Antimicrobial Resistance surveillance data: from antibiotic susceptibility testing results to treatment regimen

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The Future of Infectious Diseases in the 1970's

•~~"It is time to close the book on infectious diseases, and declare the war against pestilence won"~~
•William H Stewart, US surgeon general 1965-1969

•"Even with my great personal loyalty to Infectious Disease, I cannot conceive of the need for 309 more trainees in infectious disease…unless they spend their time culturing each other"
•Robert Petersdorf, 1978

•"If for the present we retain a basic optimism and assume no major catastrophes occur and that any wars are kept at the 'brush fire' level, the most likely forecast about the future of infectious disease is that it will be very dull."
•Frank McFarlane-Burnet, 1972

Antibiotics were discovered – not invented

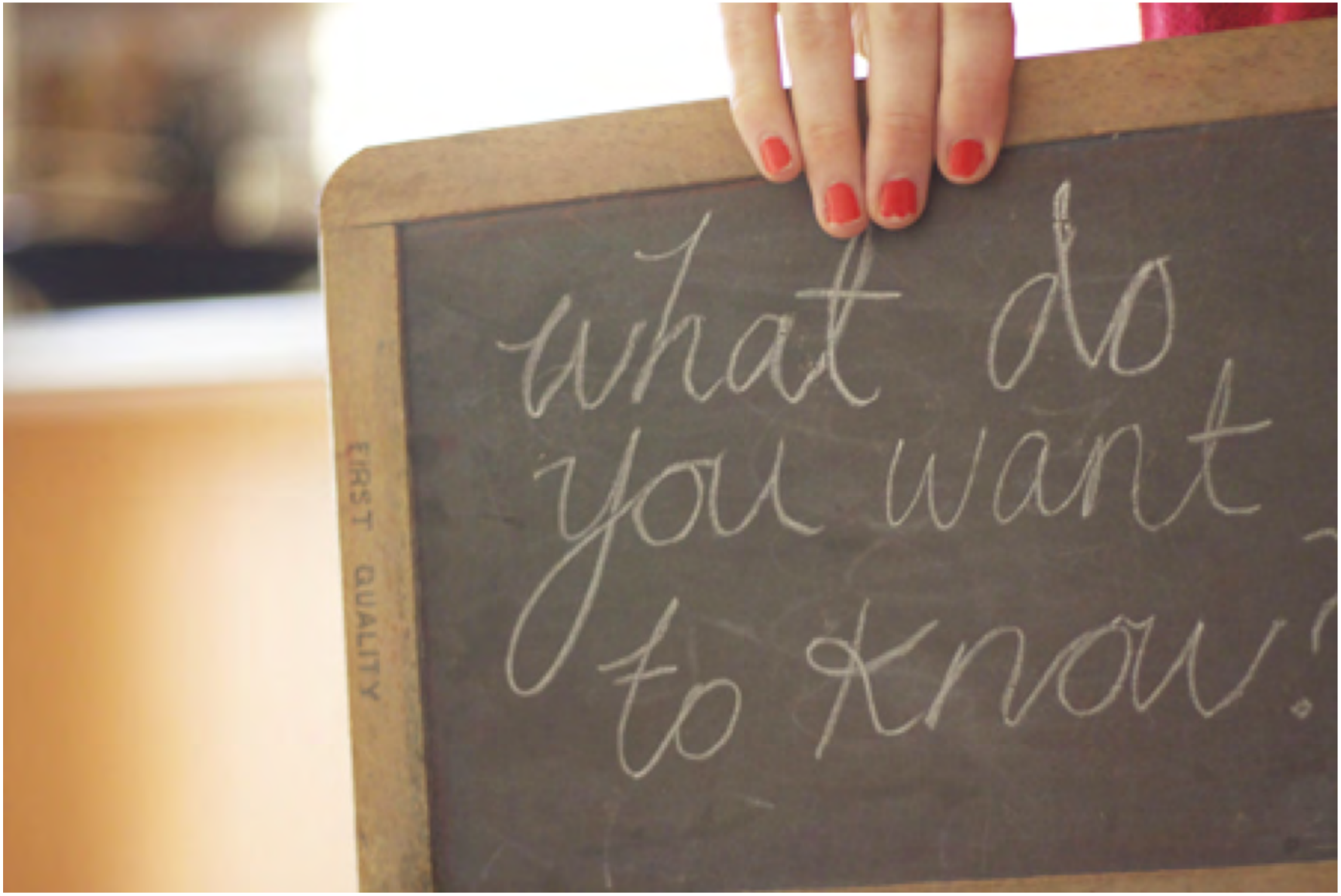
AMR and AMR genes are selected, not newly evolving or emerging

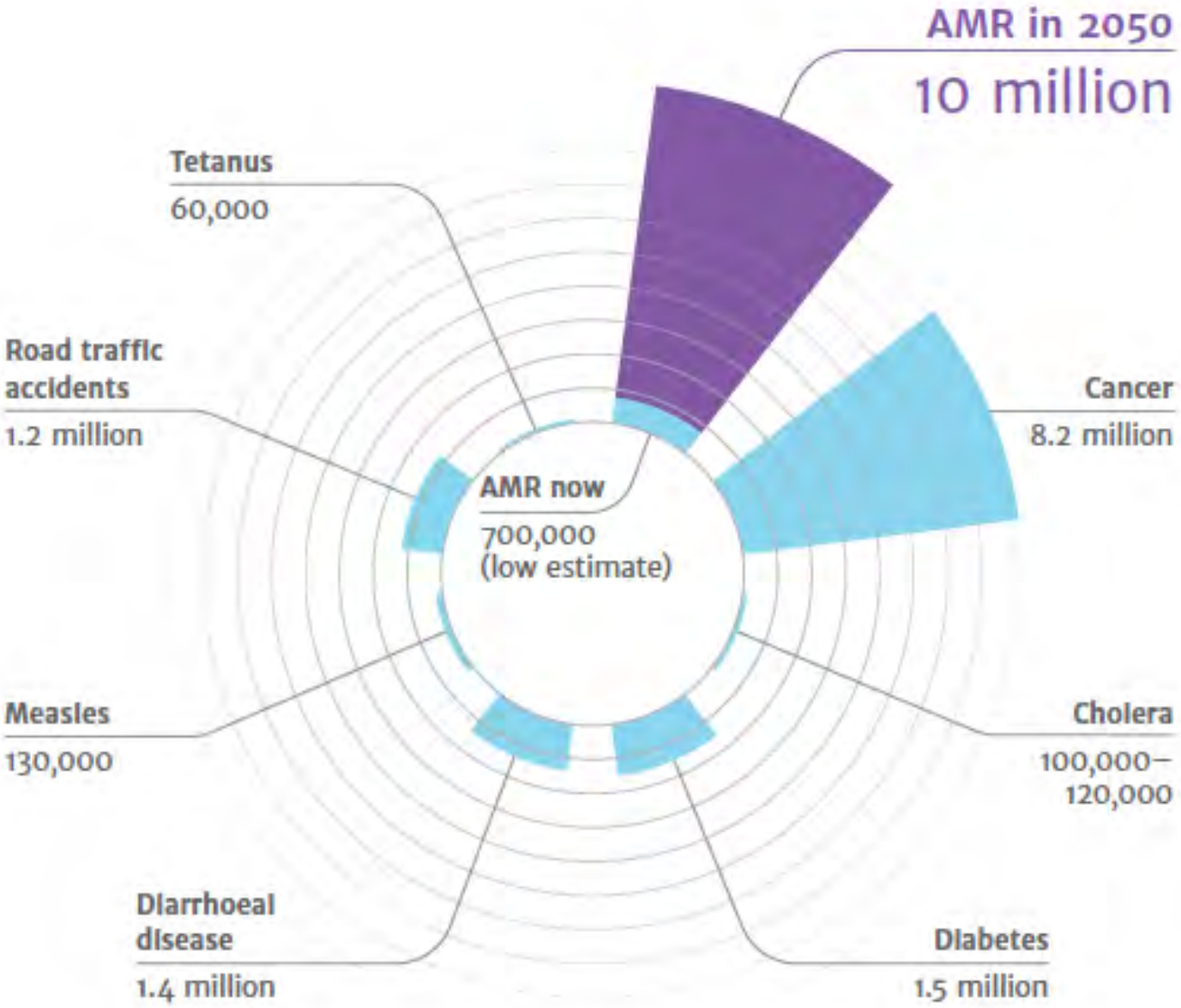
Antibiotics are like a natural resource – every use, appropriate or inappropriate, eats away at its future / total use – Tragedy of the Commons

