# Big data starts small: refocused global AMR surveillance

#### **Paul Turner**

Clinical Microbiologist Cambodia Oxford Medical Research Unit University of Oxford

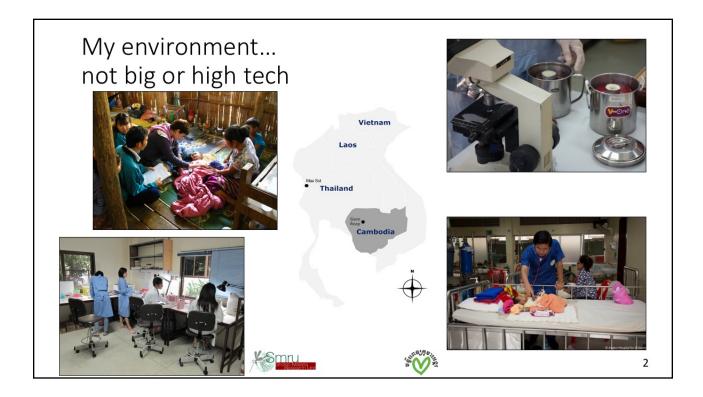
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## AMR surveillance takes all sorts...









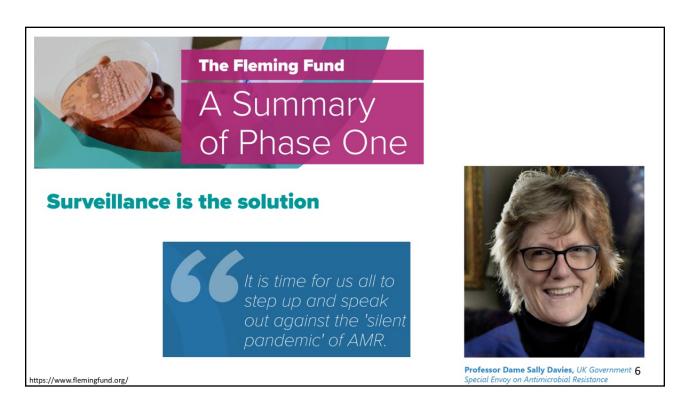


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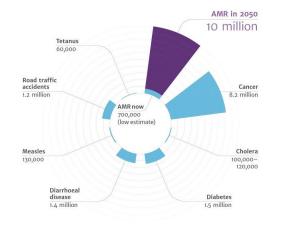
- To estimate burden of disease
- To characterise trends in space and time
- To serve as benchmark to measure the impact of interventions
- To provide local evidence for empiric treatment guidelines and clinical decision making





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### How much AMR is there and what impact does it have?





ESSA

### Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050?

Marlieke E. A. de Kraker<sup>1</sup>\*, Andrew J. Stewardson<sup>2</sup>, Stephan Harbarth<sup>1</sup>

- 1 Infection Control Program, Geneva University Hospitals and Faculty of Medicine, Geneva, Switzerland, 2 Infectious Diseases Department, Austin Health, Heidelberg, Australia
- Current global estimates of the burden of AMR are not very informative; we need
  detailed, reliable data to be able to improve AMR control measures, preferably based or
  comprehensive, population-based surveillance data from low-, middle-, and highincome countries.

  PLoS Med. 2016;13(11):e1002184

O'Neill report (2016)

### Improving the estimation of the global burden of antimicrobial resistant infections



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Direk Limmathurotsakul, Susanna Dunachie, Keiji Fukuda, Nicholas A Feasey, Iruka N Okeke, Alison H Holmes, Catrin E Moore, Christiane Dolecek, H Roqier van Doorn, Nandini Shetty, Alan D Lopez, Sharon J Peacock, Surveillance and Epidemiology of Drug Resistant Infections Consortium (SEDRIC)

Panel: Key actions to improve the estimation of the global burden of AMR infections

#### Strengthen health systems

- Increase country capability and capacity to:
  - Reliably detect the global priority list of AMR bacteria reported by WHO
  - Document clinical outcomes and link to laboratory data

8 Lancet Infect Dis. 2019;19(11):e392-e8

### Is there any good data?

- Recent review of 286 studies
- Mostly:
  - · High income countries
  - Retrospective
  - Single centre
  - Methodologically sub-optimal
- Conclusion:
  - Need better studies / data urgently
  - Policy makers are unable to act until burden is clear

Clinical Microbiology and Infection

Journal homepage: www.clinicalmicrobiologyandinfection.com

Systematic review

Methodological quality of studies evaluating the burden of drugresistant infections in humans due to the WHO Global Antimicrobial Resistance Surveillance System target bacteria

Maria Diletta Pezzani 1-, Barbara Tornimbene 2, Carmenn Pessoa-Silva 2, Marileke de Kraker 3, Sebastiano Rizzardo 1, Nicola Duccio Salerno 1, Stephan Harbarth 3, Evelina Tacconelli 1-, 4

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Clin Microbiol Infect. 2021. 10.1016/j.cmi.2021.01.004



