DESCRIBING THE ‘END OF AIDS AS A PUBLIC HEALTH THREAT’

FINAL REPORT OF A TECHNICAL WORKING MEETING CONVENED BY UNAIDS

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EXECUTIVE SUMMARY

United Nations Member States committed, through Sustainable Development Goal 3.3.1, to "end AIDS as a public threat" by 2030. This objective was conceptualized as a situation in which HIV was controlled, reducing new HIV infections and AIDS related deaths to a sufficiently low and 'locally acceptable' level. UNAIDS quantified the target as a 90% reduction in national HIV incidence and HIV related mortality between 2010 and 2030, alongside ending stigma and discrimination. The *Global AIDS Strategy 2021–2026* set out the 95–95–95 testing, treatment and other comprehensive HIV prevention targets; meeting these by 2025 is the core of a strategy to attain the 'ending AIDS' goal. In 2017, UNAIDS defined a set of epidemiological metrics to identify when a country was on track to ending the AIDS epidemic.

Many countries, particularly those most affected by HIV in eastern and southern Africa, are on track to achieve the 95–95–95 targets and reach, or nearly attain, the 90% incidence and mortality reduction targets by 2030. Current target frameworks do not prescribe anticipated HIV epidemiological outcomes or programme priorities after 2030 in these or other countries. In the absence of specific outcomes and programme priorities, language such as 'end of AIDS' may lead some to interpret that the 'end of AIDS as public health threat' would also mean the end of a concerted public health response to HIV/AIDS and large-scale HIV investments.

Uncertainties remain about: (1) probable HIV epidemic trajectories beyond 2030 in settings that have attained testing and treatment targets (or have nearly done so) in the period before 2030; (2) the package of services, policies (legal environment, government policies and instruments) and programme (interventions) implementation which will be required for the foreseeable future to sustain declining HIV infections and AIDS deaths; and (3) the core set of indicators that need to be routinely monitored to ensure that HIV infections and AIDS deaths remain low and continue to decline.

This technical meeting aimed to:

- Review long term HIV epidemic projections in high HIV burden settings sustaining high levels of HIV testing and treatment coverage and other comprehensive HIV prevention and reasons for variation in model projections.
- Assess the implications of long-term transmission dynamics for sustaining progress in reducing new HIV infections and AIDS deaths.
- Review empirical evidence on current HIV transmission dynamics and interpret implications of empirical evidence for adjudicating likely future HIV epidemic trajectories.
- Develop clear characterizations of potential HIV epidemic situations post-2030 in high burden settings that have controlled the epidemic.
- Describe how and when the HIV response in high HIV burden settings changes as it transitions from an 'emergency response' to a long-term epidemic control scenario with regard to:
  - Epidemiological indicators and metrics for maintaining disease control.
  - HIV programmes (treatment, testing, prevention, societal enablers).
  - HIV surveillance and monitoring.

Current evidence indicates that with high levels of HIV treatment and viral suppression coverage targets met and sustained, HIV incidence and mortality will be considerably lower after 2030, with new infections continuing to fall. There was broad consensus across models about incidence reductions occurring post-2030, with high levels of coverage targets. However, there are uncertainties and variations across models on the rates of decline of incidence and if incidence will plateau at some point after 2030–2040. High levels of treatment and viral load suppression coverage will be required to maintain the important incidence and mortality reductions which have been achieved, and as the epidemic progresses the average age of people living with HIV will increase over time. HIV transmission may become more concentrated in higher risk populations. Currently, what evidence is available does not support the presence of large HIV transmission clusters within sub-Saharan African epidemics, unlike the HIV transmission dynamics among men

who have sex with men and people who inject drugs seen in Europe or USA. However, as incidence declines, high HIV transmission networks may become more identifiable through phylogenetic studies, given underlying heterogeneities in transmission and intervention coverage. This is because the programmes that have led to the initial and large declines in incidence can still leave gaps, and some of these gaps may be in populations with disproportionately high risk of onward transmission. Other populations which will become a growing proportion of people living with HIV with HIV transmission risk include those who are treatment naïve, and those currently, or previously, on antiretroviral therapy but who face barriers to achieving or sustaining viral load suppression, and thus remain viraemic. Future epidemic dynamics among key populations remain an important source of uncertainty because there remain relatively few data on treatment coverage rates among these populations.

Recommendations

Some suggested metrics for maintaining disease control as the HIV response transitions include:

- Measures of cumulative/lifetime risk of HIV acquisition or mortality.
- Testing and treatment coverage rates.
- Population viral load measures such as population prevalence of viral suppression among young people.
- Measures of HIV morbidity such as the CD4 count at diagnosis.

The recommended HIV programmes that will be required for the foreseeable future for high HIV burden settings were:

- Free ART for all to enable a high level of ART coverage and viral load suppression, including continued investment in drug development to improve the availability of highly effective treatment options.
- Treatment for chronic conditions in ageing people living with HIV, with integration of noncommunicable disease (NCD) care into already existing healthcare systems. Systems for building on HIV modes of care to expand to NCD care (for those living with and without HIV) are needed.
- Scaling up of differentiated service delivery (DSD) models to improve access to treatment, accompanied by routine viral load testing.
- Access to HIV testing services, with an increased focus on index testing and HIV self-testing and retaining a focus on HIV testing among pregnant women attending antenatal services.
- Continued access to HIV prevention services, such as condoms, well targeted PrEP and HIV prevention education.
- The current 10–10–10 targets to remove social and legal barriers to HIV services, including the legal and policy environment, stigma and discrimination, and gender inequalities.

The recommended HIV surveillance and monitoring measures included:

- Sustained use of antenatal clinic surveillance, including for monitoring HIV prevalence and incidence trends and population ART coverage and viral suppression.
- Strengthened routine programmatic and data systems for monitoring mortality and advanced HIV disease.
- Strengthened community led HIV measurement activities among key populations.
- Continued presence of large, population based, household surveys, which will remain an important source of reliable data, but which can be scaled back.

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BACKGROUND

Upon adoption of the 2030 Sustainable Development Goals, specifically target 3.3.1, Member States of the United Nations committed to end AIDS as a public health threat by 2030 *(1)*. In the past 20 years, numerous countries have succeeded in dramatically reducing new infections and AIDS-related deaths through strong, well-funded HIV responses coupled with political commitment and leadership, strong health system implementation, and engaged communities. Following these successes, and achieving targets, the long-term programme implementation required to sustain low and declining new HIV infections and AIDS deaths will evolve, and HIV programmes will be integrated into strengthened health systems. The *Global AIDS Strategy 2021–2026* identified targets that need to be met to end AIDS as a public health threat by 2030 *(2)*.

The target of ending AIDS as a public health threat by 2030 was conceptualized as new HIV infections and AIDS related deaths declined to a sufficiently low, locally acceptable, level. It has been operationalized by UNAIDS as a 90% reduction in national incidence and mortality between 2010 and 2030. Countries have made different levels of progress toward these targets, with many countries in eastern and southern Africa achieving large declines. As new infections drop to low levels and countries are achieving the 95–95–95 testing and treatment targets, precise understanding of the state of the epidemic and its potential trajectory are needed to monitor the continued decline and define the programmes required to sustain these trajectories in the context of large numbers of people with HIV living to an old age with treatment and durable viral suppression for decades to come.

This includes understanding the current transmission dynamics of HIV in high burden settings, likely epidemic trajectory under alternative future scenarios, appropriate level of programme required to maintain epidemic control, health systems integration, surveillance systems, sustainable financing, community support, laws, and policies. The ‘end of AIDS as a public health threat’ does not mark the end of the multisectoral response to HIV, but rather a status that must be sustainably maintained and monitored.

In 2014, UNAIDS convened a meeting to consider the long-term goals for the global response to the AIDS epidemic. The panel agreed on ‘ending AIDS as a public health threat’ by 2030 as an ambitious, yet feasible, goal for policies and strategies *(3)*. Another meeting was held in 2017 to “refine the pathway towards ending AIDS as a public health threat by more clearly defining the meaning of epidemic control” *(4)*. From this meeting, metrics were identified to guide when a country was on track to ending the AIDS epidemic. The conclusion of that meeting was to use six different metrics that were useful for different purposes *(5)*. Since the 2017 meeting, additional countries have reached the critical testing and treatment targets (95–95–95), advancing the need for more specificity about when the HIV epidemic is sustainably under control. Thus, countries need to achieve a progressive decline in new infections and have systems in place to maintain and monitor the reduced incidence.

Several questions remain in this discussion:

(1) What are the probable HIV epidemic trajectories beyond 2030 in settings that have attained targets for HIV testing and treatment with commensurate declines in infections and deaths?
   - For how long and under what circumstances will HIV incidence continue steadily declining versus stabilizing at lower level 'simmering' and when?
   - What epidemiological (e.g. heterogeneity in transmission) or programmatic features (e.g. variation in attaining or sustaining targets) will result in simmering epidemics?
   - What is the risk of increasing new HIV infections resulting in resumption of AIDS threatening public health and on what time scale could a rebound to high incidence rates occur?

(2) What is the minimum package of services, policies and programme implementation required in perpetuity to sustain reductions in new HIV infections and AIDS deaths?

(3) What are core set of indicators routinely monitored to ensure that the minimum service packages are effectively implemented, and HIV infections and AIDS deaths remain low or declining?

Some of the epidemiological questions can be investigated using mathematical models, epidemiological, and phylogenetic data. There are further considerations about how to communicate the concept of successfully reaching targets such that AIDS is no longer a public health threat, with the need to avoid complacency and continue appropriate multisectoral HIV response and monitoring.

MEETING AGENDA

Overall objective

This technical meeting focused on characterizing current and future HIV epidemiology in eastern and southern African settings with high HIV burden and high treatment coverage. It was the first in a series of consultations convened by UNAIDS to define a situation in which AIDS is no longer a public health threat and the conditions to sustain HIV epidemic control beyond 2030. The language describing these aspired achievements should be straightforward—such that national leaders, ministers of health, and ministers of finance can effectively advocate for what they are pursuing.

Ultimately, these questions will need to be addressed for HIV epidemics in settings in all regions of the world. However, initially consultations will focus on addressing these questions in the context of sub-Saharan Africa where large vertical HIV programmes have been implemented and many countries have surpassed or are nearing attainment of many targets.

Specific objectives of the July technical meeting

- Establish a common understanding of the motivation for this exercise, review concepts, definitions and metrics applied to established ‘End AIDS by 2030’ goals and consider adaptation for applicability after 2030.
- Develop a framework and components for describing the HIV situation after 2030 in settings attaining targets.
- Review long term HIV epidemic projections in high HIV burden settings sustaining high levels of HIV testing and treatment coverage.
- Understand structural reasons, assumptions and epidemic dynamics for variation across model projections of post-2030 epidemiological trends.
- Assess the implications of long-term transmission dynamics for programmatic requirements for sustaining progress.
- Review empirical evidence on current HIV transmission dynamics, and interpret implications for adjudicating likely HIV epidemic trajectories.
- Develop simple descriptions of the HIV epidemic situation after 2030 for settings that have controlled the epidemic.
- Identify areas of confidence and key uncertainties about the HIV epidemiological situation to 2030 and beyond, and describe how epidemiological uncertainty affects: (1) the programmes required to sustain epidemic control; and (2) priorities for surveillance and monitoring.
- Describe the existing list of essential programmes, policies, and surveillance for the HIV response in current strategy (2021–2026).
- Identify commonalities across participant pre-meeting survey responses to the definition of ‘ending AIDS as a public health threat’.
- Based on changing HIV epidemiology, describe how ‘ending AIDS by 2030’ changes as the HIV response transitions from an ‘emergency response’ to a long term control scenario.

Meeting structure

The two-day meeting was organized into seven sessions. The first four sessions on day 1 were structured around plenary presentations, question and answers, and discussion, to establish the objectives of the meeting and review mathematical modelling, as well as epidemiological and phylogenetic evidence on current HIV epidemic trends in eastern and southern African countries.

The three sessions on day 2 were organized as working group sessions and plenary discussions to synthesize: (1) summary descriptions of future HIV trends and epidemiology in high burden settings sustaining high testing and treatment coverage; and (2) implications of changing HIV epidemiology for HIV programme, surveillance and monitoring priorities after 2030.

The meeting participants represented: (1) epidemiologists and mathematical modellers with specific expertise and research related to HIV transmission dynamics and projections for HIV epidemics in eastern and southern Africa; and (2) representatives from stakeholder organizations with interests in future HIV programme strategies, including; UNAIDS; World Health Organization; the President's Emergency Plan for AIDS Relief (PEPFAR) (USA); Africa Centres for Disease Control and Prevention (Africa CDC); national HIV programmes; and the Bill and Melinda Gates Foundation.

See the appendix for the list of participants and the full agenda with details of specific objectives and content in each session.

SESSION 1: GLOBAL NEEDS TO REVIEW UNDERSTANDING OF THE 'END OF AIDS'

Overview of meeting and agenda

Opening remarks established the aims of the meeting to: (1) better understand epidemiological scenarios for 2030, with a focus on high performing countries in sub-Saharan Africa; and (2) develop an initial framework for how epidemiological patterns affect future programmes and surveillance priorities. Three previous meetings, through which conceptualization of the 'End of AIDS' targets had been developed, were briefly reviewed:

(1) **2014 meeting at Jiva Hills, France**. It was agreed at this meeting that the 'End of AIDS' was possible, given the availability of effective treatment and prevention, with a bold vision for the future needed.

