Maximising the effect of combination HIV prevention through prioritisation of the people and places in greatest need: a modelling study

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Summary

Background Epidemiological data show substantial variation in the risk of HIV infection between communities within African countries. We hypothesised that focusing appropriate interventions on geographies and key populations at high risk of HIV infection could improve the effect of investments in the HIV response.

Methods With use of Kenya as a case study, we developed a mathematical model that described the spatiotemporal evolution of the HIV epidemic and that incorporated the demographic, behavioural, and programmatic differences across subnational units. Modelled interventions (male circumcision, behaviour change communication, early antiretroviral therapy, and pre-exposure prophylaxis) could be provided to different population groups according to their risk behaviours or their location. For a given national budget, we compared the effect of a uniform intervention strategy, in which the same complement of interventions is provided across the country, with a focused strategy that tailors the set of interventions and amount of resources allocated to the local epidemiological conditions.

Findings A uniformly distributed combination of HIV prevention interventions could reduce the total number of new HIV infections by 40% during a 15-year period. With no additional spending, this effect could be increased by 14% during the 15 years—almost 100,000 extra infections, and result in 33% fewer new HIV infections occurring every year by the end of the period if the focused approach is used to tailor resource allocation to reflect patterns in local epidemiology. The cumulative difference in new infections during the 15-year projection period depends on total budget and costs of interventions, and could be as great as 150,000 (a cumulative difference as great as 22%) under different assumptions about the unit costs of intervention.

Interpretation The focused approach achieves greater effect than the uniform approach despite exactly the same investment. Through prioritisation of the people and locations at greatest risk of infection, and adoption of the interventions to reflect the local epidemiological context, the focused approach could substantially increase the efficiency and effectiveness of investments in HIV prevention.

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Introduction

HIV/AIDS remains one of the leading causes of death and disability in much of eastern and southern Africa.1,2 Fortunately, several important scientific advances in recent years have provided a set of interventions that are highly effective in reducing the risk of acquisition (male circumcision, pre-exposure prophylaxis [PrEP]) and transmission (early initiation of antiretroviral therapy [ART]).3-5 The UNAIDS Investment framework6 and the US President’s Emergency Plan’s Blueprint to achieve an AIDS-free generation7 highlight the need to prioritise effective interventions for populations that are at the greatest risk of acquiring and transmitting HIV. The Global Fund to Fight AIDS, Tuberculosis and Malaria has a new strategy that focuses on effect and key affected populations.8 However, evidence is needed to identify appropriate priority populations.

Data from many large household surveys in Africa have recently shown crucial new insights about the highly uneven spread of HIV. For example, across eastern Africa (figure I), there is remarkable heterogeneity in HIV prevalence, not only between countries but also within countries. HIV prevalence in the southwestern region of Kenya and the southern tip of Mozambique is as high as the national prevalence in South Africa, despite the country-wide prevalence estimate for Kenya being about two-thirds lower than that in South Africa and that for Mozambique being one-third lower.9,10 Within South Africa, the estimated provincial HIV prevalence ranges from 9-2% in the Western Cape to 27-6% in KwaZulu-Natal.11 At the same time, the prevalence among key population groups in extremely high.12-14 Despite a national prevalence of 17-9% in South Africa, HIV prevalence in sex workers can be as high as 60%,15,16 Across sub-Saharan Africa, HIV prevalence in men who have sex with men (MSM) is estimated at 18%, substantially higher than the 5% regional adult prevalence reported by UNAIDS.16 These observations

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believe earlier assumptions that all individuals would be at high risk of acquisition of infection in generalised epidemics, and suggest that it is imperative that we move beyond the notion of national epidemics and identify the populations and geographies in greatest need of intervention.

Kenya has a wealth of subnational data that shows the diversity of the epidemic across the country. We use those data to investigate the potential gains in the efficiency and effectiveness of investments focused on the people and places at highest risk, rather than a uniform, national approach.