JAC Antimicrob Resist doi:10.1093/jacamr/dlaa130 JAC-Antimicrobial Resistance

Mortality attributable to third-generation cephalosporin resistance in Gram-negative bloodstream infections in African hospitals:

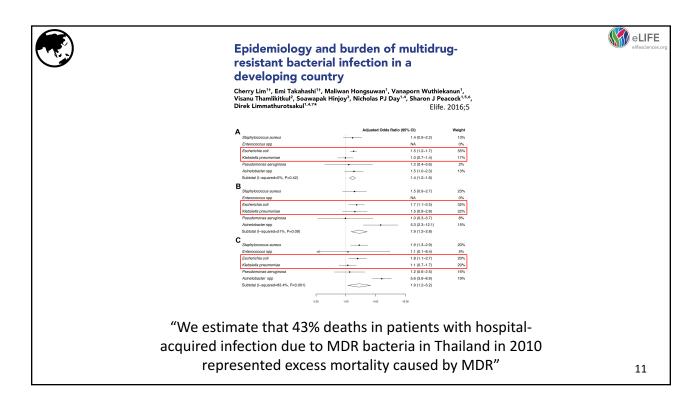
a multi-site retrospective study

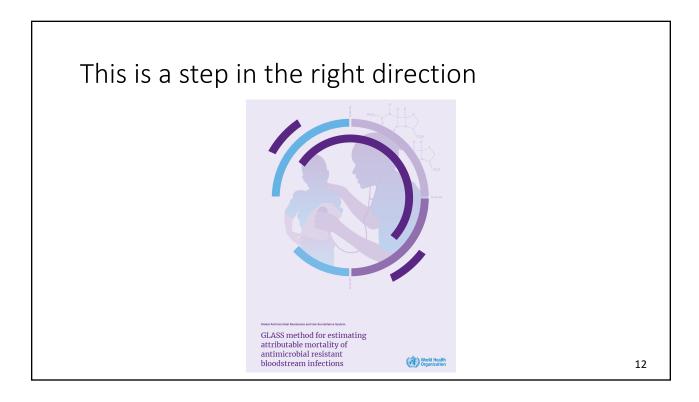
Angela Dramowski³, Gerald Ongʻayo², Andrea M. Rehman ⑥³, Andrew Whitelaw⁴, Appiah-Korang Labi⁵, Noah Obeng-Nkrumah°, Awa Ndir², Marcelyn T. Magwenziª, Kenneth Onyedibe², Martin Wolkewitz¹o, Marlieke E. A. de Kraker ⑥ ¹¹, J. Anthony G. Scatt²³a and Alexander M. Aiken ⑥ ³\* on behalf of the MBIRA study collaborators†

 $\textbf{Table 3.} \ \, \textbf{Impact of third-generation cephalosporin resistance on in-hospital mortality, discharge and length of stay in \textit{E. coli} and \textit{K. pneumoniae} \ \, \textbf{BSI} \ \, \textbf{BSII} \ \, \textbf{BSI} \ \, \textbf{BSII} \ \, \textbf{BS$ 

Comparison	HR (95% CI)			
	Cox model (death)	Cox model (discharge alive)	Fine + Gray model (death)	Excess LOS, days (95% CI)
R-E. coli versus matched controls	2.82 (2.10-3.79)	0.51 (0.44-0.59)	4.10 (3.06-5.48)	1.9 (-1.4 to 5.1)
S-E. coli versus matched controls	2.73 (2.29-3.24)	0.54 (0.50-0.58)	3.81 (3.21-4.51)	4.5 (3.1-5.8)
R-E. coli versus S-E. coli <sup>a</sup>	1.03 (0.73-1.46)	0.94 (0.79-1.11)	1.08 (0.77-1.51)	0.80 (0.59-1.09)
R-K. pneumoniae versus matched controls	2.89 (2.38-3.50)	0.47 (0.43-0.51)	4.55 (3.77-5.49)	6.2 (4.5-7.8)
S-K. pneumoniae versus matched controls	2.61 (2.03-3.37)	0.51 (0.46-0.57)	3.99 (3.11-5.12)	6.0 (3.9-8.2)
R-K. pneumoniae versus S-K. pneumoniae <sup>a</sup>	1.10 (0.80-1.52)	0.92 (0.80-1.06)	1.14 (0.83-1.55)	1.01 (0.84-1.21)

