

Targeting of resources in efforts to end AIDS: the global Optima HIV allocative efficiency model

Sherrie L Kelly, Rowan Martin-Hughes, Robyn M Stuart, Xiao F Yap, David J Kedziora, Kelsey L Grantham, S Azfar Hussain, Iyanoosh Reporter, Andrew J Shattock, Laura Grobicki, Hassan Haghparast-Bidgoli, Jolene Skordis-Worrall, Zofia Baranczuk, Olivia Keiser, Janne Estill, Janka Petravic, Richard T Gray, Clemens J Benedikt, Nicole Fraser, Marelize Gorgens, David Wilson, Cliff C Kerr, David P Wilson

Burnet Institute, Melbourne, Australia (S L Kelly MSc, R Martin-Hughes PhD, R M Stuart PhD, X F Yap MSc, D J Kedziora PhD, S A Hussain MSc, I Reporter MSc, J Petravic PhD, C Kerr PhD, Prof D P Wilson PhD)

Monash University, Melbourne, Australia (S L Kelly MSc, D J Kedziora PhD, K L Grantham MAppStat, J Petravic PhD, Prof David P Wilson PhD)

Department of Mathematical Sciences, University of Copenhagen, Copenhagen, Denmark (R M Stuart PhD)

The Kirby Institute, UNSW Sydney, Sydney, Australia (A J Shattock PhD, R T Gray PhD)

Institute for Global Health, University College London, London, UK (L Grobicki MSc, H Haghparast-Bidgoli PhD, J Skordis-Worrall PhD)

Institute of Global Health, University of Geneva, Geneva, Switzerland (Z Baranczuk PhD, O Keiser PhD, J Estill PhD)

Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland (Z Baranczuk PhD, O Keiser PhD, J Estill PhD)

Institute of Mathematics, University of Zurich, Zurich, Switzerland (Z Baranczuk PhD)

Institute of Mathematical Statistics and Actuarial Science, University of Bern, Bern, Switzerland (J Estill PhD)

World Bank Group, Washington, DC, USA (C J Benedikt PhD, N Fraser PhD, M Gorgens MPH, D Wilson PhD)

School of Physics, University of Sydney, Sydney, Australia (C Kerr PhD)

Correspondence to:

Sherrie L Kelly

Infectious Disease Modelling

Burnet Institute

85 Commercial Road

Melbourne VIC 3004

Australia

sherrie.kelly@burnet.edu.au

Word count

Abstract: 300 words

Main text: 3954 words

Keywords: HIV epidemic, cost-effective HIV investment

SUMMARY

Background: To move towards ending AIDS by 2030, HIV resources should be allocated cost-effectively. We estimated how global HIV resources could be re-targeted for greatest epidemiological impact and how many additional new infections could be averted by 2030.

Methods: For 44 countries, capturing 80% of people living with HIV globally, we collated standard data used in country modelling exercises (including demographic, epidemiological, behavioural, programmatic, and expenditure data from 2000 through 2015). These data were used to parameterize separate subnational and national models within the Optima HIV framework. To estimate an optimal resource allocation at the subnational, national, regional, and global level, we used an adaptive stochastic descent optimization algorithm in combination with the epidemic models and cost functions for each programme in each country. Optimal allocation analyses were conducted with international HIV funds remaining the same to each country and by redistributing these funds between countries.

Findings: Without additional funding, if countries were to optimally allocate their HIV resources from 2016 to 2030, we estimate that an additional 7.4 million (3.9 million–14.0 million) new infections could be averted, representing a 26% (13%–50%) incidence reduction. Redistribution of international funds between countries could avert a further 1.9 million infections, a 33% (20%–58%) incidence reduction overall. To reduce HIV incidence by 90% compared to 2010, we estimate that an over three-fold increase of current annual funds will be necessary until 2030. The most common priorities for optimal resource reallocation are to scale up treatment, followed by prevention programmes targeting key populations at greatest risk in each setting. Prioritization of other HIV programmes depends on the epidemiology and cost-effectiveness of service delivery in each setting, as well as resource availability.

Interpretation: Greater reductions in global HIV incidence are possible through further targeting of international and national HIV resources.

Funding: World Bank and NHMRC Australia.

Introduction

The global community is committed to reducing new HIV infections by 90% by 2030 compared to 2010 to end the AIDS epidemic as a global health threat.¹ To help reach this goal, the Joint United Nations Programme on HIV and AIDS (UNAIDS) has set ambitious diagnosis, treatment, and viral suppression targets supplemented with high coverage of prevention as a roadmap to achieving this goal. However, as international funding declined by 7% in 2016,² national governments are being urged to mobilize new domestic HIV resources to cover the billions of dollars in additional funds anticipated to be needed to achieve these targets.³

As part of their “Investment Framework for the Global HIV Response”,⁴ UNAIDS directs national governments to invest strategically in HIV programmes. Siapka et al.⁵ conducted a systematic review of cost-effectiveness of the six most essential HIV programmes included in this framework and showed that further evidence was needed to better understand how to best achieve efficiency gains in HIV programmes. One type of gain is known as allocative efficiency, whereby funding is allocated across a mix of interventions in the right combination to yield the greatest health outcomes. The objective of this modelling study is to estimate how to minimize the number of HIV infections by 2030 by targeting global resources to the most cost-effective combination of interventions and locations worldwide.

International funding organizations including the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM) now require applicants to provide evidence that their proposed budget will be invested cost-effectively. Many countries have used HIV modelling tools such as Goals,⁶ the AIDS Epidemic Model (AEM),⁷ and Optima HIV⁸ to assist in developing their investment strategy. Since 2011, over 40 national governments have requested Optima HIV

modelling analysis support,^{9, 10} led by the World Bank, United Nations agencies, or the Centers for Disease Control and Prevention, to improve the allocative efficiency of their HIV responses. This study incorporates expansions of previously generated Optima HIV country models as well as the generation of new subnational and national models (55 Optima HIV models in total) to represent over 80% of the number of people living with HIV (PLHIV) worldwide. We combined subnational and national models to generate a global Optima HIV model. We then projected the potential epidemiological gains that could be achieved through the most cost-effective investment in HIV programmes to minimize new HIV infections by 2030 at the subnational, national, regional, and global level if international funding remained the same or if these funds were redistributed across countries.

