Optimal resource allocation to reduce HIV incidence across sub-Saharan Africa: a mathematical modelling study

Jessica B McGillen, Sarah-Jane Anderson, Mark R Dybul, Timothy B Hallett

Department of Infectious Disease Epidemiology, Imperial College London, London, UK (J B McGillen PhD, S-J Anderson PhD, Prof T B Hallett, PhD); **The Global Fund, Geneva, Switzerland** (Amb M R Dybul, MD)

Correspondence to: Jessica B McGillen, Department of Infectious Disease Epidemiology, Imperial College London, Norfolk Place, Praed Street, London W2 1PG, UK
j.mcgillen@imperial.ac.uk

Summary

Background Advances in HIV prevention methods offer promise to accelerate declines in incidence, but it has been unclear how these can be deployed to best effect on the heterogeneous landscape and drivers of the pandemic. We hypothesised that using this landscape to inform the allocation of resources for combination prevention could enhance the impact of HIV funding across sub-Saharan Africa.

Methods We developed a compartmental mathematical model of HIV transmission and disease progression by risk group to subnational resolution in 18 countries, capturing 80% of the adult HIV burden in sub-Saharan Africa. For each top-level administrative division, the model was calibrated to historical data on HIV prevalence, sexual behaviours, treatment scale-up, and demographics. We then evaluated four strategies for allocating prevention funding over a 15-year period from 2016 to 2030, which exploited epidemic differences between subnational regions to varying degrees.

Findings For a \$20 billion expenditure over the 15-year period, scaling up prevention along current funding channels could avert 5·3 million infections (relative to no scale-up). Prioritising key populations could avert 3·7 million more infections than current funding channels, and additionally prioritising by within-country geography could avert 400,000 more infections in turn. Removing national constraints from this could avert a further 600,000 infections. Risk prioritisation thus has more marginal impact than geographical prioritisation, but across multiple expenditure levels, doing both is best for total impact and could achieve up to a three-fold gain over current channels. Shifting from the current to optimal pattern would rebalance resources toward more cost-effective interventions and emerging epidemics.

Interpretation If domestic and international funders were to align strategically to build an aggregate funding pattern that is guided by the epidemiology of HIV, and particularly by the emerging understanding of local dynamics and epidemic drivers, more cost-effective and impactful HIV prevention investments could be achieved across sub-Saharan Africa.

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Introduction

New HIV infections have dropped by one third over the past decade, but the pandemic will rebound with population growth if the global response stagnates¹. Sub-Saharan Africa (SSA) continues to bear more than 70% of the global burden of people living with HIV, and its population suffers losses in length and quality of life as well as slowed economic development. In resource-limited settings, expansion of treatment will remain vital to the response against HIV, but without arresting the spread of the epidemic, the long-term provision of treatment represents an economic burden comparable in magnitude to the sum-total of the national debt for many countries.² However, a powerful suite of available prevention interventions offers an immediate opportunity to capitalise on previous progress and drive down HIV transmission.³

Exploitation of combination prevention calls for optimal allocation of resources at each of four levels: between countries, geographically within countries, between subnational population groups, and between intervention methods. This is complicated by heterogeneity in the epidemic and its drivers: in 2013 the adult HIV prevalence averaged 4.7% across sub-Saharan Africa but ranged from 0.2% in Bas-Congo, DRC to 27% in parts of Swaziland.⁴ Female sex workers (FSW) have an HIV prevalence as high as 60% in South Africa,⁵ and limited data put prevalence among men who have sex with men (MSM) at 18% across the continent.⁶

