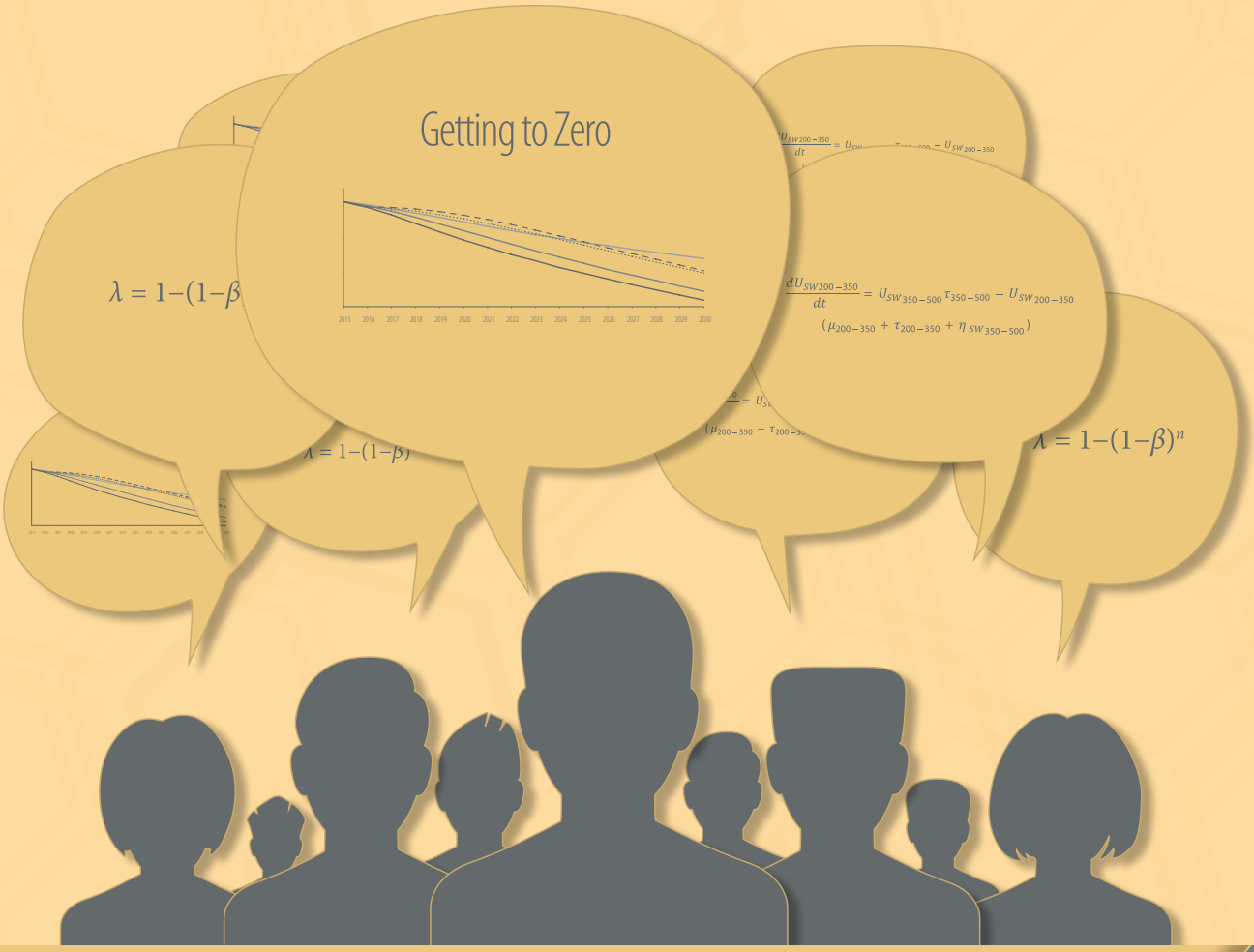
THE REPUBLIC OF UZBEKISTAN

Modelling an Optimised Investment Approach for Uzbekistan



Sustainable Financing of National HIV Responses

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Modelling an Optimised Investment Approach for Uzbekistan

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Table of Contents

Abbreviations **6**
Acknowledgments **7**

Foreword **8**

Executive summary **9**

1. Why is this document needed? **11**
The HIV response is heavily dependent on international sources 11
The current HIV response is insufficient to meet all commitments 11
International aid is unlikely to increase 11
Objectives 11

2. How much is spent? Where does the money come from? **13**
The national HIV response has been dependent on international aid 13
Breakdown of funding by programme components 13

3. What are the results of current investments? **17**
Investments have averted infections 17
HIV prevalence is declining, but slowly 17
HIV testing high, but needs further improvement 17
Treatment coverage: depending on the way of calculation – but too low 17
Treatment needs continue to rise 18

4. Scenario 1: Maintaining the current investment allocations and budget level, what will the HIV epidemic look like by 2020? **19**
HIV incidence and prevalence are expected to decline slowly 19
HIV transmission mode shifting from injecting towards sexual 19
Number of PLHIV eligible for ART is expected to increase with guideline update 20
Return on investment – Scenario 1: 'Maintaining 2012 investment allocations and budget level' 21

5. Scenario 2: What can be improved by optimising efficiencies under the current budget envelope? **22**
More value for money through technical efficiency 22
More value for money through allocative efficiency 22
Background for allocative efficiency 22
Methods for allocative efficiency 22
Modelling results for allocative efficiency 23
Improved impact – but still insufficient service coverage 25
Return on investment – Scenario 2: 'Optimising the investment allocations under 2012 budget level' 26

6. Scenario 3: Fulfilling the commitments for people in need – the rights-based investment case 27
Shortfalls of the current and optimised investment case under the current budget ceiling 27
Modelling the scale-up to universal coverage of essential HIV services 27
Background on universal coverage 27
Methods for modelling universal coverage of essential HIV prevention, treatment and care services 28
Modelling results for a rights-based investment case approach 28
Return on investment – scenario 3: 'Scaling up to universal coverage by 2020 29

7. Rights-based investment today – the highest impact now and in the future 30
The rights-based investment approach – highest impact on HIV infections and DALYs in the short-term 30
The rights-based investment approach – highest impact on HIV infections and DALYs also in the long-term 30

8. Remarks 32

Annex 34

Annex 1. Model description 34
Overview of analytical methods 34
Relationships between spending and risk behaviours 38
Counterfactual scenarios 38
Cost-effectiveness calculations for past evaluations 39
Future impact of HIV programmes and optimal allocation of resources 40

Annex 2. Data inputs 41
Summary of costs and unit costs 41

Abbreviations

AIDS	Acquired immunodeficiency syndrome
ART	Antiretroviral therapy
DALY	Disability-adjusted life year
GF	Global Fund to Fight AIDS, Tuberculosis and Malaria
HIV	Human immunodeficiency virus
HR	Human resources
HTC	HIV testing and counselling
LRF	Low-risk females
LRM	Low-risk males
MDG	Millennium Development Goal
MSM	Men who have sex with men
NFM	New funding model (of the GF)
OI	Oportunistic infections
OVC	Orphans and vulnerable children
PLHIV	People living with HIV
PMTCT	Prevention of mother-to-child transmission
PWID	People who inject drugs
RAC	Republican Centre to Fight AIDS
SDG	Sustainable development goal
STI	Sexually transmitted infection
SW	Sex workers

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Foreword

Owing to the National Strategic Programmes to Fight HIV / AIDS in the Republic of Uzbekistan that are implemented in the country since 2003, and reinforcing strong commitment of the Government to reduce the burden of the disease among the country's population, comprehensive prevention and treatment activities are being implemented to stabilize the epidemiological situation in the country.

The implementation of the Strategic Programme to Fight HIV for 2007-2011 was supported by the leadership of the country through the President's Resolution dated December 2008 that regulates financial allocations and organization of HIV prevention and treatment programmes in the country.

In order to implement the Resolution, the National Action Plan for 2009-2011 has been developed with increased state budget allocations embedded: The Republican Centre to Fight AIDS and all its branches in 14 administrative territories of the country have been equipped with modern diagnostic and laboratory equipment to ensure increased HIV testing and counselling services available for all. Important to note that along with these initiatives, enhancement of the normative and legislative work concerning HIV/ AIDS are ongoing.

A lot has been achieved in the area of HIV prevention and treatment, however it is important to understand what lies ahead for the country and what should be done in order to stop the spread of the infection in the country and the whole region. I hope that this report will greatly contribute towards achieving this goal.

Nurmat Atabekov
Director Republican Centre to Fight AIDS
Republic of Uzbekistan

Executive summary

- The new SDG 3[1] calls for ending the HIV/AIDS epidemic by 2030 and the provision of universal access to essential health services, including HIV prevention and treatment services, thereby re-enforcing the UNAIDS Getting-to-Zero Strategy and the fast track approach for upscaling such services from current coverage levels[2,3].
- While considerable progress has been made, Uzbekistan is still struggling to reverse the spread of HIV/AIDS, key populations at higher risk for HIV exposure still face discrimination and criminalization, and ART coverage is well below the MDG6 target.
- As a low middle-income country, Uzbekistan's national HIV response is still dependent on external funding, mainly provided through the Global Fund to Fight AIDS, TB and Malaria (GF). Demands are increasing for higher domestic funding as pre-condition for external support, and while there is a renewed commitment to scale up the HIV response under the new Strategic Programme for Fighting HIV Infection in the Republic of Uzbekistan, for 2013-2017 of the Republic of Uzbekistan[4] external funding is rather stagnating at current levels.
- This report aims to contribute to the development of sustainable financing strategies for the national HIV response in the short-, mid-, and long-term perspective by modelling the impact of alternative investment approaches. As part of the short-term contribution, the report provides a rational for improved allocative efficiency that can be used for the GF concept note under the GF New Funding Model (NFM).
- For the modelling, the following key questions of primary relevance for investment decisions related to the national HIV response were identified and addressed through modelling three investment scenarios using 2012 as the reference year:
  - What is the HIV epidemic in Uzbekistan likely to look like if the response continues unchanged? And what will be the return on investment by 2020?

Scenario 1: Continue with the current investment allocations and current budget ceiling

  - Can be more achieved with the same amount of resources, and how? What would then be the return on investment by 2020?

Scenario 2: Continue with optimised investment allocations and current budget ceiling

  - Using optimised efficiencies, what would need to be done and how much would it cost to achieve universal coverage of the key prevention and treatment services? What would then be the return on investment by 2020?

Scenario 3: Continue by scaling up to universal coverage of essential HIV prevention and treatment services

1 United Nations, General Assembly. Transforming our world: the 2030 Agenda for Sustainable Development. New York: United Nations, General Assembly; 2015.

2 Joint United Nations Programme on HIV/AIDS. Getting to Zero: 2011–2015 strategy. Geneva: Joint United Nations Programme on HIV/AIDS; 2010.

3 Joint United Nations Programme on HIV/AIDS. Fast-Track: ending the AIDS epidemic by 2030. Geneva: Joint United Nations Programme on HIV/AIDS; 2014.

4 Republic of Uzbekistan. Strategic programme for fighting HIV infection in the Republic of Uzbekistan for 2013-2017. Tashkent: Government; 2012.

- For all three scenarios, what would be the long-term impact by 2030?

The model results suggest:

- Maintaining the current investment allocations and budget level should be the absolute minimum target in order not to fall back behind the impact the national HIV response has achieved so far.
- Technical and allocative efficiencies can be improved and recommendations are provided in the report. However, the current budget ceiling is too low to achieve universal coverage of essential HIV services. Due to the resulting rationalization, only improving efficiencies without addressing the overall budget constraints (scenario 2) will not be sufficient in Uzbekistan for 'Getting-to-Zero', ending the HIV/AIDS epidemic by 2030 and fulfilling the basic rights for access to essential HIV services for those in need.
- To achieve these goals and targets (scenario 3) the overall investment until 2020 would need to be increased by about 40% in order to achieve universal coverage for all essential HIV services.
- As return on the investment, around 103,000 new HIV infections would be averted between 2014 and 2030 under scenario 3 using the 'test and treat' approach (around 91,000 using WHO 2013 guidelines, 88,000 using 2012 national guidelines). Scenario 2 and 1 avert significantly lower numbers of HIV infections, approximately 70,000 and 65,000, respectively.
- In addition, about 870,000 DALYs would be averted between 2014 and 2030 under scenario 3 using the 'test and treat' approach (822,000 using WHO 2013 guidelines, 796,000 using 2012 national guidelines). Scenario 2 and 1 avert significantly less DALYs, approximately 516,000 and 430,000.
- Despite the significantly higher number of HIV related deaths averted under scenario 3, the model predicts for this scenario the lowest number of PLHIV by 2030.
- Detailed information about the mathematical model used is provided in the Annex.

The key message of this report:

With a moderate increase of the investment volume until 2020 combined with an optimised investment allocation the national HIV response in Uzbekistan can be brought on a trajectory which fulfils the basic rights to access to all essential HIV services for those in need and makes ending the epidemic threat of HIV/AIDS in Uzbekistan a realistic goal if an environment without stigma and discrimination is provided so that services available will be accepted and used by the affected communities.

1. Why is this document needed?

The HIV response is heavily dependent on international sources

- Uzbekistan is a lower-middle income country. While some components of Uzbekistan's economy have increased substantially, the government is aiming for further improvements in a number of regional and global indicators.
- The Uzbekistan government has exercised leadership in financing substantial parts of its HIV response at a sustained level in recent years. However, the national HIV response is still dependent on international sources, particularly from the GF.

