

GARDP, RKI, OXFORD, KENYA MEETING
Friday 11th November 2022

MEETING SUMMARY/MINUTES

Opening and welcome remarks: *Andrew Farlow*, Centre for Tropical Medicine and Global Health, University of Oxford

Chair

- **Andrew Farlow,**
- The Chair introduced a brief framework for the meeting, which was followed by a series of talks by those invited
- Colleagues from Robert Koch, Oxford and Kenya, as well as The GARDP team introduced themselves and gave a brief description of the various projects they are involved in.
- There were calls for more collaboration amongst those present

Attendees:

Name	Organisation/Project	Email
Yann Ferrisse	GARDP Business Development & Partner Engagement Director	
Jennifer Cohn	GARDP Lead, Global Access Strategy Development & Implementation	
Andrew Farlow & Team	Global Health Initiative, Univ of Oxford	
Tim Eckmanns	Head, Division for healthcare-associated infections, surveillance of antimicrobial resistance and consumption/RKI Germany	
Benn Sartorius	Head of modelling of the GRAM Project: University of Oxford and IHME and Global AMR Collaborators	
Christiane Dolecek	Associate professor, Centre for Tropical Medicine and Global Health, University of Oxford and Mahidol-Oxford Tropical Medicine Research Unit, Scientific Lead and Co-PI on the GRAM study	

Andrew Jack	Financial Times, Antibiotic Accountability Tracker	
Sebastian Haller	Senior Epidemiologist, RKI, Germany	
Sam Akech	PI CINAMR, KEMRI/Wellcome Trust Programme, Kenya	
Edna Mutua	Co-Investigator in the CINAMR and HIGH-Q projects, KEMRI/Wellcome Trust Programme, Kenya	
Michuki Maina	Health-Systems Researcher, KEMRI/Wellcome Trust Programme, Kenya	
Hermine Mkrtchyan	Professor of Microbiology, Head of Research, School of Biomedical Sciences, University of West London	
Taniya Sharmeen	Oxford Centre for Global Health Research, Bio-cultural Anthropology, ABACUS II Project	
Katy Thomson	Postdoctoral Research Associate, BARNADS II, Oxford INEOS Institute	
Mahmoud Eltholth	Lecturer in Global Health, Department of Health Studies , Royal Holloway, University of London	
Jennifer Cole	Director of Research for the Department of Health Studies , Royal Holloway, Univ of London	
Jacob McKnight	Post-doctoral researcher, Centre for Tropical Medicine & Global Health, Co-PI CINAMR	
Ben Cooper	Professor of Epidemiology, MORU, Tropical Health Network	
Koen Pouwels	Senior Researcher, Oxford Population Health- Health Economics Research Centre (HERC)	

Tim Eckmanns & Sebastian Haller: New Collaborating Centre Launched during the [World Health Summit 2022](#), in Berlin

- A new World Health Organization Collaborating Centre for Antimicrobial Resistance, Consumption and Health Care-Associated Infections which was started half a year ago launched during the World Health Summit in September.
- The Launch report can be found [here](#)
- This is part of a network of over [25 collaborating centres \(CC\)](#) in 17 countries (most are in the Global North) including South Africa, coordinated by the WHO with support from the Robert Koch Institute (RKI)

