Bridging the gap between evidence and policy for AMR: How models can aid AMR containment decision-making

Gwen Knight
Associate Professor, Deputy Director AMR Centre

LONDON SCHOOL of HYGIENE & TROPICAL MEDICINE

RADAAR: Virtual Workshop – Southeast Asia

AMR containment decision-making

What do we want to know?

- where AMR is coming from?
- how much from where?
- what impact will different AMR containment decision-making have?
- what will it cost?

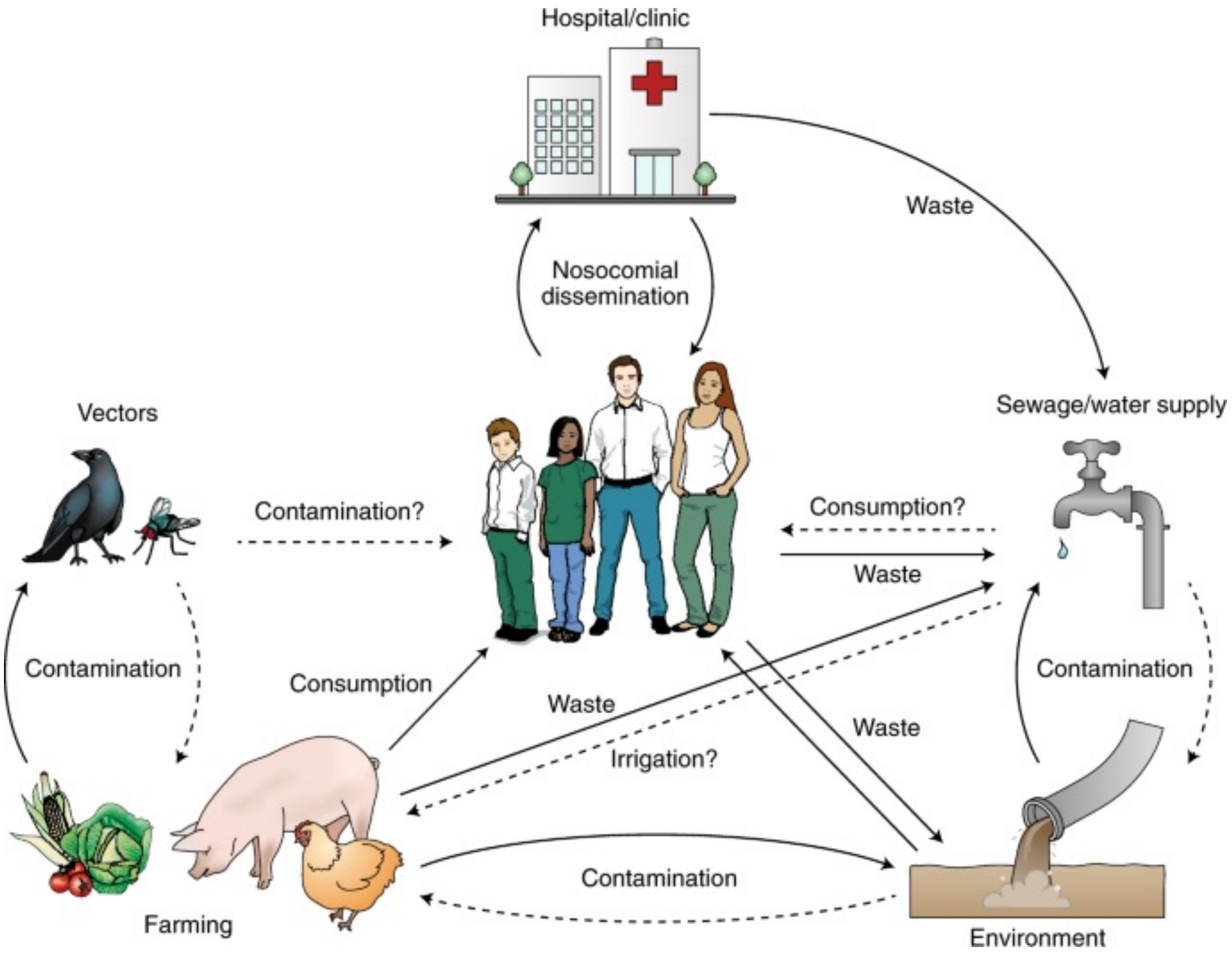
Not AMR are equal…

How can we find this out?