(2) **2015 Lancet Commission on Defeating AIDS.** This meeting enumerated measurement needs and essential indicators (new infections, proportion of people living with HIV diagnosed, retained in care, receiving ART and receiving viral load monitoring) for ending AIDS.

(3) **2017 meeting in Glion, Switzerland**. This meeting aimed to more clearly define the meaning of 'epidemic control' and identify metrics to capture when countries were progressing toward epidemic control. It identified four potential metrics (percentage reductions, an absolute *rate, an incidence-mortality ratio, and an incidence-prevalence ratio)* that could complement existing indicators as countries move along the pathway to ending the AIDS epidemic.

Since these three meetings, a number of countries in eastern and southern Africa are on track to reach the 95–95–95 testing and treatment targets before 2025, and some countries have reached the epidemic control thresholds defined at the Glion meeting. This has raised the question of whether these countries have 'ended AIDS as a public health threat'. It was also noted that success is not always across all populations, with gaps still existing for men and children in attaining the 95–95–95 targets and little data on the treatment cascade among key populations. Some challenges with the epidemic control metrics defined at the Glion meeting were also raised, such as the incidence-mortality ratio, which is considered misleading in settings with low ART coverage and high mortality, or the poor performance of the incidence prevalence ratio in key population driven epidemics. These questions have motivated a desire for a summary metric that signals progress towards the end of AIDS.

Guiding perspectives from stakeholders

Participants representing stakeholders, such as PEPFAR, the National AIDS and Health Promotion Agency in Botswana, Africa CDC, and the Bill & Melinda Gates Foundation, provided guiding perspectives on motivations for revisiting understanding of the 'Ending of AIDS as a Public Health Threat' and target outcomes from this meeting.

Irum Zaidi, representing PEPFAR, stated that the discussions on the 'end of AIDS as a public health threat' should include considerations on the epidemiological impact, development (health infrastructure and economic progress) and security (economic disruption, health across age groups) of a nation. The importance of changing demographic trends across countries and their implications on the epidemic were highlighted. Data from Eswatini, which has attained the UNAIDS 95–95–95 targets (97–98–98; 2023 UNAIDS estimates) showed that despite marked reductions in incidence across the general population, incidence remains high among 15–24-year-olds (particularly in females), who make up a considerable proportion of the sexually active population. In Uganda, where important progress has also been made (90–94–94, 2023 UNAIDS estimates), infections have only fallen modestly among 15–24-year-olds in recent years. Data from the recent PHIA survey in Uganda (2020) highlighted how age disparities in viral suppression, lower among younger adults, contributes to HIV transmission potential among young sexually active adults. Zaidi also noted that the target audiences for the outputs of this meeting includes political leaders, funders, ministry staff, communities, programme technical staff, and surveillance and monitoring staff, and it would be important consider how best to communicate the future of the HIV epidemic to

each of these groups. Finally, Zaidi highlighted the PEPFAR *Sustainability Roadmap Plan*, underway in parallel, which involves working with host country governments on transforming HIV programmes from an emergency response to a sustained response with impact.

Robert Selato, representing Botswana's National AIDS and Health Promotion Agency, described Botswana's experience towards epidemic control. This included an overview of its achievements in reducing incidence significantly over time and important progress in attaining the 95–95–95 targets. Data on the age distribution of people living with HIV from Botswana currently shows a shift towards older ages among these people, with plans needed to address the health needs of the ageing HIV population. The need to expand and refocus testing initiatives to reach the last pockets of infections was also noted, given that testing is the route of entry into the HIV cascade. Communities and local nongovernmental organizations (NGOs) need to be empowered to achieve a broader reach if no one is to be left behind, especially key populations. Botswana has commenced planning beyond 2030 on ways to increase efficiencies and domestic funding for HIV. A sustainability and transition readiness assessment and roadmap is currently ongoing and some elements of these include:

- Integration of HIV care into other health services, including noncommunicable diseases (NCDs).
- Increased prevention funding for sustained reductions in new infections.
- Planning how to sustain the national HIV response independently.

Important thresholds identified which could affect decision-making about Botswana's HIV strategy include: (1) future funding availability and the national economic situation; (2) the political commitment to invest in HIV; (3) involvement of communities in continuing the fight against HIV; and (4) competing priorities from other emerging and future epidemics.

Participants were interested in the forms of HIV prevention being planned for the future in Botswana and how the younger generation is being involved in the fight against HIV. Selato noted that future prevention activities will include provision of condoms, interventions to reduce risky sexual behaviour and plans to continue with the cross-border project which helps identify and cater to people living with HIV from neighbouring countries. It was also noted that legislation has also been provided within the country to decriminalize sex work. Provision of funding for youth organizations to support HIV campaigns, including the use of youth radio stations for messaging and the PEPFAR DREAMS initiative, were listed as important tools that have been employed to engage young people in the fight against HIV.

Abdulaziz Mohammed's presentation, representing the Africa CDC, highlighted that the Africa Union 'Agenda 2063' and 'The Catalytic Framework to End AIDS, TB and Eliminate Malaria in Africa by 2030' specifically set targets and mention ending AIDS as a public health threat by 2030. The Africa CDC is working with its Member States to create an integrated Africa CDC strategy and this strategy will focus on: leadership; governance; multisectoral coordination; diagnostics; technologies; treatment; surveillance and information systems; and workforce development such as the increased use of community health workers. Some emerging themes and priorities at the continental level following conversations with Member States include: (1) paediatric/adolescent HIV/AIDS; (2) increasing community access to decentralized services; (3) understanding gaps in funding and advocacy for domestic financing; (4) tackling co-morbidities and supporting integrated service delivery; (5) PMTCT via the triple elimination approach; and (6) documenting best practices and scaling up their implementation. Important areas that were also noted and are currently being worked on by Member States include: (1) increased domestic financing — by supporting Member States to take ownership of their HIV programmes; (2) expanding local manufacturing of health products — by advocating for the removal of trade and intellectual property related barriers to support local production of health products, including innovation in Africa; (3) promoting respectful, action-oriented partnerships — by coordination of activities between partners in support of country priorities to maximize efficiency and reduce duplication of efforts; (4) strengthening African institutions; and (5) workforce development — through continuous training of healthcare worker and integration of community healthcare workers as a key component of the workforce. Finally, it was noted that the vision for success in ending HIV/AIDS based on the Africa Union Catalytic Framework is attaining the following targets: (1) less than 150 000 AIDS related deaths per year

with a treatment coverage of 95–95–95; (2) less than 150 000 new HIV infections per year; (3) zero infection in children and mothers; (4) all men and women have access to HIV combination prevention and SRH services; and (5) all key populations have access to HIV combination prevention services. These targets were aligned with the UNAIDS established thresholds of reducing new HIV infections and AIDS deaths by 90% between 2010 and 2030.

Guiding perspectives from the Bill & Melinda Gates Foundation HIV delivery team included an overview of the epidemiological pillar of its draft HIV Sustainability Framework. This includes: (1) identifying fit for purpose metrics to track the evolution of HIV epidemics; (2) evolution of surveillance methods as the epidemic evolves; (3) strengthening granular, timely data for decision-making; (4) characterizing the evolution of risk; and (5) identifying and supporting multiple methods to track networks of high transmission as well as population level 'background' events. It was noted that the HIV epidemic is progressing to a new phase of rapid disease burden reduction, which will require new approaches. Also noted was the possibility that key lessons learnt from responses to polio and malaria as they shifted from high burden to significant burden reduction curves should guide the HIV response. Some of these key lessons were: the need for granular, precise surveillance; multiple methods of population level surveillance; shift to a decentralized governance structure; an investment strategy for end stage; a mix of data and model driven interventions; and engaging communities to reach underserved populations. Confidence in the progress achieved against the HIV epidemic so far was expressed, given the marked reductions in incidence in eastern and southern Africa between 2010 and 2020, and the achievement of 95–95–95 by countries such as Botswana, Eswatini, Rwanda, United Republic of Tanzania and Zimbabwe. However, it was acknowledged that uncertainties, such as the expected future incidence trajectory and availability of donor funding, remain.

To understand some of these uncertainties, the foundation conducted some analyses and identified a set of future state scenarios for HIV incidence and three country archetypes. The country archetypes identified are: (1) higher burden settings, mostly in southern Africa, that have achieved significant progress in service coverage but still have relatively high incidence; (2) high achievement settings, mostly east African countries with low incidence levels that are continuing to decline; and (3) mixed trajectory countries in east, west and central Africa which have lower incidence but a flatter trajectory. Three potential trajectories of incidence identified include: (1) new infections concentrated in higher risk populations, with a plateau in incidence occurring in 10–15 years; (2) diffuse transmission across populations, with plateau emerging in the long term (15+ years); and (3) sustained decline in incidence over time. The different scenarios have different implications for the Foundation's portfolio, and understanding these is key.

Participants also acknowledged that funding for HIV is unlikely to continue at current levels forever and it is important to understand the impacts of a potential funding shock on the HIV epidemic. It was suggested that while understanding the implications of funding is essential, participants should come from a programme needs and programmes risk perspective to inform the funding.

SESSION 2:
FRAMEWORK TO DESCRIBE THE 'END OF AIDS AS A PUBLIC HEALTH THREAT'

The objectives of Session 2 were to:

- Review concepts, definitions, and metrics applied to 'End AIDS by 2030'.
- Develop a framework and components for describing HIV post-2030 in settings attaining targets.

The terminology 'End of AIDS as a Public Health Threat' by 2030 was first adopted in 2014 by the UNAIDS Programme Coordinating Board (PCB) as the main goal for the post-2015 development agenda *(6)*. No specific definition was attributed to what constitutes a public health threat, or the conditions under which AIDS represents a threat. AIDS 'no longer being a public health threat' was equated to the concept of ***disease control*** set out in the 1997 Dahlem Workshop on the Eradication of Infectious Disease, alluding to similar language used in World Health Organization declarations in the 1990s to 'end as a public health problem' in the context of neglected tropical diseases *(7)*. 'Disease control' was defined as a "reduction in disease incidence, prevalence, and morbidity to a locally acceptable level *as a result of deliberate efforts*" and noted that "*continued intervention efforts* are required to maintain the reduction" *(8)*.

The UNAIDS PCB meeting provided a working definition for 'ending the AIDS epidemic':

> *"Reducing new HIV infections, stigma and discrimination experiences by people living with HIV and key populations, and AIDS-related deaths by 90% from 2010 levels, such that AIDS no longer represents a major threat to any population or country."*

In 2015, the United Nations Sustainable Development Goal (SDG) 3 included the target:

> *"By 2030, end the epidemics of AIDS, tuberculosis, malaria and neglected tropical diseases and combat hepatitis, water-borne diseases, and other communicable diseases".*

SDG indicator 3.3.1 established a "number of new HIV infections per 1,000 population not living with HIV, by sex, age and key populations" as the main indicator for monitoring the 'end of AIDS' target. However, the SDG monitoring frameworks did not specify a threshold for considering the target attained *(1)*.

In 2015, the UNAIDS–Lancet Commission on Defeating AIDS — Advancing Global Health identified **low level endemicity** as the outcome of successful efforts to end AIDS by 2030 *(9)*. The Commission emphasized the need for long term control measures (beyond 2030), consistent with the Dahlem Workshop definition of 'epidemic control', and acknowledged that disease 'elimination' or 'eradication' were unlikely for HIV short of curative therapies. However, it did not establish a specific definition or threshold for what 'low-level endemicity' entailed and noted this as an urgent priority. Such a level was envisioned as a situation in which HIV/AIDS was "*no longer ranked among the leading causes of a country's or high-risk community's disease burden*" and the Commission contemplated approaches to defining the 'acceptable level for new infections' target based on transmission level, where a partially effective vaccine could eventually eliminate HIV. The Commission also enumerated a measurement need:

> *"Progress towards epidemic control can be measured by the rate at which new hot spots emerge and by reductions in HIV incidence in each hot spot or high-risk population identified."*

In addition, it identified new infections, proportion diagnosed, retained in care, receiving ART and viral load monitoring as essential indicators, disaggregated by age and sex or data on high risk populations.

In 2018, Granich et al., defined the 'End of AIDS' as the

"abstract political target of ending HIV as a major public health threat but includes achieving the epidemiological target of reducing both AIDS cases and HIV incidence to less than 1 per 1000 population per annum." (10).

Epidemic control indicators: definitions, strengths and weaknesses, applications and open questions

The objectives of the 2017 Glion meeting were to: (1) build consensus around an epidemiological definition of 'epidemic control'; (2) provide mathematical modellers with a clear goal towards 2025, 2030, 2035 and beyond to inform future programmatic targets, estimates of the impact of the response and of resource needs; and *(3)* ensure that the definition of 'epidemic control' is sufficiently nuanced to allow for heterogeneity across subpopulations. Four important epidemic control metrics were identified *(4)*. These were: (1) percentage reduction in new infections and deaths from a baseline in 2010; (2) absolute rates of HIV incidence and AIDS related mortality of less than 1 per 1000 adults per year, or less than 1 per 10 000 adults per year; (3) the incidence mortality ratio, which assesses the epidemiological tipping point; and (4) the incidence prevalence ratio, which incorporates ART success. The main strengths and weaknesses of the metrics were also outlined, as shown in the table below.