AMR is a “wicked problem”

Antibiotics are part of our societal and healthcare infrastructure – losing our ability to rely on their effectiveness will have profound consequences

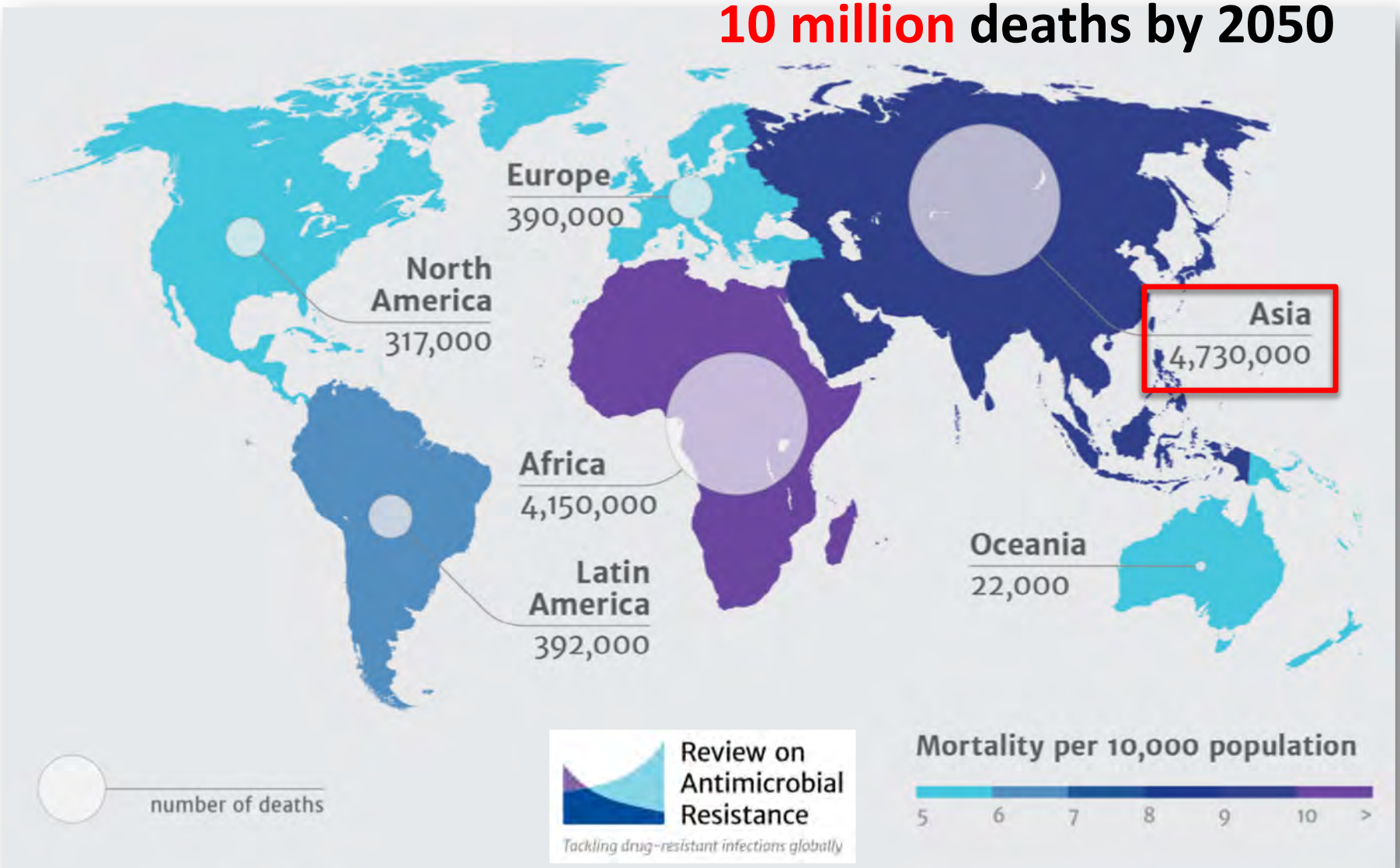
AMR is a pandemic that has been and will be among us globally for the foreseeable future – “The lobster and the frog”


what do
you want
to know?
FIRST QUALITY



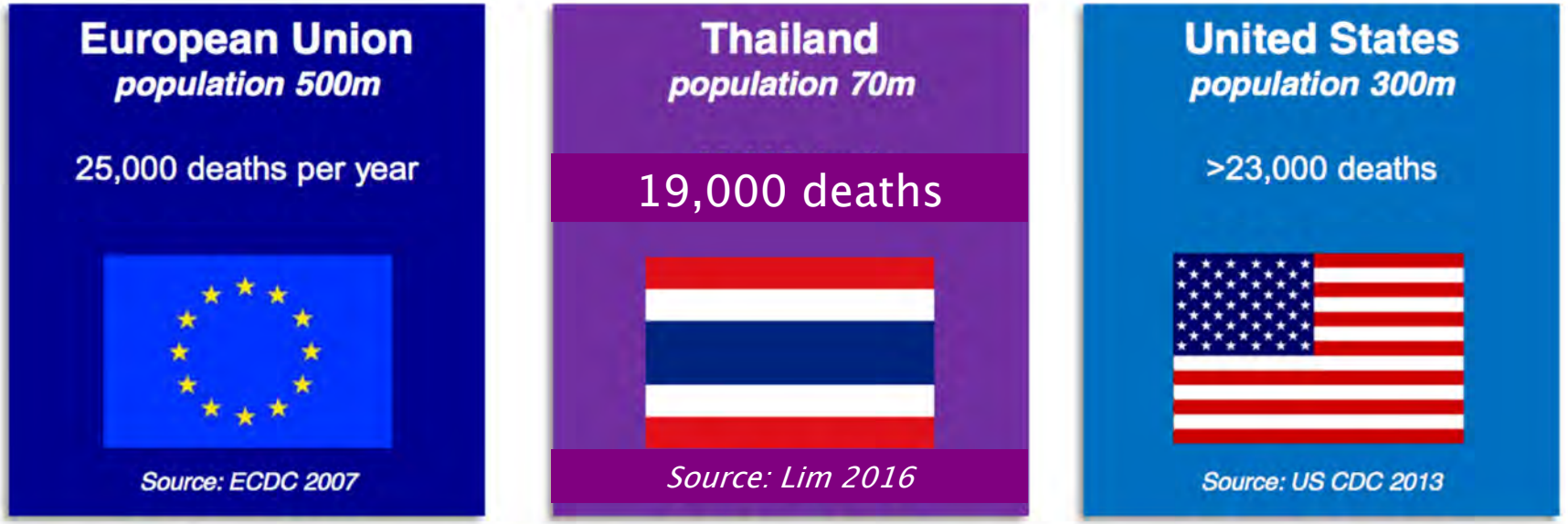
amr-review.org

10 million deaths by 2050



Currently 700,000 deaths (low estimate) due to antimicrobial resistant infection amr-review.org

