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Title: Maximising the Impact of Combination HIV Prevention through Prioritising the People and Places in Greatest Need

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Corresponding Author: Dr. Timothy B Hallett, PhD

Corresponding Author's Institution: Imperial College London

First Author: Sarah-Jane Anderson, MSc

Order of Authors: Sarah-Jane Anderson, MSc; Peter Cherutich, MBChB; Nduku Kilonzo, PhD; Íde Cremin, PhD; Daniela Fecht, PhD; Davies Kimanga, MD; Malayah Harper, MSc (Eco); Ruth Laibon Masha, MPH; Prince Bahati Ngongo, MBA; William Maina, MPH; Mark Dybul, MD; Timothy B Hallett, PhD

Abstract: Background: Epidemiological data indicate that there is 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 for HIV infection could significantly improve the impact of investments in the HIV response.

Methods: Using Kenya as a case-study, a mathematical model was developed that described the spatio-temporal evolution of the epidemic and which incorporated the demographic, behavioural, and programme differences across subnational units. Modelled interventions (male circumcision, behaviour change communication, early antiretroviral therapy (ART), and pre-exposure prophylaxis (PrEP)) could be provided to different population groups according to their risk behaviours or their location. For a given national budget, we contrasted the impact of a uniform intervention strategy, where 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 HIV prevention intervention could reduce the total number of new HIV infections by forty percent over a fifteen year period. With no additional spending, this impact could be increased by 14% over the fifteen year period, and result in 33% fewer new HIV infections occurring each 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 over the fifteen year projection period could be as great as 22% if the budget is limited and the unit costs of interventions are high.

Interpretation: The focused approach, which prioritises resources to the people and places at greatest risk of infection, and adapts the interventions provided to reflect the local epidemiological context, could substantially increase the efficiency and effectiveness of investments in HIV prevention.

Funding: The Bill and Melinda Gates Foundation and UNAIDS.

Maximising the Impact of Combination HIV Prevention through Prioritising the People and Places in Greatest Need

Sarah-Jane Anderson¹, Peter Cherutich², Nduku Kilonzo³, Ide Cremin¹, Daniela Fecht¹, Davies Kimanga², Malayah Harper⁴, Ruth Laibon Masha⁴, Prince Bahati Ngongo⁵, William Maina², Mark Dybul⁶ & Timothy B Hallett^{1*}

¹Imperial College London, London, UK

²National AIDS/STD Control Program (NASCOP), Nairobi, Kenya

³Liverpool VCT, Care and Treatment, Nairobi, Kenya

⁴UNAIDS, Nairobi, Kenya

⁵International AIDS Vaccine Initiative (IAVI), Nairobi, Kenya

⁶The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland.

*for correspondence: timothy.hallett@imperial.ac.uk

+44(0)2075941150

Abstract

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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, there have been several important scientific advances in recent years that 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, 4} The UNAIDS Investment framework⁵ and the US President's Emergency Plan's Blueprint to achieve an 'AIDS-free generation'⁶ highlight the need to prioritize 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 impact and key affected populations.⁷ However, evidence is needed to identify appropriate priority populations.

Data from many large household surveys in Africa has recently revealed critical new insights about the highly uneven spread of HIV. For example, across eastern Africa (Figure 1), there is remarkable heterogeneity in HIV prevalence levels not only between countries but also within countries. HIV prevalence in the south-western 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 and Mozambique being approximately two thirds and one third lower than in South Africa, respectively.⁸⁻¹⁰ Within South Africa, the estimated provincial HIV prevalence ranges from 9.2 percent in the Western Cape to 27.6 percent in KwaZulu-Natal.¹¹ At the same time, the prevalence among key population groups remains extremely high.^{12, 13} Despite a national prevalence of 17.9 percent in South Africa, HIV prevalence among sex workers can be as high as 60 percent.^{10, 13, 14} Across Sub-Saharan Africa, HIV prevalence in MSM is estimated at 18 percent, considerably higher than the five percent regional adult prevalence reported by UNAIDS.¹² These observations belie earlier assumptions that all persons would be at high risk of acquisition of infection in generalized epidemics,^{15, 16} and suggest that it is imperative that we move beyond the notion of national epidemics to understanding geographic and key affected population epidemic "strongholds".

Kenya has a wealth of sub-national data that highlights 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 HIV strongholds rather than a uniform, national approach.

Methods

We aim to examine how a fixed amount of resources for HIV prevention can be used to generate reductions in the rate of new HIV infections under 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: (i) Specification of the spatio-temporal course of the HIV epidemic in Kenya; (ii) Assessment of the impact and cost of uniform, national implementation of interventions; and, (iii) Assessment of the optimal form of intervention when constructing programs specific to each locality (county or city). The methods for each part are discussed in turn and further details are found in the Supplementary Materials.

(i) Specification of the spatio-temporal course of the HIV epidemic in Kenya

A dynamic mathematical model is used to represent the epidemic in each county or large city (in the case of Nairobi, Mombasa, and Kisumu). Building upon our previous work,^{17, 18} the model represents the spread of HIV through sexual contact and tracks disease progression in HIV-positive individuals.

Information on the scale-up of male circumcision and of ART in each county was extracted from official reports.¹⁹ Information on the proportion of men and women that have casual partners and that buy or sell sex are evaluated from national survey data.²⁰ The proportion of men who have sex with men (MSM) was informed from review of the literature and an extensive national mapping of key populations.²¹ 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 referenced to the most recent nationally-representative household survey.^{20, 22} For both sources of prevalence data, spatial interpolation techniques are used to generate local-level estimates.^{23, 24}

The model includes four forms of intervention (Table 1) and it assumed that these can be provided to four population groups independently; Female Sex Workers (FSW), other women, Men who have Sex with Men (MSM), and other men. The key assumptions regarding the efficacy, cost and coverage of these interventions are described in Table 1. 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 impact (defined as the number of infections averted over 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 each possible permutation of interventions and population group in a county or city.

ii) Assessment of the impact and cost of a uniform approach

Under the best circumstances for decision-making at country level, the relative costs and impacts of different forms of intervention -- when applied uniformly to the whole country -- are compared.