Methods

Model design

Using Optima HIV⁸ (version 2.3.6, available at www.hiv.optimamodel.com) we generated a global HIV model to estimate the optimal resource allocation across HIV programmes to minimize new infections from January 1, 2016 to December 31, 2029 (hereafter referred to as “by 2030”) at the subnational, national, regional and global level. Optima HIV is a population-based compartmental model that uses a linked system of ordinary difference equations to track the transmission of HIV among and between context-specific population groups. We have provided a diagram of the Optima HIV model structure in figure S1 and additional details surrounding the methodology and modeling approach in appendix 1. We used demographic, epidemiological, and behavioural data by population group, along with expenditure and coverage levels of HIV programmes from 2000 to 2015 to inform the model. It captures elements including sexual and injecting risk behaviour and mother-to-child

transmission, and dynamically tracks people as they move across clinical categories, disease states, and age and risk groups. Following the 2016 World Health Organization guidelines,¹¹ we have specified in the model that all PLHIV are eligible for treatment regardless of CD4 count. Further information about the Optima model is available elsewhere.⁸

Forty-four countries with the greatest numbers of PLHIV in their respective regions were selected for inclusion in the study to capture 80% of all PLHIV (table S1), representing an estimated 29.5 million of the 36.7 million PLHIV worldwide.¹² Regional representation varied based on data availability as follows: 86% of PLHIV in Asia and the Pacific (Asia-Pacific), 70% in Eastern Europe and Central Asia (EECA), 75% in Latin America and the Caribbean (LAC), 56% in the Middle East and North Africa (MENA), and 88% in sub-Saharan Africa (SSA). Countries with low-HIV prevalence (including all upper-middle- and high-income countries) were not included in this study.

Data sources

We generated one Optima HIV modelling file for each country in this study, including subnational models for countries with particularly heterogeneous epidemics and where data were readily available. Country Optima HIV models that were previously generated to inform national strategic planning or funding proposals with country governments were also included. Data to inform these models, originally collated and endorsed in partnership with country governments, were updated where possible. For newly created national and subnational models, data were collated from UNAIDS Global AIDS Monitoring and National AIDS Spending Assessments, United States President's Emergency Plan for AIDS Relief (PEPFAR), Demographic and Health Surveys, and Integrated HIV Bio-behavioral Surveillance reports, as well from the Avenir Health Unit Cost, Vital Statistics, and the

World Bank databases supplemented with context-specific sources including national annual reports and strategic plans for HIV and AIDS. Input data and assumptions for Optima country models are available on request, with non-public country-owned data subject to approval from the respective country. Models were representative of national or subnational areas with generalized, concentrated, or mixed HIV epidemics, as well as with diverse HIV spending patterns and responses.

Model calibration and cost functions

We calibrated the epidemic model with UNAIDS¹² and/or locally provided estimates for HIV prevalence per key population and age group, number of PLHIV, number of people on antiretroviral therapy (ART), new HIV infections, and AIDS-related deaths (see appendix 2 for calibrations).

Uncertainty estimates were generated around the model projections using an approximate Bayesian computation algorithm, with prior distributions defined for HIV prevalence in each population, transmission probabilities, and the key parameter values needed to define each projection. For cost functions these are: (a) the average cost of reaching someone with the program at the current level of operations, (b) the estimated maximal attainable coverage of the program, and (c) the program impact in terms of behavioural or clinical outcomes. The cost function parameter values were allowed to vary uniformly over ranges within 10% of best assumptions. For each analysis, we calculated interquartile ranges around the estimated cumulative number of infections and deaths expected from the model outputs based on n=100 simulations with parameters sampled from the joint prior distributions. Model parameters are described in appendix 3. Cost-functions are provided in appendix 4. We considered past expenditures for all services and components of the HIV response as representative of the

costs required to implement these responses in future. The latest reported unit costs for each HIV programme were applied and did not vary over time. Estimated costs are reported in 2016 United States dollars.

Optimization algorithm

A unique feature of the Optima HIV model is its optimization algorithm.¹⁴ Kerr et al. developed an adaptive stochastic descent algorithm to calculate the optimal resource allocation against defined constrained objective functions.¹⁴ The algorithm forms probabilistic assumptions about which parameters (changes in spending on programmes, which influences changes in programmatic coverage levels, which influences prevention, treatment and other outcomes) have the greatest effect on minimizing new infections and uses optimal step sizes for each parameter. For the optimizations we used Monte Carlo initializations to minimize the possibility of finding a local optimum. The default for optimizations is that they start 10 times from the initial allocation and 10 times from random allocations. We applied this algorithm to estimate the optimal allocation of HIV resources across available HIV interventions for every jurisdiction and across jurisdictions to minimize new infections from 2016 to 2030, compared with last reported budget allocations in each jurisdiction.

We differentiated between targeted and non-targeted HIV programmes (see table S2 for programme list). Targeted programmes include treatment and prevention programmes with a clear potential impact on reducing HIV transmission, morbidity, or mortality. Non-targeted programmes are those that may be essential in an HIV response, but do not have a direct impact on health or cannot be attributed to population-specific outcomes. As non-targeted HIV programme expenditures do not have a direct impact on outcomes, they were considered

to be fixed, remaining in the HIV response, but were not included in the optimization. To reflect ethical treatment approaches, the optimization was subject to constraints such that funding to treatment programmes (antiretroviral therapy, opiate substitution therapy (OST), and prevention of mother-to-child transmission (PMTCT)) could not be decreased.

Optimization analyses were based on reallocation of last reported HIV funding amounts performed to: (1) redistribute funding among programmes within each country with international resources¹² remaining the same to each country or (2) redistributing funding within each country as well as redistributing international funding among countries. International funds were considered from funding organizations including GFATM, PEPFAR, and bi- and multi-lateral agencies, whereas domestic HIV resources were not redistributed between countries in our analyses.

Using different combinations of coverage for HIV programmes, the change in risk behaviour and morbidity and mortality outcomes were modelled. New HIV infections and AIDS-related deaths were projected to 2030 under different funding amounts and programmatic allocations; specifically, across every possible combination of allocation. The optimization algorithm within the Optima HIV model was then used to estimate global minima for the optimal allocation of resources to minimize new HIV infections. Each programme had defined effectiveness assumptions with justifications from available international evidence (e.g. ART was assumed to reduce CD4-stratified mortality¹⁵ and when viral suppression is achieved to reduce infectiousness by 96% (73%–99%)).¹⁶ Model output was aggregated from subnational projects to the national level, and national output to the regional and then global level. Our global optimization analyses were assessed not only at currently available global HIV resources, but if the levels of HIV funding varied from 0% to 200% of last reported

spending levels in 20% increments. We measured the impact of these funding changes, with optimal resource allocation, on the cumulative new HIV infections and AIDS-related deaths by 2030.

Role of the funding source

The World Bank provided funding to support country applications and the Australian NHMRC (APP1086540) provided modelling research funding for this study. The funders of the study had no role in study design. Staff at the World Bank contributed to data collation and review of this article. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication. SLK received a Graduate Scholarship and International Postgraduate Research Scholarship from Monash University. DPW received a Senior Research Fellowship from the Australian NHMRC. OK received a professorship grant from the Swiss National Science Foundation (163878).