The distribution of domestic funding across countries in SSA directly reflects neither disease burden nor financial need,⁷ whilst international donors vary in how they prioritise countries; but a better funding configuration has not been offered. Some previous studies have argued for targeting HIV treatment and prevention efforts by geography⁸ or risk group,⁹ and reaching marginalised high-risk populations is widely viewed as crucial to epidemic control.¹⁰ However, it is not always clear what priority these concerns receive in programmes over other considerations such as achieving scale or rolling out new interventions. Finally, new interventions or additions to health programmes have typically been evaluated in isolation^{11–13} and held in comparison to an estimate of the cost-effectiveness of interventions already funded, an approach that ignores the relative costs and impacts of alternative options. Exceptions in Africa include a national-level cost-effectiveness analysis of prevention portfolios¹⁴ and an exploration of combination prevention in a hyperendemic setting.¹⁵ The Optimal model¹⁶ has informed national priority setting and programme planning in several African countries, though to date countries tend not to account explicitly for subnational heterogeneity in choosing intervention packages for population groups. A notable exception is Kenya, which changed its strategic plans¹ following a modelling case study by Anderson et al.¹⁷ that synthesised subnational transmission modelling and combination prevention optimisation under a constrained national budget for HIV spending.

We seek to determine whether the results of Anderson et al.¹⁷ could scale beyond Kenya, and how funds could be optimised across multiple countries under a single analytical framework. Moreover, we aim to unpack the sources of epidemic heterogeneity and examine their roles in the potential cumulative impact of prevention efforts. Our hypothesis is that an integrated strategy—one which confronts epidemic heterogeneity, considers available interventions in combination along with their efficacies and costs, and allocates resources optimally—can achieve a significantly greater impact across SSA than maintaining current patterns.

Methods

Model design

We employ a mathematical model that builds upon our previous work^{17–19} to describe the dynamic spread of HIV. Equations are available in the Supplemental Appendix of the paper by Anderson et al.¹⁷ Here we describe key details of the model structure (appendix p. 1).

The adult (age 15–49) population is grouped by risk of HIV acquisition and transmission. Groups comprise low-risk women in stable long-term partnerships; moderately high-risk women who form casual partnerships; female sex workers (FSW) at very high risk; low-risk heterosexual men in stable long-term partnerships; moderately high-risk heterosexual men who form casual partnerships; very high-risk heterosexual men who are clients of FSW; and men who have sex with men (MSM). In the absence of detailed data on MSM outside Kenya, we assume that all MSM form partnerships with both men and women and are moderately high-risk. Persons over age 50 are assumed to have negligible risk. Men and women are linked by heterosexual HIV transmission, with risk structure further differentiating how the groups interact and how HIV is transmitted among and between them. Following infection, the model tracks CD4 progression. All subnational regions in 18 countries (appendix p. 2) are included in the modelling framework, such that it represents 80% of all people living with HIV across SSA.

Data sources

Parameters governing the biology of HIV are held constant, whilst parameters governing sexual behaviour or population demographics are calibrated to produce epidemic dynamics consistent with historical data for each region (appendix p. 2–34). The calibrated model allows us to explore one possible future for the epidemic that is consistent with available evidence. This possible future shows considerable heterogeneity in the spread of the HIV epidemic in SSA (figure 1), with the highest prevalence in the southeast but additional high-prevalence regions in Nigeria, western Kenya and Ethiopia, and parts of Tanzania. The model also anticipates heterogeneity in epidemic drivers (appendix p. 34).

We approximate the current HIV funding pattern using the most recent available UNAIDS data for the modelled countries²⁰ (appendix p. 35). Assuming donor funding will continue to flatline²¹ and avoiding assumptions around uncertain domestic growth,⁷ we can suppose that the prevention share in HIV spending will approach 25%²² and 90% of this will go toward scaling up current methods (vs. research into new methods). This generates a 'representative' expenditure of \$20 billion over the 15-year period from 2016 to 2030.

Analysis

In the model, anti-retroviral therapy (ART) is given to all persons who would be likely to seek care. Initially in ART scale-up, we assume that treatment goes preferentially to persons with CD4<200 cells per microlitre, as they are most likely to present to the clinic, and expand this to CD4<350 cells per microlitre to accommodate shifts in ART eligibility. The assumption throughout is that ART is supplied to all persons presenting for care. Prevention interventions are then considered over and above this treatment level. Treatment costs are thus implicit in the framework, and the counterfactual scenario (no future scale-up of prevention interventions) is not a zero-cost scenario. All expenditures considered herein are net prevention expenditures relative to this baseline treatment cost.

