



SOUTH AFRICAN HIV AND TB INVESTMENT CASE

REFERENCE REPORT

Phase 1 | March 2016



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FOREWORD

The publication of the HIV and TB Investment Case report comes at a crucial time for our country's HIV and TB response. Over the past decade, we have seen large decreases in new HIV infections and deaths from AIDS. Tuberculosis prevalence and deaths have levelled off. In large part due to the massive roll-out of antiretroviral treatment (ART), the country has recovered from the significant decrease in life expectancy in the early years of the epidemic. We are on the way to reaching the target of an average life expectancy of 70 years for all by 2030, as envisaged in the National Development Plan.

At the same time, the country still has a long way to go before we can declare the war on these two diseases to be won.

Large groups of the population, such as young women, still experience high HIV infection rates; testing and treatment uptake is lagging behind in men, who continue to bear the brunt of mortality from both HIV and TB.

Although we have a number of new prevention methods available, such as medical male circumcision and pre-exposure prophylaxis, demand for these will have to be increased and sustained.

We have the world's largest number of people on ART, but the public health system needs to ensure that everyone who is on treatment receives their drugs every month and remains in care for life.

The Investment Case has helped us in four ways:

- by reviewing the evidence base for all known interventions against HIV and TB, including those that are currently part of our HIV and TB programmes and a number of those that we could add;
- by comparing the impact and cost of each of these interventions and suggesting an optimal package of services to reach important targets in controlling the two diseases;
- by calculating the total budget needed to implement the optimal package over 20 years so that the return on our initial investment becomes clear;
- and by pointing out in greater clarity where the gaps are in our collective knowledge on what works against the two diseases.

The Investment Case is the first exercise that compares all known HIV and TB interventions at the same time, and calculates their impact on both HIV and TB across all layers of the population. The team that made this possible, by reviewing the evidence, fashioning powerful tools to do the maths, and creating relevant scenarios that are easy for policymakers to implement, deserve our praise.

As a country, South Africa has shown the world what political will and leadership can achieve in combating a disease. We cannot however be complacent. The fight goes on, and the results of the Investment Case point the way.

In implementing the recommendations of the South African HIV and TB Investment Case, I would like to ask for everyone's help in making HIV and TB history. This includes the programme planners, policy makers and decision makers at national, provincial and district levels; researchers, evaluators and analysts in South Africa

FOREWORD

and abroad; and especially clinicians, nurses, counsellors, pharmacists and pharmacy assistants, community health workers, laboratory technicians and specialists, dietitians and social workers, and many many volunteers and peer counsellors.

It also includes the many ordinary South Africans - and citizens of other countries living here - that choose to take HIV and TB seriously, get tested for HIV, be screened for TB, follow the necessary steps into care if required, protect themselves and those nearest to them by using condoms regularly, get circumcised, get tested early in pregnancy to protect their baby from HIV, take their treatment every day and endure its side effects, and stay with the programme.

I am thankful for the efforts of these millions of people. All of us need to join in and be part of the struggle to overcome HIV and TB.

A handwritten signature in black ink that reads "Cyril Ramaphosa". The signature is written in a cursive, flowing style.

Deputy President Cyril Ramaphosa
Chair, South African National AIDS Council



PREFACE

The South African HIV and TB Investment Case is the result of two years of intense work by the Investment Case Task Team, a group of technical experts in HIV and TB, and the Steering Committee, which was chaired by Dr Yogan Pillay (DOH) and Dr Fareed Abdullah (SANAC Secretariat). The Investment Case aims at informing, and if need be, changing national policy with regards to these two diseases, which continue to claim thousands of lives every year in South Africa. It has fulfilled this objective in providing five important results.

Firstly, the main result shows that we are right to aim high in HIV programming, to aim at getting every South African to know their HIV status, encouraging every person living with HIV to initiate treatment immediately, and scaling up all prevention interventions that we know work to the maximum. For the first time, the results also show that our response to TB needs to be scaled up as dramatically, by screening everyone at high risk for TB annually, starting with miners, inmates in correctional facilities and those living in communities near mines, testing everyone with TB symptoms using state-of-the-art diagnostics, and making sure everyone who is found to have TB starts appropriate treatment and continues until he or she is healed.

This is why the final outcome of the Investment Case is the recommendation to identify 90% of people living with TB and/or HIV, initiating treatment in 90% of those with TB and HIV, and 90% treatment success for TB and viral suppression for HIV. While this is the logical next step for a country in which testing and treatment coverage is already much higher than in our peers, it also helps us fulfil targets set by UNAIDS, the Stop TB Partnership and the World Health Organization.

Secondly, the Investment Case shows that as a result of maximising coverage, we can bring the two diseases closer to elimination than ever before. If we scale up testing and treatment initiation for HIV to 90%, we can bring HIV incidence almost to the low levels that UNAIDS defines as necessary for HIV elimination. While this has a large impact on bringing down TB as well, it is only if we additionally scale up screening, testing and treatment success for TB to 90% that we can start seeing massive reductions in deaths from TB, and a halving of the number of TB cases.

A third important finding is that while going to the maximum in every aspect of dealing with the two diseases, we will also be able to save money in the long term- which is important since the fight against both diseases is largely paid for by South African tax money. For both HIV and TB, scaling up the response means that we will need to invest a lot more funding over the medium term. But it also means that after 5 years for TB, and after 10 to 15 years for HIV, we will start saving money every year because our prevention efforts will start paying off and we will have less people needing expensive treatment.

The fourth result is that, despite living in a country that is host to a great amount of research and knowledge around these two diseases, much remains unknown. The fact that the Investment Case task team, despite engaging many of the country's best researchers and programme implementers in the process, identified so many gaps in the evidence base points to how much still needs to be done. Because of its focus on solid evidence, the Investment Case ended up including mostly medical interventions whose beneficiaries are easy to count and whose impact is easy to quantify.

It is clear that we need to now focus our curiosity and resources to measure the impact of those critical enablers that might not have a direct impact on HIV and TB infections or deaths but without which the medical interventions will never reach full coverage or will cease to work. Such enablers include interventions that increase community involvement in planning and implementing programmes, reduce stigma, and help to remind everyone in South Africa that AIDS and TB are not over- not just yet.

Finally, the Investment Case also serves as a reminder that while we as a country have done much to improve the lives of people living with HIV or TB, and much to prevent others from contracting the diseases, we can do a lot better. Even though we have already started to “bend the curves” of HIV incidence and mortality from HIV (in other words, both new infections and deaths have decreased, significantly, over the last few years), and new TB cases and deaths from TB have stopped increasing, we need to strengthen our resolve and improve implementation of our programmes in order to bring about the large impacts we are aiming for, as well as the cost savings mentioned above.

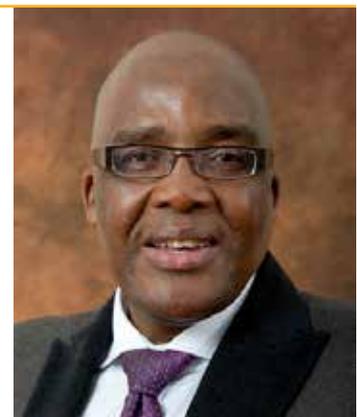
Many of the results of the Investment Case are not new. We have known for a long time that we need to increase condomisation. We have dramatically increased access to HIV and TB testing and treatment over the last years; even novel technologies such as medical male circumcision to prevent HIV, and GeneXpert testing for TB, have been scaled up quickly and to high levels. What the Investment Case shows is that we need to continue and increase our efforts along these upward trajectories, while also bringing services closer to beneficiaries and communities to make it easier for people to take up and adhere to these interventions.

While some of us had hoped that the Investment Case would point to ways to reduce the number of interventions in our HIV and TB programmes, it instead showed that we need to continue doing everything that works, and do more of it, in order to make our substantial previous investments count and to end these epidemics in our lifetime.

We are grateful for the energy and time that South Africans have already invested in this effort in general, and in the Investment Case project in particular- this project owes a debt to the hundreds of people who contributed their insights, expertise, time and passion during the course of the exercise. I am sure that the findings and recommendations of the Investment Case will be implemented with the same passion and rigour that we saw during its preparation- amongst others by guiding the development of the next National Strategic Plan for HIV, TB and STIs.



Dr Aaron Motsoaledi, MP
Minister of Health



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The South African HIV and TB Investment Case was a joint effort of the National Department of Health (NDOH) and the South African AIDS Council (SANAC). It was developed through an intensified national dialogue about investment choices and priority setting involving all key national partners, including civil society groups at all stages. SANAC and NDOH would like to thank everyone who contributed to the development of the South African HIV and TB Investment Case.

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PREFACE

NDOH and SANAC also give special thanks to the many colleagues from partner organisations who participated in the National stakeholder meeting at the beginning of the Investment Case process in August 2014. This work was made possible by financial support from UNAIDS, UNICEF, United States Agency for International Development (USAID) and the Global Fund for AIDS, TB and Malaria.

Two handwritten signatures in black ink. The first signature is 'Pillay' and the second is 'Fareed Abdullah'.

Dr Yogan Pillay (NDOH) and Dr Fareed Abdullah (SANAC)
Co-Chairs, Investment Case Steering Committee



ACRONYMS

aHR	Adjusted hazard ratio
ACF	Active case finding
ACSM	Advocacy, communication and social mobilisation
AIDS	Acquired immune deficiency syndrome
AFB	Acid fast bacilli
AFRO	World Health Organization African Region
AIM	AIDS Impact Model
ANC	Antenatal care
aOR	Adjusted odds ratio
ARV	antiretroviral
ART	Antiretroviral therapy
BAS	Basic Accounting System
BCG	Bacillus Calmette-Guérin
BDQ	Bedaquiline
CBI	Community-based intervention
CCMT	Comprehensive care, management and treatment of HIV
CCP	Comprehensive condom programming
CCT	Conditional cash transfer
CFR	Case fatality rate
CG	Conditional Grant
CHAPS	Centre for HIV and AIDS Prevention Studies
CHBC	Community and home based care
CHCT	Community-based HIV counselling and testing
CHER	Children with HIV Early Antiretroviral Therapy study
CHW	Community health worker
CI	Confidence interval
CPD	Continuing professional development
CPU	Central procurement unit at NDOH
CTX	Cotrimoxazole
CYPR	Couple year protection rate
DALY	Disability-adjusted life year
DBS	Dried blood spot
DCS	Department of Correctional Services
DOD	Department of Defence
DOE	Department of Education
DOH	Department of Health
DOTS	Directly observed treatment short course
DR	Drug resistant
DS	Drug sensitive
DSD	Department of Social Development
DTD	Demonstration and training districts
DVA	Domestic Violence Act
EA	Expenditure analysis
ECD	Early childhood development
ECG	Electrocardiogram
EDRweb	Electronic drug resistant TB register
EFR	Enhanced Financial Report
EID	Early infant diagnosis
EIMC	Early infant male circumcision
EMTCT	Elimination of mother-to-child HIV transmission
EPI	Expanded programme on immunisation
EPWP	Expanded Public Works Programme
ES	Equitable share
E&S	Earmarked and specific

ACRONYMS

ETB	Extra-pulmonary TB
EVISAT	Evidence to Inform South African TB Policies
FET	Further education and training
FP	Family planning
FPD	Foundation for Professional Development
FSW	Female sex worker
FY	Financial year
GBV	Gender based violence
GF, GFATM	Global Fund to Fight AIDS, TB and Malaria
Govt	Government
GP	General practitioner
GXP	GeneXpert
HAART	Highly Active Antiretroviral Therapy
HBT	Home based testing
HCT	HIV counselling and testing
HCW	Health care workers
HE²RO	Health Economics and Epidemiology Research Office
HEAIDS	Higher Education and Training HIV/AIDS Programme
HIV	Human immunodeficiency virus
HMIS	Health management information system
HSRC	Human Sciences Research Council
HSS	Health systems strengthening
HTA	Hight Transmission Area
IC	Investment case
ICF	Intensified case finding
IMCI	Integrated Management of Childhood Illnesses
INH	Isoniazid
IOM	International Organization for Migration
IP	Implementing partner (PEPFAR)
IPV	Interpersonal violence
IPT	Isoniozid preventive therapy
JHHESA	Johns Hopkins Health and Education in South Africa
KZN	KwaZulu-Natal
M&E	Monitoring and evaluation
MAT	Medication assisted therapy
MatCH	Maternal, Adolescent and Child Health
MCH	Maternal and child health
MDGs	Millennium Development Goals
MDR	Multi-drug resistant
MNCH	Maternal, newborn and child health
MSP	Multiple sexual partners
MSM	Men who have sex with men
mHealth	Mobile health technologies
MMC	Medical male circumcision
Mtb	Mycobacterium tuberculosis
MTEF	Medium Term Expenditure Framework
N/A	Not available/ applicable
NACM	National ART Cost Model
NACOSA	Networking HIV, AIDS Community of South Africa
NASA	National AIDS Spending Assessment
NAT	Nucleic acid testing
NCS	National HIV Communication Survey
n.d.	not disaggregated
NDOH	National Department of Health
NDP	National Development Plan
n.e.c.	not elsewhere classified

NFM	New Funding Model (Global Fund)
NHA	National Health Accounts
NHI	National Health Insurance
NIMART	Nurse initiated and managed ART
NSP	National Strategic Plan
NSP	Needle and syringe programme
NSWP	National Strategic Plan for HIV Prevention, Care and Treatment for Sex Workers
NTP	National TB Programme
OIs	Opportunistic infections
OMC	One Man Can
OPD	Outpatient department
OR	Odds ratio
OSD	Occupation specific dispensation
OVC	Orphans and vulnerable children
PCR	Polymerase chain reaction
PEP	post-exposure prophylaxis
PEPFAR	President's Emergency Plan for AIDS Relief (USG)
PFIP	Partnership Framework Implementation Plan (PEPFAR)
PHC	Primary health care
PHRU	Perinatal HIV Research Unit
PICT	Provider-initiated counseling and testing
PLHIV	People living with HIV
PM	Programme Management
PMTCT	Prevention of mother-to-child transmission of HIV
POC	Point of care
PPP	Public-private partnership
PR	Principal Recipient (GF)
PrEP	Pre-Exposure Prophylaxis
PTB	Pulmonary TB
PWD	People with disabilities
PWID	People who Inject Drugs
RCT	Randomised controlled trial
Rif	Rifampicin
RR	Rifampicin-resistant
SA	South Africa
SABCOHA	South African Business Coalition on HIV and AIDS
SADC	Southern African Development Community
SAG	South African government
SANAC	South African National AIDS Council
SANBS	South African National Blood Service
SAPS	South African Police Service
SA NTP	South African National TB Programme
SBCC	Social and behaviour change communication
SDA	Service Delivery Area (for Global Fund Principal Recipients)
SDC	Step down care
SFH	Society for Family Health
SHIPP	Sexual HIV Prevention Programme
SMS	Short message services
STI	Sexually transmitted infection
SW	Sex worker
SWEAT	Sex Worker Education and Advocacy Taskforce
TAC	Treatment Action Campaign
TasP	Treatment as Prevention
TB	Tuberculosis
TBMAC	TB Modelling and Analysis Consortium

ACRONYMS

TB-NEAT	Evaluation of multiple novel and emerging technologies for TB diagnosis in smear-negative and HIV-infected persons in high burden countries
TBPT	Tuberculosis preventive therapy
TE	Technical efficiency
TIME	TB Impact Model and Estimates
TST	Tuberculin skin test
TTT	Technical Task Team
TWG	Technical Working Group
UNAIDS	Joint United Nations Programme on HIV/AIDS
UNFPA	United Nations Population Fund
UNICEF	United Nations Childrens Fund
USG	United States government
UTT	Universal Test and Treat
VAW	Violence against women
VCT	Voluntary counselling and testing
WBOT	Ward-based outreach team
WHO	World Health Organization
XDR	Extensively drug-resistant TB
XPHACTOR	Xpert MTB/RIF for people attending HIV care: an interventional cohort study to guide rational implementation
XTEND	Xpert for TB - Evaluating a New Diagnostic
ZAR	South African Rand

EXECUTIVE SUMMARY

AN INVESTMENT CASE FOR HIV AND TB IN SOUTH AFRICA

With an eye towards maximizing the impact of investments in HIV and TB programmes – and to ensure the sustainability of the national response to these epidemics – South Africa has developed an Investment Case for HIV and TB. The Investment Case aims to inform the development of a clear national plan for ending the HIV and TB epidemics through identification of the most cost-effective mix of interventions to address HIV and TB over the next 20 years. The Investment Case will be taken into account in the development of the next National Strategic Plan for HIV, TB and STIs in 2016.

South Africa's Investment Case (IC) is envisaged as an iterative process that will evolve over time based on changes in circumstances and expansion of the evidence base. The national-level results summarized here is an effort to strengthen the use of an investment approach to inform and strengthen national efforts to end HIV and TB in South Africa. Future phases of the IC project will include results and recommendations at provincial (phase 2) and sub-provincial (phase 3) levels. It is anticipated that as the evidence base increases future iterations of the IC will take account of a greater array of interventions, with recommendations to be updated as deemed necessary.

BACKGROUND: THE STATE OF THE NATIONAL EPIDEMIC AND RESPONSE

The HIV and TB epidemics in South Africa

HIV and TB represent among the most serious of all health threats to the people of South Africa. In 2013, HIV accounted for 21 938 deaths in South Africa, while TB accounted for an estimated 89 000 deaths. Expanded access to antiretroviral therapy has had a profound impact on South Africa's HIV and TB epidemics; the number of AIDS-related deaths in 2014 in South Africa, while still substantial, was less than half the number in 2005.

South Africa is home to 6.3 million people living with HIV, or 18% of all people living with HIV worldwide (2013). An estimated 12.2% of South Africa's population – including 18.8% of adults ages 15-49 – were living with HIV in 2012. Geographically, HIV prevalence is highest in KwaZulu-Natal and Mpumalanga provinces.

An estimated 340 000 people in South Africa were newly infected with HIV in 2013 – a sharp decline since 2005, when 560 000 people acquired HIV. The number of new HIV infections among children – 16 000 in 2013 – has fallen by more than half since 2009, when 33 000 children were newly infected. Women are almost twice as likely to become infected with HIV as men, with young females (15-24 years) four times more likely to acquire HIV as young males (UNAIDS Spectrum, 2013).

An estimated 450 000 new cases of TB occurred in South Africa in 2013, including more than 26 000 cases of drug-resistant TB. South Africa's HIV epidemic has largely driven the country's TB epidemic.

South Africa's response to HIV and TB

The National Strategic Plan guides South Africa's response to HIV and TB. The South African National AIDS Council (SANAC), a representative body of all stakeholders in government, the private sector, non-governmental organisations and civil society, oversees and coordinates the national response.

EXECUTIVE SUMMARY

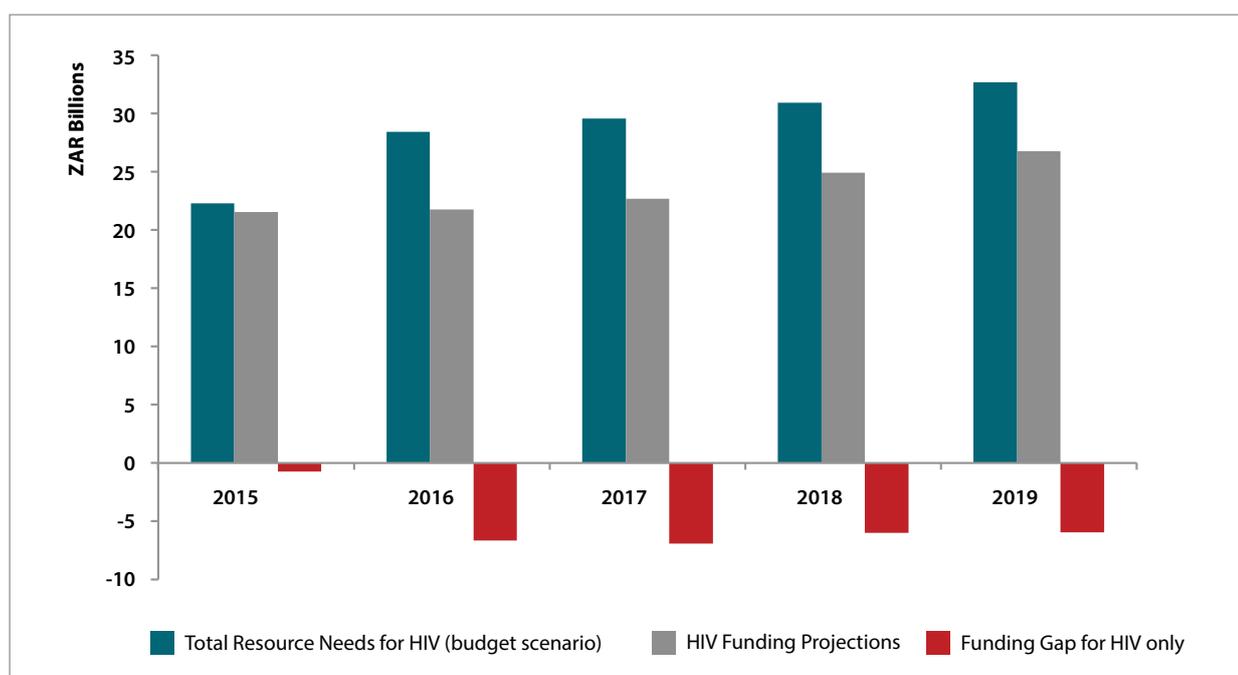
The national response includes evidence-based actions to prevent new HIV infections, scale up antiretroviral therapy and reduce AIDS-related mortality, lower TB infections and deaths, ensure an enabling environment that protects and promotes human rights, and reduce stigma related to HIV and TB. South Africa has emphasized HIV treatment scale-up; in 2015, the country began recommending use of 500 CD4 cells/ml³ as the threshold for HIV treatment initiation, and the country has also enthusiastically embraced the UNAIDS 90-90-90 target for treatment scale-up¹. Steps have been taken to ensure the integration of HIV and TB services.

Taking into account spending by the government, the Global Fund to Fight AIDS, Tuberculosis and Malaria (GF) and the United States President’s Emergency Plan for AIDS Relief (PEPFAR), R22.1 billion was invested in HIV- and TB-related activities in South Africa in 2013. In 2011-2013, total funding for HIV and TB activities increased by 27% (including a 15% increase in 2013 alone). Over those three years, the share of spending by the South Africa government rose (from 76% to 80%), while the proportion financed by PEPFAR declined (from 22% to 17%), as a function of the transition of responsibility for PEPFAR-funded programmes from the U.S. government to South Africa.

In 2011-2013, HIV care and treatment accounted for 39% of all spending on HIV and TB activities, with an additional 5% devoted to HIV counselling and testing. The proportion of total HIV and TB spending devoted to HIV care and treatment has increased over time, a trend that is continuing. TB activities represented 19% of all spending, while social and programme interventions designed to extend the reach and impact of programmatic efforts consumed 8% and 5%, respectively, of total spending.

It is projected that spending on HIV and TB will continue to increase in future years and that the share of spending covered by the South Africa government will also continue to rise. However, current projects indicate that these projected increases are unlikely to meet resource needs, with a substantial resource gap projected for each of the next five years.

Potential Funding Gap for HIV in South Africa (ZAR, 2015/16-2018/19)



a The 90-90-90 target provides that by 2020: (a) 90% of all people living with HIV will know their HIV status; (b) 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy; and (c) 90% of all people receiving antiretroviral therapy will achieve viral suppression.

METHODOLOGY

Given the gap documented by the Investment Case between needed funding and amounts projected to be available for HIV and TB in South Africa in coming years, the country confronts the need both to identify new, sustainable sources of funding and to maximize the strategic impact and efficiency of funding. To develop the Investment Case to inform such efforts, SANAC convened an intensified national dialogue on future directions for the country's response to HIV and TB. A broad array of partners were engaged in development of the Investment Case, including civil society and leading scientific researchers. Development of the Investment Case was directed by a steering committee, which included senior officials from relevant government departments, civil society representatives, UN organisations, donor agencies and experts from academia.

A review of the evidence base

For the South Africa Investment Case, the following nine (9) basic programme activities were taken into consideration:

- Focused interventions for key populations at higher risk
- Elimination of new HIV infections among children
- Social and behaviour change programmes
- Comprehensive condom promotion and distribution
- Treatment, care and support for people living with HIV
- Voluntary medical male circumcision
- HIV counseling and testing
- Tuberculosis screening, diagnosis and treatment
- Other biomedical prevention (e.g., pre-exposure prophylaxis, post-exposure prophylaxis, STI treatment).

In each of these programmatic areas, a sub-working group was formed to rigorously examine and analyse the evidence base for the effectiveness and efficiency of relevant interventions. Each sub-working group developed an initial list of interventions to be included in the Investment Case, with input also provided by large stakeholder consultation held on 30-31 July 2014.

In the review of data for various interventions, preference was given to randomized controlled trials and other well-designed studies, with particular preference for studies conducted in South Africa, although numerous observational studies were also taken into account. In addition, interventions sanctioned by official government policy were also included in the Investment Case. Each sub-working group evaluated the strength of the evidence for each intervention, using these findings to assign a grade for each intervention (see box).

- 1 – IN** (good evidence)
- 2 – IN** (existing government policy)
- 3 – OUT** (weak evidence)
 - 3a** – Likely more data by Phase 2
 - 3b** – Important research question
 - 3c** – Exclude altogether
- 4 – Transfer elsewhere**
 - 4a** – to other programme area
 - 4b** – to social enablers
 - 4c** – to programme enablers
- 5 – OUT** (can't be modelled)
- 6 – IN** (consider cost only)

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Interventions with strong evidence of effectiveness, as well as those reflecting official government policy, were included in the Investment Case and taken into account in the modelling of various scenarios.

For each intervention, the sub-working group also analysed the evidence base for technical efficiency, or TE factors. These are intervention-specific factors that improve the efficiency of an intervention (for example, by enhancing the impact of an intervention or by reducing costs associated with delivery of an intervention).

In addition to the nine programmatic categories, sub-working group also analysed the evidence base for critical enablers and development synergies. Programme enablers (such as incentives, organizational capacity-building) help create demand for key services and improve the performance of basic programme activities, while social enablers (which often focus on human rights and other social conditions that influence service uptake) make environments more conducive to sound HIV and TB responses. Development synergies involve strategic linkages between HIV and other sectors, which may reduce vulnerability, mitigate the impact of HIV and improve service uptake and retention. The sub-working groups for critical enablers and development synergies took a similar, although slightly modified, approach to the evaluation of evidence as was adopted by the programmatic sub-working groups.

In identifying interventions and TE factors for inclusion in the modelling exercise for the Investment Case, sub-working groups often confronted gaps in the evidence base. In many cases, there was a strong consensus within the relevant sub-working group that a particular intervention or TE factor was highly effective, yet the rigorous evidence review was unable to identify clear evidence supporting this consensus. As one important component of the Investment Case exercise, priority evidence gaps were identified, with the aim of guiding efforts to build the evidence base for future efforts. As South Africa's Investment Case is envisaged as a long-term, ongoing exercise, it is expected that revisions and adaptations in the Investment Case will be needed as new evidence emerges and as research gaps are closed.

Based on this multi-step exercise, the following interventions were included in the final analysis for the Investment Case:

Programme area	Intervention	Impact represented in model
ART	Cotrimoxazole	ART uptake
	ART at current guidelines	ART uptake in children and eligible adults (CD4 < 500)
	Universal test and treat	ART uptake in children and all HIV-positive adults HCT uptake
Male medical circumcision	General population MMC	MMC uptake in highly sexually active men
	Early infant male circumcision	EIMC uptake
	MMC age group targeting (10-14, 15-19, 20-24, 25-49)	MMC uptake in highly sexually active men
Comprehensive condom programming	Condom availability	Condom use
	Male and female condom education	Condom use
Key populations	PrEP for sex workers	PrEP uptake for sex workers
PMTCT	PMTCT (Triple ART initiation in pregnant women)	ART uptake in pregnant women
	Infant testing at birth	Uptake of infant testing at birth
	Infant testing at 6 weeks	Uptake of infant testing at 6 weeks

Programme area	Intervention	Impact represented in model
HCT	General population HCT	HCT uptake
	Testing of pregnant women	HCT uptake in pregnant women
	Testing of adolescents	HCT uptake in adolescents
Social and behaviour change communication	SBCC campaign 1 ^b	HCT uptake in adolescents Multiple sexual partners
	SBCC campaign 2	Condom use
	SBCC campaign 3	Condom use HCT uptake MMC uptake
Prevention	PrEP for discordant couples	PrEP uptake
	PrEP for adolescents	PrEP uptake for adolescents
	Microbicides ^c	Microbicides uptake

The following TE factors and critical enablers were also taken into account in the modelling exercise:

Programme area	TE factor/ enabler	Impact represented in model
TE factors		
ART	GP down referral	Mortality on ART Infectiousness on ART ART retention
	Home-based ART	ART cost (Cost model)
	Community based adherence supporters	Mortality on ART Infectiousness on ART ART retention
	Adherence clubs	Mortality on ART Infectiousness on ART ART retention ART cost (Cost model)
	Point-of-care CD4 testing	ART uptake

^b A number of organisations responsible for SBCC campaigns were involved in a government tender submission process at the time of analysis, so we anonymized the campaigns in order to not influence the tender process.