Research in context

Evidence before this study

We searched PubMed from January 1, 2000 to July 31, 2017 with the terms “HIV” AND (“efficiency” OR “optim*” OR “allocation”) AND (“resources” OR “fund*”) AND “model*”. Several studies have shown that there are common principles for determining the optimal allocation of HIV resources at the national (e.g. Kenya, USA) and regional levels (e.g. sub-Saharan Africa (SSA)). Findings show that targeting resources to more cost-effective programme combinations and to geographical hotspots (e.g. Kenya) can lead to reductions in new HIV infections by up to approximately 30%. Two other well-known HIV resource allocation models, Goals and AEM, have been extensively used in partnership with

countries to guide strategic planning. The Goals model has also been applied to estimate programme coverage requirements and resource needs for achieving global HIV targets. However, neither model was specifically designed to identify optimum HIV resource allocations. Remme et al. have shown for countries across SSA that while additional domestic funds have yet to be leveraged, international funds will still be required to meet global AIDS goals. According to Stover et al., to reach global HIV targets, the current 2016 annual HIV budget of \$19.1bn for low- and middle-income countries will need to be increased to \$26.2bn by 2020, with a decline to \$23.8bn by 2030.

Added value of this study

Although studies have examined targeting HIV resources more cost-effectively, these have been carried out at either the subnational, national, and regional level. Our study is unique in that it is the first global HIV allocative efficiency analysis. We estimated that reductions in new infections of approximately 30% could be achieved from reallocating funds to the most cost-effective mix of HIV programmes, confirming findings from a previous study conducted for SSA. We showed that similar gains are possible in regions across the world in both generalized and concentrated epidemic settings using different mixes of programme prioritization. We also showed that redistributing international funds between countries across the world, could lead to additional gains. International funds were mainly shifted towards countries in SSA, as previously recommended. By 2030, if allocations are optimized at the subnational and national level and international funds reallocated between countries an absolute reduction in incidence of over 30% is possible. In addition, if global HIV funding is either increased or as forecasted continues to decline, we have identified funding priorities for HIV investment. Our modelling results also confirm that reaching the global HIV incidence

target by 2030 is possible, but that substantially more resources are needed (to approximately \$40bn total each year until 2030).

Implications of all the available evidence

Findings from modelling studies can be useful for programme planners and funders in making evidence-based decisions to invest limited funds towards the most cost-effective HIV programmes to improve health outcomes.

Results

Worldwide, if the last reported HIV expenditure amounts and allocations are held constant from January 1, 2016 to December 31, 2029, we project a gradual rise in new HIV infections (figure 1), thus moving further from the target to reduce infections by 90% compared to 2010 and of ending AIDS by 2030.¹ However, if the same global budget is invested in the optimal mix of HIV programmes, we estimate that annual new infections would be decreased by almost 30% compared with 2010 levels. To achieve these improved global health outcomes, the highest priority is to scale-up ART funding from 40% of annual global HIV spending in 2015 (\$5.1bn) to 48% (\$6.1bn) through to 2030 (figure 2). This would represent a cumulative shift of \$14.5bn in global HIV spending towards ART by 2030, effecting a 9% increase in coverage of people receiving ART. We also estimate that it is possible to reduce incidence by 90% globally by 2030, but considerably more resources will be needed, to an approximate increase to \$40bn in total annual funds for countries modelled. This means it is even more important to allocate resources most cost-effectively, as well as to explore other types of efficiencies, for example, delivering high quality HIV services at reduced costs and reducing commodity costs. Globally, at current funding channels, the next priorities are to

increase funding towards PMTCT and programmes targeting key populations, including people who inject drugs (PWID) and men who have sex with men (MSM).

In sub-Saharan Africa (SSA), a region that accounts for nearly 70% of all PLHIV, with mainly generalized or mixed HIV epidemics, we estimate that new HIV infections could be reduced by 23% (3%–59%) from 2016 to 2030, (4.6 million infections (670,000 to 11.6 million) could be averted if resources were optimally allocated (table S4). With no increase in the annual funding available over this period, the incidence reductions would largely be accomplished by shifting approximately \$550 million towards ART, increasing total budget allotment on ART from 38% to 46% (figure 2). An optimized allocation for this region would also see investments shifting towards PMTCT (57% relative increase from approximately \$340 million to \$530 million) as well as key population prevention programmes including programmes for female sex workers (FSW) (124% relative programme budget increase from \$26 million to \$58 million) and under last reported budget, away from less contextually cost-effective programmes targeted at the general population, such as condoms and social behaviour communication change.

At the national level, the most common prioritization of resource reallocation is towards ART, as shown in 75% or 33 of 44 countries modelled (figure 3). For 34 of 44 countries (77%), the next priority is to scale up one or more prevention and testing programme targeting key populations.

Another potential opportunity to consider for achieving further reductions in HIV infections and moving closer to global HIV targets is to evaluate the impact of redistributing HIV funds from international sources between countries. In this analysis, only international funds

exceeding non-targeted and treatment programme (ART, PMTCT, and OST constrained for ethical reasons) amounts, were considered for redistribution between countries. International HIV funding accounted for \$4.6bn (36%) of the \$12.8bn budget for countries modelled, with \$1.3bn available for redistribution according to our imposed constraints for the analysis. The proportion of international to domestic funds varies widely between countries, with the majority (64%) of international funds invested in countries in SSA.¹² We found that an optimal redistribution of international funds between countries would see the largest share shifted to countries in SSA, primarily to countries in central and western Africa, which otherwise do not receive equitable donor funding compared with eastern and southern African countries. Specifically, we found that country allocations are generally already well-distributed, but our estimated optimal allocation had a very modest increase in funding for SSA, from 55% or \$7.0bn to 56% or \$7.2bn of total global budget, and to a lesser extent there were shifts towards countries in EECA and MENA (figure 2). In SSA and MENA, the gains in international funds are prioritized towards scaling up ART, whereas in EECA, OST, needle and syringe programmes (NSP), and prevention and testing programmes targeting sex workers are of highest priority. At the global level, we estimate that this shift could lead to an additional 7% incidence reduction compared with optimal allocation within countries alone, representing an overall 33% reduction in new HIV infections globally. This could avert an additional 9.3 million (4.2 million to 18.3 million) additional new infections compared with maintaining the latest reported allocation over this period, with a reduction to 1.3 million infections annually by 2030 (figure 1 and table S4). Therefore, by better targeting HIV resources towards the most cost-effective mix of programmes in the right locations, it is possible to significantly reduce global infections by 2030 without additional resources.

If total global HIV funding were increased, then it would become affordable to include several programmes in the most cost-effective programmatic mix that were not found to be part of the optimization under last reported budget. As more funding is available, there is more opportunity to shift funds towards the next most cost-effective programme(s), including HIV testing, and more towards programmes targeting key populations (i.e. PWID, MSM, and FSW) (figure 4A and table S6). However, if global HIV resources were reduced by 20% (to 80% of the last reported amount) then several critical programmes would fall out of the most cost-effective mix; however, as budget varies, so do the priorities for cost-effective allocation (table S6). We estimated that if funding was reduced by 20% from 2016 to 2030 new infections would increase globally by 41% (22%-62%) (29.0 million (23.6 million to 35.1 million) cumulative new infections) compared with an estimated 20.6 million (17.0 million to 27.0) infections with 100% of global funds optimized over this period (figure 4B and table S6). If the last reported global spending amounts were doubled, distribution towards prevention programmes targeting key populations at greatest risk would increase from 14% of the last reported budget allocation to an estimated 21% of the optimized budget, which is better aligned with the 25% advocated by UNAIDS to be spent on prevention.¹⁷ At double budget, the proportion of optimized funds for HIV testing would also increase <1% to 9%. Lastly, to achieve a nearly 90% reduction in global HIV incidence from 2010 to 2030 with optimal allocation, an increase to approximately \$40bn in annual budget is estimated to be required for countries modelled.

