ECONOMIC IMPACT OF HIV

AN OVERVIEW OF GAPS IN CURRENT RESEARCH

Health Economics and Epidemiology Research Office
HE²RO
Wits Health Consortium
University of the Witwatersrand

WITS UNIVERSITY

BOSTON UNIVERSITY

UCL

CONTENTS

This report was written by Markus Haacker from University College London, UK, and Harvard T.H. Chan School of Public Health, US, and Gesine Meyer-Rath from the University of the Witwatersrand, South Africa, and Boston University, US, who are also the primary authors of the technical and policy briefs. Michael Obst contributed research support.

Input to the briefs was provided by Kate Harris (formerly Bill & Melinda Gates Foundation), Arjun Vasan (US Treasury), Stef Bertozzi (UCSF Berkeley), Lorna Tumwebaze (Bill & Melinda Gates Foundation), and attendants of the webinars representing academic institutions, governments of low- and middle-income countries, and non-state actors. The project was funded by the Bill & Melinda Gates Foundation. The views and opinions expressed in the webinars and the policy briefs do however not necessarily reflect the positions or policies of the Bill & Melinda Gates Foundation.

BACKGROUND TO RESEARCH GAPS REPORT

The *Economic Impact of HIV* project aimed at not only reviewing the available evidence on the economic impact of HIV but also, while doing so, taking stock of gaps in this evidence, with an aim of informing future research in this area. This report summarises our findings regarding this aspect- in other words, on the evidence that is still missing. The report starts with an overview of how the role of economic analysis has changed as both the HIV epidemic and the response to it have changed over the last decades (Section I), then summarises main research themes and the gaps in current research in the areas of HIV programming (Section II), the macro-economic impacts of HIV (Section III), a fiscal perspective on HIV (Section IV), and a health-sector perspective (Section V).

In each section, outstanding research questions are highlighted in bold.

Finally, we summarise all research gaps and suggest methodologies for specific studies to close these gaps in the evidence in a Table.

I.
THE ROLE OF ECONOMIC ANALYSIS AS HIV AND HIV RESPONSE CHANGE

The shape of the HIV pandemic – in terms of the transmission dynamics, the population groups most affected, and the health consequences – has changed drastically over the last decades. These developments are predominantly a consequence of the scaling-up of the HIV response and especially of universal access to HIV treatment (Brief #1). This has resulted in reduced mortality among people living with HIV (Brief #2), and contributed to declining HIV incidence. However, due to opposing effects of increased survival and reduced incidence, the number of people living with HIV has often changed only little. Moreover, increased survival and reduced HIV incidence contribute to an ageing of the population living with HIV, the health needs of whom are changing accordingly (Brief #3).

These developments have implications for the economic costs and consequences of HIV, and the contribution of economic analysis for motivating investments in HIV and refining the HIV response. The focus has shifted from preventing imminent deaths and averting severe economic disruptions to improving health outcomes among people living with HIV (further), shifting the trajectory of the epidemic on a path towards "ending AIDS," and improving the effectiveness and cost-effectiveness of the HIV response (Brief #16) contemporaneously (technical and allocative efficiency) and over time (returns to investment).

The interplay between the shape and perception of the HIV pandemic on the one hand, and economic approaches to framing and supporting HIV policies on the other hand, is apparent across different phases of the HIV response. The "tipping point" in the global perception of HIV around 2000 – which saw AIDS elevated "to levels at which no health issue has ever been discussed before" (Piot, 2012) – was supported by mounting evidence on the appalling socio-economic consequences of AIDS. In this phase, HIV was framed not only as "one of the most formidable challenges to human life and dignity," but also one "which undermines social and economic development throughout the world" (United Nations General Assembly, 2001).

Economic analysis, however, played a subordinate role at this time as the evidence was only emerging, and the fundamental concerns – regarding HIV threating economic development, its devastating economic consequences, and the dramatic situation especially in sub-Saharan Africa (United Nations General Assembly, 2001) – were valid in their own right and did not call for a finely calibrated economic evaluation.

The situation changed over the next decade, in part as a consequence of the global effort to fight HIV/AIDS. The scaling-up of treatment contributed to a steep decline in the number of AIDS deaths (from 1.9 million at the peak in 2005 to 1.3 million in 2010, see Brief #1 and UNAIDS (2021)), and the more negative scenarios regarding possible macroeconomic effects did not play out (Brief #7). At the same time, the HIV response became an important and recurrent component of global health financing, with annual spending of US$ 15.1 billion across low- and middle-income countries, split roughly evenly between domestic resources and external support (Ávila, Loncar, Amico, and De Lay, 2013). HIV had thus become a dominant aspect of health overseas development aid (ODA), accounting for 41 percent of ODA in the areas of health and population policies, and an important component of ODA overall (5 percent of total; OECD (2022)). Because external assistance was concentrated on less developed countries with low domestic resources, domestic HIV spending in the most heavily affected countries only very rarely exceeded 0.3 percent of GDP (Haacker, 2016). This, however, often amounted to a significant share of public health spending.

A second important development was the global financial crisis of 2008/09, which had lasting consequences for fiscal space in high-income countries and thus resulted in increased scrutiny of ODA (and any other) budgets. While causality is difficult to establish, the global financial crisis also coincided with a shift in HIV financing. Between 2000 and 2008, the bulk of increases in HIV financing across low- and middle-income countries came from external funders. Since 2008, however, external funding has stagnated (in real terms), and has declined relative to GDP of advanced economies. Meanwhile, contributions from domestic public resources nearly doubled and now account for more than 60 percent of funding across low- and middle-income countries (Brief #14).

For the global HIV response, this means that there is greater scrutiny and accountability on the effectiveness and cost-effectiveness of the HIV response, in relation to other health investments but also – considering that external HIV financing usually comes from ODA budgets and domestic HIV funding involves trade-offs with other sectors through the budget envelope – across objectives of the national development agenda (Brief #12). One influential approach which aimed to address these challenges is the UNAIDS investment framework (Schwartländer and others, 2011), which responds to these challenges in several ways: (1) Framing HIV spending as investment, thus emphasizing the lasting benefits (or "returns") and placing HIV alongside other investments and contributors to economic developments; (2) emphasising on economic returns in addition to health gains, e.g., by emphasising the financial savings that can be achieved by effective HIV prevention. Another influential effort at the same time – associated with the Global Fund's [year] investment case and frequently replicated in global health since then – involves estimating the production gains resulting from longer survival and improved health of people living with HIV (Resch and others, 2011, see Briefs #3, #6, and #7)). While not focusing on HIV, the report of the Lancet Commission on Investing in Health (Jamison and others, 2013) also contributed to developing this perspective, and emphasised the economic value of health gains per se as contributor to the returns to investment (Brief #2).

Assessing recent and ongoing changes in the role of economic analysis is a tad more difficult, without the benefit of hindsight, especially as the simultaneous health and economic crises caused by Covid-19 are playing out. Owing to the high fiscal costs of managing the economic fall-out of Covid-19 in advanced economies, it is plausible that there will be even more scrutiny on ODA budgets and any other forms of public expenditures – similar to the period following the global financial crisis of 2008/09. The situation on health spending, though, is somewhat different, as the impact of Covid-19 has driven home the consequences of underinvesting in health sector capacities for health and economic security.

At the same time, there are longer-term developments related to the changing shape of the HIV epidemic and the response to it. The success in extending access to treatment in most countries has two distinct consequences. First, for most of the populations living with HIV, extending treatment coverage further means initiating treatment somewhat earlier, which leads to improvements in long-term survival and realizing prevention gains through viral suppression but has less immediate health benefits for the individual (Brief #2). This means that arguments for HIV investments based on economic returns (which largely rely on increased survival) have become much less forceful, while HIV poses similar long-term health systems and health financing challenges as other chronic diseases (Atun and Bataringaya, 2011). Second, aggregate high treatment coverage rates may mask sub-populations without adequate access to treatment, for HIV-specific reasons (e.g., stigma) and/or because they lack adequate access to health services overall. For these populations, extending access to HIV services remains a pressing concern, but effective approaches need to be tailored to the relevant barriers.

Much of the discussion so far – and throughout this document – focuses on the global picture and general lessons from the experience of HIV and the HIV response. However, countries differ in terms of the maturity and transmission patterns governing their HIV epidemics, their health systems and barriers in access to health and HIV services, their financial resources, and the contribution of domestic and external sources to the financing of their HIV programmes. Meanwhile, the role and presumably influence of global funders has been waning, and HIV often has evolved from an acute and pressing health challenge into a stable epidemic and a cause of chronic disease. As a consequence, HIV policies are increasingly embedded and subordinated in national health strategies. For example, South Africa has developed an integrated strategy on HIV, TB, and sexually transmitted diseases (SANAC, 2011), and Botswana has merged aspects of its HIV and NCD control programmes. At the same time, the transitions in funding have contributed to increased integration of HIV services and other health services (Brief #12), with generally positive results (Bulstra and others, 2021), and this trend is likely to be reinforced as the populations living with HIV are aging (Haacker, Bärnighausen, and Atun, 2019).