^c It is important to note that this report refers to the results of Phase 1 of the Investment Case, for which we took all evidence into account that had been published, or brought to our attention, by 31 January 2015 the latest. This meant that some very recent updates, such as the new data regarding the effectiveness of microbicides presented during CROI 2015, or the results of the START and TEMPRANO trials, could not be included in this process.

EXECUTIVE SUMMARY

Programme area	TE factor/ enabler	Impact represented in model
Critical enablers		
	SASA! Community-based gender-based-violence intervention	Multiple sexual partners
	Life skills and vocational training for adolescent girls	Condom use in adolescents
	Risk reduction for alcohol and substance users	Condom use
	Risk reduction for substance users	Condom use
	School-based HIV/STI risk reduction	Multiple sexual partners Condom use
	Teacher support	Multiple sexual partners
	Parental monitoring	Multiple sexual partners Condom use in adolescents
	School feeding	Condom use in adolescents
	Positive parenting	Multiple sexual partners
	Supporting adolescent orphan girls to stay in school	Age of sexual debut
	State-provided child-focused cash transfers	Age disparate sex

Identifying unit costs

The Investment Case exercise identified unit costs for each intervention and Technical Efficiency (TE) factor, which enabled projections of future costs for specific interventions and for all programmatic interventions, TE factors, critical enablers and development synergies in different scenarios. Where unit costs were available from published or unpublished sources, the model generated cost analyses that represented implementation of the intervention under the most recent guidelines and at the most relevant level of care. Where necessary, published unit cost estimates were updated to reflect more recent costs. Where no unit cost could be found in the literature, costs were established using ingredient-based costing or by consulting recent budgets or expenditure records.

Modelling of results

To be able to model an intervention, TE factor or enabler or synergy, three types of information were required: (1) the precise population targeted with each intervention, (2) the effectiveness of the intervention in terms of mortality, HIV or TB incidence, and/or a number of other epidemiological or behavioural parameters, and (3) the cost of the intervention. Of these three types of evidence, effectiveness data alone determined which interventions were included in the Investment Case.

A team of modellers from the economic sub-working group reviewed the data findings of the programme area sub-working groups, reapplying the same grading criteria for each proposed intervention. This review primarily aimed to identify interventions that, while supported by strong evidence of effectiveness, were unable to be modelled because either the reported effect or the target population of each intervention could not be modelled.

The primary model used to evaluate future options for South Africa's HIV response was Thembisa, an integrated demographic and epidemiological model of the HIV epidemic in South Africa. To address the fact that Thembisa does not currently consider HIV transmission among men who have sex with men or the result of sharing of contaminated injecting equipment, a secondary analysis for key populations was undertaken using Spectrum model (AIM and Goals modules).

For the TB Investment Case, the TIME model was used, a dynamic compartmental TB model developed by the TB Modelling and Analysis Consortium (TB MAC), in the version calibrated to the South African TB epidemic.

Examining future scenarios for the HIV and TB response in South Africa

Modelling the future of the HIV response

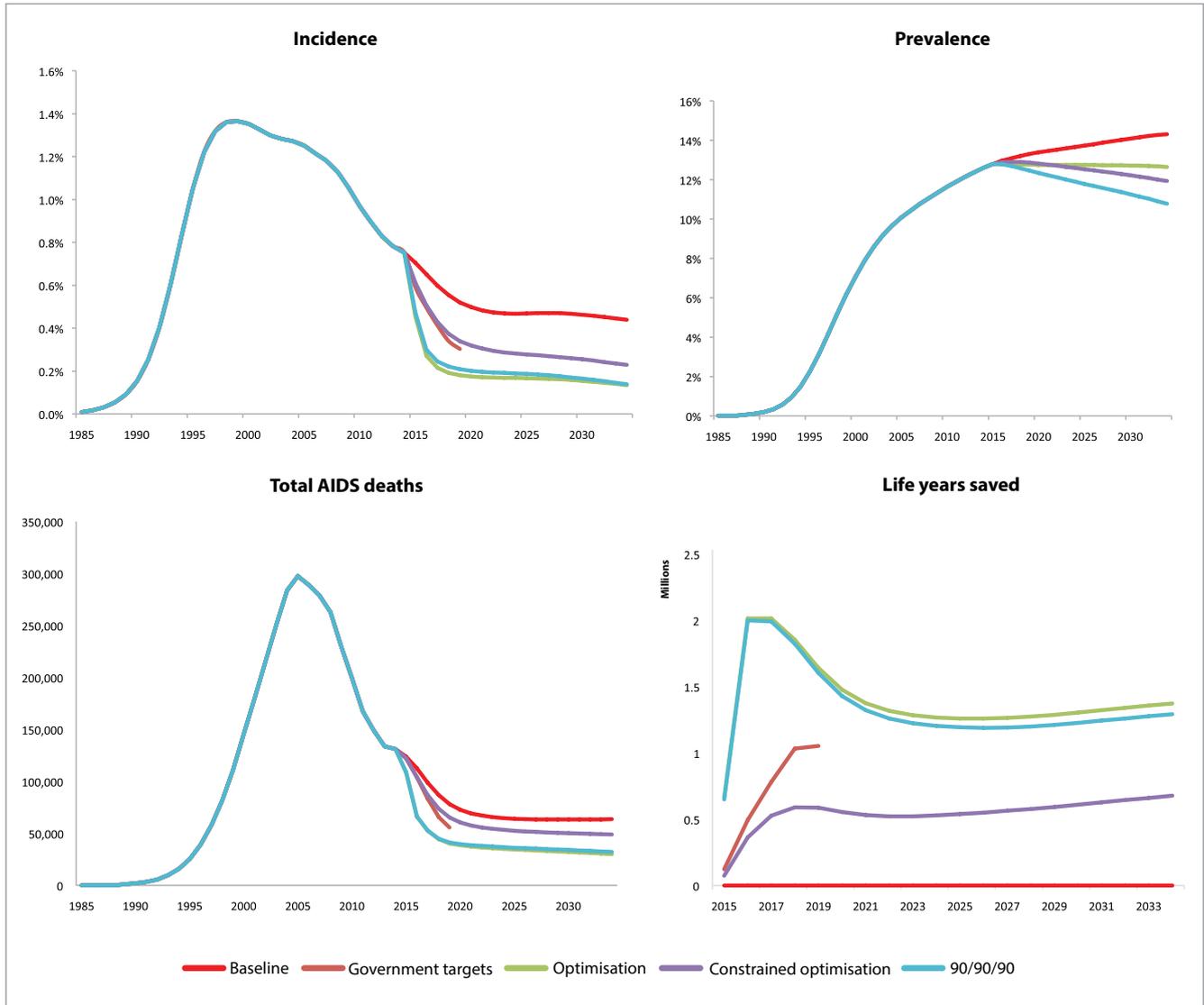
The modelling team assessed the epidemiological impact, cost and cost-effectiveness of the following six scenarios:

1. *Baseline*: This scenario, which was used as a comparison for all the other scenarios, maintained coverage with all interventions and TE factors at current (2014) coverage levels throughout the 20-year projection period.
2. *Government targets*: The project analysed the full and incremental cost and incremental cost-effectiveness of the current mix of interventions against HIV and TB over the next 5 years, at current coverage targets endorsed by the government. As with the baseline scenario, separate analyses were undertaken for current and optimal levels of technical efficiency.
3. *Optimisation scenario without constraints*: An analysis was conducted to ascertain the full and incremental cost and incremental cost-effectiveness of the *most efficient mix* of interventions against HIV and TB, with efficiency measured in cost per live year saved, over the next 20 years. This exercise (Scenario 3) also identified optimal coverage targets and assessed the impact of achieving them with both current and optimal levels of technical efficiency. No budgetary limitations were assumed with respect to Scenario 3.
4. *Optimisation scenario with budget constraints*: A separate exercise (Scenario 4) repeated the analysis for Scenario 3, but assessed outcomes with the current budget envelope (including domestic and important external sources) maintained over time. This step aimed to identify the most efficient mix of interventions in the absence of additional resources. As in prior scenarios, analyses were made with both current and optimal levels of technical efficiency.
5. *90-90-90*. Another exercise repeated the analysis for Scenario 3, but with the aim of determining the most cost-effective package of interventions to achieve the 90-90-90 targets.
6. *Budget*: To inform relevant domestic and donor budgets, the 90-90-90 scenario was adapted for a more budget-relevant scenario. This scenario started with the current financial year (2015/16) rather than the original start year of 2014/15. The scenario also added a number of interventions and enablers that were not part of the optimisation package despite being current government policy because their effectiveness could not be established based on the evidence reviewed.

Each of the six HIV scenarios resulted in declines in new HIV infections and AIDS-related deaths. All non-baseline scenarios (2-6) resulted in substantial reductions in new HIV infections compared to baseline, with the unconstrained optimisation and 90-90-90 scenarios achieving the greatest declines in new HIV infections through 2030. The same pattern is seen with regard to AIDS-related deaths, with scenarios 2-6 representing an improvement over baseline and with the unconstrained optimisation and 90-90-90 scenarios proving most effective in minimizing HIV-related mortality. Similar patterns are evident with respect to life years lost due to AIDS, with the unconstrained optimisation and 90-90-90 scenarios saving 38% and 37%, respectively, over five years, and 47% and 45%, respectively, over 20 years.

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HIV incidence, prevalence, life years saved and total AIDS deaths, by scenario



Among the scenarios that improve results in the HIV response over baseline (2-6), cost per life saved and new infection averted is lowest for the government targets and constrained optimisation scenarios. Among the two scenarios with the greatest impact in terms of new HIV infections, AIDS-related deaths and life-years lost to AIDS – the unconstrained optimisation and 90-90-90 scenarios – the 90-90-90 scenario appears most cost-effective based on cost per life-year saved and new infections averted.

Effectiveness, cost, and cost effectiveness of HIV programme by scenario5 at optimal technical efficiency

	Baseline at current technical efficiency	At optimal technical efficiency				
		Baseline	Government targets	Optimisation without constraint	Optimisation with constraint	Optimisation towards 90-90-90
Total new HIV infections						
2014/15 - 2018/19	1,439,654	1,365,376	989,957	600,343	1,017,432	668,569
2014/15 - 2033/34	5,115,877	4,788,710	-	1,705,291	3,035,413	2,052,180
HIV infections averted (% change on baseline)						
2014/15 - 2018/19	-	74,278	449,697	839,311	422,222	771,085
2014/15 - 2033/34	-	327,167	-	3,410,586	2,080,464	3,063,697
Total life years lost due to AIDS						
2014/15 - 2018/19	21,711,080	19,808,720	17,289,300	12,688,780	17,713,070	12,801,000
2014/15 - 2033/34	59,425,080	52,386,990	-	29,390,930	43,252,040	30,507,923
Life years saved (% change on baseline)						
2014/15 - 2018/19	-	1,902,360	4,421,780	9,022,300	3,998,010	8,910,080
2014/15 - 2033/34	-	7,038,090	-	30,034,150	16,173,040	28,917,157
Total cost [billion 2014 ZAR]						
2014/15 - 2018/19	122	124	132	193	131	158
2014/15 - 2033/34	688	691	-	953	676	743
Incremental cost [billion 2014 ZAR] (% change on baseline)						
2014/15 - 2018/19	-	2	10	71	9	36
Incremental cost per life year saved						
2014/15 - 2018/19	-					
2014/15 - 2033/34	-	1,287	2,357	7,874	2,294	4,042
Incremental cost per HIV infection averted						
2014/15 - 2018/19	-					
2014/15 - 2033/34	-	32,965	23,179	84,641	21,722	46,705

In the separate analysis undertaken for key populations, results were modelled for standard service packages for each key population, using the Spectrum model. For each of the key populations – young women, men who have sex with men, people who inject drugs, and sex workers – each of the packages had a limited impact on total infections averted or life-years saved compared to baseline. However, these findings need to be interpreted with caution, as they use a different baseline than the earlier general population analysis and fail to take into account the impact of scaling up interventions in the general population.

Modelling the future of the TB response

To analyse impact and cost of the future course of the national response to TB, two scenarios were modelled:

1. A baseline scenario, which maintains coverage of all interventions at current (2014) levels throughout the 20-year projection period.

EXECUTIVE SUMMARY

2. A 90-90-90 scenario, which provides that by 2020 90% of prevalent TB cases will be diagnosed and treatment, with 90% of those on treatment achieving treatment success.

Continuing current coverage, as in the baseline scenario, would result in 2.1 million TB-related deaths over the next 20 years and only a somewhat modest 24% decline in the rate of TB deaths in the population at large. By contrast, the TB 90-90-90 scenario would reach the international target of a 35% reduction in TB deaths by 2020 and a 75% reduction by 2035. Meeting current government targets for TB will achieve international epidemiological targets for TB by 2020, but longer-term efforts will be needed to achieve the vision of ending TB as a public health threat over the next 20 years.

At its peak in 2020/21, the TB 90-90-90 strategy would require double the annual TB expenditure required by the baseline scenario. Over the first five years (from the base year 2015/16 to 2020/21), implementation of the TB 90-90-90 strategy would demand a 46% budget increase, including costs associated with a mass TB screening campaign. Over 20 years, a 22% budget increase will be needed to implement the TB 90-90-90 strategy.

Costs to the South African National TB Programme, ZAR millions 2015 to 2020

Cost component	2015/16	2016/17	2017/18	2018/19	2019/20	2020/21
Diagnostics	814.2	785.4	829.4	1 931.4	4 135.5	4 736.8
Smears	95.7	94.7	105.9	99.5	82.1	64.5
Culture	245.4	236.8	260.5	236.6	190.1	144.5
Xpert	429.8	414.4	420.5	1 395.1	3 232.7	3 659.4
LPA	8.2	5.3	6.3	7.5	7.5	6.6
X-rays	35.1	34.1	36.2	192.7	623.0	861.9
Treatment	529.2	539.1	627.9	700.6	672.2	577.1
Drug sensitive TB	111.1	107.6	114.8	101.6	80.0	62.2
MDR and XDR TB	418.1	431.5	513.1	599.0	592.2	514.9
Patient support	219.7	539.1	627.9	700.6	672.2	577.1
Patient health service usage	1 810.0	1 856.4	2 186.0	1 981.4	1 518.5	1 019.6
Non-MDR	180.6	174.9	186.4	164.9	129.8	100.8
MDR	1 629.3	1 681.5	1 999.6	1 816.5	1 388.7	918.7
HIV-TB	668.6	749.4	781.9	1 007.6	1 118.1	1 208.4
Program support	235.9	250.1	265.1	281.0	297.9	315.7
Program management	22.1	23.5	24.9	26.4	27.9	29.6
Service delivery	169.4	179.5	190.3	201.7	213.8	226.7
Health and community workforce	35.2	37.3	39.6	41.9	44.4	47.1
Community systems strengthening	9.2	9.8	10.4	11.0	11.6	12.3
Total costs	4 277.6	4 719.5	5 318.1	6 602.5	8 414.5	8 434.7

Modelling underscores that South Africa cannot achieve its TB targets solely by expanding the HIV response, as TB-related gains from expanded HIV programmes stabilize after 2025. However, reaching the HIV and TB 90-90-90 targets simultaneously would magnify results, reducing the population-based rate TB death rate by 87% over 20 years.

OPTIMISING THE FUTURE HIV RESPONSE IN SOUTH AFRICA

The Investment Case (IC) results indicate that South Africa's response to HIV is relatively efficient from an allocative perspective. Potential gains from changing the relative prioritization of interventions in South Africa's response are limited.

Given that resources will inevitably be finite, however, the IC worked to identify the optimal order of interventions to bring to scale in the event of funding limitations. To maximize allocative efficiency, the HIV response in South Africa should first scale up interventions that are cost-saving, in that they prevent HIV infections and reduce future needs for antiretroviral therapy. These include

- increasing condom availability to a maximum of about 570 million per year;
- increasing access to male medical circumcision, including for adolescents who are not currently targeted by the intervention (even though the IC results did not support prioritisation of one age group over another) to a maximum of 4 100 000 over the next five years, and
- social behaviour change communication that focuses on increasing HIV testing uptake in adolescents and discouraging them from having multiple sexual partners.

Using the money saved, the next cost-effective intervention would be to scale up ART to the greatest degree possible.

For all interventions included in the IC modelling exercise, the IC drew conclusions regarding appropriate next steps for each intervention. Using the incremental cost-effectiveness of the 90-90-90 scenario as the benchmark, the IC team grouped all interventions into three categories of cost-effectiveness.

Recommendation by intervention

Intervention	ICER (Cost per life year saved, ZAR)	Recommendation
1. Cost-effective		
Condom availability	Cost saving	Scale up, as this is the most cost-effective intervention amongst the list considered. However, since the number of protected sex acts is limited, it is not necessary to oversaturate the country with condoms as per current government targets.
MMC	Cost saving	Scale up as much as possible. However, the intervention will reach a saturation point, as there is a limit to the number of men willing to undergo circumcision even after taking into account demand creation efforts.
SBCC 1	Cost saving	Scale up
MMC targeting	Cost saving	Scale up as much as possible, and extend age targeting to younger age groups (aged 10-17) that are not covered under current policy. (Note that targeting each of the age groups is equally cost-effective.)
Testing at 6 weeks	749	Scale up
ART		
- Current guidelines	1,043	Scale up ART as much as possible. Increasing coverage under current guidelines is more cost-effective than extending the eligibility criteria to UTT, but the latter is necessary if achieving UNAIDS' 90-90-90 targets is a priority.
- Universal Test and Treat (UTT)	14,644	
HCT	5,978	Scale up. As the entry point in the treatment cascade, scaling up HCT is a prerequisite to scaling up ART.
SBCC 3	13,111	Scale up.

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Intervention	ICER (Cost per life year saved, ZAR)	Recommendation
2. Neutral		
PMTCT (Initiation of ART in pregnancy)	2,940	Although the model suggests scaling down the initiation of ART in pregnancy, this is primarily a result of PMTCT being made redundant once very high levels of ART coverage have been achieved. The IC does not recommend scaling down PMTCT under the status quo.
SBCC 2	N/A	The model is indifferent between scaling down and maintaining the high baseline levels of SBCC 2.
Testing of pregnant women	N/A	The model is indifferent between scaling down and maintaining the high baseline levels of testing of pregnant women.
3. Not cost-effective compared to cost-effectiveness of UTT, and once all of the above have been scaled up		
Testing of adolescents (15-19)	15,303	None of these interventions should be prioritised before universal testing and treatment (UTT) coverage has been achieved, as each is less cost-effective than UTT. For PrEP and microbicides in particular, this result hinges on the cost of the intervention; the likely public sector costs of these interventions remains unknown, requiring the IC modelling team to use assumptions.
Birth testing	36,710	
PrEP		
- for sex workers	106,452	
- for adolescents	304,776	
- for discordant couples	710,321	
Microbicides	304,776	
Condom education	5,781,471	
EIMC	295,239,305	

With respect to TE factors, critical enablers and development synergies, the largest potential impacts are gained by TE factors that reduce the loss to follow-up between HIV testing and ART initiation (point-of-care CD4 testing and provider-initiated testing). The only TE factor or enabler that is cost saving is adherence clubs for ART, which reduce the average cost of ART provision per patient as well as the total cost of the HIV programme. Generally, there is limited published evidence that critical enablers and development synergies have a considerable impact on life-years saved from preventing HIV infections and deaths. The enabler with the greatest impact is a community-based intervention for gender-based violence, through its reported impact on a reduction of multiple sexual partners.

Target population, coverage and impact on total cost and effectiveness for TE factors and enablers included in the Budget scenario

TE factor/ enabler	Target population	Coverage	% change in	
			total life years lost	total cost
1. TE factor				
a. for ART				
Adherence clubs	All adults currently on ART	2015: 10%	5%	-1%
		2016: 10%		
		2017: 20%		
		2018: 30%		
		2019: 40%		
		2020: 50%		
		2021: 60%		

TE factor/ enabler	Target population	Coverage	% change in	
			total life years lost	total cost
Home-based ART ^d	All adults currently on ART	2015: 0% 2016: 0% 2017: 3% 2018: 7% 2019: 10% 2020: 13% 2021: 17%	-	-1%
Point-of-care CD4 testing			8%	1%
b. for HCT				
Provider initiated HCT	All adults undergoing testing	25% of tests	5%	3%
Mobile HCT		25% of tests	3%	2%
Home-based HCT		15% of tests ^e	3%	2%
HCT invitations to pregnancy partners			6%	5%
2. Critical enablers				
SASA! Community-based gender-based-violence intervention	Intense intervention to adults 18-35 + community outreach; in HTA ^f only		3%	6%
Life skills and vocational training for adolescent girls	All adolescents aged 16-25 who aren't in education or employment		1%	1%
Risk reduction for alcohol and substance users	Alcohol and substance using adults		0.2%	1%
Risk reduction for substance users	Meth- and cannabis-using women 15+		0.1%	0.3%
School-based HIV/STI risk reduction	Same as Life skills curriculum ^g		2%	8%
2. Critical enablers				
Teacher support	Adolescents in informal settlements and rural areas with >28% ANC prevalence		1%	0.2%
Parental monitoring			2%	4%
School feeding			0.2%	2%
Positive parenting	High schools in low-income districts		1%	5%
Supporting adolescent orphan girls to stay in school			0.2%	6%
State-provided child-focused cash transfers	Adolescent orphan girls		0.01%	2%

d We did not assess the cost impact of this TE factor in isolation. We know that home-based care reduces the cost of first-line adult ART by 6%, but this likely doesn't translate into a saving in total cost.

e The remaining 36% of tests are assumed to be done through traditional stand-alone, clinic-based, non-targeted HCT.

f HTA: high transmission area

g These values are based on covering all adolescents, not only those covered by the life skills curriculum.

EXECUTIVE SUMMARY

BUDGET IMPLICATIONS OF IC RECOMMENDATIONS

Investments needed to reach the budget scenario for the HIV response are substantially greater than those currently available in South Africa. Distribution between programming areas remains roughly the same in the budget scenario as in the current national response.

Although annual investments in HIV and TB will need to increase in coming years to reach ambitious targets, including 90-90-90, required investments will begin to decline in 15-20 years.



CHAPTER 1

CONTEXT AND
BACKGROUND TO THE
INVESTMENT CASE



In 2011, UNAIDS convened a panel of leading experts to examine the optimal way forward in financing the global HIV response. The result was a proposed new approach that sought to shift the focus from spending *needs* to key *investments* required to achieve optimal results.[1] In essence, this new investment framework proposed a new way to approach HIV financing, with the ultimate aim of maximizing the strategic impact of HIV investments.

The investment framework called for prioritized spending on a limited set of basic programme activities – prevention of new HIV infections among children; condom promotion and distribution; focused programmes for certain key populations (notably female sex workers, men who have sex with men and intravenous drug users); treatment, care and support for people living with HIV (including HIV testing and antiretroviral therapy); voluntary medical male circumcision; and behaviour change programmes.[1] Under the framework, basic programme activities should be supported by critical social^a and programme enablers^b and by synergies with other development sectors.

Modelling used to inform development of the investment framework projected that up-front spending aligned with investment principles would enable HIV-related resource needs to decline in future years. As the investment framework was released, the first results emerged from a large-scale clinical trial indicating that antiretroviral therapy substantially reduces HIV transmission.[2] Following launch of the investment framework, several clinical trials also demonstrated the efficacy of pre-exposure antiretroviral prophylaxis, and clinical trial results in 2015 found that very early initiation of antiretroviral therapy confers a clear health benefit for people living with HIV.

The investment approach garnered broad support in the HIV and broader global health fields, although it was recognized that the continued evolution of the evidence base for HIV prevention and treatment might affect the precise funding levels or comparative allocations among various interventions, critical enablers and development synergies. Indeed, the investment approach outlined for the HIV response motivated other fields within global health to develop their own investment frameworks.[3]

In particular, the importance of taking an investment approach in the HIV response was underscored by evidence of more modest increases in international HIV support and the replacement of sharp annual increases in overall HIV spending with more modest increases more recently.[4] The uncertain financial outlook for the HIV response highlighted the need to leverage every iota of spending to achieve maximum impact. Aligning their efforts with investment principles, both the Global Fund to Fight AIDS, Tuberculosis and Malaria (GF) and the United States President's Emergency Plan for AIDS Relief revised their funding models and strategic priorities to maximize the strategic impact of investments.[5]

More recently, a strong global consensus has emerged that the tools now exist to end the AIDS epidemic by 2030.[6] In particular, South Africa has endorsed a new global target that provides that by 2020: (a) 90% of all people living with HIV will know their HIV status; (b) 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy; and (c) 90% of all people receiving antiretroviral therapy will achieve viral suppression.[6] Investments principles that aim to maximize the impact of investments will be essential to reaching these ambitious new targets to end the AIDS epidemic.[6]

a Critical enablers, which include both social and programme enablers, are 'activities that are necessary to support the effectiveness and efficiency' of basic programme activities. Social enablers make environments more conducive to sound HIV and TB responses. Social enablers include outreach for HIV testing and HIV treatment literacy, stigma reduction, advocacy to protect human rights, communications to raise awareness and promote changes in social norms, and monitoring of the equity, quality and results of programme access.

b Programme enablers help create demand for key services and improve the performance of basic programme activities. Programme enablers include incentives for programme participation, interventions to improve retention among patients receiving antiretroviral treatment, capacity building for community organisations, strategic planning, infrastructure for communications, dissemination of information, and improving service integration and linkage to care.

AN INVESTMENT CASE

To implement an investment approach to the HIV response, UNAIDS issued guidance regarding the development of a national investment case.^[7] Development of an Investment Case involves a systematic, data-driven, inclusive process to inform future investments in the national response, enhance the sustainability of the response, and enable forward-looking strategic planning. Dozens of countries have either development national investment cases or are in the process of doing so.^[5]

In developing an Investment Case, countries collect, analyse and synthesize available epidemiological data; evidence regarding the efficacy and cost-effectiveness of basic programme activities, critical enablers and development synergies; unit costs; and information on the national fiscal space, including the possibility of innovative ways of financing the national response. The process involves an exploration of service delivery models and approaches that are optimally effective and efficient. The process encourages other inquiries to enhance the impact and efficiency of national responses, such as better focusing programmes and resources on geographic settings and populations with heavy HIV burden and an unmet need for essential services.

A key element of the investment approach is to link investments with impact. After assembling an optimally strategic portfolio as a national response, the investment case uses available data on unit costs to estimate total investments required to implement the strategic plan of action. Drawing from available data on the impact of particular interventions and activities, modelling is used to project the short- and long-term impact of these investments on health outcomes and resource needs.

Through the investment case, national decision-makers and stakeholders are able to project the gap between resources likely to be available and amounts needed to implement an investment approach to achieve national health aims. The investment case offers an opportunity for agreement on the way forward to close these resource gaps.

SOUTH AFRICA'S INVESTMENT CASE FOR HIV AND TB

South Africa's Investment Case aims to inform the midterm review and the development of the next national plan for ending the HIV and TB epidemics through identification of the most cost-effective mix of interventions to address HIV and TB over the next 20 years. To assess cost-effectiveness, South Africa has used the cost per HIV or TB infection averted, as well as the number of life years saved, by the national programme as a whole. By charting an investment plan linked to clear health impacts, the Investment Case seeks to provide a roadmap for national decision-makers and to unite diverse stakeholders in a common undertaking.

As noted, an investment approach is useful for a broad array of health issues, as funding for any health priority is inevitably finite. Although developed specifically for HIV, the investment approach has particular relevance for South Africa's response to TB, an epidemic closely linked with HIV and a major health priority in its own right.

The South Africa investment case outlined here will inform development of a new National Strategic Plan for HIV, TB and STIs (NSP). The investment case differs from the National Strategic Plan in that the former explicitly quantifies the returns on health investments.

To develop South Africa's investment case for HIV and TB, the South African National AIDS Council (SANAC) convened an intensified national dialogue on future directions for the country's response to HIV and TB. A broad array of national partners has been engaged at all stages in this dialogue, including civil society groups. SANAC structures and other governance bodies, as well as various partnership forums, were used to obtain input on investment priorities. One

important aspect of the process for development of the Investment Case has been an intensification of dialogue between HIV and TB programmes and between the HIV and TB sectors and authorities responsible for guiding national development efforts.