We find the optimal intervention strategy for a given total cost through constructing Health Production Functions (HPF).²⁵ The HPF is created through plotting the cost and impact of all possible candidate strategies. We then remove those which are subject to dominance (i.e. provide a lesser health return at a greater cost than an alternative strategy). Successive points that fall on the frontier (i.e. 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*, since decisions are made for the whole country.

iii) Assessment of impact 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 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 HPFs (using the same method as above) to identify those sets of interventions that maximize health returns for a given total cost with a location. We used these local-level HPFs to inform the allocation of resources between locations as follows:

- Consider a small increment in the budget for the whole country.
- For each locality, quantify the health returns that could be gained through the use of that increment using the local-level HPFs.
- Compare the potential health gains across each locality.
- Allocate that increment to the locality that can produce the greatest health gains (i.e. infections averted).
- Repeat these steps 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 based on where it will have most impact. We term this the *Focused Health Production Function*, as it represents the health returns that can be achieved across the whole country when programs can be implemented such that they are tailored to specific populations at the local level (counties and major cities). This will be compared with the Uniform HPF, described in point (ii).

Intervention	Efficacy Assumption	Coverage Assumption	Range of Unit Cost Considered*	Default Unit Cost Value*
Voluntary Medical Male circumcision	Risk of acquisition for circumcised men 60% less than for uncircumcised men ^{26, 27}	80% of eligible men	\$30-\$120 per one man circumcised	\$60 ⁵
Behaviour Change Communication	20% reduction in risk of acquisition for each low risk person reached, 50% reduction in risk of acquisition for	100% of the relevant population group	\$5-\$80 per person per year reach	\$10 in low risk women and heterosexual men, \$20 in FSW and MSM ⁵

	high risk groups (MSM and FSW) ⁵			
Early ART (ART initiated at CD4 cell count > 350 cells per microliter)	85% reduction in risk of onward transmission for a person on ART relative to others ²⁸	33% in low risk women and heterosexual men, 66% in FSW and MSM	\$250-\$1000 per person on ART per year	\$515 ²⁹
Pre-exposure prophylaxis	75% reduction in risk of acquisition for a person on PrEP ³⁰	25% in low risk women and heterosexual men, 50% in FSW and MSM	\$100-\$1000 per person on PrEP per year	\$250 ³⁰

Table 1: Interventions and assumed unit costs. In each case, these estimates were chosen to be consistent with the assumptions used in the UNAIDS Investment Framework analysis.^{29 5}

* Neither impact nor costs was discounted in the analysis.

Further details of the methods used and intervention related assumptions can be found in the Supplementary Materials.

Role of the Funding Source

The funding source had no role in the collection, analysis and interpretation of data, in writing the report or in 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 markedly, from 0.3% to 22.1%. In the model, the estimated number of new infections is concentrated in five counties 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 HPF by allocating funds to particular combinations of interventions for the whole country (Figure S1). The Uniform HPF 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 programs are implemented. This is followed by a region of “diminishing returns”, whereby greater impact is possible by scaling up early ART and PrEP, but at a much greater cost.

Next, we constructed the local-level HPFs (Figure 3). Differences in the demography and epidemiology across the different counties and cities result in local-level HPFs that vary

markedly in both shape and scale (Figure 3A). The order in which additional interventions are added in each county or city as costs increase displays some broad consistency but also significant variation. It is these differences that are exploited in a Focused approach for HIV prevention (Figure S2).

Figure 3B contrasts the configuration of interventions across localities under the Uniform and Focused forms of programming over the 15 year period, with a budget of \$60M. In the Uniform approach, if an intervention is implemented it is scaled-up across all localities. In contrast, under the Focused approach, every county or city has its own mix of interventions. In many localities, male circumcision programs are not required. In some places but not others, a significant intervention is provided for female sex workers, whilst in others the focus is more on MSM. In some localities the total cost of programs is far greater than in others, as the high incidence of HIV infection could justify the widespread use of expensive interventions, such as early ART. There is a relationship between the total costs allocated to each location and the number of persons living with HIV in that location (Figure S3) but this does not fully explain the variation in allocated costs, as the scope of potential HIV prevention impact and the cost of the most appropriate intervention also have an effect.

The difference in the total health gains between the Uniform and Focused approaches is summarised in Figure 4. The difference in the projected number of new infections in the two strategies, at a budget of \$60M, is considerable and increases over time (Figure 4A). Figure 4B describes the difference in impact 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 \$60M between the years 2015-2029, the total additional health gain for the Focused approach is almost 100,000 extra infections averted over the 15 years period, a 14% increase, and there would be 33% fewer new HIV infections in the year 2029 under the Focused approach than there would be in the Uniform approach. Repeating the analysis using different assumptions for the unit cost of interventions at the same total budget (Table 1) reveals that the marginal health gain may reach 22% additional HIV infections averted with the Focused approach (Figure 4C).

Discussion

We compared two approaches to tackling a large HIV epidemic and found that an investment strategy that focuses on epidemiologic strongholds of HIV could yield substantially greater impact than a strategy that allocates resources in a uniform way across a country.

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 the WHO and UNAIDS, with emphasis on detailed epidemiological data collection and beginning prevention programming with a 'Know Your Epidemic' assessment.³² The strategic direction of resources is a fundamental principle in the

UNAIDS investment framework.⁵ There is now increasing recognition of the potential to leverage geographical variation in epidemics for program planning.³³ Although prioritisation is applied in countries it is unclear at what geographic 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.³⁴⁻³⁸ Nevertheless, this is the first report synthesizing epidemiological data from a country, including data on high-risk groups in specific locations, to estimate the value of a focused approach for HIV. Data from many low- and middle-income countries,^{39,40} and indeed also high-income countries,^{41,42} demonstrate significant variation in HIV rates geographically and/or by key affected populations, making this approach widely applicable.

