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“Population simulation modeling to guide product development, evaluation, and scale up”

How population modeling can contribute to the LA field – what does individual-level data mean for the population at large?

Process map.

Light bulb is science and innovation (preclinical and clinical development).

Around the light bulb are stages where we can link in population simulation modeling.

Understand the epidemiologic context.

Much of what we know about epidemics arises from population modeling – informs what is going on, who is getting access to treatment and who isn't, routes of transmission, risk of death, etc.

Identify points of leverage.

Identifies targets with the most beneficial impact; Informs what we should be looking for across studies.

Assist evaluation design.

Informs the design and interpretation of studies.

Assess potential health impact of a new intervention.

Efficacy in an individual in a trial does not equate to population-level effectiveness.

Estimate the potential value of an innovation.

Often considers the opportunity costs, resource use, feasibility, equity, etc.

Epidemiological context and points of leverage – the most important things we need to understand about epidemics are not directly observable.

Modeling enables inference from disparate pieces of data to inform resource allocation.

- The route of transmission for most HBV infections is not readily apparent at the global level.
 - Modeling available data shows change over time, revealing that mother-to-child transmission is increasingly the main route of HBV transmission worldwide.
Prevention efforts should focus on birth dosing and treatment during pregnancy.
- Understanding low uptake despite availability of HIV prevention innovations in rural Zimbabwe.
 - Modeling estimates the number of avertable HIV infections among different demographics (i.e., the technology is available to the people at that location, and if used the new cases of HIV infection could have been averted).
 - The main reasons for low uptake were then examined, revealing knowledge, motivation, and fear as targets for intervention.
LA HIV PrEP could overcome some of these barriers.
- Which global priority is the most powerful in reducing HCV incidence and mortality?
 - An enormous model representing HCV epidemics in every key population in the world identifies three global priorities (general population risk reduction; PWID harm reduction coverage; and proportion diagnosed).
 - The proportion diagnosed demonstrates the steepest gradient in HCV incidence and mortality.
Diagnosis is a massive point of leverage for the HCV epidemic and should be the focus of research and innovation.

Evaluation Design.

A priori modeling is increasingly being used to determine P3/P4 study design and project outcomes.

- HPTN Modelling Centre is devoted to understanding the dynamics that study interventions are going to have.
- Modeling informs power, design, maximum correlation between communities, and data that need to be captured to make inferences for the future.
- HPTN 071 PopART trial – Projected outcomes of universal testing and treatment in a generalized HIV epidemic in Zambia and South Africa.
 - Modeling added considerable interpretational clarity – untangled study arms and made a projection about what would happen if that intervention were to be implemented over time.

Potential health impact of a new intervention.

The population-level impact always seems to be less than what people hope.

- HPTN 052 trial results.
 - The Economist thought that ART would be the end of AIDS based on the large reduction in HIV transmission, yet it wasn't.
- In extrapolating an individual trial result across a population over time, population modelers must consider:
 - Population heterogeneities among behaviors, access, and risk.
 - Feasibility and frailties of real-world implementation given the epidemiological/program context.
 - Knock-on effects.

Beware of the trap – the best intervention is the one that isn't quite here.

- When HIV PrEP was on the horizon, we modeled the beneficial health impact, and now years of studies have revealed the difficulties of real-world implementation.
**Before an intervention is here, all the weaknesses are not apparent.*

Potential value of a new intervention – cost-effectiveness is not always obvious.

Value-based pricing – a simple definition using health gain and cost.

- Incorporating a new intervention (health gain and cost) into a health system with finite resources means an existing intervention (health gain and cost) will be displaced.
- A net health benefit means the displaced intervention is being replaced with something better.
Need health gain of the new intervention > the health gain of the displaced intervention.
- Cost-effectiveness is required for a product to be usable and accessible, thus the health benefit is a function of the cost for the whole intervention (C).
 - Provider point of view (i.e., the State): The greater the health benefit, the higher the cost can be.
*Need Health gain – C/normalizing threshold (CET) > 0; therefore C < Health Gain * CET.*
 - Very setting-specific: depends on intrinsic product value and what else the healthcare system is doing.
**LA products will have the greatest public health impact in places where the C-value is very low.*

Additional value considerations – a broader definition that is normally used.

- Cost to patients (co-pay; time out of their lives; transport costs; difficulty finding childcare).
One-shot cures, LA therapies, and less contact with healthcare system are beneficial to patients.
- Health equity (often an explicit aim of healthcare systems in LMICs).
A special value is attached to LA products that help populations access care that wouldn't otherwise be able to.
- Financial risk protection (prevent down-the-line costs related to treatment, complications of acquiring disease, and palliative care).
A special value is attached to interventions for prevention.
- Return on Investment (assigns a dollar amount to all the benefits of a new intervention).
 - Instrumental value of health approach: Reductive way of thinking about health.
My investment in the intervention is leading to economic growth (the person will now be able to work/contribute to the economy).
 - Intrinsic value of health approach: Survey-based estimates that often yield eye-catching values.
The value that beneficiaries themselves place on the reduced risk of having the disease (i.e., what they would pay for the intervention/cure, if they could).
**Used by GAVI or the Global Fund to make their case for the investment.*

Summary.

- LA products from the first plenary session are at different stages along the development pipeline.
 - How could modeling be linked into that?
- Would be interesting to use population modeling for LA HCV treatment.
 - Designing a TPP for that kind of product, then exploring its value-based pricing, ROI, contribution to health equity, etc.