We consider four HIV prevention interventions currently on the market: voluntary medical male circumcision (VMMC); behaviour change communication (BCC), such as encouraging

condom use; pre-exposure prophylaxis (PrEP); and anti-retroviral therapy as prevention ('early' ART). Early ART comprises outreach testing and offering of ART to all HIV-positive persons, and tends to attract persons who are earlier in disease progression than those presenting for care. Unit costs for these interventions are listed in table 1 and derived in the appendix (p. 35–36). Each intervention can be applied independently to the target populations as follows: VMMC can be applied to uncircumcised men, PrEP and BCC to HIV-negative persons, and early ART to HIV-positive persons who have not already presented for care. The interventions are bundled together to form combination strategies, with all possible combinations of interventions and target populations considered.

In a given region (national or subnational, to be described below), we identify the optimal combination of interventions for a given total expenditure via creation of a health production function (HPF). We enumerate all possible intervention combinations across all risk groups, subnational regions, and costs, and select those that provide the greatest health return—in terms of infections averted—for the lowest cost. Successive points on this optimal cost-effectiveness frontier are joined to form a piecewise linear HPF. We use these HPFs to allocate a 15-year block of funding for SSA under four sets of constraints that represent intervention strategies (figure 2).

The 'uniform' strategy distributes the funding block to the modelled countries in proportions matching current channels (appendix p. 35). Each country then uses its funding portion to roll out a single combination of prevention interventions—chosen using a national-level HPF—uniformly across its subnational regions. Roll-out is constrained such that each intervention can be applied either to all relevant populations or to none. This strategy is intended to approximate scale-up under current patterns in funding and intervention programmes.

If we suppose that prevention programmes will begin to prioritise key populations effectively, we capture a less constrained scale-up. This 'semi-uniform' strategy allocates funding to countries in current proportions, then selects optimal prevention bundles nationally but allows these to include interventions targeted by risk. Further relaxing within-country constraints, we again distribute the funding block in current proportions, but from there allow local epidemiology to dictate choices of subnational prevention bundles. For a given country, a subnational-level HPFs is constructed that identifies optimal sets of local interventions for a given total cost. Defining a small increment in the national funding allocation, the health gains achievable for this increment in each subnational region are compared, and the increment is awarded to the subnational region whose locally-optimal intervention strategy produces the greatest health gains. The process is iterated until the national funding allocation has been reached. We call this the 'semi-focused' strategy as it permits allocation by local epidemiology within the confines of national boundaries. It is a direct extension of the method developed by Anderson et al.¹⁷ to multiple countries.

Finally, we move beyond national boundaries and allow all subnational regions across the continent to 'compete' directly with each other for funding. Subnational HPFs are constructed for all regions in all countries, and small budget increments are optimally allocated between them until the entire funding block has been distributed. This 'focused' strategy allows intervention bundles to compete within each region and the best choices of these to compete between regions across SSA, resulting in allocation that is freely optimised to the local epidemiology.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Given a set of assumptions around costing and achievable coverage levels (table 1), for our \$20 billion representative expenditure, the model suggests that scaling up prevention efforts following current funding channels (the uniform strategy in figure 2) could potentially avert a total of 5·3 million infections between 2016 and 2030, relative to a baseline of continued treatment but no further prevention scale-up (in which 17·6 million new infections would occur). Relaxing the current channels to permit a focus on marginalised populations (the semi-uniform strategy) could avert an additional 3·7 million infections, a 70% marginal increase over uniform allocation. Allowing geographical targeting within national boundaries (the semi-focused strategy) could avert a further 400,000 infections. Finally, letting the optimisation engage fully with subnational epidemiology (the focused strategy), could avert another 600,000 infections in turn. Focused allocation could thus avert a total of 10 million infections relative to no scale-up, nearly doubling the gain achievable with uniform allocation for the same expenditure (figure 3A). The largest marginal gain comes from relaxing within-country constraints to allow risk targeting (i.e. shifting from uniform to semi-uniform allocation), but the greatest total impact requires targeting by both risk and geography.