Administrative regions (counties) are the main unit of analysis here as 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, each county is large (average size is 12000km² with a population of ~800,000 people).⁴³ Fine-scale targeting to particular venues within an area can be informed by other approaches, such as the successful PLACE methodology.⁴⁴ Further data will be essential to refine this analysis, in particular on the spatial variation in unit cost: for instance, the cost of services in more remote areas could be much higher than in more central areas.⁴⁵ The analysis could be expanded to assess the benefit of updating the configuration of the interventions through time, which may further enhance efficiency.

There are a number of critical points which must be considered when assessing the 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 is aggregated to regional level in an area with otherwise very low prevalence. It is important to ensure that accurate data on key affected populations are collected both across and within areas of each country. The issue of key affected populations, often marginalized and even criminalized in many countries pose unique challenges. Cultural norms around highly effective interventions, for example voluntary male circumcision and condoms, can also pose obstacles.

Although there has been significant progress in preventing the transmission of HIV, recent scientific advances afford the opportunity to drive rates to lower levels. A uniform strategy, which does not utilise available intelligence on the epidemic, will fail to be as effective as one that does. By using a public health approach that focuses resources based on an epidemiological understanding of sub-national geographic areas and key affected populations, and selects the package of interventions most likely to have an impact according to the drivers of each HIV stronghold, it may be possible to greatly increase efficiency and effectiveness of programming, and so maximize the return on investment in

HIV prevention. It must be stressed that increased effectiveness and efficiency does not mean fewer resources are needed, at least in the near term, but rather that 'smarter spending' can generate even greater impact.

Research in Context

Review of Current Evidence

We searched PubMed for the terms HIV AND (priorit* OR target* OR focus*) AND (spatial OR geog* OR subnational) AND (model OR modelling OR modeling).

Very few relevant modelling studies were found. One model showed how male circumcision interventions could be distributed in South Africa, in light of variation in HIV prevalence.⁴⁶ However, this examined only one intervention and did not consider the dynamic infectious transmission of HIV. Early studies which consider the epidemic at different geographical scales suggested that the impact of the epidemic on population structure is most visible at fine resolution.⁴⁷ The need for data at finer geographical scales to allow for better estimates of the geographical burden of infection has been emphasised.⁴⁸ Studies have noted the apparent inadequacy of models that do not capture significant within-county epidemiological variation.⁴⁹ The use of transmission models of subnational units has been proposed in the evaluation of interventions,⁵⁰ but we have not found further examples of such models in prospective programming.

Other studies simply described the spatial distribution of infection, HIV related mortality or service availability, or looked for factors associated with prevalence. Significant variation in prevalence within countries and local level clustering of the burden of infection has been observed.⁵¹⁻⁵⁶ A number of studies have examined the spatial distribution of healthcare services, in particular ART and sexual and reproductive health, and assessed implications for access to care for the surrounding populations.⁵⁷⁻⁵⁹

Additional studies returned in the search documented real world examples of a focused approach being deployed programmatically. In particular, India has used epidemiological indicators to classify districts into categories which partly determine programme design there.⁶⁰ South Africa has also set targets for care provision at the local level.⁶¹ In Mozambique, there are tailored health services for key populations in specific high risk locations.⁶² Furthermore the need to identify high risk populations at key localities, such as those who work in high risk sectors in mapped geographies, has been emphasized.⁶³

Interpretation

This is the first study to integrate spatial analyses, transmission dynamic modelling of HIV and economic evaluation to examine the optimal configuration of the full set of HIV prevention interventions available. Despite all of the elements of a spatially structured modelling analysis present in the literature, we found no examples of integration of these methods for intervention planning.

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Figure Legends

Figure 1: The spatial distribution of the HIV epidemic

An interpolated map of HIV prevalence taken from DHS surveys (conducted between the years 2006-2012) across Eastern Africa. Ordinary kriging was used to interpolate between observed HIV prevalence at sample cluster locations.

Figure 2: Modelled new infections by county for the year 2013

(A) An untransformed map of the counties of Kenya; the colours correspond to the number of modelled new infections for the year 2013.

(B) A cartogram of modelled new infections by county in the year 2013. The cartogram is a distorted map; with the area of the counties transformed to be proportional to the number of new infections modelled to occur in that county whilst preserving the topology. Those counties with a high number of new infections (shown as red and pink on the map) have expanded to dominate the figure. The Scapetoad application was used to create this plot; which uses the Gastner/Newman 2004 diffusion based algorithm for the transformation.³¹

Figure 3: The intervention expansion pathway using the Uniform and Focused approach. (A)

Local Level Health Production Functions (HPFs). Each curve displays the maximum possible impact (number of infections averted, 2015-2029) at a given cost, for each county or city. The HPFs are overlaid to highlight the difference in scale and shape seen across the country. The HPFs were grouped according to the maximum impact possible in each location for ease of reading. The locations in each group are as follows: Group 1 (Maximum Impact <10 000 Infections Averted): Lamu, Garissa, Isiolo, Wajir, Tana River, West Pokot, Turkana, Samburu, Marsabit, Laikipia, Tharaka, Kwale, Baringo, Machakos, Embu, Kitui, Nyeri, Busia, Kajiado, Kirinyaga, Mombasa, Uasin Gishu, Taita Taveta, Kilifi, Nyandarua, Elgeyo-Marakwet, Mandera, Nyamira, Meru, Nandi. Group 2 (Maximum Impact >10 000 and <20 000 Infections Averted): Murang'a, Makueni, Nakuru, Bomet, Bungoma, Trans Nzoia, Kiambu, Narok. Group 3 (Maximum Impact >20 000 Infections Averted): Kisumu City, Vihiga, Kisumu County, Siaya, Kakamega, Nairobi, Homa Bay, Kisii, Migori, Kericho.