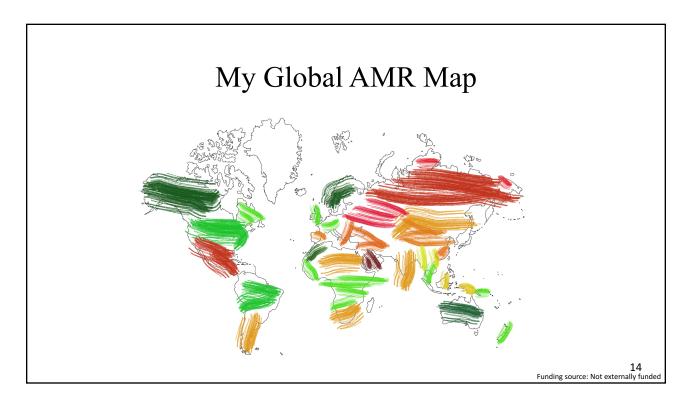
"...there did not appear to be an impact of 3GC-resistance on mortality in *E. coli* or *K. pneumoniae* BSI in African hospitals, as compared with susceptible BSI with equivalent species"



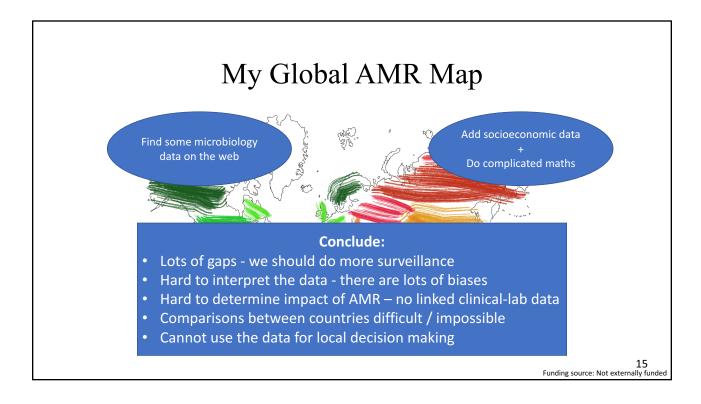


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### Can big data save the day?



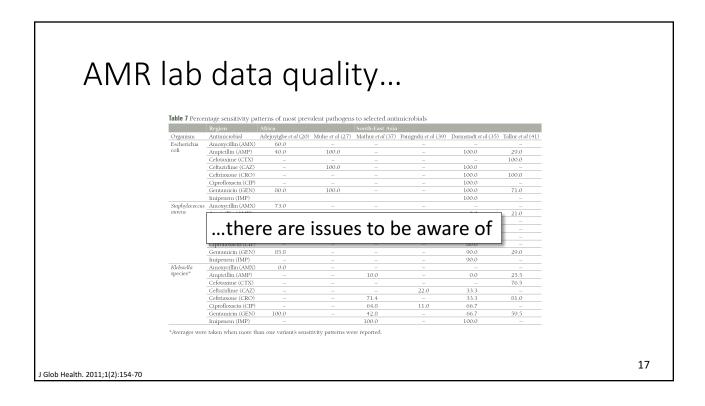
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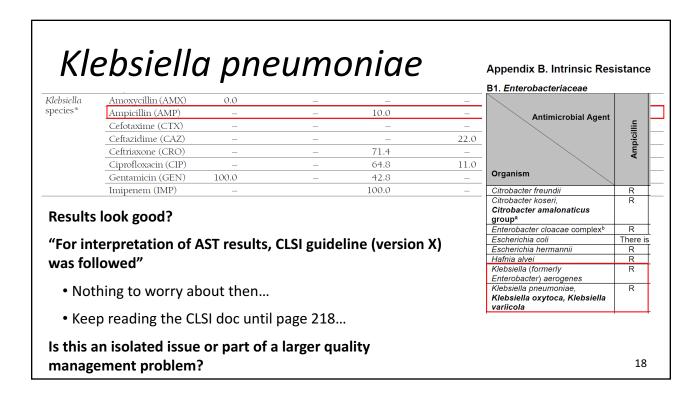


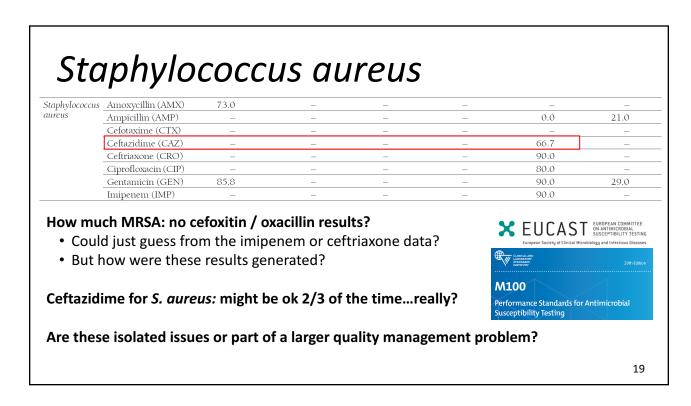
### Things to ponder whilst looking at an AMR map

- What does country level resistance actually mean?
- · Community acquired versus hospital acquired infections
  - Mash them together or keep separate?
- · Sites of infection
  - Adults vs Children vs Neonates
  - Are bugs in urine the same as those in blood cultures?
- AMR data issues
  - Data quality more coming on this
  - Changes in breakpoints over time
    - Fluoroquinolones and Enterobacterales
    - Penicillin and Streptococcus pneumoniae
  - Equivalence of breakpoints
    - CLSI vs EUCAST
    - What did they do with "I"?