The intent of the Investment Case is to aid diverse governmental decision-makers, including the Cabinet, SANAC, and premiers and AIDS councils at the provincial, district and local levels. In recognition of the multi-sectoral nature of the HIV and TB challenge and the focus in the Investment Case on financing, potential users of the Investment Case extend well beyond the health sector, encompassing the national Treasury and key non-health national departments. Recognising the central role that civil society plays in the national response, it is hoped that civil society advocates and civil society participants on AIDS councils will be key users of the Investment Case.

The Investment Case is also closely linked with development of a new proposal for funding from the GF during a funding round which will extend from 1 April 2016 through 31 March 2019. Informed by the work of the Investment Case, the new proposal will support implementation of the 90-90-90 strategy.^c

For the South Africa Investment Case, the following nine (9) basic programme activities were included:

- Focused interventions for key populations at higher risk
- Elimination of new HIV infections among children
- Social and behaviour change programmes
- Comprehensive condom promotion and distribution
- Treatment, care and support for people living with HIV
- Voluntary medical male circumcision
- HIV counseling and testing
- Tuberculosis screening, diagnosis and treatment
- Other biomedical prevention (e.g., pre-exposure prophylaxis, post-exposure prophylaxis, STI treatment).

Gaps in available data posed a challenge to the development of South Africa's Investment Case. Although South Africa's HIV and TB epidemics are arguably the most carefully studied in the world, questions nevertheless persist regarding certain aspects of the epidemic and response. Likewise, as this report's review of the evidence for the efficacy of various programmatic activities indicates, the available evidence base is not always enlightening as to everything that would be ideal to know for each of these interventions. It was also impossible for this Investment Case to predict or reliably anticipate how technologies and strategies to address HIV and TB might evolve in future years. The Investment Case here is based on the best evidence available as of January 2015, as interpreted by the experts who participated in the development process.

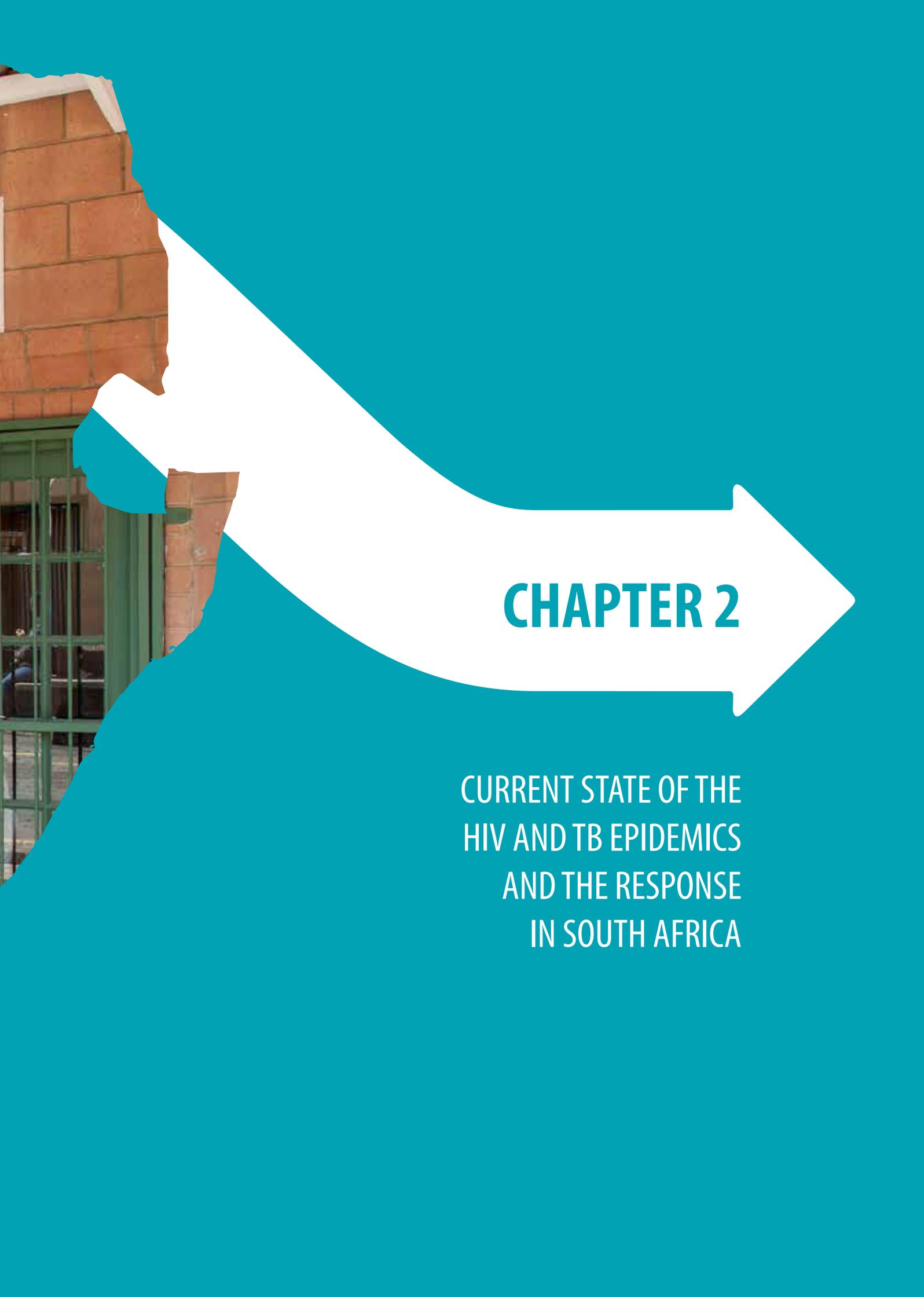
^c The 90-90-90 strategy refers to a new global target for the AIDS response. By 2020: (a) 90% of all people living with HIV will know their HIV status; (b) 90% of all people with diagnosed HIV infection will receive sustained antiretroviral therapy; and (c) 90% of all people receiving antiretroviral therapy will achieve viral suppression.

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CHAPTER 2

CURRENT STATE OF THE
HIV AND TB EPIDEMICS
AND THE RESPONSE
IN SOUTH AFRICA

2.1 STATE OF THE HIV AND TB EPIDEMICS IN SOUTH AFRICA

HIV and TB represent among the most serious of all health threats to the people of South Africa. In 2014, HIV alone accounted for nearly one-third of all deaths in South Africa. However, important progress has been made in reducing the toll that these two disease exact on the health and well being of South Africa’s people.

2.1.1 State of the HIV epidemic

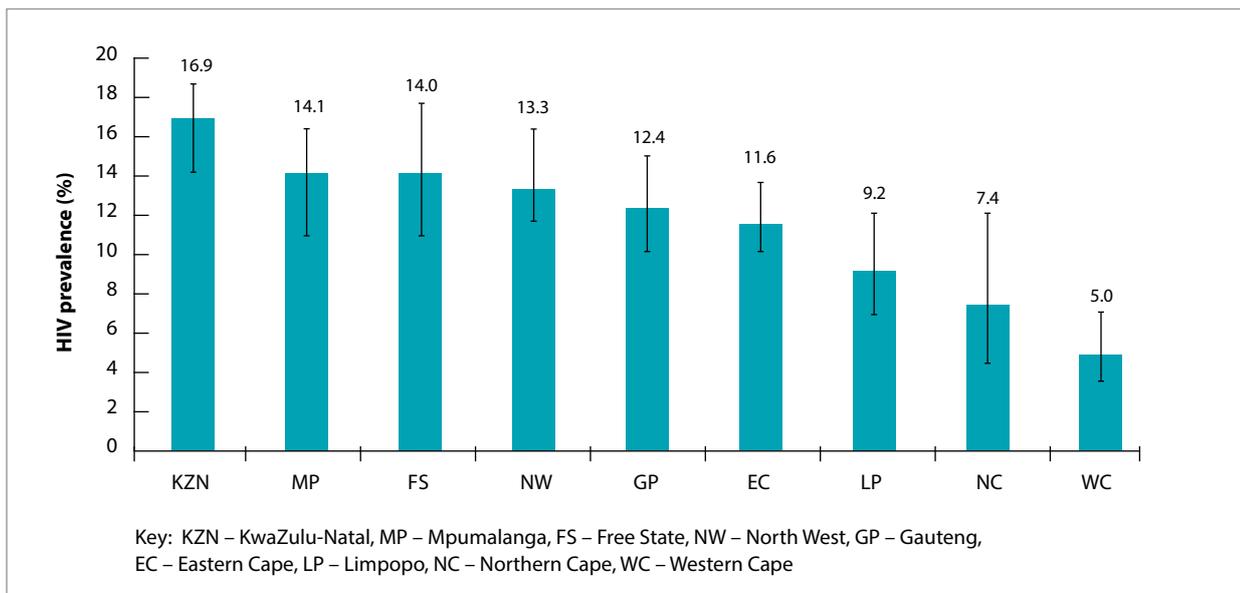
An estimated 6.3 million people in South Africa were living with HIV in 2013, representing 18% of all people living with HIV worldwide [1]. An estimated 12.2% of South Africa’s population, including 18.8% of adults ages 15-49, were living with HIV in 2012 [2].

HIV prevalence appears to be increasing. National surveys by the Human Sciences Research Council (HSRC) found that the percentage of the overall population living with HIV rose from 10.6% in 2008 to 12.2% in 2012 [2]. The number of people living with HIV in South Africa has also increased, from 5.6 million in 2005 to 6.3 million in 2013 [1]. The increased life expectancy of people receiving antiretroviral therapy is primarily responsible for the increase in HIV prevalence [3].

Variations in South Africa’s HIV epidemic

Although every corner of South Africa has been affected by HIV, certain parts of South Africa experience much heavier HIV burden than others (Figure 1). Provincial HIV prevalence in 2012 ranged from a low of 5.0% in the Western Cape to 16.9% in KwaZulu-Natal [2]. Next to KwaZulu-Natal, Mpumalanga has the second highest provincial HIV prevalence, at 14.1% [2]. The epidemic’s impact also varies within provinces, with a district-level analysis finding that the epidemic is most heavily concentrated in 13 districts in the provinces of KwaZulu-Natal, North West and Mpumalanga [4].

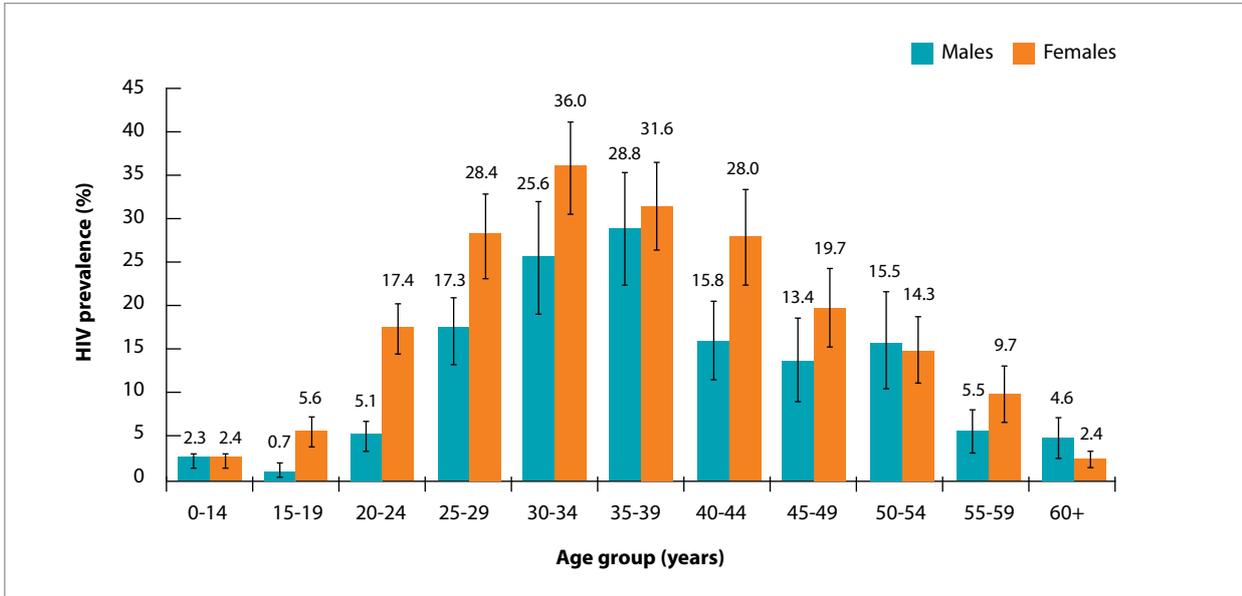
Figure 1: HIV prevalence by province (from [4])



HIV prevalence is higher among women than among men in every age cohort except people over age 50 (Figure 2).[2] Especially striking gender imbalances in HIV risk are apparent in younger age cohorts. While 5.6% of females ages 15-19

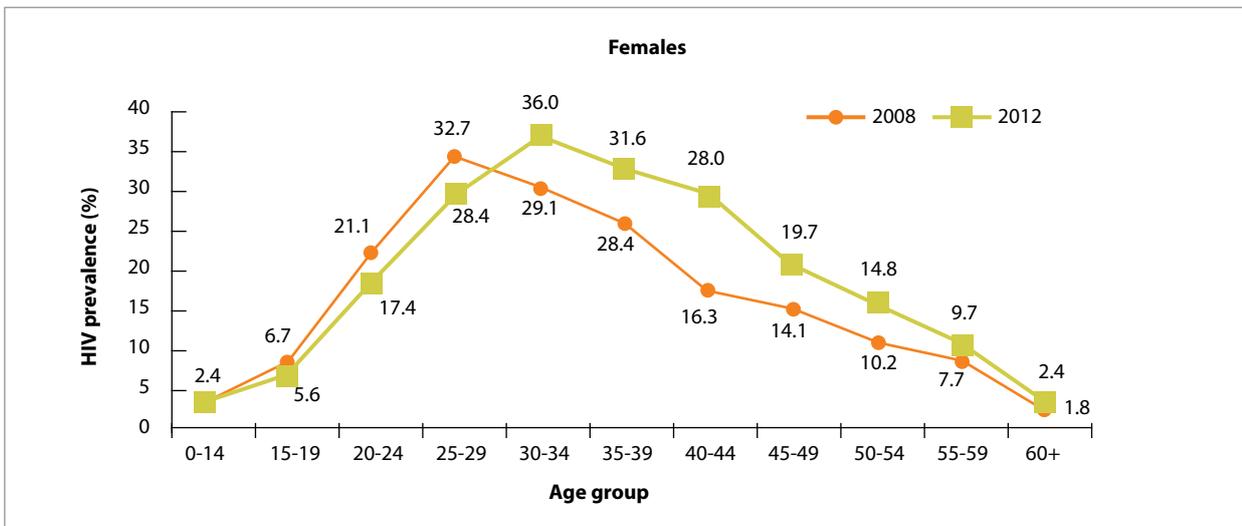
were found to be living with HIV in 2012, only 0.7% of males in these age group tested HIV-positive.[2] Among 20-24-year-olds, females are more three times more likely to be living with HIV than their male counterparts (17.4% to 5.1%).[2]

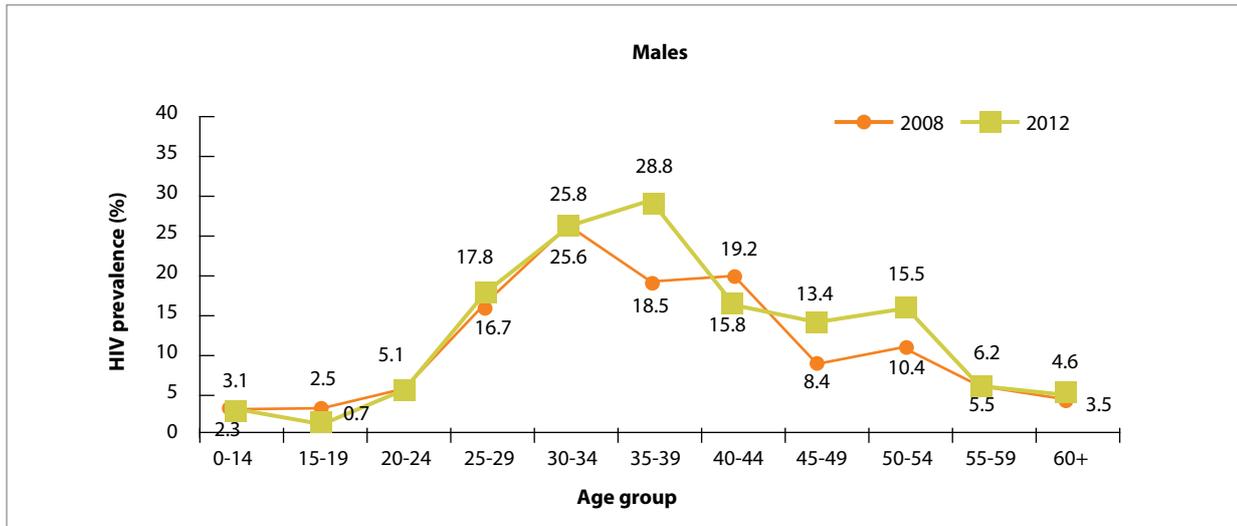
Figure 2: HIV prevalence by sex and age (from [4])



Among age groups, HIV prevalence is highest among people over age 25 (19.9% in 2012).[2] Thereafter, HIV prevalence declines with age, with 12.6% of those over 50 living with HIV in 2012.[2] Peak HIV prevalence tends to occur earlier in life for women (30-34 years) than for men (35-39 years), a reflection of the disproportionate risk and vulnerability experienced by adolescent girls and young women .[2]

Figure 3: HIV prevalence in females (a) and males (b) by age, 2008 and 2012 (from [4])





New HIV infections

An estimated 340 000 people in South Africa were newly infected with HIV in 2013.[1] This reflects major progress in the AIDS response since 2005, when 560 000 people acquired HIV infection in South Africa.[1]

HIV incidence is the rate at which new HIV infections are occurring within a population, as measured by the proportion of the population newly infected within a given time period (typically a year). Between mid-2011 and mid-2012, it is estimated that South Africa nationally had an HIV incidence rate of 1.5% to 1.7%.[5]

In 2012, women in South Africa (2.28% incidence) were almost twice as likely to become infected with HIV as men (1.21). [2] Among 15-24-year-olds, young females (2.54% incidence) were more than four times more likely to become infected as young males (0.55%).[2] Of all population groups studied, women ages 20-34 had the highest HIV incidence in 2012, with 4.5% becoming infected each year.[2]

Risk of HIV acquisition involves a combination of biological and behavioural factors. South Africa’s national HIV survey in 2012 offered cause for concern regarding behavioural trends, finding a decrease in reported condom use compared to 2008 in every age group except those over age 50.[2] Among sexually active people over age 15, the 2012 survey also noted an increase in multiple sexual partnerships.[2]

HIV among children and young people

In 2013, 16 000 children under age 15 were newly infected with HIV.[1] The number of new HIV infections among children in 2013 was less than half the number reported in 2009, when 33 000 children acquired HIV.[1] From 2002 to 2012, HIV prevalence among children ages 2-14 fell from 5.6% to 2.4% -- a notable departure from the increase in HIV prevalence in recent years among adults.[2]

Rapid expansion of services to prevent mother-to-child HIV transmission is primarily responsible for this sharp decline in the number of children newly infected. The share of South African newborns exposed to HIV has not declined, as HIV prevalence among pregnant women attending antenatal clinics has remained steady, at 29.5% in 2012.[2] Highest HIV prevalence among women attending antenatal clinics in 2012 was in KwaZulu-Natal (37.4%), Mpumalanga (35.6%) and Free State (32.0%).[2]

Although the epidemic continues to pose profound risks for young people in South Africa, especially adolescent girls and young women, there is good news here as well. Among 15-24-year-olds, HIV prevalence fell from 8.7% in 2008 to 7.1%

in 2012.[2] While trends in HIV prevalence are an imperfect proxy for HIV incidence in the larger population, in large part due to the effects of antiretroviral therapy on life expectancy, declines in HIV prevalence among young people are much more likely to reflect actual reductions in new HIV infections.

HIV among key populations

In South Africa, as in every other country, some populations are more heavily affected by HIV than others. According to the 2012 national survey, the highest HIV prevalence was found in the following populations for whom national-level data were available:

- Black African women (ages 20-34) – 31.6%
- People living together but not married – 30.9%
- Black African men, 25-49 years – 25.7%
- Disabled persons over age 15 – 16.7%
- High-risk drinkers over age 15 – 14.3%^[2]

South Africa lacks national data on HIV prevalence in other populations that experience elevated risks globally, such as men who have sex with men (MSM), female sex workers (FSW) or people who inject drugs (PWID). However, cohort studies have found high prevalence among these populations. One survey of MSM in the Soweto found that 13.2% of study participants were living with HIV.^[6] Other studies have detected elevated HIV prevalence among PWID ^[7] and FSWs.^[8]

AIDS-related mortality

AIDS remains an important cause of mortality in South Africa. In 2014, 171 733 people die of AIDS-related causes in South Africa, representing 31% of all deaths in South Africa that year.^[9]

Despite the continuing gravity of the HIV epidemic, far fewer people in South Africa are dying of AIDS-related causes today than in previous years. The number of AIDS-related deaths in 2014 was less than half the number in 2005, when 363 910 people died.^[10] The proportion of deaths in South Africa attributed to AIDS has also fallen, from 51% in 2005 to 31% in 2014.^[10]

2.1.2 State of the TB epidemic

Tuberculosis (TB), the disease caused by *Mycobacterium tuberculosis*, is a global public health threat. The World Health Organization (WHO) estimated that in 2013 there were 9 million TB cases and 1.5 million deaths from TB globally ^[11]. WHO classifies South Africa as having a high burden of TB, including a high burden of drug-resistant (DR) TB. In 2013, South Africa reported and initiated on treatment 328 896 TB cases, including 10,663 multi-drug resistant (MDR) TB cases. In 2013, an estimated 89 000 people (low estimate: 62,000; high estimate: 121,000), including HIV-negative and HIV-positive persons, died of TB in South Africa ^[11].

The TB epidemic in South Africa has largely been driven by the HIV epidemic. Key populations in South Africa who are at increased vulnerability for TB infection and active TB disease include people living with HIV, household contacts of people with TB, miners, inmates, health care workers, correctional services officers, and people with diabetes. TB was the leading cause of death reported in South Africa in 2011 (10.7% of all deaths), 2012 (9.9%) and 2013 (8.8%) ^[12].

TB incidence, prevalence and case notifications

Prevalence and incidence of active TB in South Africa is estimated from transmission models, as South Africa has not yet completed a national TB prevalence survey. According to WHO estimates, 450 000 (410 000 to 520 000) new cases of TB occurred in South Africa in 2013. TB prevalence was estimated at 380 000 (210 000 to 590 000) in 2013. As Figure 4 and Figure 5 indicate, these figures are equivalent to an incidence rate of 860 (776 to 980) and prevalence rate of 715 (396 to 1,126) per 100 000 population [11].

Figure 4: WHO estimates for incident TB cases in South Africa, 1990 - 2013

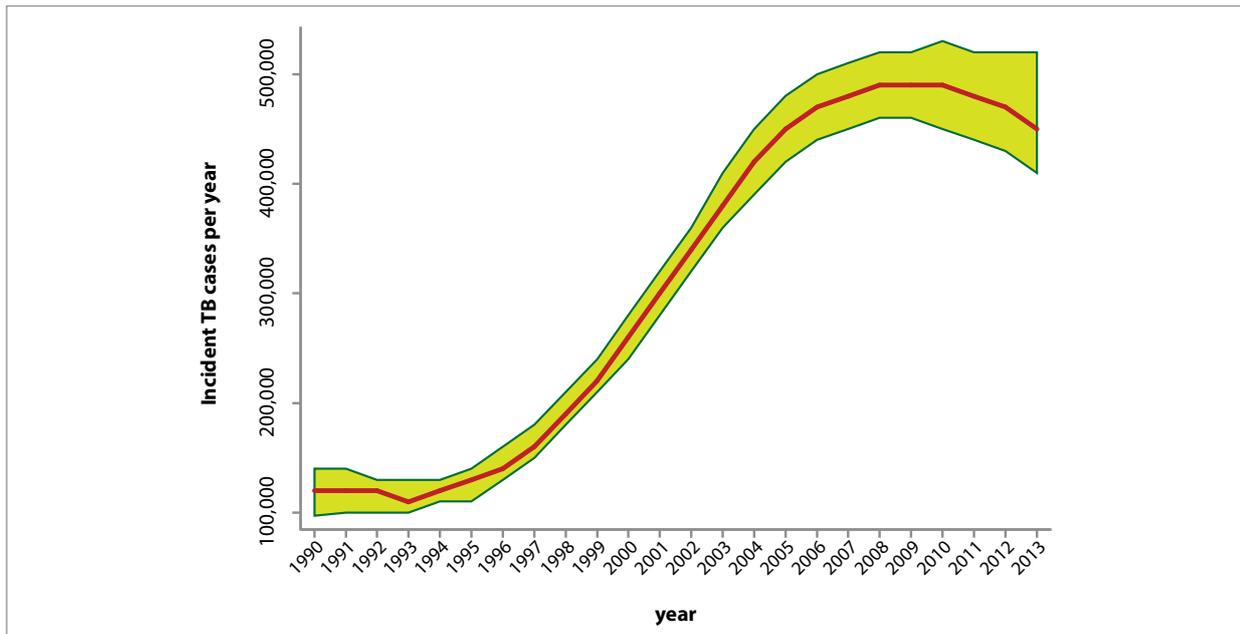


Figure generated using data downloaded from the WHO TB database, accessed May 2015 [13]

Figure 5: WHO estimates for prevalent TB cases in South Africa, 1990 – 2013

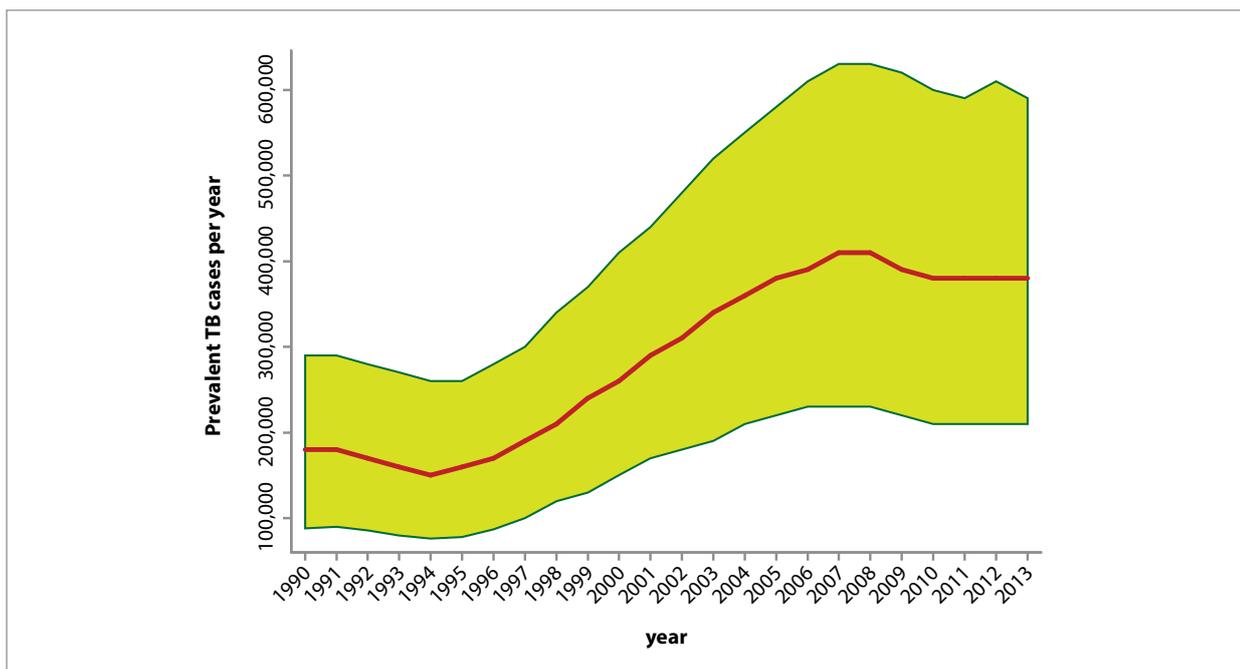


Figure generated using data downloaded from the WHO TB database, accessed May 2015 [13]

Persons who have active TB disease may self-cure (i.e., the disease resolves without medication) or die prior to being diagnosed. Persons with TB disease may also die after diagnosis but prior to initiation of TB treatment. Based upon case registration data reports, WHO estimates that only 69% of prevalent TB in South Africa is detected and initiated on treatment [11]. As Figure 6 indicates, the number of individuals who have TB and whose TB is diagnosed and reported as a case to the TB programme on a paper-based or electronic TB register (ETR.net) began increasing in the late 1990s and peaked in 2009 at 405 982 cases. In 2013, 328 896 cases of TB were reported in South Africa, equivalent to a case registration rate of 621 per 100,000 population. Children under 15 years of age accounted for 11% of all case registrations. Pulmonary TB accounted for 87% of TB cases; 10% were classified as retreatment cases (i.e., patients with a previous history of TB) [11].

