Mapping pathways to HIV prevention
Developing evidence-based, people-centred strategies for the use of antiretrovirals

Some 34 million people worldwide live with HIV, and the human and economic costs impose a heavy burden, particularly on the world’s poorest countries. Over 2 million new infections are reported each year, and existing prevention options such as condoms, counselling, testing and needle exchange have not fully stemmed the tide. Clinical trial data show great promise for antiretroviral (ARV) drug-based strategies to fight HIV. However, the science is rapidly evolving and real-world implementation is complex, shaped by local political and social circumstances.

Mapping Pathways is the first study of its kind to synthesise evidence and views about ARV-based prevention strategies in diverse global contexts, looking at South Africa, India and the United States. Six partner organisations collaborated to review the social, economic and clinical impacts of four strategies: Testing, Linkage to Care Plus Treatment (TLC+), which provides linkage to care and the offer of earlier treatment for HIV-positive people; pre-exposure prophylaxis (PrEP), which provides ARVs to HIV-negative people to prevent transmission; microbicides, topical ARV-based applications, also for use by HIV-negative people to prevent HIV transmission (still in development); and post-exposure prophylaxis (PEP), which offers ARVs to people with a recent possible exposure to HIV. Our aim is to provide a resource for communities and policymakers that brings together evidence, voices and views about ARV-based prevention strategies in a manner that lays out a future agenda for policymaking and further research.

Integrating scientific and societal perspectives
We used four complementary methodologies to provide ‘snapshots’ of a rapidly evolving scientific landscape and its implications in the three countries. A systematic review of published literature was an essential starting point to understand the scientific evidence base and highlight knowledge gaps. We analysed 520 articles, 40 per cent of these published since 2011, illustrating the dynamic nature of the field. To further explore the evidence, we sought the views of a multidisciplinary panel of HIV experts from the three countries, using an iterative Delphi-based ‘ExpertLens’ approach to stimulate online debate and insights on patient-related, social, economic and clinical delivery conditions.

Key insights on ARV-based prevention:
- **Structural factors** such as cost and access are as important as individual behaviours
- **Policymakers and communities need more information** to develop successful local strategies
- **Local context** shapes perception: the same scientific data will be viewed and interpreted differently by stakeholders in different countries and groups

A ‘grassroots’ survey captured views and experiences from 1069 community members who were living with or alongside people with HIV, or helping to deliver HIV services, in order to understand the practical challenges of implementing strategies in different contexts. At the ‘grasstops’, we conducted semi-structured interviews with 38 policymakers and public health stakeholders to clarify the concerns and evidence needs of a group facing new choices as a result of rapid scientific advances.

All science is local
The evidence snapshots from this project highlight the importance of local views and the need for a multidisciplinary approach to understand why different strategies may or may not be effective in a particular community. Context is critically important; for example, the favourability of the four strategies for the grasstops varied markedly by country (see Fig. 1).

The literature review highlighted the dominant role of clinical trials in shaping current policy. We found a strong focus on efficacy – in terms of trial or laboratory results – but significantly less evidence on real-world effectiveness. Since behaviour and adherence are central to success, along with factors such as cost, access, drug resistance, side effects and health system capabilities, further research is needed into the conditions that should now shape community-based ‘trials’.
Developing evidence-based, people-centred strategies for the use of antiretrovirals as prevention

Mapping Pathways is a community-led initiative to synthesise evidence and views on the social, economic and clinical impacts of four prevention strategies based on antiretroviral (ARV) drugs in South Africa, India and the United States.

New approaches to prevention are needed

What does the literature say?
- Clinical trial results play dominant role in shaping current policy
- Strong focus on efficacy, limited evidence on effectiveness
- Behaviour central to success
- Further research needed to clarify implementation

What are the ‘grassroots’ perspectives?
- More info needed to make decisions on how/whether to adapt ARV-based approaches locally
- General support for ARVs as prevention
- Concerns include drug resistance, adherence, resource allocation, cost trade-offs, need for improved education, systems capacity
- Weight given to different concerns varied by country/context

What do policymakers say?
- Limited evidence available for policymakers to make decisions on ARV-based prevention
- Reluctance to make determinations from one study
- Generally positive, but science interpreted, framed and perceived differently based on local context:
  - India – most scepticism that efficacy would translate to effectiveness
  - South Africa – concerned about resource allocation, need for trade-offs
  - U.S. – most optimistic, willing to accept science at face value

What do the experts say?
- Online discussion forum harnessed group wisdom to explore faultlines in evidence
- Strong agreement science justifies more funding for earlier treatment
- Agreement on importance of adherence, biological reliability of ARVs; disagreement on importance of potential risk behaviour increase
- Little consensus on essential delivery conditions

Key insights on ARV-based prevention:
- Structural factors such as cost and access are as important as individual behaviours
- Policymakers and communities need more information to develop successful local strategies
- Local context shapes perception: the same scientific data are viewed and interpreted differently by stakeholders in different countries and groups

The science is dynamic and fast-changing. Providing insight from diverse communities and stakeholders will enrich policies to ensure that ARVs can reach their prevention potential at local and global levels.
The grassroots survey showed that people need more information to make appropriate local decisions. The weight given to different concerns varied by country, but the issues raised in each included possible effects such as drug resistance and adherence, resource and cost trade-offs, education needs and healthcare capabilities.

While grasstops leaders in all three countries were generally positive about ARV-based strategies, they were somewhat reluctant to make determinations on the basis of one clinical trial or study. The same scientific data were interpreted, framed and perceived very differently.

Stakeholders in India were most sceptical that efficacy in one clinical trial would translate to effectiveness on the ground, noting cultural barriers and complexity around treatment and testing. In South Africa, stakeholders were primarily concerned about trade-offs and resource decisions, while in the U.S. stakeholders interpreted the scientific data most optimistically.

The ExpertLens exercise highlighted key faultlines in the evidence base. The experts agreed that the scientific evidence justified more funding for TLC+ strategies, and also agreed on the importance of adherence and biological reliability. They disagreed on the implications of patient risk behaviours and on which delivery conditions were essential to success.

**An adaptive approach to innovation policy**

The scientific landscape is dynamic and fast-changing. Our approach to understanding the evidence base for future policy development is an inherently adaptive one. Our findings suggest we can develop much more tightly integrated understandings of both the scientific data about efficacy, which tell us whether recent innovations in the use of ARV drugs work or not, and the ‘social’, multidisciplinary data about effectiveness. This approach, drawn from innovation policy thinking, considers the interplay between ‘physical technologies’ such as drug protocols and trials, ‘social arrangements’ such as health clinics and community education, and ‘organisational frameworks’ such as regulation and funding. All three need to be complementary for any scientific innovation to be useful, appropriate and adaptable.

The next step is to work directly with communities to map locally driven but globally informed pathways to effective decisions about ARV-based prevention strategies. Iterative and reflexive knowledge exchange between communities will be captured so that real-world insights across diverse contexts can be shared. This will enrich each individual pathway and facilitate adaptive policy decisions to unlock the full prevention potential of ARVs. Strategies must be successful at a local level before they can have a global impact.
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