Discussion

Limited HIV resources must be invested cost-effectively. We have shown that by optimizing global HIV resources from 2016, approximately 30% more new infections and AIDS-related deaths could be averted by 2030 compared with current allocations. Across all countries and

regions analyzed, the most common first priority towards these reductions should be to scale up ART. This is followed by priority scale-up of one or more prevention and testing programmes targeting key populations.

If international HIV resources were redistributed, with a priority shift in funds to countries in SSA, further reductions in incidence and deaths could be achieved. International funding organizations like the GFATM and PEPFAR may choose to consider enhancing their strategic investment from the global perspective towards countries or settings where the greatest health outcome could be achieved.²⁰ Should additional funds become available, certain programmes not prioritized at current funding levels, will become a higher priority for funding (for example HIV testing programs within the allocations for SSA and LAC).

These findings are consistent with previous modelling studies conducted in specific countries^{10, 21} and for the SSA region.^{22, 23} With a constant HIV budget, optimal reallocation towards ART and programmes targeting key populations would require funds to be shifted away from lower impact programmes. While it is not surprising that recommendations are to increase ART funding, the optimal allocation of remaining resources was found to be context-specific. Funding to other programmes in a prioritized HIV strategy depends on local epidemiology and cost-effectiveness of local service delivery. Moreover, with varying budget, different programmes are prioritized for funding. Lastly, we reaffirm the ongoing gap in global HIV resource needs. More resources will be needed to achieve HIV incidence targets by 2030.

While not included in the optimization, almost half of total HIV funds from modelled countries are being spent on non-targeted programmes, with wide variation in spending by

region and at the national level. This likely reflects different accounting and administrative frameworks and suggests an opportunity to capitalize on reducing spending on non-targeted programmes and to optimally reinvest any savings in targeted programmes to further improve health outcomes.

As with any modelling study, there are limitations to this global HIV model analysis. First, the model only includes countries with the greatest numbers of PLHIV by region capturing 80% of all PLHIV and only \$12.8bn of the approximate \$19.2bn in annual HIV spending reported for all low- and middle-income countries.² Second, limitations in data availability and reliability can lead to uncertainty surrounding projected results. While the model optimization algorithm accounts for inherent uncertainty, it may not be possible to account for all aspects of uncertainty given often poor quality or paucity of data, particularly for critical cost values. Cost functions, which were applied to every HIV programme in every country, were the primary driver – coupled with epidemic burden – of optimal resource estimations. Third, we used evidence from systematic reviews of clinical and research studies to inform model assumptions. These assumptions may be conservative; in certain settings more optimistic values may exist, for example the level of programme efficacy, which would lead to even further projected health gains. We conducted a sensitivity analysis by varying key parameters and showed the impact on model outcomes. Fourth, we do not capture the effect of migration of PLHIV across countries, but rather model countries in isolation. Fifth, due to limited data availability we did not include the potential impact of pre-exposure prophylaxis (PrEP) and cash transfers within the optimization analysis, but are working to augment the models in future to include these interventions. Sixth, we did not incorporate time varying optimization where it may be optimal to scale-up or scale-down programmes over time. We anticipate this approach would have more appropriately prioritized funding to programmes for which health gains from early investment will only be realized in later years.

We expect this limitation to most affect funding for VMMC in generalized epidemic settings, as shown by Shattock et al.²⁴ for South Africa. Seventh, for the optimization scenario whereby international funds were permitted to be shifted between countries, we assumed that redistribution would not be limited to investment in select programme(s), as is often specified by some funding organizations. Lastly, it is important to keep in mind that these findings are only modelling analysis projections and have not been confirmed in practical settings. The models used in this study have been calibrated to reflect country- and UNAIDS-endorsed epidemiological estimates, but validation of results showing that optimal allocations are indeed more efficient in practice has not been possible. Shifting resources based on evidence from resource optimization studies is not always feasible nor is it necessarily politically favourable, but if there is the will to make a greater impact, it should be considered. Resource redistribution towards programme combinations identified as more cost-effective in allocative efficiency studies, including towards ART and key population HIV prevention and testing, has been demonstrated from Optima HIV modelling cases e.g. in Sudan²⁵ and Belarus.²⁶ As well as for many other countries who have used Optima HIV in Global Fund Concept Notes and National Strategic Plan development and target setting.¹⁰ It is anticipated that epidemiological impacts of these programmatic changes will be realized; however, rigorous impact evaluations have not been established nor would they be simple to conduct at national levels due to lack of an empirical counterfactual. Our choice of objective to minimize new HIV infections resulted in optimal reallocation of funds towards treatment, which would in turn lead to reductions in AIDS-related deaths. However, different objectives, for example to minimize AIDS-related deaths or disability-adjusted life years, will result in somewhat different optimal allocations and outcomes.⁸ Finally, it was outside the scope of this model and study to examine accrual and spread of genotypic resistance.

Using allocative efficiency analyses we have estimated where shifts in resource allocation could lead to greater impact for the same funding or similar impact with less funding. These findings have been used at the national level and may now also be used at the regional and global levels to guide programme planners, policy makers, and donors in their decisions for improving population health outcomes.²⁷ However, allocative efficiency will only take us so far in improving the HIV response. Innovations must also be realized to deliver treatment and prevention services at lower costs by revising policies to allow procurement of more affordable antiretrovirals, to deliver services at quality for less,⁵ and aim to support essential health environments at appropriate cost. Ultimately, resources must be invested in the most cost-effective HIV programmes targeting populations and locations where they will have the highest health impact.

Authors' contributions

SLK and DPW conceived the study. SLK, RMH, DPW, RMS, CCK, DJK, and KLG developed the global HIV modelling approach. SLK, RMH, XFY, RMS, KLG, AH, IR, AJS, LG, HHB, ZB, OK, JP, RTG, CJB, NF, and CCK compiled the data and conducted original country analysis. RMH, SLK, RMS, and CCK performed the global analyses. SLK wrote the first version of the manuscript. MG and DW provided guidance. All authors reviewed and approved the final version.

Conflict of interest statement

Authors declare no conflicts of interest.

Ethics approval

This study did not require ethics committee approval.

Acknowledgments

We thank Andrew Craig for help with data collation, Zara Shubber for contribution to in-country applications, and national representatives for their input.