II.
RESEARCH CHALLENGES POSED BY A CHANGING HIV EPIDEMIC

The evolving HIV epidemic does fundamentally change the role of economic analysis. It also poses new policy challenges and creates new research needs in support of these challenges. Most of these new challenges are connected to the scaling-up of HIV services which has occurred so far (Brief #1). Following rapid success in scaling up treatment and other HIV services, the focus is shifting to populations which so far have been underserved. Increased survival means that people living with HIV live longer and get older, and their health needs change accordingly (Brief #2). Moreover, in countries with high HIV prevalence, these changes have significant demographic implications.

The success of efforts to extend access to HIV services is predominantly measured by national-level indicators like treatment coverage or along the cascade of care from HIV infection to diagnosis, treatment initiation, and effective viral suppression. Underneath these indicators, the **understanding of gaps in service coverage** remains weak (Briefs #8 and #9). For many countries, there is limited evidence on service coverage among key populations, with programme analyses relying on small sample surveys and infrequently collected data- which for some sub-populations reflects barriers in access related to stigma or criminalization.) And national household surveys like Demographic and Health Surveys (if they include an HIV module) offer a wealth of data on the socio-economic gradient of HIV, but only little data on prevention service access (typical through questions on HIV awareness) and no data on barriers to treatment access.

These data challenges are not new. The scaling-up of HIV services, and specifically of treatment, has however changed the picture. When access to treatment is low and extending both treatment and testing prevents imminent death, increased treatment and testing coverage is an obvious indicator of progress. At higher coverage rates, the usefulness of treatment-based indicators is compromised. If access to treatment is uneven, then populations where people living with HIV normally receive treatment early and have near-normal life expectancy and populations where AIDS-related mortality remains high coexist. Under these circumstances, the ***distribution* of treatment access and of additional gains in extending access** matters for programme effectiveness in terms of lives saved, but also to assess how effective the HIV programme is in terms of supporting broader health policy goals like improving health equity and progress on universal health coverage (Briefs #8 and #9).

There is however very **limited data on sub-national differences in treatment coverage.** Sub-national regional estimates from Kenya suggest that while

national adult treatment coverage was 75 percent in 2017, regional coverage rates ranged from 23 percent to close to 100 percent (Ministry of Health (of Kenya), 2018). In Nigeria national treatment coverage was estimated at 89 percent in 2020 but differed between 33 percent and close to 100 percent by state (UNAIDS, 2021). These estimates document that sub-national differences in treatment coverage can be an important part of the picture and that reliance on national aggregates obscures the understanding of program effectiveness and health equity implications.

These ambiguities in interpreting national-level coverage rates are compounded by the fact that coverage rates are weak indicators of treatment access. One reason is attrition bias, which arises from the fact that people not receiving treatment are more likely to die, and cross-sectional coverage rates therefore tend to overstate the odds of progressing to treatment. Second, some of the ongoing increases in treatment coverage reflect low mortality among people on treatment, without progress in getting people on treatment more effectively and earlier. For these reasons, cross-sectional differences in treatment coverage rates (as in the illustration on Kenya and Nigeria) tend to understate **gaps in effective access to treatment.**

Addressing research gaps in effective treatment first requires more comprehensive analysis of routine data including viral suppression, not just treatment initiation and retention, and validating such clinical data against population level HIV trends. Assessing gaps in service coverage would first require larger surveys sampled and designed to capture sub-populations by age, sex, geography, risk, and socio-economic factors. Where such data remain unavailable, some insights can be drawn from increasingly available sub-national estimates on the state of HIV and access to treatment.

Estimating attrition bias requires longitudinal data which capture treatment coverage as well as HIV diagnosis, transition to treatment, and of course deaths. These data are essentially unavailable, in their absence some insights can be gained from vital statistics from countries with HIV prevalence where trends in mortality can be attributed to changes in the state of HIV and treatment access, and dedicated as well as opportunistic (using established HIV models) modeling

The second major evidence gap arises with regard to **underserved populations who carry a disproportionate HIV burden** (Long and others, 2021). Concentrated sub-epidemics exist even in countries where the HIV epidemic is classified as generalized, and – against the backdrop of increased treatment coverage and often declining HIV incidence overall, the role of these sub-epidemics is changing, and understanding HIV transmission among populations who carry a disproportionate HIV burden is crucial for reaching a sustainable path towards "ending AIDS." However, effective outreach and targeting is compromised not only by stigma and other barriers, but also by lack of reliable data on the size of and transmission patterns among these sub-populations (Brief #9). **On this issue of data availability, there is no obvious fix – challenges of access are linked closely to the status of key population-, although intentional oversampling of these population groups in surveys of risk and service coverage might be a first step.**

The third major research challenge in connection with the changing shape of the epidemic arises from the survival effects of increased access to treatment, and the resulting aging of the population living with HIV. This aging has consequences for the health needs of the population living with HIV which are in part well-researched and predictable. Because the prevalence of important NCDs, including diabetes, cardiovascular disease, and cancer, increases with age, the aging of the population living with HIV means that the prevalence of NCDs in this population will increase, and people living with HIV increasingly suffer from multi-morbidities.

Beyond this age link, which applies to the general population as well as to people living with HIV, there are important unresolved questions. One is the **contribution of HIV and a history of long-term treatment for HIV to the incidence of NCDs**. Some evidence suggests that HIV has been a contributing factor to the increase in diabetes and cardiovascular disease in LMIC (see Haacker, Bärnighausen, and Atun (2019) for an overview). There is, however, considerable uncertainty around the relevance and magnitude of such estimates in the context of the population-level scaling-up of treatment, the role of different types of treatment, and the extent to which treatment could be adapted to mitigate such effects of HIV and long-term treatment on the occurrence of NCDs.

The growing prevalence of NCD multi-morbidities among people living with HIV leads up to the challenge of effective care. Much of the current drive towards improving effectiveness and cost-effectiveness of HIV services is about standardising and simplifying treatment for stable patients. In contrast, increasing age-related NCDs and the presence of multi-morbidities require a more individualised approach and some measure of **integration of HIV and NCD services.** On this, there

is no established template at present, as most of the experience on the integration of HIV services with other health services regards other areas (Bulstra and others, 2021; the only NCD-themed study on integration with HIV services identified in this review regards screening for NCD, but not treatment (Golovany and others, 2018)).

This is an area where conventional medical and health economic studies on HIV-NCD interactions and the implementation of effective service delivery to people living with HIV, those affected by NCDs, and the intersecting group affected by both HIV and (sometimes multiple) NCDs, are effective. However, an effective response relies on continuously building and synthesizing the empirical evidence across low- and middle-income countries.

In countries with high HIV prevalence, the increased survival of people living with HIV has important demographic consequences. The HIV epidemic plays out against a backdrop of **demographic transition and general population aging** – though with considerable differences across countries in the stage of the demographic transition. Against this backdrop, HIV initially slowed the growth of the old population as most people who contracted HIV did not reach old age. As cohorts who have benefitted from comprehensive access to treatment and, as a result, have suffered much less AIDS-related mortality reach old age, this slowdown is reversed and the HIV becomes a factor that increases the growth of the old population (see Haacker, Bärnighausen, and Atun (2019) on Botswana; and Brief #3 for overview). For countries with high HIV prevalence, the **increase in HIV/NCD co-morbidities** thus will coincide with **increased growth of the demand for age-related NCD services overall, the health systems and fiscal implications of which are not fully understood yet.**

Research challenges on this twin health systems burden to some extent coincide with the agenda on the intersection of HIV and NCD on the patient level or at the point of delivery, but understanding and responding to the growing health system burden requires additional modeling – taking in the stage of the demographic transition, the age and scale of the HIV epidemic, and the timing and scale of the scaling-up of treatment.

III. ECONOMIC IMPACTS OF HIV

The global response to HIV was in part motivated by concerns about the devastating economic impacts of HIV, brought about by (at least in modern times) unprecedented high mortality among young adults and the disruptions this causes to households, the economy, and society. Broadly speaking, these negative economic effects have not materialized. Countries with high HIV prevalence have not experienced markedly lower rates of economic growth (Brief #7), and poverty has not increased by more (or declined less) in these countries (Brief #8).

The comprehensive policy response to HIV, in particular the rapid scale-up of HIV treatment, has obviously played a role, by reversing the devastating health effects and mitigating the economic fallout. We thus did not wait to see the devastating economic consequences sustained horrific mortality rates could have had. This by itself is an achievement of the global HIV response and a valid response to the concerns raised in the UN 2001 Declaration of Commitment on HIV/AIDS and other policy documents at the time.

The absence of a clear economic footprint of the massive health shock posed by HIV, however, raises a number of research questions – on the limitations of economic theory and evidence, and the suitability of macroeconomic indicators as measures of the economic impact of a health shock.

Growth Effects

Economic growth theory does not offer clear guidance on the macroeconomic fallout of a health shock like HIV. The neoclassical growth accounting framework is a suitable vehicle for calibrating the growth effects based on estimates of the impacts of HIV on productivity, the health and size of the labour supply, and investment (successively discussed in Briefs #3 to #6, and synthesized in Brief #7). However, much of the academic work on economic growth over the last 30 years (under the label of "new growth theory") regards the determinants of productivity growth, and in particular of human skills, through the accumulation of "human capital" through education, training and so on.