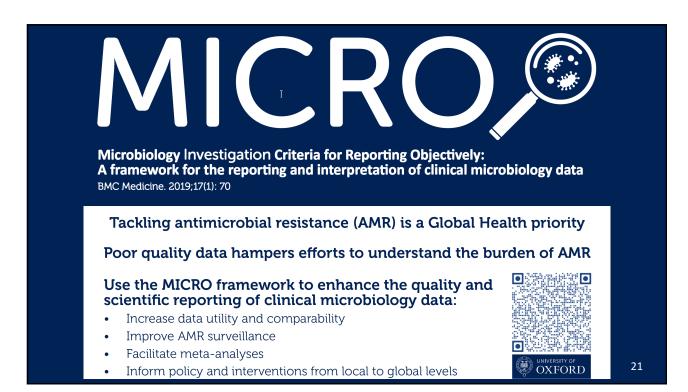






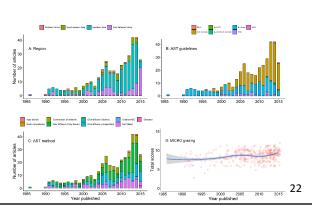






### MICRO applied at scale

- Antimicrobial resistance patterns in bacteria causing febrile illness in Africa, South Asia and Southeast Asia: A systematic review of published aetiological studies from 1980-2015
  - 371 articles from 39 countries
  - · Core MICRO checklist items scored
    - No study scored 13/13
    - Only 52% reported full information for their AST method



Roberts T et al. Submitted

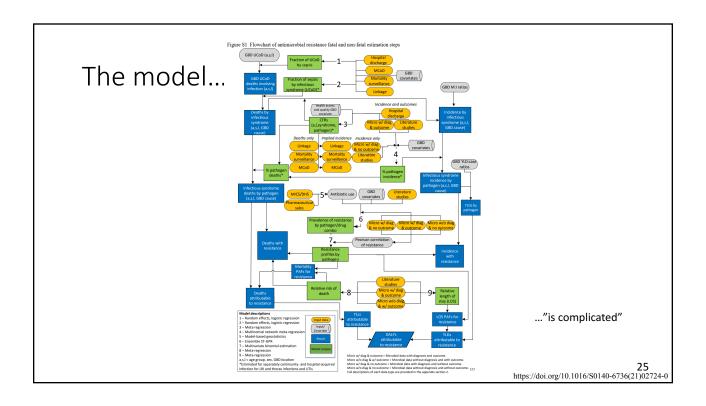


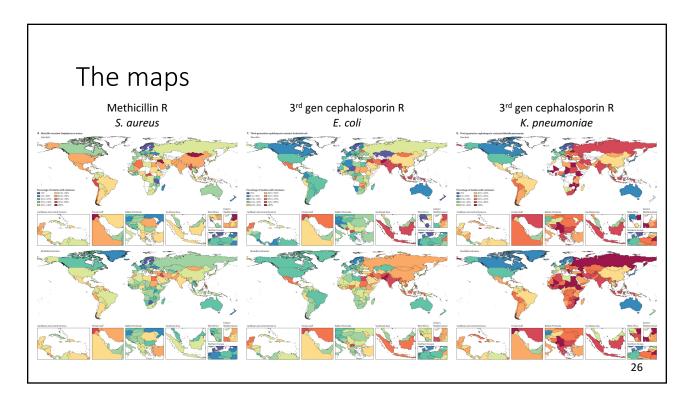
Lancet. 2022: doi.org/10.1016/S0140-6736(21)02724-0

#### The data sources

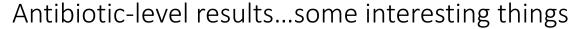
- Could be best summarised as a little data went a long way for many locations
  - Impressive number of bacterial isolates / outcome data overall though
- Need to review all 130 pages of supplementary material to get a complete understanding of how it went down...bring your own magnifying glass:

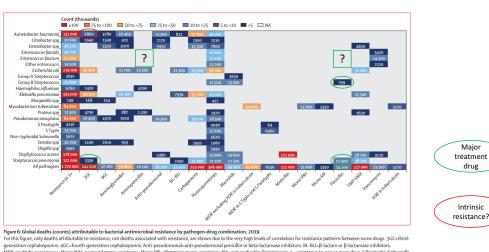
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generation cephalosporins. 4GC=fourth-generation cephalosporins. Anti-pseudomonal=ant MDR=multidrug resistance. Mono INH=isoniazid mono-resistance. Mono RIF=rifampicin mo serotype Paratyphi. S Typhi=S enterica serotype Typhi. TMP-SMX=trimethoprim-sulfamethoxazole. XDR=extensive drug resista

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#### Limitations

#### Not much data from LMICs

This study has several limitations, the most important being the sparsity of data from many LMICs on the distribution of pathogens by infectious syndrome, the prevalence of resistance for key pathogen-drug combinations, and the number of deaths involving infection; and the severe scarcity of data linking laboratory results to outcomes such as death.

