HIV prevention policy and programme planning: What can mathematical modelling contribute?
Hankins, Catherine

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Summary

This thesis explores the potential contribution of mathematical modelling to informed decision-making on policy and programme planning for novel HIV prevention tools. Its hypothesis is that, under certain conditions, modelling results can be a useful addition to the evidence and other factors that influence the HIV prevention policy and programme development process. The emerging HIV prevention tools that serve to illustrate this are voluntary medical male circumcision (VMMC), systemic pre-exposure prophylaxis (PrEP) with antiretroviral drugs, HIV vaccines, and structural interventions for people who inject drugs (PWID).

Chapter 1 sets the stage, beginning first with some basic background on the state of our knowledge about how HIV attacks the immune system, how many people live with this retrovirus worldwide, and what we understand about the importance of tailored, combination HIV prevention. It then summarises the current evidence on emerging biomedical HIV prevention tools, with a focus on VMMC, PrEP, and HIV vaccines, before introducing the theme of the potential contribution of mathematical modelling to evidence-informed decision-making about novel HIV prevention strategies.

In Part 1, Background to the HIV epidemic and HIV prevention, Chapter 2 provides an overview of changes in the state of the global HIV epidemic and is followed by two chapters that define combination HIV prevention. The first refers to its broad meaning of combining biomedical, behavioural, and structural HIV prevention components (Chapter 3) while the second focuses on the more narrow concept of combining components of biomedical HIV prevention (Chapter 4).

Part 2 Voluntary Medical Male Circumcision: Policy Background presents the example of male circumcision (MC) for HIV prevention as a new HIV prevention technology, albeit possibly the oldest surgical procedure in the world and one that has been undertaken heretofore primarily for cultural, social, or religious reasons. It covers some of the inputs to policy making on MC scale-up, including the scientific evidence (Chapters 5 and 7), the sociolegal barriers (Chapter 6), male circumcision and HIV risk for women (Chapter 8), and factors influencing country adoption and scale-up of VMMC (Chapter 9).

Part 3 Voluntary Medical Male Circumcision: Costing and Modelling discusses the contribution of mathematical modelling and costing to decision making on VMMC for HIV prevention (Chapter 10), including the result of practical application of the Decision Makers Programme Planning Tool in 13 priority countries (Chapters 11-12) and the challenge of costing demand creation activities (Chapter 13).

Part 4 Pre-Exposure Prophylaxis outlines the promise of PrEP (Chapter 14) and presents a systematic review of oral PrEP cost-effectiveness studies that
concludes that prioritising key populations at highest risk of HIV acquisition would likely be the most cost-effective strategy (Chapter 15).

In Part 5 *Vaccines*, the findings of 5 modelling teams are analysed. These modellers explored the potential population impact of an HIV vaccine regimen similar to that of the RV144 regimen that had shown moderate effectiveness in a community-based trial in Thailand (Chapter 16).

Part 6 *Structural Interventions* presents mathematical modelling-derived results estimating the impact on HIV incidence of increasing coverage of needle syringe programmes, opioid substitution treatment, and antiretroviral therapy among people who inject drugs in Odessa (Ukraine), Karachi (Pakistan), and Nairobi (Kenya). It also estimates the impact of alleviating key structural barriers to the uptake of risk reduction measures (Chapter 17).

Chapter 18 highlights lessons drawn from this body of work about how mathematical modelling can contribute to policy formulation and programme decision-making on novel HIV prevention tools. The most salient example is the body of VMMC modelling work and its practical application in a useful programme-planning tool. The systematic review of PrEP modelling sends a signal that factors such as context, adherence, and coverage clearly influence cost-effectiveness, suggesting that this is an HIV prevention tool that should be tailored specifically to those most likely to benefit. The HIV vaccine modelling provides a measure of encouragement to a field that has a first proof of concept result, but one of low efficacy with wide confidence bounds. The modelling work undertaken for the Lancet series on injecting drug use in 2010 breaks new ground in its effort to assess the potential impact of interventions to address structural determinants of HIV risk.

The convening of modellers to address the impact of emerging biomedical HIV prevention trial results began in 2005 and eventually involved three VMMC modelling meetings (Geneva in 2005, Stellenbosch in 2007, and London in 2008); two PrEP modelling meetings (Geneva in 2010 and Montreux in 2011); and an HIV vaccine modelling satellite (Atlanta in 2010). In presenting their work, modellers received constructive criticism from researchers and public health practitioners about unrealistic parameter values, including assumptions about sexual behaviour, timing of introduction, speed of scale-up, and maximum coverage levels that could be achieved, among others. As more trial data emerged along with context-specific information on sexual practices, HIV prevalence, HIV incidence, and costs, they populated well-constructed models that were increasingly able to shed light on the cost and epidemic impact of different HIV prevention programming options over the short-, medium-, and long-term. Comparing model structures and findings, including the results of sensitivity analyses, through consensus processes, systematic reviews, and other methodologies served to strengthen the potential contribution that modelling could make to HIV prevention policy.
Looking forward, integrating mathematical modelling in the design, conduct, and analysis phases of the large cluster randomised combination HIV prevention trials that are now underway will potentially facilitate trial adaptations, such as accelerated roll-out or modified trial duration, to reduce the likelihood of inconclusive trial outcomes. Modelling will increasingly be useful to biomedical HIV prevention trial design, given the evolving standard of prevention being offered to all trial participants. Populating mathematical models with up-to-date, context-relevant, and accurate information will remain a key challenge, along with effective knowledge translation strategies. Engaging policy makers from the start can help ensure that modelling addresses relevant policy questions, is informed by the best available locally available information, and finds a receptive audience when results are presented.

This thesis concludes that modellers can play an important role in evidence-informed policy making and programme planning processes. They can generate modelling results on questions of key importance that provide insights into the potential impact of competing HIV prevention scenarios in the context of constrained resources. In effect, they can paint pictures for policy makers of the paths that can lead to a future in which HIV transmission is increasingly rare.