Differences in estimates and projections based on these two strands of growth theory with regard to the impact of HIV can be large. Neoclassical growth accounting exercises typically arrive at a small and stable impact of HIV on GDP per capita – accounting for some productivity losses owing to disruptions to economic activity from increased mortality or the state of health of people living with HIV, lower investment as resources are absorbed by the HIV response, but acknowledging that available productive assets are shared among fewer people owing to AIDS-related mortality which by itself increases GDP per capita (Brief #7). The predicted net effect is typically small, as the effects on GDP per capita in different directions largely offset each other. Thus, HIV does not make (surviving) populations poorer in terms of GDP per capita, although GDP is smaller because the population size is smaller as a consequence of AIDS-related mortality. This finding is broadly consistent with the growth experience across countries facing high HIV prevalence, i.e., the absence of a slowdown in growth in those countries.

In contrast, relevant models of "new growth theory" link economic growth to investments in human capital. Because high mortality among young adults reduce the incentives to invest in education/human capital, and other disruptions affect access to education, these models can predict a permanent decline in economic growth as a result of AIDS-related mortality. This decline, however, occurs only slowly as it largely works through education and training, but the macroeconomic consequences occur only gradually as new cohorts enter the labour supply.

On the face of it, there is little support to suggest that such predicted effects on human capital have played or (considering the lags involved) are playing a role. While "new" growth models focusing on human capital kick the can in terms of growth effects (which involve long delays), there has been no evidence suggesting that there have been large shifts in decisions on investments in education in line with drastically reduced returns to education as a consequence of reduced life expectancy (Brief #4). (The limited evidence there is suggests a role in household-level disruptions, e.g., with somewhat lower school enrolment rates for orphans.)

One potential reason for the **absence of an impact of HIV on the accumulation of human capital** is the role of life expectancy in measuring the expected length of the productive life span and thus returns to investments in education, for two reasons. Life expectancy – or remaining life expectancy at ages where relevant decisions are made – is defined as the projected duration of life based on current age-specific mortality. The actual life span an individual can be expected to live, however, depends on mortality rates expected in future periods. High current mortality may not affect the expected life span by much if there is an expectation that they will decline, e.g., as a consequence of treatment or as a disease may abate. Moreover, individuals' subjective expectations – the basis of their decisions – may adapt to demographic and health data only with a delay, and in case of HIV stigma could compromise the rational processing of available information. These issues, and their relevance for economic decision-making, are so far little understood and explored in the context of HIV.

Beyond these high-level theoretical and empirical considerations there are important unresolved issues around the measurement of **productivity effects of HIV** (Brief #6). Available empirical studies on productivity effects have been focusing on manual labour where output can most readily be measured. However, these activities are not necessarily representative for the economy overall – it is possible that productivity in less strenuous employments is less affected by health impairment. The practice observed in the scant available literature to move workers (e.g., tea pluckers; see Larson and others (2013) whose health is impaired

to less strenuous jobs suggest that productivity effects of HIV indeed are different across employments, within the agricultural section but perhaps even more across the economy.

Perhaps even more importantly, the bulk of empirical work regards data around and after initiation of treatment of symptomatic HIV patients. With the scaling-up of treatment, this situation has become less typical – patients often initiate treatment earlier, before health and productivity impairments become apparent (so they do not suffer a steep drop in productivity preceding treatment). People receiving treatment earlier also tend to enjoy better health (as evident from subsequent differences in AIDS-related mortality depending on the CD4 count at treatment initiation). And with increasing numbers of people living with HIV on treatment, often for years and even decades, the productivity effects of HIV are dominated by the long-term effects on these populations – on which evidence is weak – rather than any effects around treatment initiation.

Aside from formal education/training, skills are acquired on the job by accumulating experience. This is typically estimated using data on the profile of wages by age-controlling for other factors, and assuming that such differences in wages are a reflection of productivity. HIV, by increasing mortality across the working-age population, is reducing experience, as the average age of the working population declines (by several years in some countries highly affected by HIV). Some models calibrating the macroeconomic effects of HIV therefore include such measures of experience among the determinants of productivity. Whether this approach is appropriate to capture the consequences of a health shock like HIV, however, is debatable. While premature mortality destroys experience, it offers accelerated opportunities to acquire experience to survivors through earlier advancement. In summary, a **firm macroeconomic understanding of the impacts that HIV has had on productivity** remains lacking.

The **empirical evidence on the effects of HIV and of the HIV response on economic growth is weak** (brief #7). In part, this reflects the difficulties around growth regressions in general – there are not so many data points (=countries). For HIV, this shortcoming is compounded by the fact that HIV is heavily concentrated in a few countries. HIV indicators may therefore simply reflect how these countries differ on average from comparator countries. And as many countries with high HIV prevalence share borders and are often highly economically integrated, growth outcomes across these countries are correlated, diminishing the information content of the multiple observations from these countries in growth regressions. Among explanatory variables, indicators like HIV prevalence, mortality, or treatment coverage could be endogenous (influenced by similar factors as economic growth), resulting in biased estimates. Opposed to these challenges, HIV is a large health shock which occurred over a fairly short period; with considerable variation across countries and over time, it therefore represents a good opportunity to study the growth impacts of a health shock (within the limitations of cross-country growth regressions.

Available empirical evidence on the growth effects of HIV is inconclusive (see brief #7). Some studies report a significant growth effect of HIV. On closer inspection, these studies however (1) empirically link growth and life expectancy or mortality, and then (2) link life expectancy or mortality to HIV. This approach boils down to re-affirming the robust link between growth and life expectancy in the empirical growth literature, and then asserting that HIV therefore has a large impact on growth. In contrast, empirical studies linking economic growth to HIV-specific impacts (e.g., AIDS-related mortality) tend to find no impact, or a miniscule one only. Which suggests that the studies finding a link might be based on misspecification, and that any impacts of HIV on economic growth occur along different pathways than those underlying the correlation between growth and life expectancy. A third approach focuses on the scaling-up of treatment. One recent study finds large growth impacts of extending access to treatment (Tompsett, 2020), which however appear implausible in the absence of a preceding slowdown in growth as the impact of HIV unfolded.

The (lack of) evidence on the impact of HIV on economic growth raises questions on the macroeconomic consequences of health shocks. HIV – as a large health shock – offers opportunities to better understand how macroeconomic costs add to and exacerbate the direct consequences of health shocks. However, some aspects of the disease such as its concentration in a few countries compromise empirical inference, and other aspects of the disease, e.g., its transmission and mortality patterns, are highly idiosyncratic. Looking ahead, the question **what lessons can be drawn from the experience with HIV on the growth effects of future health shocks** remains open and has not been systematically addressed. However, there are three areas of work which could contribute to improving the understanding of the growth impacts of HIV and develop a more robust understanding of the economic fall-out of health shocks.

First, much of the uneven results of empirical studies on HIV and economic growth reflects differences in specification of the state of health. Empirical work could address these inconsistencies by encompassing the main approaches – capturing overall health indicators (e.g., all-cause mortality, life expectancy) as well as contributions from HIV.

Second, address the absence of an impact of HIV on the accumulation of human capital. What lessons can be learned on how expectations on the life outlook and returns to investment in human capital are formed? To the extent that investments in human capital are driven by expectation of life prospects, the experience on HIV suggests a need for better understanding of the process through which relevant expectations are formed, and what role stigma of death and HIV may (have) play(ed). Much of this cannot be addressed ex post, but the experience with HIV suggests that this is an important knowledge gap going ahead.

As with the issue on expectations of life outlook, the opportunity to substantially improve the evidence base on the productivity impacts of HIV has passed. This knowledge gap (and corresponding knowledge gaps in aggregate indicators like disability weights incorporated in DALYs), however, could be addressed by building and systematically reviewing evidence on productivity impacts of bad health across professions. And the experience on HIV suggests raising the bar for extrapolating results on productivity across unrelated types of work, which might also contribute to encouraging more work.

Poverty

Concerns about the impacts of HIV on poverty, by reversing development gains and through the adverse economic impacts for households of people living with HIV, have played a prominent and integral role in the policy discourse on HIV. The evidence on such effect, however, is mixed (Brief #8). There is considerable evidence on the adverse economic effects of HIV on household of people living with HIV. However, HIV has not had the devastating macroeconomic consequences feared to trigger an increase in poverty across the population (Brief #7), and high HIV prevalence has not been associated with increasing poverty, or – as poverty declined overall over the last decades – a lesser decline in poverty than in other countries.

One plausible explanation for these discrepancies is the difference between household-level effects and aggregate effects which arises if losses of households affected by HIV to some extent result in gains in other households. The most obvious such mechanism is the loss of an employment and of income by a person affected by HIV, which then is taken up by a member of another household and results in an income gain there. This mechanism has been shown to be powerful in mitigating impacts of HIV on poverty. One rare study addressing this point suggests that the household-level effects of HIV are essentially nullified when the interactions through the labour market are taken into account (Cogneau and Grimm, 2008). And the macroeconomic growth models discussed above also include such an effect – as people die because of AIDS (and cease earning income), the capital they used does not remain idle, but is reallocated and adds to income elsewhere. The findings that HIV has not has an obvious impact on GDP per capita and the finding that high HIV prevalence has not resulted in higher poverty are consistent and related.