CAI versus HAI - could not split out In future iterations of the project, we hope to improve on the identification of community-acquired and hospitalacquired infections.

#### AMR data not standardised

Additionally, no universal laboratory standard exists to demarcate resistance versus susceptibility, and we often had to defer to laboratory interpretation to classify the isolates in our data, resulting in heterogeneous classification. Whenever possible, we classified resistance using the most recent CLSI guidelines based on the minimum inhibitory concentrations provided in the data; however, CLSI breakpoints have changed over time, and many datasets did not provide sufficient detail to allow for retrospective reanalysis of the data.67

#### Some of the lab data may not have been great quality

There are many well described barriers to good-quality clinical bacteriology in LMICs, and proper quality assurance and quality-control measures are crucial for quality care and accurate laboratory-based surveillance.66



### Dame Sally's take

The study also demonstrates data disparities and the lack of infrastructure and capacity for surveillance that we need to detect and respond to pandemics.



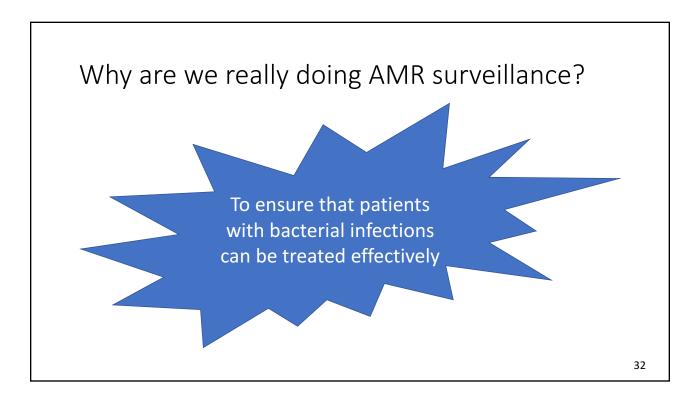
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https://www.flemingfund.org/

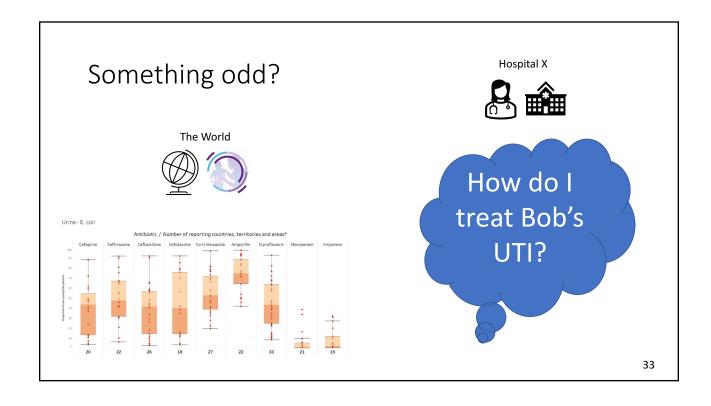
#### What does GRAM leave us with?

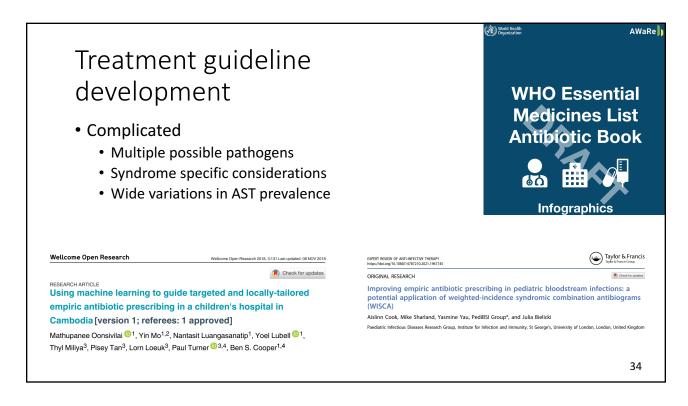
- A better sense of the magnitude of the problem and can use this to encourage urgent high-level action
  - Prioritise antimicrobial drug development
  - Invest in better diagnostics
  - Work up and test interventions
- A need to fill in the massive national and local data gaps