WHO AMR Surveillance and Quality Assessment Collaborating Centres Network

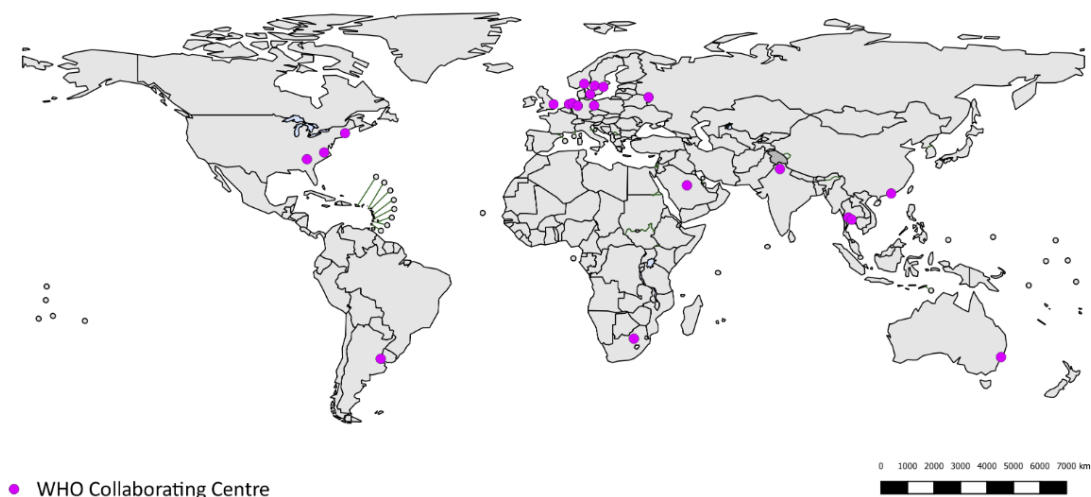


Fig 1: WHO Collaborating Centres (CC). Source: <https://www.who.int/initiatives/glass/network>

- The networks aim to support LMICS in capacity building for AMR surveillance
- The main goal of the new network is to support Surveillance (and GLASS), which is key in tackling AMR.
- Going from the findings of the recent GRAM study, a major challenge, especially in the Global South is the lack of (lab) data, which is of utmost importance for AMR surveillance
- The new CC is therefore working to support lab building capacity, infrastructure for diagnostic stewardship and most importantly, Human resources- training people
- Discussions centred around how key Surveillance and hence quality data is
- On the issue of whether this new centre will take on a One Health Approach- for now experts working at the centre are focused on Surveillance, AMR from the Human/Hospital associated infections angle, where their expertise lies
- However, they are aware of the need for a One Health Approach

- There are lessons to learn from the global climate crises- the divide between the global north and south in terms of who is responsible for the most antibiotic consumption and who the burden of AMR falls most on
- **Need for wider implementation of surveillance:** Hermine Mkrtchyan at this point asked whether the centre is going to focus on African countries. The centre has partner countries to engage with next year. These countries are:
 - i.* Namibia
 - ii.* Ivory Coast
 - iii.* Nigeria
 - iv.* West Balkan Countries, mainly Montenegro
 - v.* Iran- already being engaged
- **New poll mechanism for Reserve Antibiotics. Possible framework for GARDP use?:** a recently established mechanism in which hospitals would have to participate in the national surveillance to have access to new reserve antibiotics coming into the German market

Jennifer Cole- Antibiotic Residues in Hospital Wastewater

- Previous work in India, (see previous AMR strategy group meeting minutes and reports)
- However, due to funding, the project is now moving to Kenya
- Research looked at antibiotic residues in hospital waste water that goes into the environment, particularly waterbodies people fish from
- And whether the same strain of antibiotic resistant bacteria turned up both in humans and in livestock and the environment. Findings concluded these were the same strains