The current HIV response is insufficient to meet all commitments

- People in Uzbekistan continue to be at substantial risk of HIV infection, related morbidities and mortality.
- HIV prevention and treatment do not cover all those in need, and not all internationally recommended HIV service components are being provided.
- HIV incidence and prevalence in Uzbekistan seem largely to stabilize. Model-based estimates suggest that both incidence and prevalence are slowly declining among most key populations at higher risk of HIV exposure although with significant sub-national differences[5], but remain relatively stable among the populations with lower risk.

International aid is unlikely to increase

- The recent global economic crisis has diminished the prospects of growing or even stable international funding for national HIV responses in the region.
- Changing eligibility and co-financing requirements under the NFM of the GF – which provides primary support for key prevention, treatment and care programmes in Uzbekistan – underlines the importance of sustainability strategies for the national HIV/AIDS response.
- External funders are increasingly supporting countries to establish transitional funding mechanisms from international to domestic sources.

Objectives

- To provide model estimates of future epidemic trajectories in the context of the development of an HIV/AIDS investment case and sustainable financing strategies of the national response for Uzbekistan under three scenarios:
  - Scenario 1: Continue with the current investment allocation and current budget ceiling;
  - Scenario 2: Continue with optimised investment allocation and current budget ceiling;
  - Scenario 3: Continue by scaling up to universal coverage of essential HIV prevention and treatment services.

  2012 was used as the reference year.
- To estimate and compare the programme costs and the impact ('return on investment' expressed in new HIV infections averted and DALYs averted) of the three scenarios above in the mid-term (2020) and long-term (2030) perspective under consideration of short-term objectives such as the development

5 Republic of Uzbekistan. Analysis of HIV infection triangulation data in the Republic of Uzbekistan. Tashkent: Ministry of Health of the Republic of Uzbekistan; 2015. For example, HIV prevalence among PWID in Tashkent city is 24.5%, compared to 7.3% at the national level, HIV prevalence among SWs is above 5% in eight regions compared to 2.1% at the national level

of GF concept note under the NFM, and long-term objectives such as the UNAIDS 'Getting to Zero' goals[6], 'Together we will end AIDS' campaign[7] and the 'End of HIV/AIDS Epidemic' target by 2030 proposed for the SDGs[8].

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6 Joint United Nations Programme on HIV/AIDS. Getting to Zero: 2011–2015 strategy. Geneva: Joint United Nations Programme on HIV/AIDS; 2010.

7 Joint United Nations Programme on HIV/AIDS. Together we will end AIDS campaign.

8 Joint United Nations Programme on HIV/AIDS. Fast-Track: ending the AIDS epidemic by 2030. Geneva: Joint United Nations Programme on HIV/AIDS; 2014. United Nations General Assembly. Transforming our world: the 2030 Agenda for Sustainable Development – Draft resolution referred to the United Nations summit for the adoption of the post-2015 development agenda by the General Assembly at its sixty-ninth session. New York: United Nations General Assembly; 2015.

2. How much is spent? Where does the money come from?

The national HIV response has been dependent on international aid

- $ 18.3 million[9] and $ 23.9 million were invested in the HIV/AIDS response in Uzbekistan in 2011 and 2012, respectively. HIV funding from the international community has increased, and has surpassed domestic spending in 2012. However, domestic spending has previously dominated and has remained stable (figure 1).
- Overall investments in HIV/AIDS increased significantly between 2011 and 2012 due to increased international spending.
- The GF has been the major international funder. Its share increased and accounted for about 75% ($ 10 million) of the international funding in 2012. For the period 2014-2016, the GF has allocated $ 27.7 million for HIV grants in Uzbekistan[10] making the annual average less than the funding level in 2012.

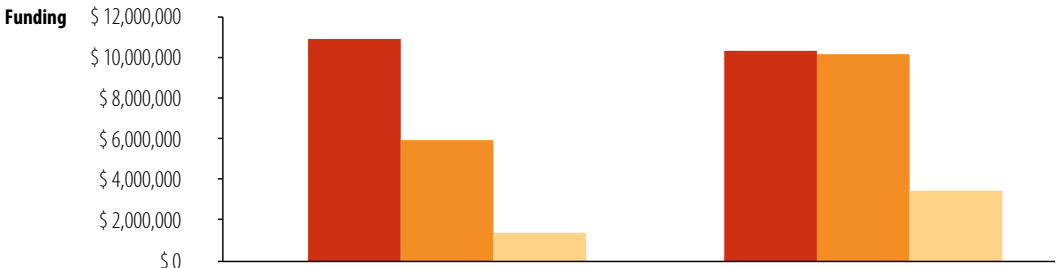
Breakdown of funding by programme components

- Approximately 49% of all HIV/AIDS funding has been allocated to prevention (figures 2 and 3a).
- Among prevention interventions the largest amounts were allocated to biomedical safety and key populations at higher risk for HIV exposure (figures 3b and 4).
- Among the key populations, funding for targeted prevention was largest for PWID and much less for SW and MSM. However, funding for PWID did not

9 All financial values in this report, including tables and figures, are expressed in United States dollars.

10 Global Fund to Fight AIDS, Tuberculosis and Malaria. Global Fund Country Allocations: 2014-2016. Geneva: Global Fund to Fight AIDS, Tuberculosis and Malaria; 2014.

Figure 1: HIV funding in Uzbekistan in 2011 and 2012 by source*



	2011	2012
Government	$ 10,950,865	$ 10,340,456
Global Fund	$ 5,932,645	$ 10,138,162
Other international	$1,379,651	$ 3,395,444
TOTAL	**$ 18,263,161**	**$ 23,874,062**

* National spending on HIV/AIDS in Uzbekistan was examined by major funding sources with the use of national statistics, sector reports, and data reported by public health service institutions for the years 2011 and 2012. Standard accountancy estimation methods were used to generate a complete dataset of national spending on HIV/AIDS spending.

include opioid substitution therapy. PMTCT was a relatively small component of the total budget.

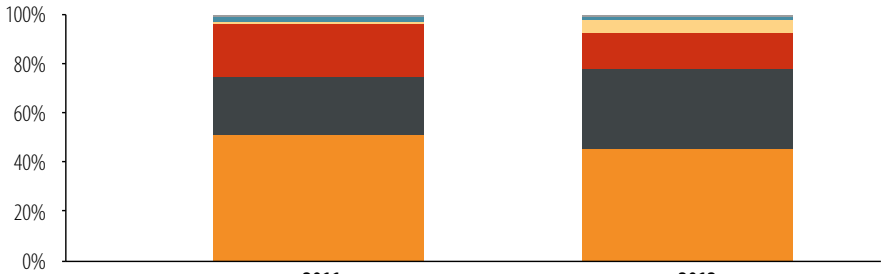
Approximately 49% of all HIV/AIDS funding has been allocated to prevention

- There was an average annual spending on prevention of $ 47.89 per PWID, $ 19.33 per MSM, and $ 31.05 per SW (based on estimates of 45,000 PWID, 21,000 SW, and 8,000 MSM[11]).

These amounts are considerably less than what is required to meet international guidelines for these populations[12].

- Expenditure on care and treatment has increased substantially between 2011 and 2012 and reached almost 30% of the total budget (figures 2, 3a, 3c and 4).
- Overall programme management and human resources costs account for 21% of overall funding in 2011-2012.

Figure 2: HIV/AIDS funding in Uzbekistan in 2011 and 2012 by programme component*



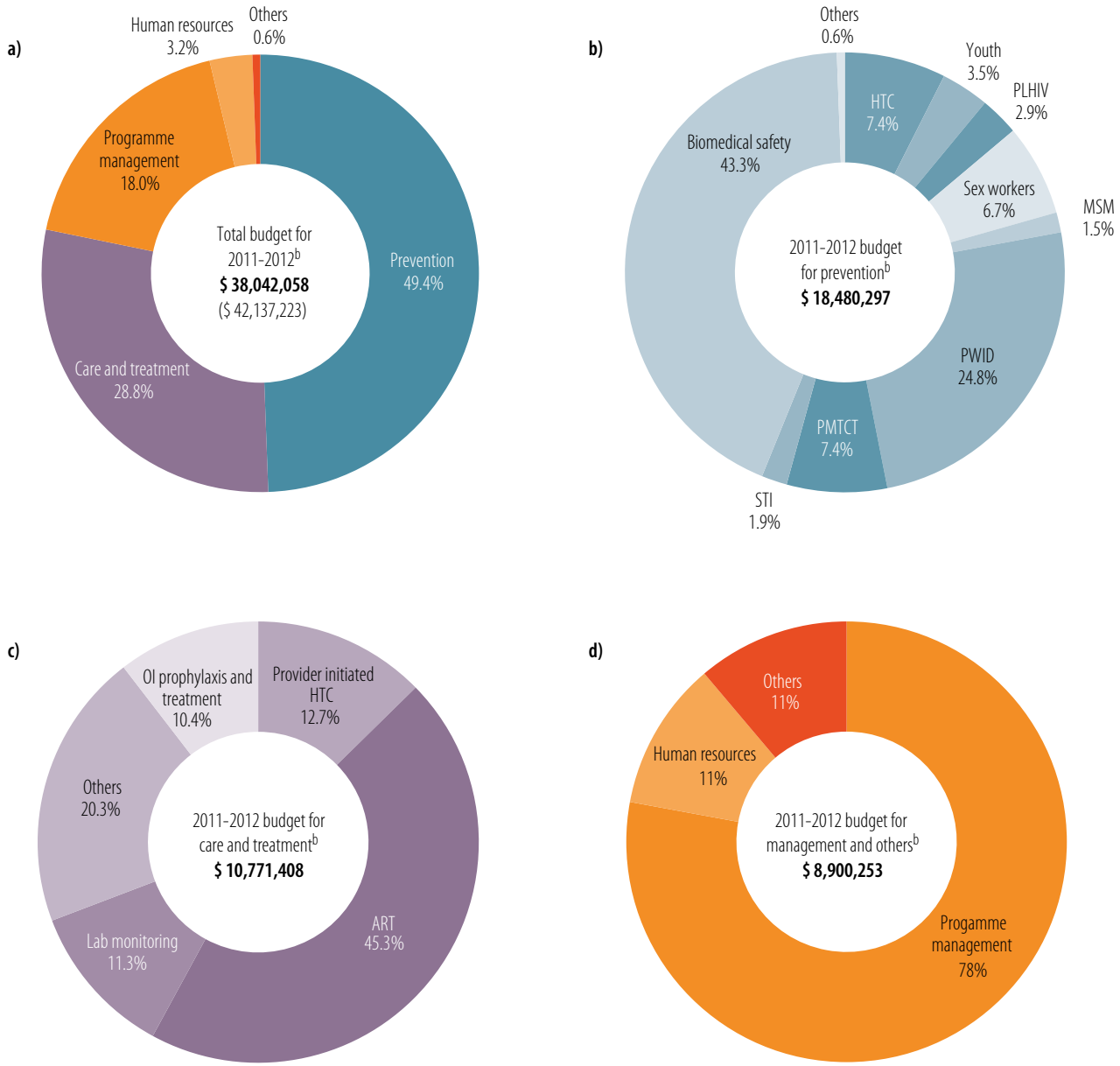
	2011	2012
Orphans and vulnerable children	$ 110,000	$ 80,000
Enabling environment	$ 353,287	$ 425,018
Human resources	$ 91,162	$ 1,089,309
Programme management	$ 3,622,303	$ 3,129,274
Care and tratment	$ 3,979,459	$ 6,791,949
Prevention	$ 8,729,691	$ 9,750,606
TOTAL	**$ 16,885,902**	**$ 21,266,156**

* The budget breakdown data were only available for $ 16.9 out of 18.3 million for 2011 and $21.3 out of 23.9 million for 2012.

11 Based on the survey on 5 regions: Tashkent city, Tashkent region, Samarkand, region, Surkhandarya region, Andijan region (UNODS methodology); MSM population size estimated in the application for GF's Rolling Continuation Channel.

12 The WHO, UNODC, UNAIDS technical guide for countries to set targets for universal access to HIV prevention, treatment and care for PWID (2012) indicates coverage in terms of sterile needle-syringes per PWID per year to be classified as low <= 100 <= mid <= 200 <= high; and coverage for opioid substitution treatment to be classified as low <= 20% <= mid <= 40% <= high. Similarly, the WB has invested in harm reduction programmes with indicated project targets of 200 needle-syringes per PWID per year and 240 condoms per SW per year. The funding required to meet these targets is substantially greater than current spending. The discrepancy for dedicated funding on prevention per MSM is even higher (Beyrer, Lancet 2012; Sullivan, Lancet 2012).

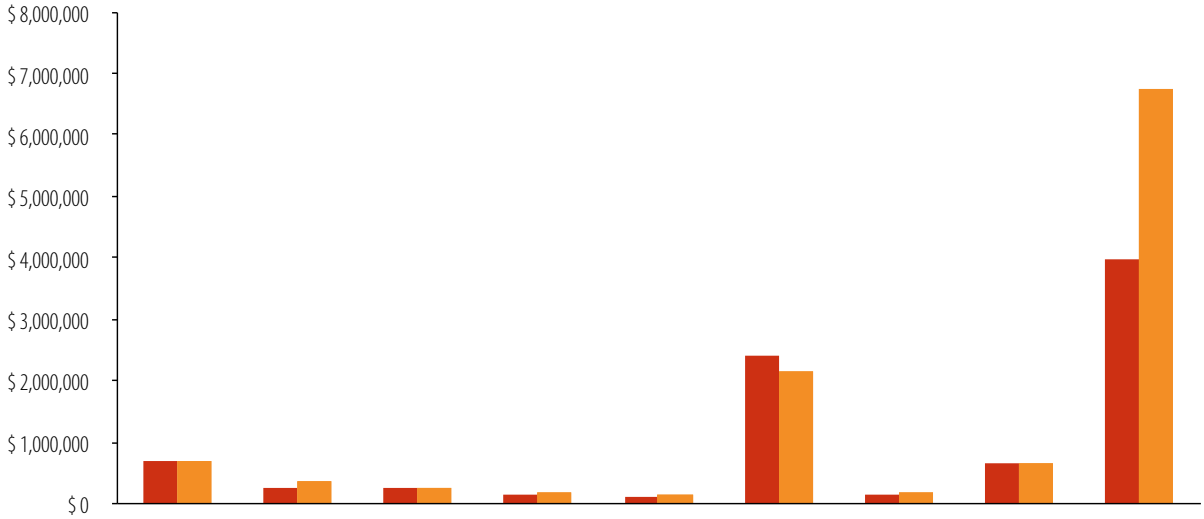
Figure 3, a-d: Detailed HIV/AIDS funding allocations in Uzbekistan, 2011-2012*,**



* National spending on AIDS in Uzbekistan was examined by major funding sources with the use of national statistics, sector reports, and data reported by public health service institutions for the years 2011 and 2012. Allocations to key populations are only referring to interventions specific for the respective key population at higher risk for HIV exposure (e.g. specific funding for key populations does not include their treatment or testing costs; on the other hand care and treatment includes care and ART for key populations).