Estimates of Burden of Antibacterial Resistance



Global information is insufficient to show complete disease burden impact and costs

| Antimicrobial Resistance
Global Report on Surveillance 2014

World Health Organization

www.who.int/antimicrobial-resistance/publications/surveillancereport/en/

Elife 2016 5:e18082

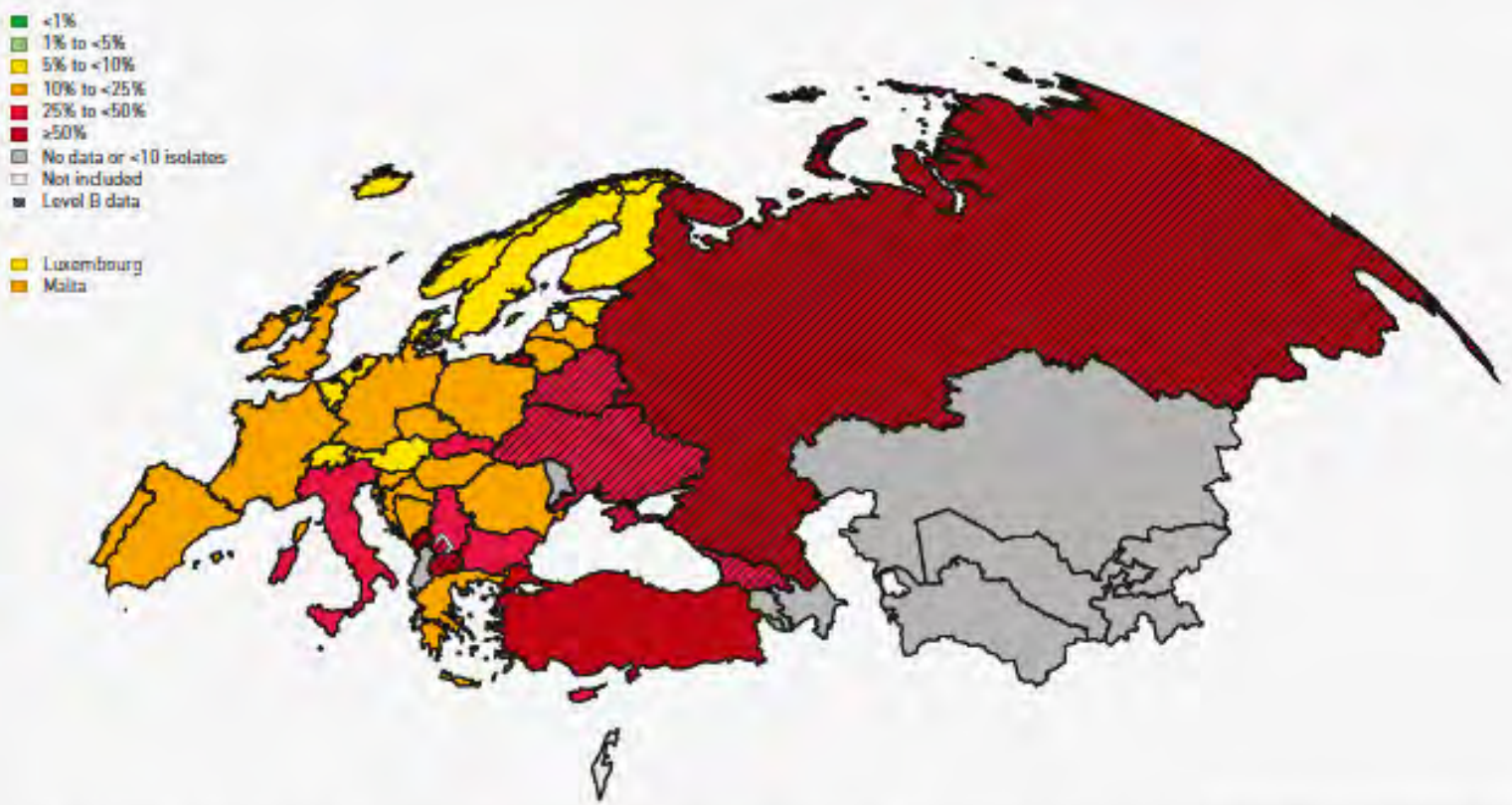
EARSnet / CAESAR

(European Antimicrobial Resistance Surveillance Network – ecdc)
(Central Asian and Eastern European Surveillance of Antimicrobial Resistance – WHO)

- Blood and CSF
- ***Escherichia coli*** – ***Klebsiella pneumoniae*** – *Pseudomonas aeruginosa* – *Acinetobacter baumannii* – ***Streptococcus pneumoniae*** – ***Staphylococcus aureus*** – *Enterococcus faecium/faecalis*
- Isolate-based
- No differentiation HAI / CAI (date of hospitalization collected)
- No information on previous antibiotics

www.ecdc.europa.eu/en/publications-data
www.euro.who.int

E. coli 3GC 2017



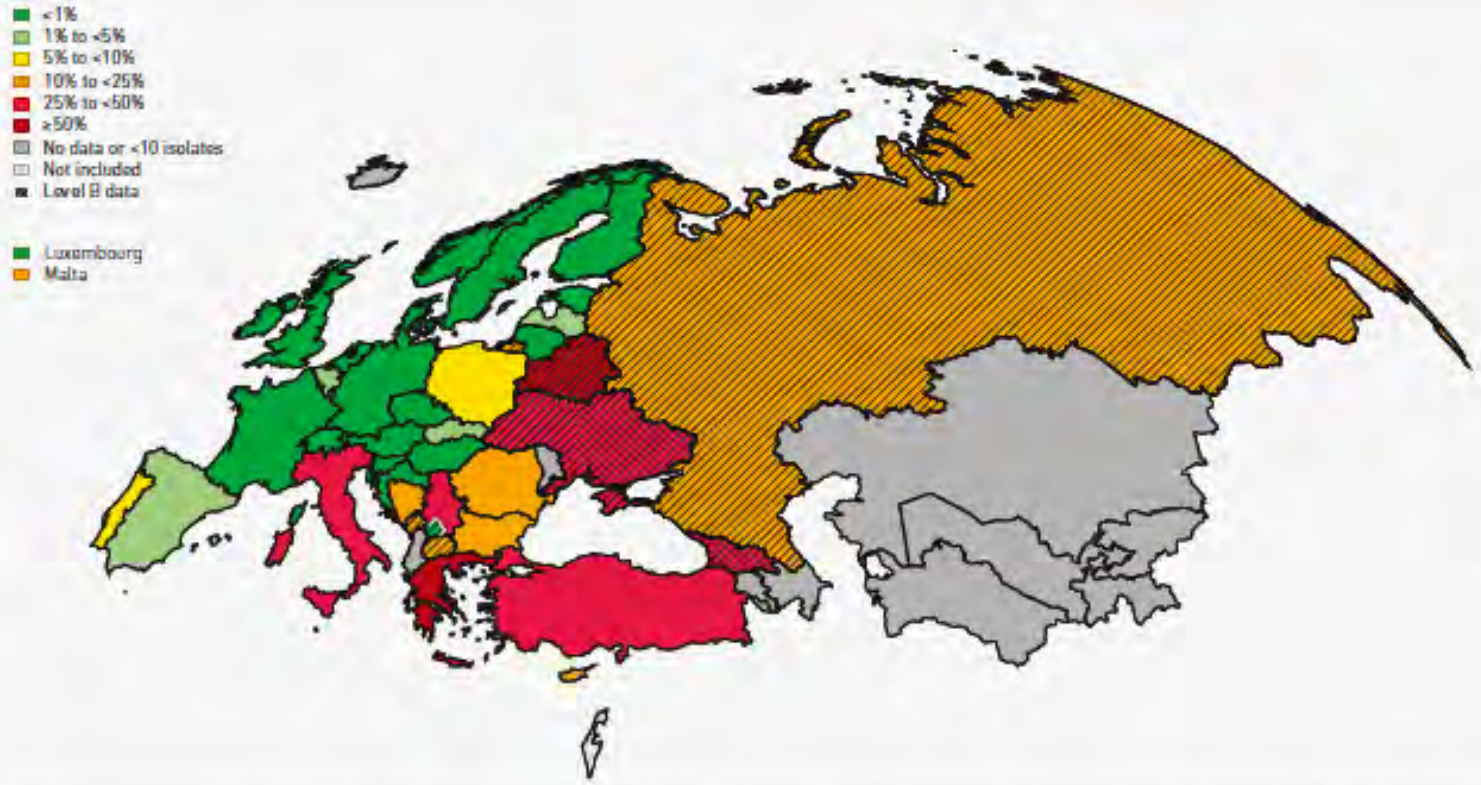
Level B data: the data provide an indication of the resistance patterns present in clinical settings in the country or area, but the proportion of resistance should be interpreted with care. Improvements are needed to attain a more valid assessment of the magnitude and trends of AMR in the country or area. See section 4.2 for more information about levels of evidence, which are only provided for CAESAR countries and areas.