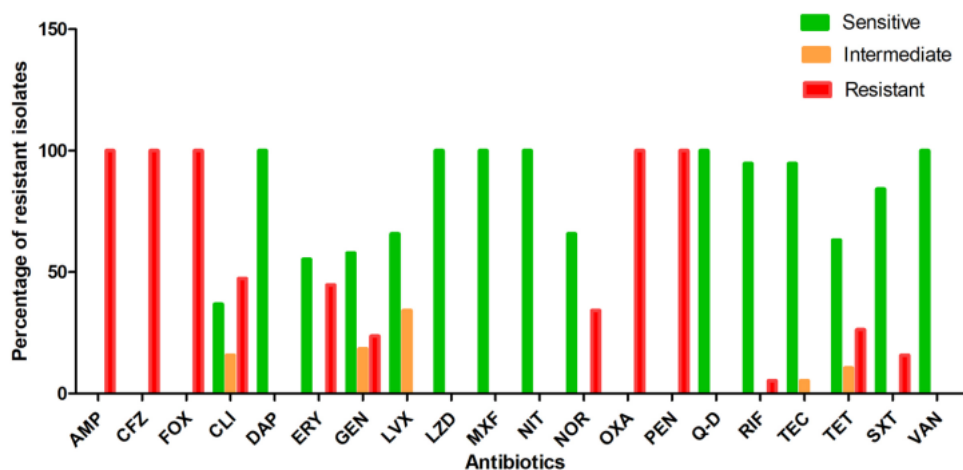


Fig 2: Percentage of isolates which are resistant, intermediate-resistant and sensitive to 13 classes of antibiotics. Source: Muneeb et al 2021

- Also, the cycle- was a particular bacterial strain in humans first, then hospital wastewater, then fish and then back into humans? i.e. the Direction of travel
- On whether the new WHO collaborating centre is looking into waste water and similar work like Jennifer Cole, Tim Eckman alluded to the fact that Germany has just begun such research with COVID, and AMR will be the next step
- An important work by a colleague in Denmark was sighted. Rene Hendrikson et al's research paper titled '[Global monitoring of antimicrobial resistance based on metagenomics analyses of urban sewage](#)'
- Rene Hendriksen is also the deputy of [WHO Collaborating Centre for Antimicrobial Resistance among foodborne pathogens in Denmark](#)- The National Food Institute
- *Links to Jennifer's work on AMR, Fish in India:*
 - <https://pure.royalholloway.ac.uk/en/publications/prevalence-of-virulent-and-biofilm-forming-st88-iv-t2526-methicil>
 - <https://pure.royalholloway.ac.uk/en/publications/virulence-and-intermediate-resistance-to-highend-antibiotic-teico>
 - <https://pure.royalholloway.ac.uk/en/publications/fish-borne-methicillin-resistant-staphylococcus-haemolyticus-carr>
 - <https://pure.royalholloway.ac.uk/en/publications/molecular-assessment-of-antimicrobial-resistance-and-virulence-in>

KEMRI/Wellcome Trust, Kenya- Sam Akech, Edna Mutua, Michuki Maina & Jacob McKnight

Microbiology Capacity in Kenya

- Various activities/projects have been set up to build Microbiology capacity in Kenya. Some by Fleming Fund, SAID with relative success
- Nevertheless, what is lacking is Active Surveillance- surveillance that's being carried out is isolated, leading to Microbiology data that is not robust
- Jacob pointed to the lack of demand for microbiology (blood culture) in settings such as Kenya, rather than just a lack of the service itself. This stems from the fact that blood culture is expensive, takes several days and a times results come back as no growth. Whereas, blood counts are inexpensive, fast and clinicians tend to make most decisions based off of this and Malaria tests.
- [Ombelet et al 2019](#) outline the challenges facing uptake of blood culture in LMICS and posit solutions, including the 'tropicalization of blood culture bottles'

Point Prevalence of antibiotic use & Guidelines

- Firstly, a point prevalence survey in 14 public hospitals was recently conducted to look at how antibiotics are used in inpatient settings in Kenya.
- The objectives were 'to examine prescription patterns and explore to what extent guidelines are available and how they might influence treatment appropriateness among hospitalised patients in Kenyan hospitals
- Guidelines, be it for microbiology testing or antibiotic treatment are a useful tool to change behaviour and provide universal results.