Metric	Strength	Weakness
Percentage reduction in new infections and deaths from a baseline in 2010	Agreed and adopted by the UN at High Level Meeting and SDGs Models of interventions and resources needed (Fast-Track) Sex/age disaggregated Estimates often available	Arbitrary, given varying 2010 baseline levels and years of epidemic peak Geographical diversity Epidemic diversity Empirical data difficult for both incidence and HIV related mortality Key populations hard to count
Absolute rates of HIV incidence and AIDS related mortality of less than 1 per 1000 adults per year, or less than 1 per 10 000 adults per year	Familiar to other programmes Easily understood Data as for percentage reduction	Threshold level lacks consensus Some countries that still consider themselves at risk, and face rising rates in particular geographies or populations, though currently below 1/10 000 Static: what happens after the threshold is reached is not implicit
Incidence mortality ratio **(Incidence:all-cause mortality rate in people living with HIV ratio <1) (IMR)**	Dynamic, shows that total number of people living with HIV is falling if population size remains stable Incidence affected by population growth, so could use numbers of new	All-cause mortality (among people living with HIV) is usually modelled, but hard to measure

	infections: numbers of people living with HIV dying of all causes PEPFAR metric for epidemic control Useful for planning and financing projections (number of people requiring ART)	Why not simply use number of people estimated to be living with HIV? Generally, occurs later in the course of epidemic control than other indicators Perverse indicator if mortality is high due to poor programme performance Reducing both mortality and incidence has unpredictable impact on indicator
Incidence:prevalence ratio (IPR) **(Incidence$_{\text{(total population)}}$:prevalence ratio < 3% or 2%**	Dynamic, accounts for treatment success Generally, occurs earlier than IMR<1 Intuitive (how few new infections should we see per 100 people living with HIV to know that we are 'on track' for control Cross-gender IPR is useful in 'generalized' epidemics	As with IMR, may be more useful to consider numbers Not always well understood

Priority open questions identified by the Glion meeting were:

(1) The delicate balance between acknowledging substantial progress has been made, while also guarding against complacency and encouraging investment at the levels required to reach the SDGs.

(2) The scalability, and disaggregation of the metrics by geography, age, gender and key populations.

(3) Structural and systemic components of success.

(4) Use of the term 'epidemic control' (or transition metrics) versus 'ending AIDS as a public health threat'.

(5) Risk of complacency, target audiences, relative complexity of ratios compared with absolute numbers or rates (noting that the 90–90–90 and 90% reduction targets have been successful because of their simplicity to communicate).

(6) Data gaps and lack of granularity, over-reliance on modelled estimates, uncertainty not always captured.

(7) Data challenges for incidence and mortality measures.

In the discussion, it was noted that the metrics defined at the Glion meeting have not been widely adopted and, despite their inclusion in the Spectrum software to guide countries, many countries have not fully utilized this feature. The Glion meeting recommended that efforts to refine and finalize the use of summary metrics should be guided by the following criteria:

(1) They should be scientifically sound, feasible, acceptable to communities and useful for AIDS programme management:

- They must be relevant for all epidemics (high prevalence and low prevalence), at all levels (global, regional, national, subnational) and be able to measure progress within subpopulations (defined by age, sex and/or population).

(2) They should be resistant to 'gaming' — intentional skewing of data to overstate programme performance.

(3) They should include inputs that measure trends in new infections, morbidity and mortality among people living with HIV.

(4) They should be packaged with improved measures of trends in HIV related stigma and discrimination, and a 'policy cascade' that measures whether an enabling legal and policy environment is in place for efforts to eliminate stigma and discrimination.

Proposed framework for describing the 'End of AIDS as a public health threat'

The meeting outlined the development of a framework for defining the 'End of AIDS as a public health threat', as well as limitations of the current definitions and metrics:

(1) The term 'end of' implies a finality inconsistent with the long-term management acknowledged for keeping a public health threat of HIV at bay. In particular, the 'as a public health threat' qualifier is often forgotten or vague, e.g. in the SDGs and UNAIDS Global Report.

(2) The concept 'public health threat' is not concretely or tangibly defined. To date it is presumed that HIV is a public health threat and there is a need to be able to define when it is no longer so. Also, it is important to be able to recognize if HIV re-emerges as a public health threat. For example, during the Covid-19 pandemic, it was established in the public discourse that the risk of '*overwhelming health system capacity*' was a 'threat to public health' and this may be a useful concept to define future risk thresholds for HIV — impact of treatment, testing, prevention burden on system capacity and resources for other needs. Two possible circumstances in which HIV re-emerges as a public health threat are: (1) Resurgent infections or deaths which could not be rapidly controlled; (2) sustained higher than expected incidence, leading to unplanned/unmanageable future treatment burden.

(3) The current working definition of a '90% reduction relative to 2010 levels' is increasingly arbitrary as 2010 recedes further in people's memory. Also, the relative definition has different levels in different settings, depending on 2010 baseline levels, and the definition does not correspond to the concept of AIDS 'no longer among the leading causes of disease burden' alluded to for 'acceptably low level'.

(4) The currently proposed set of metrics (incidence rate or change and incidence to prevalence ratio) are founded in epidemiological theory, but is not observable or tangible. These metrics are also limited in their ability to recognize and explain risk. Examples of metrics which are more tangible and correlate to epidemiological principles include in-patients admitted with advance HIV disease or viral suppression among pregnant women at first antenatal care.

A framework was proposed to reconceptualize the 'end of AIDS' from an endpoint to a **situation that is maintained**. The task for the consultation was to develop a checklist of: (1) epidemiological conditions and metrics defining 'AIDS as no longer public health threat'; (2) programmes, policies and services to ensure the epidemiological situation is maintained; (3) surveillance and monitoring requirements to ensure the epidemiological condition is sustained and programme/policies are implemented with fidelity.

For each component of the checklist, a description of what needs to be sustained in an epidemic control situation, what can be discontinued or substantially scaled-back, what needs to evolve and how, and what a return of public health threat looks like should be included.

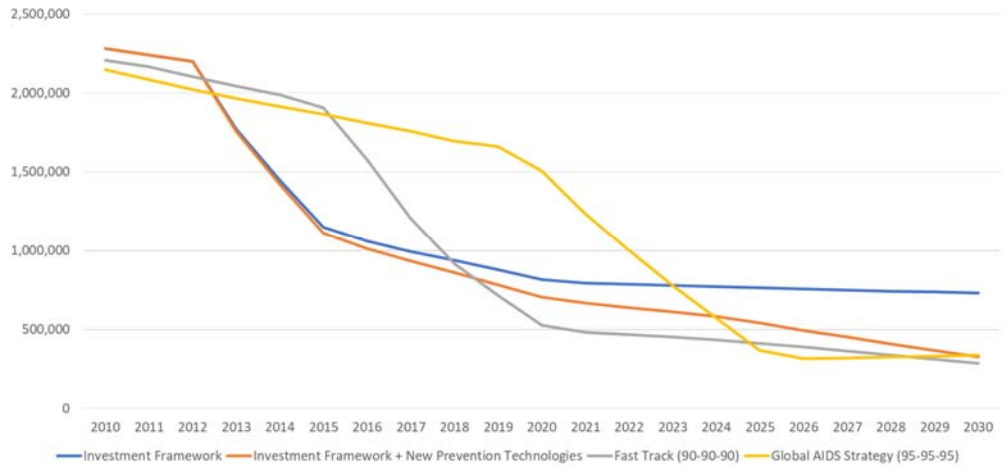
In the discussion, participants expressed discomfort with the terminology 'locally acceptable level' for HIV infections or AIDS deaths, referred to in the Dahlem Workshop definition of 'epidemic control', as it could mean different things across settings and may be futile to attempt to define. It was also suggested to think more about the AIDS-free generation of young people and how defined metrics would apply to them.

SESSION 3:
REVIEW OF LONG-TERM EPIDEMIC PROJECTIONS IN HIGH HIV BURDEN SETTINGS SUSTAINING HIGH LEVELS OF HIV TESTING AND TREATMENT

Modelling exercises to guide HIV targets

John Stover reviewed historical modelling exercises which have informed planning and target setting for the HIV epidemic. Each of these exercises have utilized updated versions of the Goals model developed by Avenir Health. The exercises included the: *2011 Investment Framework to Rationalize AIDS Investment (11)*; the *2016 Fast-Track Approach to Show What is Required to End AIDS (12)*, and the *2021 Global Strategy to Assess the Epidemiological Impact of the UNAIDS 2025 Targets to End AIDS (13)*. The target coverage assumptions in the different exercises varied from universal access (~80%) by 2015 in the *2011 Investment Framework*, 90-90-90 by 2020 with 90% prevention in the *2016 Fast-Track Approach*, and 95-95-95-95-95 with 10-10 by 2025 in the *2021 Global Strategy*. All projections showed that reaching specified strategy targets would substantially reduce HIV incidence and AIDS related deaths over time. There was a consistent pattern that global incidence reductions during each five-year period between modelling exercises had not matched the projected incidence declines under target scenarios (Figure 1); this was explained primarily by actual implementation being slower and reaching lower levels than established in strategy targets. The modelling evidence presented was for global trends; in the discussion it was questioned whether this gap might be smaller for recent years in eastern and southern African countries during the most recent period. This was proposed for further follow-up analysis.

Figure 1. Projections of new HIV infections across historical modelling exercises



Source: John Stover; Avenir Health

Across all regions, among the comprehensive scale-up targets set in the *Global AIDS Strategy 2021–2026*, increasing antiretroviral therapy coverage from current levels to the 95–95–95 targets had the greatest contribution (≥50%) to reducing new infections, compared with behaviour change, biomedical prevention, or prevention services for key populations. Comparison of the projected incidence and AIDS related deaths from the Global AIDS Strategy *2021* modelling and the current global estimates from UNAIDS indicated that incidence and AIDS related deaths are declining at a slower rate than projected if the strategy targets were on track to be achieved. The results presented reveal that the 2030 targets are achievable, but delays in commencing rapid scale-up of interventions make it harder to attain and result in more cumulative new infections and AIDS deaths. The results also show that rapid achievement of 95–95–95 targets are key to achieving the targets.

Future projections beyond 2030 from the Goals ASM (age-structured model) showed continued declining HIV incidence across countries in sub-Saharan Africa, even if future coverage of

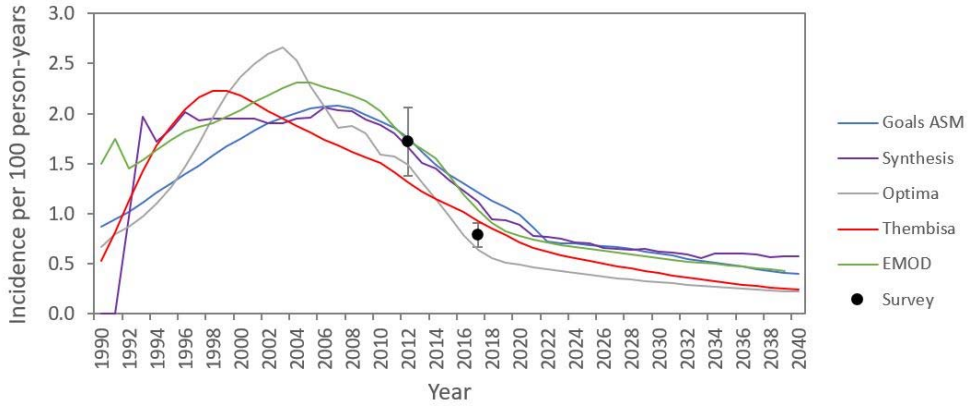
treatment and other prevention interventions are assumed to be constant at current levels (and not scaled up further). The rapid ageing of people living with HIV, from being concentrated in reproductive age groups to belonging to older adult age groups, with lower sexual risk and higher levels of viral suppression at older ages, account for the continued declines in incidence projected in Goals ASM. Even if treatment coverage and viral suppression among people living with HIV remain at current levels among young adults (below 95–95–95 targets), the reducing prevalence of HIV in these young age groups results in lower numbers of these people with viraemia and, therefore, population transmission risk.

Overview of modelling to inform HIV programmes in Sub-Saharan Africa (MIHPSA) project, South Africa model projections and Between-model Heterogeneity

The Modelling to Inform HIV Programmes in sub-Saharan Africa (MIHPSA) project is a collaboration of the HIV Modelling Consortium, east, central, and southern African Health Community, and the national HIV programmes of Malawi, South Africa, and Zimbabwe to inform the future design of national HIV programmes *(14)*. For this consultation, MIHPSA collaborators contributed model projections from 'phase 1' of the MIHPSA project, which assumed continuation of current treatment cascade and prevention coverage to 2040. Models were calibrated using common empirical data on adult HIV prevalence and number of people on ART.

For South Africa, projections from five models (Goals-ASM, HIV Synthesis, Optima, EMOD-HIV, and Thembisa) were assessed for consistency of incidence, prevalence, AIDS-deaths and 95-95-95 targets using coefficients of variation [15]. There was a large variation in estimates in the 1990s due to limited data for calibration with consistency between 2005 and 2025, with the variation increasing towards the end of the projection period. All models predicted a gradual, long-term decline in incidence, but estimates of incidence and deaths showed high variability between models (Figure 2).

Figure 2. Comparison of adult (15-49 years) HIV incidence projections in South Africa from five models



Source: Moolla H, Phillips A, ten Brink D, Mudimu E, Stover J, Bansi-Matharu L, et al. A quantitative assessment of the consistency of projections from five mathematical models of the HIV epidemic in South Africa: a model comparison study. BMC Public Health. 2023;23:2119.