- data analysis
- statistical model frameworks
- mathematical modelling

What is a model?

AMR transmission model



Walsh, T.R. A one-health approach to antimicrobial resistance. *Nat Microbiol* **3,** 854–855 (2018). https://doi.org/10.1038/s41564-018-0208-5

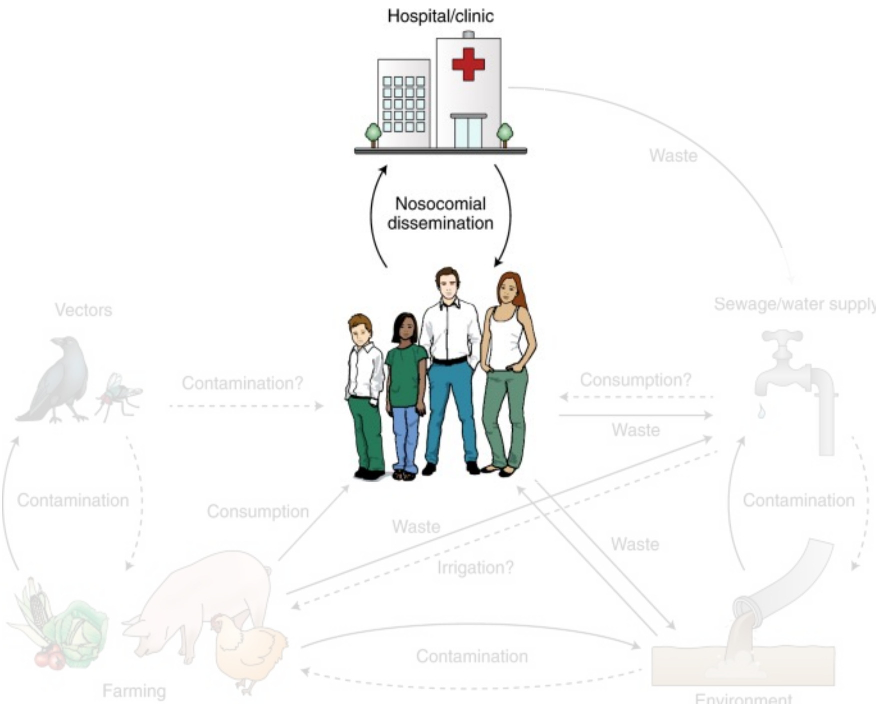
Case study

What are the risk factors for carriage of resistant bacteria?

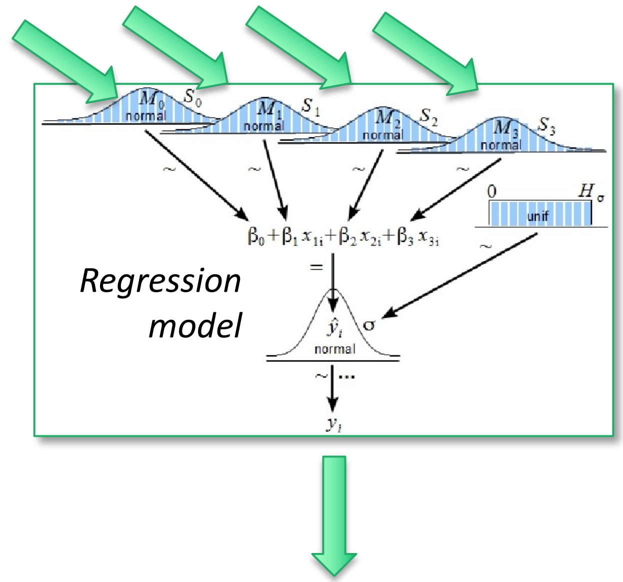
Example

- Bug: *Staphylococcus aureus*
- Resistance: Methicillin resistant (MRSA)
- Setting: Europe
- Problem: MRSA transmits between humans in hospitals (“model”), but getting more MRSA infections in community
- Question: How much is linked to hospital transmission?
- Policy:
    - Hospital linked: target control there.
    - Not hospital linked: where is it coming from? What can we do about this?
- Method:
    - Statistical modelling to extract the contributions of different risk factors