- Machuki & Jacob et al have published the research article on this [here](#) .The findings include ‘ Physical availability of treatment guidelines increased the odds of receiving appropriate treatment Odds Ratio 6.44[95% CI 4.81–8.64]’

[CINAMR](#)

- A project with 12 hospitals that are part of CIN (Clinical Information Network) that focuses on community acquired infections

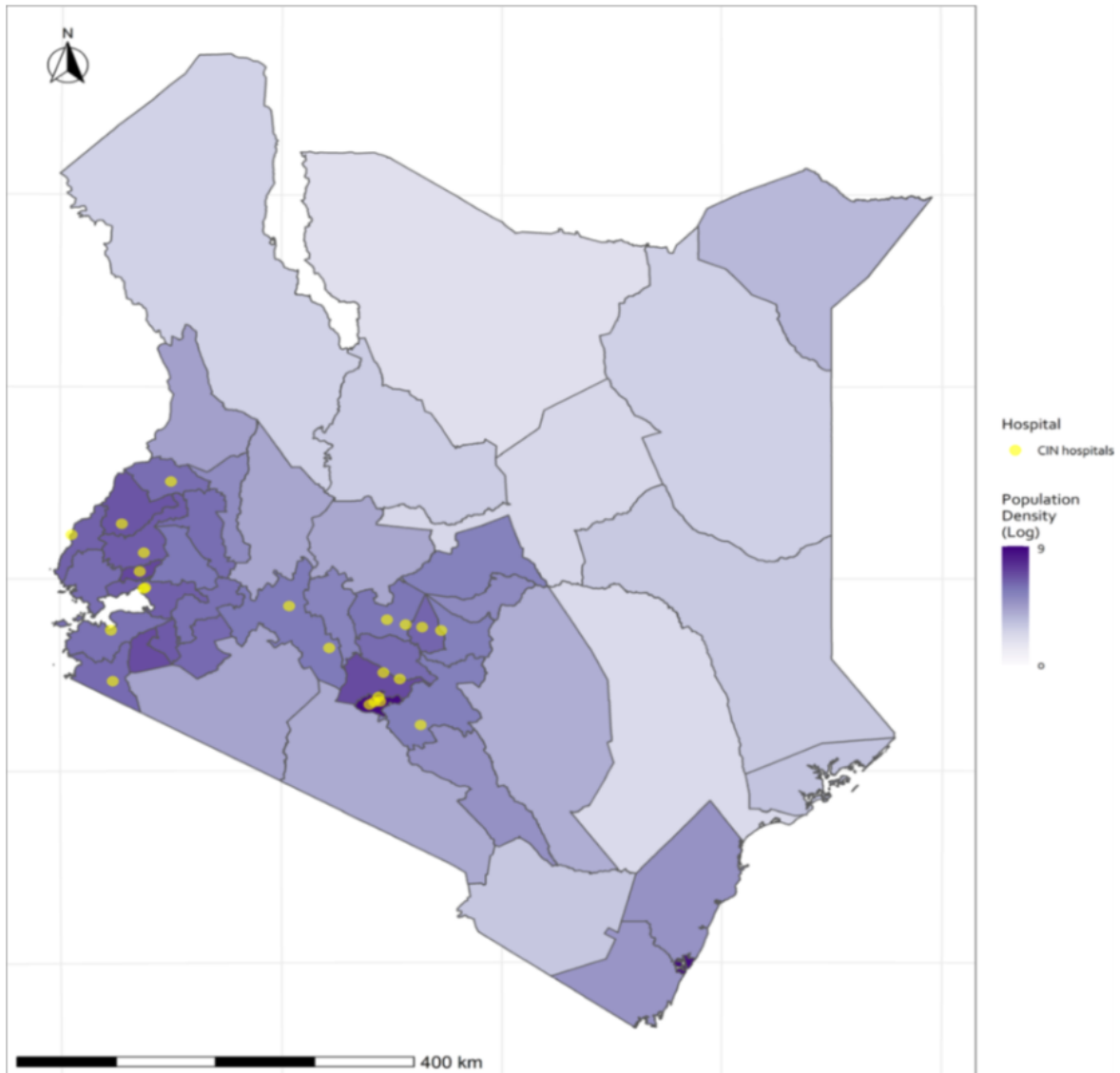


Fig 3: The CIN Hospitals in Kenya: Located in the following counties Bungoma, Busia, Embu, Kakamega, Kiambu, Kirinyaga, Kisumu, Machakos, Nairobi, Nakuru, Nyeri & Trans Nzoia. Source: <https://cin.kemri-wellcome.org/about-us/>