Figure 6: TB cases registered in South Africa, 1995 - 2013

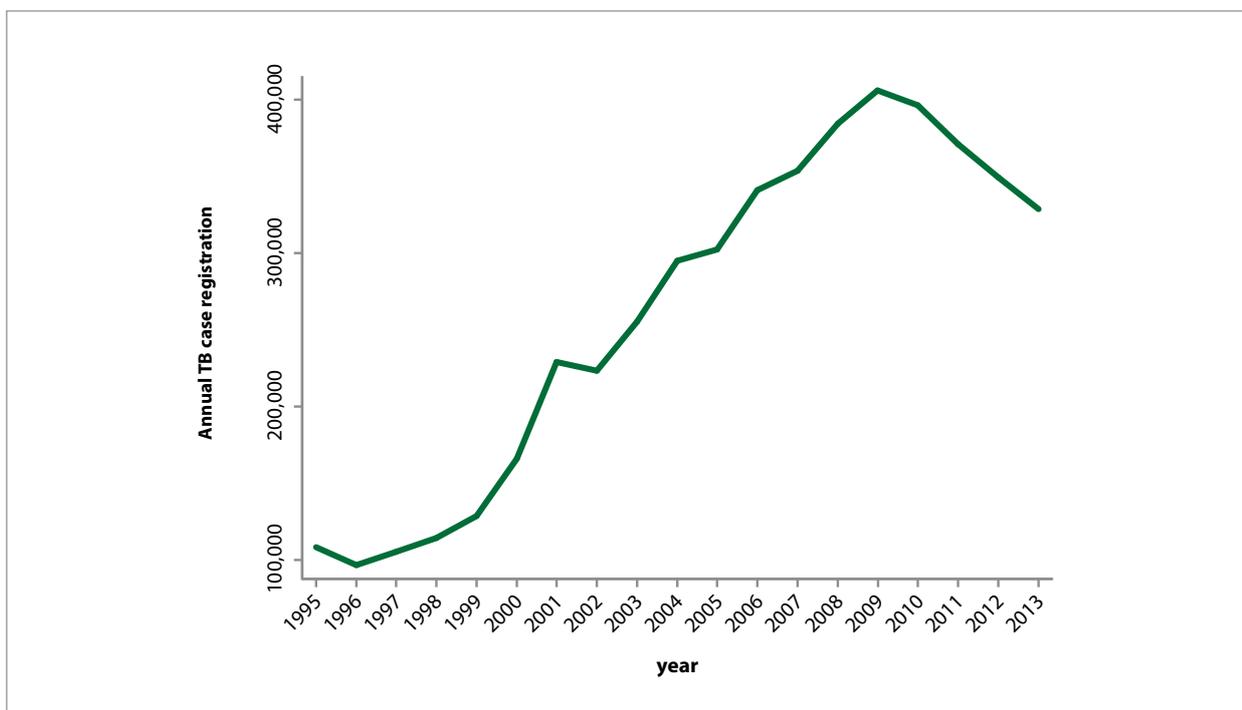


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Drug-resistant TB

First-line treatment for TB includes rifampicin, isoniazid, pyrazinamide, and ethambutol. Rifampicin-resistant TB (RR TB) – including multi-drug resistant (MDR-TB, TB that is resistant to both rifampicin and isoniazid), and extensively drug resistant TB (XDR TB, TB that is resistant to rifampicin, isoniazid, a fluoroquinolone (e.g. ofloxacin) and a second-line injectable medicine, e.g. kanamycin) – requires second-line TB treatment. A national drug resistance survey is currently underway, the first since 2001. In 2013, 26 023 persons were diagnosed with either RR TB or MDR TB [11]. As Figure 7 indicates, diagnosis of RR TB (including MDR TB) has significantly increased.

Figure 7: Diagnoses of RR TB, 2005 – 2013 in South Africa

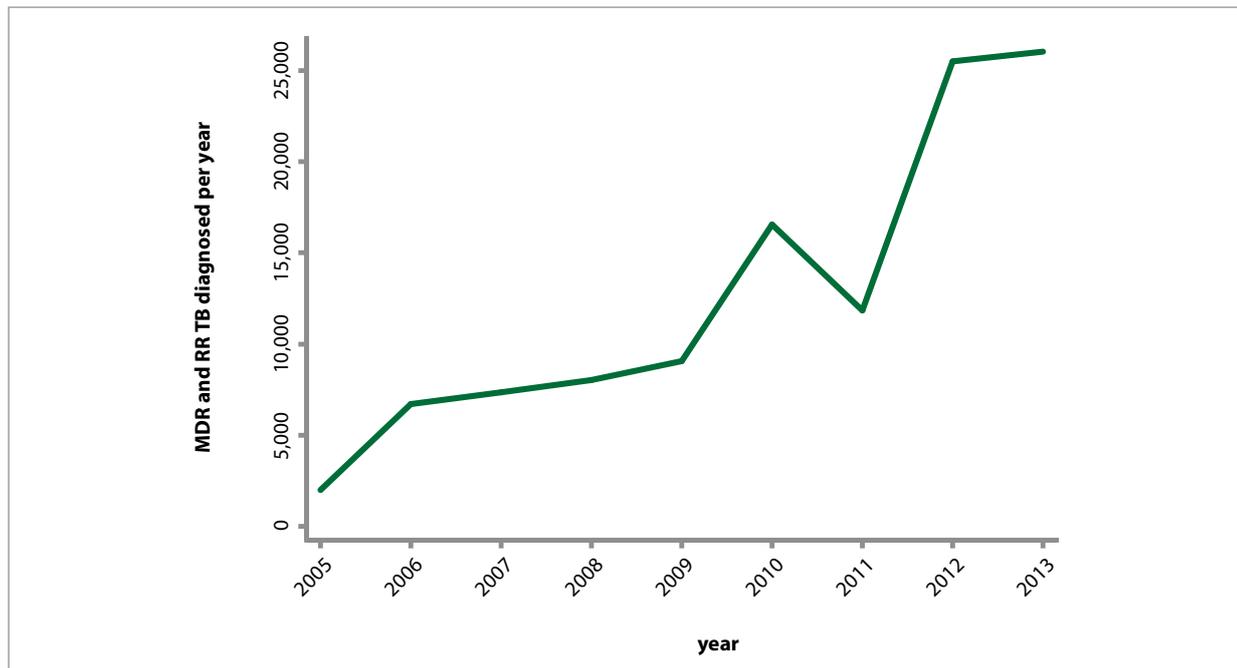


Figure generated using data downloaded from the WHO TB database, accessed May 2015 [13]

2.2 THE CURRENT HIV AND TB RESPONSE IN SOUTH AFRICA

South Africa's response to the linked epidemics of HIV and TB has inspired the world, driving many of the recent regional and global gains that have galvanized the global community to begin planning bringing an end to the global HIV and TB epidemics. However, both diseases persist as major health challenges in South Africa.

2.2.1 The current HIV response

South Africa's response to HIV and TB is guided by the NSP, which specifies five primary goals: (1) reducing new HIV infections by at least 50%; (2) initiating at least 80% of eligible patients on antiretroviral treatment (ART), with 70% alive five years after initiation; (3) reducing the number of new TB infections and deaths from TB by 50%; (4) ensuring an enabling and accessible legal framework that protects and promotes human rights; and (5) reducing self-reported stigma related to HIV and TB by at least 50%. Towards these aims, SANAC, a representative body of all stakeholders in government, the private sector, non-governmental organisations and civil society, oversees and coordinates the national response.

HIV prevention for adolescents and adults

South Africa's efforts to prevent new HIV infections reflect a combination prevention approach, including HIV counselling and testing (HCT), condom distribution, management of sexually transmitted infections (STIs) and tuberculosis (TB), as well as scale-up of ART, which has both therapeutic and preventive benefits. South Africa has also embarked on a major national effort to scale up voluntary medical male circumcision (MMC).

As noted in the previous section on the state of the HIV epidemic, the number of new HIV infections declined by nearly 40% from 2005 to 2013. This pace, while favourable, is short of the goal in the *2011 Political Declaration on HIV and AIDS* to reduce sexual HIV transmission by 50% from 2010 to 2015.

HCT. The percentage of South Africans tested in the last 12 months rose from 32.3% in 2009 to 38.1% in 2012 [14], in part as a result of a major HCT campaign launched in April 2010.

Condoms. The number of condoms distributed in South Africa declined from 492 million in 2010 to 352 million in 2013. [4] The country is now aiming to distribute 1 billion condoms in 2016.

Other key populations. SANAC collaborated with partners to develop Operational Guidelines for HIV, STIs and TB Programmes for key populations in South Africa, including MSM and FSWs. Particular strides have been made in expanding prevention services for FSWs, with 60% of FSWs reached by prevention programmes in 2014. [4] The prevention response for people who inject drugs remains limited. [4]

MMC. In 2012-2013, 514 991 men in South Africa were circumcised, representing 12% of the national target of 4.3 million circumcisions but near the national target for 2012-2013 of 600 000 MMC procedures. [4] An important challenge in the national drive to scale up MMC is the persistence of traditional circumcision practices, which vary widely and do not always meet the requirements of MMC.

Other prevention measures. National partners have launched the Zazi campaign, which aims to reduce HIV vulnerability of young girls and women. National efforts continue to focus on making youth-friendly sexual and reproductive health available and accessible in schools. HIV-related communication continues to reach large segments of the South African population, with 82% of people ages 16-55 reportedly reached with HIV-related communications in 2012. [14]

Prevention of new HIV infections among children

South Africa is committed to universal coverage of services to prevent mother-to-child transmission of HIV (PMTCT). In accordance with international guidelines, South Africa provides fixed dose combinations of ART to treat pregnant women living with HIV, regardless of their CD4 count. The proportion of pregnant women initiating lifelong ART rose from 64.1% in 2010-2011 to 75.4% in 2011-2012. [4] The six-week transmission rate from mother to child continues to fall, from 3.5% in 2010 to 2.7% in 2011. [4]

Over the last 10 years, the number of HIV-exposed children receiving early infant diagnostic services increased 100-fold, with 350 000 children tested in 2012 during the first two months of life. In 2013, an estimated 75.3% of HIV-exposed children received early infant diagnostic services – a level of coverage substantially higher than the global average. [4]

HIV treatment

South Africa has the largest ART programme in the world, with domestic sources accounting for more than 75% of all HIV spending. From 2009 to 2012, there was a four-fold increase in the number of people receiving ART in South Africa. [4] In 2012, 42% of all adults living with HIV were receiving ART. [4] Although globally children living with HIV are significantly less likely than adults living with HIV to receive ART [1], paediatric HIV treatment coverage was actually higher in South Africa in 2012-2013 (44%) than adult coverage. [4] In 2012-2013, 612 118 people in South Africa initiated ART, exceeding the national target of 500 000. [4]

South Africa has supported ART scale-up with important investments in health systems. The number of nurses trained in nurse-initiated management of ART increased from 10 000 in 2011-2012 to 23 000 in 2012-2013. [4] South Africa is also a global leader in scaling up viral load testing, leveraging its own negotiation of a favourable price from Roche, the maker of the leading viral load testing platform, to achieve a new global price ceiling that will enable more rapid scale-up of this essential diagnostic tool in other countries.

South Africa has enthusiastically embraced the 90-90-90 treatment target and taken steps to align its national programme with this ambitious new target for 2020. In contrast to earlier treatment targets, which focused exclusively on the number of people initiating ART, the 90-90-90 target addresses outcomes along the HIV treatment cascade, with the ultimate aim of maximizing the number of people living with HIV who achieve viral suppression. Retention in care for people enrolled in ART in South Africa declined in 2012-2013, underscoring the importance of enhanced results across the treatment cascade and highlighting the need to strengthen tracking systems for ART patients.[4]

Human rights and gender equality

South Africa has worked to ground its HIV response in principles of human rights and gender equality. A National Council against Gender-based Violence has been established, overseeing the 16 Days of Activism against Violence campaign. Several legislative initiatives have strengthened protections against gender-based violence (GBV). The National Prosecution Authority leads the multi-partner implementation of the Thuthuzela Project, which seeks to provide a robust, integrated response for rapid victims.

Discrimination on the basis of HIV status is illegal under South Africa law. The 2012 HSRC survey indicates that the prevalence of stigmatizing attitudes towards people living with HIV has declined.[2] SANAC is currently working to implement the People Living with HIV Stigma Index, which measures trends relating to stigma and discrimination experienced by people living with HIV.[4] The South African Human Rights Commission's Flowcentric Complaints System has been upgraded to improve the handling and investigation of complaints of human rights violations.

2.2.2 The current TB response

In 2013, WHO and the NDOH commissioned a systematic review of the epidemiology and programmatic response to TB in South Africa. The Centre for Evidence Based Health care produced six new systematic reviews to inform South African TB Policies project, EVISAT (<http://www.cebhc.co.za/research-key-outputs/research-evisat/>). These reports are available for download at <http://www.afro.who.int/en/south-africa/country-programmes/4247-tuberculosis-tb.html>.

A recent review in the South African Medical Journal [15] highlighted the successes and challenges of South Africa's TB response, listing key achievements of National TB Programme (NTP) from 1997 to 2013 (Table 1).

Table 1: South African National TB Programme (NTP) milestones, 1997 to 2013

Year	Milestone
1997	Phased implementation of directly observed treatment support Establishment of demonstration and training districts
1999	Introduction of fixed dose combination drugs Establishment of TB and HIV pilot districts
2000	MDR TB treatment guidelines endorsed Establishment of MDR treatment facilities
2001	National TB drug resistance survey
2002	Launch of the Medium Term Development Plan, 2002 - 2005 Guidelines for IPT for TST-positive, HIV-infected persons

Year	Milestone
2003	TB declared an emergency and TB crisis plan launched Electronic TB register introduced
2005	Minister of Health signs 'Declaration of TB as an emergency in AFRO region'
2006	Development of MDR TB and XDR TB action plan
2007	Launch of the National TB Strategic Plan 2007 - 2011 Development of infection control guidelines for TB
2008	Introduction of Hain M.TBDRplus as a rapid test for MDR TB First South African TB conference
2009	'Health in South Africa' series published in the <i>Lancet</i> , including recommendations for TB/HIV WHO review of the National TB Programme
2010	IPT for 6 months for all HIV-infected persons, regardless of TST status ART for TB patients living with HIV with CD4 counts <350 cells/ μ l
2011	Introduction of Xpert MTB/Rif as a replacement for sputum smear microscopy National HIV/TB campaign Management of drug-resistant TB policy guidelines approved Decentralised management of MDR TB introduced
2012	SA President signs SADC declaration on 'TB in the mines' ART for all HIV-infected TB patients Streptomycin removed from retreatment regimen
2013	NDoH guidelines for managing TB/HIV in prisons issued IPT for at least 36 months for TST-positive HIV-infected persons National drug resistance survey Independent WHO Review of NTP

TB/HIV integration

People living with HIV are at increased risk of TB disease and mortality, although initiation of ART significantly reduces these risks [15, 16]. Since 2009, the NDOH has prioritized expanded integration of HIV and TB services. As Figure 8 reveals, this has generated concrete results, reflected in increasing uptake of HCT and ART by TB patients in South Africa, 2004 to 2013.

Figure 8: HCT and ART for TB cases, 2004 to 2013

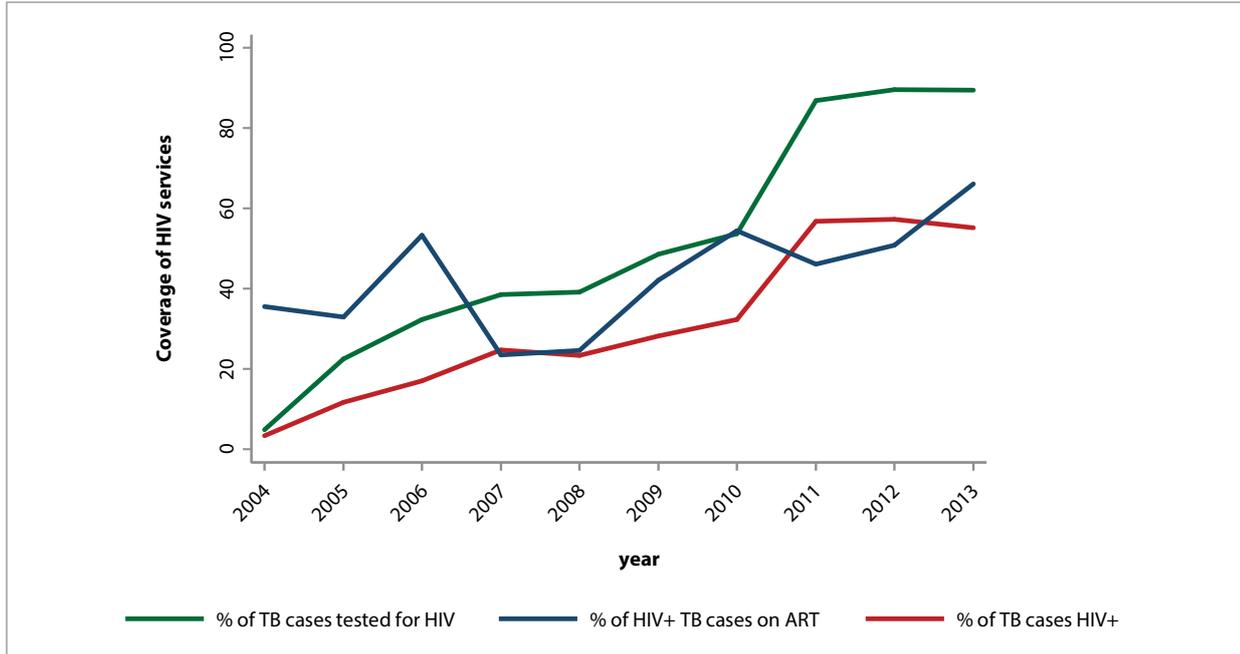
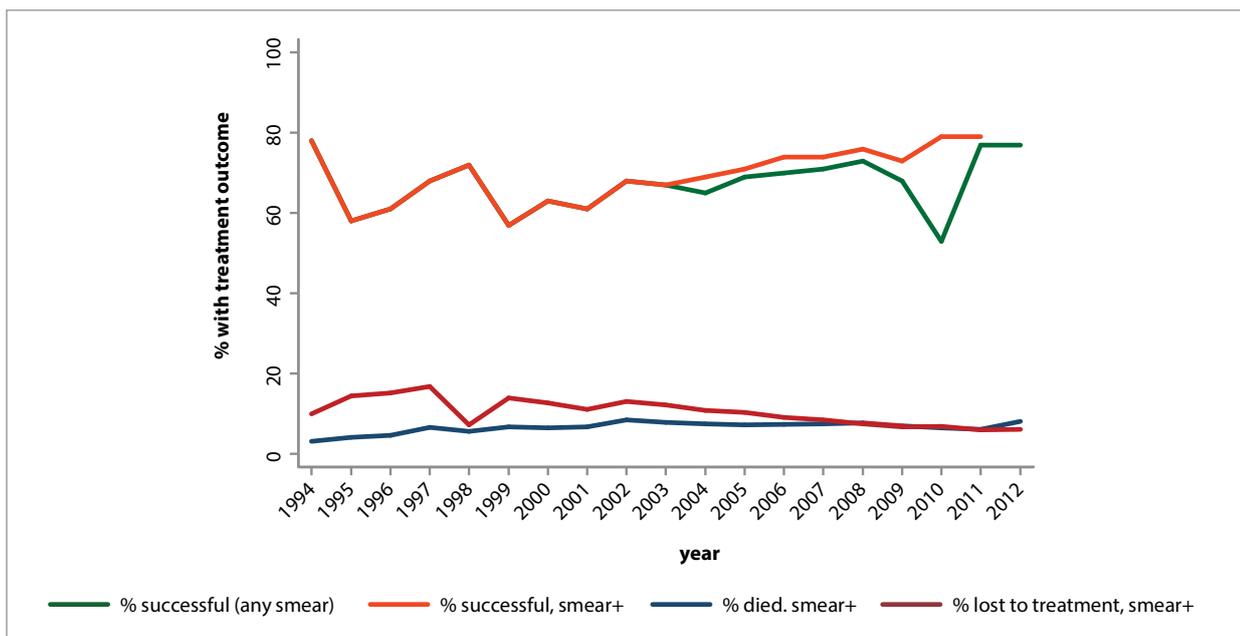


Figure generated using data downloaded from the WHO TB database, accessed May 2015 [13]

TB treatment initiation and outcomes

The combined responses to TB and HIV in South Africa have resulted in improvements in TB treatment outcomes. As Figure 9 demonstrates, the proportion of smear positive TB patients who successfully complete six months of TB treatment significantly increased from 2004 to 2012. This increase was a result of reductions the share of patients who were lost to follow up (10.2% in 2004 to 6.2% in 2012) and who died during TB treatment (7.3% in 2004 to 5.8% in 2012).

Figure 9: Trends in the proportion of smear positive TB patients who successfully completed TB treatment 1994 to 2012



Note: The 2012 data includes all TB cases (any smear status), not just smear positive TB

Figure generated using data downloaded from the WHO TB database, accessed May 2015 [13]

In 2013, 10 663 persons with either RR or MDR TB were initiated on second-line TB treatment. While access to RR TB treatment has increased, a substantial gap persists between the number of cases diagnosed with RR TB and the number of patients initiating treatment, see Figure 10. As the two data sources for this information use different methodologies – the number of cases diagnosed is based on data from the National Health Laboratory Services and the number of cases initiating treatment is based on data from the EDRweb – it is possible that methodological issues account for a portion of this gap.

Figure 10: RR TB diagnosis and RR TB treatment initiation, by year 2005-2013

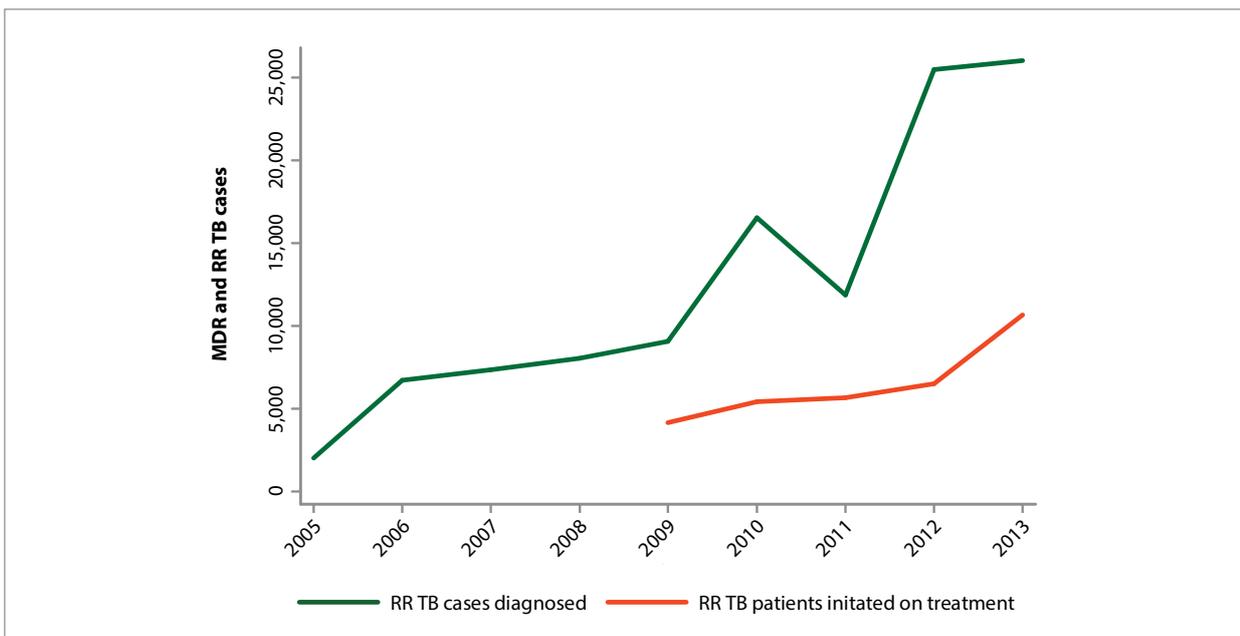


Figure generated using data downloaded from the WHO TB database, accessed May 2015

RR TB treatment has a higher frequency of adverse drug reactions and is more expensive than first-line treatment. Overall treatment outcomes are poor among patients with drug resistance, with only 45% of the RR or MDR TB patients initiated on second-line treatment in 2011 having a successful treatment outcome, i.e. were either cured or completed the 18-24 months of treatment [11]. Figure 11 depicts the rates of treatment success, loss to follow-up during treatment and death during treatment for MDR TB and XDR TB, respectively.

Figure 11: MDR and XDR TB treatment outcomes, 2007 to 2011 cohorts

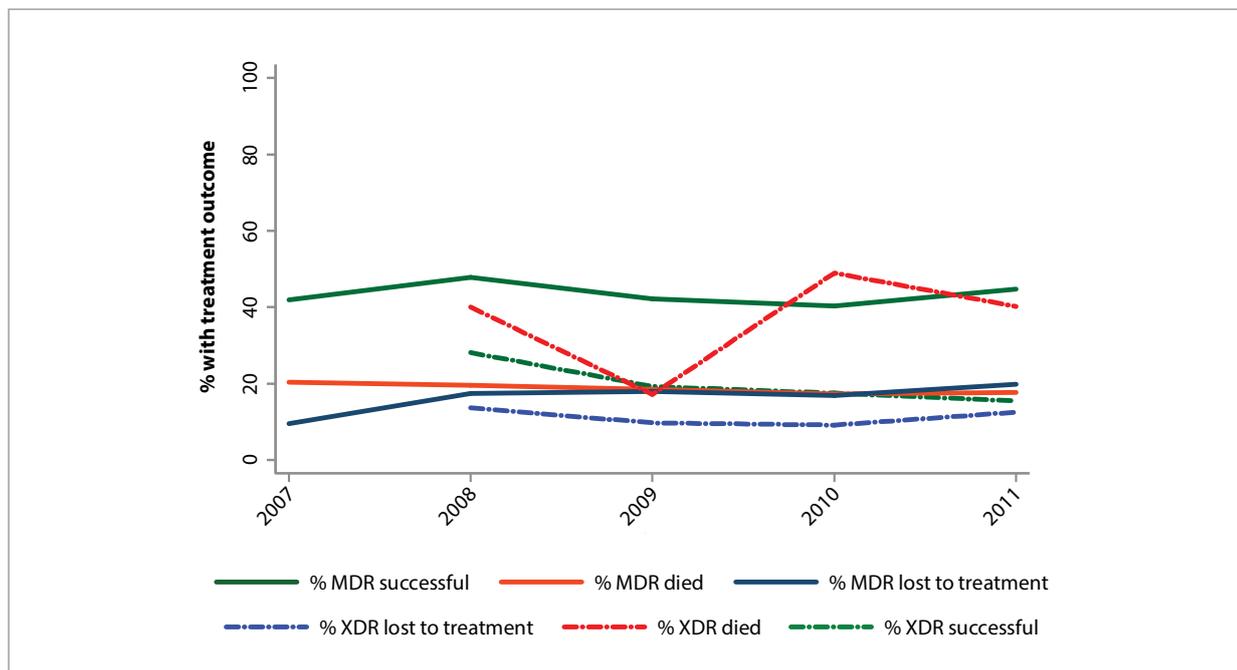


Figure generated using data downloaded from the WHO TB database, accessed May 2015 [13]

2.3 PAST AND CURRENT SPENDING ON THE HIV AND TB RESPONSE IN SOUTH AFRICA (2011/12 – 2013/14)

Understanding past trends and patterns in HIV spending provide a baseline for considering future funding. In addition, a review of funding patterns provides insight on likely funding trends for HIV and TB in the near future.

To characterise previous spending trends, a retrospective analysis was undertaken of past spending on HIV, AIDS and TB in South Africa (SA). Three funding sources were consulted: the SA government, the United States Government (USG) and the Global Fund (GF). Missing from this first phase are other external sources, which only accounted for 3% in 2010/11, and private sources, which represented 8.3% of all expenditure, according to the National AIDS Spending Assessment (NASA). Additional external sources will be added in the second phase of the South African Investment Case (SA IC). Expenditure data summarised in this chapter are presented according to the agreed interventions of the SA IC.