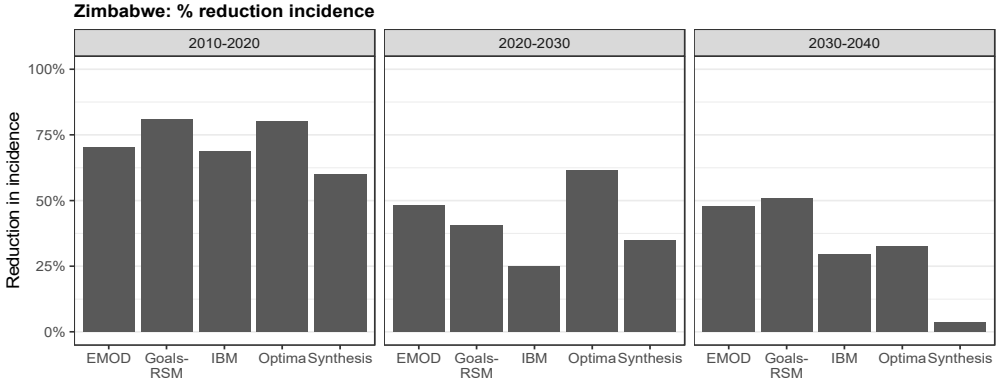
Model estimates for the 95–95–95 targets (proportion diagnosed, ART coverage and proportion on ART with viral suppression) were more consistent, but there was a higher variation in the estimates for children. Estimates and projections of HIV prevalence were also consistent, reflecting the models were calibrated to the same prevalence data. Possible reasons for the variations in the models include differences in: (1) data sources used for validation; (2) model structure (e.g. HIV-synthesis incorporates drug resistance, which influences mortality estimates); (3) age distributions of incidence; and (4) differences in modelling approaches of the status quo scenario.

MIHPSA long term projections and transmission ratios

Model projections to 2040 from five models for each of the three MIHPSA countries (Malawi, South Africa and Zimbabwe) were compared to further understand: (1) how similar are model predictions of prevalence and incidence to 2040; (2) if models predict that incidence will continue declining or will stabilize at a new equilibrium after 2030; (3) to what extent are the incidence projections determined by changes in population viremia versus other transmission and prevention dynamics; and (4) what determines the level and rate of incidence decline. Re-analyses of outputs from the MIHPSA projects were presented. Four models were applied to all three countries (EMOD, Goals, Optima, Synthesis), and one bespoke model was applied to each country: Thembisa (South Africa), PopART-IBM (Zimbabwe), and Thanzi la Onse (Malawi). Projections were also to 2040 assuming sustaining current levels of interventions.

Long term HIV prevalence trends for all three countries were consistent across models projecting steady declines in HIV prevalence among adults 15–49 years between 2020 and 2040. Consistent with the scenarios decision to maintain current (2022) intervention levels for projections, ART coverage projections for South Africa in all the models were below the 95– 95–95 target, but consistent, and near 95–95–95 for Malawi and Zimbabwe. Viral suppression projections were also slightly below the 95% target for all models for the three countries except in Goals-ASM and Optima in Malawi which were higher. Incidence was projected to decline steadily through 2040 across most models, but with a slower rate of decline between 2020 and 2030 and 2030 and 2040 compared with 2010–2020 across all models. For example, in South Africa median incidence decline in the decade 2010–2020 was 53% (range across models 48–69%), between 2020 and 2030 the median decline was 35% (range 28–43%), and between 2030 and 2040 the median decline was 30% (range 7– 41%). In Malawi, median declines (ranges) over the three decades were 67% (62–77%), 57% (41–72%), and 44% (30–58%), respectively, and in Zimbabwe it was 70% (60–81%), 41% (25–61%) and 33% (4–51%) (Figure 3).

Figure 3. Projected percentage reduction in HIV incidence for 2010–2020, 2020–2030 and 2030–2040 among adults in Zimbabwe from five models.



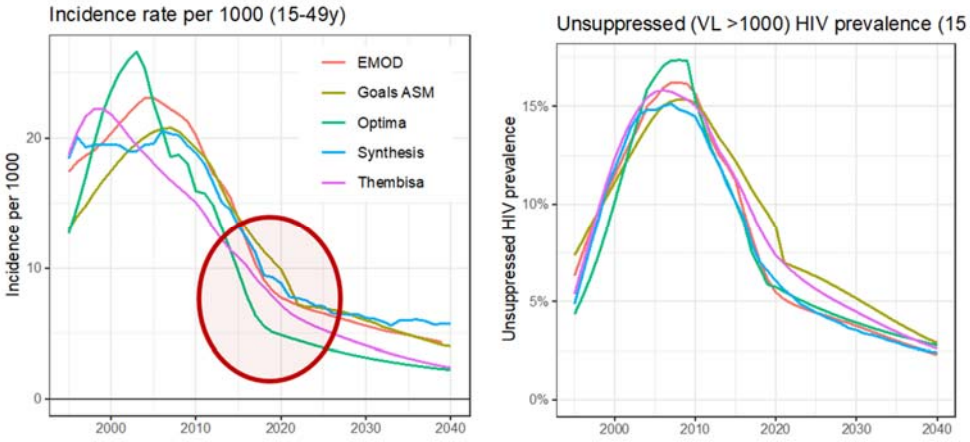
Source: Jeffrey Imai-Eaton; HIV Modelling Consortium, MIHPSA project; Moolla H, Phillips A, ten Brink D, Mudimu E, Stover J, Bansi-Matharu L, et al. A quantitative assessment of the consistency of projections from five mathematical models of the HIV epidemic in South Africa: a model comparison study. BMC Public Health. 2023;23:2119.

In South Africa and Zimbabwe, the synthesis model projected substantially slower incidence decline (nearly flattening) between 2030 and 2040 than other models (Figure 3). Overall, there was more relative variation across models in projected absolute incidence levels than in rates of decline, stemming from a relatively large variation in the current (2022) incidence level despite calibrating to similar prevalence data.

In most models, the decelerating incidence decline was characterized by a distinct slowdown around between 2018 and 2022. This change in the rate of incidence decline parallelled the change in the rate at which the prevalence of unsuppressed viraemia among adults (15-49 years) declined

— demonstrating the close relationship between incidence and prevalence of viraemia in model outcomes (Figure 4).

Figure 4. Projected HIV incidence and prevalence of unsuppressed (VL >1000 copies/mL) HIV among adults (15–49 years) in South Africa from five models



Source: Jeffrey Imai-Eaton; HIV Modelling Consortium, MIHPSA project; Moolla H, Phillips A, ten Brink D, Mudimu E, Stover J, Bansi-Matharu L, et al. A quantitative assessment of the consistency of projections from five mathematical models of the HIV epidemic in South Africa: a model comparison study. BMC Public Health. 2023;23:2119.

Between 2010 and 2020, the prevalence of viraemia declined rapidly due to the rapid scale-up of ART among people living with HIV. After 2020, as ART coverage and viral suppression saturated near the 95–95-95 targets, declining population viraemia was more closely linked to changing HIV prevalence, which declined more slowly. In the South Africa model projections, the Thembisa model reflected a less distinct deceleration in incidence declines than other models. This may be because the sustained incidence decline in Thembisa reflects the combined impacts of multiple interventions (increased condom usage, risk reduction following HIV diagnosis) more so than other models.

The transmission rate among unsuppressed adults was calculated to more directly assess the extent to which changes in incidence reflected population viraemia or other transmission dynamics (e.g. concentration of transmission in high-risk populations). Theoretically, for HIV epidemics to stabilize at a new endemic equilibrium, the transmission rate among untreated adults will increase to a level such that each individual with HIV on average transmits to one additional person (real-time reproductive number = 1). In most models, but not all (e.g. Thembisa, Optima), the transmission rate among untreated adults increased modestly between 2020 and 2040, consistent with eventual potential plateauing of incidence. However, it was not clear if, when, or at what level a new endemic equilibrium incidence might emerge.

Comparison of model projections for South Africa: Thembisa and MicroCOSM

Leigh Johnson compared future prevalence and incidence projections for South Africa among adults and key populations between the Thembisa (compartmental) and MicroCOSM (agent-based) models *(16, 17)*. Both models include age, sex and risk group stratifications for those sexually active, and includes marital status. Thembisa and MicroCOSM simulate men who have sex with men (MSM) and female sex workers with movements into and out of both populations. Key differences between the models include different assumptions about heterogeneity in condom use, sexual mixing patterns, length of relationships between MSM and data used and frequency of calibration. Both models simulate the same HIV interventions introduced in South Africa.

Both models predict reductions in incidence and prevalence beyond 2030 among adults (15– 49 years), but the Thembisa model projects much steeper declines than MicroCOSM. Among younger individuals (15–24 years), MicroCOSM projects a plateau in incidence beyond 2020, but incidence is projected to continue declining in this age group in Thembisa. Among key populations, both models predict a much slower rate of incidence decline beyond 2030 with higher estimates of incidence predicted in MicroCOSM relative to Thembisa. Projected ART coverage and condom use at last sex are higher in Thembisa than in MicroCOSM; these higher future intervention coverages in Thembisa may be important in explaining the faster incidence decline.

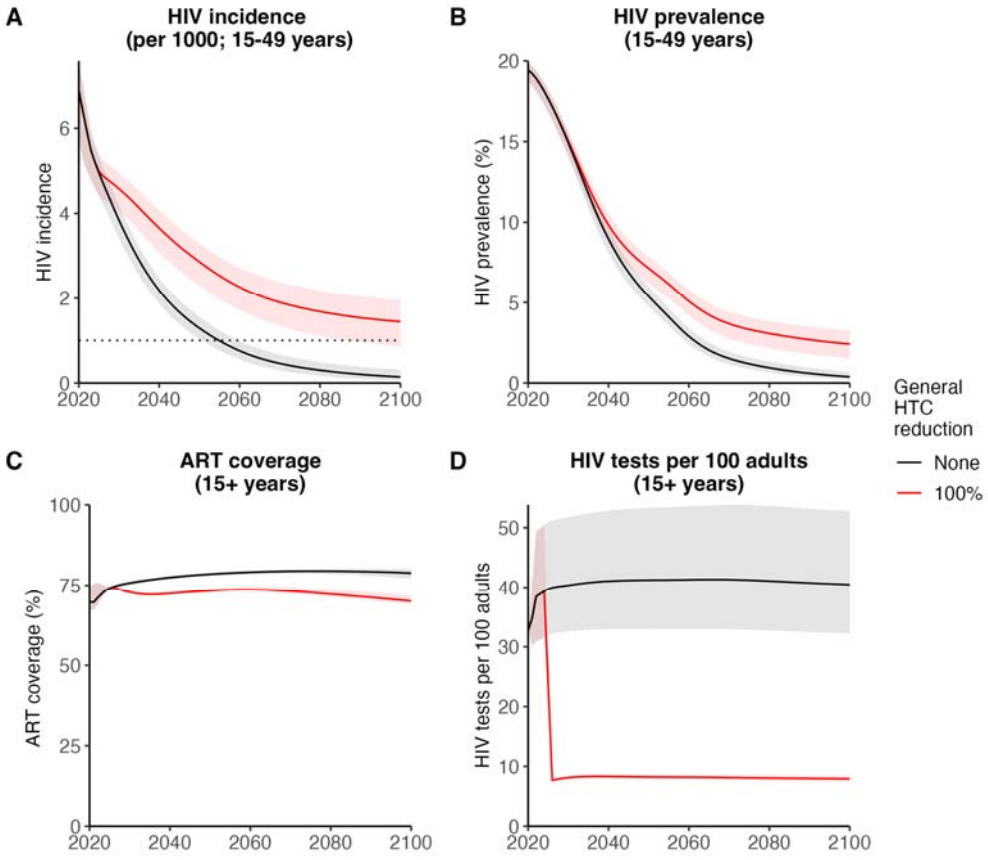
While MicroCOSM represents more detailed dynamics due to its agent based nature, it was not conclusive that its dynamics or projections were more accurate than Thembisa. Thembisa was more consistent with recent HIV incidence and prevalence data from South Africa than MicroCOSM, partly because MicroCOSM has not been calibrated recently. The continued declines in incidence projected in Thembisa are likely due to higher long term ART coverage and condom use in the model relative to MicroCOSM. Among subpopulations, incidence declines are also projected to be substantial in Thembisa, but stabilize in MicroCOSM.

Long term HIV incidence projections in South Africa and impact of reducing general HIV testing

The Thembisa model was further utilized to simulate the long-term HIV incidence projections (to 2100) in South Africa and the impact of scaling back general population HIV testing services (general HTS). The model was used to project the South African HIV epidemic to 2100, assuming continuation of current programme levels, then assuming reductions in general HTS annual volume by 25–100% at five-year intervals between 2025 and 2035 while retaining antenatal, symptom based and index testing at 2021 percentage coverage levels. Future epidemiological uncertainties were also incorporated by varying ART interruption rates (observable programme changes) and condom usage (unobservable risk environment), both by +/– 15% between 2025 and 2035.