(B) The configuration of interventions at a budget \$60 Million over a 15 year intervention period using either the Uniform Approach (without using geographical information) or Focused Approach (using geographical information). In each panel, each column represents a county or city and each row represents an intervention in a given population group. Yellow indicates an intervention is implemented or 'on', green indicates that it is not implemented and is 'off', and light green indicates it is implemented, 'on', but not at full coverage.

Figure 4: The difference in health gains between the Uniform and Focused approaches. (A)

Annual number of new infections over time (in thousands) using the Uniform approach (green line), the Focused approach (red line) and a baseline scenario of no additional

interventions (black line). (B) Health production functions for the Uniform (green line) and Focused Approach (red line), across a range of total budgets for the interventions. The vertical difference between the lines is the additional HIV infections averted when using the Focused approach versus the Uniform approach. Vertical axis gives the HIV infections averted (in thousands) 2015-2029 and the horizontal axis give the corresponding total cost in that period. Note that horizontal axis is on a log scale. (C) Histogram of marginal health gains across multivariate ranges of unit cost of the component interventions. Simulations were run using different assumptions about the unit costs of the component interventions (random sampling from the ranges indicated in Table 1) and the comparison between the two allocation approaches repeated. The percentage increase corresponds to the additional percentage infections averted using the Focused approach as opposed to the Uniform approach when each is compared to the baseline projection for new infections. These values were binned into categories (5% intervals) to allow for examination of the distribution seen across simulations. Frequency refers to the proportion of simulations which gave an additional impact of a magnitude falling within that category.

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Maximising the Impact of Combination HIV Prevention through Prioritising the People and Places in Greatest Need

Sarah-Jane Anderson¹, Peter Cherutich², Nduku Kilonzo³, Ide Cremin¹, Daniela Fecht¹, Davies
Kimanga², Malayah Harper⁴, Ruth Laibon Masha⁴, Prince Bahati Ngongo⁵, William Maina²,
Mark Dybul⁶ & Timothy B Hallett^{1*}

¹Imperial College London, London, UK

²National AIDS/STD Control Program (NASCOP), Nairobi, Kenya

³Liverpool VCT, Care and Treatment, Nairobi, Kenya

⁴UNAIDS, Nairobi, Kenya

⁵International AIDS Vaccine Initiative (IAVI), [Nairobi, Kenya](#)

⁶The Global Fund to Fight AIDS, Tuberculosis and Malaria, Geneva, Switzerland.

*for correspondence: timothy.hallett@imperial.ac.uk

+44(0)2075941150

Abstract

Background: Epidemiological data indicate that there is 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 for HIV infection could significantly improve the impact of investments in the HIV response.

Methods: Using Kenya as a case-study, a mathematical model was developed that described the spatio-temporal evolution of the epidemic and which incorporated the demographic, behavioural, and programme differences across subnational units. Modelled interventions (male circumcision, behaviour change communication, early antiretroviral therapy (ART), and pre-exposure prophylaxis (PrEP)) could be provided to different population groups according to their risk behaviours or their location. For a given national budget, we contrasted the impact of a uniform intervention strategy, where 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. ~~A total budget for the intervention was set based on historic levels of investment in Kenya.~~

Findings: A uniformly distributed combination HIV prevention intervention could reduce the total number of new HIV infections by ~~forty percent more than half~~ over a fifteen year period. With no additional spending, this impact could be increased by ~~146%~~ over the fifteen year period, and result in ~~two-thirds as many~~ ~~33% fewer~~ new HIV infections occurring each 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~~ over the fifteen year projection period could be as great as ~~2255%~~ if the budget is limited and the unit costs of interventions are high.

Interpretation: The focused approach, which prioritises resources to the people and places at greatest risk of infection, and adapts the interventions provided to reflect the local epidemiological context, ~~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, there have been several important scientific advances in recent years that 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, 4} The UNAIDS Investment framework⁵ and the US President's Emergency Plan's Blueprint to achieve an 'AIDS-free generation'⁶ highlight the need to prioritize 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 impact and key affected populations.⁷ However, evidence is needed to support decision-making-is-neededidentify appropriate priority populations.-

Data from many large household surveys in Africa has recently revealed critical new insights about the highly uneven spread of HIV. For example, across eastern Africa (Figure 1), there is remarkable heterogeneity in HIV prevalence levelsrates not only between countries but also within countries. HIV prevalence in the south-western 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 and Mozambique being approximately two thirds and one third-three times and one third- lower than in South Africa, respectively.⁸⁻¹⁰ Within South Africa, the estimated provincial HIV prevalence ranges from 9.2 percent in the Western Cape to 27.6 percent in KwaZulu-Natal.¹¹ At the same time, the prevalence among key population groups remains extremely high.^{12, 13} Despite a national prevalence of 17.9 percent in South Africa, HIV prevalence among sex workers have-ratescan be as high as 59-660 percent.^{10, 13, 14} Across Sub-Saharan Africa, HIV prevalence in MSM is estimated at 17-918 percent, considerably higher than the five percent regional adult prevalence reported by UNAIDS.¹² These observations belie earlier assumptions that all persons would be at high risk of acquisition of infection in generalized epidemics,^{15, 16} and suggest that it is imperative that we move beyond the notion of national epidemics to understanding geographic and key affected population epidemic "strongholds".

Kenya has a wealth of sub-national data that highlights 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 HIV strongholds rather than a uniform, national approach.

Methods

We aim to examine how a fixed amount of resources for HIV prevention can be used to generate reductions in the rate of new HIV infections under 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: (i) Specification of the spatio-temporal course of the HIV epidemic in Kenya; (ii) Assessment of the impact and cost of uniform, national implementation of interventions; and, (iii) Assessment of the optimal form of intervention when constructing programs specific to each locality (county or city). The methods for each part are discussed in turn and further details are found in the Supplementary Materials.

(i) Specification of the spatio-temporal course of the HIV epidemic in Kenya

A dynamic mathematical model is used to represent the epidemic in each county or large city (in the case of Nairobi, Mombasa, and Kisumu). Building upon our previous work,^{17, 18} the model represents the spread of HIV through sexual contact and tracks disease progression in HIV-positive individuals.