Another challenge with regard to the impacts of HIV on poverty links back to the discussion of socio-economic differences in the socio-economic gradient of HIV and of access to treatment. If HIV is tilted towards poorer population groups, and especially if the poor are facing barriers in access to treatment, then more poor people die because of HIV. If this is the case, there are consequences for the HIV-poverty link. First, HIV (at least through this effect) would contribute to poverty reduction, by killing moor poor people. This result, in isolation, of course is obnoxious and in fact masks a deepening of poverty – as the consequences of poverty are exacerbated. Cross-sectional poverty indicators, in the context of HIV, are thus potentially misleading, as they (similar to the ambiguities in the cascade of care, discussed above) are subject to selective mortality bias. The same challenges apply to the socio-economic gradient of HIV – while evidence, largely from DHS data, is inconclusive regarding the socio-economic gradient of HIV, these results do not take into account attrition bias which would result in an under-counting of disadvantaged populations less likely to obtain timely effective treatment.

A **firm understanding of socio-economic differences in access to treatment** (not only on a cross-sectional basis, but also in terms of progression along the cascade of care) would help resolving these ambiguities, and align the evidence on HIV and the policy dialogue on extending access to HIV services more effectively with challenges on poverty reduction and universal health coverage.

Addressing these knowledge gaps in part is a subset of the agenda on improving evidence on gaps in service coverage across sub-populations, and the notes on data availability and attrition bias made there apply to gaps according to socio-economic factors or poverty status as well. However, there are two important additional knowledge gaps.

First, poverty is endogenous, and a consequence of HIV, other health shocks, and economic factors and processes. Assessing the impacts of HIV on poverty therefore requires modeling on the dynamics of household poverty over time and across the economy, including the effects across households described above. The available evidence – especially the puzzle of the missing effects of HIV on aggregate poverty rates – suggests that these economic factors – in addition to the direct effects on households affected by HIV - are integral to the understanding of HIV-poverty links.

Second, HIV is an aspect of the issue of poverty as a barrier in effective access to health services overall. These challenges have been driven home by the ongoing fall-out of the economic disruptions encountered over the last years (Covid-19, commodity prices). The health consequences of the economic fall-out of Covid provide significant learning opportunities on poverty-related health vulnerabilities, and contribute to the impetus for creating more resilient health systems and progress towards UHC.

IV.
A FISCAL PERSPECTIVE

The fiscal perspective in a sense encompasses all other aspects of economic analysis, as economic analysis is geared towards decision support on HIV policies, i.e., it informs decisions on spending allocations (Brief #11). In this sense, the most important research gap is the gap between the menu of economic analytical tools and how findings are most commonly packaged on one hand, and the information needs and attention span of high-level policy makers on the other hand: What is – in a nutshell – the point of investing specifically in HIV/AIDS, at the expense of other policy priorities? [1]

The need to "speak to" the perspective of a Ministry of Finance raises a number of more specific questions:

- **How to summarize the impacts of HIV and of the HIV response in a way that speaks to the mindset of officials in a Ministry of Finance** (or at key donor agencies)?
- How to **understand and communicate the funding needs for HIV programs, and how these are shaped by the design and effective implementation of HIV policies?**
- **To what extent do HIV policies create long-term spending obligations** (e.g., financing the provision of treatment), and how do current HIV add to or help mitigating these obligations?
- Relatedly, **what are the boundaries – in terms of spending categories - of the fiscal costs and consequences of HIV?** The health consequences of the aging of the population living with HIV – discussed above – are mirrored in spending needs, but other categories of spending are also affected.
- The financing of the HIV program raises some issues, regarding any **specific financing instruments or linkages to achieving universal health coverage and financial protection.**

"Speaking to" the Ministry of Finance is integral to the agenda on the *Economics of HIV,* as our collaboration was in part motivated by the desire to develop more effective tools, or using existing tools more effectively, in order to improve the policy dialogue with the Ministry of Finance. For this reason, we have discussed earlier

1 The nitty-gritty questions on HIV program design and on interactions between HIV services and the health systems are addressed separately, further below.

how the perception of the economic fall-out of HIV has changed over the last two decades, and discuss aspects that a Ministry of Finance may care about above (e.g., "economic impacts") separately below.

The Ministry of Finance, however, is a government agency with experience in supporting decisions on spending allocations across the areas of government activity, which involves setting priorities and making choices across different programs and intended outcomes. As such, it is capable of evaluating the projected outcomes of an HIV program against its cost, and support spending decisions across different types of outcomes (e.g., health – education – infrastructure). Economic analysis is useful in supporting such decision processes if it provides genuine insights which effectively improve the information base of decision-making, and are connected with the outlook of the Ministry of Finance and others high-level decision makers (Brief #11).

One such area is the impact of HIV and of the HIV response on GDP and GDP per capita (discussed above). On the face of it, this is relevant because in numerous countries, the national development strategy is built around economic growth, and additional economic resources generated by the HIV response conceivably offset some of the resources absorbed by the HIV response. However, there is no evidence that estimates of the growth impacts of HIV have substantially contributed to decision-making on HIV. Relatedly, estimates of the economic returns of the HIV response in terms of "full income" or incorporating the "value of statistical life" are dominated by the valuation of health gains rather than any production gains, and so do offer little economic insights beyond interpreting the health gains. So **what role have estimates on impacts of HIV on economic growth played in informing funding decisions**, and what are the lessons for framing the case for investments in health, in different situations (e.g., from acute disasters to long-term challenges)?

In making decisions on funding allocations, it is important to understand the fiscal net costs of investments in HIV. HIV and investments in HIV are potentially associated with significant "unrelated" medical costs and affect other categories of government spending (discussed below). The more complex challenge arises from the fact that the fiscal consequences of HIV and of the HIV response are spread over decades (see points on communicable chronic diseases, below). However, there is little work on how to incorporate such sustained current costs or future costs in policy analysis. In this area, the research gaps arise in two directions: (1) **Improve the understanding of the life-time consequences of HIV, the medical needs and demand for health services, and the health systems consequences** this will have (see discussion above, also Brief #2); (2) **Develop better and readily deployable tools capturing the long-term consequences of HIV** (life-cycle perspectives, spending commitments implied by policy decisions), and develop an **empirical understanding of how such insights and expectations are utilised by policy makers** (e.g., effective time horizons, discount rates applicable to or applied across low- and middle-income countries).

The question of valuing costs over time leads up to the challenges of an integrated valuation of health gains and the costs of achieving them, and of applying such analysis in decision support. Applying estimates of the value of statistical life (VSL) across low- and middle-income countries faces considerable challenges, notably owing to the paucity of relevant empirical evidence from these countries (Briefs #2 and #10). Applications of the VSL in low- and middle-income countries therefore rely on extrapolation of estimates from advanced economies. Because of limited evidence on how the VSL changes with the level of income (the income elasticity of the VSL), however, VSL estimates thus generated are subject to very high uncertainty (Robinson, Hammitt, and O'Keeffe, 2019). Filling this knowledge gap will require **substantially more evidence on valuations of life from low-and middle-income countries**, a point well recognized in the literature on benefit-cost analysis, and an area where the evidence is slowly improving.

Relatedly, there is little established practice on utilising benefit-cost or cost-effectiveness analysis on deciding whether interventions should be implemented in a particular context. The limitations of the common practice of benchmarking against GDP per capita (the one- and three-times GDP per capita thresholds) are well recognized (Brief #13). However, there is little **country-level evidence on cost-effectiveness thresholds applied in actual policy decisions** (but see Ochalek and others (2018) on Malawi, Meyer-Rath and others (2017) on South Africa), and extrapolations based on well-documented threshold from advanced economies run into the same challenges as extrapolations on the VSL and are therefore subject to very high uncertainty when applied to low- and middle income countries (Woods, Revill, Sculpher, and Claxton, 2016; Briefs #13 and #16).

Spending Needs

The design of HIV programs affects spending needs in two ways. Most directly, effective spending allocations contribute to containing the costs of the program, improving cost-effectiveness and – by offering better value for money – making investments in HIV more compelling (Brief #16). For these aspects, there is well established body of cost-effectiveness analysis available (see discussion on health sector, below). The more complex challenges arise from the transition of HIV into a chronic disease, but one that is also communicable – compounding analytical challenges associated with either type of disease.

With chronic disease, a life-cycle approach is usually appropriate to capture cost-effectiveness of approaches on prevention and care, and it may be necessary to include "unrelated costs" (van Baal and others, 2018) in policy evaluations. This means concretely that if people living with HIV survive into old-age, the increasing years of survival are associated with increasing medical costs unrelated to HIV, and counting only HIV-related treatment costs but the full survival gains biases estimates of cost-effectiveness. Moreover, HIV itself or a history of long-term antiretroviral therapy may increase the prevalence of some non-communicable diseases.