Methods

Study design

We aimed to examine how a fixed amount of resources for HIV prevention can be used to generate reductions in the rate of new HIV infections using two forms of resource allocation. In the first, the rollout of particular interventions is uniform across the country. In the second, interventions can be focused on geographic or key affected populations that contribute to HIV strongholds.

This analysis requires three steps: (1) specification of the spatiotemporal course of the HIV epidemic in Kenya; (2) assessment of the effect and cost of uniform, national implementation of interventions; and (3) assessment of the optimum form of intervention when constructing programmes specific to each locality (county or city). The methods for each part are discussed in turn and further details provided in the appendix.

Specification of the spatiotemporal course of the HIV epidemic in Kenya

A dynamic mathematical model was used to represent the epidemic in every county or large city (in the case of Nairobi, Mombasa, and Kisumu) in Kenya. Building upon our previous work, the model represents the spread of HIV through sexual contact and tracks disease progression in HIV-positive individuals.

Information about the scale-up of male circumcision and of ART in every county was extracted from official reports. Information about the proportion of men and women that have casual partners and that buy or sell sex are assessed from national survey data. The proportion of MSM was informed from review of the literature and an extensive national mapping of key populations. The model was calibrated to these data and also to the available prevalence data, with the time-trend based upon the data from antenatal clinics and levels of prevalence informed by the most recent nationally representative household survey. For both sources of prevalence data, spatial interpolation techniques were used to generate local-level estimates.

The model includes four forms of intervention (table) and assumed that these can be provided to four population groups independently; female sex workers (FSW), other women, MSM, and other men. The table shows the key assumptions regarding the efficacy, cost, and coverage of these interventions. In the absence of compelling evidence to the contrary, we assume homogeneity in the individual-level efficacy of PrEP and early ART across the risk groups. The model is used to estimate the effect (defined as the number of infections averted during a 15-year period from the start of the intervention in 2015) and cost (approximated here by constant unit costs multiplied by the corresponding modelled estimate of consumption) for every possible permutation of interventions and population group in a county or city.
Assessment of the effect and cost of a uniform approach
Under the best circumstances for decision making at country level, the relative costs and effects of different forms of intervention when applied uniformly to the whole country are compared.

We identified the optimum intervention strategy for a given total cost through construction of health production functions. The health production function is created through plotting the cost and effect of all possible candidate strategies. We then remove those strategies that are subject to dominance (ie, provide less health return at a greater cost than an alternative strategy). Successive points that fall on the frontier (ie, are non-dominated) are then joined together by straight-line segments to form a piece-wise linear function. We call this the uniform health production function because decisions are made for the whole country.

<table>
<thead>
<tr>
<th>Interventions</th>
<th>Efficacy assumption</th>
<th>Coverage assumption</th>
<th>Range of unit cost considered</th>
<th>Default unit cost value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Voluntary medical male circumcision</td>
<td>Risk of acquisition for circumcised men 60% less than for uncircumcised men25,26</td>
<td>80% of eligible men</td>
<td>$30–120 per one man circumcised</td>
<td>$6025,26</td>
</tr>
<tr>
<td>Behaviour change communication</td>
<td>20% reduction in risk of acquisition for every low-risk person reached, 50% reduction in risk of acquisition for high-risk groups (MSM and FSW)</td>
<td>100% of the relevant population group</td>
<td>$5–80 per person per year reach</td>
<td>$10 in low-risk women and heterosexual men, $20 in FSW and MSM</td>
</tr>
<tr>
<td>Early ART (ART initiated at CD4 cell count &gt;350 cells per mL)</td>
<td>85% reduction in risk of onward transmission for a person on ART relative to others25,26</td>
<td>33% in low-risk women and heterosexual men, 66% in FSW and MSM</td>
<td>$250–500 per person on ART per year</td>
<td>$515</td>
</tr>
<tr>
<td>PrEP</td>
<td>75% reduction in risk of acquisition for a person on PrEP28</td>
<td>25% in low-risk women and heterosexual men, 50% in FSW and MSM</td>
<td>$100–1000 per person on PrEP per year</td>
<td>$25028</td>
</tr>
</tbody>
</table>