The results showed that when maintaining current HIV testing, linkage and retention levels and risk environment (status quo projection; ~79% ART coverage), HIV incidence declined steadily for decades. Virtual elimination (incidence <1/1000) was achieved among adults (15–49 years) around 2055 and projected incidence was 0.14/1000 in 2100. HIV prevalence declined from 17.7% in 2025 to 0.4% in 2100. Maintaining the status quo (40 tests per 100 adults each year) required about 20 million tests by 2040 and a stable ART coverage of about 78% was achieved. With a 25% reduction in general HTS, incidence still declined steeply but time to virtual elimination was delayed by about five years, to around 2060. There were around 360 000 additional new HIV infections over 50 years (a 10% increase which is approximately equal to current new infections in two years) and 115 000 more AIDS deaths (7% increase). With complete cessation of general HTS (100% reduction), total testing reduced by 80% to around 9 tests per 100 adults per year, incidence continued to decline, with no resurgent incidence (Figure 5). However, incidence declined more slowly and virtual elimination was not attained by 2100. There were an estimated 2.5 million and 795 000 additional new HIV infections and AIDS deaths over 50 years, respectively.

Figure 5. Changes in incidence, prevalence, ART coverage and HIV tests over time when general HIV testing was reduced. (A) Representative figures of HIV incidence rate (15–49 years) per 1000 (mean and 95% CI) including an indication of when incidence <1/1000 ('virtual elimination') was attained (dotted line); (B) HIV prevalence (15–49 years); (C) ART coverage of adults (over 15 years); (D) HIV tests per 100 (over 15 years) between 2020 and 2100 showing status quo (no testing reduction) and general HIV testing reductions of 100% from 2025



Source: Rautenbach SP, Whittles LK, Meyer-Rath G, Jamieson L, Chidarikire T, Johnson LF, Imai-Eaton JW. Future HIV epidemic trajectories in South Africa and long-term consequences of reductions in general HIV testing: a mathematical modelling study. MedRxiv 2023; 2023.12.19.23300231. https://doi.org/10.1101/2023.12.19.23300231

The results were reassuring that there is substantial momentum to HIV incidence declines in South Africa and scaling back testing would not lead to a resurgence in new infections. In discussion about the presentation, more information was requested on the cost implications of scaling back general HTS and concerns were raised about the potential unintended consequences of scaling back general HTS, such as a reduction in linkage to primary prevention following a negative test and increases in late diagnosis and advanced HIV disease.

Evolving HIV epidemic dynamics in Eswatini, sources of infection and the reproduction number

Model simulations of the HIV epidemic in Eswatini with the EMOD-HIV model were presented to understand future HIV epidemic dynamics and sources of infection in a setting with high HIV prevalence and ART coverage *(18)*. The model was calibrated to HIV prevalence and ART

coverage by age, sex and year for Eswatini and validated using data from the 2021 PHIA survey in the country.

Results from the model showed that even when the 90–90–90 or 95–95–95 targets are met, the HIV epidemic is predicted to still persist, with adult incidence remaining above 0.75–1%, primarily due to transmission occurring prior to interventions and during long term ART. The model showed that the contribution of HIV infection stages to transmission has changed over time. Before ART scale-up, latent stage (person-time between acute infection and AIDS for people living with HIV not in AIDS stage or on ART) transmissions accounted for about 70% of incidence and this has reduced to about 40% in the universal test and treat (UTT) era (using 2016 as a cut-off). The contribution from people with acutely acquired HIV (<three months from acquisition) to incidence increased following ART scale-up, representing about 20% of incidence in the UTT era. In the UTT era, the model estimated that about 40% of infections were due to people living with HIV on ART.

The generation time (time from index infection to secondary transmission) has increased from a median of 3.67 years in men and 4.25 in women pre-UTT to 7.25 and 10.00 in men and women, respectively, in the UTT era due to increased life expectancy among people living with HIV on ART, and the large share of transmissions arising from people on ART with imperfect viral suppression. There are also important age differences in the proportion of transmission from individuals who acquired HIV less than one year (which includes the acute stage). Among 15–24 year olds, 50–70% of all transmissions originate from those who acquired HIV less than a year prior, while in 25–34 and 35+ year olds, it was about 40% and <20%, respectively. Irrespective of time since infection, transmission index cases shifted sharply to older aged people living with HIV in the UTT era compared with pre-UTT (UTT defined as 2016 onwards).

Parameters identified to be important determinants of variation in the model results include: how much more infectious exposure is during acute versus latent stage; duration of the acute phase; time from infection to ART initiation; time from ART initiation to viral suppression; and ART effectiveness at reducing transmission.

In summary, the results suggested that the HIV epidemic will persist for decades under UTT due to the extended duration of disease with treatment and the imperfect efficacy of the ART regimen. It is also due to the inability to limit the contribution of the acute stage to onward transmission. Even with a more aggressive treatment approach (increasing ART to 100%), the incidence in Eswatini will not decline to epidemic control levels without improvement in ART effectiveness and scale-up of primary prevention to reduce infections from those with acute stage HIV.

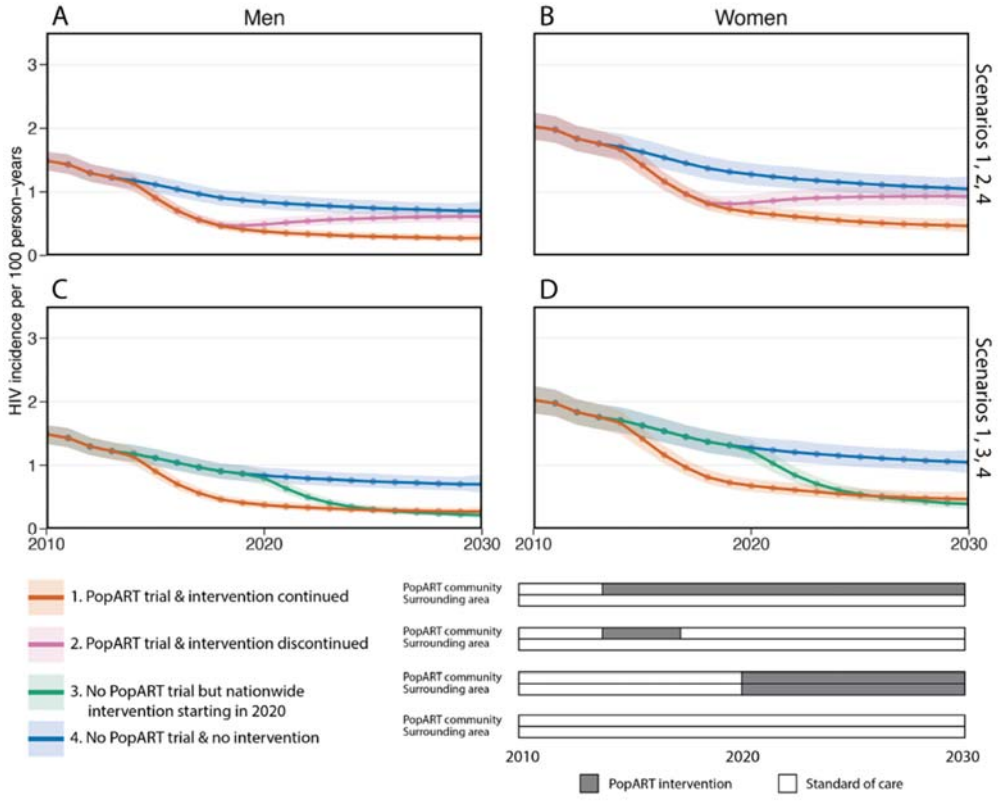
Long-term impact of the HPTN 071 (PopART) intervention, prospects of elimination, and evolving transmission

The HPTN071 (PopART) trial of a combination HIV prevention package, including universal HIV testing and treatment, was conducted between 2013 and 2018 in 21 high prevalence communities in Zambia and South Africa. Mathematical model simulations were presented, representing the long term impact of sustaining trial interventions in these communities *(19)*. The trial involved randomization of communities into one of three arms — Arm A: home based HIV testing; immediate ART offer for those living with HIV; linkage to care offer; retention on ART promotion and VMMC offer. Arm B: Same intervention as arm A, but ART offered based on national guidelines. Arm C: Standard of care. Arms A and B became aligned when universal ART was offered to everyone living with HIV in mid-2016. The trial showed a relative reduction in HIV incidence of 7% (statistically non-significant) in arm A compared with arm C and 30% (statistically significant) in arm B compared with C *(20)*.

An individual based model (PopART-IBM) was used to model all individuals in the community, with each community modelled separately. The model incorporated demographics, partnerships, HIV transmission, disease progression and AIDS death, background HIV care and the PopART intervention. Only heterosexual partnerships were modelled, with the inclusion of three categories of sexual risk-taking behaviour that differed in their maximum number of concurrent partners and mean duration of partnerships. The model does not explicitly include HIV pre-exposure prophylaxis (PrEP) or the modelling of key populations.

Model simulations reproduced well the 30% reduction in HIV incidence in arm B relative to C, but were not able to explain the 7% reduction in arm A relative to C (which may be due to random chance in the sampled trial communities or other unexpected factors). The model also performed well at predicting absolute HIV incidence level in arms B and C. The model was used to simulate four scenarios to 2030: (1) continuation of the intervention after the PopART trial; (2) discontinuation of the intervention after the PopART trial; (3) no PopART trial but nationwide intervention starting in 2020; and (4) no PopART trial and no intervention. The model predicts a reduction in HIV incidence across all scenarios, but incidence rebounded with discontinuation of the intervention (scenario 2) (Figure 6).

Figure 6. Projected mean HIV incidence across total population of arm A and B communities for the period 2010–2030. For ease of comparison, the top row (A, B) shows scenarios 1, 2 and 4, and the bottom row (C, D) shows scenarios 1, 3 and 4. Solid lines show the median of the distribution of the arithmetic mean of HIV incidence per 100 person-years across all intervention communities, while the shaded areas show 95% credible intervals of mean HIV incidence *(19)*



Source: Probert WJM, Sauter R, Pickles M, Cori A, Bell-Mandla NF, Bwalya J, et al. Projected outcomes of universal testing and treatment in a generalised HIV epidemic in Zambia and South Africa (the HPTN 071 [PopART] trial): a modelling study. Lancet HIV. 2022;9(11).

In the scenario of continued PopART intervention (scenario 1), the 95–95–95 targets were met by 2030 when averaged across all intervention communities, but not met by all communities individually. The reproduction number was estimated to remain below 1 if the intervention was continued, but would rise back and remain slightly above 1 with discontinuation of the intervention after the PopART trial. Model predictions showed that with the continuation of the UTT intervention to 2030, the proportion of incidence cases in the group with the highest level of sexual risk taking behaviour will increase.

SESSION 4:
CURRENT AND FUTURE HIV EPIDEMIOLOGY AND TRANSMISSION DYNAMICS IN SETTINGS SUSTAINING HIGH HIV PROGRAMME COVERAGE

Contemporary HIV transmission dynamics from phylogenetic data and mathematical modelling: implications for current and future epidemic trends and transmission drivers

The Phylogenetics and Networks for Generalised Epidemics in Africa (PANGEA) Consortium is a collaboration of general population HIV studies that use genomic sequencing and phylogenetic linkage to transmission pairs to understand not only who is acquiring HIV, but also the characteristics of persons most likely to *transmit* HIV in contemporary HIV epidemics in eastern and southern Africa. Recent analysis from the consortium have focused on quantitatively explaining the 'Prevention Outcome Gap'—the gap between the observed and expected reductions in rates of new infections based on progress in achieving population viral load suppression.

Phylogenetically-linked transmission analysis used data collected between 2013 and 2019 in Zambia (PopART Phylogenetics study) and Botswana (Ya Tsie trial). Out of 300 and 82 transmission pairs identified in Zambia and Botswana, respectively, 53% and 55% of pairs had a male source, with 43% and 38% of pairs having a male source aged between 25 and 40 years. The peak age of transmission was younger for women than men; the age distribution was consistent with predictions from the PopART individual based model (IBM) *(21, 22)*.

In addition to identifying men aged 25–40 years as the most likely to transmit HIV, the analysis also found that men were four times as likely to transmit HIV than women, 11% of transmission sources had drug resistant virus (pre-dolutegravir), transmissions were mostly within communities, and transmission clusters were small (mostly two–three linked transmissions per cluster). The study also found that the generation time in most transmissions was short. The distribution of duration spent living with HIV before transmission shows a large group of individuals who have never been tested (assumed to have acquired HIV recently) and also a fairly large group of individuals on ART and unsuppressed or who have dropped out of care.

These results suggested that in PopART and Ya Tsie, there is no magic bullet, with most infections arising from relatively 'ordinary members' of the communities, i.e. transmission is characterized by a large number of potentially infectious individuals with relatively low transmission risk, rather than large transmission clusters from a few highly infectious individuals ('many who infect few, not by few who infect many'). Individuals with newly acquired and long-term HIV are both contributing to new infections.

Patterns of phylogenetic clustering in the PANGEA-HIV studies showed that HIV transmission in Zambia lacks the large transmission clusters that characterize HIV transmission dynamics in Europe or the USA (primarily persons who inject drugs or MSM transmission). Up to six clusters with more than ten individuals were recorded in the European samples, with the largest cluster including 35 individuals *(23)*. In contrast, the two largest clusters in the Zambian samples had only seven individuals. Even when both epidemics were subsampled to include only samples from a similar epidemic phase relative to ART roll out in each setting, the results remained similar, with the larger transmission clusters found in the European data set (largest cluster size of 11 in the European data set versus 3 in the Zambian data set). Similar patterns of clustering were found in the Botswana data set and across other PANGEA studies: PopART, Zambia; Rakia, Uganda; and Ya Tsie, Botswana. The results were verified by comparing clustering patterns from two agent based mathematical models (PopART IBM calibrated to the Zambian epidemic and IDM EMOD calibrated to the epidemic in Eswatini) *(22)*.