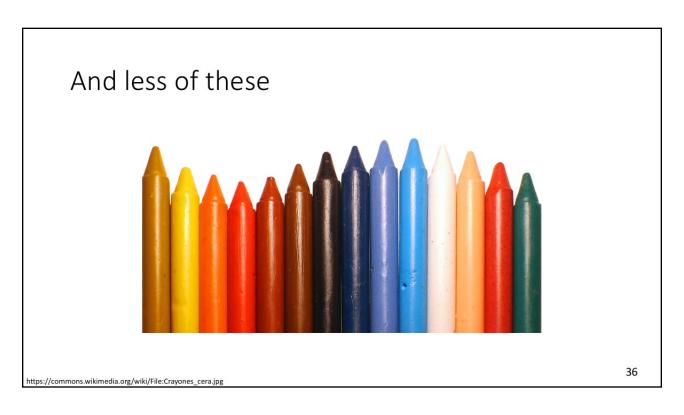
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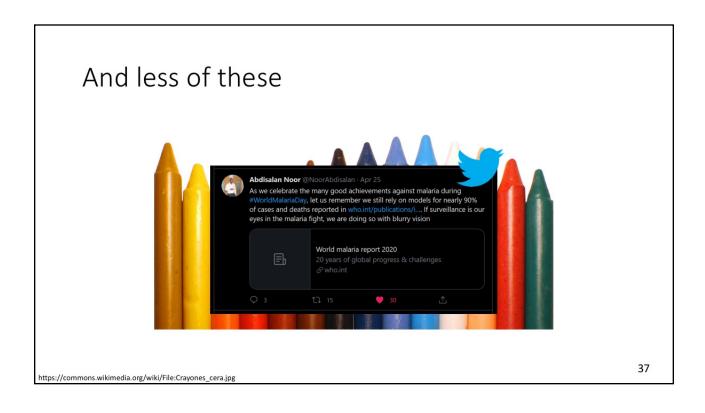


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### Better local clinical surveillance (in LMICs)

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#### What tools are needed

- Money
- · Good microbiology
  - · Several excellent capacity building initiatives on-going
  - · Important to connect labs to clinical services
- · Human resources
  - Clinical staff require support to use microbiology effectively
  - In the absence of fully electronic patient, pharmacy, and lab information systems surveillance takes time and requires effort
- · Case definitions
  - That are simple and do not require serial bloods / radiology

Lancet Infect Dis. 2018;18(8):e248-e58

#### What tools are needed

#### 3.3 Pneumonia (PN1-PN5)

Two or more serial chest X-rays or CT-scans with a suggestive image of pneumonia for patients with underlying cardiac or pulmonary disease. In patients without underlying cardiac or pulmonary disease, one definitive chest X-ray or CT-scan is sufficient.

And at least one of the following:

- fever > 38 °C with no other cause
- leukopenia (< 4 000 WBC/mm³) or leucocytosis (≥ 12 000 WBC/mm³).

and

at least one of the following (or at least two, if clinical pneumonia only = PN4 and PN5):

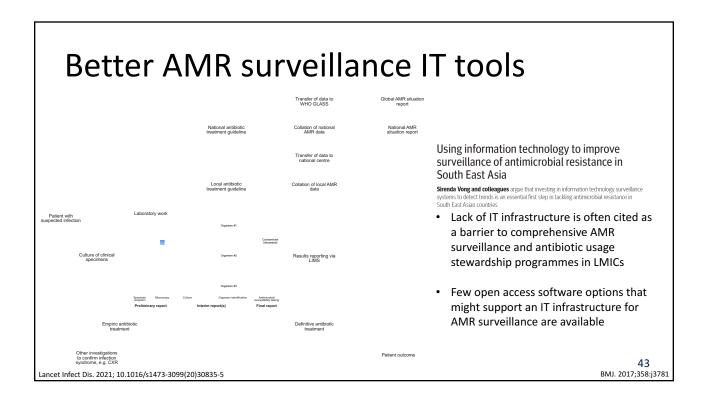
- new onset of purulent sputum, or change in character of sputum (colour, odour, quantity, consistency)
- Symptoms cough or dyspnea or tachypnea
  - suggestive auscultation (rales or bronchial breath sounds), rhonchi, wheezing
  - worsening gas exchange (e.g. O<sub>2</sub> desaturation or increased oxygen requirements or increased ventilation demand).