** The budget breakdown data were only available for $ 16.9 out of 18.3 million for 2011 and $21.3 out of 23.9 million for 2012.

Figure 4: HIV/AIDS investment in Uzbekistan in 2011 and 2012 by target population and intervention type*



	HTC	Youth	PLHIV	SW	MSM	PWID	STI	PMTCT	Care and treatment
2011	$ 700,820	$ 282,975	$ 274,537	$ 162,032	$ 117,356	$ 2,430,912	$ 162,032	$ 690,646	$3,979,459
2012	$ 675,820	$ 372,324	$ 255,056	$ 184,853	$ 154,657	$ 2,155,154	$ 184,853	$ 671,958	$6,751,949

* Allocations to key populations in figure 4 are only referring to interventions specific for the respective key population at higher risk for HIV exposure (e.g. specific funding for key populations does not include their treatment or testing costs; on the other hand care and treatment includes care and ART for key populations).

3. What are the results of current investments?

Investments have averted infections

- Modelling of the HIV epidemic in Uzbekistan confirms that if the prevention and treatment programmes had not been implemented, current HIV prevalence and incidence would be far greater, especially among PWID.

HIV prevalence is declining, but slowly

- Current HIV prevention policies appear to be keeping HIV prevalence stable or declining in key populations, but still high and increasing in some regions among PWID and SW.
- HIV prevalence among PWID is still high, but it has declined significantly from 19.7% in 2005 to 7.3% in 2013 at national level, but it is considerably higher in certain parts of the country (e.g. in Tashkent city – 24.5%)[13].
- The prevalence among MSM is unclear – the most recent estimate of prevalence (3.3% in 2013) was very different from previous estimates (e.g. 6.8% in 2009, 0.7% in 2011) and there are uncertainties about the representativeness of these findings. Forecasts for the HIV epidemic among MSM are therefore difficult to make.
- The prevalence among SW seems to be stable during the last several years, at around 2%, but still high is some regions[14].
- Modelling indicates that HIV prevalence may also slow down among intimate female partners of males who inject drugs. However, estimates of prevalence in the general lower-risk population are highly uncertain due to the lack of prevalence data.

HIV testing high, but needs further improvement

- In 2012, RAC estimated that 66% of PLHIV were aware of their infection.
- Many people are still diagnosed late, which results in late initiation of ART. This in turn leads to poorer clinical outcomes as well as longer and higher infectiousness due to uncontrolled viral load.

Some 34% of PLHIV are not aware of their infection

Treatment coverage: depending on the way of calculation – but too low

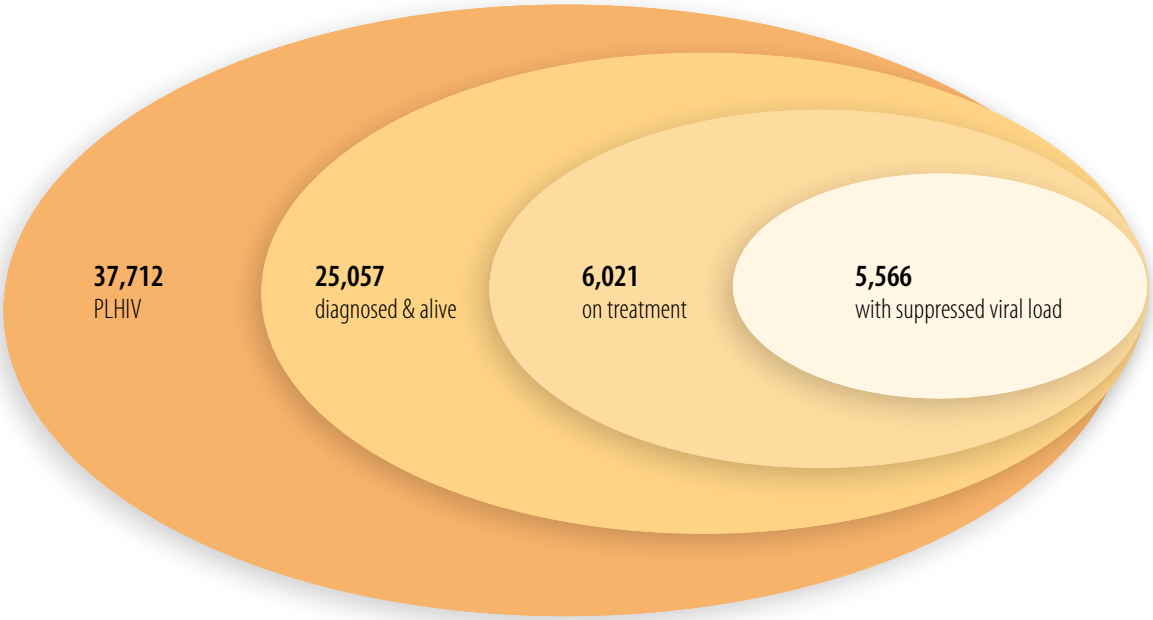
- According to RAC estimates, there were 37,712 PLHIV in Uzbekistan in 2012, of which 25,057 have been diagnosed. Of these 6,021 (16%) were on ART at the end of 2012, including 5,556 with suppressed viral load assuming standard compliance and drug efficacy[15] (figure 5).
- RAC estimated that about 13,350 PLHIV were eligible for ART in 2012 under the 2012 national guideline (according to model results). Estimates for ART coverage ranged therefore from 45% (6,021/13,350) to 74% (6,021/8,189) based on the 2012 national guideline and from 16% (6021/37,712) to 24% (6,021/25,057) based on the estimated and registered PLHIV, respectively. While

13 Republic of Uzbekistan. The results of epidemiological surveillance of HIV infection among people who inject drugs in 2013. Tashkent; 2014.

14 Republic of Uzbekistan. Analysis of HIV infection triangulation data in the Republic of Uzbekistan. Tashkent: Ministry of Health; 2015.

15 Own model estimation.

Figure 5: Treatment cascade for Uzbekistan in 2012*



* Source: RAC (estimated number of PLHIV, number of PLHIV diagnosed and alive, number of PLHIV on treatment), own model estimation (number of PLHIV with suppressed viral load).

ART treatment greatly improves a person's quality of life, many PLHIV were still without treatment in 2012. Furthermore, the proportion of people on treatment is too small to have a significant preventive effect on HIV transmission at the population level.

Treatment needs continue to rise

16% of the estimated number PLHIV were on ART at the end of 2012

- AIDS-related mortality is declining slowly.
- The number of PLHIV requiring ART outstrips supply and is expected to increase further in the near future, including the need for second-line regimens.
- In 2013 WHO released an integrated and consolidated ART guideline. The new recommendations are based on evidence that treating PLHIV earlier can both keep them healthy and lower the amount of virus in the blood, thus reducing the risk of onward infection. According to the 2013 guidelines ART should be initiated in adults living with HIV when their CD4 cell count falls to 500 cells/mm^3 or less if not indicated otherwise on clinical grounds. This will increase the number of PLHIV eligible for ART considerably compared to the previous WHO guidelines and the 2012 national guideline in Uzbekistan which still recommends ART initiation at a CD4 count of 350 cells/mm^3 or less if not indicated otherwise on clinical grounds.
- For 2014 and 2015, the Government has allocated $ 2 million as part of the cost sharing agreement that helped to cover around 2,000 new patients in 2014 and additional 2,015 new patients in 2015.

4. Scenario 1: Maintaining the current investment allocations and budget level, what will the HIV epidemic look like by 2020?

This chapter summarises key model outputs for the following questions: What is the HIV epidemic in Uzbekistan likely to look like if the response continues unchanged? And what will be the return on investment by 2020?

Scenario 1: 'Maintaining the 2012 investment allocations and budget level'

HIV incidence is expected to decline slowly

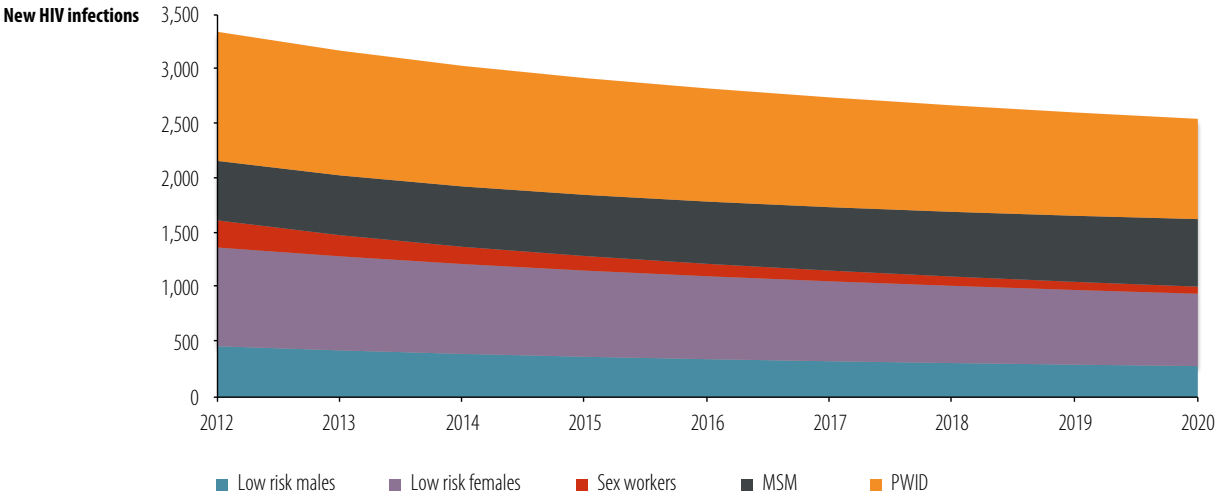
- The first HIV case in Uzbekistan was recorded in 1987. However, before the 2000s, there was little known about HIV in Uzbekistan. By the end of 2000 there had been a cumulative of 230 people diagnosed with HIV and officially registered which then increased to 31,864 at the end of 2012 of which 25,057 were still alive.
- For the future projection, the model-estimated annual HIV incidence shows a moderate decline from approximately 3,300 in 2012 to around 2,500 in 2,020.
- The projected declining incidence is driven by both key populations at higher risk for HIV exposure and general population; in SW incidence is projected to decline by 74%, in PWID by 22%, but also in low risk males (39%) and females (27%), while it is estimated that the incidence in MSM will increase by 14%.

HIV transmission mode shifting from injecting towards sexual

- In 2012, 54.2% of newly diagnosed HIV infections were transmitted sexually, 31.8% through injecting drug use and 3.5% from mother to child. HIV will continue to be transmitted among PWID in Uzbekistan but the trend towards a larger share of sexual transmissions will progress (figure 6).

54.2% of newly diagnosed HIV infections were transmitted sexually in 2012

Figure 6: Model-estimated trend in HIV incidence under Scenario 1 ('maintaining 2012 investment allocations and budget level')



Number of PLHIV eligible for ART is expected to increase with guideline update

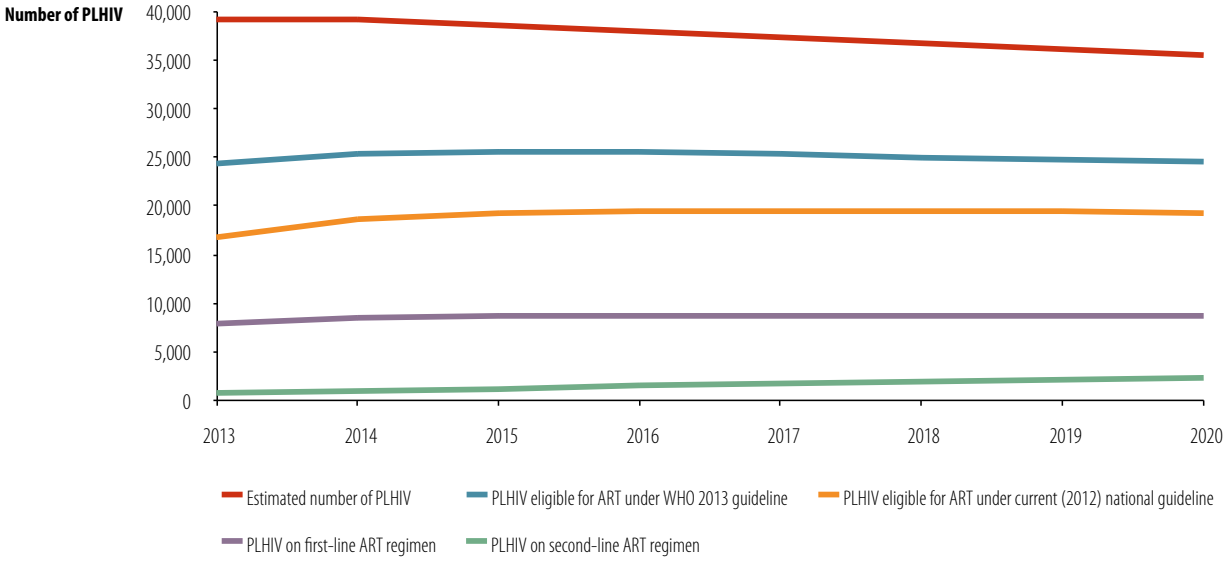
- Proceeding with current investment allocations at the current budget level, the estimated number of PLHIV is projected to slightly decrease from around 37,000 in 2012 to 35,000 in 2020 (figure 7).
- The number of PLHIV eligible for ART is estimated to reach 19,200 in 2020 based on the 2012 national guideline, and 24,400 based on the WHO 2013 guidelines.