- ‘Implementation will produce AMR surveillance data from CIN hospitals, but also demonstrate the feasibility of the ‘ Hub-and-Spoke Approach’ for other settings, build capacity for uptake of microbiology data in Kenyan hospitals and describe the impact of these data in clinical practice’
- ‘CINAMR will also feed into other initiatives such as ACORN network in Southeast Asia, WHO’s Global Antimicrobial Resistance Surveillance System (GLASS), and the Global Research on Antimicrobial Resistance (GRAM) Study’

- A social science component will look at whether the Hub & Spoke method is sustainable, other uses of the method i.e. periodic surveillance to track AMR evolution, environmental sampling within hospitals
 - There is capacity to do in-country Genome sequencing at the Kemri-Wellcome trust program, however, there is a need for funding to continue supporting this and for personnel that can perform Bioinformatic Analysis
- IPC in Kenyan Hospitals & the role of Leadership*
- It is imperative to understand IPC infrastructure in public and private hospitals
 - *Research carried out by Machuki et al used the WHO WASH Approach*
 - They developed a survey tool and scoring approach (WASH-FAST) modified from the [WHO 'WASH-FIT'](#) to assess WASH across 4 domains in 14 public hospitals in Kenya, including specific assessments of individual wards and 65 indicators

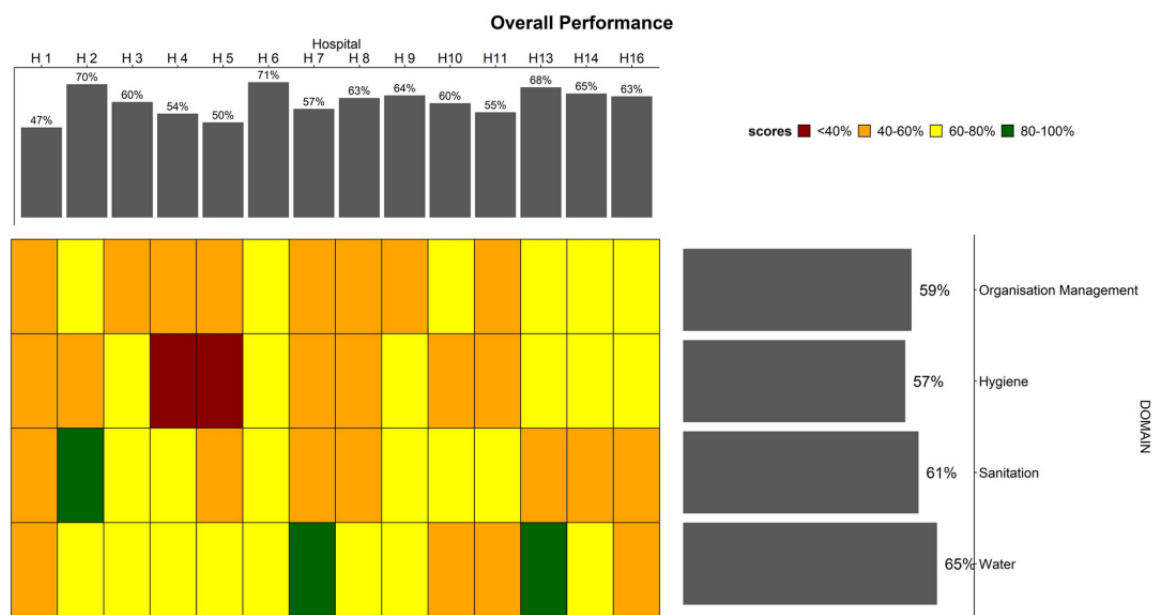


Fig 4: Overall WASH performance. The overall WASH facility performance based on all 65 indicators in four domains is shown by the upper vertical bars. The right horizontal bars summarise the performance of each domain across 14 hospitals. The tiles in the central grid are coloured according to the performance classification of each domain in each hospital, as shown in the colour legend. Source: Maina et al 2019

