensures that all perspectives are considered
- Builds trust
- Enhance decision-making
- Significantly improves the chances of project success
- Critical in externally funded studies, where local and regional health
 authorities must be informed at every stage
- Kick-off workshops followed by regular in-person and online meetings

AMR SURVEILLANCE | DATA SHARING AGREEMENTS



- Between project team/grantee and institution/government
- Outlines responsibilities, data handling protocols, and security measures to prevent misuse or unauthorised access
- Sharing of data securely and ethically, per relevant legal and regulatory requirements.
- Promotes transparency in data management

AMR SURVEILLANCE | DATA SHARING AGREEMENT TEMPLATE



Date

Parties

Definitions

Terms of Reference Obligations for all stakeholders Storage Data breach and reporting Financial angles Regulation/legislation

Signatories

PROTECTION OF SENSITIVE DATA



GDPR - General Data Protection Regulation

- Protection of personal data
- Applies to EU-based users

Health Insurance Portability and Accountability Act

- Protection of health information (Protected Health Information -PHI)
- Applies to US-based users

Methods of data protection

- Masking (only sensitive data is obscured; as commonly done in finance organizations)
- De Identification (all personally identifiable information [PII] is anonymized; commonly done for research, analysis, and other purposes without the need for patient consent)

PROTECTION OF SENSITIVE DATA

1. TEAM FORMULATION	Masking	De Identification
) ר	John Dawn, SSN: 123-45-6789	John Dawn,
2. PROBLEM STATEMENT & OBJECTIVES	(original)	Date of Birth: January 1, 1980,
-_{}Q}		Address: 123 George Street
3. STAKEHOLDER ENGAGEMENTS		(original)
DATA SHARING AGREEMENTS	Jane Smith, SSN:***	Male,
RE	(altered)	Age Range: 40-45,
5. SITE SELECTION		City: Unspecified
		(altered)
6. DATA MANAGEMENT COLLECTION, CLEANING,	Obscuring only sensitive data with	Removing all direct & indirect identifiers
ANALYSIS	fictitious data	that are personal attributes
7. PRESENTATIONS	Hash, random numbers, pseudonyms	pseudonymization and anonymization
±/₩-	does not provide complete anonymity;	irreversible and provides complete
8. REPORT WRITING	and individual can be identified through	anonymity
	ways	

Break See you in shortly.

01:00:00
SITE SELECTION



Single-centre

Multi-centre

Determine the number of sites/laboratories (as per budget/resources)

Mapping

Sampling strategy- Random/quality-based

ign Questionnaire General - Laboratory name, level of service, affiliations, co-location with pharmacy and clinical units

Quality management systems – personnel, biosafety, sample management, QC, EQAS, accreditation/certification, audits, LIS, inventory management, etc.

Approvals from responsible authorities on final choice

SITE SELECTION



Single-centre

Multi-centre

Determine the number of sites/laboratories (as per budget/resources)

Mapping

Sampling strategy- Random/quality-based

Design Questionnaire General - Laboratory name, level of service, affiliations,

co-location with pharmacy and clinical units

Quality management systems – personnel, biosafety, sample management, QC, EQAS, accreditation/certification, audits, LIS, inventory management, etc.

Approvals from responsible authorities on final choice

See you tomorrow. 10:00 London, same link.











Day 3/5: AMR Series: Surveillance in Human Health II

Dr Geetanjali Kapoor

Acting Head and Researcher, One Health Trust (formerly CDDEP)

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DATA COLLECTION



Framework prior to actual data collection

- Data collection questionnaire
- Glossary/directory of terms
- Training manual



Data collection questionnaire

- Patient level variables demographic clinical, laboratory
- Facility level variables
- Country level factors



- Patient level demographic variables
 - Age
 - Gender
 - Weight
 - Education level
 - Pregnancy status if female patient,
 - Premature birth status if child
 - Childhood vaccination status
 - Adult vaccinations status
- Patient level clinical variables
 - Diagnosis & ICD code
 - Complaint
 - Comorbidity
 - Outcome
 - Infection type- hospital acquired/community acquired,
 - Placement of associated device/catheter, intervention/surgery, antibiotic
 - Admission & discharge dates



- Patient level laboratory variables
 - Specimen type/site
 - Specimen date of collection
 - Culture test name
 - Culture test results
 - Bug-drug combinations of interest
- Patient level pharmacy variables
 - Antimicrobials dispensed
 - Dose
 - Duration



- Facility level variables
 - Ownership/Affiliation
 - Level of care
 - Co-location with lab & pharmacy
 - In-patient and out-patient volume
 - Departments
 - Human resources
 - Formats of patient clinical records- electronic/paper
 - AMS & IPC practices
 - Bed strength
- Country factors
 - Antibiotic consumption
 - Global Health Security index scores on AMR prevention
 - Primary education
 - GDP per capita
 - Physicians density
 - Nurses density
 - Universal health coverage
 - Access to improved drinking water source
 - Access to improved sanitation facilities