EARS-Net countries: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden and the United Kingdom.
CAESAR countries and areas: Albania, Armenia, Azerbaijan, Belarus, Bosnia and Herzegovina, Georgia, Kazakhstan, Kyrgyzstan, Montenegro, the Republic of Moldova, the Russian Federation, Serbia, Switzerland, Tajikistan, the former Yugoslav Republic of Macedonia, Turkey, Turkmenistan, Ukraine, Uzbekistan and Kosovo (in accordance with United Nations Security Council resolution 1244 (1999)).

Data sources: 2017 data from the Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR, ©WHO 2018) and 2017 data from the European Antimicrobial Resistance Surveillance Network (EARS-Net, ©ECDC 2018).

Fig. 7.1 Third-generation cephalosporin-resistant *E. coli* in the European Region (EARS-Net and CAESAR), 2017

K. pneumoniae CPE 2017



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Data sources: 2017 data from the Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR, ©WHO 2018) and 2017 data from the European Antimicrobial Resistance Surveillance Network (EARS-Net, ©ECDC 2018).

Fig. 7.4 Carbapenem-resistant *K. pneumoniae* in the European Region (EARS-Net and CAESAR), 2017

GLASS

Global Antimicrobial Resistance Surveillance System

Table 2. Priority specimens and pathogens for surveillance of AMR

Specimen	Laboratory case definition	Surveillance type and sampling setting	Priority pathogens for surveillance
Blood	Isolation of pathogen from blood[a]	Selected sites or national coverage Continuous Patients in hospital and in the community	*E. coli* *K. pneumoniae* *A. baumannii* *S. aureus* *S. pneumoniae* *Salmonella* spp.
Urine	Significant growth in urine specimen[b]	Selected sites or national coverage Continuous Patients in hospital and in the community	*E. coli* *K. pneumoniae*
Faeces	Isolation of *Salmonella* spp.[c] or *Shigella* spp. from stools	Selected sites or national coverage Continuous Patients in hospital and in the community	*Salmonella* spp. *Shigella* spp.
Urethral and cervical swabs	Isolation of *N. gonorrhoeae*	Selected sites or national coverage Continuous Patients in hospital and in the community	*N. gonorrhoeae*

Blood – Urine – Faeces – Urethra

Isolate based with guidance for sample / case based surveillance data and denominator data collection (sample based)

Option to differentiate between hospital and community origin

No previous antibiotics

www.who.int/glass/en/

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Global Antimicrobial Resistance and Use Surveillance System (GLASS)