All interventions can be applied to all relevant groups, with behaviour change interventions, early ART, and PrEP for FSW, other women, MSM and other men, and voluntary medical male circumcision available to all men. In every case, these estimates were chosen to be consistent with the assumptions used in the UNAIDS Investment Framework analysis.5

MSM=men who have sex with men. FSW=female sex workers. ART=antiretroviral therapy. PrEP=pre-exposure prophylaxis. *Neither effect nor costs were discounted in the analysis.

Table: Interventions and assumed unit costs

For the ScapeToad application see http://scapetoad.choros.ch/index.php
Assessment of effect and cost of a focused approach

An alternative approach to programming would be to determine the allocation between localities by judging where those resources could be used to the greatest effect. Under this focused approach, counties and major cities are not constrained to receive the same set of interventions; instead interventions can be tailored to the local epidemiological setting. To simulate this approach, we first constructed local-level health production functions (within the same method as above) to identify those sets of interventions that maximise health returns for a given total cost with a location. We used these local-level health production functions to inform the allocation of resources between locations as follows: we first define a small increment in the budget for the whole country and for each locality and quantify the health returns that could be gained through the use of that increment using the local-level health production function. The potential health gains across localities are then compared and the increment allocated to the locality that can produce the greatest health gains (i.e., infections averted). These steps are repeated until a maximum value for the budget in the whole country is reached. In this way, the national budget is allocated between locations and populations on the basis of where it will have most effect. We term this approach the focused health production function because it represents the health returns that can be achieved across the whole country when programmes can be implemented that are tailored to specific populations at the local level (counties and major cities).

Figure 3: Intervention expansion pathway using the uniform and focused approaches

(A) Local level health production functions. Each curve displays the maximum possible effect (number of infections averted, 2015–29) at a given cost, for each county or city. The health production functions are plotted on the same axes to show the difference in scale and shape seen across the country. The health production functions were grouped according to the maximum effect possible in every location for ease of reading. The locations in the group are as follows: group 1 (maximum effect >10 000 infections averted). Lamu, Garissa, Isiolo, Wajir, Tana River, West Pokot, Turkana, Samburu, Marsabit, Laikipia, Tharaka, Kwale, Baringo, Machakos, Embu, Kiambu, Nyeri, Ruiru, Kajado, Kericho, Narok, Laikipia, Marsabit, Nyamira, Men, Marsabit; group 2 (maximum effect >5000 and <10 000 infections averted): Vihiga, Kisumu county, Uasin Gishu, Ta Ta Taveta, Kilifi, Nyandarua, Elgeyo-Marakwet, Mombasa, Mombasa, Men; group 3 (maximum effect <5000 infections averted) Limpopo, Vihiga, Kisumu county, Siaya, Kakamega, Nairobi, Naivasha, Kisii, Migori, Kimaru, Kiambu. (B) Plots to show the patterns of implementation of the constituent interventions by location under both the uniform strategy and focused strategy at a budget US$600 million over the 15-year intervention period. We construct the focused and uniform approaches from a total of 13 possible constituent intervention strategies; each strategy referring to a different intervention method (male circumcision, behaviour change, early ART, and PrEP), which can be applied to the different population groups as appropriate (female sex workers, other women, men who have sex with men, other men). In each panel, each row represents one of these 13 constituent interventions and each column represents a country or city. The colour code indicates whether an intervention strategy is used in a given location. Yellow indicates an intervention is implemented, green indicates that it is not implemented, and light green indicates it is implemented but not at full coverage. In the uniform approach, the same set of interventions is used in all locations, as the allocative decisions are made for Kenya as a whole. In the focused approach, different interventions can be used in different locations, and allocation of interventions between locations is driven by the achievable impact an intervention can have and where. Although patterns of interventions are broadly conserved between locations, the choice by location is no longer restricted to be identical as in the uniform approach. Under the focused approach, generally those locations which have a higher HIV prevalence (to the right hand side) will receive a fuller complement of interventions. All of the interventions are specified such that the characteristics of the intervention strategy are the same (coverage, efficacy and unit cost) throughout this analysis (Table). The difference between the approaches is whether or not they are implemented by location. MSM=men who have sex with men. ART=antiretroviral therapy. PrEP=pre-exposure prophylaxis.
This approach will be compared with the uniform health production function. The appendix provides further details of the methods used and intervention-related assumptions.

