RESIST2 : TRANSMISSION

How did transmission to this patient happen? A bacterium, either a susceptible strain which later mutates to gain resistance, or a strain with a resistance-conferring gene, has to somehow arrive to colonise a patient. Symptom-free carriage is likely to occur in many patients before infection. Can we estimate the impact of interventions or the size of transmission using mathematical modelling?

Mathematical models should exploit the increasing data on cross-transmission between environments to estimate the relative contribution of different AMR transmission hotspots and hence support intervention design

Resistant bacterial colonization in neonatal intensive care units

Julia Bielicki
MD, PhD

The Problem:

- High rate of at risk care
- Greater crowding due to presence of accompanying carers
- Care needs require extensive physical contact

Transmission and acquisition networks in NICU: If you introduce a baby into this environment in the presence of a colonised infant, you get silent chains where babies transmit resistant bacteria to other babies. Most infants will not go on to be sick, but they may eventually spill the bacteria further into the unit environment and then also into the community.

Recommendations:

- Unit-level intervention investigated
- Participation of all babies on the unit
- Frequent testing of all babies to capture colonisation and transmissions
- Sequencing to identify transmission events

Challenges:

- Ethical barriers high for clinical trial involving extremely vulnerable population
- High-volume microbiological assessment costly
- Whole genome sequencing following traditional microbiological testing may not focus on isolates of interest

Key questions for transmission modelling

- From incomplete data, can transmission routes and levels be inferred?
- What hotspots and hence what interventions can be identified and evaluated without compromising

Mathematical modelling can help

Drug Resistant TB Household Contact Management in Children

The Problem:

- Drug resistant TB is an important component of AMR (30% of deaths)
- ~0.5 Million cases annually, 38% enrolled on treatment, 57% of those successfully treated
- >30,000 cases in children, with case detection ratio at best ~19%
- Most DR-TB resulting from transmission rather than acquisition
- Substantial proportion of children infected in their households
- Nearly 8% of household contacts of DR-TB had co-prevalent TB, nearly 50% had infection
- Proportion of cases attributable to household transmission likely to have risen as a result of COVID-19

Finn McQuaid
PhD

Should we be advocating for wider coverage of drug resistant TB **household contact management (HHCM)?**

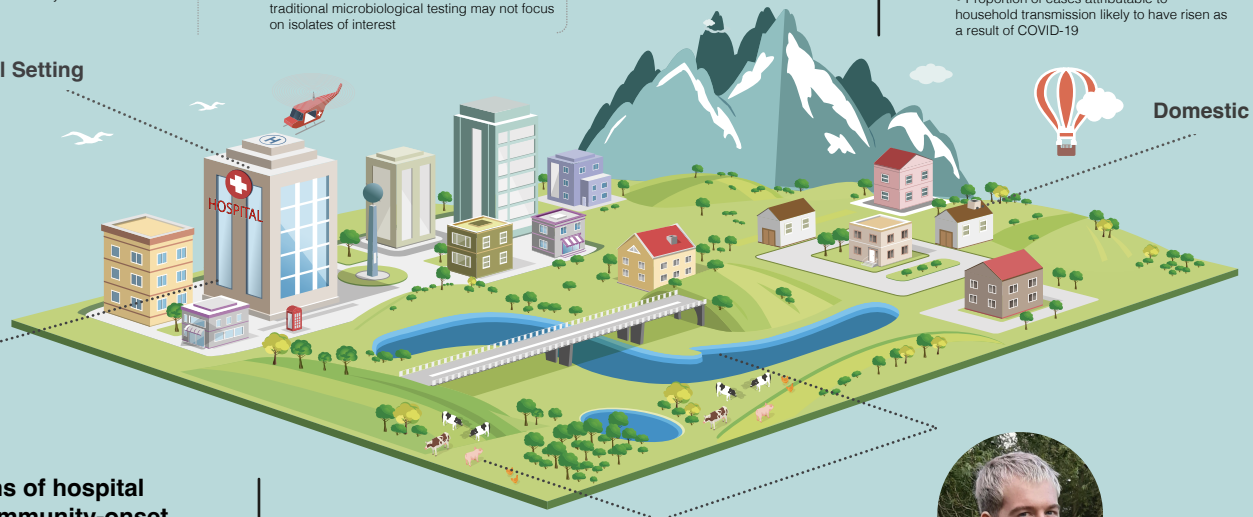
How can modelling be useful:

- Explore the impact of HHCM for DR -TB on transmission
- Estimate the effect on patient cost & equity (particularly as these are DR-TB-affected households already)

Key questions:

- How does a changing DR-TB and treatment landscape affect this?
- How do we best improve drug susceptibility testing coverage (& how important is concordance)?
- How should we prescribe empirically where coverage is low?

Nina J. Zhu
PhD, MPH, MSc, BEng



Hospital Setting

Hospital Setting

Domestic Setting

Changing patterns of hospital -acquired and community-onset infections in the COVID-19 context

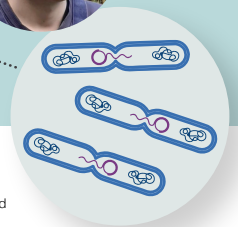
Background:

Using modelling to explore questions like the impact of COVID-19 on AMR.
Research has four policy streams:
- Priority pathogens
- Precision prescribing (aimed at optimising antibiotic treatment)
- Practice, design and engineering
- Population health and policy

> "Plasmids often carry clinically important antibiotic resistant genes, so understanding their evolutionary histories is crucial to managing resistance as a whole."

Human bloodstream infections, livestock, wastewater, and waterways

Will Matlock
DPhil student



Enterobacterales-associated plasmid sharing amongst human bloodstream infections, livestock, wastewater, and waterway niches: a genomic surveillance study in Oxfordshire, UK

Case study:

Monitoring hospital-acquired bloodstream infections. Analysis of microbiology data of Imperial College Healthcare NHS Trust patients revealed increases in hospital -acquired bloodstream infections in both COVID-19 and non-COVID-19 patients during COVID-19 waves. We are exploring the role of multidrug-resistant organism carriage.

Gaps and challenges

- How to identify and address the gaps in surveillance coverage (e.g. patient populations, settings, locations, and time periods) across the health economy?
- Why is data linkage not more widely established, across sectors and patient pathways?
- How can we fully exploit what is currently available in terms of linked data and scale up good practice?

Summary:

- Plasmid sharing across human and non-human niches in *Enterobacterales* is not uncommon
- Different plasmid clusters have different dynamics
- We need new ways of interrogating plasmid evolutionary histories
- The next step - mathematical modelling of different plasmid types (of potentially different backbones) to determine where we need to focus our surveillance in the future.

Method:

To address these limitations and better explore the overlap in plasma diversity and sharing across niches, a geographically and temporally restricted sample was assembled. This comprised of large isolate collections from human bloodstream infections, livestock, wastewater, and waterway niches in Oxfordshire between 2008 and 2020

The Problem:

The extent to which important species of *Enterobacterales* and mobile genetic elements are shared across human and non-human niches remains poorly understood. Previous studies are often:
- Limited in size given the genetic diversity in these niches
- Restricted to single species or phenotypes
- Have not fully evaluated the dissemination of mobile genetic elements