Regional Surveillance & “The Wellcome Experience”

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Antimicrobial Resistance in the Asia Pacific & Its impact on Singapore
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The Oxford Tropical Network in Asia:  
A regional presence since 1979

- **MORU: Mahidol-Oxford Tropical Medicine Research Unit**
  - Bangkok
  - Mae Sot (SMRU)
  - Vientiane (LOMWRU)
  - Siem Reap (COMRU)
  - Yangon (MOCRU)

- **OUCRU: Oxford University Clinical Research Unit**
  - Ho Chi Minh City
  - Hanoi
  - Jakarta (EOCRU)
  - Kathmandu (OUCRU-NP)
Diverse locations

Farm images: Juan Carrique-Mas
Mortality attributable to AMR in Thailand

Epidemiology and burden of multidrug-resistant bacterial infection in a developing country

Cherry Lim††, Emi Takahashi††, Maliwan Hongsuwan†, Vanaporn Wuthiekanun†, Visanu Thamlikitkul², Soawapak Hinjoy³, Nicholas PJ Day¹, ⁴, Sharon J Peacock¹, ⁵, ⁶, Direk Limmmathurosakul¹, ⁴, ⁷*
Used routinely available data from microbiology laboratory and hospital databases of nine public hospitals in northeast Thailand from 2004 to 2010

In 2010, 19,122 deaths were attributable to multidrug-resistant bacterial infection

Lim C et al. eLife 2016;5:e18082
Global burden and impact of AMR

Improving the estimation of the global burden of antimicrobial resistant infections


1. ICD principle (GBD main cause of death)

2. All-cause mortality

3. Attributable mortality (counterfactual approach)

4. IMPROVED MODELS...
Viet Nam Resistance: VINARES

Number of isolates per hospital

Legend

- National
- General
- Specific
- Provincial

Hospitals:
1. Bach Mai Hospital
2. National Hospital of Pediatrics
3. National Hospital for Tropical Diseases
4. Viet Tri Hospital
5. Saint Paul Hospital
6. National Children's Hospital
7. Viet Duc Hospital
8. Vietnam-Swedish Uong Bi Hospital
9. General Binh Dinh Hospital
10. General Da Nang Hospital
11. Hue Central General
12. Cao Bang Hospital
13. Ninh Binh General Hospital
14. Ho Chi Minh Children's Hospital
15. Hospital of Tropical Disease (HTD)
16. Quang Tri Provincial Hospital

Graph:
- 2012-13
- 2016-17

Rogier van Doorn

## VINARES “bug-drug combinations” – Blood & CSF

<table>
<thead>
<tr>
<th>Species</th>
<th>Antibiotic</th>
<th>2012-2013</th>
<th>2016-2017</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>% (N)</td>
<td>% (N)</td>
</tr>
<tr>
<td><strong>Acinetobacter baumannii</strong></td>
<td>Imipenem</td>
<td>45.1 (244)</td>
<td>56.8 (192)</td>
</tr>
<tr>
<td></td>
<td>Colistin</td>
<td>0.0 (15)</td>
<td>2.5 (122)</td>
</tr>
<tr>
<td><strong>Pseudomonas aeruginosa</strong></td>
<td>Imipenem</td>
<td>27.9 (129)</td>
<td>36.7 (147)</td>
</tr>
<tr>
<td></td>
<td>Ceftazidime</td>
<td>32.3 (133)</td>
<td>37.3 (150)</td>
</tr>
<tr>
<td><strong>Escherichia coli</strong></td>
<td>Imipenem</td>
<td>3.7 (403)</td>
<td>6.6 (1504)</td>
</tr>
<tr>
<td></td>
<td>ESBL</td>
<td>68.9 (183)</td>
<td>60.1 (1167)</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin</td>
<td>47.4 (397)</td>
<td>64.3 (1414)</td>
</tr>
<tr>
<td><strong>Klebsiella pneumoniae</strong></td>
<td>Imipenem</td>
<td>17.7 (361)</td>
<td>19.5 (477)</td>
</tr>
<tr>
<td></td>
<td>ESBL</td>
<td>52.9 (172)</td>
<td>35.0 (380)</td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin</td>
<td>41.9 (332)</td>
<td>40.1 (431)</td>
</tr>
<tr>
<td><strong>Staphylococcus aureus</strong></td>
<td>MRSA</td>
<td>60.9 (184)</td>
<td>69.4 (533)</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
<td>2.9 (70)</td>
<td>0.0 (669)</td>
</tr>
<tr>
<td><strong>Streptococcus pneumoniae</strong></td>
<td>Penicillin</td>
<td>0.0 (6)</td>
<td>43.1 (102)</td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone</td>
<td>17.3 (52)</td>
<td>14.9 (134)</td>
</tr>
</tbody>
</table>
Limitations of VINARES data

• Only culture positive laboratory data submitted through WHONET
  – No clinical diagnosis
  – No data on denominator / negative cultures
  – No data on admission – transfer relative to sampling date. i.e. hospital or community acquired
  – No data on antibiotic usage