- The study showed serious deficiencies in water- broken pipes and seals, lack of functional hand washing stations in wards
- The role of leadership was a salient factor. Over and above infrastructure, the key team driver was a passionate team leader that prioritized WASH
- This study was done prior to the pandemic, hospitals took feedback from the research findings, therefore, there probably would be more availability of certain resources post-pandemic

Similar work in Thailand on IPC

- Ben and colleagues have conducted a similar study-step-wise trial in a resource limited hospital in Thailand

- There's was also limited hand washing sinks, although alcohol-based hand rubs were available
- The biggest limitation noted was staff did not have to follow the WHO multimodal intervention framework. This is because it is time consuming. E.g. part of the hand hygiene strategy is direct observation. This is time that neither IPC personnel nor ward staff have

The One Health Approach & Socio-economic Drivers of AMR- Mahmoud Elthouth

- Understanding the socio-economic drivers and impacts of AMR is key
- From this, better suited interventions that are grounded in One Health could pave the way for tighter AMR control
- <https://www.sciencedirect.com/science/article/pii/S0044848621003975>
- <https://www.sciencedirect.com/science/article/pii/S0048969719327056>
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Jennifer Cohn & Yann Ferrisse- SECURE/GARDP



Fig 5: Key Operational SECURE Activities

- SECURE is GARDP's access portfolio
- Looking at human health while recognizing the intersection of human, animal and environmental health

- Currently focusing on increasing access to Cefiderocol as a pathfinder to introduce novel antibiotics into LMICS in a rapid manner while ensuring appropriate introduction and uptake (Stewardship)
- This will then be used as a case-study on how to improve access to new, reserve antibiotics in regions with higher burden of infections
- SECURE is also trying to:
 - i. analyse the Product-to-Patient pathway
 - ii. Barriers & Opportunities in patents, licensing, supply, quality assurance (WHO, regulatory reliance, harmonisation pathways), manufacture, environmental concerns and regulation
 - iii. Uptake: **uptake pathways available, market intelligence available**, linking **work to local antibiogram guidelines**, harmonization of guidelines especially for reserve antibiotics, building more market power for buyers, use existing procurements or build more pools, esp. reserve antibiotics with associated issues: fragmented demand, high cost and supply issues. Extend to other higher volume antibiotics under supply risk
 - iv. See how the above can be extended to antibiotics that are classified as Watch or Reserve (fig 6)
 - v. Financial or non-financial Incentives for appropriate stewardship