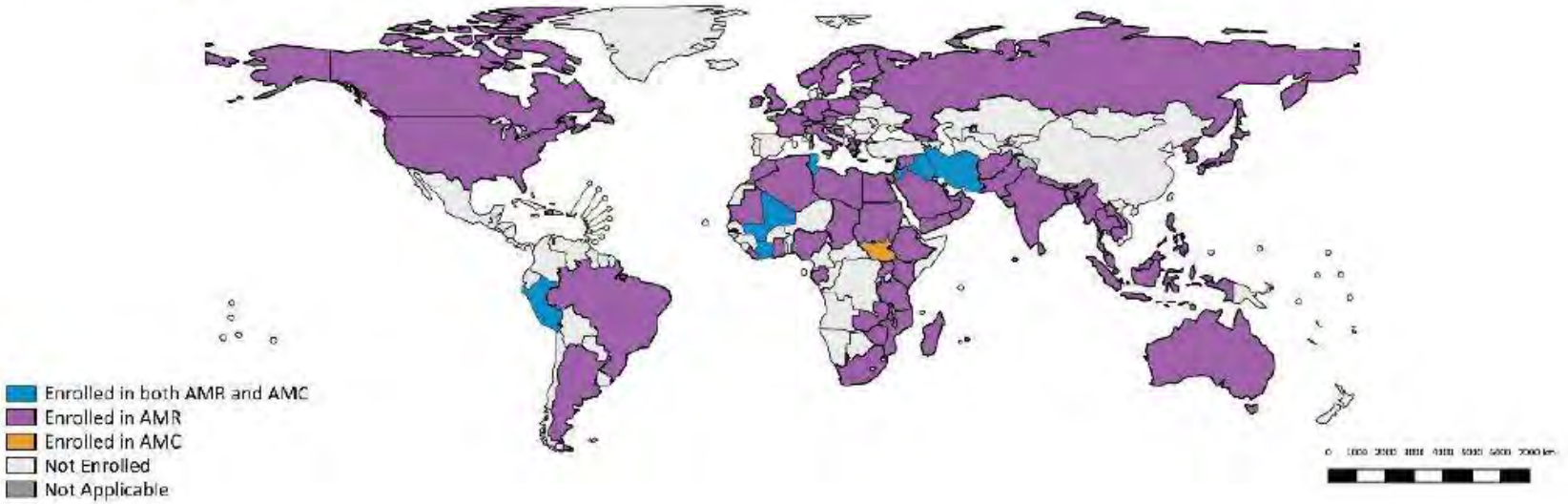
Countries enrolled in GLASS

As of 20 May 2020

GLASS

Global Antimicrobial Resistance and Use Surveillance System

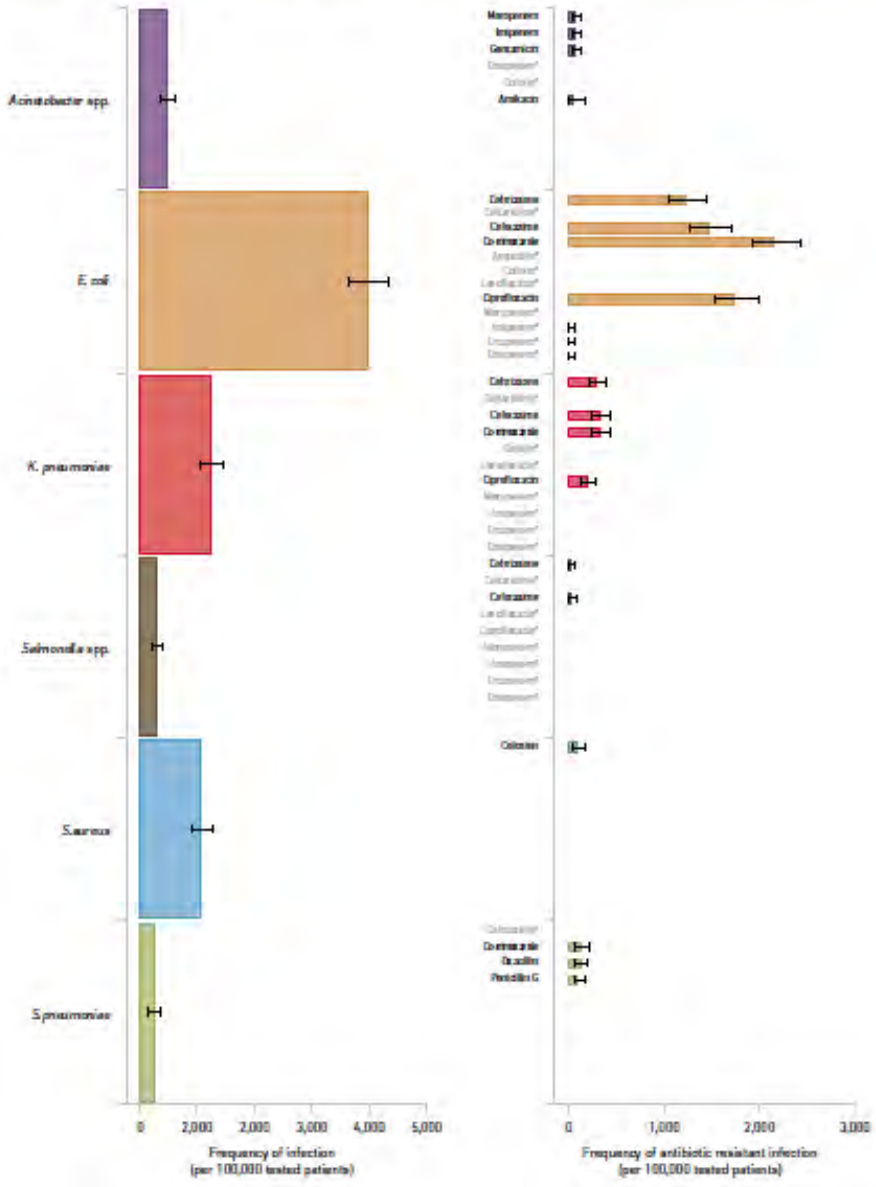
92 countries, territories and areas



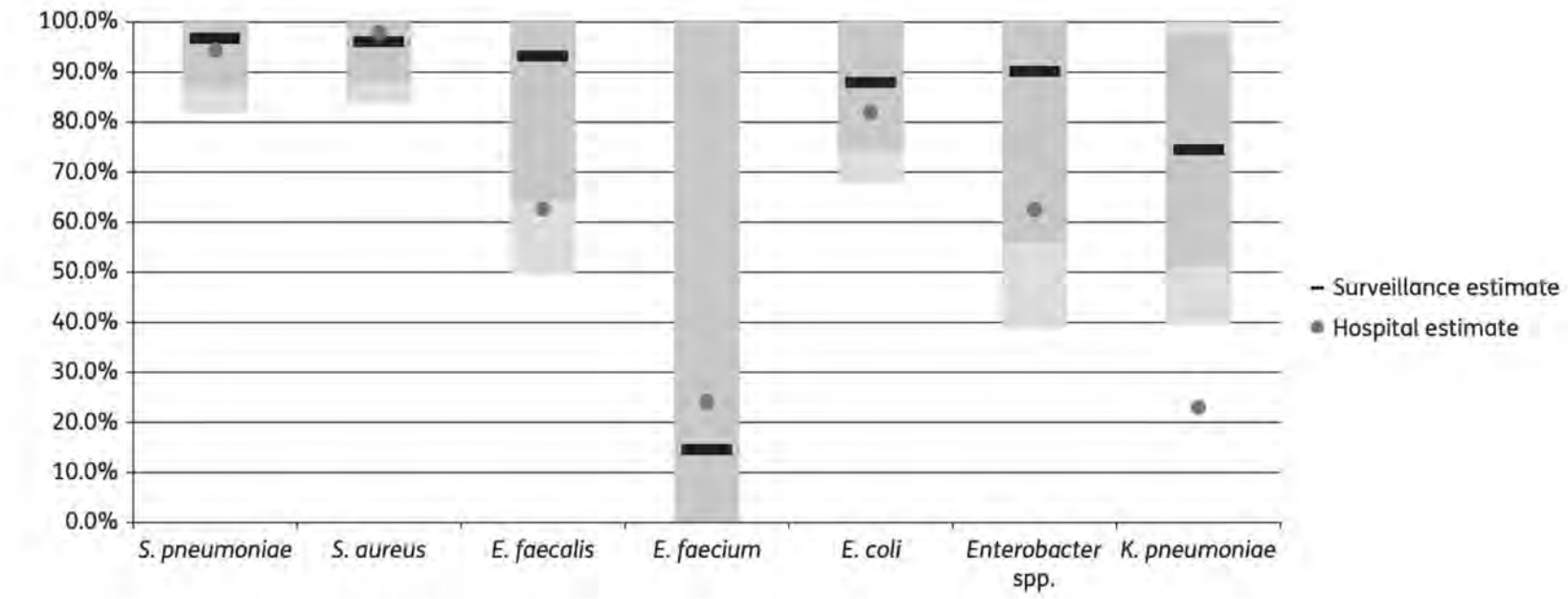
Non-susceptible pathogen-antimicrobial combination frequency

Frequency of infection caused by pathogens under surveillance per specimen and infection origin (left). Frequency of infection caused by pathogens non-susceptible to defined antibiotics under surveillance, per specimen and infection origin (right).

BLOOD- Community origin (n tested = 5733)



Weighted-incidence syndromic combination antibiograms (WISCAs)



Vietnam

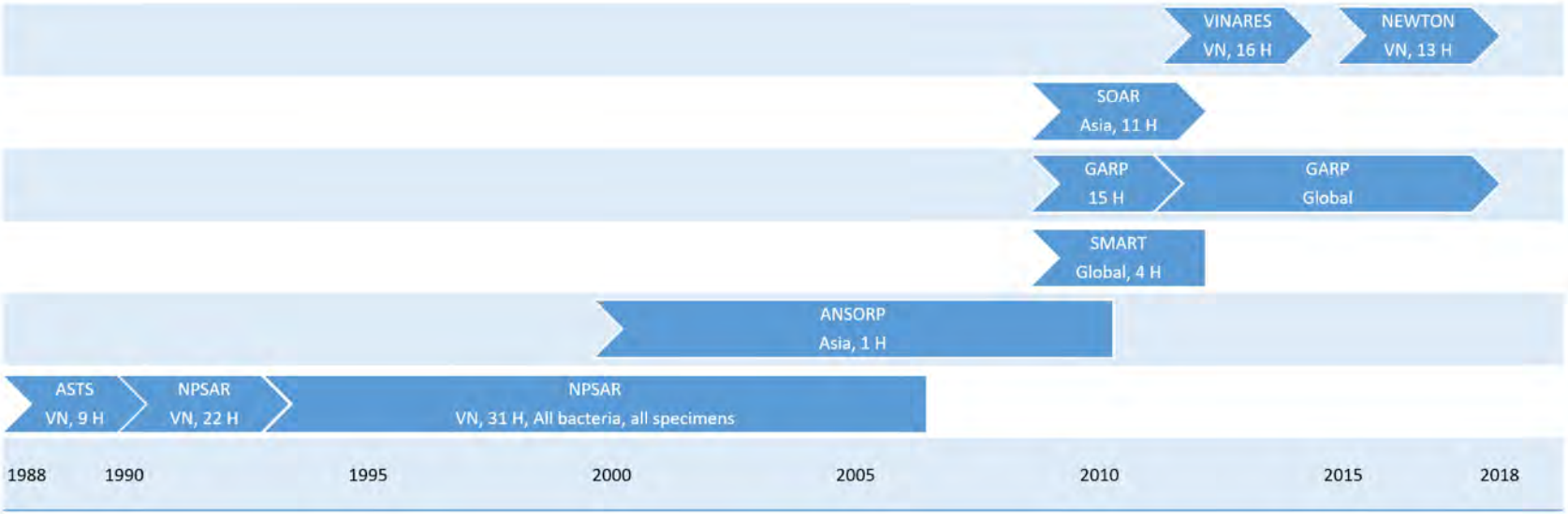


Figure 1: List of AMR surveillance network implemented in Viet Nam from 1988 to 2018