2.3.1 Overview: Financing for HIV and TB in South Africa

HIV and TB services in South Africa are funded through public revenue, external development partners (donors) and the private sector (individuals and some businesses). The last comprehensive expenditure tracking effort, the NASA, found that in 2009/10 the split between these sources was 75% public, 16% external and 8% private sector [17]. The public health HIV allocations have grown from R966 million in 2004/5 to R13.6 billion in 2014/15, representing a 1300% growth in nominal public allocations in a decade. The HIV budget has experienced an annual average nominal growth rate of 15% between 2013/14 and 2015/16 [18].

Looking forwards over the Medium Term Expenditure Framework (MTEF) period (2013/14 - 2016/17), Ndlovu & Meyer-Rath (2014) found that R43.5 billion is budgeted for HIV programmes over three years (2014/15 – 2016/17) as part of the

national health HIV allocations, which include the Conditional Grant (CG) and the Equitable Share (ES) spending by the national and provincial departments of health, up from a budget of R41 billion over the previous five years (2009/10 – 2013/14) [19]. The total national health HIV allocation has grown by 9.6% from 2013/14 to 2014/15, with an expected real growth of 7.6% over the next three years. With regards to the provincial health budgets, the HIV budget has also increased as a share of *consolidated* (provincial and national) health spending (7% in 2012/13, 9% in 2014/15 and to a projected 10% in 2016/17).

2.3.2 Expenditure tracking scope and methodology

Scope

This expenditure review undertaken for the development of the IC covers the period 2011/12 to 2013/14 (using the SA government financial year (FY)), and includes all SA government funding for HIV and TB (for all departments, conditional and voted funds), as well as the GF and USG contributions. The SA government and PEPFAR data have been disaggregated by province, but the GF spending could not be disaggregated among provinces, as the GF's Principal Recipients (PRs) did not allocate their expenditure by location.

Sources of data

Implementing departments', National Treasury, and donors' expenditure records were the sources of expenditure on HIV and TB.

For all public spending, the Basic Accounting System (BAS) provides expenditure details for every transaction, permitting the tracing of expenditure for HIV and TB. This labelling of expenditure is routine for the HIV conditional grants (CG) for the National Department of Health (NDOH) and the Department of Education (DOE), but was done less systematically for the voted (non-conditional or discretionary) spending of the DOH, the Department of Social Development (DSD) and other departments.

The DOH's data in the BAS records identifies as TB expenditure only those labelled as such for MDR and XDR TB, and for the TB hospitals. Thus, the bulk of spending on prevention and outpatient treatment of pulmonary TB (PTB) could not be easily identified in the BAS records. At the request of NDOH, these costs were estimated by applying a unit cost per patient to the number of patients each year.

The expenditure analysis (EA) for the U.S. President's Emergency Plan for AIDS Relief (PEPFAR) provided spending data for the USG. The EA includes spending reported by PEPFAR's implementing partners for 2012/13 and 2013/14. As no EA was undertaken for 2011/12, USG spending for that year was estimated using the NASA figures for 2010 and interpolating to data for 2012, assuming a straight-line increase and similar proportional split between programmes as for 2012.

PRs' Enhanced Financial Reports (EFRs), which capture actual expenditure for each of their Service Delivery Areas (SDAs), or programme areas, provided spending data for the GF.

Exclusions

The expenditure review could not identify in- or out-patient costs related to the treatment of opportunistic infections (OIs), as such costs are embedded in the general health care spending of the NDOH. Other external donor funding to NDOH was not included in this initial phase.

Financial years

Matching the reporting periods for all three data sources proved somewhat challenging. The SA government's fiscal year (FY) extends from 1 April to 31 March, while the USG's runs from 1 October to 31 September. The GF did not have a fixed financial year during the period under review, but rather the GF reporting periods matched the dates when the grants commenced, which differed grant among the multiple grants. PEPFAR EA data was provided in annual amounts according to the USG FY and could not be adapted to the SA government FY. In an effort to align spending according to the SA government's FY, the SA government FY 2012/13 (commencing in April 2012) was labeled as 2012 and matched with the PEPFAR EA data for their FY 2011/12 (commencing in October 2011). The following Table 2 illustrates the best possible overlap match for spending by the SA government and the USG. For the GF data, the EFRs per quarter were used to match more closely to the SA government FY, to the extent possible.

Table 2: Matching the South African and US government financial years for the expenditure analysis

Labeled as:	SAG		USG	
	Start	End	Start	End
Common Year				
2011	Apr-11	Mar-12	Oct-10*	Sep-11*
2012	Apr-12	Mar-13	Oct-11	Sep-12
2013	Apr-13	Mar-14	Oct-12	Sep-13

*No EA data (2010/2011) to match with SA Govt 2011/12 - estimated

Crosswalking categories

The three funding sources also used different categorisations for their activities and programmes. Again, some effort was required to match these multiple datasets with respect to activities and programmes, including the agreed-upon activities and interventions in the IC. Matching these activities among the various data sources necessitated an in-depth understanding of each source's programmes and their coding, and involved discussions with programme managers to find the best match. The PEPFAR EA data uses a few more aggregate categories that could not be disaggregated to the level available in the other two datasets, and hence some estimations based on PEPFAR's suggestions had to be computed. For example, the PEPFAR category "Facility-Based Care, Treatment, & Support" included ART and TB/HIV activities; estimated spending on these two sets of activities was 75% and 25%, respectively (as per PEPFAR instructions for a previous analysis undertaken by Results for Development) [20]. Table 3 displays the PEPFAR-BAS match in greater detail, as well as assumptions made to match activities and programmes.

Table 3: Crosswalking the PEPFAR expenditure analysis (EA) categories to the SA government (BAS) categories

PEPFAR EA category	Matching BAS category
25% of Facility-Based Care, Treatment, & Support	TB/HIV
Sexual & Other Risk Prevention-General Population (certain sub-categories only)	Communications (BCC)
Condoms (in the EA cost category and not by programme)	Condoms
HCT	HCT
Sexual & Other Risk Prevention-Key Populations	High Transmission Areas (HTA)
VMMC	MMC
PEP	PEP
PMTCT	PMTCT

PEPFAR EA category	Matching BAS category
75% of Facility Based Care, Treatment, & Support ARVs (cost category)	ART Treatment
75% of Surveillance (as per PEPFAR suggestion) Strategic Information	Monitoring & Evaluation
25% of Surveillance (as per PEPFAR suggestion) Non-Activity Level Health Systems Strengthening	Policy & Systems Development
Blood Safety	Blood Banks
OVC	OVC
Sexual & Other Risk Prevention-General Population (certain sub- categories only) Infection Control	Other Prevention
Lab Strengthening	Lab Strengthening

The labelling of the categories in BAS (i.e., names of the interventions) were not standardised across programmes, provinces and even within provinces. Even the conditional grant spending, which has a core set of activities, exhibited variation in how activities were named. In addition, the required detail of the activity was not always classified under the same variable (BAS Objective levels 6 and 7). Therefore, all possible variables had to be searched for potential information on activities, leading to a standardised sub-set of 'common BAS codes' to categorise all public spending according to a more limited list of activities. Thus, the more than 300 different codes found for all the public HIV and TB activities were collapsed into 38 common BAS codes (see Appendix 2.1). These formed the basis against which all the PEPFAR and GF activities were matched (see Appendix 2.2). In addition, these categories were matched to the NASA categories and the National Health Accounts (NHA^a) (for global comparisons) and, at a later stage, will be matched to the new GF New Funding Model (NFM) Modular Template categories^b.

The discussion below describes the key findings of the analysis of the past and current HIV and TB spending in South Africa.

2.3.3 Total spending on HIV and TB by funding source and activity (intervention)

Total spending by the SA government, USG and GF on HIV and TB totalled R17.4 billion in 2011, R19.2 billion in 2012 and R22.1 billion in 2013 (representing a 15% increase in the latter year). The SA government was the largest contributor over the three years, with the SA share increasing from 76% in 2011 to 80% in 2013. USG provided the second most substantial source of funding, with its share decreasing from 22% in 2011 to 17% in 2013. The GF's share of HIV and TB spending in South Africa rose from 1% in 2011 to 3% in 2013. Details for both HIV and TB spending provided in Table 4 below, while Figure 12 shows the **HIV only** spend.

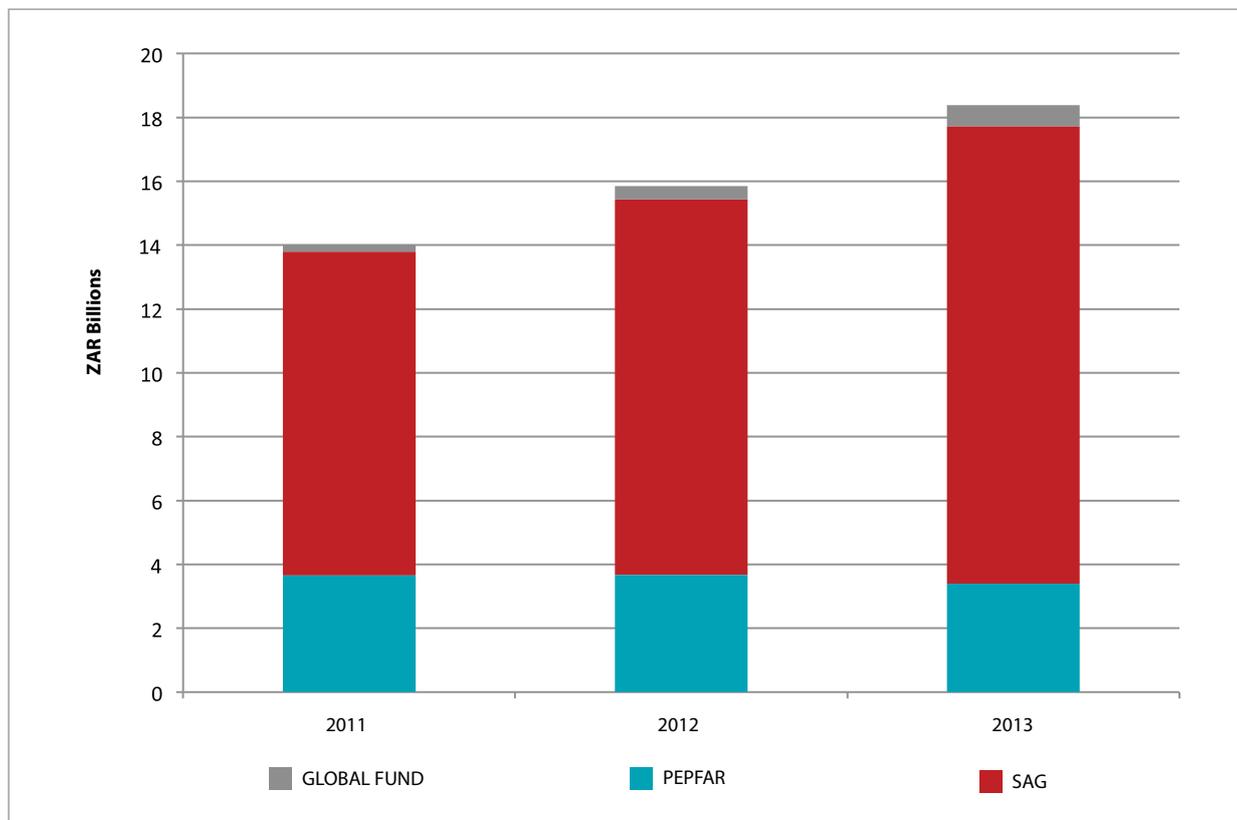
Table 4: Total spending on HIV and TB in South Africa by source (ZAR, %, 2011-2013)

Spending (ZAR)	2011	2012	2013	% (2011)	% (2012)	% (2013)
SA Govt.	13 293 518 754	14 882 754 276	17 773 204 828	76%	77%	80%
PEPFAR	3 870 712 658	3 900 724 859	3 694 922 752	22%	20%	17%
Global Fund	214 389 089	420 631 044	661 639 365	1%	2%	3%
Grand Total	17 378 620 502	19 204 110 179	22 129 766 946	100%	100%	100%

a The NHA in SA is being planned for 2016/17-2017/18.

b The GF will be piloting its new categories in 2016/17.

Figure 12: Total spending on HIV in South Africa by Source (ZAR, 2011-2013)



* SAG = South African Government. This graph excludes TB spending.

The SA government's public funding for HIV has substantially increased over the three years, including a 12% rise in 2012 and a 19% increase in 2013. GF spending also rose dramatically in the three-year period due to initial delays in the start-up of the Single Stream Funding grant (2011); early delays in disbursement associated with enrolling new PRs; and in meeting WHO quality assurance requirements (which occurred only in 2013). The 5% reduction in PEPFAR spending from 2012/13 and 2013/14 was anticipated under USG-SA government Bilateral Partnership Framework Implementation Plan (PFIP).

Table 5 provides a breakdown of total spending in HIV, HIV/TB integrated programmes and TB. HIV/TB integration activities accounted for only 1% of total funding in 2013/14, while 81% supported HIV activities and 18% for TB activities (noting again that outpatient treatment costs for TB were estimated).

Table 5: Total spending by HIV, TB and HIV/TB (ZAR, 2011-2013)

Spending (ZAR)	2011	2012	2013	Grand Total	% Share (over 3 years)
HIV	13 774 978 081	15 686 235 058	17 999 562 790	47 460 775 929	81%
HIV/TB	226 762 744	170 405 661	388 817 295	785 985 700	1%
TB	3 376 879 676	3 347 469 461	3 741 386 861	10 465 735 998	18%
Grand Total	17 378 620 502	19 204 110 179	22 129 766 946	58 712 497 627	100%

HIV and TB spending activities by the SA Investment Case categories

The spending review identified spending for each of the agreed SA IC programmatic areas, namely:

- Care and treatment (including pre-ART, ART, NIMART)
- MMC
- Comprehensive condom programming
- HCT
- PMTCT
- Other biomedical prevention (PEP, PrEP, STI treatment, microbicides)
- Key populations
- Social behaviour change communication
- TB
- Programme and social enablers – refer to the Annex 2 for specific interventions included under these.

Some HIV-related spending, on such items as home-based care, could not be classified within any of the IC programmatic areas and were categorized instead as 'non-SA IC'. In addition, some spending could not be disaggregated^c into specific programmes and were labeled as 'not disaggregated' (n.d.). Table 6 below shows the spending per IC programme area.

Table 6: Total spending according to the South African Investment Case programme areas (ZAR, %, 2011-2013)

Spending (ZAR)	2011	2012	2013	Grand Total	% Share
HIV					
Care and treatment	6 415 825 156	7 486 329 034	8 906 380 884	22 808 535 073	39%
Comprehensive condom programming	46 533 198	211 891 054	175 406 347	433 830 599	1%
HCT	833 546 557	1 048 788 653	1 141 046 035	3 023 381 245	5%
HIV not disaggregated	96 005 160	137 979 411	286 337 033	520 321 604	1%
Key populations	237 471 479	274 924 351	248 853 952	761 249 782	1%
Medical male circumcision	408 514 701	379 441 921	566 686 471	1 354 643 092	2%
Other biomedical prevention	143 932 376	188 690 835	244 393 863	577 017 074	1%
PMTCT	590 055 927	472 239 901	483 086 386	1 545 382 215	3%
Programme enablers	818 448 373	997 903 407	1 315 284 868	3 131 636 648	5%
Social behaviour change communication	247 211 514	262 726 025	319 492 166	829 429 706	1%
Social enablers	1 693 432 074	1 522 875 270	1 395 408 130	4 611 715 475	8%
TB	3 603 642 421	3 517 875 121	4 082 497 592	11 204 015 134	19%
Non SA IC	2,244,001,565	2,702,445,194	2,964,893,219	7,911,339,978	13%
Grand Total	17 378 620 501	19 204 110 177	22 129 766 945	58 712 497 623	100%

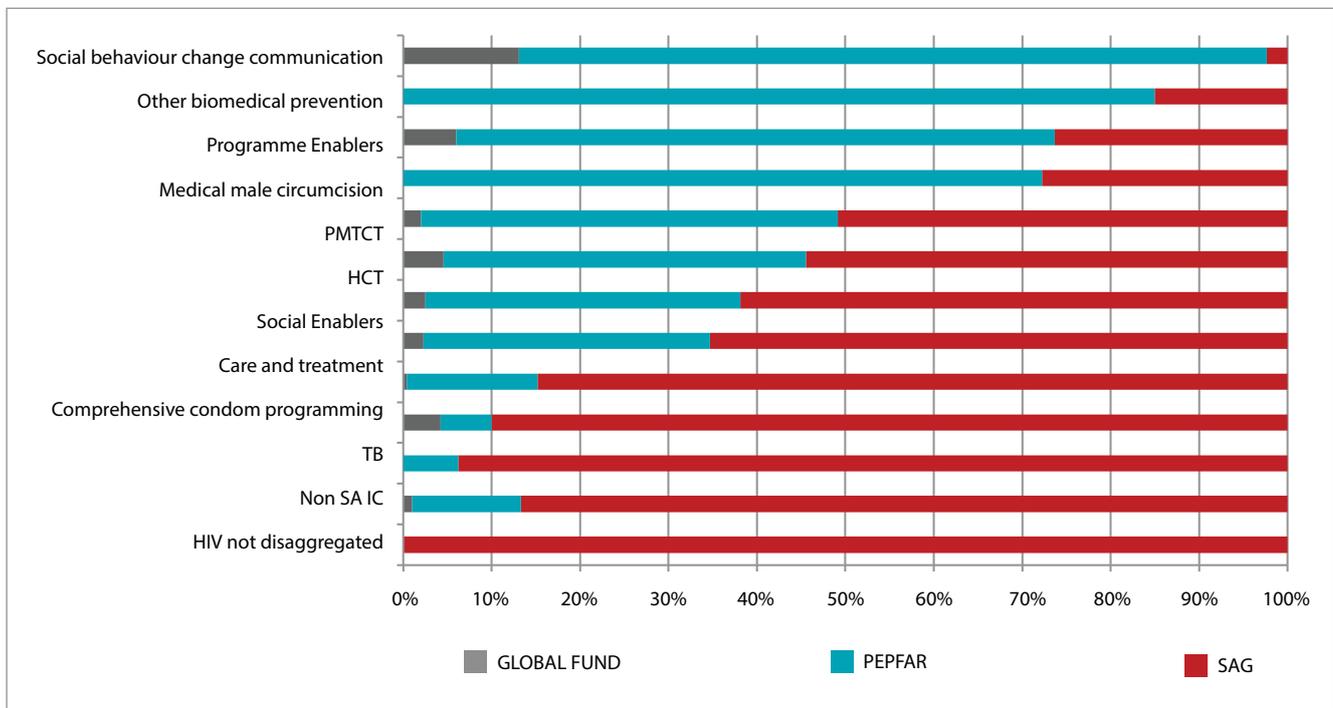
^c The 'not disaggregated' spending was mainly for public sources, where the BAS records did not give any detail, but only labelled the spending as 'HIV/AIDS'. Only one province's BAS records were poorly disaggregated.

Care and treatment activities (ART, pre-ART, adherence support, and nurse-administered ART) accounted for the largest share of spending (39%) during these three years. TB activities (including diagnosis and treatment of PTB, ETB, MDR TB and XDR TB) accounted for the second largest share of spending (19%). An additional 13% of spending focused on care and treatment activities not included in the SA IC treatment activities. Social enablers received 8% of all funding and programme enablers 5%.

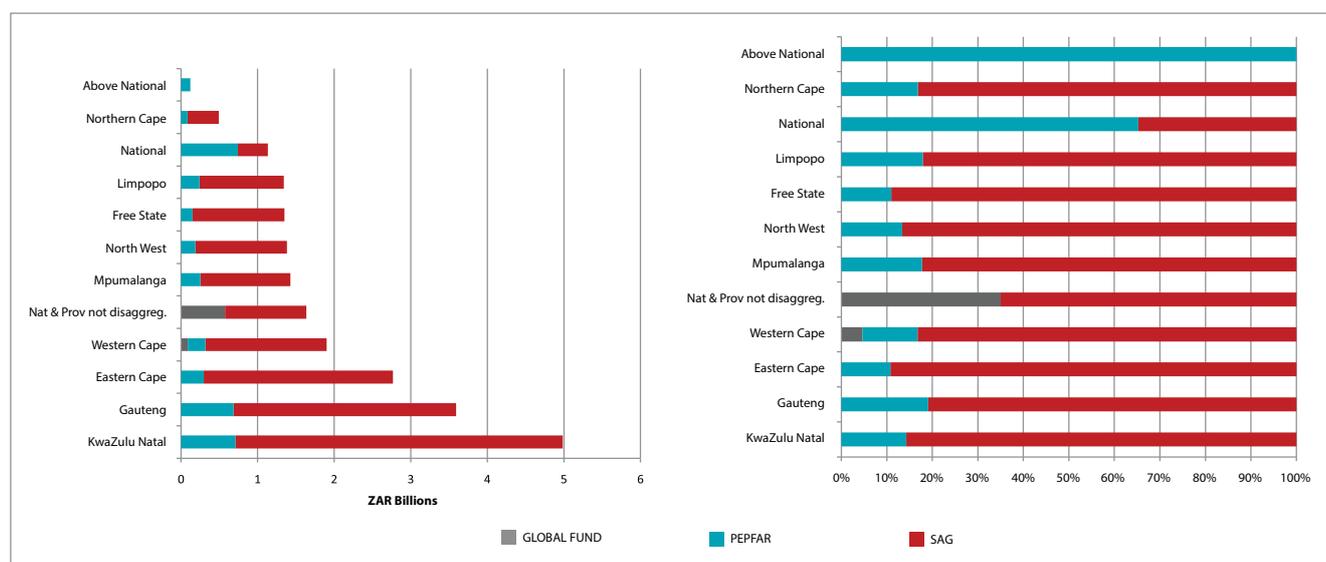
Over the three years, the proportion of total spending devoted to HIV care and treatment increased from 37% to 40%, while share of TB spending decreased from 21% in 2011 to 18% in 2013. The share of spending on social enablers declined from 10% to 6%, while spending on programme enablers increased slightly from 5% to 6% in 2013.

Figure 13 displays the respective contributions of the SA government USG and GF in each of the programmatic areas in 2013.

Figure 13: Proportional spending on HIV and TB of sources by SA IC categories (2013)



Among provinces, as Figure 14 indicates, the largest shares of total funding supported activities in KwaZulu-Natal (23%), Gauteng (16%) and Eastern Cape (12%). The smallest share went to Limpopo, Free State, North West (all with 6%) and Northern Cape with 2%. (As noted, GF spending could not be split by province and hence was captured in the 'national & provincial not disaggregated' category). PEPFAR spending that occurs outside the country but benefits South Africa is labelled as 'above national' in the figure below.

Figure 14: Spending on HIV and TB of sources by province (ZAR billions, %, 2011-2013)

2.3.4 South African Government's public spending on HIV and TB in South Africa

Total domestic public sector spending on HIV and TB in South Africa is presented in Table 7 below, including the conditional grants (CG) for both DOH and DOE and all equitable share (voted funds). The CG for HIV that flows through NDOH is the single most significant public funding mechanism (providing 57.2% of all funding), reaching R10.5 billion in 2013/14, followed by funds voted to HIV and TB by NDOH from its equitable share (33.8%), reaching R5.7 billion in 2013/14. The expenditure analysis estimated that TB in-patient costs were covered through the voted funds and hence were included in the voted share. Other funds for HIV and TB, such as the Hospital Revitalisation grant and others, made up 2.4% of total domestic public sector spending on HIV and TB. As Table 7 reveals, 93.4% of all the public funding for HIV and TB is channelled through NDOH (excluding donor funds flowing through NDOH). Domestic public sector funding for HIV and TB has steadily increased over the three-year period.

Table 7: Public sources for HIV and TB by department and funding mechanisms (ZAR, 2011-2013)

Sources of Public Funding (ZAR)	2011/12	2012/13	2013/14	Grand Total	% Share ('11-13)
DOH Voted	4 717 797 529	5 090 185 003	5 737 885 479	15 545 868 011	33.8%
Other DOH public funds	340 351 936	288 490 907	456 899 576	1 085 742 419	2.4%
DOH HIV Conditional Grant	7 246 240 201	8 515 582 501	10 515 916 337	26 277 739 039	57.2%
DOE CG (Lifeskills)	189 000 000	203 000 000	204 000 000	596 000 000	1.3%
DSD Voted	744 565 666	734 917 000	806 518 000	2 286 000 666	5.0%
DOD Voted	34 269 915	16 521 279	23 109 487	73 900 681	0.2%
SAPS Voted	4 895 651	4 943 893	4 144 332	13 983 876	0.0%
DCS Voted	16 397 855	29 113 693	24 731 618	70 243 166	0.2%
Grand Total	13 293 518 754	14 882 754 276	17 773 204 828	45 949 477 858	100%

Source: BAS records: 2011/12 – 2013/14. National Treasury Records.

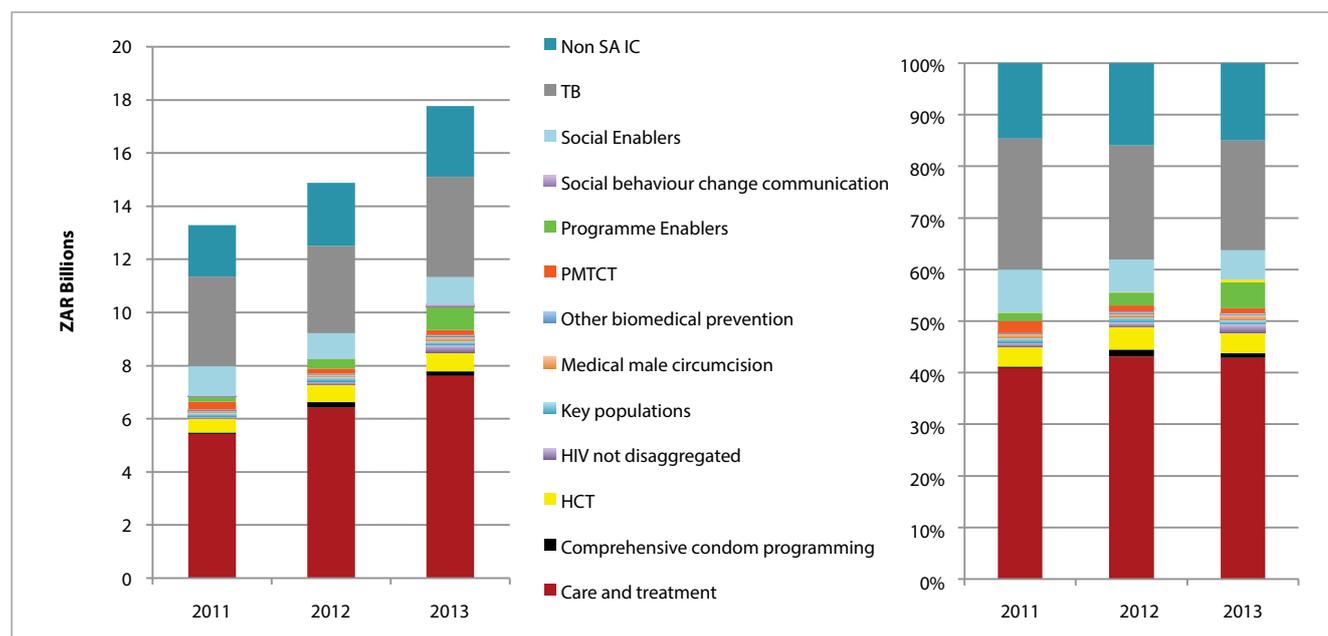
* DOH: Department of Health, DOE: Department of Education, DSD: Department of Social Development, DOD: Department of Defence, SAPS: South African Police Service, DCS: Department of Correctional Services.

While departments other than NDOH make important contributions to the national HIV and TB response, their share of spending is notably lower than NDOH (Table 7). The Department of Social Development (DSD) accounted for 5% of the total public funds, primarily as a result of HIV community and home-based care (CHBC). The Department of Education's Life Skills conditional grant, which benefits youth in school, represented 1.3% of spending. The Defence, Police and Correctional Services also have important HIV services for the army, police and inmates of correctional facilities.

Figure 15 displays the spectrum of national public sector spending among the programme categories of the SA IC. Among total public sector spending on HIV and TB, spending on care and treatment activities increased nominally (by 40% over the two years) as well as proportionally, from 41% of all spending in 2011/12 to 43% in 2013/14. Activities not included in the programme categories of the IC – notably, community and home-based care (CHBC), step down care (SDC) and palliative care^d – accounted for 15% of all national public sector spending.