Information on the scale-up of male circumcision and of ART in each county was extracted from official reports.¹⁹ Information on the proportion of men and women that have casual partners and that buy or sell sex are evaluated from national survey data.²⁰ The proportion of men who have sex with men (MSM) was informed from review of the literature and an extensive national mapping of key populations.²¹ 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 referenced to the most recent nationally-representative household survey.^{20, 22} For both sources of prevalence data, spatial interpolation techniques are used to generate local-level estimates.^{23, 24}

The model includes four forms of intervention (Table 1) and it assumed that these can be provided to four population groups independently; Female Sex Workers (FSW), other women, Men who have Sex with Men (MSM), and other men. The key assumptions regarding the efficacy, cost and coverage of these interventions are described in Table 1. In the absence of compelling evidence to the contrary, we assume homogeneity in [our metric of the](#) individual-level efficacy of PrEP and early ART across the risk groups. The model is used to estimate the impact (defined as the number of infections averted over 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 each possible permutation of interventions and population group in a county or city.

ii) Assessment of the impact and cost of a uniform approach

Under the best circumstances for decision-making at country level, the relative costs and impacts of different forms of intervention -- when applied uniformly to the whole country -- are compared.

We find the optimal intervention strategy for a given total cost through constructing Health Production Functions (HPF).²⁵ The HPF is created through plotting the cost and impact of all [possible](#) candidate strategies, ~~where impact is defined by the number of HIV infections averted due to that strategy~~. We then remove those which are subject to dominance (i.e. provide a lesser health return at a greater cost than an alternative strategy). Successive points that fall on the frontier (i.e. are non-dominated) are then joined together by straight-

line segments to form a piece-wise linear function. We ~~call term~~ this the *Uniform Health Production Function*, since decisions are made for the whole country.

iii) Assessment of impact 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 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 HPFs (using the same method as above) to identify those sets of interventions that maximize health returns for a given total cost with a location. We used these local-level HPFs to inform the allocation of resources between locations ~~using an incremental approach~~ as follows:

- Consider a small increment in the budget for the whole country.
- For each locality, quantify the health returns that could be gained through the use of that increment using the local-level HPFs.
- Compare the potential health gains across each locality.
- Allocate that increment to the locality that can produce the greatest health gains (i.e. infections averted).
- Repeat these steps until a maximum value for the budget in the whole country is reached.

In this way the national budget is allocated ~~incrementally~~ between locations and populations based on where it will have most impact. We term this the *Focused Health Production Function*, as it represents the health returns that can be achieved across the whole country when programs can be implemented such that they are tailored to specific populations at the local level (counties and major cities). This will be compared with the Uniform HPF, described in point (ii).

Intervention	Efficacy Assumption	Coverage Assumption	Range of Unit Cost Considered*	<u>Default</u> Unit Cost Value*
Voluntary Medical Male circumcision	Risk of acquisition for circumcised men 60% less than for uncircumcised men ^{26, 27}	80% of eligible men	\$30-\$120 per one man circumcised	\$60 ⁵
Behaviour Change Communication	20% reduction in risk of acquisition for each low risk person reached, 50% reduction in	100% of the relevant population group	\$5-\$80 per person per year reach	\$10 in low risk women and heterosexual men, \$20 in FSW and MSM ⁵

	risk of acquisition for high risk groups (MSM and FSW) ⁵			
Early ART (ART initiated at CD4 cell count > 350 cells per microliter)	85% reduction in risk of onward transmission for a person on ART relative to others ²⁸	33% in low risk women and heterosexual men, 66% in FSW and MSM	\$250-\$1000 per person on ART per year	\$515 ²⁹
Pre-exposure prophylaxis	75% reduction in risk of acquisition for a person on PrEP ³⁰	25% in low risk women and heterosexual men, 50% in FSW and MSM	\$100-\$1000 per person on PrEP per year	\$250 ³⁰

Table 1: Interventions and assumed unit costs. In each case, these estimates were chosen to be consistent with the assumptions used in the UNAIDS Investment Framework analysis.^{29 5}

* Neither impact nor costs was discounted in the analysis.

Further details of the methods used [and intervention related assumptions](#) can be found in the Supplementary Materials.

Role of the Funding Source

The funding source had no role in the collection, analysis and interpretation of data, in writing the report or in 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 markedly, from 0.3% to 22.1%. In the model, the estimated number of new infections is concentrated in five counties that account for almost 40% of all new HIV infections in the country (Figure 2A). The south-western counties dominate the epidemic (Figure 2B).³⁴

The first step in our analysis was to calculate the Uniform HPF by allocating funds to particular combinations of interventions for the whole country (Figure S1). The Uniform HPF 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 programs are implemented. This is followed by a region of “diminishing returns”, whereby greater impact is possible by scaling up early ART and PrEP, but at a much greater cost.

Next, we constructed the local-level HPFs (Figure 3). Differences in the demography and epidemiology across the different counties and cities result in local-level HPFs that vary markedly in both shape and scale (Figure 3A). The order in which additional interventions are added in each county or city as costs increase displays some broad consistency but also significant variation. It is these differences that are exploited in a Focused approach for HIV prevention (Figure S2).

Figure 3B contrasts the configuration of interventions across localities under the Uniform and Focused forms of programming over the 15 year period, with a budget of \$60M. In the Uniform approach, if an intervention is implemented it is scaled-up across all localities. In contrast, under the Focused approach, every county or city has its own mix of interventions. In many localities, male circumcision programs are not required. In some places but not others, a significant intervention is provided for female sex workers, whilst in others the focus is more on MSM. In some localities the total cost of programs is far greater than in others, as the high incidence of HIV infection could justify the widespread use of expensive interventions, such as early ART. There is a relationship between the total costs allocated to each location and the number of persons living with HIV in that location (Figure S3) but this does not fully explain the variation in allocated costs, as the scope of potential HIV prevention impact and the cost of the most appropriate intervention ~~must also be considered~~ also have an effect.