TRAINING



- Data collection device and its configuration
- Data collection tool
- Training manual
 - Directory/glossary (Each of the variables is given a code together with choices/entry options)
 - Device use & troubleshooting
- Recruitment of data collectors
- Training of data collectors

DIRECTORY/GLOSSARY



Purpose: to convert raw entries to standardized information

Variable name	Code (abbreviation for variable name)	Code (numeric Id)
Patient identification number	Patient_code	Patient ID
	12345	2ad3x
Gender	GENDER	Gender ID
Female	FEMALE	1
Male	MALE	2
Specimen	Spec_code	Specimen ID
Blood	BI	12
Urine	Ur	11
Joint Fluid	Jf	153
Organism	ORGANISM	ID
Acinetobacter baumannii	aba	21
Staphylococcus aureus	sau	155

WHONET



https://whonet.org/index.html

DATA COLLECTION



- On the day of data collection
 - Letter of introduction
 - Meet focal points
 - Route to be followed for data collection
 - Understanding workflow in the laboratory
 - Data collection
 - Data storage (automatically saved on the device; whenever a network connection is available, it is synced with the server)
 - Supervisory visits to monitor data collection
- Questions to be answered
 - Data collection timelines
 - How many records to be collected (if paper-based data)

DATA REVIEW/CHECK/CLEANING



- Review all entries to establish
 - Data completeness
 - Data accuracy (match the glossary-defined choices for the respective variables; glossary-defined choices can be sourced from WHONET which is in open domain).
 - Any additional entry outside the glossary are flagged to data collector for clarification; may be included if required
 - All date entries in the import file must follow the same format (ddmmyy or dd/mm/yyyy depending on protocol established)
 - Script used to review large scale data

DATA REVIEW/CHECK/CLEANING



- Review AST entries and ensure inclusion of only valid tests for rate estimation
 - Microbiologist guidance required
 - Examples of invalid tests
 - E. coli with vancomycin
 - S. pneumoniae with penicillin disk
 - Enterobacterales with oxacillin
 - Enterococcus with oxacilin
 - S aureus with oxacilin disc

DATA SUMMARIZATION (POST DATA REVIEW)



Summarization of review findings

- Quantum of cultures
 - Total
 - Positive
 - with AST
- Quantum of cultures with complete pathogen identification



AMR rate estimation

- 'Proportion non-susceptible': To what extent is a pathogen resistant to a particular antimicrobial agent/class
- <u>Number of non susceptible isolates</u> X 100 (Cl 95%)
 Number of susceptible & non susceptible isolates)
- All non-susceptible isolates (I+R) are classified as resistant
- Analyse as per resistance interpretation submitted by the laboratories
 - Adjust based on updated breakpoints
 - Present at antimicrobial class

Ref: Clinical and Laboratory Standards Institute. CLSI. Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition. CLSI Document M39-A4.; 2014.



AMR rate estimation

- Eliminate duplicates
 - Include only the first isolate of a species/patient/analysis period, irrespective of body side or AST profile (CLSI M39-A4)
- There is no need to present statistics on every drug tested, especially when you are combining data from different laboratories.
- Analyze for a broad set of "recommended/usual" antibiotics, and try to get those to be complete as possible
- Data are analyzed only when 30 or more isolates were tested against an antibiotics
- Careful state the limitations, then you can present results that potentially might have some relevance.

Clinical and Laboratory Standards Institute. CLSI. Analysis and Presentation of Cumulative Antimicrobial Susceptibility Test Data; Approved Guideline—Fourth Edition. CLSI Document M39-A4.; 2014.

Ref:



AMR rates - Examples

	Laboratory A	Laboratory B
Bug 1 Drug 1	40%	25%
Bug 2 Drug 2	30%	15%
Bug 3 Drug 3	60%	30%
Bug 4 Drug 4	80%	50%





AMR estimates statistics

- Confidence interval
 - Wilson score method (assumes all samples are independent)
 - Wilson cluster-robust (assumes correlations likely exist within and between laboratories serving similar populations

Ref: Kalanxhi E, Osena G, Kapoor G, Klein E. Confidence interval methods for antimicrobial resistance surveillance data. Antimicrobial Resistance & Infection Control. 2021 Jun 9;10(1):91.



Drivers of resistance

Patient level

- Age
- Gender
- Diagnosis
- Comorbidities
- Antimicrobial usage
- Presence of device (catheter, central line, ventilator)
- Origin of infection (hospital or community)

Facility level

- Implementation of infection prevention program
- Implementation of antimicrobial stewardship
- & more



Drivers of resistance

Country level

- Antibiotic consumption
- Global Health Security index scores on AMR prevention
- Primary education
- GDP per capita
- Physicians density
- Nurses density
- Universal health coverage
- Access to improved drinking water source
- Access to improved sanitation facilities
- Access to basic handwashing facilities including soap and water
- Enrolment in Global Antimicrobial Resistance Surveillance System (GLASS)
- & more

See you next week. Mon 9:00 London, same link.