AMR transmission model



Risk factors

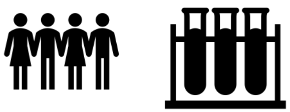


Carriage of AMR

Statistical modelling

DATA

Samples



MRSA

Demography

Medical records of antibiotic usage & healthcare contact

Multilevel modelling

Risk factors	Model 1: AMR	
	No resistance (0) versus resistance to at least one antibiotic (1)	
	OR	95% C.I.
Risk factors		
Age Patient (quartile 1 = ref category)	0.88*	0.82–0.94
Gender Patient (male = ref category)	0.97	0.85–1.11
Number of GP visits (0 visits = ref category)	1.13	1.00–1.28
Work: Nursery	0.84	0.54–1.29
Work: Health care	1.03	0.78–1.37
Work: Livestock	1.08	0.70–1.66
Living with children (no = ref cat)	1.18	0.96–1.45
Skin condition	1.0	0.79–1.26
Prescriptions Total (quartile 1 = ref category)	1.04	0.94–1.15
% Penicillin (quartile 1 = ref category)	1.09*	1.00–1.18
Random effect		
Country level variance (SE)	0.148 (0.08)	
Practice level variance (SE)	0.034 (0.024)	
Intercept	1.168 (0.241)	

*significant p<0.05

doi:10.1371/journal.pone.0135094.t002

Evidence

Penicillin use at the GP level

Variation between countries

Implications for policy

Target primary care use

National plans

van Bijnen EM, Paget J, de Lange-de Klerk ES, den Heijer CD, Versporten A, Stobberingh EE, Goossens H, Schellevis FG; collaboration with the APRES Study Team. Antibiotic Exposure and Other Risk Factors for Antimicrobial Resistance in Nasal Commensal Staphylococcus aureus: An Ecological Study in 8 European Countries. PLoS One. 2015 Aug 11;10(8):e0135094. doi: 10.1371/journal.pone.0135094. PMID: 26262679; PMCID: PMC4532423.