At the representative net expenditure, the total yearly prevention cost peaks in the initial years of investment (between 2016 and 2020) then declines due to alleviated treatment demands. This 'front-loading' is more dramatic for focused than uniform allocation, and individual countries show the same pattern (appendix p. 37). Net spending is lower in moderate-burden countries (Tanzania, Ethiopia, Zambia, Kenya) and higher in high-burden countries (Mozambique, Nigeria) for focused relative to uniform allocation over time. Ethiopia and South Africa experience net cost-saving in later years with focused allocation, a benefit not achieved with uniform allocation.

Differences between strategies vary in magnitude with total expenditure (figure 3B) and are widest for \$4 billion, with the focused strategy having a marginal impact of three times the uniform scenario at this expenditure. All strategies plateau near \$1 trillion, at which point most interventions can be funded in most places even with constraints. Although African countries have recently increased their financing by 150%²³, flatlining donor funding since 2008²¹ renders the highest expenditures unlikely. Nevertheless, a reduction on 2010 incidence of up to 80% can be achieved by 2030, nearing the UNAIDS global goal of 90%²⁴ even with imperfect intervention coverage and effectiveness (table 1).

Regional patterning of intervention bundles is markedly different between the strategies (appendix p. 38). The constraints imposed by the uniform strategy trap money in inefficient allocations, such that only early ART and VMMC are affordable in the highest-burden countries. For the same expenditure, the focused strategy allows interventions to shift into regions and subpopulations where they are most cost-effective. This gain in efficiency facilitates the use of more expensive and effective interventions for those at greatest risk, such as PrEP for sex workers and early ART in more locations, thereby achieving incidence reductions that are larger in all countries and more equitable across risk groups (appendix p. 39).

Focused allocation produces a resource distribution across the modelled countries that differs from the current distribution (figure 4A). Shifting to the focused distribution would involve mostly small changes in proportional funding (<5% in 14 of 18 countries), with the result being a rebalancing of expenditure away from countries with declining or historically well-funded epidemics (e.g. Kenya, South Africa) and into countries with high burdens by people living with HIV or emerging epidemics (e.g. Mozambique, Nigeria) (figure 4B). Nigeria is a notable case due to its rising HIV burden and current funding shortfall. Whilst it emerges as an important country in this analysis, the results also hold without it, with prevention funds rebalancing toward other high-burden epidemics in its absence (not shown).

An alternative set of costing assumptions produces similar results (appendix p. 40–43) despite the importance of relative unit costs in the optimisation. An alternative set of coverage assumptions offers a scenario wherein early ART and PrEP are scaled up more modestly and key populations are not amenable to higher coverage than the general population. Again the qualitative conclusions hold (appendix p. 44–45). Finally, a univariate sensitivity analysis of the cost of ART shows that the strategies are insensitive to economies and diseconomies of scale (appendix p. 46). This reveals a strength of our approach: the results are robust because the optimisation is adaptive, with resource allocation responding to changes in intervention characteristics in order to preserve impact.

Discussion

Here we took the strategic perspective of the African continent to analyse the potential impact of a localised, integrated approach to HIV prevention funding. We found that this approach could reduce new infections between now and 2030 by substantially more than one which did not respond to epidemic heterogeneities when allocating funds within and across countries. The marginal impact of responding to risk heterogeneity was consistently greater than that of responding to geographical heterogeneity. This suggests that countries may benefit from focusing national programmes on marginalised groups even if varying programmes between subnational regions proves infeasible. Nevertheless, the largest total impact emerged from full resource flexibility, and this held true over multiple expenditure levels and assumptions about intervention characteristics. Rebalancing prevention funds from the current channels to the fully flexible pattern would shift priorities toward emerging epidemics and thereby increase the cost-effectiveness of prevention investments.