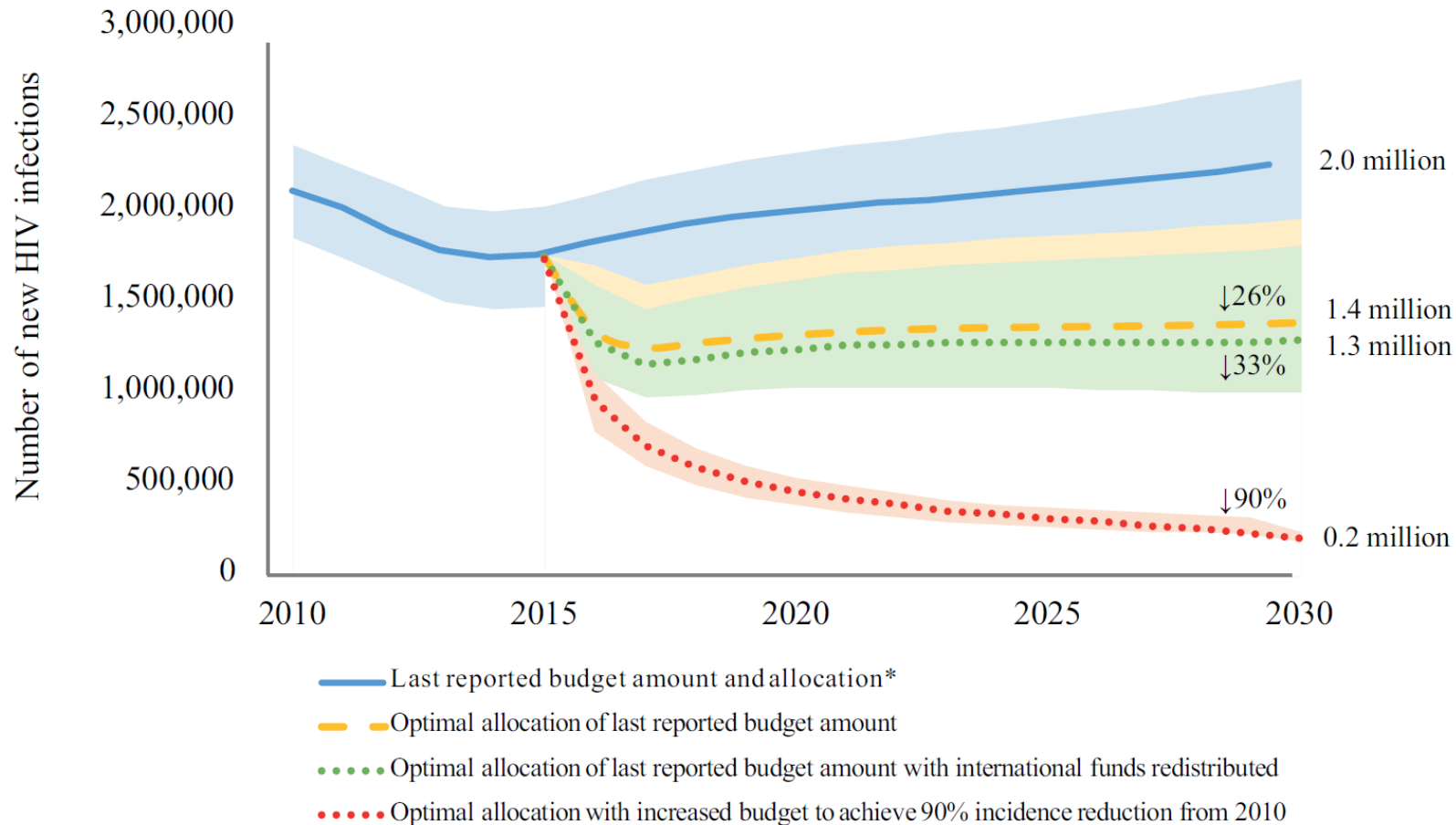


Figure 1:

Estimated global trends in new HIV infections with different resource allocations

Modelled global HIV incidence from 2010 to 2015 with projections from 2016 to 2030 using the last reported global budget amount and allocation applied over this period (solid blue line); optimal resource allocation to minimize new infections by 2030 with the last reported budget amount (dashed yellow line); and optimal allocation with last reported budget amount, but with international funds redistributed between countries (dotted green line), and optimal allocation with increased annual global budget from 2016 to 2030 to achieve a 90% incidence reduction from 2010 levels (dotted red line), with uncertainty bounds (shaded to match respective line colours). *Increasing funding trend not continued, but last reported spending amount and allocation remaining fixed from 2016 to 2030.

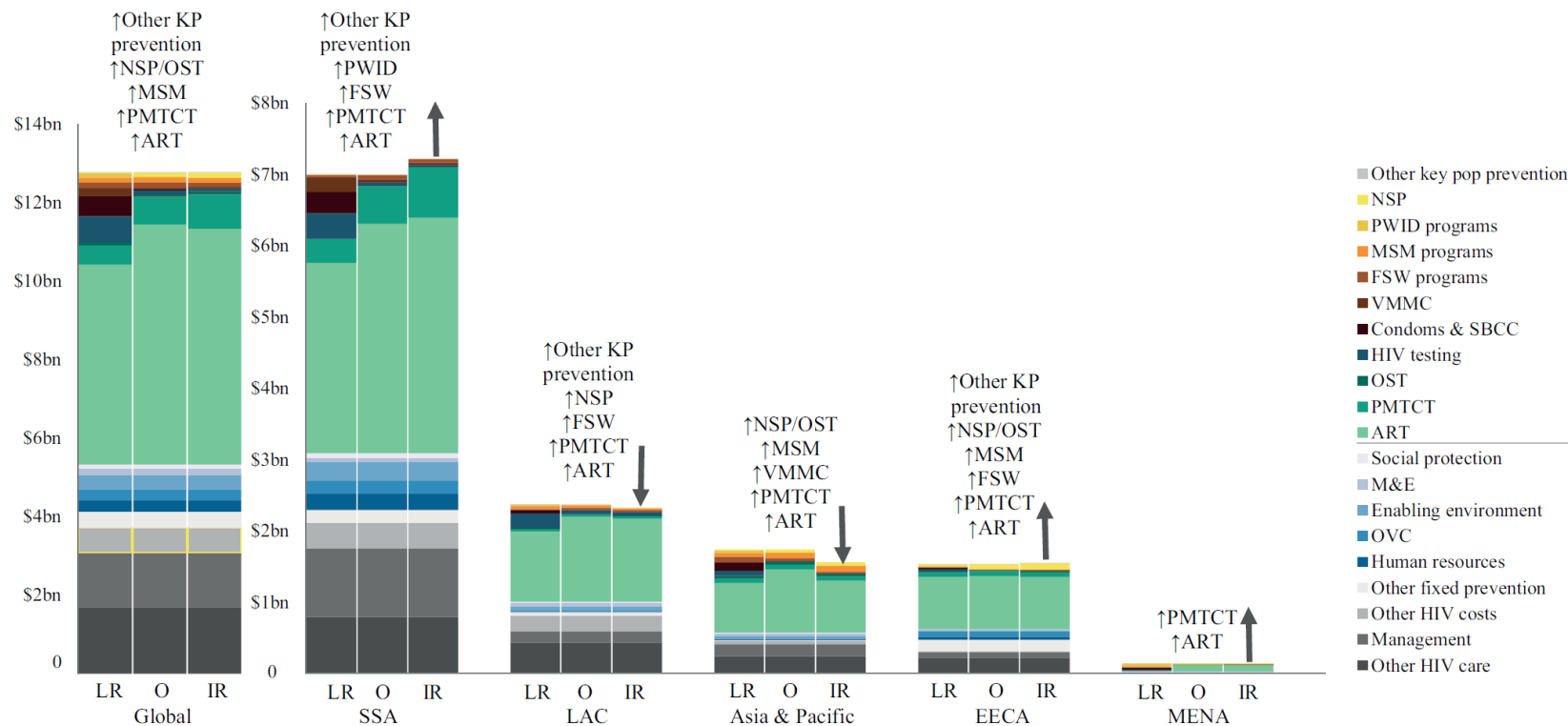
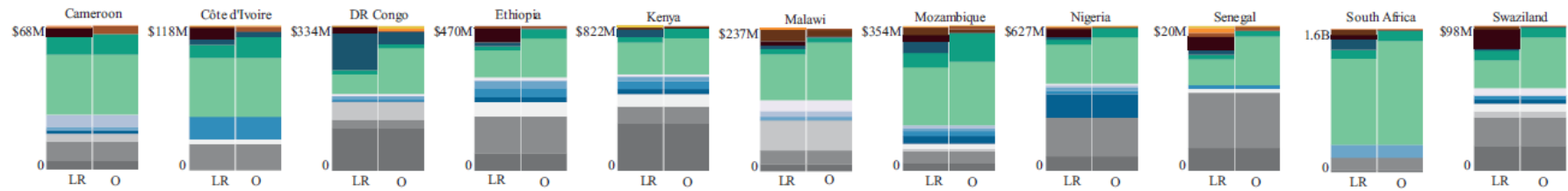