With communicable diseases, it is necessary to take into account population-level effects which arise through disease transmission. This is well known and reflected in standard epidemiological models. It is, however, not well-captured in most cost-effectiveness analyses. The 10- to 20-year horizons adopted in most HIV policy analyses may have been appropriate when HIV interventions were averting imminent deaths and HIV prevention interventions would result in adverse health consequences within a few years. (Even then, the health consequences of prevention outcomes late in the policy period did not get captured, resulting in some bias.) These issues have become exacerbated through the transformation of HIV into a chronic disease. As a result, cost-effectiveness analyses especially on prevention efforts that rely on deaths averted (or the resulting loss in DALYs) within the policy period have become an increasingly blunt and misleading tool (Haacker, Hallett, and Atun (2020)), and results are highly sensitive to the time horizon applied (White and others, 2008). **These challenges on time horizons have rarely been acknowledged or addressed explicitly in HIV research, and a consensus on best practice for capturing the health and economic consequences of HIV interventions over time is lacking.**

Relatedly, HIV policies are often motivated in terms of permanently shifting the trajectory of the epidemic, that is, in terms of "ending AIDS." Such policies have long-term consequences beyond the period during which they are implemented. **There are methods available to evaluate the effects of such a permanent shift in the trajectory of an infectious disease,** as the disease settles on a new steady state (e.g., a constant incidence rate). These methods have been applied in the context of immunization programs (Ultsch and others (2016), Mauskopf and others, 2018), **but so far they have not been adapted to HIV and "ending AIDS."**

The scope of costs beyond the health sector which are relevant to evaluating the fiscal consequences of HIV and HIV policies also deserves some more attention (Briefs #10 and #11). Good practice in cost-effectiveness analysis involves adopting a broad "societal" perspective, capturing all fiscal or societal costs caused by a disease or affected by an intervention (Sanders and others, 2016). Significant fiscal costs outside the health sector can arise especially in the area of social security – as a result of increases in morbidity and mortality the costs of disability payments or in support of orphans go up, while fewer people reach old age and would qualify for pensions and other grants linked to old age as a consequence of HIV. These fiscal costs can be significant – in the case of South Africa, it was estimated that fiscal savings owing to reduced old-age grants were of a similar order of magnitude as the immediate costs of the HIV response (Haacker and Lule, 2012). Some of these repercussions (e.g. disability payments), though, have diminished as HIV has transformed into a less severe, chronic disease.

The knowledge gaps described in the preceding three paragraphs are largely linked to the transition of HIV into a chronic disease. Addressing them will require methodological innovations drawing on the literature on chronic diseases (life-cycle horizons capturing the changing needs over time, supported by the specific evidence on the needs of the aging HIV population and HIV-NCD intersections, discussed further above), life-cycle approaches in public finance, as well as methods

designed to capture a shift in the trajectory of a disease (drawing, e.g., from immnunisation economics).

The question on the scope of fiscal costs and cost savings linked to the impact of HIV and the HIV response leads up to the question of how much of any economic gains (in GDP etc.) can be counted as offsets against the fiscal costs of HIV. Output gains increase the tax base, a proportion of these gains thus yields additional fiscal revenues. The tax-GDP ratio, typically in the range of 15-25 percent of GDP, is a useful benchmark on the magnitude of revenue gains as a consequence of higher GDP. However, many public services are linked to the size of the population (including some of the "unrelated" medical costs discussed earlier) and economic activity, so some of an increase in revenues from higher GDP is absorbed by higher non-HIV spending and not available for refinancing the HIV program or other spending priorities.

Additionally, public spending could be refinanced by higher taxes or national insurance contributions. This is relatively straightforward when HIV investments result in higher GDP per capita. If some or all of this gain is taxed, households are on average not worse off in terms of income and still benefit from the health gains. However, the bulk of GDP gains comes from (and is largely absorbed by) increased survival and not from GDP per capita, so there is little scope for actual or potential taxation of survival gains leaving households not worse off in terms of income.

However, household benefit from and value reduced mortality risks, and this valuation is estimated on an aggregate level applying the value of statistical life or "full-income." While these valuations include survival gains (so the same issues as discussed above apply), they are dominated by the valuations of health. To the extent that households are willing and able to pay for improvements in the health outlook, estimates of "full-income" gains thus point to a potential for refinancing HIV investment through higher taxes or contributions.

In summary, while there is a considerable amount of work on the direct cost consequences of HIV and investments in the HIV response over time, and broad understanding on the macroeconomic consequences, **the fiscal implications of HIV – in terms of the scope of costs and actual or potential revenue gains – and the interpretation of economic gains from a fiscal perspective are much less understood. Addressing this gap will require more explicit economic modeling beyond the growth effects of HIV, that also takes into account how much of the additional output accrues to the government through increased revenues, and how much of these additional revenues are absorbed by increased population-driven spending needs across the board.**

Financing

HIV programmes around the world are almost entirely funded from external and domestic public resources – a reflection of the consensus that HIV is an infectious disease for which a public health approach is appropriate (brief # 15). Where significant contributions from private spending are reported in spending assessments, these are typically estimates of the private costs of accessing care or of private spending on items like condoms which contribute to HIV prevention.

In light of this, most of the policy discourse on HIV financing involves convincing the domestic government or donors to commit sufficient funding – from general resources or ODA budgets, respectively – for supporting and attaining the program's objectives, as described in costed strategies or "investment cases." Nevertheless, part of the policy discussions on sustainable financing have regarded dedicated funding instruments – e.g., through (portions) of taxes dedicated to the HIV program and administered through a special fund, or "development bonds" the proceeds of which are contributing to specific objectives. However, so far there is only one functioning example of an HIV trust fund – the "AIDS levy" (a surcharge on income tax) in Zimbabwe (Brief #11), while efforts to establish a fund have stalled in other countries (e.g., Kenya) or the funds play a marginal role so far (Tanzania). To focus the policy discourse on "innovative" financing, it would be useful to **assess this experience, the additionality of such specific funding instruments, the purposes they serve, and the extent to which they have met these objectives.**

The other area in which considerable research and policy gaps exist is the **integration of HIV programmes into national health insurance schemes, and especially their role in attaining universal health coverage** (Briefs,

#12, #15). HIV programmes have been important contributors to progress towards universal health coverage, in terms of extending coverage to essential health services, providing access to high-quality care, and financial risk protection (through public provision of treatment and other services). The drive towards universal health coverage, and introducing national health insurance, raises two types of questions. Firstly, **what are the implications for any integration of HIV services and other health services of a wider transformation of the health system?** Secondly, if HIV services are integrated into the benefit package offered by a national health insurance, **does this open the possibility of raising domestic funding from private sources (through contributions) for funding HIV services?** In part, this research challenge is part of the wider agenda in support of progressing towards universal health coverage. There are, however, three HIV-specific considerations which need to be taken into consideration. (1) Any arrangement would have to be consistent with the public health approach to HIV, i.e., not introduce barriers in access to treatment. (2) Compulsory national insurance contributions are similar to taxes, and the distributional effects of switching from public (=tax) financing to funding by compulsory private contributions need to be taken into account. (3) Using national health insurance as an instrument to attain universal health coverage typically involves subsidies to enable lower-income households to participate within their means. The objective of attaining high coverage imposes constraints on how much of the costs of a medical benefits package can be funded from contributions.

V.
A HEALTH-SECTOR PERSPECTIVE

In this section we describe research gaps relating to decision-support and trade-offs within the health sector, building on briefs # 12, 13, 15, and 16.

In addition to securing additional funding, resources for the HIV response can also be unlocked through improved efficiency (Briefs #16, #11). Improved efficiency, in turn, contributes to the value-for-money proposition and helps improving the case for additional funding. Assessments of program efficiency, and opportunities for efficiency gains, have been integral to economic analyses in support of HIV strategies. Methodologically, it is useful to distinguish the issue of technical efficiency (how effectively and cost-effectively specific services are delivered, and how this effectiveness can be improved) and allocative efficiency (how best to allocate financial resources across program components). In practice, though, the two issues are inter-related, as technical efficiency drives funding needs, and optimal allocations across interventions reflect their technical efficiency.

Technical Efficiency

Capturing technical efficiency is conceptually straightforward as long as it regards specific services and concrete outcomes, and is adequately addressed through analyses of unit costs. Identifying scope for improving cost-effectiveness, though, also requires comparisons – between sites, across countries, or against some derived benchmark. Much of the literature in this area regards estimating unit costs, understanding its determinants, and separating systematic differences (e.g., according to HIV prevalence which affects the yield of testing, or the number of patients by site) from differences which can not be explained in this way and point to inefficiencies and waste.

There are two types of knowledge gaps in translating this evidence into actionable policy advice. With regards the health systems context, a remaining question is **to what extent do measured inefficiencies reflect**

health systems challenges which apply more widely and which are not adequately addressed at the (HIV) programme level- e.g., **to what extent does observed under-utilization of resources apply across health services on site or across sites? Do inefficiencies in the delivery of HIV services reflect inefficiencies across the entire health sector or the public sector overall,** e.g., insufficient equipment and supplies? **And to what extent do health workers (need to) supplement their incomes through other sources, absorbing some of their working time?** The common theme behind these questions is the need to benchmark findings on the technical efficiency of HIV services against evidence on the efficiency of health services in general, by comparison with existing evidence or including non-HIV health services in empirical studies.