The PopART IBM agent-based simulation calibrated to the Zambian epidemic reproduced the clustering patterns seen in the Zambian phylogenetic data set. However, it was noted that with increases in sampling fractions, more clusters would become apparent. The differences in cluster sizes between the UK data set and African data sets were robust to sensitivity analyses accounting for differences in sampling fraction.

A branching process model in which the amount of superspreading could be varied by a single dispersion parameter was used to understand the reasons for the clustering differences between the African data sets and the data from the UK or Europe. The model showed that superspreading has a dramatic effect on the cluster size distribution, i.e. large amounts of superspreading is required to see large cluster sizes. The effect of migration on clustering was also explored, demonstrating that migration breaks up clusters. However, to counteract through migration the clustering to the low degree seen in the African data, no less than about 50% of people in the community would need to have acquired HIV outside the community *(23)*.

One possible explanation for the clustering differences was differences in sexual networks between different populations. Men who have sex with men who are at risk of acquiring HIV in the United Kingdom have been shown to report more partners compared with heterosexual men and women in rural Zimbabwe, with this distribution characterized by power laws which may or may not be scale free *(24)*. Epidemics with scale-free power law distributions tend to take off very quickly. Similar power law coefficients have been found in the PopART study and older studies in Zimbabwe.

In summary, in multiple epidemic settings in eastern and southern Africa, the plurality of HIV transmission appears to occur in small clusters compared with large transmission clusters that characterize HIV epidemics involving men who have sex with men in the global north. This was broadly consistent with models with lower variance in the offspring distribution. Key populations, including female sex workers, are at high risk but are mobile and transient, and so may not appear as distinctly in phylogenetic clusters constructed from geographically defined study populations. There is a need for more studies that focus on phylogenetics with key populations within general populations.

These findings suggest that while the focus on HIV prevention for small subpopulations at high risk of transmission may provide much needed benefit to those receiving the prevention efforts, the risk of acquiring and transmitting HIV is diffuse in these populations and focusing on small subpopulations is unlikely to have a large immediate indirect effect on curtailing population wide HIV incidence.

HIV epidemiology and transmission dynamics in a setting with high population viral suppression and combination prevention: the Rakai Community Cohort Study

The Rakai Community Cohort Study (RCCS) is a longitudinal, open, population based census and cohort study and includes eligible adolescents and adults (15–49 years) in 34 communities in south–central Uganda. Following rapid scale-up of biomedical interventions (ART and voluntary medical male circumcision (VMMC)) and sustained high population viral suppression over the last decade in the study population, there have been substantial declines in HIV incidence, HIV associated mortality, and orphanhood. HIV incidence has declined across all ages and both sexes. However, incidence declines have been more rapid among men than women, leading to a growing gender disparity in the relative fraction of incidence cases among women. The median age of HIV infection among women has increased *(25)*. RCCS data also show a correlation between faster declines in incidence among men and faster declines in population viral load among women *(25)*. Phylogenetic data analysis of HIV transmission sources reveal an increasing proportion of HIV transmissions from men and transmission from men are shifting to older ages. Adolescent girls and young women acquire HIV from male partners about a decade older. However, as women age, the age difference between the woman and her infecting partner decreases *(25)*.

Most participants in RCCS have durable viral suppression with few rebounds. Those remaining viraemic are largely individuals with persistent high-level viremia and newly diagnosed persons. Persistently viraemic persons are more likely to be young, male, have more partners, inconsistently use condoms, have hazardous alcohol use, have lower income, and have recently migrated *(26)*. Prior to dolutegravir roll-out, pre-treatment drug resistance was increasing among pre-treated people living with HIV. However, the overall population prevalence of pre-treatment HIV drug resistance declined as the coverage of treatment and viral load suppression increased in the population. The post-dolutegravir resistance landscape is currently being assessed in the study population.

Study data since 2020 in RCCS fishing and inland communities in the study area reveal significant reductions in annual HIV testing among HIV seronegative men and women. Coverage of ART and viral suppression among people living with HIV remains high, but increases in coverage are slowing. The uptake of VMMC in older age groups also slowed. HIV incidence continued to decline, but at a slower rate, particularly among men. Among recently seroconverted people living with HIV, substantial declines in annual HIV testing resulted in less timely HIV diagnosis; recently seroconverted individuals were less likely to be aware of HIV status, self-report ART use, and be virally suppressed than in recent study rounds. HIV testing declined among all HIV risk categories.

Preliminary data from ongoing surveillance studies were also presented. Recent contact tracing studies showed that male HIV incident cases were more likely to report a female sex worker partner compared with age, community and religion matched controls. HIV seroprevalence among female sex workers is high with high levels of viral suppression. However, self-reported PrEP usage among those HIV seronegative is low. These studies also showed that more than half of viraemic people living with HIV are ‘pre-treatment/ART-naïve With the exception of the increasing age of sexual debut among adolescent girls and young women, no major changes in HIV risk behaviours have been observed. Despite high rates of PrEP eligibility in the RCCS general population, the level of PrEP use is low, and non-HIV sexually transmitted infections are very prevalent in the region *(27–30)*.

SESSION 5:
CONSENSUS STATEMENTS ON THE DESCRIPTION OF HIV EPIDEMIOLOGY POST-2030 IN SETTINGS ACHIEVING TARGETS

Session 5 consisted of working group discussions to synthesize summary descriptions of the HIV epidemic situation beyond 2030 in settings attaining and sustaining HIV testing and treatment targets, based on the evidence presented in Sessions 3 and 4. Three working groups were each asked to address three objectives [Working Groups (Task 1)]:

- Develop simple descriptions of the HIV epidemic situation post-2030 in settings that have controlled the epidemic. Summary descriptions of HIV epidemiology in settings controlling HIV.
- Identify the confidence level and key uncertainties about the future epidemiological description.
- Describe how epidemiological uncertainty affects: (1) the programmes required to sustain epidemic control; and (2) priorities for surveillance and monitoring.

Each group reported back on their discussions, and plenary sessions were convened to reach consensus descriptions and areas of uncertainty, as described below.

Summary descriptions of HIV epidemiology in settings controlling HIV

The general consensus was that in high HIV burden settings while meeting and sustaining HIV treatment and viral suppression targets:

- HIV incidence after 2030 will be much lower and will continue to decline for at least another decade. However, the **rate of incidence decline will likely be slower** than over the past decade (2010–2020), when ART coverage and population viral suppression increased rapidly.
- There was an expectation that HIV incidence would likely eventually plateau at a lower equilibrium level, with **HIV infection and transmission more concentrated among higher risk/core populations**. However, there was great uncertainty about when, among whom, or at what level HIV incidence would stabilize and what would determine this. There was a high level of consensus that **key populations or core at-risk populations will have disproportionate risk of acquiring HIV and require sustained, more intensive, HIV prevention services** for a long period (decades).
- HIV prevalence among reproductive age (15–49 years) adults will steadily decline for the next decades (irrespective of uncertainty about current and future incidence), reflecting lower incidence compared with earlier cohorts and ageing of the HIV population. The prevalence of HIV among older adults may continue to rise, slightly, before eventually declining. The age distribution of the **HIV population will shift dramatically towards older ages with more chronic health conditions**, substantially increasing the healthcare needs of the HIV population and value proposition for engaging in care.
- People living with HIV who are treatment naive, and those currently on, or previously on, treatment but who face barriers to achieving or sustaining viral load suppression, and thus remain viraemic, will also become a growing proportion of people living with HIV with potential transmission risk.
- As HIV incidence declines, it is likely that inequalities will increase and become more polarizing. In these settings, high HIV transmission networks will become more visible, with this having important implications for potentially fuelling increased stigma and discrimination, which must be actively addressed to sustain an effective HIV response and protect individual rights and wellbeing.
- High levels of treatment coverage and viral suppression are needed in these settings to sustain declines in incidence, while the impacts of interventions such as VMMC that currently contribute to suppressing population HIV transmission will continue to benefit programmes in the future.

Priority areas of uncertainty about future epidemiology

While it was expected that HIV incidence would continue to decline, it was unclear how quickly this incidence will decline, the level at which it will plateau (if this occurs), and if trends in declines in incidence noted in countries with data are generalizable to other regions with limited data. It is also uncertain if HIV infections will concentrate among key populations or remain diffuse, and if seeding of infections from key populations into a larger but lower risk population will occur. The quality of data on key populations is currently poor, with consequent limitations on assumptions about key populations (including their mixing patterns) in models. There are further uncertainties about attainment of targets within all subpopulations.

Other priority uncertainties are on the need to continue monitoring all 95–95–95 targets (split by subpopulation), particularly the first 95, which is more difficult to measure. It is believed that the availability of data on the second and third 95 targets alone should provide key information on patient and population health and service needs, including the population level prevalence of detectable viremia (PDV). There is also limited knowledge on the possible impacts of treatment failure, following long term ART usage in ageing populations, which can occur due to drug resistance mutations, changes in adherence, or migration. Better understanding of the role in transmission of individuals on ART with low level viremia is also needed.

We need more data on the characteristics and risk profile of men who are missing from HIV services to distinguish if programmes are failing to reach them, or if they are unwilling to use currently available and accessible services. We also have knowledge gaps on behaviour change with respect to primary prevention practices, particularly in the context of evolving social media connectivity (apps) and on the role mobility will play in the future of the epidemic.

Implications of uncertainty for programme and surveillance priorities

Uncertainties about the level at which HIV incidence plateaus will have implications on new infections and deaths, and therefore long-term treatment need and expenditure. If transmission becomes more concentrated among key or high-risk populations, programmes will need to adapt, focusing more narrowly on engaging these populations in HIV prevention, and including a need for more structural and systemic changes.

Programme priorities include understanding how the functionality of existing health systems will need to change to cater to the ageing epidemic requiring lifelong treatment and considering calls for integration of HIV services into existing healthcare systems. There is also a need to identify inequalities and challenges to access services and identify ways to address them. These will include identifying ways to reach the populations dropping out of treatment to improve retention and reinitiation, understanding how HIV testing patterns need to evolve and promote reinitiation of ART after interruption, developing mobility friendly and male centric HIV programmes.

Key surveillance priorities for programmes will include improving on currently existing key population and HIV case surveillance activities and the use of electronic medical records (EMRs) to inform programmes. Better systems are needed to monitor populations that are dropping out of care and improve detection of drug resistance. Improved understanding of the populations susceptible to HIV infections and those most likely to transmit new infections are needed to optimize the targeting of interventions.

SESSION 6:
IMPLICATIONS OF EPIDEMIOLOGICAL CHANGES FOR HIV PROGRAMME AND SURVEILLANCE AND MONITORING PRIORITIES POST-2030

Session 6 focused on discussions about the implications of epidemiological changes for HIV programme and monitoring priorities in 2030 and beyond. The sessions was introduced by two presentations summarizing: (1) the current global AIDS strategy and monitoring framework; and (2) a summary of responses to a pre-meeting survey of meeting participants to solicit ideas towards defining AIDS as no longer being a public health threat.

Following this, three working groups were tasked with completing an exercise to articulate how the HIV response should change and evolve in response to sustaining the epidemiological situation described in Session 5. The working groups were prompted to discuss the following topic:

Based in changing HIV epidemiology, describe how "ending AIDS by 2030" changes as the HIV response transitions from an 'emergency response' to a long-term control scenario.

Three dimensions:

- Epidemiological indicators and metrics for maintaining disease control.
- HIV programmes (stratify into treatment, testing, prevention, societal enablers).
- HIV surveillance and monitoring.

For each dimension, describe:

- What needs to be sustained beyond 2030/does not change.
- What can be discontinued or substantially scaled back in the transition from emergency response to control scenario.
- What needs to evolve.
- What a return of public health threat from HIV/AIDS look like.

Global AIDS Strategy and Global AIDS Monitoring 2021–2026

As a baseline for considering future transitions in the HIV response, the three Strategic Priorities of the *Global AIDS Strategy 2021–2026* and their corresponding Result Areas were presented. **Strategic Priority 1 (SP1)** is to *maximize equitable and equal access to HIV services and solutions*. This highlights that HIV services are not always designed or tailored for the populations or age groups most affected by HIV, and often fail to meet their needs. SP1 includes a new prioritized Result Area 1 on HIV prevention, and two high level targets: (1) ensure 95% of people at risk for HIV have access and use HIV prevention; and (2) 95% of women of reproductive age have their HIV and SRH needs met. Result Area 2 features the range of services in the HIV cascade, with 95–95–95 to be reached in all subpopulations, age groups and settings. Result Area 3 focuses on meeting the needs of children living with or at risk of HIV, currently one of the most glaring disparities in the HIV response. The strategy prioritizes smarter programming to end vertical transmission and to reduce the inequalities that worsen outcomes for HIV exposed infants and children.

Strategy Priority 2 (SP2) aims to *break down barriers to achieving HIV outcomes and specifically address the effects of criminalization, stigma, discrimination, gender inequalities, gender based violence and other human rights violations in the context of HIV*. SP2 includes four Result Areas (RA), including [RA4]: support for community-led responses, and [RA5]: human rights, stigma, and discrimination free lives for people living with HIV, key populations and people at risk of HIV. Across this Strategic Priority, the **10–10–10 targets** are critically important, whereby by 2025 less than 10% of countries will have punitive legal and policy environments, less than 10% of people living with HIV and key populations experience stigma and discrimination, and less than 10% of women, girls, people living with HIV and key populations experience gender inequality and violence.