TB spending, including XDR/MDR TB and the estimated PTB costs, accounted for 22% of total public sector spending over the three years. Although total national public sector spending on TB-related activities increased by 12% during the three-year period, TB's share of total public spending declined from 25% to 21%. National public sector spending on programme enablers more than doubled between 2011/12 and 2013/14 to 5% of total public spending on HIV and TB. Refer to Table 11 below for the detailed figures.

Figure 15: Public expenditure on HIV and TB according to the Investment Case programme areas (ZAR billions, %, 2011/12-2013/14)



NDOH spending on HIV and TB (conditional grants and voted funds)

Among public sector spending that flows through NDOH, 57% is derived from the CG for HIV, which has steadily increased over the years. However, the voted portion is also a significant contribution (36%) and represents the provincial departments' commitment to the response. From the BAS records, the expenditure review identified a number of other grants and voted sources, although their contributions to overall spending on HIV and TB were relatively small. These included: the Expanded Public Works Programme (EPWP), the Health Infrastructure Grant, the Hospital Revitalisation Grant, the National Health Insurance (NHI) Grant, the National Tertiary Services Grant, and other national and provincial

^d Palliative care is included in the IC cost estimates for every person dying of AIDS.

'earmarked and specific' (E&S) funds (these have been lumped together in Table 8 below). It is not clear why these grants may have been used for HIV and TB, or if it was incorrect labelling of the source (Fund_Level in BAS).

Table 8: Department of Health's sources of public funds for HIV, AIDS and TB (ZAR, %, 2011/12-2013/14)

Source of DOH Public Funds (ZAR)	2011/12	2012/13	2013/14	Grand Total	% Share ('11-13)
CG Comprehensive HIV	7 246 240 201	8 515 582 501	10 515 916 337	26 277 739 039	61%
Voted funds	4 717 797 529	5 090 185 003	5 737 885 479	15 545 868 011	36%
Other grants/ voted	340 351 936	288 490 907	456 899 576	1 085 742 419	3%
Grand Total	12 304 389 667	13 894 258 411	16 710 701 392	42 909 349 470	100%

Source: DOH (national and provincial) BAS records: 2011/12 – 2013/14.

Table 9 shows CG, voted and total NDOH spending, in 2013/14, across 30 BAS codes.

Table 9: Total DOH public spending on HIV and TB by funding channel (CG vs voted), according to the BAS categories (ZAR, 2013/14)

DOH HIV & TB Interventions	DOH HIV CG	DOH Voted	Other DOH public funds	Grand Total	% Share (2013)
HIV					
ART	7 237 529 245	362 537 000	362 896	7 600 429 142	45.5%
CHBC	521 322 513	1 692 853 564	34 179 791	2 248 355 868	13.5%
Condoms	112 696 543	-	53 779 490	166 476 032	1%
HCT (or VCT)	694 225 887	22 139 176	15 898	716 380 961	4.3%
HIV not disagg.	19 440 030	43 533 907	223 363 096	286 337 033	1.7%
HIV treatment not disaggregated	16 554 928	649 628	-	17 204 556	0.1%
HTA (CSW & clients)	101 866 748	-	1 576 200	103 442 948	0.6%
Key pop prevention other nec.	-	13 585 474	-	13 585 474	0.1%
M&E	-	102 127	-	102 127	0%
Mass media/ soc. mob.	-	-	93 250 000	93 250 000	0.6%
MMC	171 327 688	52 733	3 800	171 384 222	1.0%
Palliative / hospice care	-	21 456 953	-	21 456 953	0.1%
PEP/ OPEP/ NOPEP	55 221 781	427 789	-	55 649 570	0.3%
PM	722 130 908	137 133 328	24 765 000	884 029 236	5.3%
PMTCT	181 597 872	327 501	-	181 925 373	1.1%
Prevention not disaggregated	99 030 164	17 637 447	-	116 667 611	0.7%
Step-down care	120 288 313	175 306	-	120 463 619	0.7%
STI	229 419	370 400	-	599 819	0%

DOH HIV & TB Interventions	DOH HIV CG	DOH Voted	Other DOH public funds	Grand Total	% Share (2013)
TB					
TB control/ management/ surveys	14 485 421	47 712 869	8 025 811	70 224 101	0.4%
TB treatment (clinics or outpatient)	-	832 439 237	-	832 439 237	5.0%
TB treatment (hospitals)	(15 711)	1 058 829 158	17 577 392	1 076 390 840	6.4%
TB XDR/MDR treatment	-	447 238 461	201	447 238 662	2.7%
TB/HIV (integration)	340 892 100	218 632	-	341 110 731	2.0%
Training	107 092 488	15 761 541	-	122 854 030	0.7%
Workplace prevention	-	1 703 248	-	1 703 248	0%
TB diagnostics	-	1 021 000 000	-	1 021 000 000	6.1%
Grand Total	10 515 916 337	5 737 885 479	456 899 576	16 710 701 392	100%

Source: DOH (national and provincial) BAS records: 2011/12 – 2013/14. * HTA: High transmission areas – interventions for commercial sex workers & truck drivers/ other clients. OVC support – the DOH and DSD collaborate to provide these services.

Overall, 75.6% of NDOH public revenue for HIV and TB supported HIV, while 24.4% focused on TB services and 1.6% on HIV/TB integration activities. NDOH spending on ART reached R7.6 billion in 2013/14, representing 46.7% of the NDOH spending on HIV and TB. During the three-year period, NDOH spending on ART rose by an average 23% each year. Funding for CHBC amounted to R2.2 billion in 2013/14 (14%), including all NDOH community services (mostly from voted funds), which could not be disaggregated into HIV and non-HIV related (hence will have overestimated the CHBC spending for HIV). Spending on step-down care (follow-on care in lower-level hospitals after an admission to a tertiary- or secondary-level hospital) represented less than 1% of total spending and is likely to be phased out completely. A small amount of spending (1.7%) could not be disaggregated, as the BAS records did not specify a specific activity, but simply indicated 'HIV/AIDS'. These were labelled 'HIV treatment not disaggregated'. About 9.1% supported activities to address MDR/XDR and in-patient treatment (specifically for MDR-TB), while 5% supported PTB treatment either through clinics, community health centres and mobile clinics.

NDOH Conditional Grant spending on HIV and TB

Table 10 reveals that nearly 70% of funding from the NDOH HIV CG supported ART over the three-year period, with ART-related funding increasing by 46% from 2011/12 to 2013/14. CG spending on condoms tripled over the three years, from R44 million to R113 million, while spending on programme management quadrupled during the period. Spending on HCT accounted for 7% of the total CG over the three years, with total CG-related HCT spending increasing by 35%. Although small proportions (1.4%) of the CG supported MMC, there was a large increase (50%) in CG-related MMC spending between 2011/12 and 2013/14, from R113 million to R171 million. Only 2.5% of the CG went towards PMTCT and 2.1% went towards TB treatment, and shares to the other activities were relatively small.

Table 10: DOH spending (Conditional Grant) on HIV and TB (ZAR, %, 2011/12-2013/14)

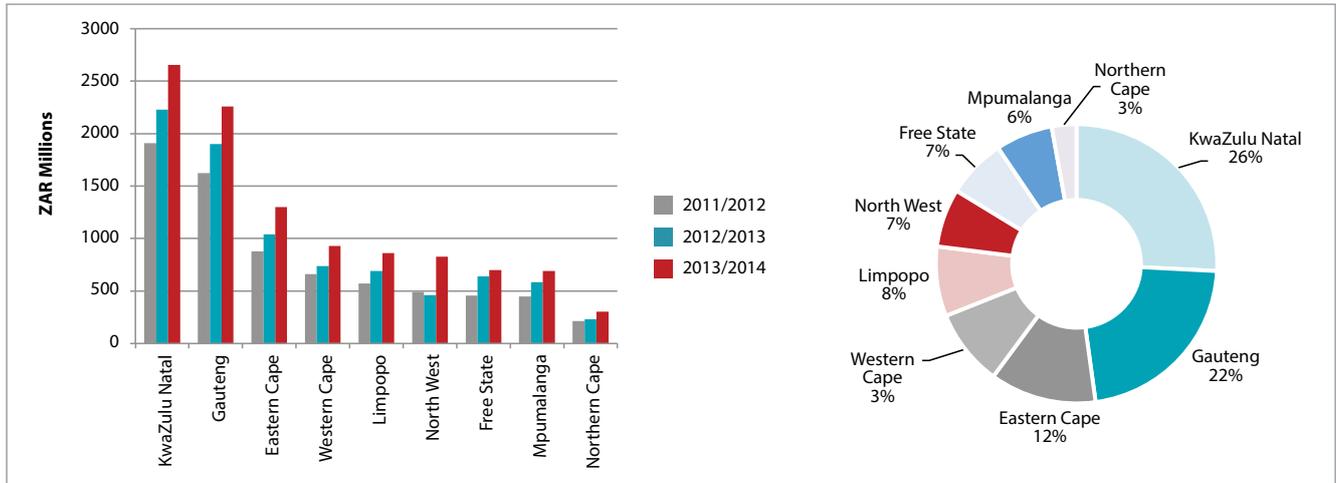
Spending by Activity (ZAR)	2011/12	2012/13	2013/14	Grand Total	% Share ('11-13)
HIV Sub-Total	7 222 684 966	8 343 035 208	10 160 554 527	25 726 274 700	97,9%
ART	4 959 619 397	5 875 133 174	7 237 529 245	18 072 281 816	68,8%
CHBC	420 652 317	485 447 541	521 322 513	1 427 422 371	5,4%
Condoms	44 542 610	89 448 736	112 696 543	246 687 888	0,9%
HCT (or VCT)	514 530 638	653 677 152	694 225 887	1 862 433 677	7,1%
HIV not disaggregated	15 110 854	5 132 964	19 440 030	39 683 847	0,2%
HIV treatment not disaggregated	386 066 083	261 544 412	16 554 928	664 165 423	2,5%
MMC	113 292 235	75 215 258	171 327 688	359 835 182	1,4%
PEP/ OPEP/ NOPEP	3 823 488	47 711 965	55 221 781	106 757 234	0,4%
PM	173 590 671	272 623 481	722 130 908	1 168 345 060	4,4%
PMTCT	299 865 689	181 007 442	181 597 872	662 471 002	2,5%
Prevention not disaggregated	207 307	72 002 015	99 030 164	171 239 486	0,7%
Step-down care	96 822 071	106 769 764	120 288 313	323 880 148	1,2%
STI	81 829	535 169	229 419	846 417	0,0%
Training	81 698 724	97 983 578	107 092 488	286 774 791	1,1%
HTA (CSW & clients)	112 781 052	118 802 558	101 866 748	333 450 357	1,3%
TB Sub-total	23 474 590	172 544 381	355 377 521	551 396 493	2,1%
TB control/ management/ surveys	26 194	2 753 540	14 485 421	17 265 155	0,1%
TB/HIV integration	23 448 396	169 790 842	340 892 100	534 131 338	2,0%
Grand Total	7 246 159 556	8 515 579 589	10 515 932 047	26 277 671 193	100%

Source: DOH (national and provincial) BAS records: 2011/12 – 2013/14.

NB. Some provinces labelled a small portion of HIV spending as 'Sexually transmitted disease interventions' hence captured under STI above.

Figure 16 illustrates the steadily increasing NDOH CG spending in each province over the three years, with KZN and Gauteng having the largest shares (26% and 22% respectively), followed by Eastern Cape (12%). Other provinces received relatively small shares of NDOH CG funding (9% or less), with Northern Cape (3%) receiving the smallest share.

Figure 16: DOH CG for HIV per province (ZAR millions, %, 2011/12-2013/14)

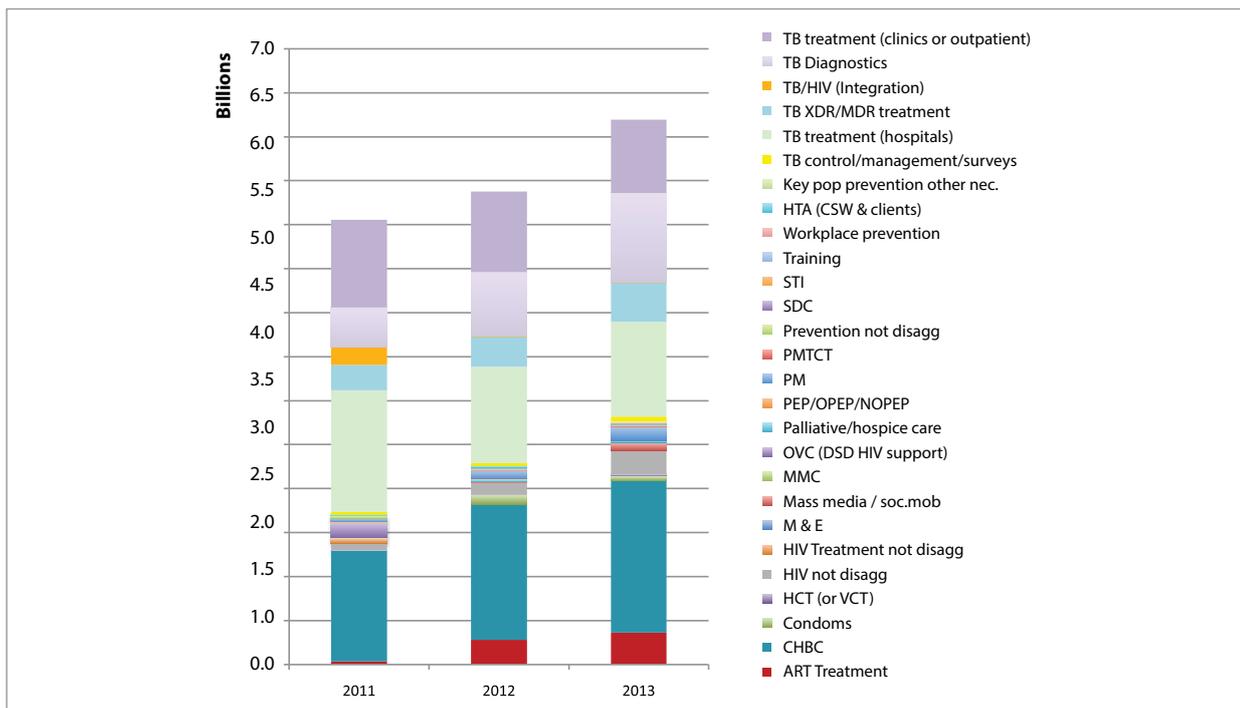


Source: Provincial DOH BAS records: 2011/12 – 2013/14.

NDOH voted funds spending on HIV and TB

With respect to NDOH voted funds for HIV and TB, illustrated in Figure 17, roughly 60% of voted funds during the three-year period supported TB-related activities. Approximately half of TB-related spending from voted funds supported out-patient treatment of PTB (including diagnostics), and the other half for MDR/XDR TB and hospital treatment. Slightly more than one quarter of voted funds (27%) financed CHBC, but this could not be disaggregated between HIV-related care and non-HIV, and therefore is possibly an overestimation of HIV CHBC spending. Only 4% of voted funds supported ART, although amounts of voted funds directed towards ART programmes increased each year, from R37 million in 2011/12 to R363 million in 2013/14, almost 10-fold. The sharp increase in ART funding from voted funds may indicate that CG allocations for ART have become insufficient, prompting provinces to top up the CG funding with their equitable share (voted funds).

Figure 17: NDOH spending (voted funds) on HIV and TB (ZAR millions, 2011/12-2013/14)



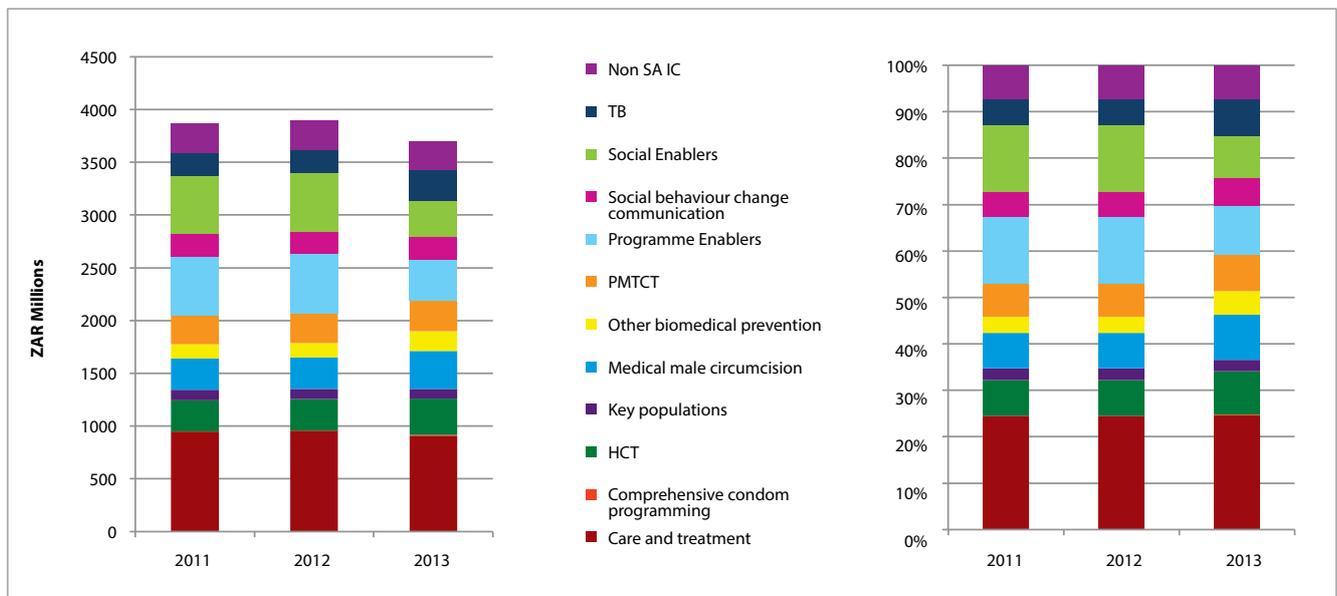
Source: DOH (national and provincial) BAS records: 2011/12 – 2013/14.

2.3.5 PEPFAR spending on HIV and TB

PEPFAR funding data, primarily provided through their Expenditure Analysis (EA) reports, were analysed in more depth by Results for Development (2013). As previously noted, spending activities for PEPFAR were matched with SA government BAS and IC codes for comparability, but no EA data were available for 2011/12. To estimate the 2011/12 spending, the PEPFAR data were interpolated between the 2010 NASA and the EA 2012 data, assuming a linear progression between these two data sets. Figure 18 summarises PEPFAR funding trends over the three years.

Despite the 5% decrease in PEPFAR contributions resulting from the transition outlined in the PFIP, PEPFAR spending actually increased during the three-year period for certain types of programmes, such as blood safety, facility-based treatment and care (which includes HIV and some TB treatment), HCT, strategic information and MMC. Other activities experienced considerable reductions in PEPFAR support, including programmes for orphans and vulnerable children (OVC) (32% reduction) and health systems strengthening (HSS) (19% reduction). Programme management spending in 2013/14 was allocated across the various programme categories, per the latest EA approach.

Figure 18: PEPFAR spending according to the Investment Case programme areas (ZAR millions, %, 2012-2013)

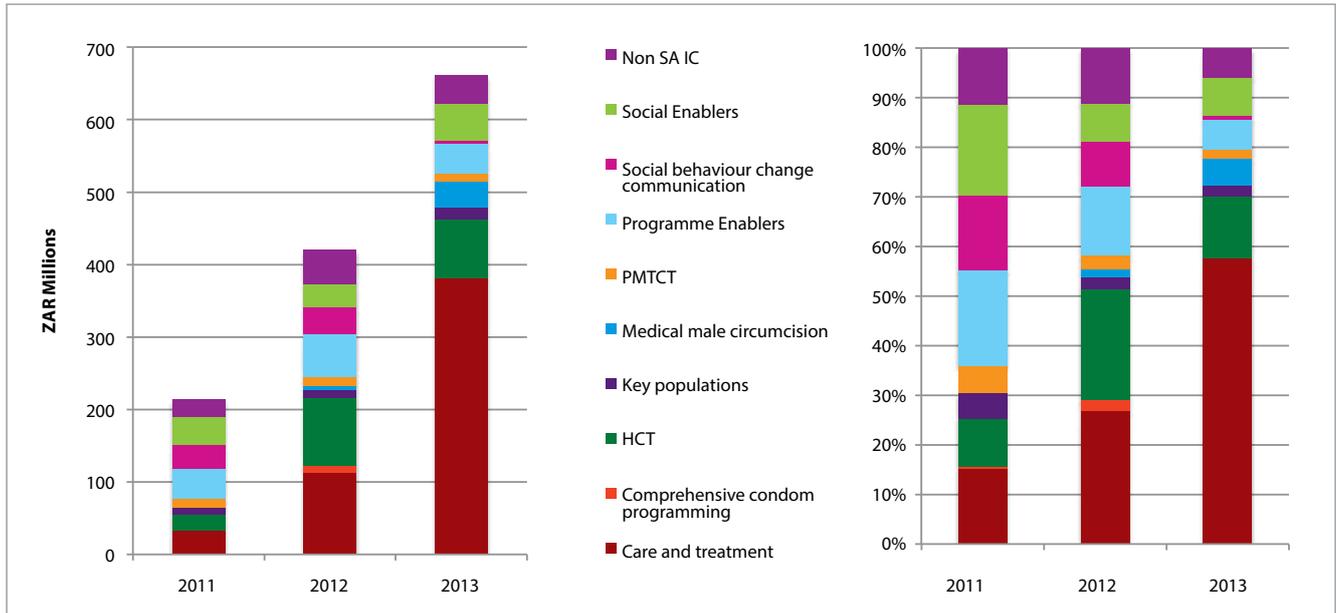


Source: PEPFAR EA data.

2.3.6 Global Fund spending on HIV and TB

As Figure 19 indicates, GF spending on HIV and TB in the IC programmatic categories sharply increased over the three years, from just over R200 million in 2011 to R650 million in 2013, mainly as a result of the increase in the care and treatment spending.

Figure 19: Global Fund spending according to the Investment Case programme areas (ZAR millions, %, 2011-2013)

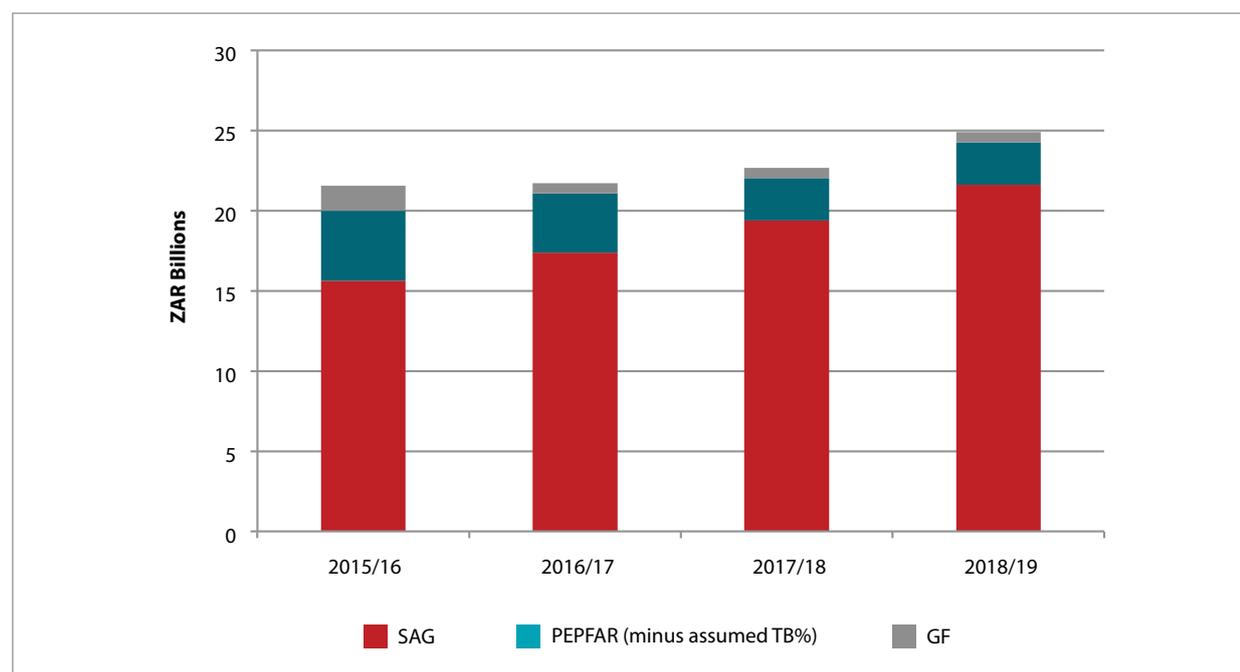


Source: Global Fund Principal Recipients’ Enhanced Financial Reports

The comparatively modest spending by the GF in 2011 stems primarily the new Single Stream Funding (SSF) grant, which required new processes as well as a new PR. In addition, the increase in ART spending occurred after WHO quality assurance requirements were met (only in 2013) and the NDOH established the Central Procurement Unit (CPU), which assumed responsibility for procurement and supply management of the ARV stocks.

2.3.7 Future allocations/ commitments for HIV and TB

The SA government’s mid-term expenditure framework (MTEF) budget allocations for 2015/16 to 2017/18, summarised in Figure 20, indicate the allocation of funding for HIV and TB in the near future. The GF confirmed grant amounts for 2014/15 and 2015/16 pertain to the remaining contract amounts for current grants that may not fully convert into actual disbursements (these will be based on the ‘burn rates’, that is, the PRs’ percentage expenditure from their total budget). Projected amounts from the GF for 2016/17 to 2018/19 are drawn from the country’s new Concept Note but these may not be fully realised. Figure 20 projects future PEPFAR spending based on the commitments outlined in the PFIP, but these, too, may not fully convert into available funding. Until contracts with implementing partners are finalised for GF and PEPFAR, and until SA government department business plans and detailed budgets are in place, it is difficult to project accurately the funding available the various IC programmatic categories.

Figure 20: Estimated future funding commitments for SA government, GF and PEPFAR (ZAR, 2014/15-2017/18)

SA govt. sources: Estimates of National Expenditure and Provincial Budgets (2015/16). Excludes provincial discretionary (voted) budgets. Historical spending by DCS, DOD, SAPS and adjusted for inflation. PEPFAR: PFI agreement. GF: remaining budget for current grant (2013/14-2015/16) and indicative funding ceiling for new Concept Note (2016/17). Subsequently, the GF has approved some additional 'above allocation' funding for SA.