Under scenario 1, 19,200 (24,400) PLHIV will be eligible for ART by 2020 under the current national (under WHO 2013) guideline

- If testing rates are not increased, 14,200 PLHIV will go undiagnosed, representing about 40% of all PLHIV.

Since the total number of PLHIV on ART would slightly decrease because of budget constraints and the increasing number of second line ART, and since the model predicts the number of PLHIV to only slightly decrease, ART coverage in 2020 would remain low between 31% and 57%: 31% of the estimated number of PLHIV (11,000/35,000), 45% of PLHIV eligible for ART according to WHO 2013 guidelines (11,000/24,400), 57% of PLHIV eligible for ART according to the 2012 national guideline (11,000/19,200). Following the 2012 national guideline (the WHO 2013 guideline) around 8,200 (13,300) of the PLHIV would be eligible but without ART; 5,100 (10,300) of them would know their status and be on a waiting list for ART.

Figure 7: Estimated numbers of PLHIV, of PLHIV eligible for ART and of PLHIV on ART (Scenario 1 – 'Maintaining 2012 investment allocations and budget level')



Return on investment – Scenario 1: 'Maintaining 2012 investment allocations and budget level'

- Compared to the counterfactual scenario of no HIV/AIDS programmes at all, 'maintaining current investment allocations and budget ceiling' would avert about 12,500 new HIV infections and 49,000 DALYs until 2020 at a total programme cost of $167.1 million (2014 – 2020, not counting inflation).

5. Scenario 2: What can be improved by optimising efficiencies under the current budget envelope?

This chapter summarises key model outputs for the following questions: Can more be achieved with the same amount of resources, how can this be achieved and what would be the return on investment by 2020?

Scenario 2: 'Optimising the investment allocations at the 2012 budget level'

More value for money through technical efficiency

- With the need to achieve more, with less funding, it is important to consider how unit costs can be reduced. If unit costs are reduced, more can be done with the same resources.
- Overall programme management costs account for 18% of overall funding in 2011-2012. This is deemed to be generally acceptable.
- Using the most efficient models of service delivery and removing barriers that limit the effectiveness and efficiency of service delivery, a 5% technical efficiency gain was considered as realistic for the model.

A 5% technical efficiency gain was considered realistic for the model

More value for money through allocative efficiency

Background for allocative efficiency

- The resource allocation in Uzbekistan has to take into account the disease burden, the distribution among sub-populations and the potential for impact. There is an important opportunity to further improve the allocation of resources to the populations and programmes that will result in the greatest impact.
- Allocative efficiency can be considered the allocation of resources in the best combination across various programme components that leads to optimal outcomes and impact within a defined budget envelope. It should be noted that allocative efficiency does not tell us how big the overall budget envelope (over time) should be. In addition, allocative efficiency is assessed here from the perspective of an individual disease programme, and not across the health sector or beyond.

Methods for allocative efficiency

- A formal mathematical optimisation procedure surrounded an epidemiological transmission model to calculate the allocations of funding across HIV programme components which is likely to result in the least number of new HIV infections and DALYs over the 2014-2020 period; it uses the 2012 investment allocations as a starting point and keeps the budget constant on 2012 amounts (see table A2 in Annex for more details). The model was informed by available epidemiological, behavioural and clinical data, as well as likely programme outputs and other outcomes associated with possible funding combinations over all programmes.

- The most cost-effective interventions are those which have proven effectiveness in reducing risk behaviours and/or biological transmissibility, or improving survival and health, and are targeted to groups of people at greatest risk of acquiring or transmitting HIV. The optimisation procedure automatically factors these considerations into the calculation of ideal allocations taking into account costs and the level of effectiveness to meet a given objective.

Allocative efficiency is considered here as an optimal allocation mix to reach the objectives of minimizing new HIV infections and DALYs

- There will be different optimal allocations for different objectives. For example, objectives could include: minimising the number of new infections with current resources; minimising the number of deaths with current resources; or minimising the amount of money required to achieve a certain percentage decline in new infections or to meet the targets of the National Strategic Plan, such as providing universal coverage for prevention and treatment services.
- Here, the initial objective is designed to reflect the UNAIDS 'Getting to Zero'[16] visions by minimising both DALYs (accounting for disease progression and death) and new HIV infections by 2020 with current (2012) resources. Each additional infection was considered equivalent to 20 DALYs, a value which takes into account both DALYs outside the window of the intervention period as well as the effect of subsequent infections. While the model is optimised for the period until 2030, the outputs are discussed in this chapter for the short- and mid-term period until 2020 to focus on the current programming needs under the GF new funding model in Uzbekistan.

The model assumes that ART reduces the probability of HIV transmission by 70%

- The model takes into account the dual impact of ART: 'treatment as prevention'[17]. It could be assumed that treatment reduces transmission risk by as much as 96% based on the HPTN-052 clinical trial setting (Cohen et al. NEJM 2011)[18], but this may be an overestimation. In an observational cohort study of serodiscordant couples in China it was shown that HIV transmission was reduced by only 26% due to ART[19]. Based on a large review of literature we conducted across many settings, adherence to ART was estimated as 75% for the model; at 92-96% efficacy for full adherence, this weights to approximately 70% efficacy of ART in reducing infectiousness when accounting for observed adherence patterns. Therefore, we assumed that ART reduces transmission by 70%[20].
- In the model, we kept biomedical prevention programme components (blood safety, safe medical injections and universal precautions), condom provision, community mobilization and prevention for PLHIV constant.

Modelling results for allocative efficiency

- Current resource allocation strikes a compromise between an optimal incidence-reduction strategy and an optimal DALY-reduction strategy. Generally, it is considered that the allocation of resources across programme components in Uzbekistan is well balanced and close to optimal for minimizing HIV incidence and DALYs (with the exception of the unclear situation of MSM). However, there is

16 UNAIDS 'Getting to zero' strategy for 2011-2015 has three visions: to get to zero new infections, to get to zero AIDS-related deaths and to get to zero discrimination.

17 World Health Organisation. Antiretroviral treatment as prevention (TASP) of HIV and TB. Geneva: World Health Organisation; 2012.

18 Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. N Engl J Med. 2011;365:493–505.

19 Jia Z, Mao Y, Zhang F, Ruan Y, Ma Y, Li J, et al. Antiretroviral therapy to prevent HIV transmission in serodiscordant couples in China (2003-11): a national observational cohort study. Lancet. 2013;382:1195–203.

20 Regional studies on the impact of ART on preventing HIV transmissions in key populations at higher risk are not available; such studies would be useful to improve investment decisions.

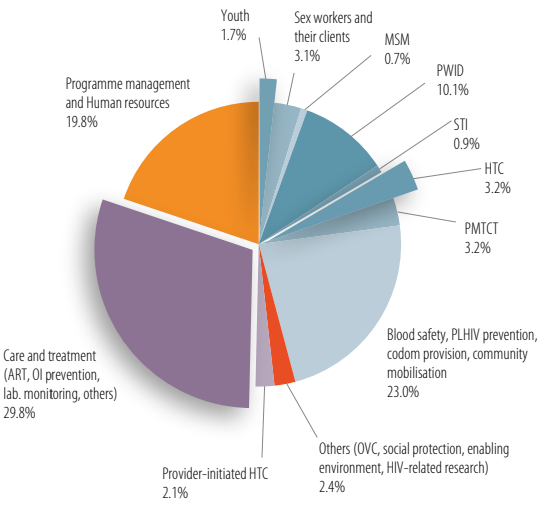
still some potential for refinement towards better allocative efficiency.

The current budget is insufficient to scale up essential HIV interventions to universal coverage, even under optimised efficiencies

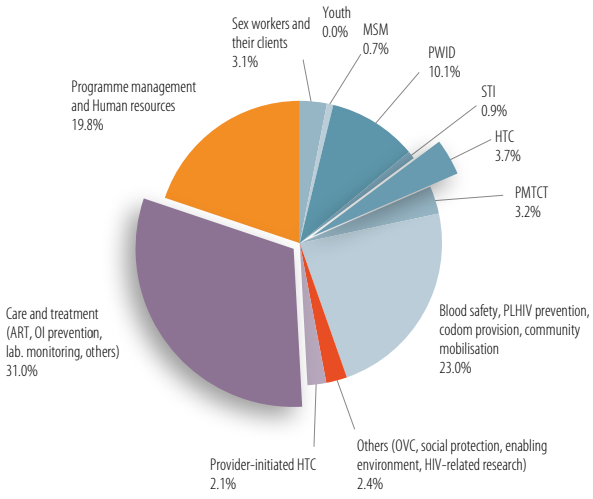
- It was identified that overall the current (2012) budget envelope is insufficient to scale up all effective standard interventions to achieve universal coverage. Therefore, the results for an optimised allocative efficiency for the currently underfunded programme must be interpreted with caution in the context of service rationalization under consideration of competing effectiveness of essential key interventions with regard to reduction of infections, disease burden and death.
- With these constraints in mind, the model suggests only small changes for an optimised resource allocation under the 2012 budget constraints by shifting resources from general prevention among youth towards HTC and treatment (figure 8, table 1).

Figure 8, a, b: Comparison of budget allocations under the current (2012) budget envelope; a) current (2012) allocations, b) optimised allocations*,**

a) Current



b) Optimised



* Allocations to key populations in figure 8 are only referring to interventions specific for the respective key population at higher risk for HIV infection (e.g. specific funding for key populations does not include their treatment or testing costs; on the other hand care and treatment includes care and ART for key populations).

** The budget breakdown data were only available for $ 16.9 out of 18.3 million for 2011 and $21.3 out of 23.9 million for 2012.

Table 1: Comparison of budget allocations under the current (2012) budget envelope: current (2012) allocation mix and optimised allocation*

	Budget allocation in $	
	a) 2012 allocation	**b) optimised allocation**
HIV spending TOTAL	**21,266,156**	**21,266,156**
Prevention SUBTOTAL	**9,750,606**	**9,490,066**
Prevention – biomedical safety, PLHIV prevention, other prevention	4,883,715	4,883,715
HTC	675,820	787,604
Prevention – SW	652,125	652,125
Prevention programmes for MSM	154,657	154,657
Harm reduction programmes for PWID	2,155,154	2,155,154
Prevention – youth	373,324	0
Prevention – STI	184,853	184,853
PMTCT	671,958	671,958
Care and treatment SUBTOTAL	**6,791,949**	**7,052,489**
Provider initiated testing and counselling	454,315	454,315
Care and treatment – ART, opportunistic infection prevention, lab. monitoring, others	6,337,634	6,598,174
Programme management and human resources SUBTOTAL	**4,218,583**	**4,218,583**
Others – OVC, enabling environment SUBTOTAL	**505,018**	**505,018**

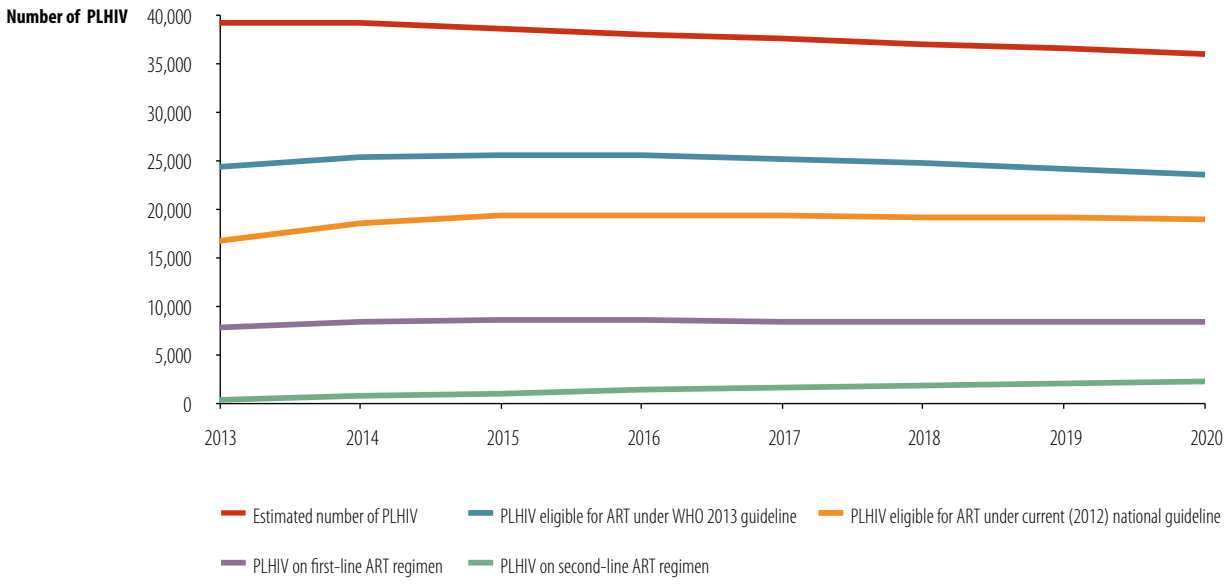
* The budget breakdown data were only available for $ 16.9 out of 18.3 million for 2011 and $21.3 out of 23.9 million for 2012.