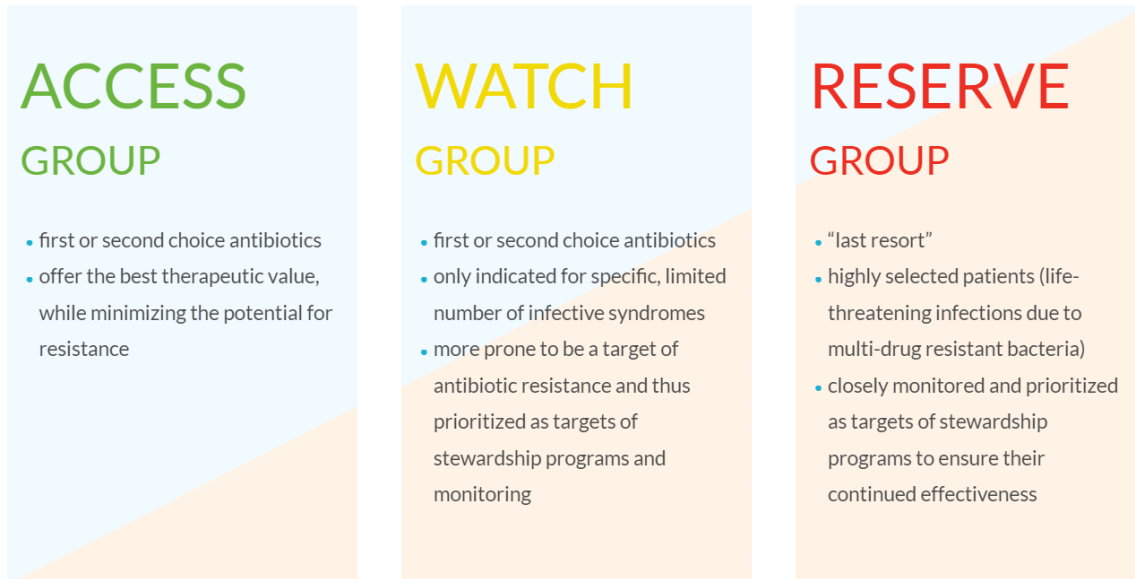


Fig 6: WHO AWaRe classification of antibiotics. Source: <https://aware.essentialmeds.org/groups>

Projects by Koen Pouwel

- There are major gaps in our understanding what kind of antibiotics are used in what volume and for what conditions in many countries- there's also a lot of retrospective data with several limitations
- Koen and Ben's research is a global point prevalence survey for primary care. By employing the WHO AWARE Guidance, the research seeks to understand what conditions patients are consulting for, what antibiotics are prescribed, including duration of antibiotic use
- In particular, research focuses on statistical power: how to steer surveillance and how much to invest, how many sites and how often, patient sample sizes etc. Study a few years back in the UK: can we benchmark different countries/sites against each other for good prescription practice
- Another area of focus: How to carry out Surveillance (how frequently to sample, number of sites, sample size in each site) in order to have precise estimates to correctly inform policy makers, policy decisions. **This is underpinned by how economically justifiable these methods will be**

INEOS Institute- Katy Thompson

- Specialising in neonatal sepsis in LMICS & antibiotic usage in neonates. This includes how cost and availability could impact antibiotic usage, AMR prevalence
- Other INEOS Projects: Impact of flies of Hospital acquired infections, Adult sepsis & its impact on Antibiotic resistance, **development of new antibiotics for human and animal health**
- **Possible Future collaboration with GARDP:** [BERNADS study](#) is looking at efficacy of commonly used antibiotics. Might be helpful to have conversations when data from the study has been analysed; if the study finds more effective antibiotics, how GARDP could help in improving access



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BARNARDS

Burden of antibiotic resistance in neonates from developing societies

Neonatal sepsis is one of the leading causes of infant mortality, particularly in LMICs, and is commonly linked to drug resistance. However, the burden and mechanisms of AMR linked to neonatal sepsis remain poorly explored, particularly in rural areas where healthcare is severely restricted.

The BARNARDS study was one of the first studies to blend clinical and molecular epidemiology from LMICs to characterize neonatal Gram-negative infections and their AMR profiles, and link this to clinical outcomes and risk factors (including social deprivation, access to clean water, sanitation and hygiene conditions, and antibiotic use).



The BARNARDS study

Fig 7: The BARNARDS Study, INEOS

The GRAM Study- Christiane Dolecek & Benn Sartorius

- Phase II of the study has begun
- This involves a framework to generate sustainable estimates of associated/attribution AMR burden globally for priority bacterial antimicrobial combinations; a component on the impact of substandard/falsified (SF) antimicrobials on AMR in collaboration with Paul Newton, IDDO; incorporating environmental and animal data in future estimates based on collaborations with other groups; importantly; a capacity building component to improve the quality of data especially in sub-Saharan Africa (SSA)
- WASH: a very important component in AMR. Currently there's a project with Oxford-Berlin Collaboration, involving Friederike Mehler (see AMR strategy group meeting report). Perhaps GARDP could incorporate WASH in improving access to antibiotics, and look at the essential medicines list