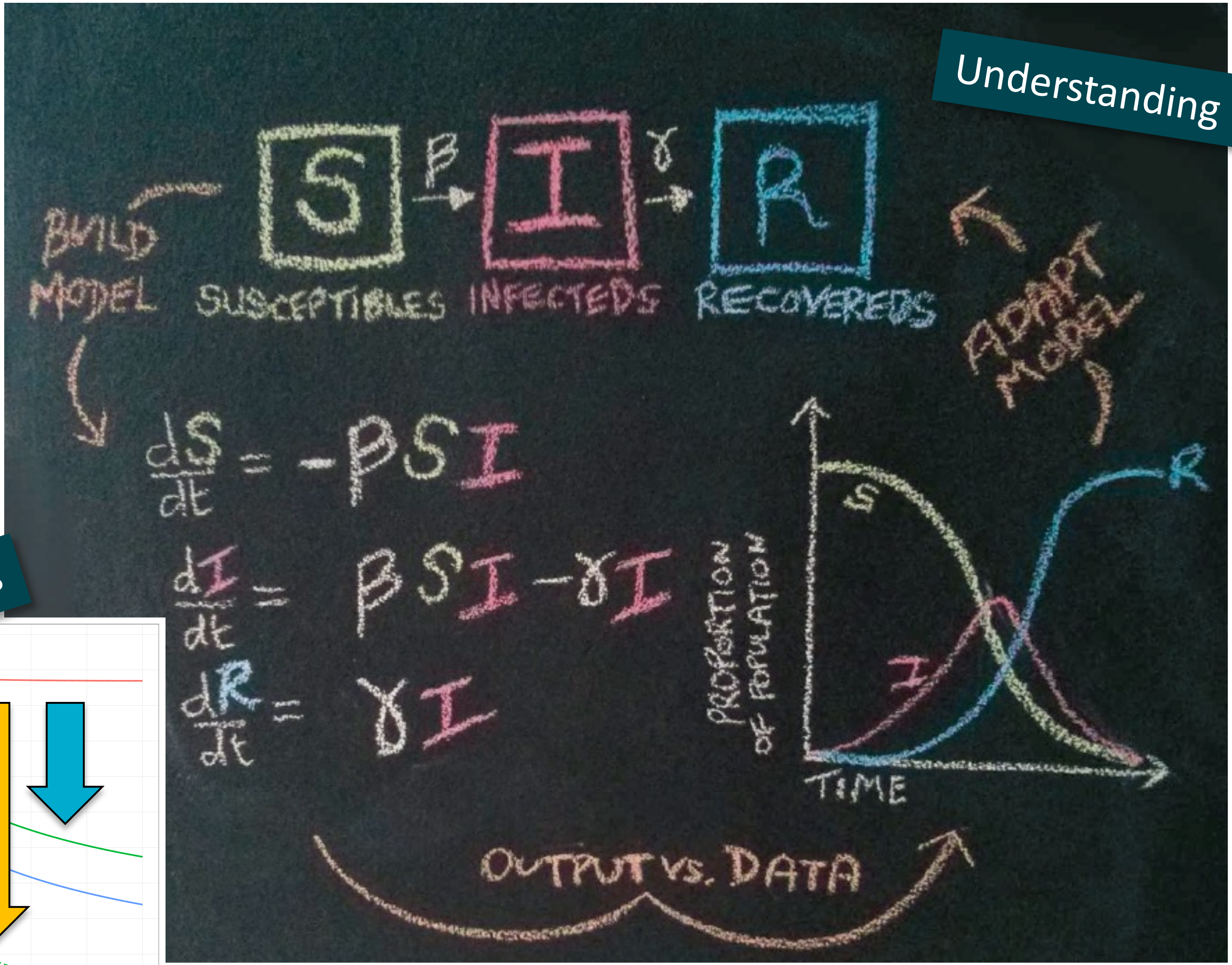
Case study

How many people carry drug-resistant bacteria?

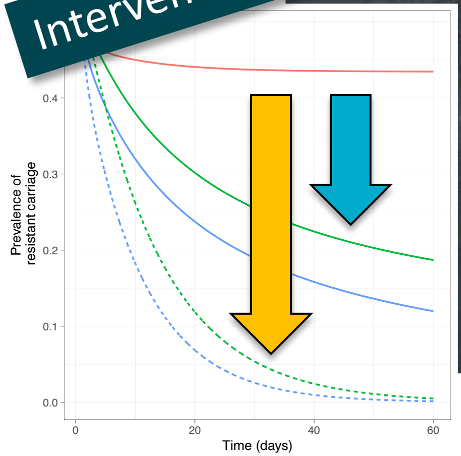
Example

- Bug: *Mycobacterium tuberculosis*
- Resistance: Multi-drug (INH/RIF) (MDR-)
- Setting: Global
- Problem: Cannot sample the bacteria causing latent infection, but big risk factor for subsequent diseases.
- Question: How much latent infection is with MDR-TB?
- Policy:
    - Who should we give prophylactic therapy to?
    - Where is MDR-TB coming from? Latent reactivation?
- Method:
    - Mathematical modelling
    - Trend data analysis + cohort simulation model