Improved impact – but still insufficient service coverage

In late 2013 the Government of Uzbekistan committed $ 2 million in ART and other costs. Until June 2015, $ 894,697 was expended: $ 775,312 for procurement and delivery of ARV and $ 119,395 for CD4 and viral load tests. Taking this into account and adding it to the 2012 budget ceiling, modelling allocative efficiency results by 2020 in:

- an estimated 36,000 PLHIV,
- an estimated 19,000 of PLHIV eligible for ART based on the 2012 national guideline, and 24,000 based on the WHO 2013 guidelines,
- 10,500 PLHIV on ART (8,300 on the first-line and 2,200 on the second-line) with an estimated ART coverage of 55% among the estimated number of PLHIV eligible for ART according to the 2012 national guideline (10,500/19,000), 44% (10,500/24,000) according to the WHO 2013 guidelines and 29% among estimated number of PLHIV (10,500/36,000). About 5,000 (7,500) diagnosed PLHIV and eligible for ART would be without treatment access according to the 2012 national guideline (WHO 2013 guideline).

Figure 9: Estimated numbers of PLHIV, of PLHIV eligible for ART and of PLHIV on ART (Scenario 2 – 'Optimising the investment allocations at the 2012 budget level')



Return on investment – Scenario 2: 'Optimising the investment allocations under 2012 budget level'

- Compared to the counterfactual scenario of no HIV/AIDS programmes at all, 'optimizing the current investment allocations under the current budget ceiling' would avert about 13,000 new HIV infections and 74,000 DALYs until 2020 at a total programme cost of $174.1 million[21] (2014 – 2020).

21 Additional $ 1 million annually from the Government included.

6. Scenario 3: Fulfilling the commitments for people in need – the rights-based investment case

This chapter summarizes key model outputs for the questions: Using optimised efficiencies, how much would it take to achieve universal coverage of the key prevention and treatment services, and what would then be the return on investment by 2020?

Scenario 3: 'Scaling up to universal coverage by 2020'

Shortfalls of the current and optimised investment case under the current budget ceiling

- The modelling results of scenario 1 and 2 clearly demonstrate the limitations of the current budget level: too many PLHIV will remain undiagnosed and without essential services, even under optimised allocative efficiency and reduced programme management and HR costs; the impact on HIV incidence and DALYs remains limited.

Keeping the current budget envelope means: too many PLHIV will remain undiagnosed and without essential services

- 'Doing more and better with less' is an important call for continuous quality improvement and efficiency gains, but there is clearly a threshold below which a budget simply becomes insufficient to fully meet the objectives.
- The current epidemic indicators, service coverage and the modelling forecast show that overall the HIV response is underfunded in Uzbekistan to meet its objectives of 'getting to zero' and of fulfilling the commitments for universal coverage of essential HIV services.

Modelling the scale-up to universal coverage of essential HIV services

Background on universal coverage

- Commitment to universal coverage of HIV service in Europe and Central Asia is reflected in a number of declarations, including the 2004 'Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia'[22], the 2004 'Vilnius Declaration on Measures to Strengthen Responses to HIV/AIDS in the European Union and in Neighbouring Countries'[23], and the 2007 'Bremen Declaration on Responsibility and Partnership – Together Against HIV/AIDS'[24]. Uzbekistan is

22 Dublin Declaration on Partnership to fight HIV/AIDS in Europe and Central Asia. Breaking the Barriers – Partnership to fight HIV/AIDS in Europe and Central Asia Conference; 2004, Feb 23-24; Dublin, Ireland.

23 Vilnius Declaration on Measures to Strengthen Responses to HIV/AIDS in the European Union and in Neighbouring Countries. Europe and HIV/AIDS – New Challenges, New Opportunities Conference; 2004, Sept 17; Vilnius, Lithuania.

24 Bremen Declaration on Responsibility and Partnership – Together Against HIV/AIDS. "Responsibility and Partnership -Together Against HIV/AIDS" Conference; 2007, Mar 12-13; Bremen, Germany.

one of 55 countries included in the monitoring of progress against the commitments of the Dublin declaration[25].

Without universal coverage of essential HIV services, ending the epidemic by 2030 will be unrealistic

- The main goals of the Strategic Programme for Fighting HIV Infection in the Republic of Uzbekistan for 2013-2017 are to ensure the reduction of the spread of HIV in Uzbekistan and to ensure universal access to HIV prevention, treatment, care and support[26].
- Universal health coverage is one of the targets under the proposed Sustainable Development Goal for health and it plays a key role in the positioning of health in the post-2015 development agenda[27].
- Without universal coverage of key prevention and treatment services, the target of ending the epidemic of HIV/AIDS by 2030 under SDG 3 will be unrealistic[28].

Methods for modelling universal coverage of essential HIV prevention, treatment and care services

- Using the same model structure as described in the previous chapter and detailed in the Annex, the objective of a rights-based investment approach is to reach universal coverage of essential HIV prevention services and ART by 2020;
- Starting at estimated service coverage for HTC, ART, PMTCT and special interventions for key populations in 2012, the model assumed an approximately linear increase over time to reach universal coverage for the key prevention and ART services by 2020;
- For ART services, the model investigated alternatively the following three options to determine universal coverage:

Option A: 95% of diagnosed PLHIV and eligible for ART under the 2012 national guideline;

Option B: 95% of diagnosed PLHIV and eligible for ART under WHO 2013 guidelines;

Option C: 95% of all diagnosed PLHIV ('test and treat' concept[29]);

- For PMTCT, the objective of the modelling was to achieve 95% coverage; for harm reduction specific to PWID and special preventive service for other key populations an 80 % coverage of estimated need was used. For HTC the objective was that 80 % of key populations at higher risk would know their status.

Modelling results for a rights-based investment case approach

With a rights-based investment approach the number of PLHIV on ART would increase 5 to 6-fold

- To achieve universal treatment access under scenario 3 option C ('test and treat') the number of PLHIV on ART would need to reach around 25,800, for option B (WHO 2013 guideline) approximately

25 European Centre for Disease Prevention and Control. Thematic report: Combined reporting – Monitoring implementation of the Dublin Declaration on Partnership to Fight HIV/AIDS in Europe and Central Asia: 2012 progress report. Stockholm: European Centre for Disease Prevention and Control; 2013.

26 Republic of Uzbekistan. Strategic programme for fighting HIV infection in the Republic of Uzbekistan for 2013-2017. Tashkent: 2012.

27 World Health Organisation. Positioning Health in the Post 2015 Development Agenda – WHO Discussion Paper. Geneva: World Health Organisation; 2012.

28 United Nations General Assembly. Transforming our world: the 2030 Agenda for Sustainable Development – Draft resolution referred to the United Nations summit for the adoption of the post-2015 development agenda by the General Assembly at its sixty-ninth session. New York: United Nations General Assembly; 2015.

29 Dodd PJ, Garnett GP, Hallett TB. Examining the promise of HIV elimination by 'test and treat' in hyperendemic settings. AIDS. 2010;24(5):729-35.

23,300 and for option A (2012 national guideline) about 20,000 by 2020. This reflects a 5- to 6-fold increase to 2013 ART figures.

- Since coverage for PMTCT services is already high they would see only modest scale-ups by 2020, same as for harm-reduction programmes for PWID with the exception of opioid substitution therapy which is currently not being offered.

Return on investment – scenario 3: 'Scaling up to universal coverage by 2020'

- Under the assumption of the universal coverage for key preventive interventions, the epidemic impact would depend on the applied criteria for ART eligibility, as shown in table 2.

Table 2: Projected estimated epidemiological impact and programme costs* (point estimates) using three options for ART eligibility criteria for Scenario 3: 'Scaling up to universal coverage by 2020'**

	Universal ART coverage		
By 2020	**Option A**	**Option B**	**Option C**
Estimated PLHIV	39,586	38,755	33,799
Estimated new HIV infections averted***	20,270	21,150	26,818
Estimated DALYs averted***	222,622	229,149	232,061
Total programme costs 2014-2020	210,619,371	228,104,257	248,786,151

* 2014-2020, not accounting for inflation.
** See narrative for further explanation of option A, B and C.
*** Compared to the counterfactual scenario of no HIV/AIDS programmes at all.

7. Rights-based investment today – the highest impact now and in the future

This chapter summarises key model outputs for the long-term impact until 2030 of scenario 1 ('maintaining the 2012 investment allocations and budget level'), scenario 2 ('optimising the investment allocations at the 2012 budget level') and scenario 3 ('scaling up to universal coverage').

The rights-based investment approach – highest impact on HIV infections and DALYs in the short-term

- In the previous chapters, model predictions showed the highest impact for scenario 3 'scaling up to universal coverage' in terms of averting new HIV infections and DALYs by 2020; this is also the only scenario fulfilling international commitments made and core objectives of the National AIDS Programme. Comparisons of projected impact and costs are summarized in table 3.

The rights-based investment approach – highest impact on HIV infections and DALYs also in the long-term

- The long-term impact of scenario 3 until 2030 is even more impressive; figure 10 shows comparisons of all scenarios.
- Under scenario 3, the estimated number of PLHIV would be around 35,000 by using the 2012 national guideline, approximately 33,000 using WHO 2013 treatment guideline, and about 23,000 using the 'test and treat' approach. This compares to an estimated 33,000 PLHIV for scenario 2 and 35,000 for scenario 1 (figure 10a). Differences can be explained by long-term dynamics of differences in averted HIV infections and averted HIV-related deaths.
- An estimated cumulative total of about 103,000 new HIV infections would be averted between 2014 and 2030 under scenario 3 using the 'test and treat' approach (around 91,000 using WHO 2013 guidelines, 88,000 using the 2012 national guidelines. The differences are mainly caused by the higher impact in earlier years through options with

Table 3: Cumulative new HIV infections averted, cumulative DALYs averted and total programme costs under the three different scenarios (2014-2020)

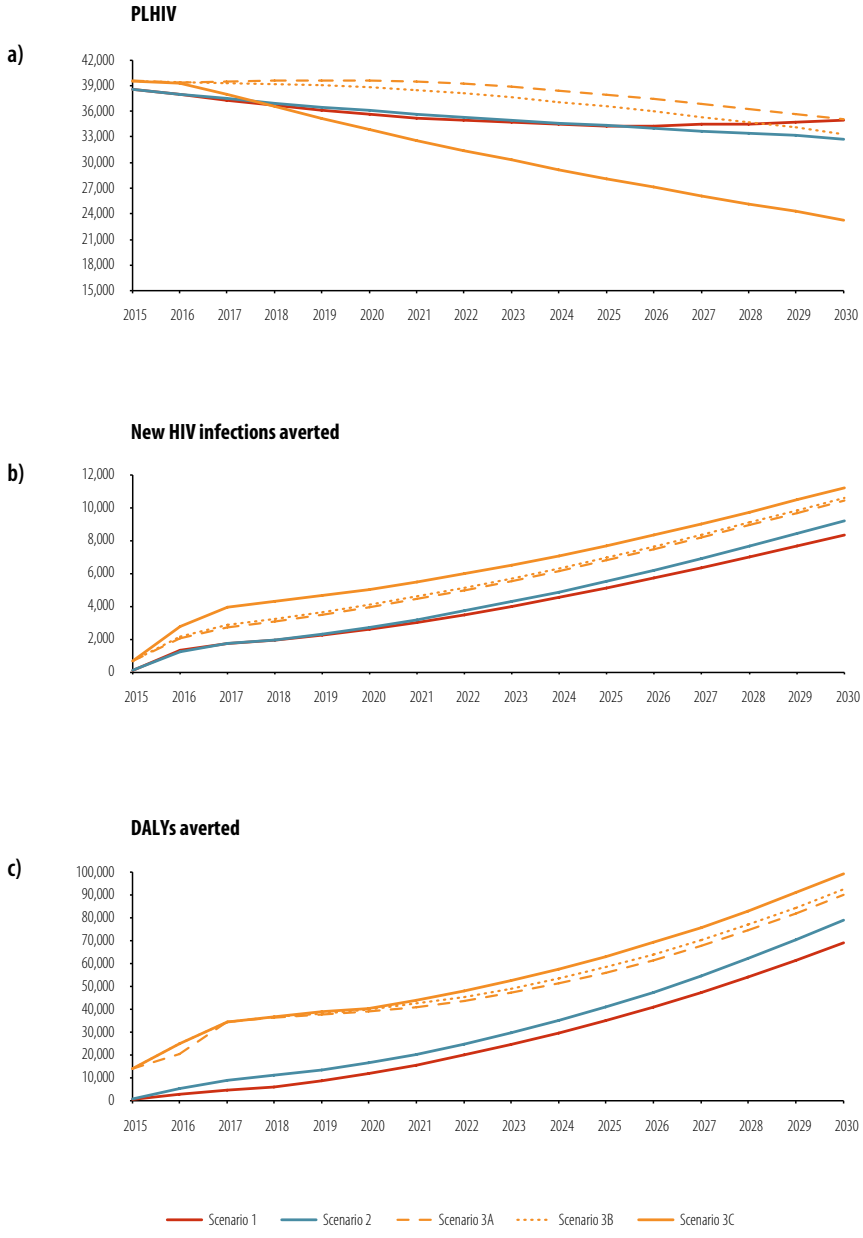
	Scenario 1	Scenario 2	Scenario 3 Option A*	Scenario 3 Option B*	Scenario 3 Option C*
New HIV infections averted	12,869	13,151	20,270	21,150	26,818
DALYs averted	49,218	74,110	222,622	229,149	232,061
Total programme costs	$ 167.1 million	$ 174.1 million	$ 210.6 million	$ 228.1 million	$ 248.8 million

* Option A: 95% of diagnosed AND eligible PLHIV by 2020, 2012 national guideline; option B: 95% of diagnosed AND eligible PLHIV by 2020, WHO 2013 guidelines; option C: 95% of all diagnosed PLHIV by 2020 ("test and treat").

more inclusive eligibility criteria for ART. Scenario 2 and 1 achieve significantly lower numbers of averted HIV infections, approximately 70,000 and 65,000, respectively (figure 10b).

