RESIST2 :

Interventions

Can mathematical models determine what would be the most effective intervention (infection prevention control/vaccine) or place to intervene in the drivers of resistance? Which interventions should we fund? - A key policy question that modelling has a long history of helping due to its integration of different data sources, such as economics.

Emulating a target trial with observational data: an application to estimating mortality of delays in concordant antibiotic treatment for bacteraemia accounting for time-varying confounding and immortal time biases

[Cherry Lim, Wellcome Trust Training Fellow
DPhil Student of Clinical Medicine, Oxford University]

Using mathematical modelling and observational data to look at the impact of delaying concordant antibiotic treatment on mortality.

Advantages with using observational data:
- Useful source of data when randomised controlled trial is not feasible/ethical
- Sample represents the "reality" better than that from randomised controlled trial
- Large sample size is achievable

Does delaying concordant antibiotic treatment impact patient's survival in a low- and middle- income country setting?

Designed target trials → **Identified key variables** → **Applied weights to individuals and create pseudo-population** → **Applied model to pseudo-population**

What we learnt
- Emulating target trials to evaluate impact of discordant antibiotic can be a useful tool to disentangle the causal relationship between empirical antibiotic use and mortality
- Appropriate analysis to adjust for potential biases arising from data is important to estimate the causal relationship between exposure and outcome

Gaps / what we don't know
- We need a good balance between access and excess of antibiotics, also taking into account the duration of treatment, admin route, dosage and frequency of antibiotic treatment.
- A cost effective analysis on over prescriptions to support the design of empirical antibiotic guidelines, based on local data that can reflect the local epidemiology of AMR infections and patient characteristics is needed.
- We need detailed data on patient characteristic and severity of infection from LMICs

How to use modelling to select efficient policies?

[Nichola Naylor, Research Fellow of AMR, LSHTM &
Senior modeller at the UK Health Security Agency]

How do we use modelling to select efficient policies and interventions to tackle AMR?

A framework was developed to look how modelling and wider evaluation tools can be used to evaluate AMR from a One Health (OH) and cross-sectoral perspective.

Aims:
- Collate and describe previous methods used in the quantitative evaluation of interventions related to OH and other cross-sectoral issues
- Offer an explicit approach for evaluating such interventions, and apply this approach to the case of AMR-related interventions

Results:
- 75 Individual evaluations & 16 reviews
- Spanning climate change, vaccinations, zoonic diseases and AMR
- Narrative discussions of methods & outcomes used to help build a framework to help select efficient policies

Outlining the interventions, considering the stakeholders and their objectives within your system, tailoring your economic models to get an outcome that fits into those objectives, allows us to then rank interventions across different factors.

What are the gaps and challenges?

Data Inputs
- Basic epidemiological and economic inputs (e.g. with GRAM & WHO VAF studies)
- Intervention trial data (how to scale this?)
- Expand data sharing and access

Modelling Processes
- Open access and good documentation
- Participatory and explorative processes

Modelling Outputs
- Knowledge mobilisation
- Working with experts; software engineers, communication managers, artists

Within-host models to designing resistance-reducing therapies

[Alison Hill, Assistant Professor
Johns Hopkins University]

AMR evolution occurs on multiple scales
AMR is a worldwide problem. But despite its global scale, all infections first occur (and all drugs are first administered, thus all drug resistance first takes place) within individual hosts or patients - before it can potentially spread between individuals in a population and eventually become a global problem.

Understanding how the natural history of infection and the way in which we prescribe treatments (inc. how these treatments are actually taken and the evolutionary landscape of a pathogen) are all critical to understanding how resistance risk emerges and how we can prevent it from arising in the first place.

Challenges to modelling within-host therapy and AMR

- Pathogen population structure
- High resolution longitudinal data (+ across transmission chains)
- Role of immune system (+ benefit of immunotherapy)
- Available resistance pathways
- Acute vs chronic infections - drug resistance is also an important issue for many acute infections

Using mathematical models to understand how this dynamic interaction between infection (and therapeutics used to treat infection) impacts the risk of resistance within individual patients is key.

Models show how we can bring together a lot of diverse data sources, such as laboratory characterisation of resistant strains, pharmacological data on drug levels and knowledge of host pathogen interactions in order to make better predictions.

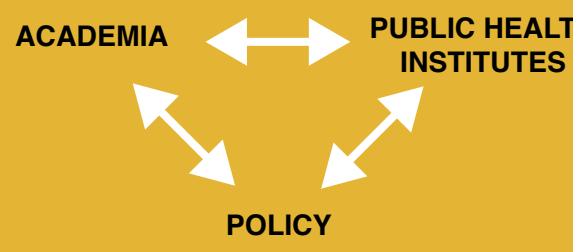
How to use modelling to select efficient policies?

[Alice Ledda,
Senior Infectious Disease Modeller,
UK Health Security Agency]

How different is modelling for policy in academia versus in public institution?

Academia
- Start with the question
- Choose your collaborators
- Develop data and model
- Combine these together to learn something new
- Use this to inform policy

Public Health
- Start with a public health problem, something that's not working, or just a question.
- Bring together the question, the samples, and the data.
- Model
- Find something actionable to put it back into policy.



We can find a balance between deciding pragmatic, simplifying assumptions for AMR versus building in a full realistic model complexity.