The difference in the total health gains between the Uniform and Focused approaches is summarised in Figure 4. The difference in the projected number of new infections between in the two strategies, at a budget of \$60M, is considerable and increases over time (Figure 4A). ~~This difference is the additional benefit which can be gained using exactly the same resources, but by allocating them differently.~~ Figure 4B describes the difference in impact 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 ~~\$60m~~ 2bn between the years 2015-2029, ~~which would represent a continuation of current level of spending in Kenya,~~ the total additional health gain for the Focused approach is ~~98250~~ almost 100,000 extra infections averted over the 15 years period, a ~~1416%~~ increase, and there would be ~~two-thirds~~ half as many ~~33% fewer~~ new HIV infections in the year 2029 under the Focused approach relative than there would be in the Uniform approach. Repeating the analysis using different assumptions for the unit cost of interventions at the same total budget (Table 1) reveals that the marginal health gain may reach ~~could 22%~~ be as high as 55% additional HIV infections averted with the Focused approach (Figure 4C).

Discussion

We compared two approaches to tackling a large HIV epidemic and found that an investment strategy that focuses on epidemiologic strongholds of HIV could yield substantially greater impact than a strategy that allocates resources in a uniform way across a country.

Prioritising interventions to areas-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 the WHO and UNAIDS, with emphasis on detailed epidemiological data collection and beginning prevention programming with a 'Know Your Epidemic' assessment.³² The strategic direction of resources is a fundamental principle in the UNAIDS investment framework.⁵ There is now increasing recognition of the potential to leverage geographical variation in epidemics for program planning.³³ Although prioritisation is applied in countries it is unclear at what geographic 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.have been lacking.

Focusing on 'hot spots' is standard practice for infections such as malaria and schistosomiasis and, to a lesser extent, tuberculosis.³⁴⁻³⁸ Nevertheless, this is the first report synthesizing epidemiological data from a country, including data on high-risk groups in specific locations, to estimate the value of a focused approach for HIV. Data from many low- and middle-income countries,^{39,40} and indeed also high-income countries,^{41,42} demonstrate significant variation in HIV rates geographically and/or by key affected populations, making this approach widely applicable.

Administrative regions (counties) are the main unit of analysis here as 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, each county is large (average size is 12000368km² with a population of ~800,000 people).⁴³ Fine-scale targeting to particular venues within an area can be informed by other approaches, such as the successful PLACE methodology.⁴⁴ Further data will be essential to refine this analysis, in particular on the spatial variation in unit cost: including in rural areas for instance, the cost of services in more remote areas could be much higher than in more central areas-where the overall unit costs of services could be much higher.⁴⁵ The analysis could be expanded to assess the benefit of updating the configuration of the interventions through time, which may further enhance efficiency.

There are a number of critical points which must be considered when assessing the feasibility of applying such a strategy in practise. The political and practical issues of focusing resources in certain areas of a country, in particular in countries with complex cultural and ethnic geographical divisionssociocultural variation, must not be underestimated. ~~It is important to ensure that accurate data on key affected populations are collected both across and within areas of each country.~~ Extremely high rates of HIV could be masked if data is aggregated to regional level in an area with otherwise very low prevalence. It is important to ensure that accurate data on key affected populations are collected both across and within areas of each country. The issue of key affected populations, often marginalized and even criminalized in many countries pose unique challenges. Cultural norms around highly effective interventions, for example voluntary male circumcision and condoms, can also pose obstacles.

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Although there has been significant progress in preventing the transmission of HIV, recent scientific advances afford the opportunity to drive rates to lower levels. A uniform strategy, which does not utilise available intelligence on the epidemic, will fail to be as effective as one that does. By using a public health approach that focuses resources based on an epidemiological understanding of sub-national geographic areas and key affected populations, and selects the package of interventions most likely to have an impact according to the drivers of each HIV stronghold, it may be possible to greatly increase efficiency and effectiveness of programming, and so maximize the return on investment in HIV prevention. It must be stressed that increased effectiveness and efficiency does not mean fewer resources are needed, at least in the near term, but rather that 'smarter spending' can generate even greater impact.

Research in Context

Review of Current Evidence

We searched PubMed for the terms HIV AND (priorit* OR target* OR focus*) AND (spatial OR geog* OR subnational) AND (model OR modelling OR modeling).

Very few relevant modelling studies were found. One model showed how male circumcision interventions could be distributed in South Africa, in light of variation in ~~numbers of uncircumcised men and~~ HIV prevalence.⁴⁶ However, this examined only one intervention and did not consider the dynamic infectious transmission of HIV. Early ~~studies models~~ which consider the epidemic at different geographical scales suggested that the impact of the epidemic on population structure is most visible at fine resolution.⁴⁷ The need for data at finer spatial-geographical scales to allow for better estimates of the geographical burden of infection ~~and demographic implications~~ has been emphasised.⁴⁸ Studies have noted the apparent inadequacy of models that do not capture significant within-county epidemiological variation.⁴⁹ The use of transmission models of subnational units has been proposed in the evaluation of interventions,⁵⁰ but we have not found further examples of such models in prospective programming.

Other studies simply described the spatial ~~distribution disruption~~ of infection, HIV related mortality or service availability, or looked for factors associated with prevalence. Significant variation in prevalence within countries and local level clustering of the burden of infection has been observed.⁵¹⁻⁵⁶ A number of studies have examined the spatial distribution of healthcare services, in particular ART and sexual and reproductive health, and assessed implications for access to care for the surrounding populations.⁵⁷⁻⁵⁹

Additional studies returned in the search documented real world examples of a focused approach being deployed programmatically. In particular, India has used epidemiological indicators to classify districts into categories which partly determine programme design there.⁶⁰ South Africa has also set targets for care provision at the local ~~district~~ level.⁶¹ In Mozambique, there are tailored health services for key populations in specific high risk

locations.⁶² Furthermore the need to identify high risk populations at key localities, such as those who work in high risk sectors in mapped geographies, has been emphasized.⁶³

Interpretation

This is the first study to integrate spatial analyses, transmission dynamic modelling of HIV and economic evaluation to examine the optimal configuration of the full set of HIV prevention interventions available. Despite all of the elements of a spatially structured modelling analysis present in the literature, we found no examples of integration of these methods for intervention planning.