Strategic Priority 3 aims to *fully resource and sustain efficient HIV responses and integrate HIV into systems for health, social protection, humanitarian settings, and pandemic responses*. These include [RA8]: to ensure a fully resourced, fully funded HIV response, with total annual resource

needs of $28.5 billion per year by 2025; [RA9]: integrating HIV into systems for health and social protection to ensure 45% of people living with, at risk and affected by HIV have access to one or more social protection benefits; and [RA10]: ensuring HIV responses protect people living with, at risk of, and affected by HIV in humanitarian settings and from the adverse impacts of current and future pandemics and other shocks.

The routinely reported indicators for the Global AIDS Monitoring framework which help track the top-line targets for 2025 were also outlined.

Pre-meeting survey: identify commonalities across responses to the definition of 'ending AIDS as a public health threat'

In advance of the meeting, participants were sent a short survey to guide discussion themes at the July meeting and obtain initial ideas about key elements of defining a situation in which AIDS is no longer a public health threat. Participants were asked to give **concise, actionable, measurable and simple definitions** of: (1) the epidemiological conditions and applicable metrics in which AIDS would be considered not a 'public health threat'; (2) the essential policies, health system capabilities, and provision of services that must be implemented in perpetuity to ensure that AIDS does not remain a public health threat; and (3) the key monitoring and surveillance capabilities and/or indicators that must be in place to ensure that required programmes are effectively maintained and epidemiological conditions are sustained. Participants were also asked to provide any additional comments on priority discussion topics or on framing the description of the 'end of AIDS as a public health threat'.

A total of 21 participants responded. The key themes in responses about metrics for determining that HIV was not a public health threat were as follows:

- The majority of respondents suggested epidemiological conditions and metrics which included a **measure of HIV incidence**, with measures of **HIV related deaths** being next most common.
- Some raised concerns about using mortality measures, given the difficulties in defining mortality thresholds, and suggested focusing instead on **attainment of ART coverage goals**.
- There was a general preference for **'absolute'** over 'relative' targets. However, few respondents suggested conditions of consistent and stable declines in incidence and deaths as being sufficient to define that AIDS was no longer a threat.
- The majority of respondents recommended that all metrics should be applicable across all subpopulations (age, gender and key populations). Metrics suggested included: a <1% cumulative risk of acquiring HIV by age 50; risk of onward transmission lower than 1 per lifetime or AIDS deaths as a proportion of all-cause deaths.
- Some respondents also suggested maintaining the 95–95–95 target, particularly the 'third 95'.
- Some suggested including measures of stigma and quality of life among people living with HIV.

Regarding essential programmes and policies that should be sustained:

- Participants consistently responded that free, accessible, high quality antiretroviral therapy needs to be sustained for all people living with HIV.
- Most respondents also mentioned the **maintenance of HIV testing services.** However, responses were divided between maintaining high levels of testing for all versus focusing HIV testing among pregnant women, those with symptoms or at high risk of HIV infection.
- Comprehensive **HIV prevention services,** including PrEP, PEP, VMMC, harm reduction and opioid substitution therapy for vulnerable populations, were also consistently reported as being an essential provision and there were suggestions for these to be integrated into broader STI prevention efforts.
- Most respondents also reported the need for **policies on stigma reduction, non-discrimination** against people living with HIV and **decriminalization of same sex**

partnerships, sex work, injecting and using drugs among key populations, with a need for all services provided to be person centred and to uphold the human rights of all persons, including people living with HIV.

The key monitoring and surveillance capabilities consistently reported were surveillance activities to detect and respond to outbreaks. Some suggestions were for antenatal HIV surveillance to continue, improvement of current key population surveillance activities and case-based surveillance in programmes. Some respondents called for the continuation of population-based surveys, such as the Population-based HIV Impact Assessment, while others suggested less reliance on these surveys and more focus on data collected during routine service delivery supplemented by 'programme driven surveys'. Other key monitoring capabilities mentioned were improved tracking of ART retention, viral suppression, drug resistance, migration patterns, supply chains and monitoring of policies on stigma and discrimination.

Session 5 working group consensus summary

Epidemiological indicators and metrics for maintaining disease control as the HIV response transition:

- **Cumulative risk of HIV acquisition** over a given period was identified as a preferred metric for communicating progress at sustaining low risk of HIV infection. This could be expressed, for example, over an individual's lifetime or up to age 30. The period measure is consistent with standard demographic measures, such as the probability of death before age 5 (child mortality), or the probability of death between ages 15 and 60 ($_{45}q_{15}$).
- This measure was recommended because it is intuitive for a non-specialist audience. Particularly at low levels of incidence, understanding a "3.5% lifetime risk of infection" is more tangible than a "1 per 1000 annual risk".
- The 'lifetime risk' aligns to the lifelong nature of HIV infection and connotes the intention to sustain low risk of HIV infection in perpetuity (versus reduce annual incidence rate in a given year or age).
- It can be compared across populations and measured over time periods and the measure could potentially be ranked with other diseases in a country to serve as a comparison of the threat posed by HIV.
- The measure can be reported 'positively', for example a '99% probability of remaining HIV-free at age 30'.
- However, it will require estimates of age-specific HIV incidence rates to be ascertained, likely through modelling (similar to current approaches to global reporting on HIV incidence metrics).
- **Cumulative/lifetime risk of death from HIV** was suggested as a summary measure of the health impact of HIV. This metric is comparable to risk of death from other disease burdens in a local setting, as envisioned for a situation in which HIV was controlled by the 2015 Lancet Commission on Ending AIDS. However, a key limitation of this indicator (similar to other AIDS related mortality metrics) is that reliably measured data on AIDS related mortality are limited or do not exist in many settings, and therefore AIDS death estimates are heavily modelled based on assumptions about ART coverage and its impacts on mortality.
- **Population prevalence of viraemia** (unsuppressed HIV viral load) was proposed as a proxy metric for monitoring HIV incidence risk in a population. In modelling and empirical analyses, this outcome is highly correlated to incidence changes, but is likely more directly measurable in a low cost way than directly monitoring incidence, possibly using programme data.
- Continued monitoring of the **95–95–95 targets** was also recommended, particularly the ART coverage and viral suppression outcomes. The 'first 95' HIV awareness target, which is difficult to measure accurately over time given repeat diagnoses, deaths and (unrecorded) emigration of diagnosed people living with HIV, can be discontinued.
- Instead of monitoring 'awareness' (first 95), **time from infection to HIV diagnosis**, **low CD4 count** at diagnosis or **AIDS/advanced HIV disease (AHD)** at diagnosis were suggested. These outcomes indicate the timeliness of HIV diagnosis, ensuring that the duration spent with unsuppressed viraemia (and therefore cumulative transmission

potential) is low. The prevalence of low CD4 or AHD at initial diagnoses or in the population of people living with HIV on ART are also a key proxy for monitoring the effectiveness of testing and treatment programmes at averting morbidity and mortality from HIV. They may also be easy to monitor from routine programme data in settings where CD4 count testing is routinely done.

Suggested indicators for monitoring susceptibility and transmission risk include: population prevalence of viral suppression among under 35 year olds (by sex); percentage non-suppression among those on ART (by age and sex); fraction of the population that is at negligible risk to HIV; incidence to population viremia prevalence ratio and proportion of antenatal care women living with HIV and with viral suppression.

The preference for suggested indicators to be measured across subpopulations and sub-nationally was highlighted. It was also suggested that other functional forms of current targets can be explored, such as 'the probability of it being lower than particular values'.

HIV programmes requirements (stratify into treatment, testing, prevention and societal enablers)

HIV treatment. High levels of ART coverage (95%) and viral load suppression (95%) and prevention of mother-to-child transmission services need to be sustained. However, while sustaining the 95–95–95 targets is important, HIV programme implementers need to actively consider about how to achieve these targets. The role of long acting ART in the future needs to evolve.

Attention to chronic conditions among older people living with HIV needs to evolve to sustain the clinical benefits of care for the ageing people living with HIV. We also require continued investment in drug discovery to increase the availability of effective ART options for treatment and prevention.

More differentiated service delivery (DSD) models, including multi-month dispensing (MMD) with a focus on reducing the 'medicalization' of HIV treatment as part of patient-centred care is needed. We also need to leverage more on DSD models to increase access to viral load testing and identify ways to improve the availability of test results so they can be used to make timely treatment decisions, including regimen switch. It was noted that the current cost of viral load testing in sub-Saharan Africa remains high and reducing this cost should be a priority.

HIV testing. Maintaining high rates of HIV testing among populations at risk of acquiring HIV is critical to enable timely ART linkage, and therefore avert risk of onward HIV transmission. There was general consensus that current HIV testing approaches need to evolve, with the focus of testing on identifying new infections and getting people living with HIV on treatment. Testing modalities that should be retained include index testing, HIV self-testing and ANC testing, while traditional modes of untargeted testing such as voluntary counselling and testing (VCT) may be scaled back. Access to HIV self-testing needs to increase and self-referral as a key part of HIV testing needs to evolve and become an integral component of HIV testing strategy. Ways to incorporate contact tracing into self-testing should be considered.

HIV prevention. Primary HIV prevention (condoms, behaviour change, VMMC) has had a large impact on reducing HIV incidence before ART scale-up and continues to have an important suppressive effect on incidence that must be sustained. However, current approaches of providing expensive or resource intensive HIV prevention services to general populations will become less cost-effective over time as incidence declines, and these need to become more targeted. Similarly, modes of providing pre-exposure prophylaxis (PrEP) need to evolve. The promotion of condoms as an important primary prevention tool should be sustained given its low cost and effectiveness in preventing HIV transmission, unwanted pregnancies, and other sexually transmitted infections.

Policies and programmes that address societal barriers.: The current 10–10–10 targets for stigma and discrimination should be sustained, including ongoing work on policies, services and programme implementation (such as person centred healthcare) to reduce stigma and discrimination. There is a need to focus on where barriers to access services exist to help reduce inequalities in HIV prevention, treatment and health outcomes. Health systems also need to

continue to strengthen community engagement and community leadership to empower people with the right information on concepts such as U = U, given that misconceptions about HIV still exist in some settings. However, methods to assess the impact of such interventions remain a challenge.

Potential developments that should be monitored to inform programmatic shifts include the: probable increasing concentration of new infections among core populations; poorer treatment outcomes such as ART linkage; retention on treatment or viral suppression among subpopulations; and the introduction of discriminatory laws that amplify barriers in access to care.

HIV surveillance and monitoring requirements

- High quality routine antenatal care testing data should be sustained to monitor national population trends in HIV prevalence. Antiretroviral treatment coverage and viral suppression, and routine programmatic data and mortality reporting systems need to be strengthened.
- Sustain (and as locally relevant, improve upon) focused HIV surveillance programmes with key populations, other marginalized populations, and particularly high transmission networks. Surveillance approaches may need to be adapted to reflect changes in the local HIV epidemiology (i.e. changes in high transmission networks) and in the local health system and the sociopolitical context. Such monitoring should focus on monitoring service coverage and barriers to accessing effective treatment and prevention services.
- Viral load suppression and antiretroviral resistance need to be monitored, though the optimal frequency and density of monitoring will need to be evaluated.

Surveillance will play an important role in the future to help monitor trends across subpopulations and identify inequalities.

Large population based household HIV surveys like the PHIAs will be less effective and efficient as population prevalence of primary outcomes decreases. This loss of efficiency may be mitigated by reducing the target precision of surveys or, alternatively, incorporated into other large surveys such as MICS and DHS to share the operational costs more widely. However, it was strongly noted that nationally representative surveys still need to be retained in some form to provide reliable data to guide the HIV response in many settings where routine programme data remain insufficiently precise for surveillance purposes.