Within the HIV programme, the most important challenge is that a large portion of spending is not linked to specific services but is used for **programme management.** While there is some scrutiny on such spending (e.g., through external funders benchmarking across countries), there is limited understanding on the **contributions of programme management to overall service delivery, and how management expenditure is linked to the scale of the programme.** (E.g., the leading tool on HIV program analysis – Spectrum/Goals – captures it as a simple mark-up on the costs of services, not necessarily informed by empirical data.) These uncertainties cumulate in a general **uncertainty regarding the statistical properties of average service costs (or "unit costs",** as they are often referred to), and undermine the generalization of cost estimates from one setting to another- a nonetheless common practice. These shortcomings could be addressed by reviewing and unpacking programme management costs as documented in "National AIDS Spending Assessments," empirically study how program management costs are linked to the scale and other aspects of the HIV program (to identify systematic drivers of these costs but also outliers which might point to inefficiencies and waste), and incorporating the findings of such an analysis in HIV modeling and policy analysis.

Allocative Efficiency

Capturing allocative efficiency of HIV programs is more complex, as it requires estimates on the cost-effectiveness across HIV services, and as the relevant outcomes – unlike for technical efficiency – are not unique (Brief #16). Outcomes of HIV policies include HIV infections averted, AIDS-related deaths averted or delayed, they target different age groups and populations, and the effects are spread over time (the lifetimes of people living with HIV, and even longer time horizons if the transmission dynamics are fully taken into account, see above). This leads up to two questions where going practice in HIV policy analysis is particularly unsettled.

One question regards the **valuation of outcomes and costs over time.** HIV policy analyses exhibit great variation in time horizons applied (Haacker, Hallett, and Atun, 2020), and are inconsistent across studies in the methods applied to capture the consequences of the policy beyond this period (survival, costs, state of HIV epidemic, see discussion under "fiscal" heading). Results regarding cost-effectiveness are sensitive to the choice of the policy period and the methods of accounting for longer-term consequences; the lack of an established practice therefore introduces an arbitrary element into these results, and compromises external validity.

Second, and relatedly, many **HIV policy analyses focus on HIV-specific outcomes like HIV infections and AIDS-related deaths,** and not standardized health metrics like DALYs. Because of the focus on HIV-specific outcomes, **much of the evidence on the cost-effectiveness of HIV interventions does not allow direct comparisons with other diseases, and therefore does not support allocative efficiency analysis between HIV and other health services.** One important illustration of this disconnect is the Global Burden of Disease III study, which – in spite of very considerable work that has been done on the cost-effectiveness of HIV interventions – identifies and includes very few studies reporting standardized health outcomes (e.g., only 3 studies on VMMC; see Horton (2017)). This knowledge gap could be addressed by encouraging/enforcing more consistent reporting of standardized health outcomes. To facilitate such reporting ex ante and ex post, reduce burden on individual researchers, and ensure consistency and quality, an authoritative study on the mapping of typical outcomes of HIV interventions and policies (not only deaths averted where it is straightforward, but also HIV infections averted or placing people on treatment) would be useful. This calculus would also need to take in research gaps discussed elsewhere, notably on the

needs of people living with HIV – realizing full DALY gains requires an ongoing financial commitment to sustain treatment.

Cost-effectiveness analysis, however, is an area in which there has been a disconnect between academic practice (which often applied GDP-based "cost-effectiveness thresholds" popularized early on by the WHO (see Commission on Macroeconomics and Health (2001), Hutubessy, Chisholm, and Edejer (2003), and – on academic application - Griffiths, Legood, and Pitt (2016)), and political practice, where these thresholds played no apparent role. This state of affairs is slowly changing, with general academic practice moving on from an unreflected use of such thresholds (Marseille and others (2014), Bertram and others (2016)), and a growing small body of work building on thresholds implied by governments' (and donors') observed willingness to pay for health improvements in low- and middle-income countries (Ochalek and others (2018), Edoka and Stacey (2020)). Research on the economics of HIV has several stakes in this agenda. Empirically, it offers a wealth of evidence on governments' and donors' willingness to pay (and their interplay, through joint funding of HIV programmes), and how this willingness may change in response to economic and health circumstances (notably the global financial crisis of 2008/09, and the ongoing disruptions from Covid and acutely from war in Europe. Looking ahead, a **consistent body of knowledge on decisions regarding funding allocations and implied willingness to pay** will be instrumental for addressing challenges posed through funding transitions, and managing the changing health needs of people living with HIV.

Methods for Informing HIV Budget Trade-Offs

The methods used in answering research questions aimed at the optimal allocation not only of the health, but in particular of the HIV budget have increased in both use and complexity over the last decade (Brief #16). If the main aim in the early years was to help make the economic case for more access in particular to treatment, in recent years the focus has been on moving away from blanket programming targeting average potential clients at known and average costs and average plannable budget amounts to closing coverage gaps by targeting the underserved with more tailor-made services at, potentially, higher-than-average cost (Avanceña and others (2020), Long and others (2021); for a modelled application, see Maheu-Giroux and others (2019)). One such approach is targetting interventions to populations based on risk behaviour and/ or geography (Anderson and others (2014), optimising programmes over time (Stopard and others (2019), Shattock and others (2016)) or while considering diminishing returns to investment (Chiu and others (2017)). Recommendations from these targeted modelling applications have been criticised for being impractical when budget lines cannot be shifted easily or quickly (Stopard and others (2019)) or when recommendations go against other policy aims, including those of international organisations and funders.

In this situation, a number of empirical questions remain unanswered:

- **Is the front-loading of HIV investment net beneficial?** Higher short-term population coverage with both treatment and prevention theoretically shortens the time to epidemic control and "ending AIDS". It is however also contingent on the long-term development of costs which are unknown. Addressing this question involves methodological and practical work to better capture the long-term effects of HIV interventions, systematically exploring the timing of interventions and changing effectiveness and cost-effectiveness as the epidemic evolves, and capturing the cost-effectiveness of policies which shift the trajectory of an epidemic, and greater attention to the uncertainties of projecting HIV outcomes and costs over long periods.
- **What is the shape and determinants of local and global cost functions for HIV interventions and HIV programmes are; and how do costs evolve over time?** This involves two activities. (1) Building on and expanding evidence on unit costs and their determinants across facilities, depending on local or national characteristics, scale, and over time. (2) Empirically assessing how local or national costs of HIV services have been changing over time in line with changing input process and economic context, and developing best practice on projecting costs.
- Does the **uncertainty associated with more granular data** from household surveys (such as PHIA) and other

sources **overwhelm the benefits of more granular model types,** potentially leading to findings and resulting recommendations that are net detrimental? Addressing this question involves learning from the experience in translating results from granular modelling into policy, and incorporating uncertainty around localized data into models

An important methodological concern over the years has been how to best deal with overlapping effects of interventions aimed at the same target group or at the same underlying issue (for example, improving retention on treatment). Adding together the effects of individual interventions and their costs ignores that the same interventions would have likely been less effective if added onto an already existing interventions, and, due to integration effects, potentially less costly. One suggestion for this would be to evaluate interventions in packages to see **how packaging of interventions for particular target groups effects their costs and effectiveness.**

Additionally, the focus on budget constraints inherent in allocative efficiency models risks ignoring the presence of constraints on the supply and demand side that are unknown or hard to quantify at the time of analysis, including human resource constraints or limited global supplies with novel drugs or diagnostic technologies (Vassall and others (2016)).

This leads to the question on **the relevance of such non-monetary health systems constraints for HIV programmes and across the health sector,** and how to best incorporate such factors into allocative efficiency and other decision models by adding opportunity costs and non-monetary constraints into models and assessing the implications for cost-effectiveness and effectiveness. This question may be less pressing for HIV service delivery now (as the situation is no longer one of rapid service expansion), but it is relevant in the context of allocative efficiency across the health sector and integration of HIV services into a health system characterized by multiple resource constraints.