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NHTD
NATIONAL HOSPITAL OF TROPICAL DISEASES

LINKÖPINGS UNIVERSITET

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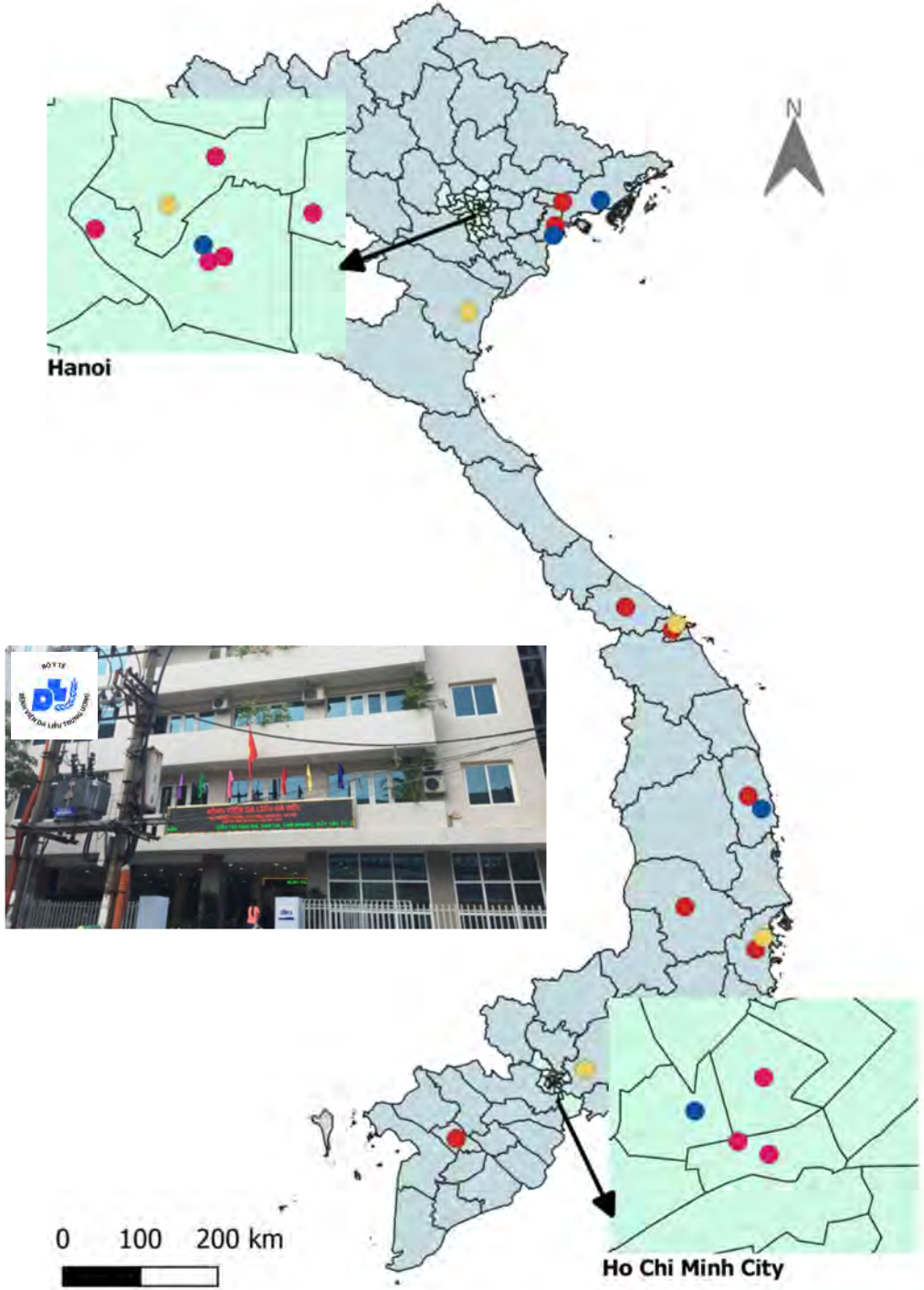

- National AMR surveillance network

National Hospital for Tropical Diseases
Bach Mai Hospital
Vietnam National Children Hospital
Saint Paul Hospital
Viet Duc Hospital
Viet Tiep Hospital
Viet Nam - Sweden, Uong Bi Hospital
Binh Dinh Provincial General Hospital
Da Nang Hospital
Hue Central Hospital
Khanh Hoa Provincial General Hospital
Dak Lak Provincial General Hospital
Cho Ray Hospital
Children Hospital No 1
Hospital for Tropical Diseases, Ho Chi Minh City
Can Tho Central General Hospital

- AMR surveillance in Neisseria gonorrhoeae (since 2017)

National Hospital of Dermatology and Venereology
Hospital of Dermato Venereology, Ho Chi Minh City
Hai Phong Dermato Venereology Center
Quang Ninh Center of Disease Control
Quy Hoa Dermato Venereology Hospital

- AMR surveillance in Neisseria gonorrhoeae (since 2019)

Ha Noi Hospital of Dermatology and Venereology
Dong Nai Hospital of Dermatology and Venereology
Da Nang Hospital of Dermatology and Venereology
Thanh Hoa Hospital of Dermatology and Venereology
Khanh Hoa Hospital of Dermatology and Venereology

“Bug-drug combinations” – Blood & CSF

Bacteria	Antibiotic	2016-2017	Thailand	Philippines	Korea	Sweden
		% (N)	%	%	%	%
Acinetobacter baumannii	Imipenem	56,8 (192)	17	40	69	2
	Colistin	2,5 (122)	-	6	0	-
Pseudomonas aeruginosa	Imipenem	36,7 (147)	-	-	-	-
	Ceftazidime	37,3 (150)	-	-	-	-
Escherichia coli	Imipenem	6,6 (1504)	3	5	1	1
	ESBL	60,1 (1167)	42	38	36	11
	Ciprofloxacin	64,3 (1414)	38	40	40	14
Klebsiella pneumoniae	Imipenem	19,5 (477)	8	22	3	1
	ESBL	35,0 (380)	50	54	30	8
	Ciprofloxacin	40,1 (431)	30	40	25	10
Staphylococcus aureus	MRSA	69,4 (533)	14	62	53	2
	Vancomycin	0,0 (669)	-	-	-	-
Streptococcus pneumoniae	Penicillin	43,1 (102)	51	5	21	8
	Ceftriaxone	14,9 (134)	-	1	15	2

resistancemap.org (CDDEP)

J Glob Antimicrob Resist. 2019 18:269–278

Biases

Underuse of microbiology
Isolate based - No clinical denominator
More severe and unresponsive infections
Transfers
Pre-admission antibiotic use
Hospital vs. community acquired

All bias towards resistance

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ACORN

www.acornamr.net

Why ACORN?

Antibiotic access prior to healthcare visit / hospitalization

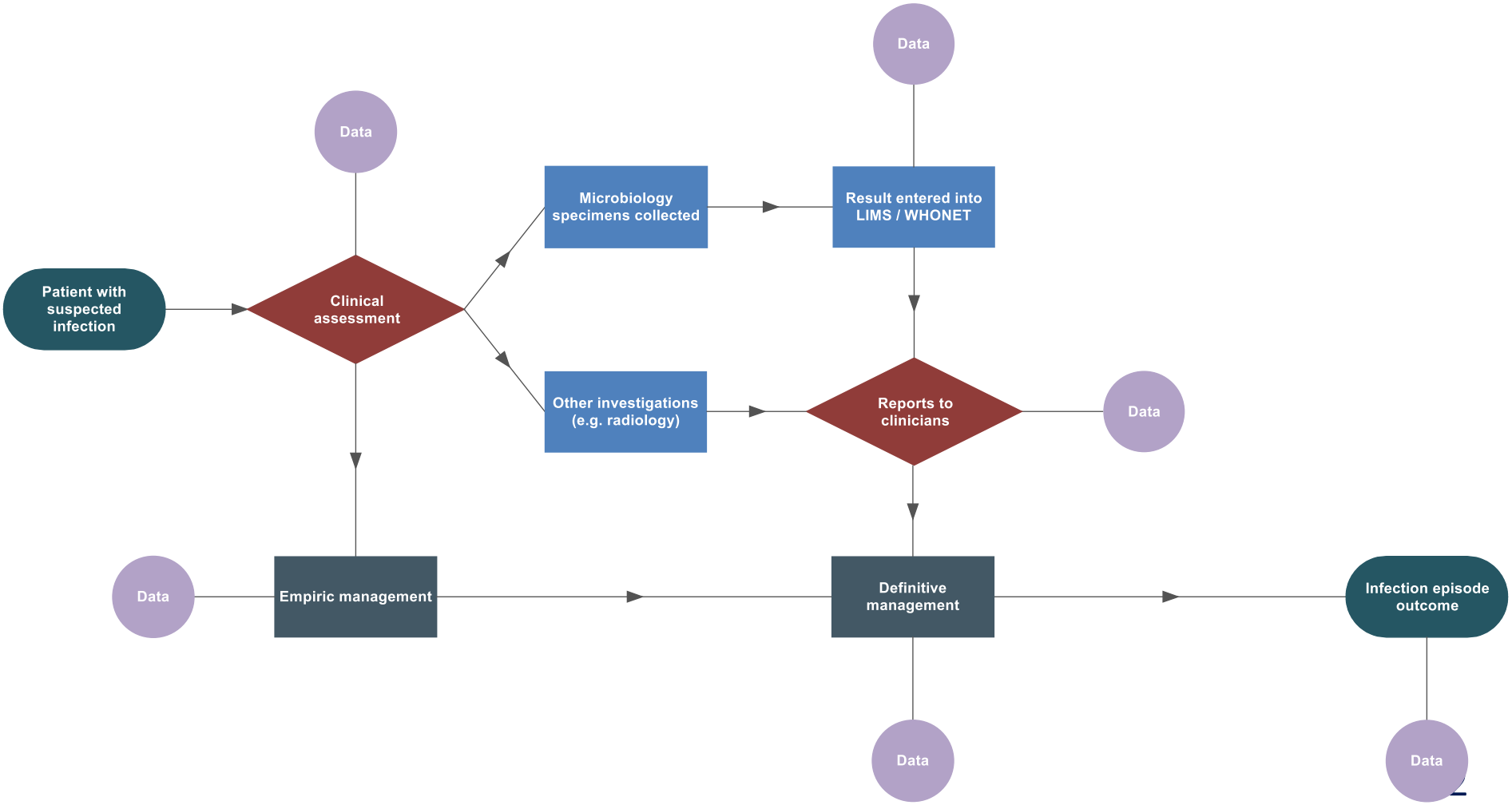
Microbiology services only available at higher levels hospitals