Our integration of multiple data sources introduces a host of uncertainties. In particular, reliable data on FSW and MSM are scarce and comprise a major public health need. Non-response bias in the DHS is likely to be small,²⁵ and in agreement with UNAIDS and WHO, we make no corrections for this. A large body of work also confirms that, despite suggestions that ANC surveillance can exaggerate trends,²⁶ such data provide a reasonable guide to historical dynamics. The analyses presented herein consider the potential impact of intervention strategies within one possible epidemic future, but confronting uncertainties in the underlying model structure and data could permit explorations of other possible futures.

We do not explicitly consider migration between subnational regions in estimating impact, although important HIV transmission dynamics have been observed among, for example, migrant workers in southern Africa.²⁷ The potential consequences of such dynamics are not clear *a priori*; whilst migration could reduce heterogeneity in well-connected regions, movement patterns would themselves be heterogeneous, as would interregional service-

seeking behaviours. To the extent that migrating populations could be targeted specifically, the benefits of a focused approach could be amplified. This is a promising area for future investigation. Our modelling scope of sexual HIV transmission precludes consideration of injecting drug use, suggested by limited data to be a potential emergent concern in SSA.²⁸ Programmes are increasingly aiming to address the needs of adolescent girls in recognition of their vulnerability to HIV.²⁹ We expect that extending our analysis to allow for their prioritisation as a third key population would further increase the benefits of a focused approach to combination prevention. In the absence of additional data, we have assumed that cost and effect size are scale-invariant, and populations are all equally accessible. However, accessibility varies with geography and socioeconomics³⁰ such that rural areas may be more expensive to reach than urban ones. Moreover, we have imposed no costs on changing intervention mixes or funding patterns, or on sustaining a programme in only part of a country. Whilst in some countries, resource allocation choices may be driven by non-scientific factors such as policy or discriminatory practices, our results serve as a proof-of-principle that basing those choices instead on epidemiology would benefit both underserved groups and the general population.

This work sets out the most impactful pattern of funding to decrease HIV incidence over the coming 15 years. Because of the high resource needs, to a varying extent among countries, domestic and external international funds will be required. As countries increase their own funding, international funding would be most impactful if aligned with greater strategic focus under one resource envelope. By exploiting the emerging understanding of the geographical and key population epidemiology of HIV, and providing the optimal bundles of interventions, the global goal of ending AIDS as a public health threat by 2030 can be achieved.

Research in context

Evidence before this study

We searched PubMed for studies up to 21 January 2016, with the terms HIV and (spatial or geog* or subnational) and (model*) and (heterogeneity or priorit* or focus* or optim* or resource or allocation) and Africa. Several studies have observed spatial clustering of the HIV burden in Africa, argued for targeting treatment and prevention efforts by geography or risk group, or considered implications of spatial variations in HIV-related healthcare. Prevention interventions have been evaluated in isolation or on a national scale. A recent case study of Kenya was the first to synthesise spatial analysis, dynamic transmission modelling, and economic evaluation for optimisation of prevention bundles under a constrained budget. The Optima model has informed priority-setting in several African countries.

Added value of this study

Whilst many studies have partially addressed issues surrounding HIV prevention focusing in resource-limited settings, these have been on a within-country basis, with none considering the potential impact of rebalancing total prevention funds across countries. Our study is unique in that it confronts local-level HIV heterogeneity at scale, with the pulled-back strategic perspective often taken by donor governments and international funders. Moreover, we are the first to unpack how the components of this multifaceted heterogeneity contribute to incidence reduction. Our results show that whilst greater marginal gains come from optimising by risk than geography, doing both is more impactful overall and favours prioritisation of emerging epidemics.

Implications of all available evidence

For investors in HIV programmes in resource-limited settings, including governments of affected countries and international donors, the first-order question is how funds should be used to achieve the greatest impact. This study addresses this central question in light of the full array of available interventions, from the perspective of optimising resource allocation and with the scope of the African continent. We thus anticipate it having substantial value for funders and governments in our collective push toward the global goal of ending AIDS as a public health threat by 2030.