Day 4/5: AMR Series: Surveillance Reports, Challenges, and Mitigation

Dr Geetanjali Kapoor

Acting Head and Researcher, One Health Trust (formerly CDDEP)

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PRESENTATIONS



	Why	Audience	When	How				
S	Why • •	 Why Accountability & Ownership Foster collaborative efforts Cross learn with other groups if multi consortia grant Inform policies Contribute to broader public health efforts 						
	Audie •	ence Funders Healthcare provide	rs					

- PolicymakersResearchers
- Community organisations





Cover Page Executive Summary Overview Institution(s) profile & relevant policies Break each activity and mention methodology/approach & results Challenges Recommendations Limitations References Appendices



Cover Page

- Institution(s)
- Project Name
- Programme Name
- Funder
- Year
- Project Team Name

Executive Summary

Overview

Institution(s) profile & relevant policies Break each activity and mention methodology/approach & results Challenges Recommendations

- Limitations
- References
- Appendices



Cover Page

Executive Summary

- Problem statement/purpose
- Key findings
- Approach
- Actionable insights

Overview

Institution(s) profile & relevant policies Break each activity and mention methodology/approach & results Challenges Recommendations Limitations References Appendices



Cover Page Executive Summary

Overview

- Problem Statement/purpose in detail
- Against the above backdrop, relevance for the report/proposal/study/surveillance
- Objectives and timelines
- Key engagements
- Any ethical dilemmas

Institution(s) profile & relevant policies Break each activity and mention methodology/approach & results Challenges Recommendations Limitations References Appendices



Cover Page Executive Summary Overview

Institution(s) profile & relevant policies

- [Institution Name]; Established in [year]
- Mission
- Key Areas of Expertise
- Key Programs and Initiatives
- Collaborations and Partnerships
- Recent Achievements
- Leadership and Governance
- Location

Break each activity and mention methodology/approach & results Challenges Recommendations Limitations References Appendices



Cover Page Executive Summary Overview Institution(s) profile & relevant policies

Break each activity, tie it to each objective, detailed methodology/approach, results, infographics, special considerations

- Activity 1: Laboratory/Site selection
- Activity 2: Data Collection
- Activity 3: Data Review
- Activity 4: Data Analysis

Challenges Recommendations Limitations References Appendices



Cover Page Executive Summary Overview Institution(s) profile & relevant policies Break each activity and mention methodology/approach & results Challongos

Challenges

- Contributing laboratories vs population
- Routine testing or special cases
- Surveillance standards
- Testing practices
- Access to clinical records and antimicrobial usage
- Lack of integrated AMR surveillance

Recommendations Limitations References Appendices


Cover Page Executive Summary Overview Institution(s) profile & relevant policies Break each activity and mention methodology/approach & results Challenges

Recommendations

- Standardize AMR Surveillance Protocols Globally
- Platforms that allow for real-time exchange of surveillance data
- Expanding access to rapid diagnostic tools
- Capacity-building initiatives
- Promote Antibiotic Stewardship Programs
- Foster Public Awareness
- Multisectoral Engagement
- Incentivize public-private partnerships
- Regular evaluations of AMR surveillance systems
- Funding for research

Limitations References

Appendices



Cover Page Executive Summary Overview Institution(s) profile & relevant policies Break each activity and mention methodology/approach & results Challenges Recommendations

Limitations

- Timeline
- Funding
- Governance related
- Permissions

References Appendices



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Appendices

- Questionnaires- laboratory selection, data collection, any other?
- Directory/Glossary
- Training Manual

See you tomorrow. 10:00 London, same link.











Day 5/5: Conclusion and Open Discussion

Dr Geetanjali Kapoor

Acting Head and Researcher, One Health Trust (formerly CDDEP)

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CONCLUSION

Reliable estimates of the true AMR burden are scarce

Diagnostic Gaps

Lack of Standardized Surveillance

Variability in Data Collection

Underreporting

Overlapping Factors

CONCLUSION

Approach to large scale AMR surveillance



CONCLUSION

Reporting

Cover Page Executive Summary Overview Institution(s) profile & relevant policies Break each activity and mention methodology/approach & results Challenges Recommendations Limitations References Appendices

ACKNOWLEDGEMENT

Hamied Foundation UK-INDIA AMR Fellowship Yusuf and Farida Hamied Foundation The Academy of Medical Sciences Office of the Chief Medical Officer (CMO) for England

Professor Ben Cooper Dr Christiane Dolecek Dr Barney McManigal Isabela Cabrera Lalinde Sophie Patten Nuffield Department of Medicine, University of Oxford

The Global Health Network, University of Oxford

Dr John Stelling

One Health Trust



Please take a moment to fill in the feedback survey for this lecture series.

Your feedback is important in helping us understand to what extent this event has met your learning needs, how events could be improved for future participants and what you feel you have learned. Thank you.



https://app.onlinesurveys.jisc.ac.uk/s/oxford/tghn-webinar-workshop-feedback-survey-v4

Thank you.