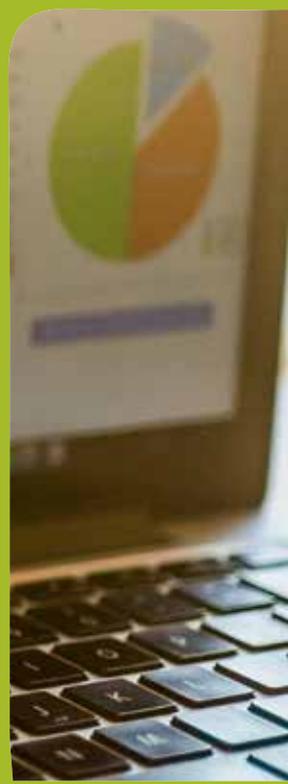
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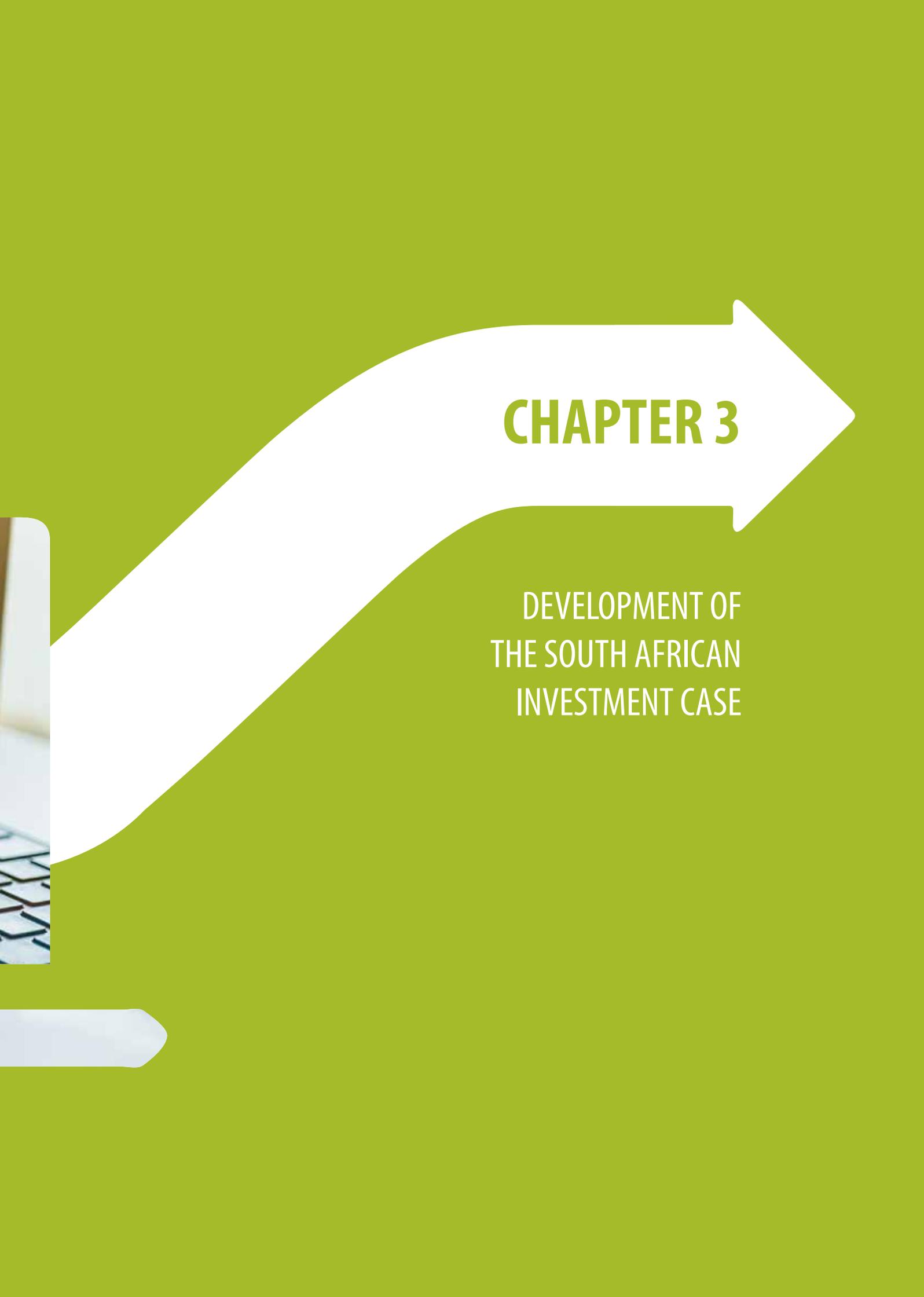
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12/4/14	30min 12s	3.25	10min 0s
14/4/14	30min 0s	3.00	20min 27s
16/4/14	30min 42s	3.25	12min 0s
18/4/14	30min 0s	3.00	10min 0s
21/4/14	30min 24s	4.00	10min 30s





CHAPTER 3

DEVELOPMENT OF
THE SOUTH AFRICAN
INVESTMENT CASE

3.1 THE PROCESS

The Investment Case aimed to engage and respond to all sectors of society while remaining scientifically rigorous in the assessment of available evidence. This section describes the timelines, key stakeholders and structures involved in developing the IC. The section also describes the evidence collection and verification process that supported the decisions regarding the specific interventions to include, as well as the process of the reviewing and endorsing the results by the stakeholders.

3.1.1 An innovative analytical framework

The South African Investment Case started with the concept for the Investment Framework suggested by Schwartländer et al (Schwartländer 2011) but added a number of innovations, summarised below.

In contrast to the original Investment Framework approach, the South African HIV and TB IC:

- Included both the HIV and the TB epidemics, rather than only the HIV/TB integration aspect (which focusses on TB care for HIV-positive people only). This made sense due to the closely linked nature of these epidemics in South Africa. TB accounts for the largest share of AIDS-related deaths in South Africa, while HIV prevention and treatment interventions represent the most effective measures to reduce TB mortality and incidence.
- Used a larger number of basic programme areas than suggested in the Investment Framework. In particular, other biomedical prevention was added as a basic programmatic activities, as studies validating this category of interventions largely emerged after the Investment Framework was created. In addition, a separate category was created for HIV Counseling and Testing; rather than treat HCT as a sub-set of HIV treatment and care, the intervention was deemed sufficiently critical to stand on its own.
- Focused on the quality of evidence concerning the effectiveness of the interventions to be included.
- Added – in addition to the Investment Framework's categories of basic programme interventions, critical enablers and development synergies – the category of technical efficiency (TE) factors. These are defined as activities that improve the technical efficiency^a of existing programmes but only affect a single intervention, in contrast to enablers and synergies that have the potential to affect a number of interventions.
- Constructed a novel optimisation method to choose the optimal expansion path for the South African HIV programme, with the aim of maximizing allocative efficiency^b among the interventions included in the IC. (This analysis is as yet outstanding for the TB Investment Case.)

Most importantly, the South African HIV and TB IC is a long-term exercise that aims to update the evidence base regarding the best HIV and TB interventions on an ongoing basis. Analysis and recommendations to optimize the HIV and TB response will be updated annually. Towards this end, SA will organise recurring stakeholder engagements and data collection exercises and urge all stakeholders, implementers and researchers engaged in HIV and TB programmes and evaluations to continue submitting new evidence to this process as it is generated.

a Technical efficiency in the context of this analysis refers to the maximisation of output (for example, HIV tests done) given a set level of inputs (for example, healthcare staff).

b Allocative efficiency in the context of this analysis refers to the maximisation of a socially desirable output (for example, life years saved) given a set level of funding.

3.1.2 Timelines and phases

The South African IC exercise involves several phases:

- **Phase 1** (Feb 2014 - June 2015): Results and of recommendations at the national level
- **Phase 2** (July 2015 - April 2016): Results and of recommendations at the provincial level
- **Phase 3** (May - July 2016): Results and of recommendations at the sub-provincial level, including collection of unit costs and use of geospatial models of the HIV epidemic

The current report summarises results from Phase 1. (Additional details regarding planned analyses for Phases 2 and 3 are provided in Chapter 7.)

3.1.3 Key stakeholders in the development of the Investment Case

The South Africa IC was developed through an intensified national dialogue regarding investment choices and priority setting. At all stages, this dialogue involved all key national partners, including government departments at national and provincial level, SANAC, National Treasury, civil society, the private sector and development partners. Forums for this dialogue included existing multi-stakeholder structures and processes, such as SANAC structures and other governance bodies and partnership forums. For a detailed list of organisations involved in development of the IC, see Annex 3.

3.1.4 Coordination with other exercises and processes

Given the nature and global importance of the South African HIV and TB epidemics, a number of similar analytical exercises and processes were ongoing at the same time as the IC, each with somewhat different objectives and methods but all with an aim of informing South African HIV or TB policy. The IC Steering Committee sought to coordinate and, where possible, align the IC with as many of these as possible. These processes included the following:

- HIV Think Tank
- TB Think Tank
- TB Targets project of the TB Modelling and Analysis Consortium (TB-MAC).

Beyond this, the results of the IC will be used to inform development of a new national strategic plan, as well as the GF concept note, and will also inform both South African and donor budgets (for more detail see chapter 7).

3.1.5 Structures for developing the Investment Case

Governance of the Investment Case process involved a steering committee and a task team as well as a number of programmatic and cross-cutting working groups.

Steering committee

A Steering Committee consisting of senior officials of relevant government departments, representatives of civil society, UN organisations and donor organisations, and experts from academia and consulting organisations (see Box 1 for the Steering Committee members) directed the IC process. The Steering Committee was co-chaired by Dr Yogan Pillay, the Deputy Director General: Special Programmes in NDOH, and Dr Fareed Abdullah, the Chief Executive Officer of SANAC. The Committee worked to align the IC process with similar ongoing processes; determine the overall objectives, scope and process of the IC; coordinate the process; maintain engagement with and motivate contributions of relevant stakeholders; and finally to provide stewardship for effectively using the recommendations of the IC. The Steering Committee met four times during the course of Phase 1, starting in October 2013.

Box 1: Steering Committee members

1. David Allen (BMGF)
2. Benjamin Alli (UNAIDS)
3. Fareed Abdallah (SANAC)
4. Faith Kumalo (DBE)
5. James Maloney (US Embassy)
6. Mark Blecher (National Treasury)
7. Nancy Knight (CDC)
8. Nono Simelela (The Presidency)
9. Patrick Osewe (World Bank)
10. Siphon Senabe (DPSA)
11. Tshiamo Moela (Civil Society Representative)
12. Yogan Pillay (NDOH)

Secretariat: UNAIDS

Task team

The development of the IC was led by a Task Team comprising subject matter experts from academia, UN organisations and funders, as well as key government structures such as SANAC, the GF Country Coordinating Mechanism, NDOH and Treasury. Two conveners, Eva Kiwango from the South African office of UNAIDS and Dr Nevilene Slingers from SANAC, led the Task Team. The Task Team decided on the methods used in the evidence review and modelling involved in the IC, selected the interventions to be considered, graded the evidence supporting each of the interventions, reviewed and refined the results of the modelling, and developed this report. Much of the work was done in 10 sub-working groups, each of which were co-led by a Task Team member together with an official of the NDOH or SANAC (see Table 11). Nine of the working groups were each responsible for one of the nine basic programme areas, with one additional sub-working group focused on social and programme enablers and development synergies and one on the economic aspects of the Investment Case. The Task Team met bi-weekly, in February and March 2014, then monthly until November 2014.

Table 11: Sub-working group co-leads^c and linkages with other groups

	Sub-working group	Task team co-lead	NDOH/ SANAC co-lead	Linkages with other groups
1	Care and treatment	Augustin Ntilivamunda, WHO Gesine Meyer-Rath, HE ² RO	Letta Seshoka, CCMT	NDoH: Adherence working group; Affordable Medicines Unit
2	Key populations	Heidi O’Bra, CDC	Eva Maruma, Prevention Directorate, NDoH	Key populations working group
3	Comprehensive condom programming	Leonard Kamugisha, UNFPA	Thato Chidarikire, Director Prevention, NDoH	NDOH Condom working group

^c For some sub-working groups, the co-leads changed during the process.

	Sub-working group	Task team co-lead	NDOH/ SANAC co-lead	Linkages with other groups
4	PMTCT	Sanjana Bhardwaj, UNICEF	Precious Robinson, Director PMTCT, NDoH	NDOH PMTCT working group
5	HCT	Eva Kiwango, UNAIDS	Thato Chidarikire, Director Prevention, NDoH	SANAC Nerve Centre meetings
6	SBCC	Tshiamo Moela, Deputy Chair CCM	Nditsheni Mungoni, SANAC	SANAC Prevention TTT
7	MMC	Paul Pleva, USAID	Collen Bonnecwe, Director MMC, NDoH Dayanund Loykissoonalal Programme Manager, MMC, NDoH	MMC working group
8	TB	Alasdair Reid, UNAIDS	David Mamejta, Chief Director TB, NDoH	
9	Economics	Gesine Meyer-Rath, HE ² RO	Nthabiseng Khoza, Chief Director HIV Conditional Grant, NDoH	SANAC Costing TTT
10	Critical enablers	Petro Rousseau, SANAC		SANAC Human Rights TTT

3.1.6 Evidence collection and verification

To be able to model an intervention, TE factor or enabler or synergy, three types of information were required: (1) the precise population targeted with each intervention, (2) the effectiveness of the intervention in terms of mortality, HIV or TB incidence, and/or a number of other epidemiological or behavioural parameters, and (3) the cost of the intervention. Of these three types of evidence, effectiveness data alone determined which interventions were included in the IC, making the availability of high-quality effectiveness data a key to the entire process. Where cost data were missing, the Task Team used other strategies to estimate costs (see chapter 4.3). Using one of two epidemiological models (see chapter 3.2), modelling was used to derive target population data for each of the interventions.

Selection of interventions by programme area sub-working groups

Sub-working groups for each of the 10 above-described intervention categories began meeting in April 2014, deciding on a preliminary list of interventions in each area to include in the IC. For a number of programme areas, sub-working groups were able to link with existing government-initiated technical task teams that were already working in the same area; in other programme areas, representatives of such task teams were invited to the sub-working group meetings but did not always attend. All programme area sub-working groups met at least once before the stakeholder workshop. The number of interventions and TE factors suggested by each programme area before the workshop are summarised in the first column of Table 12.

In preparation of the stakeholder workshop, the co-chairs of the sub-working groups and associated resource persons received a 2-hour training focused on deciding which interventions to consider during the workshop.

Stakeholder consultation workshop

A large-scale, two-day stakeholder consultation workshop was held on 30-31 July 2014, attended by about 250 participants representing government, academia, civil society, non-governmental organisations and the health care

profession. Starting from a provisional list of interventions drafted by the sub-working groups for each programme area, the workshop solicited ideas regarding new interventions from participants and facilitated discussion on the merits and demerits of existing interventions. The conference also served as a comprehensive data collection exercise, as participants were urged to bring evidence, published or unpublished, regarding the effectiveness and, where available, cost of all interventions they wanted added to the list of interventions.

After an introduction to the format, purpose and analytical framework for the IC, attendees on the first day split into 11 working groups – nine for the basic programme areas and one each for the social and programme enablers and development synergies. Each working group spent several hours on the first and second day discussing the suggested interventions and their target populations, as well as any available evidence regarding the effectiveness and cost of these interventions. On the second day, each working group summarised the discussion by providing a list of interventions, TE factors and enablers deemed relevant to their focus area. These lists were then discussed during a “marketplace”-type session on the second day, during which members of all other working groups were invited to review, comment and suggest additions on these lists, including an invitation to add other interventions missing from the lists developed by the sub-working groups. The intervention lists from the sub-working groups, along with additions from the “marketplace” session, were listed on a single slide, along with primary challenges, for the final summary session. The number of interventions and TE factors suggested by each programme area by the end of the workshop are summarised in the first column of Table 12.

Grading of evidence by sub-working groups

In the days following the workshop, participants were invited to forward papers and other data to the co-chairs of their working group, with co-chairs following up actively for any missing submissions. The results were summarised in a generic Word data template, submitted to the chair of the economics sub-working group for scrutiny and discussed at the next Task Team meeting. At this stage, not all interventions were supported by papers or other documents demonstrating their effectiveness. Based on these templates, co-chairs and resource persons compiled the evidence for each intervention in greater detail into generic Excel data templates, which were submitted together with the cited documents (see the second column of Table 12). The number of interventions had decreased at this stage because not all suggestions from the stakeholder workshop could be supported by evidence.

Box 2: Grading scale for evidence review

- 1 – IN** (good evidence)
- 2 – IN** (existing government policy)
- 3 – OUT** (weak evidence)
 - 3a** – Likely more data by Phase 2
 - 3b** – Important research question
 - 3c** – Exclude altogether
- 4 – Transfer elsewhere**
 - 4a** – other programme area
 - 4b** – social enablers
 - 4c** – programme enablers
- 5 – OUT** (can't be modelled)
- 6 – IN** (consider cost only)

Using this interim list, sub-working group co-chairs and resource persons assigned grades to each intervention, using a grading scale agreed by the Task Team (see Box 2). This process determined whether evidence for the effectiveness of a proposed intervention was available, and if so whether this evidence was of a high enough quality (**grade 1**- criteria for this were left at the discretion of the working groups) to warrant inclusion in the list of IC interventions. The grading process also identified interventions that needed to be placed in a different programme area from the one initially suggested (**grade 4a**) or classified as an enabler (**grade 4b or 4c**). If evidence for an intervention was deemed to be weak, further decisions were made whether more data were likely to become available in Phase 2 (**grade 3a**), whether it was an important question for further research (**grade 3b**- some of these are summarised in chapter 8), or if the intervention should be excluded from the IC altogether (**grade 3c**). Interventions and TE factors without strong evidence regarding their effectiveness

could also be included based on the fact that they were endorsed by government policy (**grade 2**). Finally, interventions and especially TE factors were included if evidence existed that their effectiveness was comparable to another intervention but that the cost was (likely or proven to be) different (**grade 6**). In the case of HIV interventions, the latter two categories, grade 2 and 6, were not included in the optimisation exercise, as their effectiveness could not be modelled; they are, however, included in the IC's Budget scenario.

The sub-working groups on social and programme enablers and development synergies followed a slightly different process after the stakeholder workshop, due in large part to the wide-ranging nature of these enablers and synergies. These required the engagement of a broader spectrum of experts, many of whom were involved at an individual rather than working group level. However, both of these sub-working groups used the same grading system for reviewing evidence as the basic programme areas working groups and submitted the evidence using the same data templates, albeit in a slightly altered version. In reviewing the evidence for social enablers, each publication reviewed was deemed to represent a separate intervention, as each published study focused on a somewhat different version of interventions or on a different target population.

The results of this grading exercise are summarised in the third column of Table 12. Chapter 4 provides details of the interventions considered by each of the working groups, as well as the grades allocated by the working groups to the evidence supporting them.

Grading of evidence by modellers

Four members of the economic sub-working group who were most closely involved with the project's modelling work reviewed the Excel data templates submitted by the sub-working groups. Re-applying the same grading criteria as above, this review also noted interventions that, although supported by strong evidence, could not be modelled because a) the reported impact or b) the target population for the intervention was not represented in the model. For example, neither of the two models used in the IC analysis tracked the viral load of people receiving ART, making it impossible to model the impact of virological failure. Likewise, one of the models used, the Thembisa model, did not permit modelling of interventions for MSM or PWID (although a separate analysis for these populations was undertaken using the Spectrum model). The last column of Table 12 summarises interventions that had good quality evidence but could be included in either model.

Although the TB process was identical with respect to collecting and grading evidence for proposed interventions, modelling of TB interventions is currently still much less advanced than that of HIV. Thus, for Phase 1 of the IC, only a few of TB-related interventions could be represented in the TB model. TE factors are not yet addressed by the TB model, and the details of how to achieve the targets are not captured in the model.

Evidence collected for the programme enablers and development synergies was also reviewed. It was observed that none of the programme enablers reported an impact on more than one programme area. A large number of suggested programme enablers had already been included as TE factors in the care and treatment and HCT programme areas.

Table 12: Tally of suggested interventions and TE factors by programme area at every stage of review

Programme area	Before workshop	After workshop	Included in Excel data templates	Good evidence	Included in models		
					Thembisa	Spectrum	
1. Interventions							
Care and treatment	9	14	45	6	2		
Medical male circumcision	6	2	19	3	6		
Comprehensive condom programming	9	4	26	2	2	1*	
Key populations	20	18	38	12	1	6	
PMTCT	26	8	23	4	3		
HIV counselling and testing	26	4		4	3	1*	
Social behaviour change communication	24	11	17	1	3		
Other biomedical prevention	5	4	26	4	3	1*	
Total HIV	125	65	194	36	23	9	
TB	31	50	26	25	5	-	
Total	156	115	220	61	6	9	
2. TE factors							
Care and treatment	21	23		22	9		
Medical male circumcision	12	14		2	-		
Comprehensive condom programming	4	9		-	-		
Key populations	3	8		-	-	8	
PMTCT	9	10		9	-		
HIV counselling and testing	28	12		20	19		
Social behaviour change communication	5	7		-	-		
Other biomedical prevention	-	22		15	4		
Total HIV	82	105		64	32	8	
TB	31	14		- ^d	-	-	
Total HIV + TB	113	119		64	32	8	
3. Enablers and synergies							
Social enablers and synergies	-	- ^e	65 ^f	13	13	3	
Programme enablers and synergies	-	26	52	- ^g	-		
Total interventions, TE factors and enablers	269	260	337	138	51	3	

*The Spectrum-based analysis included these as part of a package targeted at young women only.

d The TB Investment Case did not include any TE factors in Phase 1.

e The social enablers working group at the stakeholder workshop felt that it was impossible to synthesise the large amount of data during the 2-day workshop.

f Note that for social enablers we treated each publication as a separate intervention since it was impossible to summarise them further as each was reporting on a slightly different version of an intervention and/ or a different target population.

g Note that a large number of the suggested programme enablers had already been included as TE factors in the Care and treatment and HCT programme areas. Amongst the programme enablers that we could model, we found none that reported an impact on more than one programme area.

3.1.7 Review of modelling results

The modelling initiative analysed four different scenarios (for more detail, see chapter 5): (1) baseline; (2) achievement of government targets; (3) unconstrained optimisation; and (4) constrained optimisation. After the Task Team, Steering Committee and Minister of Health reviewed results, they were shared with a wider audience. The Steering Committee made several recommendations for additions and adaptations to the modelling:

- A separate scenario focussed on reaching the 90-90-90 testing and treatment target;
- Additional social and programme enablers, regardless of their cost effectiveness;
- Inclusion of interventions that were already endorsed by current policy and/ or mentioned in the National Strategic Plan for HIV/AIDS, TB and STIs 2012-2016;
- The reporting of results towards the health targets in the National Development Plan.

Accordingly, two additional scenarios were modelled: one using the “90-90-90” optimisation scenario and a “budget” scenario that was based on the 90-90-90 scenario but included a number of additional TE factors and enablers (regardless of cost-effectiveness) that were mentioned in the NSP or other government documents but had not been part of the other scenarios.

3.1.8 Stakeholder engagement regarding results of Investment Case

The results of all six scenarios have been shared with a range of key stakeholders:

- Minister of Health
- SANAC Programme Review Committee
- SANAC Costing Task Team
- SANAC Board of Trustees
- Representatives of civil society
- International experts at several UNAIDS meetings
- PEPFAR South Africa
- National Treasury
- GF Country Coordinating Mechanism.

Comments received from these audiences will be incorporated in an updated analytical framework for Phases 2 and 3.

3.2 INVESTMENT CASE DESIGN PRINCIPLES

3.2.1 Methods of the HIV Investment Case

Objectives and process

The IC aims to establish the most cost-effective mix of interventions against HIV and TB in South Africa over the next 20 years, taking into account both current and future technical efficiency^h, with the goal of optimising both the impact and allocative efficiencyⁱ of the country's HIV and TB programmes. The exercise measured cost-effectiveness as the cost per life year saved by the entire programme of interventions, incremental to a baseline of maintaining *current* coverage with all interventions.

Following the evidence review phase, the following scenarios were modelled by members of the economics sub-working group:

1. *Baseline:* As a baseline for the incremental analysis, a scenario was modeled that maintained coverage with all interventions and TE factors at current (2014) coverage levels throughout the 20-year projection period. This mix of interventions was analysed based on current levels of technical efficiency (Scenario 1a), as well as optimal levels of technical efficiency (Scenario 1b). Scenario 1a serves as the comparison for all other scenarios.
2. *Government targets:* The project analysed the full and incremental cost and incremental cost-effectiveness of the *current mix* of interventions against HIV and TB over the next five years, at *current* coverage targets endorsed by the government. As with the baseline scenario, separate analyses were undertaken for current and optimal levels of technical efficiency. The analysis (Scenario 2) provided insights on both potential impact and feasibility of these targets, while also providing insights into incremental improvements in outcomes associated with enhanced technical efficiency.
3. *Optimisation scenario without constraints:* An analysis was conducted to ascertain the full and incremental cost and incremental cost-effectiveness of the *most efficient mix* of interventions against HIV and TB, with efficiency measured in cost per live year saved, over the next 20 years. This exercise (Scenario 3) also identified *optimal* coverage targets and assessed the impact of achieving them with both current and optimal levels of technical efficiency. No budgetary limits were assumed.
4. *Optimisation scenario with budget constraints:* A separate exercise (Scenario 4) repeated the analysis for Scenario 3, but assessed outcomes with the current budget envelope (including domestic and important external sources) maintained over time. This step aimed to identify the most efficient mix of interventions in the absence of additional resources. As in prior scenarios, analyses were made with both current and optimal levels of technical efficiency.
5. *90-90-90.* Another exercise repeated the analysis for Scenario 3, but with the aim of determining the most cost-effective package of interventions to achieve the 90-90-90 target.

h Technical efficiency in the context of this analysis refers to the maximisation of output (for example, HIV tests done) given a set level of inputs (for example, healthcare staff).

i Allocative efficiency in the context of this analysis refers to the maximisation of a socially desirable output (for example, life years saved) given a set level of funding.

6. *Budget:* To inform relevant domestic and donor budgets, the 90-90-90 scenario was adapted for a more budget-relevant scenario. This scenario started with the current financial year (2015/16) rather than our original start year of 2014/15. The scenario also added a number of interventions and enablers that were not part of the optimisation package despite being current government policy because their effectiveness could not be established based on the evidence reviewed.

Methods

Modelling suite

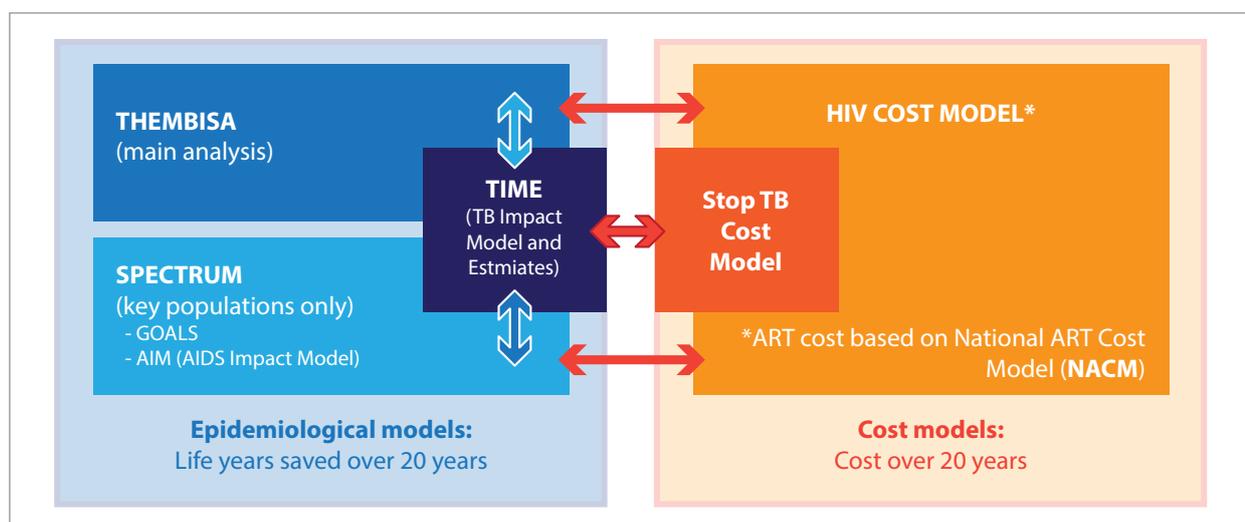
The analysis used two established models of the HIV epidemic in South Africa, as well as a cost model that was purpose-built for this exercise (described in more detail below). Figure 21 summarises the flow of information between the models.

The epidemiological models required input data on (1) the definition of the target population for each intervention, and (2) the effectiveness of each intervention. Effectiveness could be expressed as an impact of the intervention on transmission rates or mortality or on any other intermediate variable or programme indicator, such as condom usage, increase in adherence, decrease in loss to follow-up, or increase in cases diagnosed, etc. For sub-analyses 2b, 3b and 4b, intervention effectiveness was adjusted according to level of technical efficiency.

Based on these different types of inputs, as well as assumptions regarding survival and HIV transmission embedded in the models, these models generated for each intervention: a) the number of HIV and TB infections averted, and b) the number of life-years gained for the financial years 2014/15 to 2033/34.

Taking from the epidemiological model the numbers of people covered by each intervention, the cost model multiplied this number by the unit cost (i.e., the per person/ person year/ test/ visit cost) of the respective intervention. In sub-analyses 2b, 3b and 4b, the cost of scaling up relevant TE factors was added; for example, in cases where TE factors reduced cost (for example, by reducing the staff time required), the unit cost of the intervention was reduced as a result. Cost was evaluated from the government perspective, using public-sector prices, and is presented in undiscounted, nominal terms.

Figure 21: Models included in Investment Case and data flow between models



HIV epidemiological models

The two epidemiological models used to derive projections for the different scenarios were selected based on their capacity to incorporate the impact of a number of HIV interventions on both survival and HIV incidence and their ability to model interventions concomitantly, e.g. estimate the reduced need for ART that results from an expansion of an HIV prevention intervention. The project used:

- a) *Thembisa* model, a dynamic model of the HIV epidemic maintained by the Centre for Infectious Disease Epidemiology and Research at the University of Cape Town [1], and
- b) *Spectrum AIM* and *Goals* model, maintained by the Avenir Health (formerly Futures Institute).

Following recommendations by the Task Team, *Thembisa* was used for the primary analysis, with *Goals* used for the secondary analysis, including data on populations not represented in *Thembisa* (such as MSM and PWID). Because differences in model architecture and assumptions render the results of both models quite different, results from the two models are presented independently in this report.