Mathematical modelling



Interventions

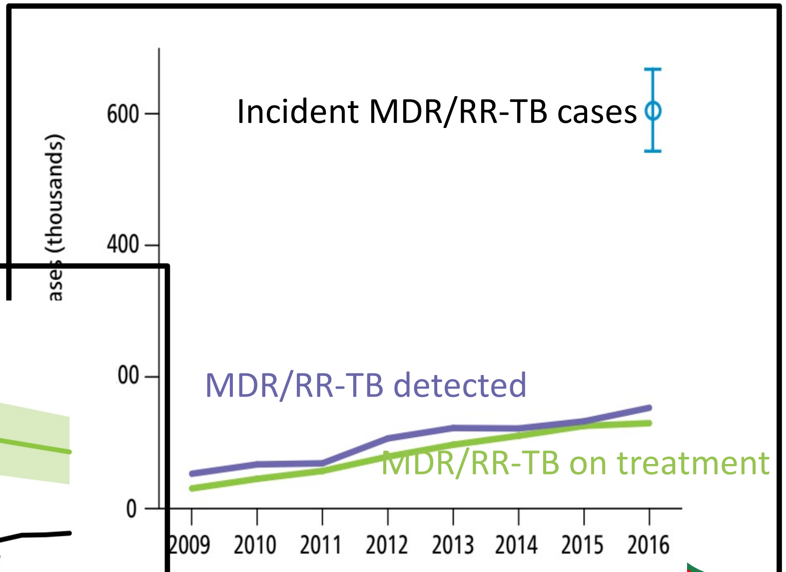


Decisions

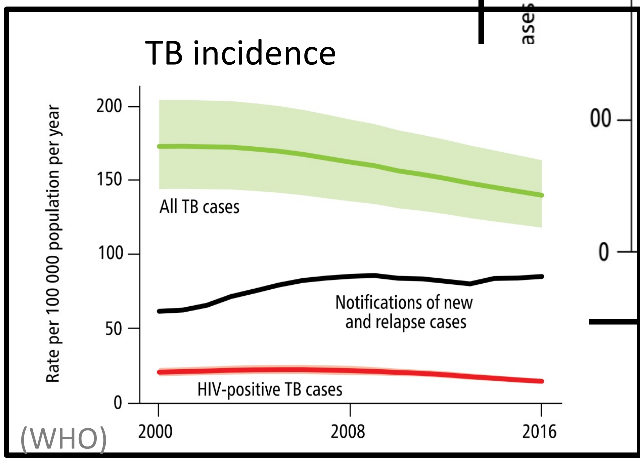
Mathematical modelling

How much latent infection is with MDR-TB?