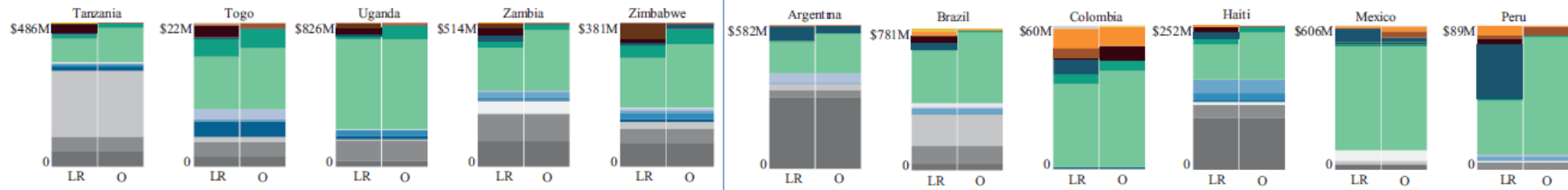
Figure 2: Global and regional HIV resource allocations

Global and regional resource allocations using last reported budget amount applied from 2016 to 2030 for last reported allocation (LR), optimal allocation to minimize new HIV infections by 2030 (O), and optimal allocation to minimize new HIV infections with international funds redistributed between countries (IR). Optimal allocation resulting in shifts in resources towards (↑) or away from (↓) HIV programmes are indicated accordingly. Abbreviations included for regions (Eastern Europe and Central Asia (EECA), Latin American and the Caribbean (LAC), Middle East and North Africa (MENA), and sub-Saharan Africa (SSA)) and HIV programmes (antiretroviral therapy (ART), female sex workers (FSW), monitoring and evaluation (M&E), men who have sex with men (MSM), needle and syringe programmes (NSP), opiate substitution therapy (OST), orphans and vulnerable children (OVC), other key population (pop) prevention, prevention of mother-to-child transmission (PMTCT), people who inject drugs (PWID), social behaviour change communication (SBCC), and voluntary medical male circumcision (VMMC)). Non-targeted HIV programmes are shaded in grey and blue and grouped below the line in the legend. See table S3 for supporting data.