Suboptimal use of microbiological diagnostics
- capacity
- culture / trust / toothless
- insurance

Probably preferential culturing of
- severe infection
- unresponsive infections
- hospital acquired infections

No denominator data

No clinical metadata



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ACORN

1. Active data collection on wards at day 0, 3 and at day 28 for patients with an infectious syndrome, weekly PPS for HAI
   a. Case based AMR data for specified subgroups that can
   b. inform local treatment guidelines and local / global AMR data
   c. Data on burden of DRI vs non-DRI

2. Diagnostic stewardship
   a. Sampling
   b. Analysis / Interpretation

3. Software solutions
   a. Tablet
   b. LIMS
   c. middleware

Clinical variable selection

Two-day workshop held in May 2019

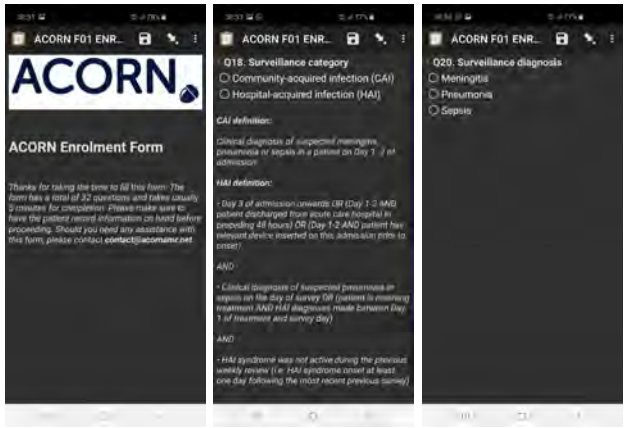
Key AMR stakeholders asked to provide 10 key clinical variables

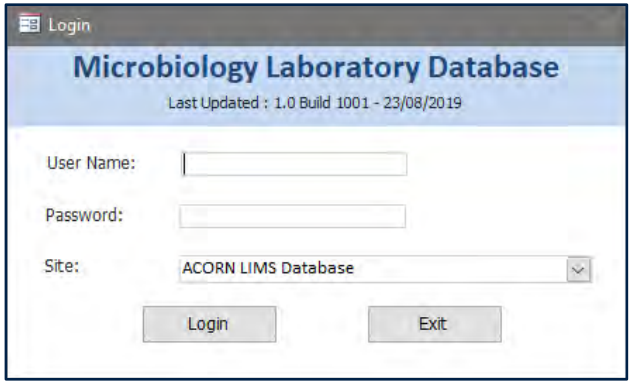
- Epidemiologist, ID clinicians, microbiologists, paediatricians, mathematical and economic modellers
- Investigators then developed a consensus list for the pilot surveillance

Simple and scalable

Efficient data capture

- Clinical data captured by smartphone / tablet app
- Carefully defined clinical dataset
- Laboratory data captured via bespoke LIMS or WHONET





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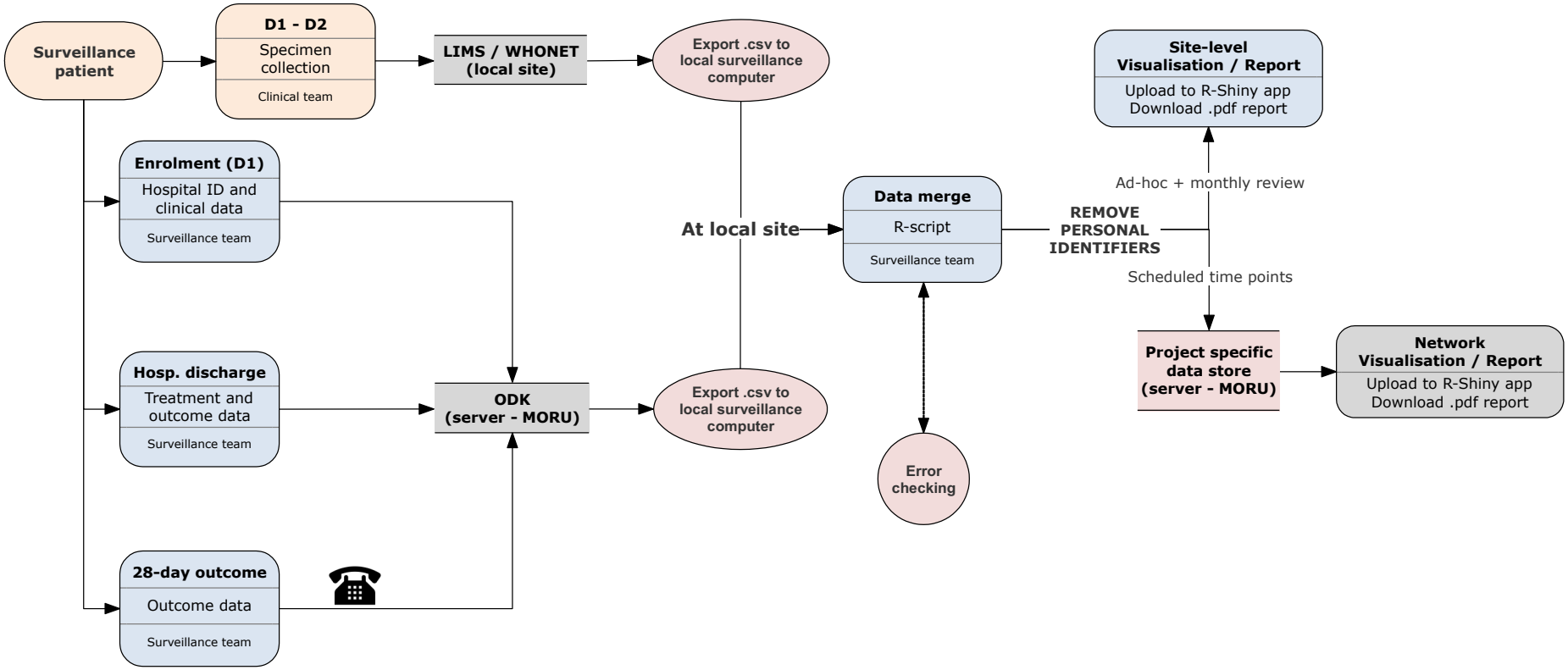
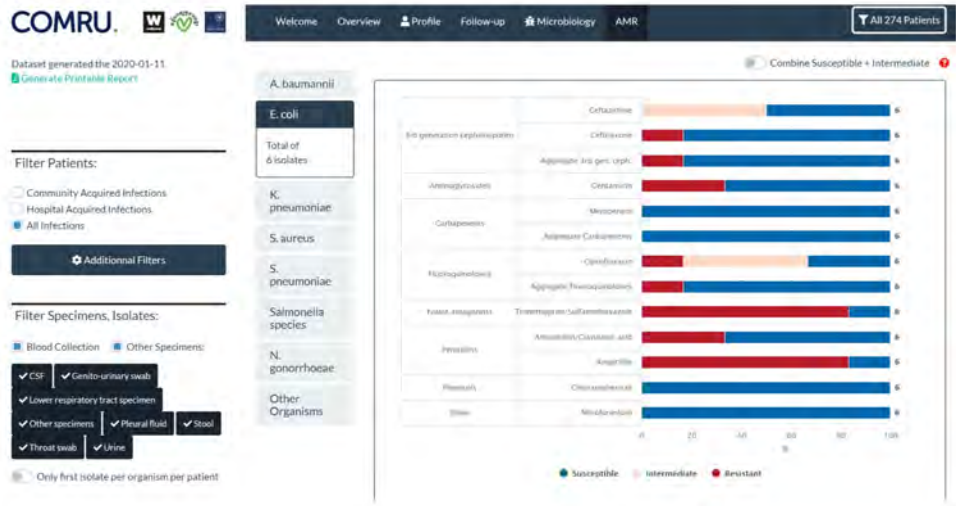
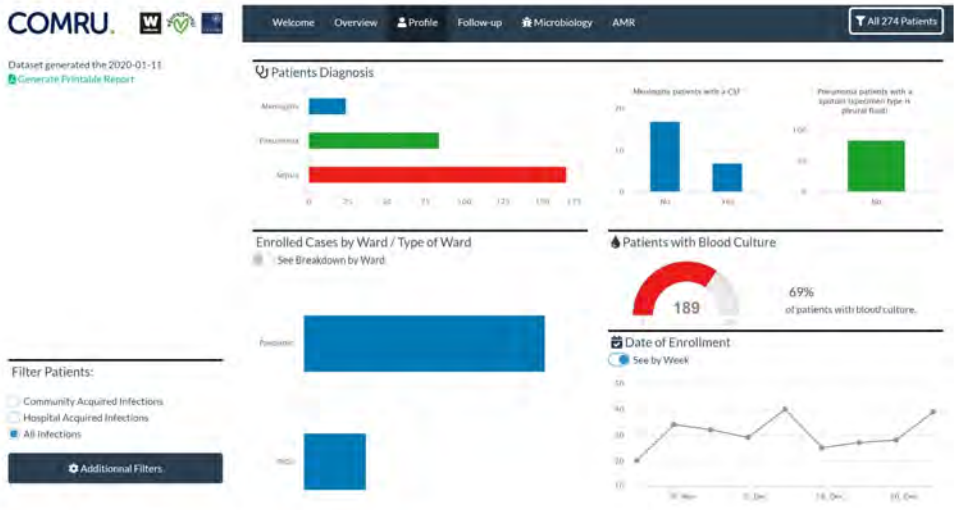