Role of the funding source
The funder had no role in the data collection, data analysis, or data interpretation; writing of the report, or in the decision to submit the paper for publication. S-JA and TBH had full access to all the data and made the decision to submit the paper for publication.

Results
The model was calibrated to epidemiological data from Kenya. Across the 47 counties in Kenya, estimated HIV prevalence varies substantially, from less than 1% to 22% in the year 2013. In the model, the estimated number of new infections is concentrated in five counties (Migori, Homa Bay, Kisii, Nairobi, and Kericho) that account for almost 40% of all new HIV infections in the country (figure 2A). The south-western counties dominate the epidemic (figure 2B).

The first step in our analysis was to calculate the uniform health production function by allocating funds to particular combinations of interventions for the whole country. The uniform health production function is available in the appendix. The uniform health production function displays a familiar form, with substantial gains in health being achieved with small increments in cost at low overall total costs, as behaviour change communication and male circumcision programmes are implemented. This corresponds to the steep rise at the beginning of the curve, which is followed by a region of diminishing returns, whereby greater effect is possible by scaling up early ART and PrEP, but at a much greater cost.

Next, we constructed the local-level health production functions (figure 3). Differences in the demography and epidemiology across the different counties and cities result in local-level health production functions that vary substantially in both shape and scale (figure 3A). The order in which additional interventions are added in every county or city as costs increase displays some broad consistency but also considerable variation. These differences are exploited in a focused approach for HIV prevention shown through a comparison of the expansion pathways in each location in the appendix.

Figure 3B contrasts the configuration of interventions across localities under the uniform and focused forms of programming during the 15-year period, with a budget of US$600 million. In the uniform approach, if an intervention is implemented, it is scaled up across all localities. By contrast, under the focused approach, every county or city has its own mix of interventions. In many localities, programmes for male circumcision are not required. In some places but not others, all relevant interventions (early ART, PrEP, and behaviour change) are provided for FSW, whereas in others the focus is more on MSM. In some localities the total cost of programmes is far greater than that in others, because the high incidence of HIV infection could justify the widespread use of expensive interventions, such as early ART. There is a relation between the total costs allocated to each location and the number of persons living with HIV in that location (appendix), but this does not fully
explain the variation in allocated costs, because the scope of the potential HIV prevention effect and the cost of the most appropriate intervention also have an effect.

Figure 4 summarises the difference in the total health gains between the uniform and focused approaches. The difference in the projected number of new infections in the two strategies, at a budget of $600 million, is considerable and increases with time (figure 4A). Figure 4B shows the difference in effect between the uniform and focused approaches over a range of total costs. At very high total cost, there is no difference between the strategies, because almost all interventions are deployed in all populations. However, at lower total costs, there can be very large differences in the overall health gains. For a cost of $600 million between 2015 and 2029, the total additional health gain for the focused approach is almost 100 000 extra infections averted during the 15-year period, a 14% increase. Further, 33% fewer new HIV infections would occur in the year 2029 under the focused approach than under the uniform approach, equivalent to 8000 fewer infections in that year. Repeat analysis with different assumptions for the unit cost of interventions (from within the plausible cost ranges given in the table) at the same total budget (table) shows that the additional infections averted under the focused approach compared with the uniform approach might be as high as 150 000 during the 15-year period (figure 4C).