- Between 2014 and 2030 about 870,000 DALYs would be averted under scenario 3 using the 'test and treat' approach 822,000 using WHO 2013 guidelines, 796,000 using 2012 national guidelines). For new HIV infections averted, the differences are mainly caused by the higher impact during the earlier years through options with more inclusive eligibility criteria for ART. Scenario 2 (516,000) and scenario 1 (430,000) avert about half the number of DALYs.

Figure 10 a-c: Long term comparisons (2015-2030) of the epidemiological impact of scenario 1, 2 and 3; a) estimated number of PLHIV, b) estimated number of new HIV infections averted, and c) estimated DALYs averted



8. Remarks

All mathematical models have their limitations and results should therefore be interpreted with the necessary caution. In particular, the following points should be considered:

- All model forecasts are subject to uncertainty. Therefore, point-estimates indicate trends rather than exact figures.
- The model calibration depends as much on the quality of input data as on the quality of the model itself. The country and study teams including the RAC paid much attention to assure data quality and completeness. However, there is room for improvement for further studies, both in terms of data quality as well as for further improvements of the model structures.
- The best model calibration will rarely achieve an exact match of historical data, but mirror as closely as possible the key trends of them.
- Modelling the optimization of allocative efficiencies depends critically on the availability of evidence-based parameter estimates of the effectiveness and cost-efficiency of individual intervention packages or intervention components.
- Particularly interventions related to the so-called critical enablers[30] such as interventions against punitive laws and discrimination, community mobilization, but also interventions related to health systems strengthening often lack 'hard' effectiveness data in relation to the key impact indicators such as new HIV infections or DALYs averted. Under resource constraints like the scenario 2, the model will therefore suggest to reduce or even stop such interventions which require to set model restrictions like fixing allocations to certain minimum amounts.
- Even for some of the more clinical interventions, the effectiveness in general but particularly in a specific country or population setting is less clear than commonly thought. Assumptions need therefore to be made in a transparent way so that they can be subject of discussion and review. One of the critical assumptions – the effectiveness of ART on HIV prevention – have been presented in detail, others are referred to in the Annex.
- The model operates largely with current unit costs. Although the effect of increases or decreases of unit costs can be estimated with the model, the model itself cannot suggest what unit cost is adequate to achieve a defined standard of service quality or even what the defined standard should be. There is very little information about service quality and its contextual effect on impact available for Uzbekistan or for the region. This is an area which deserves much greater attention particularly in times in which funding mechanisms such as the new funding model of the GF structurally incentivise reduction of unit costs without having adequate quality monitoring measures in place.
- Finally, no allocative efficiency optimization within a budget framework that is not sufficient to meet the needs for essential health services can replace the rights for basic health services. On the other hand, waste of resources under conditions of global resource constraints, low service coverage and inequities in service access make the fulfilment of these basic rights even more difficult. The key message of this document is therefore: With a moderate increase of the investment volume until 2020 combined with an optimised investment allocation covering all essential HIV services the national HIV response in Uzbekistan can be brought on a trajectory which fulfils the basic

30 United Nations Development Programme, Joint United Nations Programme on HIV/AIDS. Understanding and acting on critical enablers and development synergies for strategic investments. New York: United Nations Development Programme; 2012.

rights to access to essential HIV services for those in need and makes ending the epidemic threat of HIV/AIDS in Uzbekistan a realistic goal if an environment without stigma and discrimination is provided so that services available will be accepted and used by the affected communities.

Annex

Annex 1. Model description

Overview of analytical methods

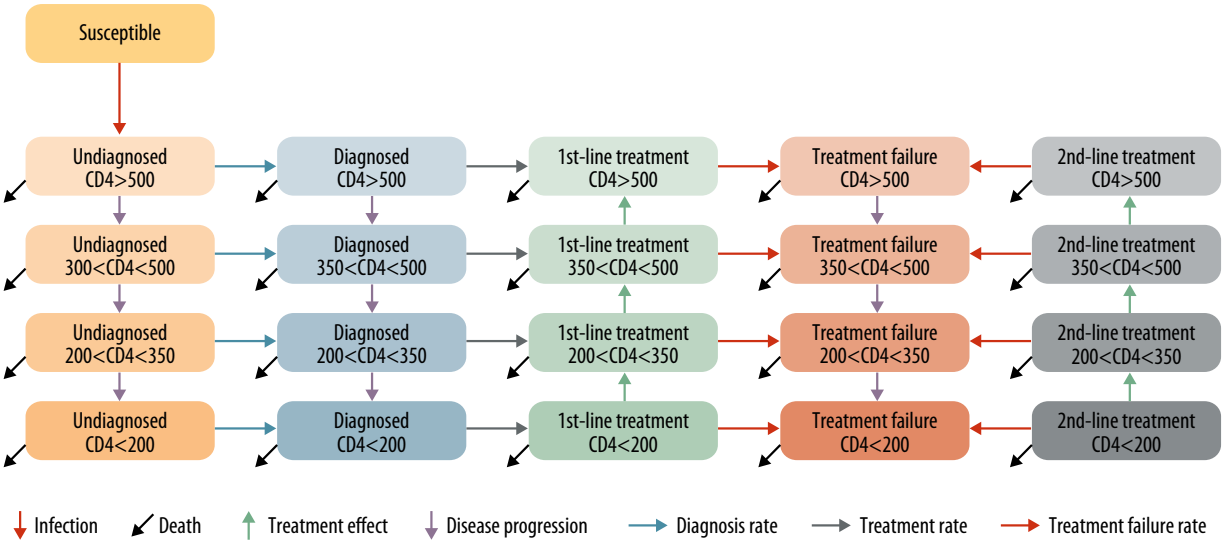
To assess HIV epidemic trends, resource needs, the cost-effectiveness of past programmes, and the impact of potential future programmes, we developed a detailed mathematical model of HIV transmission and disease progression, called the Projection and Evaluation Tool (Prevtool).

Prevtool is an flexible population-based HIV model. The basic disease progression implemented in the model is shown in figure A1. This is the only aspect of model structure that is fixed, and specifies it as being an HIV model instead of a universal epidemic model.

In contrast to most other HIV models, the population groups used in Prevtool are not fixed. Instead, up to 14 user-defined population groups may be used. A typical example for a concentrated HIV epidemic, such as used in Uzbekistan, is shown in figure A2. Here, five population groups are used, including low-risk ('general') males and females, SW, PWID and MSM.

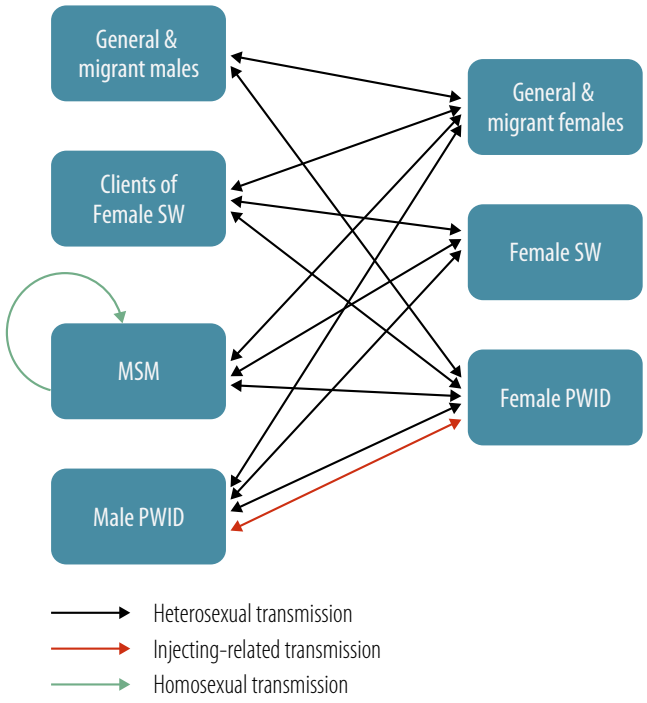
Data are entered into Prevtool by means of an Excel spreadsheet, as shown in figure A3. Data entry is flexible, allowing everything from a separate data point for every population for each year, or a single data point for all populations over the entire time period.

Figure A1: Schematic diagram of model structure*



* Each compartment represents a single population group with the specified health state, while each arrow represents the movement of individuals between health states. All compartments except for 'Susceptible' represent individuals living with HIV. 'Death' includes all causes of death.

Figure A2: Population groups and interactions in Prevtool, example



The model uses a coupled system of ordinary differential equations to track the movement of people between health states. The overall population is partitioned in two ways: by group and by health state. Individuals are assigned to a given population based on their dominant risk; however, to capture important cross-modal types of transmission (e.g., SW becoming infected via injecting drug use), relevant behavioural parameters can be set to small but nonzero values (e.g., male PWID occasionally engage in commercial sex; MSM occasionally inject drugs).

The rate at which uninfected individuals in each population group become infected is determined by the force-of-infection for that population. This depends on the number of risk events an individual is exposed to in a given period of time and the infection probability of each event. Sexual transmission risk depends on the number of people in each HIV-infected stage (that is, the prevalence of infection in the population of partners), the average number of casual, regular, and commercial homosexual and heterosexual partnerships per person, the average frequency of sexual acts per

Figure A3: Example of data entry spreadsheet for a concentrated epidemic

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Testing rate per year Тестирование (Количество протестированных и доля в ....)	Low-risk males (Мужчины с низким риском)														
	Low-risk females (Женщины с низким риском)														
	Direct FSW (Прямые работники секс-бизнеса женщины)								25.00%		44.00%		31.00%		32.30%
	Indirect FSW (Непрямые работники секс-бизнеса женщины)														
	Clients of FSW Клиенты работников секс-бизнеса														
	MSM (MCM)								18.00%		34.00%		30.70%		27.00%
	Bisexual MSM (Бисексуальные МСМ)														
	Transgender (Трансексуалы)														
	Male high-risk PWID Мужчины ПИНы с высоким риском										36.40%		28.70%		30.00%
	Female high-risk PWID Женщины ПИНы с высоким риском														
	Male low-risk PWID Мужчины ПИНы с низким риском														
	Female low-risk PWID Женщины ПИНы с низким риском														
	High-risk males Мужчины (высокий риск)														
	High-risk females Женщины (высокий риск)														
	AIDS stage (стадия СПИДа)														
Treatment rate per year Лечение (количество пролеченных и доля в ...) в ГОД	CD4(500)							0	0	0	0	0	0	0	
	CD4(350,500)							0	0	0	0	0	0	0	
	CD4(200,350)							200	820	1406	1520	2200	3552	5768	
	CD4(200)							15	108	164	235	263	301	253	
	Treatment failure (неэффективность лечения)							0	0	0	115	143	123	112	
No. of HIV diagnoses (Количество установленных диагнозов с ВИЧ)	Total (всего)	154	549	981	1836	2016	2198	2205	3167	3404	4016	3828	3584	3878	4247

partnership, the proportion of these acts in which condoms are used, the efficacy of condoms, the extent of male circumcision, and the prevalence levels of STIs (which increase transmission probability) and HIV.

The stage of infection (chronic, AIDS-related illness/late stage, or on treatment) for the HIV-positive partner in a serodiscordant couple also influences transmission risk due to different levels of infectiousness in each infection stage. Intravenous transmission risk depends on the number of injecting partners per person per year, frequency of injecting per year, frequency of sharing injecting equipment and percentage of shared syringes that are cleaned before re-use and the efficacy of cleaning.

Mathematically, the force-of-infection is given by:

$$\lambda = 1-(1-\beta)^n$$

where λ is the force-of-infection, β is the transmission probability of each event, and n is the effective number of at-risk events (thus n gives the average number interaction events with infected people where HIV transmission may occur). The value of the transmission probability β is based n average viral load of people in different stages of infection and transmissibility differs by mode of transmission (sharing of non-sterile equipment for injected drug use, unprotected, heterosexual intercourse, and homosexual intercourse), and may be modified by behavioural interventions (for example, condom use or circumcision). The number of events n not only incorporates the total number of events, but also other factors that moderate the possibility that these events are capable of transmitting infection, such as condom use or circumcision. There is one force-of-infection term for each type of interaction (for example, casual sexual relationships between low-risk males and indirect female SW), and the force-of-infection for a given population will be the sum of overall interaction types.

In addition to the force-of-infection rate, in which individuals move from uninfected to infected states, there are seven other means by which individuals may move between health states. First, individuals may die, either due to the background death rate (which affects all populations equally), due to injecting behaviour, or due to HIV/AIDS (which depends on CD4 count). Second, in the absence of intervention, individuals progress from higher to lower CD4 counts. Third, individuals can move from undiagnosed to diagnosed states based on their HIV testing rate, which is a function of CD4 count (for example, people with AIDS symptoms have a higher testing rate) and population type (for example, SW usually get tested more frequently than low-risk males). Fourth, diagnosed individuals may move onto treatment, at a rate which is dependent on CD4 count. Fifth, individuals may move from treatment to treatment failure, and sixth, from treatment failure onto second-line treatment. Finally, while on successful first- or second-line treatment, individuals may progress from lower to higher CD4 count and they will have reduced infectiousness.