Surveillance patient
D1 - D2
Specimen collection
Clinical team
LIMS / WHONET (local site)
Export .csv to local surveillance computer
Site-level Visualisation / Report
Upload to R-Shiny app
Download .pdf report
Enrolment (D1)
Hospital ID and clinical data
Surveillance team
At local site
Data merge
R-script
Surveillance team
REMOVE PERSONAL IDENTIFIERS
Ad-hoc + monthly review
Scheduled time points
Hosp. discharge
Treatment and outcome data
Surveillance team
ODK (server - MORU)
Export .csv to local surveillance computer
Error checking
Project specific data store (server - MORU)
Network Visualisation / Report
Upload to R-Shiny app
Download .pdf report
28-day outcome
Outcome data
Surveillance team

Direct & Local Utility





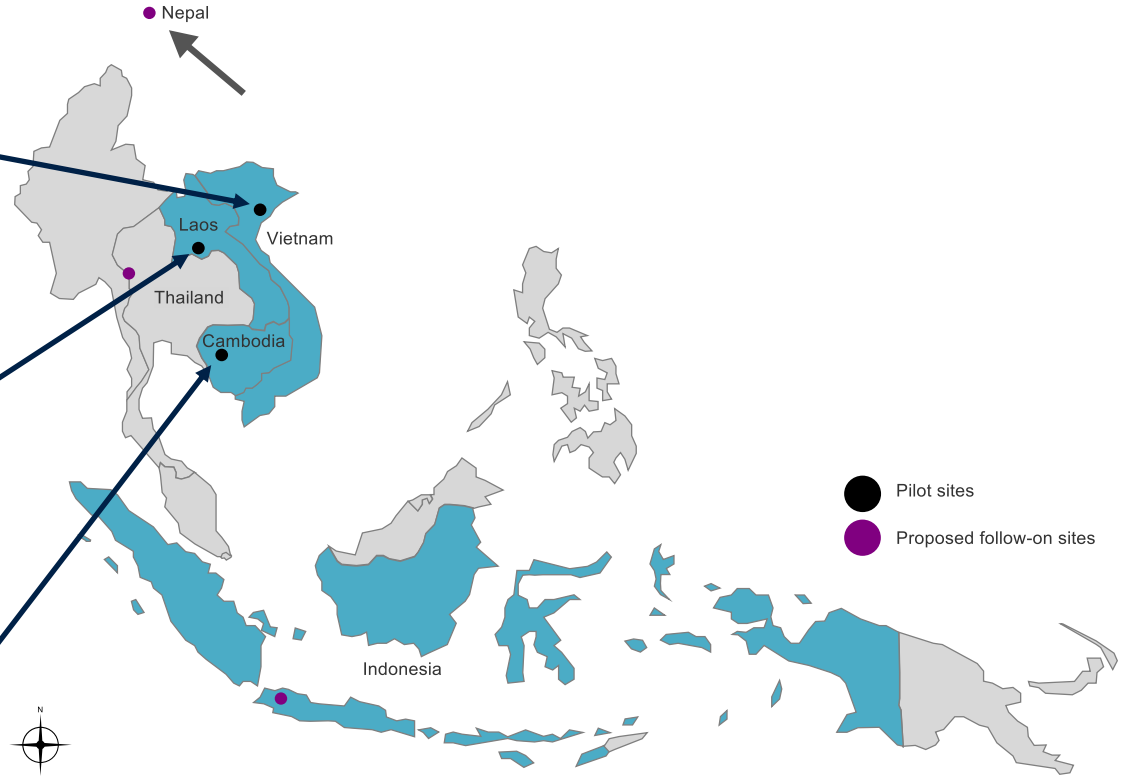
The pilot

Pilot until May2020
Extension until October 2020

National Hospital for Tropical Diseases
350/500 bed governmental hospitals
Tertiary infectious diseases

Mahosot Hospital
365 bed governmental hospital
Primary - tertiary

Angkor Hospital for Children
~100 bed non-governmental hospital
Primary – tertiary



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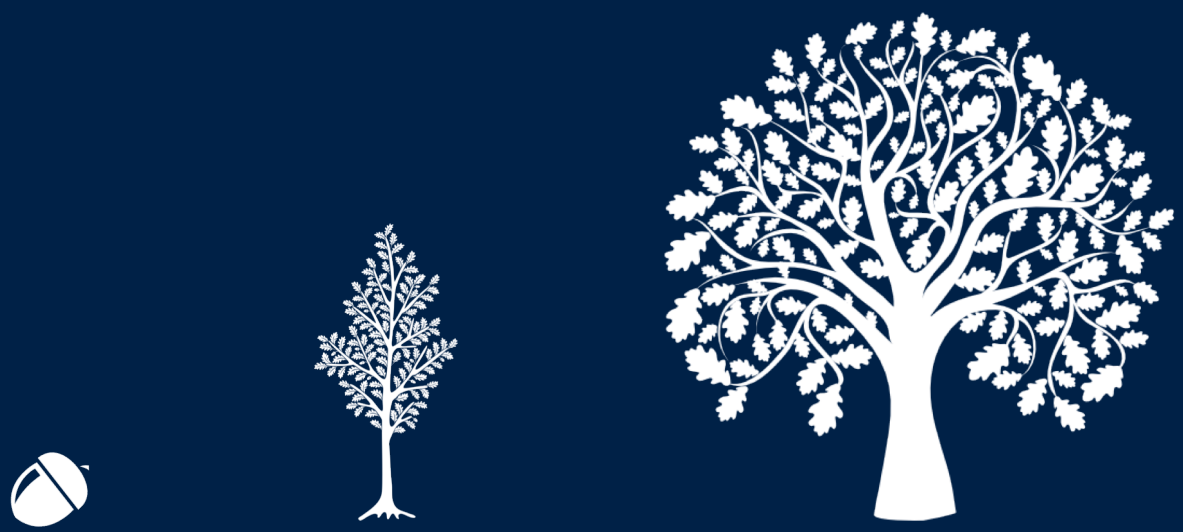
The next steps…



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