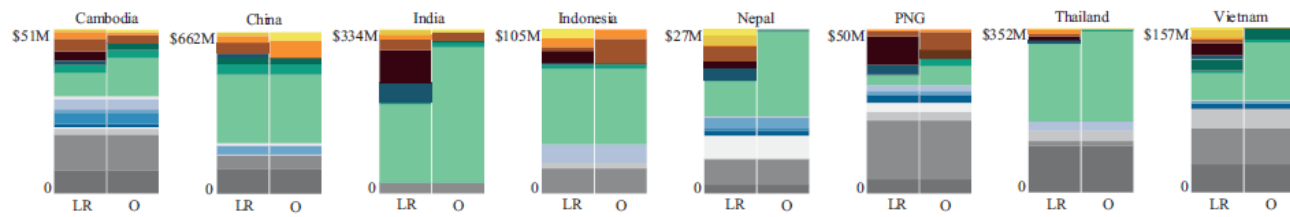
Sub-Saharan Africa



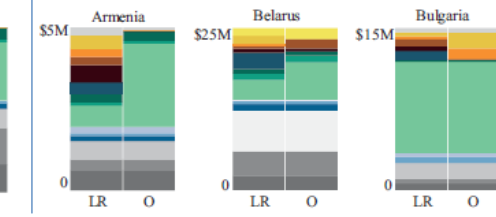
Latin America and the Caribbean



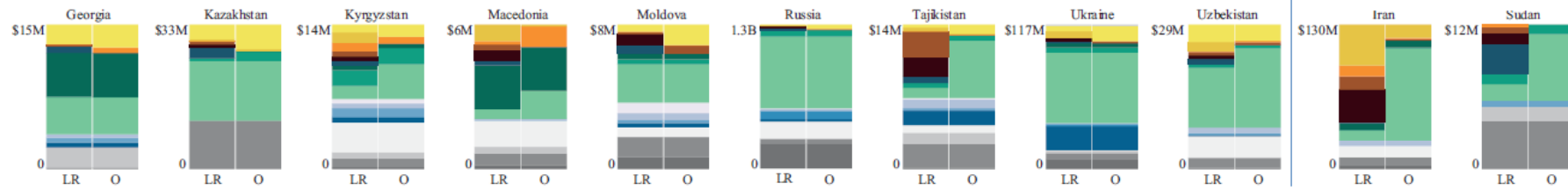
Asia and the Pacific



Eastern Europe and Central Asia



Middle East & North Africa



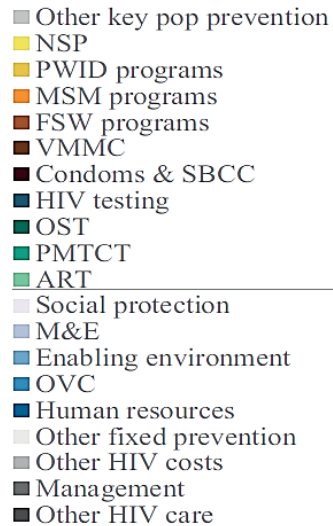
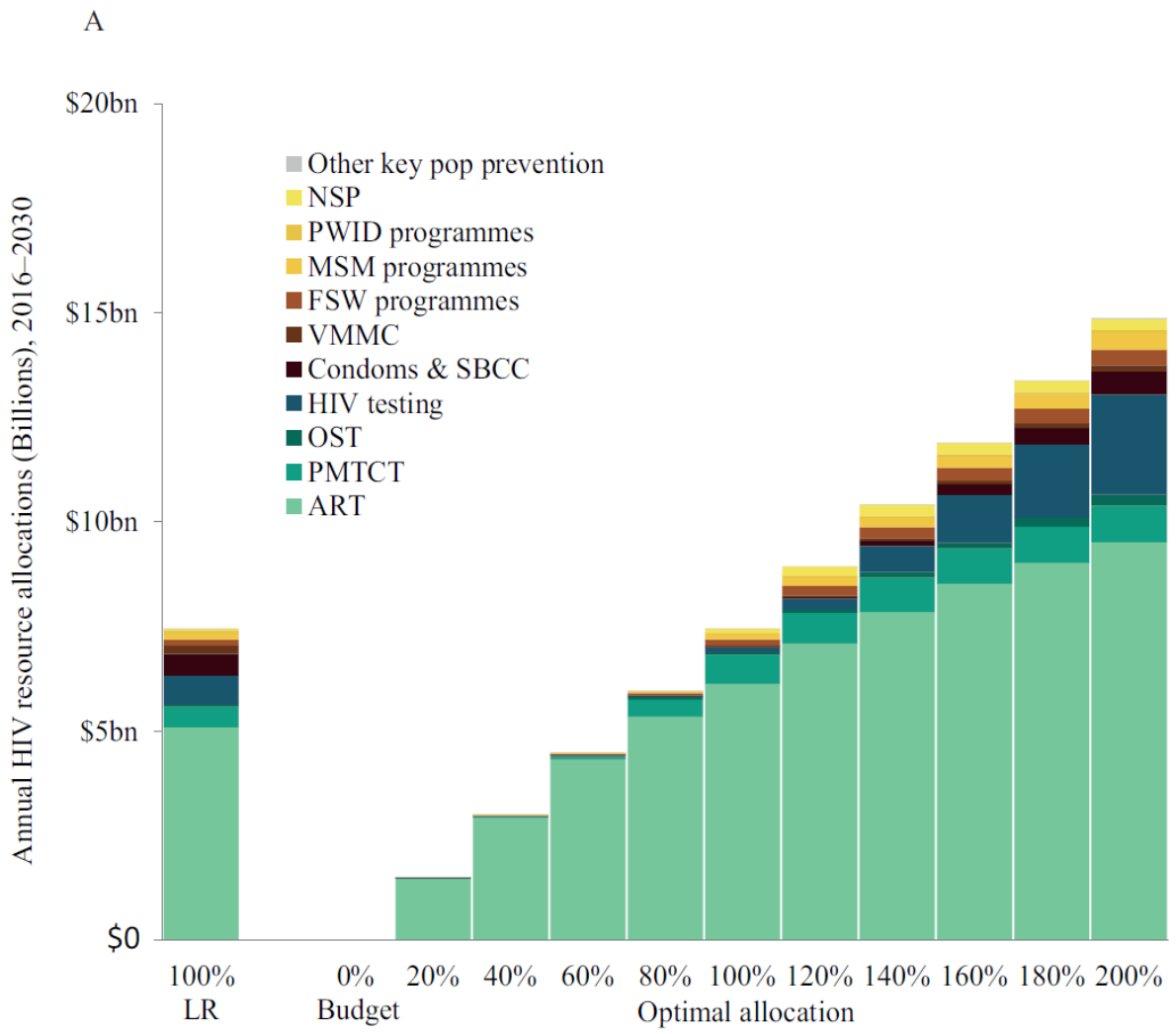


Figure 3: HIV resource allocations by country

Stacked bars showing the last reported (LR) and optimal (O) HIV programme resource allocations to minimize new HIV infections from 2016 to 2030 for each country modelled. Abbreviations included for countries (Democratic Republic of the Congo (DR Congo) and Papua New Guinea (PNG)) and HIV programmes (antiretroviral therapy (ART), female sex workers (FSW), monitoring an evaluation (M&E), men who have sex with men (MSM), needle and syringe programmes (NSP), opiate substitution therapy (OST), orphans and vulnerable children (OVC), other key population (pop) prevention, prevention of mother-to-child transmission (PMTCT), people who inject drugs (PWID), social behaviour change communication (SBCC), and voluntary medical male circumcision (VMMC)). Non-targeted HIV programmes are shaded in greys and blues grouped below the dividing line in the legend. See table S5 for a summary of allocations.