In total, the model can accommodate up to 294 compartments (14 populations each with 21 health states), and the change in the number of people in each compartment is determined by the sum over the relevant rates described above multiplied by the compartments on which they act. For example, the number of individuals in the compartment corresponding to undiagnosed female sex workers with a CD4 count between 200 and 350 cells/μL changes according to the following equation:

$$\frac{dU_{SW200-350}}{dt} = U_{SW350-500}\tau_{350-500} - U_{SW200-350}(\mu_{200-350} + \tau_{200-350} + \eta_{SW350-500})$$

where $U_{SW350-500}$ is the current population size of people with undiagnosed HIV and with a CD4 count between 350 and 500 cells/μL, $U_{SW200-350}$ is the population size of the compartment with lower CD4 count (200-350 cells/μL), τ is the disease progression rate for the given CD4 count, μ is the death rate, and η is the HIV testing rate. (Note: this example does not consider movement between populations, such as female SW returning to the low-risk female population and vice versa.) Each compartment (figure A1, boxes) corresponds to a single differential equation in the model, and each rate (figure A1, arrows) corresponds to a single term in that equation.

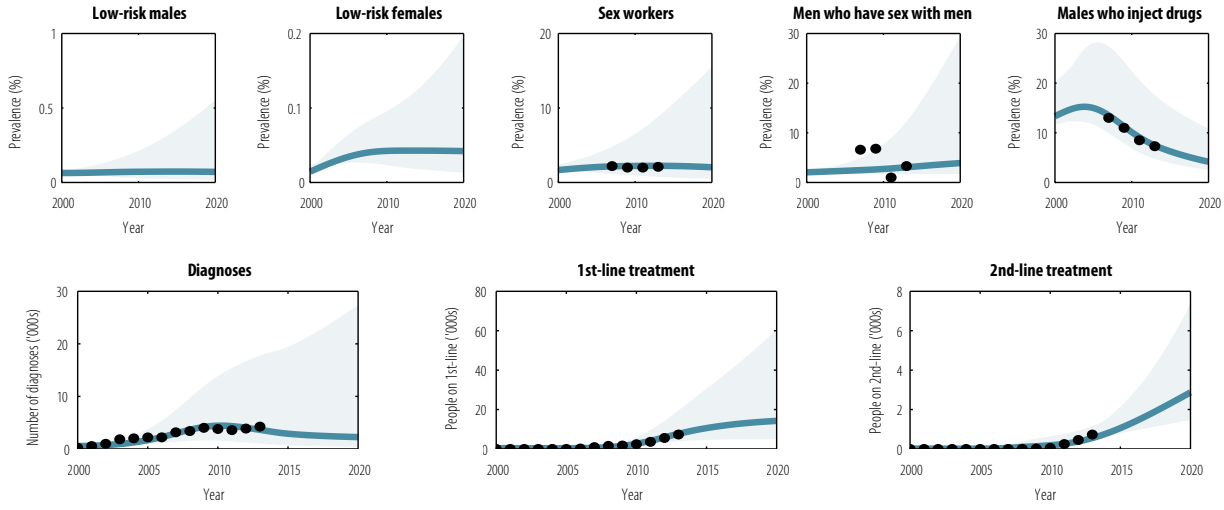
Most of the parameters in the model are related to calculating the force-of-infection; a list of model parameters is provided in table A1. Empirical estimates for model parameter values can be interpreted in Bayesian terms as prior distributions. The model must then be calibrated, which is the process of finding

Table A1: Input parameters of the model

	Biological parameters	Behavioural parameters	Epidemiological parameters
Population parameters	Background death rate		Population sizes (TP)
HIV-related parameters	Sexual HIV transmissibilities* (H) STI-related transmissibility increase* Condom efficacy* Circumcision efficacy* HIV health state progression rates (H) HIV-related death rates (H)	Number of sexual partners* (TPS) Number of acts per partner* (S) Condom usage probability* (TP) Circumcision probability* (T)	HIV prevalence (TP) STI prevalence (TP)
Mother-to child transmission related parameters	Mother-to-child transmission probability	Birth rate PMTCT access rate (T)	
Injection-related parameters	Injecting HIV transmissibility* Syringe cleaning efficacy* Drug-related death rate	Number of injections* (T) Syringe sharing probability* (T) Syringe cleaning probability* Methadone treatment probability (T)	
Treatment parameters	ART efficacy* ART failure rates	HIV testing rates (TPH)	Number of people on ART (T)

Key: T = parameter value changes over time; P = parameter value depends on population group; H = parameter depends on health state; S = parameter depends on sexual partnership type; * = parameter is used to calculate the force-of-infection.

Figure A4: Calibration of Prevtool to Uzbekistan epidemic data*



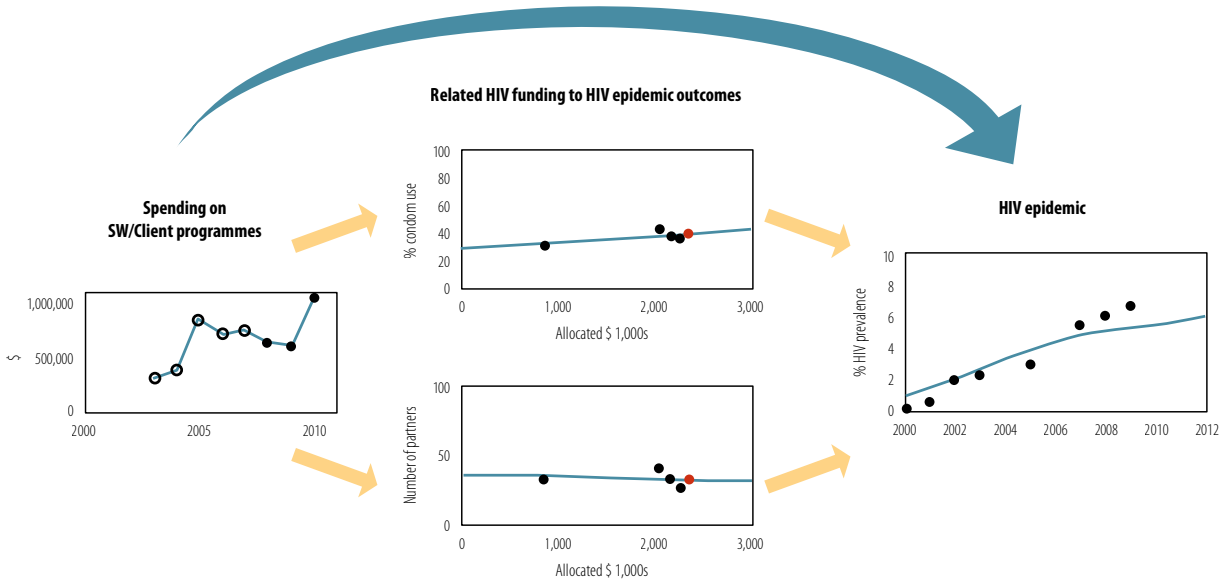
* Dots show data; lines show model outputs; shaded regions are 95% confidence intervals.

posterior distributions of the model parameter values such that the model generates accurate prevalence estimates. Given the challenges inherent in quantifying all known constraints on the epidemic, initial calibration is performed manually, with oversight by and collaboration with in-country stakeholders where possible. This prior distribution is then used in a Monte Carlo Markov chain algorithm, which uses both epidemiological and behavioural data to calculate the log-likelihood for a given set of model parameters. The distribution of parameter values produced by the Monte Carlo Markov chain is the posterior, which is then used for all epidemiological and economic analyses. An example calibration is shown in figure A4.

Relationships between spending and risk behaviours

In our analysis, we use a logistic/sigmoid function to describe the relationships between a behavioural parameter affected by a HIV prevention programme and the level of spending on that programme. Using this function with assumed uncertainties bounds, we obtain cost-outcome curve fits to available datasets for overall programme spending and associated behaviours. Indirect costs have no direct impact on HIV transmission parameters; but changes to HIV programmes may affect these costs to supply additional condoms, clean syringes, for example. Using these relationships, any change in HIV programme funding directly affects risk behaviours and changes to the HIV epidemic; an example of this is demonstrated in figure A5. The fitted cost-outcome relationships will represent the change in behaviours with spending.

Figure A5: Example of the relationship between spending on SW/client programmes and the HIV epidemic*



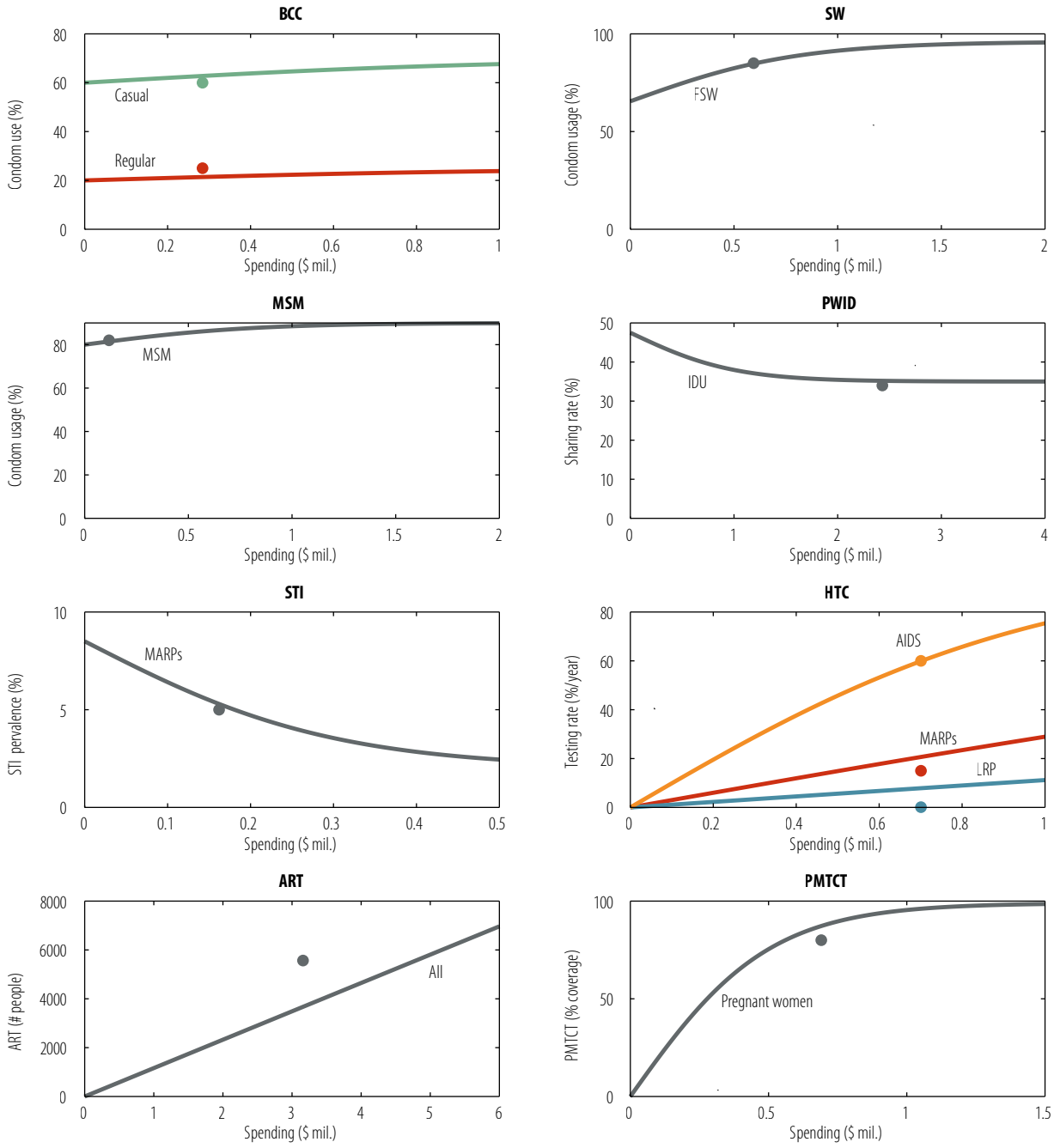
*Numerical values are for illustrative purposes only.

Counterfactual scenarios

Prevtool calculates the cost-effectiveness of past HIV programmes by comparing the expected number of new infections and AIDS-related deaths according to current and past conditions with the estimated numbers under counterfactual scenarios in the absence of funding for specific programmes.

We simulate counterfactual scenarios using Prevtool based on the assumed effect of the removal or enhancement of specific programmes. The calibrated simulations with the programmes in place represent the baseline scenario. For each prioritized population, we develop counterfactual scenarios for the behavioural parameters affected by prevention programmes prioritizing that population—with the parameters for the other populations remaining at their values obtained through the calibration process. Specific counterfactual scenarios used depend on the implementation and characteristics of HIV prevention programmes and the data available. We fit a logistic function to behavioural parameters affected by prevention programmes; figure A6 shows these cost-outcome curves for Uzbekistan.

Figure A6: Cost-outcome curves for Uzbekistan



Cost-effectiveness calculations for past evaluations

For each counterfactual scenario, we measure the health benefits of a specific HIV intervention programme in terms of HIV infections averted as well as life years and DALYs saved compared to the baseline scenario. We calculate incremental cost-effectiveness ratios (ICERs) to estimate the cost-effectiveness of each programme. These are calculated based on the counterfactual scenarios and comparing the spending of each programme (discounted annually), as well as estimated annual healthcare costs incurred/saved

(using unit health costs and utilities for each country obtained from our data synthesis), with the estimated effectiveness of the programmes. Determining whether a past HIV programme is cost-effective is dependent on country-specific thresholds. Appropriate thresholds for each country were determined after consultation with in-country stakeholders.