Discussion

We compared two approaches to tackle a large HIV epidemic and noted that an investment strategy that focuses on epidemiological strongholds of HIV could yield substantially greater effect than a strategy that allocates resources in a uniform way across a country. To our knowledge, this is the first study to integrate spatial analyses, transmission dynamic modelling of HIV, and economic evaluation to inform the configuration of available interventions for planning (panel).

Prioritising interventions to the people and places with high rates of HIV infections in this way makes intuitive sense. Focusing resources to those at greatest risk has long been a central theme in guidance issued by WHO and UNAIDS, with emphasis on detailed collection of epidemiological data and beginning prevention programming with a know your epidemic assessment. The strategic direction of resources is a fundamental principle in the UNAIDS investment framework. Recognition is increasing of the potential to leverage geographical variation in epidemics for programme planning. Although prioritisation is applied in countries it is unclear at what geographical level such decisions are made and there has been a lack of unified methods to guide national level resource allocation decisions utilising subnational epidemiological data.

Focusing on hot spots is standard practice for infections such as malaria and schistosomiasis and, to a lesser extent, tuberculosis. To our knowledge, this is the first report to synthesise epidemiological data from a country, including data for high-risk groups in specific locations, to estimate the value of a focused approach for HIV. Data from many countries with low and middle income, and also high-income countries, show substantial variation in HIV rates by geography and by key affected populations, making this approach widely applicable.

Administrative regions (counties) are the main unit of analysis in this study because they correspond to both the lowest level of resource allocation decisions and the finest resolution of available input data. We did not consider transmission between modelled locations...
(representing cross-county migration), which could reduce the value of differentiating interventions between geographies; although for Kenya, every county is large (average size 12 000 km² with a population of about 800 000 people). Further data will be essential to refine this analysis, in particular the spatial variation in unit cost: for instance, the cost of services in remote areas could be much higher than that in central areas. The analysis could be expanded to assess the benefit of updating the configuration of the interventions through time, which might further enhance efficiency.

Several crucial points must be considered in assessment of feasibility of applying such a strategy in practice. The political and practical issues of focusing resources in certain areas of a country, in particular in countries with complex sociocultural variation, must not be underestimated. Extremely high rates of HIV could be masked if data are aggregated to regional level in an area with otherwise very low prevalence. Collection of accurate data for key affected populations both across and within areas of each country is important. The issue of key affected populations, often marginalised and even criminalised in many countries, poses unique challenges. Cultural norms around highly effective interventions, for example voluntary male circumcision and condoms, can also pose obstacles.

Although substantial progress has been made towards preventing the transmission of HIV, recent scientific advances afford the opportunity to drive rates to lower levels. A uniform strategy, which does not use available intelligence on the epidemic, will fail to be as effective as a strategy that does. By use of a public health approach that focuses resources based on an epidemiological understanding of subnational geographical areas and key affected populations, and selects the package of interventions most likely to have an effect according to the drivers of each HIV stronghold, the efficiency and effectiveness of programming could be greatly increased. However, increased effectiveness and efficiency does not mean fewer resources are needed, at least in the near term, but rather that so-called smarter spending can generate an even greater effect.

**Contributors**

TBH, S-JA, and MD conceived the study. TBH and S-JA developed the methods and did the analyses. IC assisted in parameter estimation and DF provided additional maps and advice on methodology. PC, NK, DK, MH, TBH, S-JA, and MD wrote the manuscript. TBH and MD, and S-JA wrote the first draft of the report. All authors reviewed and approved the final version.

**Declaration of interests**

TBH reports grants and personal fees from the Bill & Melinda Gates Foundation during the conduct of the study; grants and personal fees from World Bank, UNAIDS, and The Bush Foundation; personal fees from the University of Washington, New York University, Children’s Investment Fund Foundation, and Global Fund outside of the submitted work. Other authors declare no competing interests.

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