• Microbiology utilization variable: potential for bias when
  – Culture not always done
  – Culture not always done before antibiotics
  – Culture preferably done for severe patients and patients failing treatment
  – Overestimate resistance of community acquired pathogen
AMR in animals: ViParc

ViParc aims

• To reduce 33-50% antimicrobial usage in chicken farms by providing farmers with a local veterinary support system

• To elucidate the relationship between antimicrobial usage, farming practices and antimicrobial resistance

• To provide recommendations to the GoV on cost-effective measures that help reduce farmer’s reliance on antimicrobials
Study design: A randomised controlled before-and-after study

Random selection of farms ≥ 100 chickens

Exclusion criteria:
• Raise <100 chickens
• Raise chickens <50% time
• Raise only layer chickens

Final selection of study farms (n=120)

Randomisation

Arm I (n=40)
• Farmer Training
• Farm Health Plan (level 1)
• Diagnostic support

Arm II (n=40)
• Farmer Training
• Farm Health Plan (level 2)
• Diagnostic support

Arm III (n=40)
• No intervention

Phase I: Baseline phase (12 months)

Phase II: Intervention phase (18 months)

Dong Thap province
Situation Analysis

• Recent GARP-supported situation analysis

• 58 papers included in review
  – ESBL becoming more common
    • First detected in clinical isolates in 2004
    • One quarter of children colonised
  – MRSA relatively rare
  – *N. gonorrhoeae* remain susceptible to ceftriaxone and spectinomycin
  – *S. Typhi* almost all non-MDR / FQ susceptible
Appropriate Antibiotic Prescribing

Building consensus antimicrobial prescribing guidelines with MoH

Building MicroGuide App in Lao language

Conducting a stepped-wedge trial in 6 hospitals to evaluate impact on prescribing

Using regular PPS to monitor antibiotic use

Using antibiotic susceptibility patterns of key pathogens to monitor appropriate guidelines through time
Angkor Hospital for Children. Siem Reap
- 100 bedded NGO hospital with NICU and PICU
- 180,000 patient visits per year
- 6,000 in-patient admissions per year

Review of 10 years microbiology data (2007-2016)
- 39,050 blood/CSF cultures
- 1,088 GLASS organism infections

Improving Antibiotic Prescribing

- Using machine learning to determine empiric antibiotics

- 245 children with bacteraemia 2013-15
  - Detailed meta-data collected

- Random forest method gave AUC of
  - 0.80 (95%CI 0.66-0.94) for predicting susceptibility to ceftriaxone
  - 0.74 (0.59-0.89) for susceptibility to ampicillin and gentamicin
  - 0.85 (0.70-1.00) for susceptibility to neither
  - Most important variables for predicting susceptibility were
    - time from admission to blood culture
    - patient age
    - hospital versus community-acquired infection
    - age-adjusted weight score

A SELECTION OF FUTURE PLANS
Involved in country applications in 2/5
SEA Fleming Fund priority countries

South East Asia

We work through all of our Global
Grants in South-East Asia and host a
regional hub in Thailand managed
by Mott MacDonald. Our Fleming
Fund pilot project and early
investment project was hosted in
Vietnam, to support the learning
and development of the Country
Grants programme since 2015.
Gather existing AMR data from around the region
- Cambodia
- Indonesia
- Laos
- Myanmar
- Papua New Guinea
- Timor Leste
- Vietnam

Partners:
- NUS, PATH, & CDDEP

Digitise
- Support labs move towards routine LIMS / WHONET data entry

Quality grade datasets
- Provide feedback to improve quality where problems are found

Model

Map
- CCDEP ResistanceMap

Share
- Global Burden of Disease AMR project
ACORN: A Clinically Oriented AMR Surveillance Network

1. Harmonised AMR surveillance network
2. Data capture & visualisation tools
3. Clinical syndromes
4. Countries
5. Minutes per patient for metadata capture
6. Pathogens

Map indicating countries: Laos, Vietnam, Thailand, Cambodia, Indonesia

Technical Development | Surveillance roll out
Capture of clinical / lab data for ACORN

Patient with suspected infection → Specimen collected

Specimen collected → Request form completed

Request form completed → Laboratory work

Laboratory work → Empiric antibiotic

Empiric antibiotic → Definitive antibiotic

Definitive antibiotic → Infection episode outcome

Result entered into LIS / WHONET → Report issued to clinician

Report issued to clinician → Infection episode outcome

Data

Data

Data

Data
Making the most of AMR surveillance data...

- How can we facilitate data capture, harmonisation, transfer, visualisation, and use to achieve AMR surveillance goals through
  - Innovation in informatics
  - Creation of a range of tools which will also incentivise and facilitate data sharing
  - Compatible with GLASS but broader in scope

SEDRIC
Surveillance and Epidemiology of Drug Resistant Infections Consortium

Streptococcus pneumoniae