Generally, as the field moves towards including aspects beyond cost and effectiveness, such as overall and intra-population equity, financial risk protection, international targets or non-financial constraints, using methods such as Multi-Criteria Decision Analysis (Baltussen and others (2006) or Expanded Cost-Effectiveness Analysis (Verguet and others (2016), two related questions arise: **Which metrics and data can these additional decision criteria best be informed by,** in order to avoid additional layers of parameter uncertainty? Additionally, **what are the best methods to elicit which criteria should apply in any given decision problem, how should they be weighted in relationship to each other- and who gets to choose both criteria and weights?**

Summary: Research Gaps & Suggested Methodologies

Research gap	Suggested methodology
1. Research challenges posed by a changing HIV epidemic (Policy brief #1)	
Gaps in *effective* treatment	Routine data including viral suppression, not just treatment initiation or retention
Contribution of HIV and long-term treatment to NCD incidence	HIV transmission models including NCDs
Health systems and fiscal implications of demographic transition and general population aging	Models capturing prevalence and budget impact of NCDs (+/- HIV)
Integration of HIV and NCD services	Implementation science
Improve the understanding of the life-time consequences of HIV, the medical needs and demand for health services, and the health systems consequences	Build evidence on co-prevalence, incidence, resource use and costs from patient data on people living with HIV across low- and middle-income countries, taking account of health systems context and the most common co-existing diseases in these countries.
2. Growth effects (Policy briefs #3-#6)	
Empirical evidence on the growth effects of HIV: Weak evidence in part reflects limitations of cross-country regressions (especially as HIV is heavily concentrated in small number of countries), but differences in specification have also contributed to ambiguities	Systematically explore (and encompass) pathways addressed across prior empirical studies, distinguish "health-growth" nexus from specific impact of HIV
Productivity effects of HIV and HIV treatment, incl. macroeconomic effects	Explore wage and employment data on people living with HIV, linking wage/employment data across regions and localities with differences in HIV and service access. Systematically review evidence on productivity effects of poor health (owing to HIV or otherwise) across employments, also covering non-manual activities.
Absence of impact of HIV on the accumulation of human capital	Explore conventional measures of life expectancy (based on current mortality) vs. forward-looking measures taking in expectations on changing mortality, and processes through which perceptions and expectations adapt.
What lessons on the growth effects of future health shocks can be drawn from the experience with HIV?	Identify more clearly, calibrate, and empirically validate the channels through which HIV affects growth. Test lessons from HIV against experience from more acute and short-terms health shocks, such as Ebola, and Covid(?).
3. Effect of HIV on poverty (Policy briefs #8, #9)	
Gaps in service coverage (sub-populations by age/ sex/ geography / risk)	Larger surveys sampled to represent these sub-populations
Barriers to service access	Household surveys complemented by longitudinal data, indirect evidence from population surveys
Distribution of additional gains in extending access	Sub-stratified models
Understanding of socio-economic differences in access to treatment (and other services)	Larger surveys sampled to represent all relevant socio-economic strata. Longitudinal data to gain insights on attrition bias.
Contrast between evidence on impact of HIV on affected households and lack of impact on aggregate poverty rates	Drawing on evidence on dynamics of poverty, economic modelling to capture "general equilibrium" repercussions across economy and households.

4. Expenditure policy (Policy briefs #11, #13, #14, #16)	
Provide evidence and build consensus on best practice for capturing the health and economic consequences of HIV interventions over time (incl. choice of time horizons)	Assess dependence of results on effectiveness and cost-effectiveness on time horizon in modelling (sensitivity analysis), and develop more robust approaches on capturing health and cost consequences.
Apply to HIV available methods to evaluate the effects of a permanent shift in the trajectory of an infectious disease	Build on work on shifting the trajectory of an epidemic permanently and valuing this shift, drawing on work, e.g., in immunization economics and economic approaches to valuing assets.
Pay more attention to the scope of costs beyond the health sector which are relevant to evaluating the fiscal consequences of HIV and HIV policies	Build on literature on "unrelated costs" in health economics, and "generational accounts" in fiscal economics
Generate more evidence on valuations of life from low-and middle-income countries	Using dedicated surveys, wage data, and indirect evidence on valuation of life implied by political or consumers' decisions.
Country-level evidence on cost-effectiveness thresholds applied in actual policy decisions	Increase body of literature deriving thresholds from specific policies and decisions, and develop cross-country knowledge base.
5. Financing (Policy brief #15)	
Assess extent to which output gains owing to reduced HIV mortality translate into additional fiscal resources	Economic modelling to capture revenue effects of increased GDP and fiscal resources absorbed by increased population-driven spending needs.
Assess experience and potential of dedicated financing instruments, such as HIV trust funds or development bonds	Simple overview on trust funds and other financing instruments (and policy processes which may or may not result in establishing one), the intended purposes, and the extent to which they have fulfilled these objectives.
Integration of HIV programmes into national health insurance schemes, and their role in attaining universal health coverage • What are the implications for any integration of HIV services and other health services of a wider transformation of the health system? • Does this open the possibility of raising domestic funding from private sources (through contributions) for funding HIV services?	Review evidence on introducing and increasing coverage of national health insurance schemes, Interpret against literature on public health approach to HIV and designing medical benefit packages.
6. Technical efficiency (Policy briefs #12, #15, #16)	
Do inefficiencies in the delivery of HIV services reflect inefficiencies across the entire health sector or the public sector overall, e.g., insufficient equipment and supplies? • To what extent does observed under-utilization of resources apply across health services on site or across sites? • To what extent do health workers (need to) supplement their incomes through other sources, absorbing some of their working time?	Integrate analysis of technical efficiency of HIV services with analysis of health sector. Do inefficiencies in HIV services replicate pattern observed elsewhere? Should we benchmark HIV against other types of services? How do constraints in HIV and health overall overlap and differ?
What are the contributions of programme management to overall service delivery, and how is management expenditure linked to the scale of the programme?	"Overhead" costs typically are a large component of HIV spending, and in modelling often represented as simple mark-up on direct costs. Using available spending data across countries and over time, explore how overhead costs change with scale of programme and other factors driving it, to identify HIV programmes where it is relatively high and provide an empirical basis for extrapolating overhead in scaling-up scenarios.

7. Allocative efficiency (Policy briefs #13, #16)	
Valuation of outcomes and costs over time, especially with regards to • methods for accounting for longer-term consequences • choice of time horizons	Address methodological challenges on HIV as a disease that is both chronic and communicable (long time horizons, transmission dynamics). More systematically address implications of choosing duration of time horizon and methods for capturing costs and consequences over time.
Generation of evidence on the cost-effectiveness of HIV interventions that allows direct comparisons with other diseases, and supports allocative efficiency analysis between HIV and other health services	Routinely report standardized outcome measures (such as DALYs, or QALYs where local quality weights exist) which allow comparisons across diseases, while taking account of challenges posed by long time horizons (including the spending needs implied by sustained treatment) and transmission dynamics of HIV.
8. Methods for informing HIV budget trade-offs (Policy brief #16)	
Is front-loading of HIV investment net beneficial?	Draw on work on allocative efficiency, build on and systematically explore results on the timing of interventions and time-varying spending allocations.
What is the shape and determinants of cost functions for HIV interventions and HIV programmes?	Compile evidence on unit costs and their determinants across facilities, depending on local or national characteristics, scale, and over time. Empirically assess how local or national costs of HIV services have been changing over time in line with changing input process and economic context, and develop best practice on projecting costs.
Does the uncertainty associated with ever-more granular data from household surveys (such as PHIA) and other sources overwhelm the benefit of more granular model types?	Incorporate error terms around survey-based model inputs into models, and review experience on use of granular data to steer HIV resources and inform localized strategies.
What is the relevance of non-monetary health systems constraints for HIV programmes and across the health sector?	Add opportunity costs or non-monetary constraints into optimisation models, and address implications for cost-effectiveness and efficiency.
In using decision criteria beyond cost and effectiveness, • which metrics and data can these additional decision criteria best be informed by? • what are the best methods to elicit which criteria should apply in any given decision problem • how should they be weighted in relationship to each other • who gets to choose both criteria and weights?	Incorporate these aspects into ongoing development of multi-criteria decision analysis; where possible, co-design these analyses in conversation with policy makers.