Conflicts of Interest

~~TBH has conducted consultancy work for the Bill & Melinda Gates Foundation.~~

Acknowledgements

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Figure Legends

Figure 1: The spatial distribution of the HIV epidemic

An interpolated map of HIV prevalence taken from DHS surveys (conducted between the years 2006-2012) across Eastern Africa. Ordinary kriging was used to interpolate between observed HIV prevalence at sample cluster locations.

Figure 2: Modelled new infections by county for the year 2013

(A) An untransformed map of the counties of Kenya; the colours correspond to the number of modelled new infections for the year 2013.

(B) A cartogram of modelled new infections by county in the year 2013. The cartogram is a distorted map; with the area of the counties transformed to be proportional to the number of new infections modelled to occur in that county whilst preserving the respecting the topology pre-existing shape constraints. Those counties with a high number of new infections (shown as red and pink on the map) have expanded to dominate the figure. The Scapetoad application was used to create this plot; which uses the Gastner/Newman 2004 diffusion based algorithm for the transformation.³¹

Figure 3: The intervention expansion pathway using the Uniform and Focused approach. (A) Local Level Health Production Functions (HPFs). Each curve displays the maximum possible impact (number of infections averted, 2015-2029) at a given cost, for each county or city. The HPFs are overlaid to highlight the difference in scale and shape seen across the country. The HPFs were grouped according to the maximum impact possible in each location for ease of reading. The locations in each group are as follows: Group 1 (Maximum Impact <10 000 Infections Averted): Lamu, Garissa, Isiolo, Wajir, Tana River, Turkana, West Pokot, Samburu, Marsabit, Laikipia, Tharaka, Kwale, Baringo, Machakos, Embu, Mombasa, Kajiado, Kitui, Busia, Nyeri, Kirinyaga, Uasin Gishu, Taita Taveta, Kilifi, Nyandarua, Elgeyo Marakwet,

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Mandera, Nyamira. Group 2 (Maximum Impact >10 000 and <20 000 Infections Averted): Nandi, Meru, Murang'a, Makueni, Nakuru, Bomet. Group 3 (Maximum Impact >20 000 Infections Averted): Trans Nzoia, Bungoma, Kiambu, Narok, Kisumu City, Vihiga, Kisumu County, Nairobi, Siaya, Kakamega, Homa Bay, Kisii, Migori, Kericho. Group 1 (Maximum Impact <10 000 Infections Averted): Lamu, Garissa, Isiolo, Wajir, Tana River, West Pokot, Turkana, Samburu, Marsabit, Laikipia, Tharaka, Kwale, Baringo, Machakos, Embu, Kitui, Nyeri, Busia, Kajiado, Kirinyaga, Mombasa, Uasin Gishu, Taita Taveta, Kilifi, Nyandarua, Elgeyo-Marakwet, Mandera, Nyamira, Meru, Nandi. Group 2 (Maximum Impact >10 000 and <20 000 Infections Averted): Murang'a, Makueni, Nakuru, Bomet, Bungoma, Trans Nzoia, Kiambu, Narok. Group 3 (Maximum Impact >20 000 Infections Averted): Kisumu City, Vihiga, Kisumu County, Siaya, Kakamega, Nairobi, Homa Bay, Kisii, Migori, Kericho.

(B) The configuration of interventions at a budget \$~~60 Million~~^{2 Billion} over a 15 year intervention period using either the Uniform Approach (without using geographical information) or Focused Approach (using geographical information). In each panel, each column represents a county or city and each row represents an intervention in a given population group. Yellow indicates an intervention is implemented or 'on', green indicates that it is not implemented and is 'off', and light green indicates it is implemented, 'on', but not at full coverage.

Figure 4: The difference in health gains between the Uniform and Focused approaches. (A) Annual number of new infections over time (in thousands) using the Uniform approach (green line), the Focused approach (red line) and a baseline scenario of no additional interventions (black line). (B) Health production functions for the Uniform (green line) and Focused Approach (red line), across a range of total budgets for the interventions. The vertical difference between the lines is the additional HIV infections averted when using the Focused approach versus the Uniform approach. Vertical axis gives the HIV infections averted (in thousands) 2015-2029 and the horizontal axis give the corresponding total cost in that period. Note that horizontal axis is on a log scale. (C) Histogram of marginal health gains across multivariate ranges of unit cost of the component interventions. Simulations were run using different assumptions about the unit costs of the component interventions (random sampling from within the ranges indicated in Table 1) and the comparison between the two allocation approaches repeated. The percentage increase corresponds to the additional percentage infections averted using the Focused approach as opposed to the Uniform approach found in each simulation when each is compared to the baseline projection for new infections. These values were binned into categories (5% intervals) to allow for examination of the distribution seen across simulations. Frequency refers to the proportion of simulations which gave an additional impact of a magnitude falling within that category.

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Response to Reviewers

We respond to each point raised by the reviewers in turn; with the reviewers comments highlighted in bold. Text taken from the manuscript is in italics. The word count of the abstract is 308, and of the main text is 2952.

EDITORIAL COMMENTS:

Please can you send all declarations of contributions with signatures of all authors. We cannot accept the paper without them.

We have uploaded these forms with the resubmission.

Please note that we have also made a slight adjustment to Figure 3B, which displays which interventions are implemented in each location, to indicate more clearly which strategies partially funded.

COMMENTS TO THE AUTHOR:

Reviewer #1: Only (minor) point: I do not understand why authors don't like to mention the work done by Sharon on the "place" methodology specifically? While Sharon et al didn't do any of the modelling as you do now, they precisely describe how infections cluster specially and how interventions should be targeted. This work should be noted.