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Author contributions

JBM, S-JA, MRD, and TBH conceived the study. JBM, S-JA, and TBH developed the methods. JBM collected data, did the analyses, and wrote 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 Rush 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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Figure 1: Modelled spatiotemporal dynamics of HIV. One possible trajectory, shown in ten-year increments from 1985 to 2025, produced by the model for subnational HIV prevalence among adults (ages 15–49) across sub-Saharan Africa, consistent with current estimates and past trends. Modelled countries are listed in the appendix (p. 2). Countries in white are not modelled. The average HIV prevalence across all modelled countries is 5·8% for 2015.

Figure 2: Four strategies for intervention allocation. The uniform strategy (dark blue) is intended to represent scale-up of interventions along funding channels following current patterns (appendix p. 35), the semi-uniform strategy (light blue) relaxes this to allow a focus on marginalised populations, the semi-focused strategy (orange) is a direct extension of the approach developed by Anderson et al¹⁷ and the focused strategy represents a continental intervention programme driven entirely by local epidemiology (red).

Figure 3: Potential performance of the allocation strategies. Strategies are uniform (dark blue), semi-uniform (light blue), semi-focused (orange), and focused (red). What might happen due to each intervention strategy under a given set of costs and coverage levels (see table 1), in terms of (A) millions of infections averted over time, relative to a baseline scenario of no further scale-up of prevention efforts, across the continent for a representative net prevention expenditure of \$20 billion over 2016 to 2030, and (B) the percent reduction by 2030 on the 2010 incidence level against increasing net prevention expenditure. Note that the x-axis in B is on a log scale. m=million, b=billion, t=trillion.

Figure 4: Changes in funding pattern between strategies. (A) Comparison of the proportional net prevention expenditure in each country (dots) under the focused strategy vs. according to the current pattern. The current pattern is a moderate predictor of how funds should be allocated under the focused strategy (Kendall rank correlation coefficient = 0.582). (B) Changes in proportional net prevention expenditure by country (ordered by increasing number of people living with HIV) upon shifting from current to focused patterns, for a representative continental expenditure of \$20 billion over 2016 to 2030. This shift moves next expenditure primarily from mid-burden into high-burden countries. The current allocation pattern comprises domestic public, international, and private contributions (appendix p. 35).

Table 1: Available prevention interventions. Each intervention can be applied independently to each relevant population group. Behavior change communication, 'early' antiretroviral therapy (ART), and pre-exposure prophylaxis (PrEP) can be applied to men and women in the general population, female sex workers (FSW), and men who have sex with men (MSM). Voluntary medical male circumcision can be applied to all uncircumcised men. Estimates are consistent with UNAIDS Fast Track framework²⁴ and unit costs are derived in the appendix (p. 36). 'Early' ART refers to a prevention strategy comprising outreach testing programmes and the offer of treatment to all people living with HIV. This is distinct from the assumption, in all scenarios, of providing treatment for those who present for care (typically with low CD4 counts). We assume homogeneity of individual-level efficacies of ART and PrEP with respect to risk. As the intention is not to make specific or quantitative forecasts, the analysis includes discounting of neither costs nor effects.

Target population	Effectiveness	Unit cost	Achievable coverage
<i>Voluntary medical male circumcision</i>			
Eligible men	60% reduction in RoA	\$68 per procedure	80%
<i>Behaviour change communication</i>			
Heterosexual men	20% reduction in RoA	\$63 pppy	100%
Low-risk women	20% reduction in RoA	\$63 pppy	100%
FSW	50% reduction in RoA	\$28 pppy	100%
MSM	50% reduction in RoA	\$28 pppy	100%
<i>'Early' ART as prevention</i>			
Heterosexual men	70% reduction in RoT	\$457 pppy	33%
Low-risk women	70% reduction in RoT	\$457 pppy	33%
FSW	70% reduction in RoT	\$457 pppy	66%
MSM	70% reduction in RoT	\$457 pppy	66%
<i>PrEP</i>			
Heterosexual men	75% reduction in RoA	\$95 pppy	25%
Low-risk women	75% reduction in RoA	\$95 pppy	25%
FSW	75% reduction in RoA	\$95 pppy	50%
MSM	75% reduction in RoA	\$95 pppy	50%