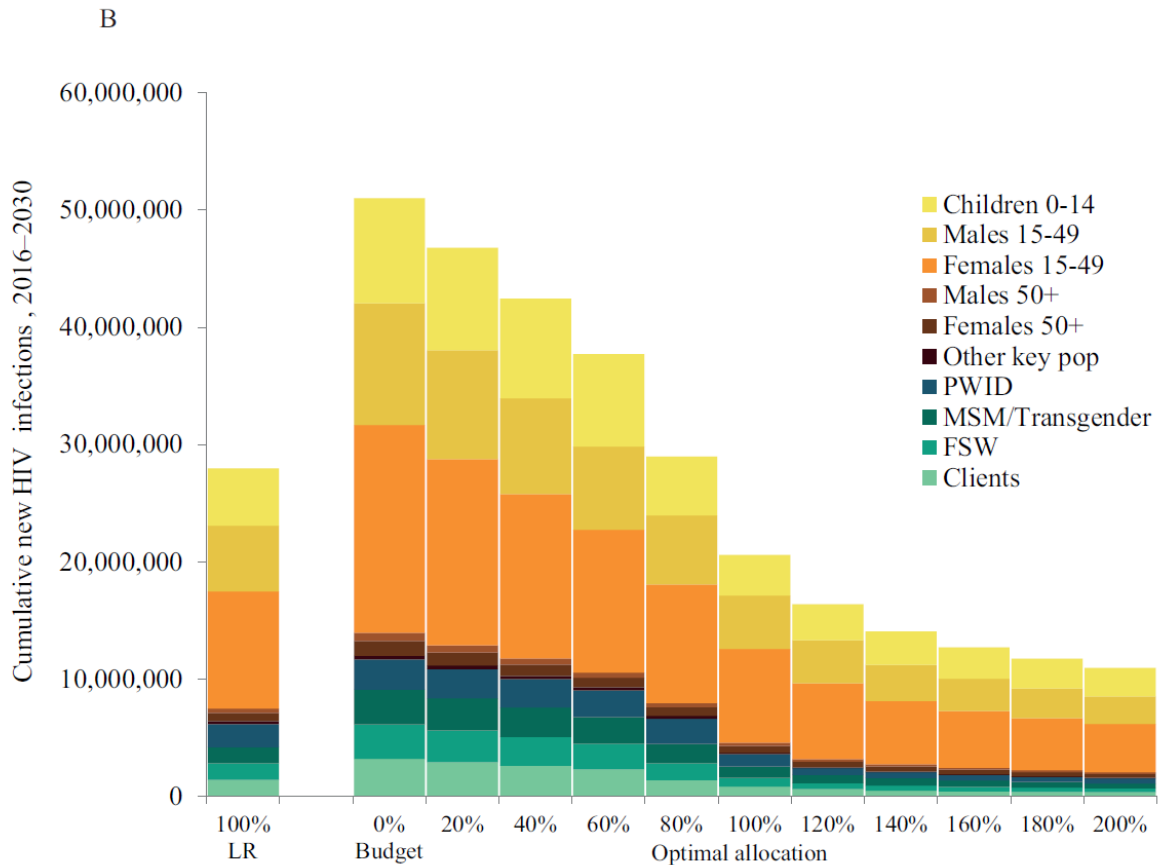


Figure 4: Global HIV resource allocations and new HIV infections with varying budget
 (A) Optimal allocation of annual global HIV programme resources to minimize new HIV infections by 2030 with 20% incremental budget increases from 0% to 200% compared with the last reported (LR) allocation with 100% budget. (B) Cumulative new HIV infections by population group from 2016 to 2030 at variable budget levels. As we did not consider non-targeted programme spending within the optimal allocation, these programmes were excluded here. Abbreviations for HIV programmes include: antiretroviral therapy (ART), female sex workers (FSW), men who have sex with men (MSM) including people who are transgendered, needle and syringe programmes (NSP), opiate substitution therapy (OST), other key population (pop) prevention, prevention of mother-to-child transmission (PMTCT), people who inject drugs (PWID), social behaviour change communication (SBCC), and voluntary medical male circumcision (VMMC); and for population groups aged 50 years and older (50+). See table S6 for supporting data.

References

1. Fast-Track: ending the AIDS epidemic by 2030. Geneva: UNAIDS, 2014.
2. Kates J, Wexler A, Lief E, UNAIDS. Donor government funding for HIV in low- and middle-income countries in 2016. Menlo Park: Kaiser Family Foundation, 2017.
3. Stover J, Bollinger L, Izazola JA, Loures L, DeLay P, Ghys PD, et al. What is required to end the AIDS epidemic as a public health threat by 2030? The cost and impact of the Fast-Track approach. *PLoS One*. 2016;11(5):e0154893.
4. Schwartländer B, Stover J, Hallett T, Atun R, Avila C, Gouws E, et al. Towards an improved investment approach for an effective response to HIV/AIDS. *Lancet*. 2011;377(9782):2031-41.
5. Siapka M, Remme M, Obure C, Maier C, Dehne K, Vassall A. Is there scope for cost savings and efficiency gains in HIV services? A systematic review of the evidence from low- and middle-income countries. *Bull WHO*. 2014;92(7):499-511AD.
6. Goals Manual: A model for estimating the effects of interventions and resource allocation on HIV infections and deaths. 2011. http://www.avenirhealth.org/Download/Spectrum/Manuals/Goals_Manual_August_2011.pdf (accessed July 31, 2017).
7. Brown T, Peerapatanapokin W. The Asian Epidemic Model: a process model for exploring HIV policy and programme alternatives in Asia. *Sexually Transmitted Infections*. 2004;80(Suppl 1):i19-i24.
8. Kerr CC, Stuart RM, Gray RT, Shattock AJ, Fraser N, Benedikt C, et al. Optima: a model for HIV epidemic analysis, program prioritization, and resource optimization. *J Acquir Immune Defic Syndr*. 2015;69(3):365–76.
9. Stuart RM, Grobicki L, Haghparast-Bidgoli H, Skordis-Worrall J, Keiser O, Estill J, et al. How should HIV resources be allocated? Lessons learnt from applying Optima HIV in 25 countries. *J Int AIDS Soc (under review)*. 2017.
10. The Optima model: HIV applications. 2017. <http://optimamodel.com/hiv/applications.html> (accessed July 31, 2017).
11. WHO. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. Geneva: WHO, 2016.
12. AIDSinfo. 2016. <http://aidsinfo.unaids.org/> (accessed July 31, 2017).
13. National AIDS Spending Assessment (NASA): Classification and Definitions. Geneva: UNAIDS, 2009.
14. Kerr CC, Smolinski TG, Dura-Bernal S, Chadderdon GL, Wilson DP. Optimization by adaptive stochastic descent. Under review preprint available from <http://thekerrlab.com/asd/asd.pdf>.
15. Maman D, Pujades-Rodriguez M, Nicholas S, McGuire M, Szumilin E, Ecochard R, et al. Response to antiretroviral therapy: improved survival associated with CD4 above 500cells/ μ l. *AIDS*. 2012;26(11):1393-8.
16. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011;365(6):493-505.
17. Political declaration on HIV and AIDS: On the Fast-Track to accelerate the fight against HIV and to end the AIDS epidemic by 2030. New York: United Nations, 2016.
18. Kelly SL, Wilson DP. HIV cascade monitoring and simple modeling reveal potential for reductions in HIV incidence. *J Acquir Immune Defic Syndr*. 2015;69(3):257-63.
19. Stenberg K, Hanssen O, Edejer TT-T, Bertram M, Brindley C, Meshreky A, et al. Financing transformative health systems towards achievement of the health Sustainable

- Development Goals: a model for projected resource needs in 67 low-income and middle-income countries. *Lancet Glob Health*. 2017.
20. Fan V, Silverman R, Duran D, Glassman A. The Financial Flows of PEPFAR: A Profile (CGD Policy Paper 027). Washington DC: Center for Global Development, 2013.
 21. Anderson S-J, Cherutich P, Kilonzo N, Cremin I, Fecht D, Kimanga D, et al. Maximising the effect of combination HIV prevention through prioritisation of the people and places in greatest need: a modelling study. *Lancet*. 2014;384(9939):249-56.
 22. McGillen JB, Anderson S-J, Dybul MR, Hallett TB. Optimum resource allocation to reduce HIV incidence across sub-Saharan Africa: a mathematical modelling study. *Lancet HIV*. 2016;3(9):e441-e8.
 23. Atun R, Chang AY, Ogbuaji O, Silva S, Resch S, Hontelez J, et al. Long-term financing needs for HIV control in sub-Saharan Africa in 2015–2050: a modelling study. *BMJ Open*. 2016;6(3).
 24. Shattock A, Kerr C, Stuart R, Masaki E, Fraser N, Benedikt C, et al. In the interests of time: improving HIV allocative efficiency modelling via optimal time-varying allocations. *J Int AIDS Soc*. 2016;19:20627.
 25. Sudan's HIV response: value for money in a low-level HIV epidemic. Washington, DC: World Bank, 2014.
 26. Optimizing investments in Belarus for the national HIV response. Washington, DC: World Bank, 2015.
 27. Kahn J, Bollinger L, Stover J, Marseille E. Using Models to Guide HIV/AIDS Policy: A Synthesis of Current Models to Determine Resource Allocation Cost-Effectiveness. In: Holmes K, Bertozzi S, Bloom B, Jha P, Nugent R, editors. Disease Control Priorities. Major Infectious Diseases. 6. 3 ed. Washington, DC: World Bank; 2016. p. 39.