References

- Anderson SJ, Cherutich P, Kilonzo N, Cremin I, Fecht D, Kimanga D, Harper M, Masha RL, Ngongo PB, Maina W, Dybul M, Hallett TB. 2014. "Maximising the Effect of Combination HIV Prevention through Prioritisation of the People and Places in Greatest Need: A Modelling Study". *Lancet*, vol. 384, no. 9939, pp. 249-56.
- Atun, Rifat, and Jacqueline Bataringaya, 2011, "Building a Durable Response to HIV/AIDS: , Implications for Health Systems," *Journal of Acquired Immune Deficiency Syndromes*, Vol. 57 Suppl. 2, pp. S91-S95
- Avanceña ALV, Hutton DW. 2020. "Optimization Models for HIV/AIDS Resource Allocation: A Systematic Review". *Value Health*, vol. 23, no. 11, pp. 1509-21.
- Ávila, Carlos, Dejan Loncar, Peter Amico, and Paul De Lay, 2013, "Determinants of Government HIV/AIDS Financing: A 10-Year Trend Analysis from 125 Low- and Middle-Income Countries," *BMC Public Health,* Vol.13, No. 1: 673.
- Baltussen R, Niessen L. 2006. "Priority Setting of Health Interventions: The Need for Multi-criteria Decision Analysis". *Cost Effectiveness Resource Allocation*, vol. 4:14.
- Bertram, MY, Lauer, JA, De Joncheere, K, Edejer, T, Hutubessy, R, Kienya, MP, & Hilla, SR 2016, "Cost-effectiveness Thresholds: Pros and Cons", *Bulletin of the World Health Organization*, vol. 94, no. 12, pp. 925-30.
- Bulstra, Caroline A, and others, 2021, "Integrating HIV Services and Other Health Services: A Systematic Review and Meta-Analysis," *PLoS Medicine,* Vol.18, No. 11: e1003836.
- Chiu C, Johnson LF, Jamieson L, Larson BA, Meyer-Rath G. 2017. "Designing an Optimal HIV Programme for South Africa: Does the Optimal Package Change When Diminishing Returns are Considered?" *BMC Public Health,* vol. 17:143.
- Cogneau, Denis, and Michael Grimm, 2008, "The Impact of AIDS Mortality on the Distribution of Income in Côte d'Ivoire," *Journal of African Economies,* Vol.17, No. 5, pp. 688-728
- Commission on Macroeconomics and Health 2001, *Macroeconomics and Health: Investing in Health for Economic Development,* WHO, Geneva.
- Edoka, Ijeoma P, and Nicholas K Stacey, 2020, "Estimating a Cost-Effectiveness Threshold for Health Care Decision-Making in South Africa, *Health Policy and Planning*, Vol. 35, No. 5, pp. 546–555.
- Golovaty, Ilya, and others, 2018, "Cost of Integrating Noncommunicable Disease Screening Into Home-Based HIV Testing and Counseling in South Africa," *Journal of Acquired Immune Deficiency Syndromes,* Vol. 78, No. 5, pp. 522-526.
- Griffiths, UK, Legood, R & Pitt, C 2016, "Comparison of Economic Evaluation Methods Across Low-income, Middle-income and High-income Countries: What are the Differences and Why?" *Health Economics,* vol. 25, pp. 29-41.
- Haacker, Markus, 2016, *The Economics of the Global Response to HIV/AIDS* (Oxford and New York: Oxford University Press).
- Haacker, Markus, Till Bärnighausen, and Rifat Atun, 2019, "HIV and the Growing Health Burden from Noncommunicable Diseases in Botswana: Modelling Study," *Journal of Global Health,* Vol.9, No. 1: 010428.
- Haacker, Markus, Timothy B Hallett, and Rifat Atun, 2020, "On Time Horizons in Health Economic Evaluations," *Health Policy and Planning*, Vol.35, No. 9, pp. 1237-1243.
- Haacker, Markus, and Elizabeth Lule, 2012, *The Fiscal Dimension of HIV/AIDS in Botswana, South Africa, Swaziland, and Uganda* (Washington DC: World Bank).
- Hontelez, Jan AC, and others, 2021, "Evidence-Based Policymaking When Evidence Is Incomplete: The Case of HIV Programme Integration," *PLoS Medicine,* Vol.18, No. 11: e1003835.
- Horton, Susan, 2017, "Cost-Effectiveness Analysis in Disease Control Priorities, Third Edition," in: Jamison, Dean T, and others (eds.), 2017, *Disease Control Priorities, Third Edition : Volume 9. Improving Health and Reducing Poverty* (Washington DC: World Bank).
- Hutubessy, R, Chisholm, D & Edejer, TT 2003. "Generalized Cost-Effectiveness Analysis for National-Level Priority-Setting in the Health Sector", *Cost Effectiveness and Resource Allocation,* vol. 1, no. 1:8
- Jamison, Dean T, and others, 2013, "Global Health 2035: A World Converging within a Generation," *The Lancet,* Vol. 382, No. 9908, pp. 1898-955.

- Larson, Bruce. A, and others, 2013, "Antiretroviral Therapy, Labor Productivity, and Gender: A Longitudinal Cohort Study of Tea Pluckers in Kenya," *AIDS*, Vol. 27, No. 1, pp. 115–23.
- Long, Lawrence C, and others, 2021, "Getting resources to those who need them: the evidence we need to budget for underserved populations in sub-Saharan Africa," *Journal of the International AIDS Society,* Vol.24, Issue S3: e25707.
- Maheu-Giroux M, Diabaté S, Boily MC, Jean-Paul N, Vesga JF, Baral S, Abo K, Wognin V, Diouf D, Alary M. 2019. "Cost-Effectiveness of Accelerated HIV Response Scenarios in Côte d'Ivoire".
- Marseille, E, Larson, B, Kazi, DS, Kahn, JD & Rosen, S 2014, "Thresholds for the Cost-effectiveness of Interventions: Alternative Approaches", *Bulletin of the World Health Organization,* vol. 93, pp. 118-24.
- Martha Ainsworth, Lieve Fransen, and Mead Over (eds.), 1998, *Confronting AIDS: Evidence from the Developing World* (Luxembourg: Office for Official Publications of the European Communities).
- Mauskopf, Josephine, and others, 2018, "Economic Analysis of Vaccination Programs: An ISPOR Good Practices for Outcomes Research Task Force Report," *Value in Health,* Vol.21, No. 10, pp. 1133-1149.
- Ministry of Health (of Kenya), 2018, *Kenya HIV Estimates Report 2018* (Nairobi: Ministry of Health).
- Meyer-Rath, Gesine, Craig van Rensburg, Bruce Larson, Lise Jamieson, Sydney Rosen, 2017, "Revealed Willingness-to-Pay versus Standard Cost-Effectiveness Thresholds: Evidence from the South African HIV Investment Case," *PloS One,* Vol.12, No. 10: e0186496.
- Ochalek, Jessica, and others, 2018, "Supporting the Development of a Health Benefits Package in Malawi," *BMJ Global Health,* Vol.3, No. 2: e000607.
- OECD, 2022, Creditor Reporting System,, accessed at https://stats.oecd.org/Index.aspx?DataSetCode=crs1 in February 2022.
- Piot, Peter, 2012, *No Time to Lose* (New York and London: Norton and Company).
- Resch, Stephen, and others, 2011, "Economic Returns to Investment in AIDS Treatment in Low- and Middle-Income Countries," *PLoS One,* Vol. 6, No. 10:e25310.
- Robinson, Lisa A., James K. Hammitt, and Lucy O'Keeffe, 2019, "Valuing Mortality Risk Reductions in Global Benefit-Cost Analysis," *Journal of Benefit-Cost Analysis,* Vol.10, No. S1, pp. 15-50.
- Sanders, Gillian D, and others, 2016, "Recommendations for Conduct, Methodological Practices, and Reporting of Cost-effectiveness Analyses: Second Panel on Cost-Effectiveness in Health and Medicine," *JAMA : The Journal of the American Medical Association,* Vol.316, No. 10, pp. 1093 1103.
- Schwartländer, Bernhard, and others, 2011, "Towards an Improved Investment Approach for an Effective Response to HIV/AIDS," *The Lancet,* Vol. 377, Issue 9782, pp. 2031-2041.
- Shattock AJ, Kerr CC, Stuart RM, Masaki E, Fraser N, Benedikt C, Gorgens M, Wilson DP, Gray RT. 2016. In the Interests of Time: Improving HIV Allocative Efficiency Modelling via Optimal Time-varying Allocations". *Journal of the International AIDS Society,* vol.19:20627.
- South African National AIDS Council (SANAC), 2011, "National Strategic Plan on HIV, STIs and TB 2012-2016" (Pretoria: SANAC).
- Stopard IJ, McGillen JB, Hauck K, Hallett TB. 2019. "The Influence of Constraints on the Efficient Allocation of Resources for HIV Prevention". *AIDS,* vol. 33, no.7, pp. 1241-46.
- Tompsett, Anna, 2020, "The Lazarus Drug: The Impact of Antiretroviral Therapy on Economic Growth," *Journal of Development Economics*, Vol.143: 102409.
- Ultsch Bernhard, and others, 2016, „Methods for Health Economic Evaluation of Vaccines and Immunization Decision Frameworks: A Consensus Framework from a European Vaccine Economics Community," *PharmacoEconomics*, Vol. 34, No. 3, pp. 227–244.
- UNAIDS, 2021, "Epidemiological Estimates Database". Accessed at https://onlinedb.unaids.org/epi/libraries/aspx/Home.aspx in February 2022.
- United Nations General Assembly, 2001, "Declaration of Commitment on HIV/AIDS", Resolution S 26/2 adopted by the General Assembly (New York: United Nations).
- van Baal, Pieter, Alec Morton, David Meltzer, and Werner Brouwer, 2018, "Future Unrelated Medical Costs Need to Be Considered in Cost Effectiveness Analysis," *European Journal of Health Economics,* Vol.20, No. 1, pp. 1-5.

- Vassall A, Mangham-Jefferies L, Gomez GB, Pitt C, Foster N. 2016. "Incorporating Demand and Supply Constraints into Economic Evaluations in Low-income and Middle-income Countries". *Health Economics,* vol. 25, supplement 1, pp. 95-115.
- Verguet S, Kim JJ, Jamison DT. 2016. "Extended Cost-Effectiveness Analysis for Health Policy Assessment: A Tutorial". *PharmacoEconomics*, Vol. 34, no. 9, pp. 913-23.
- White, Richard G, 2008, "Male Circumcision for HIV Prevention in Sub-Saharan Africa : Who, What and When?" Vol. 22, No. 14, pp. 1841-1850.
- Woods, Beth, Paul Revill, Mark Sculpher, and Karl Claxton, 2016, "Country-Level Cost-Effectiveness Thresholds: Initial Estimates and the Need for Further Research," *Value in Health,* Vol.19, No. 8, pp. 929-935.