REFERENCES

1. United Nations. The 2030 Agenda for Sustainable Development. New York: United Nations; 2015 (cited 26 September 2023). Available from: https://sdgs.un.org/goals
2. Joint United Nations Programme on HIV/AIDS. End Inequalities. End AIDS. Global AIDS Strategy 2021–2026. Geneva: UNAIDS; 2021 (cited 26 September 2023). Available from: https://www.unaids.org/en/resources/documents/2021/2021-2026-global-AIDS-strategy
3. Joint United Nations Programme on HIV/AIDS. Fast-Track — Ending the AIDS epidemic by 2030. Geneva: UNAIDS; 2014 (cited 26 September 2023). Available from: https://www.unaids.org/en/resources/documents/2014/JC2686_WAD2014report
4. Joint United Nations Programme on HIV/AIDS. Making the end of AIDS real: consensus building around what we mean by "epidemic control". Geneva: UNAIDS; 2017 (cited 26 September 2023). Available from: https://www.unaids.org/en/resources/documents/2017/glion_oct2017_meeting_report
5. Ghys PD, Williams BG, Over M, Hallett TB, Godfrey-Faussett P. Epidemiological metrics and benchmarks for a transition in the HIV epidemic. PLoS Med. 2018;15(10).
6. Joint United Nations Programme on HIV/AIDS. 34th Programme Coordinating Board Meeting, July 2014. Geneva: UNAIDS; 2014 (cited 26 September 2023]. Available from: https://www.unaids.org/en/aboutunaids/unaidsprogrammecoordinatingboard/pcbmeetingarchive/34-pcb-meeting
7. Dowdle WR, Hopkins DR. The eradication of infectious diseases : report of the Dahlem Workshop on the Eradication of Infectious Diseases, Berlin, 16–22 March 1997. Available from: https://api.semanticscholar.org/CorpusID:68721862
8. Dowdle WR. The principles of disease elimination and eradication. Bull World Health Organ. 1998;76(Suppl 2):22–25.
9. Piot P, Abdool Karim SS, Hecht R, Legido-Quigley H, Buse K, Stover J, et al. The Lancet Commissions: A UNAIDS–Lancet Commission on Defeating AIDS—Advancing Global Health Defeating AIDS—Advancing global health. Lancet. 2015;386:9989.
10. Reuben G, Somya G, Brian W. 90-90-90, Epidemic Control and Ending AIDS: Global Situation and Recommendations. Int. J. Virology and AIDS. 2018;5(1).
11. 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.
12. Stover J, Bollinger L, Antonio Izazola J, 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).
13. Stover J, Glaubius R, Teng Y, Kelly S, Brown T, Hallett TB, et al. Modeling the epidemiological impact of the UNAIDS 2025 targets to end AIDS as a public health threat by 2030. PLoS Med. 2021;18(10).
14. HIV Modelling Consortium. Modelling to Inform HIV Programmes in Sub-Saharan Africa (MIHPSA). London: University College London (cited 26 September 2023). Available from: http://hivmodeling.org/mihpsa
15. Moolla H., Phillips A., ten Brink D., Mudimu E., Stover J., Bansi-Matharu L., et al. A quantitative assessment of the consistency of projections from five mathematical models of the HIV epidemic in South Africa: a model comparison study. BMC Public Health. 2023; in press.
16. Johnson L, Dorrington R. Thembisa: mathematical model. Cape Town: University of Cape Town; 2023 (cited 26 September 2023]. Available from: https://www.thembisa.org/

17. Johnson LF, Kubjane M, Moolla H. MicroCOSM: a model of social and structural drivers of HIV and interventions to reduce HIV incidence in high-risk populations in South Africa. bioRxiv. 2018.

18. Akullian A, Morrison M, Garnett GP, Mnisi Z, Lukhele N, Bridenbecker D, et al. The effect of 90-90-90 on HIV-1 incidence and mortality in eSwatini: a mathematical modelling study. Lancet HIV. 2020;7(5).

19. Probert WJM, Sauter R, Pickles M, Cori A, Bell-Mandla NF, Bwalya J, et al. Projected outcomes of universal testing and treatment in a generalised HIV epidemic in Zambia and South Africa (the HPTN 071 [PopART] trial): a modelling study. Lancet HIV. 2022;9(11).

20. Hayes RJ, Donnell D, Floyd S, Mandla N, Bwalya J, Sabapathy K, et al. Effect of universal testing and treatment on HIV incidence — HPTN 071 (PopART). New England J. Med. 2019;381(3).

21. Hall M, Golubchik T, Bonsall D, Abeler-Dörner L, Limbada M, Kosloff B, et al. Demographics of people who transmit HIV-1 in Zambia: a molecular epidemiology analysis in the HPTN-071 PopART study. medRxiv. 2023; Available from: https://www.medrxiv.org/content/early/2023/03/24/2021.10.04.21263560

22. Magosi LE, Zhang Y, Golubchik T, Degruttola V, Tchetgen ET, Novitsky V, et al. Deep-sequence phylogenetics to quantify patterns of HIV transmission in the context of a universal testing and treatment trial: BCPP/Ya Tsie trial. Elife. 2022;11.

23. Otecko N, Di Lauro F, Herbeck J, Grabowski MK, Bonsall D, Abeler-Dörner L, et al. PANGEA-HIV consortium investigators. Patterns of phylogenetic clustering in the PANGEA-HIV studies: implications for targeted prevention, and need for follow-up studies. 2023.

24. Schneeberger A, Nat R, Mercer CH, Gregson SAJ, Ferguson NM, Nyamukapa CA, et al. Scale-free networks and sexually transmitted diseases: a description of observed patterns of sexual contacts in Britain and Zimbabwe. Sex Transm Dis. 2004;31(6).

25. Monod M, Brizzi A, Galiwango RM, Ssekubugu R, Chen Y, Xi X, et al. Growing gender disparity in HIV infection in Africa: sources and policy implications. medRxiv. 2023; Available from: https://www.medrxiv.org/content/early/2023/03/20/2023.03.16.23287351

26. Rosen JG, Ssekubugu R, Chang LW, Ssempijja V, Galiwango RM, Ssekasanvu J, et al. Temporal dynamics and drivers of durable HIV viral load suppression and persistent high- and low-level viremia during Universal Test and Treat scale-up in Uganda: a population-based study. medRxiv. 2023; Available from: https://www.medrxiv.org/content/early/2023/06/16/2023.06.15.23291445

27. Ssempijja V, Nakigozi G, Ssekubugu R, Kagaayi J, Kigozi G, Nalugoda F, et al. High rates of pre-exposure prophylaxis eligibility and associated HIV incidence in a population with a generalized HIV epidemic in Rakai, Uganda. J. Acquir. Immune Defic. Syndr. 2022;90(3).

28. Ssempijja V, Ssekubugu R, Kigozi G, Nakigozi G, Kagaayi J, Ekstrom AM, et al. Dynamics of pre-exposure (PrEP) eligibility because of waxing and waning of HIV risk in Rakai, Uganda. J. Acquir. Immune Defic. Syndr. 2023;93(2).

29. Grabowski MK, Mpagazi J, Kiboneka S, Ssekubugu R, Kereba JB, Nakayijja A, et al. The HIV and sexually transmitted infection syndemic following mass scale-up of combination HIV interventions in two communities in southern Uganda: a population-based cross-sectional study. Lancet Global Health. 2022;10(12).

30. Whittles LK, Galiwango RM, Mpagazi J, Tobian AAR, Ssekubugu R, Jackson J, et al. Age patterns of HSV-2 incidence and prevalence in two Ugandan communities: a catalytic incidence model applied to population-based seroprevalence data. J. Infect. Dis. 2023; 2023 228(9):1198–1207.

APPENDIX

Meeting participants

Participant	Affiliation
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Alison Galvani	Yale School of Public Health
Anna Bershteyn	New York University
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Shona Dalal	World Health Organization
Solange Baptiste	International Treatment Preparedness Coalition (ITPC)
Will Probert	World Health Organization

Meeting Agenda

Describing the "End of AIDS as a Public Health Threat"

Technical working meeting

20-21 July 2023, Harvard T.H. Chan School of Public Health, Boston, MA, USA
Virtual participation via Zoom (all times are EDT [UTC-4]): [Zoom link]

Day 1: 20th July 2023 (9:00 – 18:00 EDT)

Time	Duration (mins)	Topic	Presenter(s)/ Lead Discussant
Session 1: Global needs to review understanding of the 'End of AIDS' (chaired by Lucie Abeler-Dorner) • **Establish common understanding for motivation for exercise and planned outputs**			
9:00	**30**	**Welcome and introductions** **Background, overview of exercise, and outputs** **Overview of meeting and agenda**	**Mary Mahy** **Mary Mahy** **Jeff Eaton**
9:30	**60**	**Guiding perspectives from stakeholders** • **PEPFAR [10 mins]** • **Government of Botswana [10 mins]** • **Africa Centers for Disease Control [10 mins]** • **Bill & Melinda Gates Foundation [15 mins]** ***Discussion***	**Irum Zaidi** **Robert Selato** **Abdulaziz Mohammed** **Michelle Morrison & Geoff Garnett**
Session 2: Framework to describe the End of AIDS as a Public Health Threat (chaired by John Stover) • **Review concepts, definitions, and metrics applied to goals 'End AIDS by 2030' and consider adaptation for applicability post-2030** • **Develop framework and components for describing HIV situation post-2030 in settings attaining targets**			
10:30	**15**	**Overview and definitions of 'End AIDS as a Public Health Threat'" by 2030**	**Jeff Eaton**
10:50	**20**	**Epidemic control indicators: definitions, strengths and weaknesses, applications, and open questions**	**Peter Godfrey-Faussett**
11:10	**10**	**Proposed framework for describing the 'End of AIDS as a Public Health Threat'**	**Jeff Eaton**
11:20	**40**	***Discussion*** • **'End of public health threat' vs. 'epidemic/disease control'** • **Retaining/defining 'acceptably low level of inf. and deaths'** • **Need for description of 'return of a public health threat'?** • **Components and framework for description**	
12:00	**30**	**Lunch (in meeting room)**	
Session 3: Mathematical model projections of HIV epidemics beyond 2030 (chair Christophe Fraser) • **Review long-term HIV epidemic projections in high HIV burden settings sustaining high levels of HIV testing and treatment coverage** • **Understand structural, assumptions, and epidemic dynamics reasons for variation in model projections** • **Assess implications of long-term transmission dynamics for requirements for sustaining progress**			
12:30	**40**	**Modelling exercises to guide HIV targets: principles and assumptions, results, assessment of implementation, and current projections [25 mins]** ***Discussion***	**John Stover**
13:10	**50**	**Overview of *Modelling to Inform HIV Planning in Sub-Saharan Africa* (MIHPSA) projection, South Africa model projections, and between-model heterogeneity [10 mins]**	**Haroon Moolla**

		MIHPSA long-term projections and transmission ratios [15 mins] ***Discussion***	**Jeff Eaton**
14:00	**90**	**Comparison of model projections for South Africa: Thembisa and MicroCOSM [20 mins]** **Long-term HIV incidence projections in South Africa and impact of future HIV programme decisions [10 mins]** **Evolving HIV epidemic dynamics in Eswatini, sources of infection, and the reproduction number [15 mins]** **Long-term impact of the HPTN 071 (PopART) intervention, prospects of elimination, and evolving transmission [15 mins]** ***Discussion***	**Leigh Johnson** **Jeff Eaton** **Adam Akullian** **Will Probert**
15:30	**10**	**Coffee**	
Session 4: Current and future HIV epidemiology and transmission dynamics in settings sustaining high HIV programme coverage (chaired by Joseph Kagaayi) • **Review empirical evidence on current HIV transmission dynamics** • **Interpret implications of empirical evidence for adjudicating likely HIV epidemic trajectories**			
15:40	**70**	**Evidence on contemporary HIV transmission dynamics from phylogenetic data and mathematical modelling: implications for current and future epidemic trends and transmission drivers** ***Discussion***	**Christophe Fraser Lucie Abeler-Dorner**
16:50	**40**	**Contemporary HIV epidemiology and transmission dynamics in a setting with high population viral suppression and combination prevention: evidence from the Rakai Community Cohort Study** ***Discussion***	**Kate Grabowski**
17:30	**30**	***Discussion*****: consolidating questions for Day 2 morning**	**Jeff Eaton**

Day 2: 21st July 2023 (9:00 – 17:00 EDT)

Time	Duration (mins)	Topic	Presenter(s)/ Lead Discussant
Session 5: Consensus statements on description of HIV epidemiology post 2030 in settings achieving targets (chaired by Geoff Garnett) • **Develop simple descriptions of HIV epidemic situation post-2030 in settings that have controlled the epidemic** • **Identify confidence level and key uncertainties about epidemiologic description** • **Describe how epidemiologic uncertainty affects: (1) what programmes are required to sustain epidemic control, (2) priorities for surveillance and monitoring**			
9:00	**60**	**Discussion: Day 1 priorities topics**	
10:00	**45**	***Working groups*** • **Summary descriptions of HIV epidemiology in settings controlling HIV** • **Priority areas of uncertainty about future epidemiology** • **Implications of uncertainty for programme and surveillance priorities**	
10:45	**75**	**Working group report back and discussion**	
Session 6: Implications of epidemiologic changes for HIV programme and surveillance & monitoring priorities post 2030 (chaired by Sharmistha Mishra) • **Describe existing list of essential programmes, policies, and surveillance for the HIV response in current strategy (2021–2026)** • **Identify commonalities across our responses to the definition of Ending AIDS as a public health threat**			
12:00	**20**	**Global AIDS Strategy and Global AIDS Monitoring 2021–2026**	**Mary Mahy**

11:15	**10**	**Pre-meeting survey summary**	**Lanre Edun**
12:30	**30**	**Lunch (in meeting room)**	
13:00	**60**	**Working groups: completing the post-2030 transition matrix** ***Based in changing HIV epidemiology, describe how 'ending AIDS by 2030' changes as the HIV response transitions from an 'emergency response' to a long-term control scenario*** **Three dimensions:** • **Epidemiologic indicators and metrics for maintaining disease control** • **HIV programmes (stratify into treatment, testing, prevention, societal enablers)** • **HIV surveillance and monitoring** **For each dimension, describe:** ▪ **What needs to be sustained beyond 2030/does not change** ▪ **What can be discontinued or substantially scaled-back in transition from emergency response to control scenario** ▪ **What needs to evolve** ▪ **What a return of public health threat looks like**	
14:00	**70**	**Working group report back and discussion**	
15:20	**10**	**Coffee**	
Session 7: Next steps—outlining consensus working paper and wider engagement (chaired by Mary Mahy) • **Summarize plans for September meeting, including objectives and participants** • **Agree on steps to compile working paper and timeline** • **Describe linkages to Africa Union heads of state meeting**			
15:30	**90**	***Discussion***	

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