MDR-TB going up

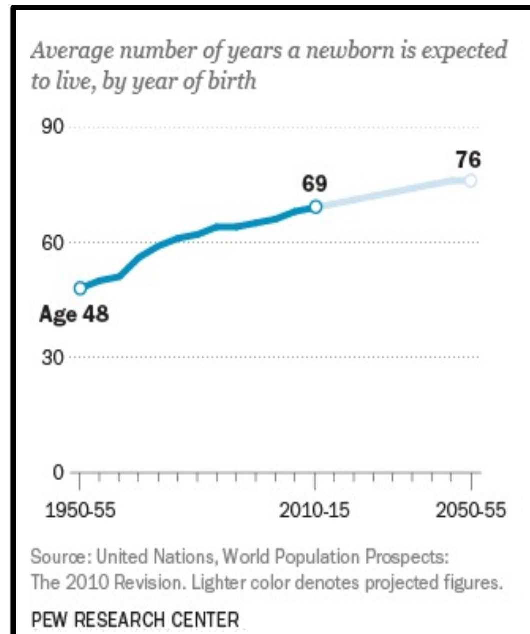


TB burden going down

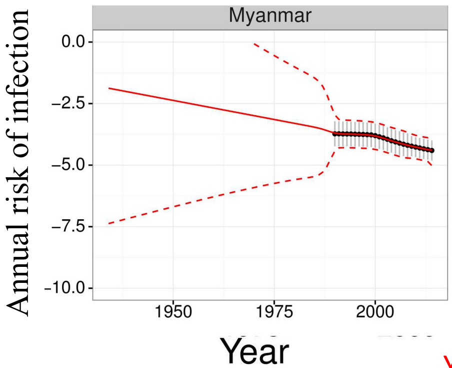


80% protection from re-infection

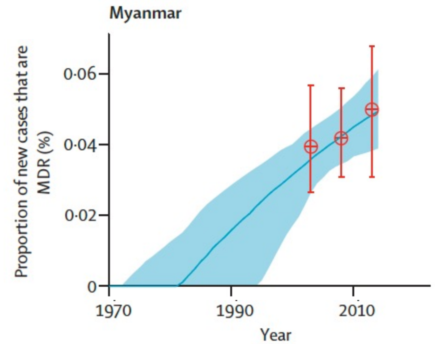
Age going up



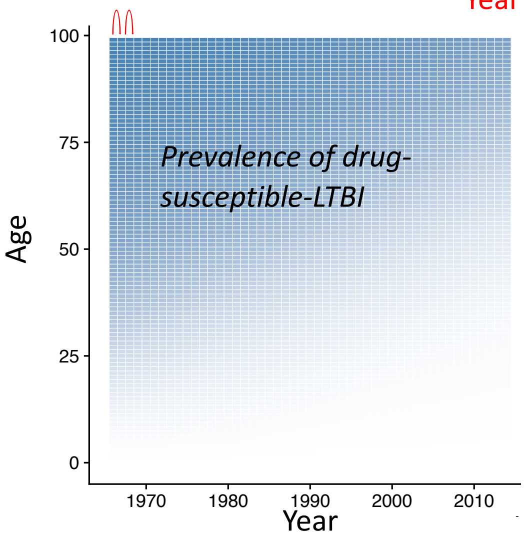
MDR-LTBI burden

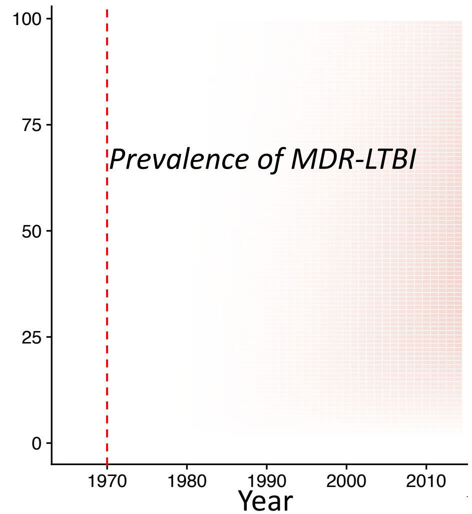


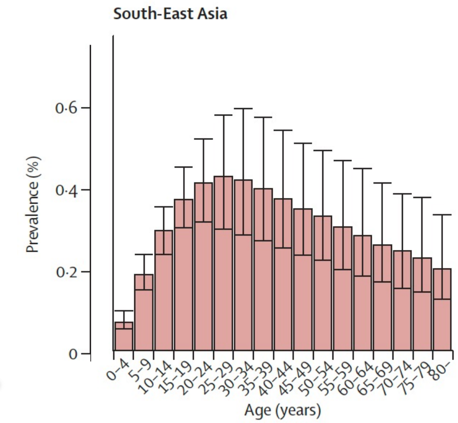
Apply ARI to age structured cohort model

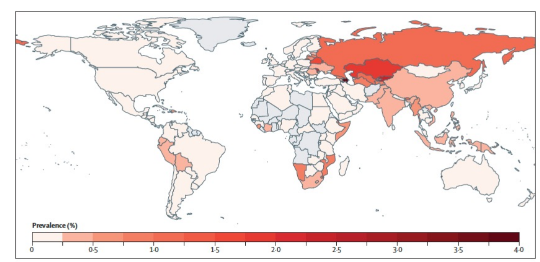


Year TB treatment introduced









Evidence
Younger ages high MDRLTBI
3/1000 carry MDRLTBI

Implications for policy
Age based
To tackle TB need to tackle latent

Knight GM, McQuaid CF, Dodd PJ, Houben RMGJ. Global burden of latent multidrug-resistant tuberculosis: trends and estimates based on mathematical modelling. Lancet Infect Dis. 2019 Aug;19(8):903-912. doi: 10.1016/S1473-3099(19)30307-X. Epub 2019 Jul 4

Modelling for AMR containment decision-making

- Modelling provides the link between data and evidence for decision making

- Complex relationships can be written in a concise and precise way
  And analysed with existing methods to generate clear results

- Rigour of mathematical / statistical model supports better decision making (e.g. uncertainty quantification)

- Important to know what the problems are and the appropriate or relevant data to collect for what decision-making evidence

Conclusion

We all have models of how things work – writing them down mathematically improves their quality and our understanding of the world

Thanks to MDR-LTBI co-authors: Rein Houben, Finn McQuaid, Pete Dodd

gwen.knight@lshtm.ac.uk

Any questions?