Modelling- Ben Cooper

- Modelling studies in primary care and hospitals
- Persisting challenge is the lack of granular data
- There is need for consumption data that is linked to up with microbiology data which in turn is linked to patient's outcome data

Taniya Sharmeen- University of Oxford

- Qualitative arm of the [ABACUS II](#) study with Proochista Ariana, Paul Newton (proportion of substandard & falsified in six countries Mozambique, Bangladesh, Vietnam, Ghana, South Africa & Thailand)

Andrew- Areas to explore/of interest

- Consumption data
- Patterns of potential demand for products because we're setting out to analyse the situation that companies face if they're trying to register products in LMICs.
- INEOS Oxford One Health Approach to AMR
- Although a lot of research is being carried out on AMR, there is a disconnect with the implementation side of things. With the growing body of data and activity, it is imperative to rope in health systems, One Health, Climate, Social policy and Economics into it all
- The interesting thing for us to study and as an economist is to look at what is the pattern of incentives and how are you influencing that or changing it sometimes distorting it sometimes improving? It? How do you tweak the incentives in a good direction in a second best world?

Discussions (chats) centred around the following themes

- Jenny Cole alluded to the **need for standardised data collection for surveillance and a central database**. It could start by linking networks that were present at the meeting. Hermine concurred on how crucial this point is, especially having surveillance data from low resource settings that matches high resource settings. Additionally, the salient point of travel- transfer of AMR from country to country
- Epidemiology & Measuring Outcomes: There's need to strengthen measuring AMR outcomes. Without this, data from studies (i.e. association studies, One health perspective) may be misleading. Modelling is not the silver bullet!
- The importance of One Health Approach
- Veterinary Support to rural Communities: Remote diagnosis, connecting farmers to vets, strengthening behavioural frameworks in One Health
- Ensuring quality lab results in low resource settings is a challenge: setting up labs, maintaining such facilities, collaboration with other centres. There needs to be support for labs to reduce the cost of blood culture bottles, improve knowledge on the correct use and also come up with fast and simple diagnostics
- **GARDP & use of local antibiograms-** proposes to use local antibiogram in their implementation activities: However, Challenges to this noted by Sam include lack of use of microbiology. In response, GARDP is in initial discussions with [FIND](#) which is supporting higher(tertiary) level hospitals in improving their antibiograms as well as devising ways to support and train clinicians on how to effectively use antibiograms. Additionally, initial landscaping done by GARDP has shown that there are antibiograms in Tertiary hospitals only. Therefore, a priority would be how to develop antibiograms in district hospitals, ensuring clinicians have access to usable data and subsequently use this data in decision making.
- **On the point above, see [MSF's work on antibiogram](#) in resource constrained/conflict settings. A detailed description has been provided in the AMR strategy meeting report for 26th January**

Diagnosis aid to treat patients with the most appropriate antibiotics

Antibiogo is a mobile app that supports non-expert laboratory technicians in low resource settings in measuring and interpreting Antibiotic Susceptibility Tests (AST), to help clinicians prescribe accurate antibiotics.

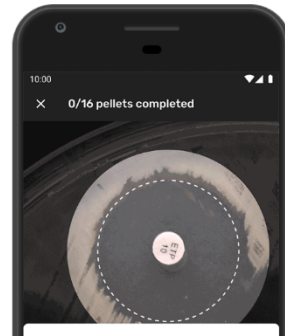


Fig 8: MSF's Antibiogo

- Noteworthy: **Peter Mugo is currently working on Pharmaceutical Procurement Models in addressing AMR in Kenya.** This is in collaboration with KEMRI & Centre for Global Development in Europe (see meeting minutes of Oxford/KEMRI for more details of the project).
- The importance of policy and adherence to guidelines
- Need for spreadsheet with the different teams present and what they are working-useful for future collaborations