We agree that the PLACE methodology is an extremely valuable approach for ensuring appropriate targeting of interventions to identifiable local hotspots. We do cite this work in the discussion (paragraph four, line six):

'Fine-scale targeting to particular venues within an area can be informed by other approaches, such as the successful PLACE methodology'.¹

We believe that our approach and that of Weir et al are complementary; both aim to enhance the efficiency of the response but are addressing the targeting of interventions at different geographical scales. We take a country-wide viewpoint in this analysis; assessing optimal resource and intervention allocation across administrative areas. In contrast, the PLACE methodology is useful in ensuring programmatic efficiency at the local scale, that interventions are focused on those places where individuals known to be most at risk can be contacted. In this way the two methods could be used concurrently for optimal targeting to key locations.

No changes made.

Reviewer #3: Overall, the manuscript has been strengthened by clearer framing that the objective is to evaluate maximum impact on HIV infections averted within a fixed budget, comparing a universal to focused approach. The figures and legends are clear. The discussion is also improved by citing how this approach is consistent with the UNAIDS investment framework and provides a specific example of how to use national data on HIV prevalence by geography and risk population to increase efficiency and impact of prevention resources.

We thank the reviewer again for their guidance on how to strengthen this manuscript.

Two specific comments:

1) In table 1 on page 5, the efficacy assumptions should reflect the durability of effect. No citations are provided for the efficacy parameters used for BCC. For the efficacy of BCC, it is unlikely that the effect is that high over a 15 yr horizon, given the data from more intensive behavioral interventions that the effects are modest and wane over time.

We cite the Investment Framework paper in the main text as this manuscript provides further discussion of the current opinion on Behaviour Change interventions.² We also provide a detailed description of the rationale behind our efficacy assumption in the technical appendix (page 10) to further explain the efficacy assumed to the reader:

The efficacy of behaviour change interventions is based on an assumption that BCC can lead to modest reductions in risk behaviour. Whilst it has been difficult to demonstrate a sustained impact of behaviour change communication (BCC); it is likely that behaviour change has been a principle driver of reductions in HIV incidence over the last ten years in places such as Zimbabwe, Malawi and Uganda. Similar assumptions have been in the Investment Framework papers and in many other analyses of prevention programming.^{3, 4}

We make no assumptions about intervention efficacy waning over time, and although a more detailed representation of the features of the intervention could be included, this would require further assumptions and would not have a substantial impact on our conclusions (see below).

2) The authors have modified their coverage estimates for interventions (point 13 in their letter), which seems appropriate for early ART and PrEP. However, they use high coverage assumptions for VMMC & BCC--80% and 100%, respectively in Table 1). Given that only a few countries are approaching their targets of VMMC, the VMMC coverage assumption seems very optimistic. It would be useful to see how much the impact is attenuated at lower coverage. It seems reasonable to assume that coverage/uptake and costs are not linear given fixed costs for infrastructure and staffing. Thus, uptake could be an important determinant of impact, and realistic coverage estimates should be used, based on model programs. The authors should better justify their coverage assumptions, and conduct a sensitivity analysis with lower coverage (e.g. 30-50% lower than used in current model, to reflect programmatic barriers and population acceptance of these interventions).

We respond to the questions raised about the assumptions for VMMC and BCC in turn:

VMMC

In the model, we assume that a circumcision intervention cannot lead to more than 80% of adult men being circumcised (in populations that do not currently circumcise widely). 80% is a target that has been set in international and national guidance frameworks.⁵

Furthermore, Kenya has made good progress in implementing VMMC.⁶ As of 2011, the VMMC program had already reached 52.2% of uncircumcised men in Nyanza Province, which historically has the lowest level of circumcision in the country. Kenya has in fact been singled out as one of the few countries on track to meet the circumcision prevalence of 80% target set.⁷ On this basis, we believe that this target is realistic and reflects the current situation and achievements of the VMMC program to date in Kenya. No changes made.

BC

We currently assume that the behaviour change intervention reaches 100% of the population, in line with how such campaigns are often administered. We conducted a sensitivity analysis as suggested by the reviewer where the coverage of behaviour change intervention was reduced to 50%.

The resulting number of new infections over time by strategy (the black line is the baseline number of new infections, green line the number of new infections using the uniform strategy and red line the number of new infections using the focused strategy) under the assumption of 50% and 100% coverage levels is shown in Figure 1 and Figure 2 respectively:

Figure 1: The number of new infections by allocation strategy. Sensitivity Analysis: 50% coverage of BCC Intervention

Figure 2: The number of new infections by allocation strategy. Original Analysis: 100% coverage of BCC intervention

The figures demonstrate that our central conclusion - that the focused strategy leads to greater intervention impact than the homogenous strategy - remains the same with the alternative assumption. The total number of infections is higher in both focused and homogenous approaches under the 50% BCC coverage assumption (Figure 1) compared to the 100% BCC coverage assumption (Figure 2) due to restriction of the use of BCC. If BCC is less effective, resources that might have been used on BCC become more likely to be redirected to other interventions.

Thus, alternative assumptions do not alter the message that a focused program will offer impact above what a uniform program can achieve.

We have added discussion of the implications of altering the assumptions regarding intervention coverage in the supplementary materials:

Technical Appendix- Page 10:

Although it is likely that changes in our assumptions regarding the efficacy, coverage and costs of our component interventions will alter the magnitude of the effect we report, these will act to modulate the difference in impact between the two allocation approaches, rather than alter the conclusion of the analysis. The current values of each of these parameters is described in Table 3, and reflect the best available evidence at this time and are in line with assumptions made in other economic studies.

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Supplementary Material

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Figure

Figure 1

Figure 2

A

B

Number of New Infections 2013

Figure 3

Figure

Figure 4

A

B

C

Figure

Figure S1

Figure

Figure S2

Figure

Figure
Figure S4

Figure S5: The Position of the 2008 DHS Clusters

Figure S6: Regional trends in HIV prevalence (Continuous Scale)

Figure S7: Regional trends in HIV prevalence (Categorical Scale)