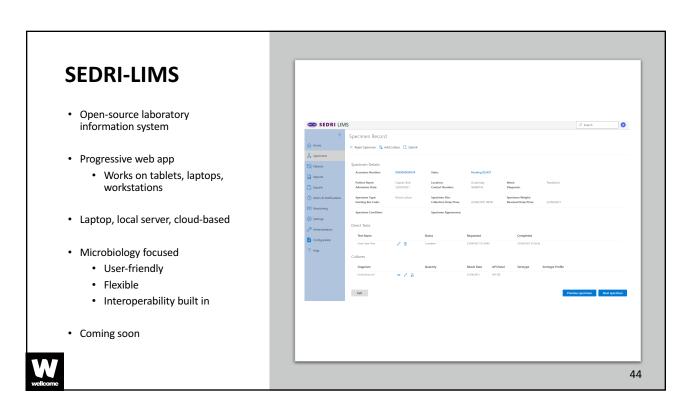


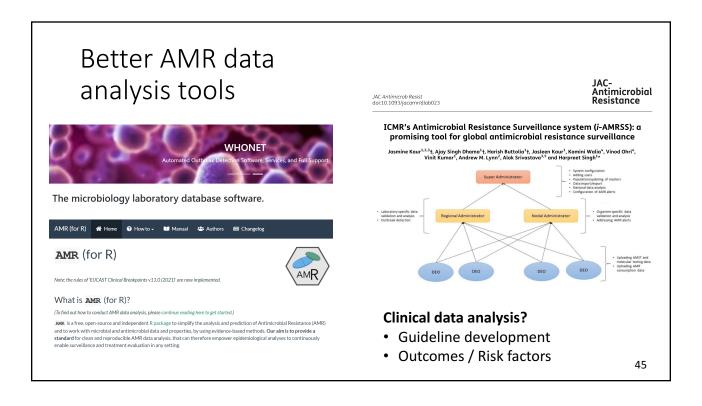
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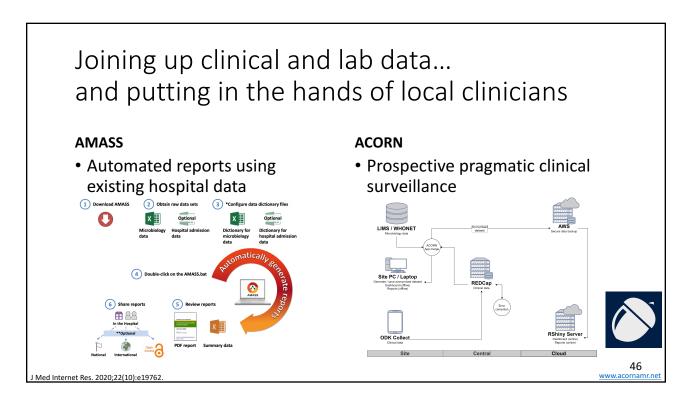
#### What tools are needed

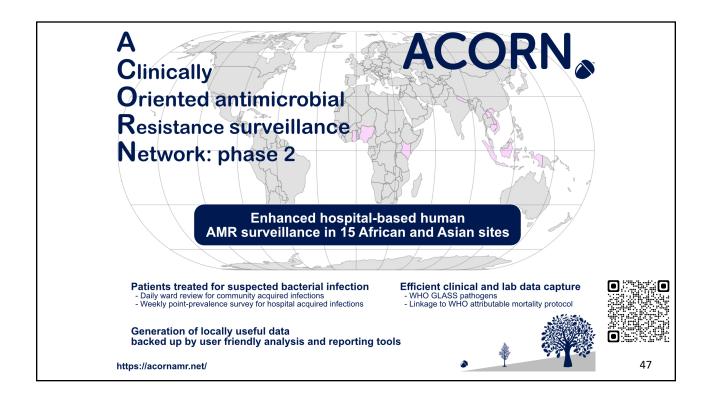
- Money
- · Good microbiology
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  - In the absence of fully electronic patient, pharmacy, and lab information systems surveillance takes time and requires effort
- Case definitions
  - That are simple and do not require serial bloods / radiology
- IT infrastructure