Future impact of HIV programmes and optimal allocation of resources

To investigate the potential impact of future HIV prevention programmes we run model projections for each scenario. Specific programme options are investigated but are based on core prevention methods (harm reduction), along with programmes based on using ART as prevention in combination with other programmes. We then compare projections where parameters and funding remain at current values and calculate the annual incidence, the number of infections averted, and the total cost required for each scenario.

Prevtool is used to determine the optimal allocation of funding using an adaptive stochastic linear gradient-descent optimization method. This calculates the allocation of funding to programmes with the minimum total infections, minimum prevalence, minimum AIDS-related deaths, or maximum DALYs saved. It is also possible to invert this analysis and calculate the minimum spend required to achieve a particular target in terms of one of those quantities.

Annex 2. Data inputs

Summary of costs and unit costs

National spending on HIV/AIDS in Uzbekistan was examined by major funding sources with the use of national statistics, sector reports, and data reported by public health service institutions for the years 2011 and 2012. Standard accountancy estimation methods were used to generate a complete dataset of national spending on AIDS. Costs were broken down by financing sources, agents, service providers, AIDS spending categories, and beneficiary populations using functional National AIDS spending assessment classifications and definitions. Data collection covered spending on AIDS response funded from domestic public and international funding sources.

Table A2: Budget for the national HIV programme by programme components

	2011 budget in $	2012 budget in $
HIV spending TOTAL*	**16,775,902**	**21,266,156**
Prevention SUBTOTAL	**8,729,691**	**9,750,606**
Condom provision	0	104,858
Community mobilization	1,200	2,550
HIV testing and counselling (HTC)	700,820	675,820
Prevention – youth in school	75,866	77,466
Prevention – youth out-of-school	207,109	294,858
Prevention of HIV transmission aimed at PLHIV	274,537	255,056
Prevention programmes for SW and their clients	594,493	652,125
Prevention programmes for MSM	117,356	154,657
Harm reduction programmes for PWID	2,430,912	2,155,154
Prevention, diagnosis and treatment of STI for general population	162,032	184,853
PMTCT not disaggregated by intervention	690,646	671,958
Biomedical safety	3,474,720	4,521,251
Care and treatment SUBTOTAL	**3,979,459**	**6,791,949**
Provider initiated testing and counselling	690,634	454,315
ART not disaggregated neither by age nor by line of treatment	2,900,447	5,216,777
Specific HIV-related lab monitoring	258,408	537,648
Psychological treatment and support service	129,970	153,156
Opportunistic infection outpatient prophylaxis and treatment	0	430,053
Orphans and vulnerable children SUBTOTAL	**110,00**	**80,000**
OVC social services and admin costs	110,000	80,000
Programme management SUBTOTAL	**3,622,303**	**3,129,274**
Planning, coordination and programme management	684,112	759,326

Table A2: Budget for the national HIV programme by programme components (cont.)		
Administration and transaction costs associated with managing and disbursing funds	63,296	333,996
Monitoring and evaluation	1,145,939	878,467
Serological-surveillance	0	134,689
Upgrading and construction of infrastructure	586,053	147,845
Programme management and admin not disaggregated by intervention	1,142,903	874,951
Human resources SUBTOTAL	**91,162**	**1,089,309**
Monetary incentives for HR not broken by staff category	0	856,318
Training	91,162	232,991
Enabling environment SUBTOTAL	**353,287**	**425,018**
Advocacy	98,657	5,000
Human rights programmes	0	63,657
AIDS-specific institutional development	105,128	233,092
AIDS-specific programmes focused on women	0	63,657
Programmes to reduce gender-based violence	149,502	59,612

* Budget breakdown data were available for $16.9 million out of $18.3 million and $21.3 million out of $23.9 million for 2012 (data presented in figure 1).

Table A3: Population size

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
LRM	12.4 mil.	12.5 mil.	12.7 mil.	12.8 mil.	13.0 mil.	13.1 mil.	13.3 mil.	13.5 mil.	13.8 mil.	14.0 mil.	14.7 mil.	14.8 mil.	15.0 mil.	
LRF	12.4 mil.	12.6 mil.	12.7 mil.	12,9 mil.	13.0 mil.	13.2 mil.	13.3 mil.	13.5 mil.	13.8 mil.	14.0 mil.	14.6 mil.	14.8 mil.	15.0 mil.	
SW							30,000						21,000	
MSM														
PWID							80,000						45,000	

LRM = low-risk males; LRF = low-risk females; SW = sex workers; MSM = men who have sex with men; PWID = people who inject drugs. Brackets are used to indicate estimates as opposed to observed data; applies to all following table.

Table A4: HIV prevalence (%)

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
LRM														
LRF														
SW						14.7		2.2		2.0		2.2		2.1
MSM						10.8		6.6		6.8		0.7		2.3
PWID						19.7		13.0		10.9		8.5		7.3

Table A5: STI prevalence (%)

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
LRM														
LRF														
SW								13.2		6.0		5.4		
MSM								1.4		0.0		1.3		
PWID								13.0		8.0		4.9		

Table A6: HIV diagnoses (no. per year)

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Total	154	549	981	1,836	2,016	2,198	2,205	3,169	3,404	4,016	3,795	3,584	3,878	4,247

Table A7: Sexual acts per person per year and condom use, and circumcision probability

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Average no. regular sexual acts	LRM														
	LRF														
	SW														
	MSM														
	PWID														
Average no. casual sexual acts	LRM														
	LRF														
	SW														
	MSM														
	PWID														
Average no. other sexual acts (e.g. commercial)	LRM														
	LRF												0		
	SW												468		
	MSM														
	PWID														
Condom use % for regular acts	LRM														(5.0)
	LRF														(5.0)
	SW								22.0		34.5		51.9		
	MSM								52.0		34.7		50.0		
	PWID								16.0		20.1		30.1		

Table A7: Sexual acts per person per year and condom use, and circumcision probability (cont.)

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Condom use % for casual acts	LRM														
	LRF														
	SW								77.4		75.6		74.8		
	MSM								82.0		95.0		82.0		
	PWID								56.0		56.9		58.9		
Condom use % for other acts	LRM														
	LRF														
	SW								76.0		84.0		85.4		
	MSM														
	PWID								77.0		99.1		77.0		
Circumcision probability	LRM														
	LRF														
	SW														
	MSM														
	PWID														

Table A8: Injecting drug use parameters

		2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Average no. injections/ person/yr	LRM														
	LRF														
	SW														
	MSM														
	PWID														
Drug use parameters	% shared injections						57.0	45.0	41.0	35.0	38.2				
	% PWID on methadone											0.2	0.8	1.1	
	% reused syringes that are cleaned								54.0	63.2	84.1	69.0	93.5		

Table A9: Biological constants

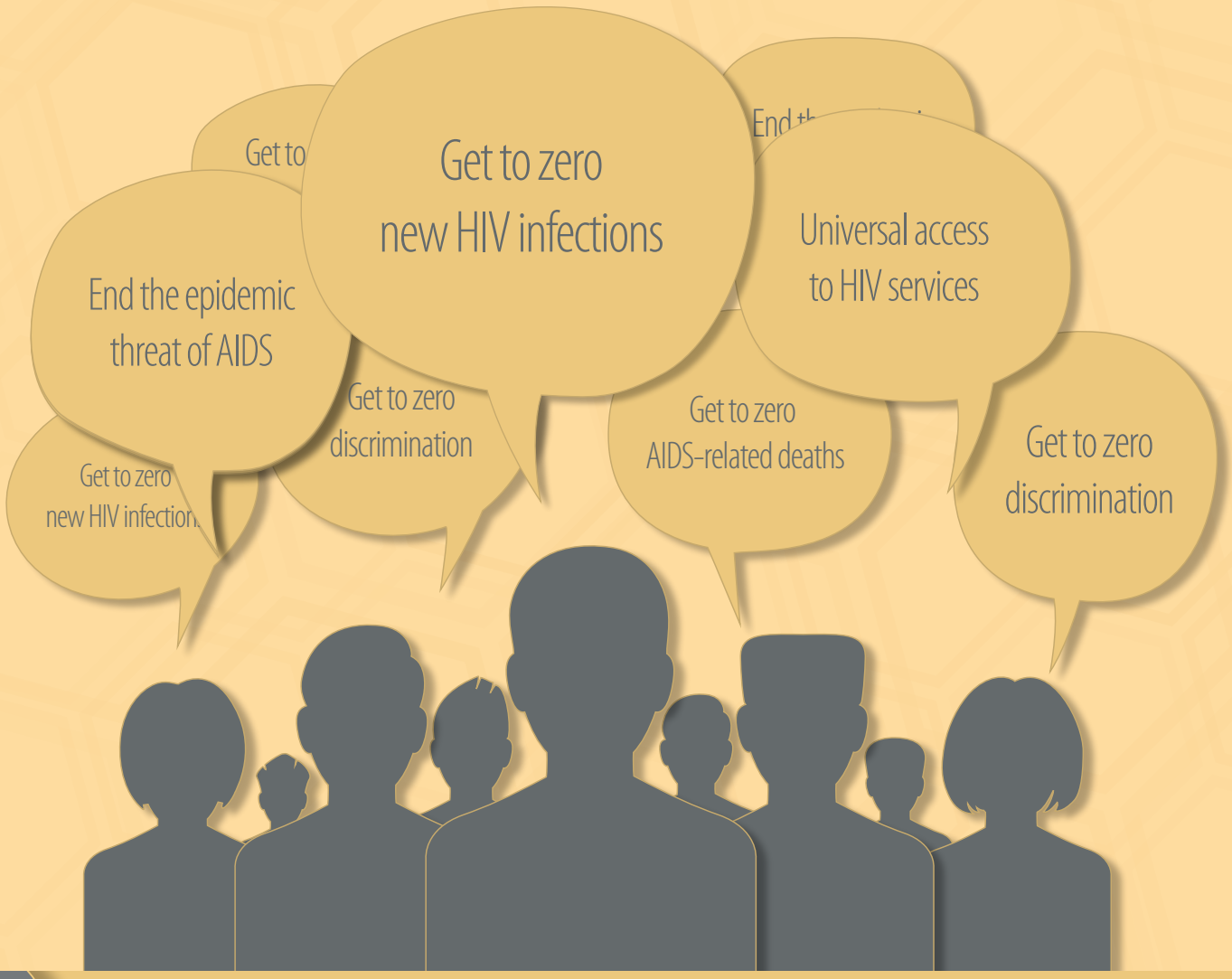
Interaction-related transmissibility (% per act)	Male & female (insertive)	0.09 (0.0001-0.1)
	Male & female (receptive)	0.25 (0000.6-0.6)
	Male & male (insertive)	0.02 (0.002-0.2)
	Male & male (receptive)	0.02 (0.002-0.2)
	Injecting	0.3 (0.1-1.0)
	Mother-to-child	35.0 (20.0-50.0)
Disease-related transmissibility	CD4(500)	4.0(1.2-5.0)
	CD4(350,499)	1.0 (0.8-1.2)
	CD4(200,349)	1.0 (0.8-1.2)
	CD4(<200)	3.8 (3.6-4.0)
	Treatment	0.2 (0.02-0.5)
Disease progression rate: (% per year)	CD4 (500) to CD4 (350,499)	24.5 (22.6-26.4)
	CD4 (350,499) to CD4 (200,349)	51.0 (47.0-55.0)
	CD4 (200,349) to CD4 (<200)	51.0 (47.0-55.0)
Treatment recovery rate (% per year)	CD4 (350,499) to CD4 (500)	45.0 (14.0-93.0)
	CD4(200,349) to CD4 (350,499)	70.0 (29.0-111.0)
	CD4 (<200) to CD4 (200,349)	36.0 (28.0-43.0)
Death rate (% mortality per year)	Background	1.4 (0.9-2.0)
	Injecting	1.0 (0.7-1.2)
	CD4 (500)	0.052 (0.035-0.068)
	CD4 (350,499)	0.128 (0.092-0.164)
	CD4 (200,349)	1.1 (.0.2-2.0)
	CD4 (<200)	50.0 (40.0-66.0)
	Treatment (CD4<200)	4.0 (1.0-10.0)
Treatment failure rate (% per year)	1st-line	4.5 (3.0-6.0)
	2nd-line	4.5 (3.0-6.0)
Efficacy/change in transmissibility due to:	Condom (%)	80.0 (60.0-99.0)
	Circumcision (%)	60.0 (50.0-65.0)
	Diagnosis (%)	30.0 (0.0-60.0)
	STI cofactor increase (%)	700.0 (100.0-1000.0)
	Syringe cleaning (%)	75.0 (70.0-80.0)
	Methadone (%)	95.0 (90.0-99.0)
	PMTCT (%)	78.0 (40.0-99.0)
	Treatment risk compensation (%)	100.0 (95.0-200.0)

Table A10: Partnerships

		LRM	LRF	SW	MSM	PWID
Regular sexual interactions	LRM		1	1		
	LRF					
	SW					
	MSM				1	
	PWID		1	1		
		LRM	LRF	SW	MSM	PWID
Casual sexual interactions	LRM		1	1		
	LRF					
	SW					
	MSM				1	
	PWID		1	1		
		LRM	LRF	SW	MSM	PWID
Other sexual interactions	LRM			1		
	LRF					
	SW					
	MSM				1	
	PWID			1		
		LRM	LRF	SW	MSM	PWID
Injecting interactions	LRM					
	LRF					
	SW					
	MSM					
	PWID					1

Table A11: Transitions (% leaving per year)

	LRM	LRF	SW	MSM	PWID
LRM					
LRF					
SW		(20)			
MSM					
PWID					


Get to
Get to zero
new HIV infections
End the epidemic
threat of AIDS
Universal access
to HIV services
Get to zero
discrimination
Get to zero
AIDS-related deaths
Get to zero
discrimination
Get to zero
new HIV infection