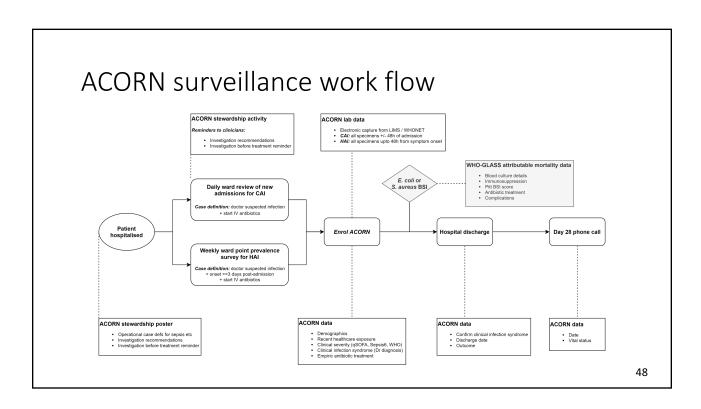




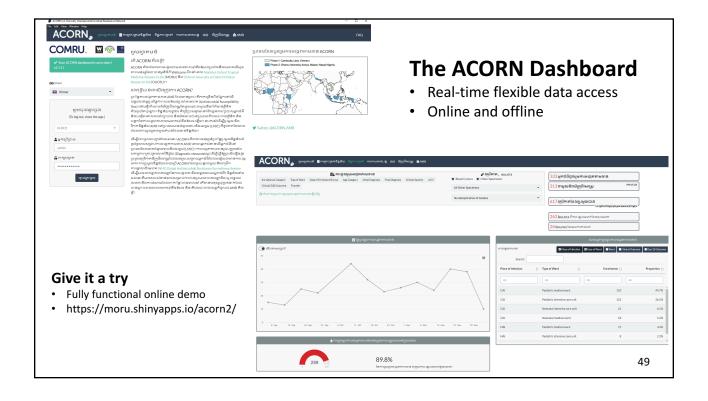


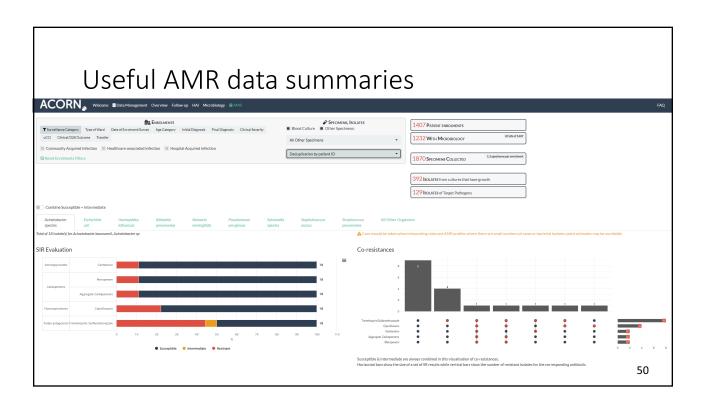


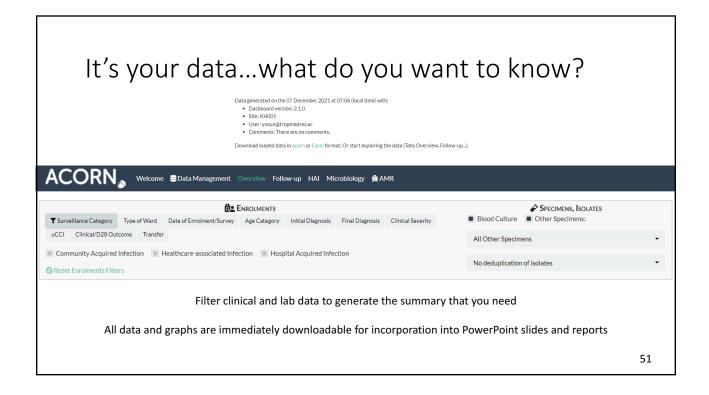




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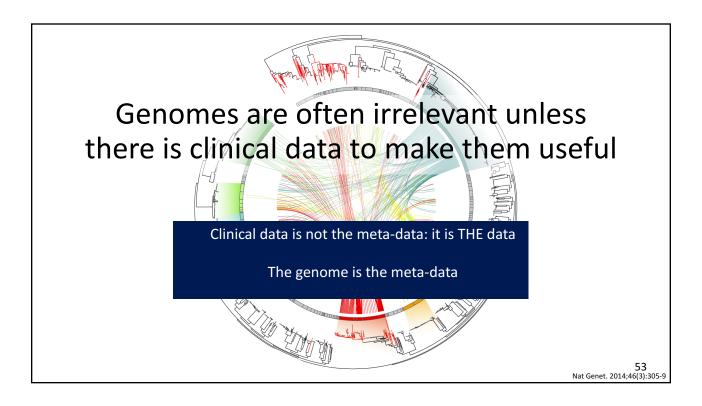






### A word about genomes

- Clearly have the potential to add considerable value to AMR surveillance efforts
- Key issues to resolve
  - Scope of WGS-based surveillance
  - · Discordances between phenotypic and genotypic AMR data
  - Decentralisation to ensure clinical utility is not lost
    - · Cost and logistics issues are challenging
  - Access to easy-to-use surveillance-appropriate bioinformatics tools
    - Pathogenwatch / CGE-DTU (online) and FlowCraft / Bactopia (local) are all available now



### To sum up...

- Generation and interpretation of AMR burden data is complicated
- There are still large data (+ data quality) and knowledge gaps
- Data management is a major road block to progress
  - Urgently need better LIMS and IT infrastructure to support this
  - User friendly analysis tools would unlock local data use
- Not enough attention is being paid to local use of data
- More focus on the local situation will improve uptake and usefulness of global surveillance
  - If we don't get the site level data sorted, then the global data will be wrong anyway

# Thanks for listening: any questions?

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www.webbertraining.com/schedulep1.php			
June 8, 2022	PULLING THE PLUG ON THE SINK DRAIN Speaker: Prof. Jean-Yves Maillard, Cardiff University, Wales		
June 21, 2022	(European Teleclass)  HOW EFFECTIVE ARE INTERVENTIONS TO IMPROVE CLEANING OF HEALTHCARE ENVIRONMENTS IN LOW-RESOURCED SETTINGS?  Speaker: Prof. Giorgia Gon, London School of Hygiene and Tropical Medicine, UK		
June 30, 2022	(FREE Teleclass) SHARING KNOWLEDGE: LEARNING FROM THOSE WHO HAVE CHALLENGED THE CIC Speaker: Sam MacFarlane, Public Health Ontario, Sandra Petersen, Ottawa Public Health, and Jeff Lee, Canadian Armed Forces Health Services Headquarters		
July 14, 2022	HEALTHCARE INFORMATICS LESSONS FROM THE PANDEMIC Speaker: Prof. Keith Woeltje, Medical College of Wisconsin		
	(European Teleclass)		