Thembisa

The *Thembisa* model is an integrated demographic and epidemiological model of the HIV epidemic in South Africa. The model is deterministic and compartmental, dividing the population into a large number of segments defined in terms of demographic, behavioural, intervention exposure and HIV disease characteristics. *Thembisa* stratifies the population by sex and age (in months, at ages 0-9, and in years, at ages 10 and older) and by level of risk (high risk and low risk, the former consisting of individuals with a propensity for concurrent partners and commercial sex activity). Within the two risk categories, *Thembisa* defines various subgroups, based on sexual experience, marital status and (in the case of married individuals) partner risk group. In the model FSW are assumed to be a sub-group of the unmarried high-risk group, and their rate of entry into sex work is assumed to be sufficient to meet the calculated male demand for commercial sex. Rates of marriage and divorce are assumed to depend on age and sex, while rates of entry into non-marital (short-term) relationships depend on age, sex, risk group, marital status and sexual experience. Assumptions regarding coital frequency and condom use depend on type of relationship, age and sex. In addition, condom use is assumed to increase over time, in response to HIV communication programmes and condom distribution programmes, although in recent years there is assumed to have been some decline in condom use relative to the historic trend.

The *Thembisa* model further stratifies individuals according to their level of exposure to different interventions (e.g., ever tested for HIV versus never tested, circumcised versus uncircumcised, currently on PrEP versus not on PrEP, and currently receiving microbicides versus not). The model distinguishes between the age-specific rates of male circumcision that existed historically, prior to the promotion of MMC as an HIV prevention strategy, and the age-specific rates of male circumcision that have resulted from MMC promotion campaigns, with the latter assumed to be highest in those men with the highest levels of HIV risk behaviour. HIV testing rates are specified separately for pregnant women, individuals with HIV symptoms and the general population. All intervention uptake parameters are assumed to change over time, based on published statistics for HIV prevention and treatment programmes.

Adults who acquire HIV are initially classified under the model as acutely infected, after which they progress through four stages of advancing immune suppression in the absence of ART (CD4 \geq 500, CD4 350-499, CD4 200-349 and CD4 < 200). *Thembisa* further classifies HIV-positive individuals according to whether they have been diagnosed with HIV or remain undiagnosed. ART initiation is modelled as occurring either at the point of diagnosis (if the individual is ART-eligible and is linked to care) or at a later date. The model stratifies adults receiving ART according to their baseline CD4 category and time since ART initiation, with mortality rates dependent on these two variables. Although treatment interruptions are not modelled dynamically, it is assumed that a proportion of patients at each ART duration are temporarily interrupting therapy, and this assumption is taken into account when calculating the model estimate of the number of adults currently on ART.

The model assumes that HIV infection in children of HIV-positive mothers occurs either at/before birth or after birth (as a result of breastfeeding), with rates of HIV disease progression differing between the two groups. Rates of mother-to-child transmission are assumed to depend on the mother's HIV stage of disease, the type of antiretroviral prophylaxis received, and (in the case of postnatal transmission) the type and duration of breastfeeding. HIV-positive children are assumed to progress from early disease to advanced disease, and in the absence of early infant diagnosis are assumed to start ART only after having progressed to advanced disease. The model allows for early infant diagnosis at birth or at six weeks (or both); following the change in South African guidelines in 2010, it is assumed that all infants who test HIV-positive are eligible to start ART immediately, even if they have not yet progressed to the advanced stage of disease. Children who start ART before progressing to advanced disease are assumed to have better survival rates than children of the same age who have already progressed to advanced disease before initiating ART.

Thembisa projects the change in the number of individuals in each compartment at monthly time steps, beginning in 1985. To ensure that results are realistic, the model is calibrated to historic HIV prevalence data from antenatal surveys and household surveys, as well as recorded death statistics. Heterosexual HIV transmission probabilities per act of sex are assumed to depend on the HIV disease stage and sex of the infected partner, the age and intervention exposure of the susceptible partner, the type of relationship and the risk groups of both partners.

A limitation of the model is that it does not consider HIV transmission among MSM or as a result of the sharing of contaminated needles. In addition, demographic parameters are preliminary, and forecasts of the future population size are thus subject to considerable uncertainty.

Spectrum/Goals

The secondary analysis for key populations was produced with the Spectrum AIM and Goals models. The AIM model comprises three sub-models for adults, children and mother-to-child transmission (MTCT). The model does not estimate HIV incidence directly, but only estimates the consequence of incidence entered into the model, from the Estimation Projection Package (EPP), Goals or direct user input. For purposes of this analysis, Goals provided the incidence input.

The Goals model captures the HIV epidemic in adult populations, 15-49 years old. Individuals enter the Goals model at age 15 and are assumed to be sexually inactive until they reach the median age at first sex of 16.3 years for men and 17.2 years for women. Individuals are then allocated to one of five risk categories, chosen on the basis of available behavioural data. The risk categories for the Goals model are: stable couples (men and women reporting a single partner in the last year), multiple partners (men and women who report more than one partner in the last year), FSWs and clients, MSM, and PWID.

Under the Goals model, HIV-positive individuals move through CD4 compartments, which is shared with the AIM model and described below. Many HIV-related parameters vary as a function of CD4 count, including progression to lower CD4 counts, HIV-related mortality, probability of initiating ART and infectiousness. Depending on the eligibility criterion and the level of first-line ART coverage, a percentage of those eligible for treatment will start first-line ART. The CD4 structure in Goals allows for the estimation of the impact and resource requirements of expanding the CD4-based ART eligibility criterion for adults to 500 CD4 cells/uL, from its current threshold of 350 CD4 cells/uL. The Goals model also draws from available evidence to estimate the changes in behaviour by risk group as a result of exposure to behaviour change interventions.

Goals calculates new HIV infections by sex and risk group as a function of behaviours and epidemiological factors such as prevalence among partners and stage of infection. The risk of transmission is determined by behaviours (number of partners, contacts per partners, condom use) and biomedical factors (ART use, male circumcision, prevalence of other STIs). Interventions may change any of these factors and, thus, affect the future course of the epidemic.

The Goals model is linked to the AIM module in Spectrum that calculates the effects on children (0-14) and those above the age of 49. The AIM module also includes the effects of programmes to prevent mother-to-child transmission on paediatric infections.

In Spectrum, cost and impact results for HIV are typically prepared using a combination of tools. Incidence impact modelling is done with Goals, utilizing its explicit transmission mechanisms and handles to via coverage input that country users can edit.

HIV cost model

While the secondary analysis using Goals included its own cost model, members of the IC economic working group created a separate cost model for the main analysis using Thembisa outputs. Unit cost assumptions in Goals were updated to represent those established for the Thembisa-based analysis.

For this, the team constructed an Excel-based unit cost model which combined information on the unit cost of each intervention with the population receiving each intervention in each of the model years under each scenario. The unit cost model calculated the cost of each ingredient used in producing one output of an intervention, then aggregated the ingredient costs to arrive at a total unit cost per output of the intervention. For some ingredients, estimates of productivity were required to estimate the ingredient's cost per output (e.g., clients counselled per day by a counsellor).

The unit costs of all interventions were assumed to be constant over time, with the exception of the cost of ART, which changed every year as a result of differing numbers of people initiating ART between the scenarios and the switch to second-line regimens for some people. (In one scenario, the 90-90-90 scenario, ART cost additionally differs as a result of the scale-up of TE factors, notably adherence clubs and home-based ART.) To inform real-world budgets, cost is presented in nominal terms (i.e., unadjusted for inflation) and undiscounted.

For those interventions whose cost was based on ingredients (rather than on literature or expenditure data), the unit cost model ensured that the cost per ingredient was the same across all interventions that included this ingredient (e.g., for every intervention that required a primary healthcare nurse's time, a minute of that nurse's time costs the same). All ingredient costs were based on the most recently available public sector data, either from sources in the public domain (such as the Department for Public Service Administration's salary scales for salaries, the Essential Drug and ARV tender price lists list for drug prices and the price lists of the National Health Laboratory Service) or from budgets from past and current South African grants with the GF. Unit costs based on ingredients are denoted as "*from ingredients*" in Table X below; unit costs based on literature updated by more recent input prices are denoted as "*from ingredients, based on Author (year)*" in Table 45 (Section 4.3.2).

For those interventions for which the unit cost came directly from existing literature, some estimates were so recent that cost items did not need to be updated. Where the literature did not include sufficient detail to permit updating, costs were forward-adjusted to 2014 to account for inflation, using South African consumer price index data from StatsSA (<http://www.statssa.gov.za>). These unit costs are denoted as "*Author (year)*" in Table 45. For a number of interventions (eg, the SASA! community-based gender-based violence intervention or the cost of palliative care) the results of an existing cost analysis had not yet been published but authors graciously shared data ahead of publication; for others, authors undertook additional analysis to permit data to fit the specific intervention or target population (eg, home-based and mobile HCT). These sources are denoted as "*personal communication*" or "*PC*" in Table 45. For those interventions for which data from the literature was available but either input costs or quantities needed adapting, the team assumed the same ingredient cost as for those interventions costed based on ingredients.

Lastly, for those interventions for which neither literature on costs nor detailed ingredients were available or budget data, most often because they were either so new that cost analyses had not yet been undertaken (such as MMC, for

which a detailed cost analysis is currently under way, or the parental monitoring/ positive parenting social enabler), the team used expenditure data instead (denoted as “*Expenditure records from implementing agencies*” in Table 45). For two of the programme enablers that are documented government policy but still in the planning phase, the supply-chain management reforms and the pharmacovigilance programme, cost was based on planned budgets drawn up by the units within the DOH responsible for their implementation.

Data sources

The following data was collected for each intervention:

1. The definition of the target population,
2. The current (2013 or, where available, 2014) coverage for the intervention or TE factor,
3. Effectiveness of the intervention, and
4. Unit cost or, in the absence of this data, as much information as possible on the quantity and cost of the ingredients required in implementing the intervention.

For the government targets scenario, information was also collected regarding the planned government targets up to 2018/19 (where available) for any intervention or TE factor included in available government documents. Data sources for all data items.

Table 13 summarises the data sources for all data items.

Table 13: Main data items included in the Investment Case and their sources

Data item	Source(s)
Definition of target population	Programme area sub-working groups
Size of target population	Epidemiological models
Current coverage	HIV/AIDS CG Annual Performance Evaluation Report 2013/14 [11]; SANAC NSP Progress Report [4]; GARP Report 2014 [12]
Effectiveness	Review of published and unpublished literature; existing assumptions in epidemiological models
Unit cost	Review of published and unpublished literature; expenditure records
Cost ingredients	Review of published and unpublished literature; RSA Global Fund Request for Funding 2013, RSA Global Fund programme budgets for rounds 6, 9, and 10

Calculation of life years

For each intervention, the primary outcome measure was life-years lost due to AIDS, with impact assessed according to the number of incremental life-years saved compared to baseline. Life-years saved was selected over HIV infections averted in order to compare interventions across different scenarios and age groups, as a focus on infections averted would have biased the analysis towards interventions for adults. Moreover, the life-years saved measure combines impacts on incidence and mortality and thus permits a comparison of prevention and treatment interventions. Since only limited data are available from South Africa regarding quality weights, and no data regarding disability weights, life-years saved was selected over compound measures such as quality- or disability-adjusted life years.

Life-years lost were calculated by multiplying the number of deaths due to AIDS in a given age group by the average life expectancy in this age group for a population with low HIV prevalence. Life expectancy values were based on the West Level 26 life table commonly used in Global Burden of Disease calculations [2]. Life years lost (or saved) were counted over the 20-year time horizon of the analysis only. In keeping with the calculation of undiscounted cost as necessary for a budget analysis (see above), neither outcomes (life-years saved) nor costs were discounted.

Selection of interventions to be included in main analysis

Interventions

Using evidence collected during the evidence synthesis process (see Chapter 3), each of the interventions, TE factors and enablers suggested by each expert group (see Chapter 5 for the details of suggested interventions) were reviewed. The analysis linked each intervention and its proposed target group to a number of assumptions and outputs in the models. Some target populations could only be modelled separately in one of the two models (notably, MSM and PWID, which could only be modelled in Goals). Both models were updated during the IC process to represent the details of the selected interventions (such as adding an incremental effect of ART adherence interventions on viral suppression). However, it was not possible to represent all suggested interventions in the current version of the models (See Appendix 1 for the full list of interventions, TE factors, and enablers suggested by each working group, and the rationale for inclusion or exclusion of each). Ultimately, it was determined that the analysis would include 24 of the 36 suggested HIV interventions, 10 of the 64 suggested TE factors, and 11 of the 76^j suggested enablers in the final version of the Thembisa model, for this phase of the Investment Case. As previously noted, Phase 2 will endeavour to review additional evidence that was not available or not presented to us during Phase 1. Table 14 lists the interventions, TE factors, and critical enablers included in the final analysis along with the impacts they had on the model. Appendix 2 provides details of changes to central model parameters for each selected intervention.

Table 14: List of intervention included in the final analysis

Program area	Intervention	Impact represented in model
Care and treatment	Cotrimoxazole	ART uptake
	ART at current guidelines	ART uptake in children and eligible adults (CD4 < 500)
	Universal test and treat	ART uptake in children and all HIV-positive adults HCT uptake
Male medical circumcision	General population MMC	MMC uptake in highly sexually active men
	Early infant male circumcision	EIMC uptake
	MMC age group targeting (10-14, 15-19, 20-24, 25-49)	MMC uptake in highly sexually active men
Comprehensive condom programming	Condom availability	Condom use
	Male and female condom education	Condom use
Key populations	PrEP for sex workers	PrEP uptake for sex workers

^j Note that the large initial list of critical enablers was partially a result of interventions being double counted in different program areas. Most notably, a significant proportion of the programme enablers (9 out of 22) evaluated were found to have been included in the other programme areas already.

Program area	Intervention	Impact represented in model
PMTCT	PMTCT (Triple ART initiation in pregnant women)	ART uptake in pregnant women
	Infant testing at birth	Uptake of infant testing at birth
	Infant testing at 6 weeks	Uptake of infant testing at 6 weeks
HCT	General population HCT	HCT uptake
	Testing of pregnant women	HCT uptake in pregnant women
	Testing of adolescents	HCT uptake in adolescents
Social and behaviour change communication	SBCC campaign 1 ^k	HCT uptake in adolescents Multiple sexual partners
	SBCC campaign 2	Condom use
	SBCC campaign 3	Condom use HCT uptake MMC uptake
Prevention	PrEP for discordant couples	PrEP uptake
	PrEP for adolescents	PrEP uptake for adolescents
	Microbicides ^l	Microbicides uptake

Technical efficiency factors and enablers

To consider the full and incremental cost and cost-effectiveness of each of the scenarios at optimal levels of technical efficiency, the cost and cost-effectiveness of each individual TE factor and critical enabler were analysed. Taken into account in the model.

Table 15 describes how each TE factor and enabler was taken into account in the model.

Table 15: List of technical efficiency (TE) factors and enablers included in main analysis

Program area	TE factor/ enabler	Impact represented in model
TE factors		
ART	GP down referral	Mortality on ART Infectiousness on ART ART retention
	Home-based ART	ART cost (Cost model)
	Community based adherence supporters	Mortality on ART Infectiousness on ART ART retention

^k A number of organisations responsible for SBCC campaigns were involved in a government tender submission process at the time of analysis, so we anonymized the campaigns in order to not influence the tender process.

^l It is important to note that this report refers to the results of Phase 1 of the Investment Case, for which we took all evidence into account that had been published, or brought to our attention, by 31 January 2015 the latest. This meant that some more recent updates, such as the new data regarding the effectiveness of microbicides presented during CROI 2015, or the results of the START and TEMPRANO trials, could not be included in this process.

Program area	TE factor/ enabler	Impact represented in model
ART	Adherence clubs	Mortality on ART Infectiousness on ART ART retention ART cost (Cost model)
	Point-of-care CD4 testing	ART uptake
HCT	Provider initiated HCT	HCT uptake
	Mobile HCT	HCT uptake
	Home-based HCT	HCT uptake
	Workplace HCT	HCT uptake
	HCT invitations to pregnancy partners	HCT uptake
Critical enablers		
	SASA! Community-based gender-based-violence intervention	Multiple sexual partners
	Life skills and vocational training for adolescent girls	Condom use in adolescents
	Risk reduction for alcohol and substance users	Condom use
	Risk reduction for substance users	Condom use
	School-based HIV/STI risk reduction	Multiple sexual partners Condom use
	Teacher support	Multiple sexual partners
	Parental monitoring	Multiple sexual partners Condom use in adolescents
	School feeding	Condom use in adolescents
	Positive parenting	Multiple sexual partners
	Supporting adolescent orphan girls to stay in school	Age of sexual debut
	State-provided child-focused cash transfers	Age disparate sex

Although TE factors could be analysed using the same methods as the main interventions, the critical enablers required an additional step. As enablers (such as cash transfers or school feeding) have broader benefits that extend well beyond HIV, it was also necessary to estimate the proportion of the cost of such enablers that should be borne by the HIV budget. By rationally limiting the share of an enabler's cost to be covered by HIV budgets, it was possible to assess its cost-effectiveness in terms of HIV. To make these determinations, the project assembled a group of experts on critical enablers who used their collective expertise to generate a fair and realistic budgetary delineation for each enabler between the HIV and non-HIV government budgets ().

Table 16: Percentage of cost borne by HIV for each enabler

Enabler	% of total cost borne by HIV budget
SASA! Community-based gender-based-violence intervention	20%
Life skills and vocational training for adolescent girls	100%
Risk reduction for alcohol and substance users	50%
Risk reduction for substance users	50%
School-based HIV/STI risk reduction	0%
Teacher support	10%
Parental monitoring	20%
School feeding	20%
Positive parenting	20%
Supporting adolescent orphan girls to stay in school	50%
State-provided child-focused cash transfers	50%

Using both the incremental cost-effectiveness ratios^m (ICERs) of HCT and ART scale up and of the overall scenarios as benchmarks, it was determined to exclude TE factors and enablers that had ICERs that were an order of magnitude greater than the highest benchmark ICER. It was decided to exclude these from the current analysis, as they would have decreased overall cost-effectiveness (although they might arguably have improved technical efficiency). The remaining TE factors and enablers were included in the final package of interventions under each of the five main scenarios at optimal levels of technical efficiency.

Interventions included in key populations analysis

South Africa's National Strategic Plan 2012-2016 identifies a number of key affected populations that are most likely to be exposed to or to transmit HIV [3]. Among this array of populations, the IC key populations working group focused on sex workers (SW), men who have sex with men (MSM) and people with intravenous drug use (PWID), following the WHO definition of key populations as population groups who are at increased risk of HIV infection and onward transmission due to high-risk sexual behaviors, and who often have legal and social issues related to their behaviours (for more details on the decision of which key populations to include, see Section 4.1.1). Additionally, it was decided to add an analysis of interventions targeting young women between the ages of 15 and 24 years.

Description of populations and interventions

A package of tailored, population-specific interventions was identified for each of the key populations studied. In addition to the package of population-specific interventions, these key populations also have some degree of access to general population interventions (e.g., ART).

Young women aged 15 to 24

Young women between the ages of 15 and 24 years are four times more likely to have HIV than males of the same age. In 2012, the estimated HIV prevalence was 11.4% among young women aged 15 to 24 years, while the prevalence for women and men together in this age group is 7.1%. On average, young females acquire HIV about five years earlier than

^m Incremental cost-effectiveness ratio (ICER): The ratio between the additional cost of an intervention and the additional effect (in life-years saved) of an intervention, measured over baseline.

males [4]. The modelled package of care for young women was based on the DREAMS initiative^m and included PrEP, cash transfers, condom promotion and provision, HIV testing and counselling, school-based HIV and violence prevention, community mobilisation.

Sex workers

Recently published HIV prevalence data for SWs varies between 26% and 59.6% across the country [4]. In 2010, 19.8% of all new HIV infections were related to CSW [3]. A community empowerment-based approach to comprehensive HIV prevention for sex workers was selected as the intervention for SWs in this analysis. The modelled package of care for SWs included STI treatment, peer outreach and counselling, condom promotion, interventions to eliminate stigma and discrimination, interventions to eliminate gender-based violence, HIV testing and treatment, and programmes addressing clients.

People who inject drugs

In 2012, the estimated HIV prevalence among PWID in South Africa was 16.2% [5]. However, it is estimated that only 1.3% of all new HIV infections nationally are related to injecting drug use [6]. A combination of three interventions was chosen as the intervention for PWID in this analysis: needle and syringe programmes (NSP), medically assisted therapy (MAT), and HIV counselling and testing (HCT). The modelled package of care for PWID consisted of initiatives to reduce the risk of spreading HIV and to mitigate other harmful effects of drug use, including harm reduction programmes, such as sterile needle and syringe programmes, as well as opioid substitution and peer outreach.

Men who have sex with men (MSM)

In 2012, the estimated HIV prevalence among MSM in South Africa was 8.6% (HSRC 2012), with 9.2% of all new HIV infections related to this group [6]. HIV prevalence among MSM varies geographically. In this analysis, the community-based behavioural intervention plus an individual intervention package of condoms with lubricant and partner reduction counselling was selected as the intervention for MSM. The modelled package of care for MSM consisted of activities that address men who regularly or occasionally have sex with other men. This includes risk-reduction activities, outreach (including by peers), prevention of sexual transmission of HIV (including condom use, prevention and treatment of STIs), voluntary and confidential HIV counselling and testing, and initiatives to ensure that these groups are able to access these services.

Implementation of scenarios in main analysis

To analyse the six scenarios, central parameters in the two models were altered to reflect changes in coverage and effectiveness of the interventions. This was especially important with respect to Thembisa, as it was the primary model used for the analysis.

Baseline scenario (Scenario 1)

The baseline scenario serves as the counterfactual for the calculation of the incremental effectiveness and cost of each of the other scenarios, but does not necessarily represent a policy option in itself. Since the default Thembisa parameters are the result of Bayesian fitting to available South African survey data, taking into account past interventions and responses to the HIV epidemic as well as current guidelines (including the planned increase in the ART eligibility threshold to 500 CD4 cells/ μ l and PMTCT Option B+ in January 2015), most of the model's default parameters were assumed to be representative of the current state of the epidemic and the response in South Africa. To determine which of the coverage levels (i.e., 0%, 30%, 60% and 90%) best reflected current coverage, government data on current levels of coverage were reviewed and mapped to the model's default coverage levels. The only exceptions to this rule were (1) early infant male circumcision, for which no coverage information from government documents was available but for which Thembisa

ⁿ The DREAMS initiative is a collaborative undertaking launched by PEPFAR, the Bill & Melinda Gates Foundation and the Nike Foundation that involves a combination of evidence-based interventions to reduce new HIV infections among adolescent girls and young women.

assumed 10.5% baseline coverage, and (2) PMTCT, for which the model default was 80% coverage. For interventions that are not currently available in the public sector, such as Universal Test and Treat (UTT), PrEP, and microbicides, a baseline coverage of 0% was assumed. Table 17 summarises the baseline coverage values from government sources as well as the baseline levels used in the model for all interventions.

Table 17: Baseline coverage levels of each intervention

Intervention	Baseline coverage level from government source	Source	Baseline coverage level used in model
Cotrimoxazole	-		90%*
ART at current guidelines	66.25% (Percentage of adults and children currently receiving ART among all adults and children living with HIV) ^o	[12]	60%
Universal test and treat	-		N/A
Medical male circumcision (MMC)	40.6% (Proportion of men circumcised 15-49)	[12]	30%
Early infant male circumcision	-		10.5%*
MMC age group targeting	-	-	-
Condom availability	58.4% (Condom use at last sex among people with multiple sexual partnerships 15-24)	[12] (citing [5])	60%* ^p
Male and female condom education	18.4%	[7]; Thembisa estimates for married women	30%
PrEP for sex workers	-		0%*
PMTCT	90% (Percentage of HIV-positive pregnant women who received antiretroviral medicine to reduce the risk of MTCT)	[12]	80%
Infant testing at birth	-		0%*
Infant testing at 6 weeks	75.3% (Percentage of infants born to HIV-positive women receiving a virological test for HIV within two months of birth/Early infant diagnosis EID)	[12]	60%
General population HCT	66.2% (HIV testing in the general population in last 12 months and know results 15-49)	[12]	60%
Testing of pregnant women			90%
Testing of adolescents		[12]	30%

^o This percentage is most likely an overestimate, based on previous results of Spectrum modelling.

^p This is based on the Thembisa's assumptions on the number of protected sex acts and data from government tenders on the number of condoms distributed.

Intervention	Baseline coverage level from government source	Source	Baseline coverage level used in model
SBCC campaign 1 ^a	17%	Programme evaluation data in conjunction with default model population estimates	30%
SBCC campaign 2	77%		90%
SBCC campaign 3	60%		60%
PrEP for discordant couples	-		0%*
PrEP for adolescents	-		0%*
Microbicides	-		0%*

*Authors' assumption

To project results through 2034/35 for the baseline scenario, coverage was assumed to remain constant for all interventions except ART. For ART, constant coverage (40%) was assumed for newly diagnosed non-pregnant, asymptomatic patients who start ART soon after diagnosis. However, in line with new guidelines, the baseline scenario assumed further uptake among pregnant women and symptomatic patients.

Government targets scenario (Scenario 2)

Current government coverage targets were available for a number of the most important interventions for the years 2014/15 to 2016/17 or 2017/18. Whenever more than one coverage estimate was available for a single intervention, the most recent source and/or the one covering the longest time period was used. which such data was available.

Table 18 summarises the values and sources for the selected government coverage targets for all interventions for which such data was available.

Table 18: Government coverage targets of selected interventions

Intervention	Metric	Coverage target from government source					Source
		2014/15	2015/16	2016/17	2017/18	2018/19	
ART	Number of people on ART	3,000,000	3,600,000	4,200,000	4,700,000	5,100,000	[8]
PMTCT B+	% of antenatal clients initiated on ART	93%	96%	98%	99%	100%	
MMC	Number of men newly circumcised	1 million	1 million	1 million	1 million	1 million	
Male condoms	Number of male condoms distributed	1 billion	1 billion	1 billion	1 billion	1 billion	[3] [3]
Female condoms	Number of female condoms distributed	17 million	22 million	25 million	25 million	25 million	
PEP	Number of rape victims receiving PEP	55,039	58,613	62,187	-	-	
HCT	Number of HIV tests conducted	11 million	11 million	11 million	11 million	11 million	[8,9]

For the majority of targets that were expressed as total numbers, exact values or values fitting variables for relevant years were manually entered. (An example of such a fitting variable is the number of adults and children initiating ART in order

^a A number of organisations responsible for SBCC campaigns were involved in a government tender submission process at the time of analysis, so we anonymized the campaigns in order to not influence the tender process.

to fit to total number of patients remaining on ART.) Goodness of fit was examined by visual inspection, and a maximum divergence of +/- 5% from the original value was deemed acceptable.

Optimisation scenario without budget constraint (Scenario 3)

The optimisation scenario permitted investigation of the maximum epidemiological impact that could be achieved if only net beneficial interventions (i.e., interventions whose scaling up (or down) resulted in an HIV programme that either costed less or was more effective than the baseline, or both) were implemented.

The team examined the impact of scaling each intervention up or down to any of the default coverage values (30%, 60% and 90%) that were not assumed to represent baseline coverage. (For example, an intervention with 60% baseline coverage was scaled down to 30% and up to 90%; an intervention with 30% baseline coverage was scaled up to both 60% and 90% coverage; an intervention with 90% baseline coverage was scaled down to 60% as well as held constant at 90%; and an intervention deemed to have zero coverage at baseline was scaled up to 30%, 60% and 90%.) For ART at current guidelines, it was not possible to reduce ART coverage to 30% without either assuming that existing patients would be taken off treatment or that patients with an opportunistic infection or pregnancy would be prevented from starting ART. Accordingly, the analysis used the lowest possible coverage under current guidelines (72% in 2019). Two UTT scenarios were analysed: the first removed any CD4 restriction to ART eligibility but maintained current testing rates, while the second increased HCT coverage to allow 90% of people living with HIV to obtain HIV treatment. Lastly, for the MMC age group targeting interventions, the exercise only modelled no targeting or a doubling in the rate of MMC uptake in the targeted age group.

We arrived at a total of 50 combinations of intervention and coverage levels to be included in the optimisation scenarios (summarised in Table 19 Table 19).

Table 19: Coverage levels modelled in optimisation scenarios

Intervention	Baseline coverage level used in model	Coverage levels modelled (coverage in 2019)
Cotrimoxazole	90%*	30%; 60%
ART at current guidelines	60%	Lowest possible coverage (72%); 90%
Universal test and treat	0%*	Eligibility change only (no impact on testing); 90%
Medical male circumcision (MMC)	30%	60%; 90%
Early infant male circumcision	10.5%*	30%; 60%; 90%
MMC age group targeting (10-14, 15-19, 20-24, 25-49)	-	0%; double the coverage of the general population
Condom availability	60%	30%; 90%
Male and female condom education	30%	60%; 90%
PrEP for sex workers	0%*	30%; 60%; 90%
PMTCT	80%	30%; 60%
Infant testing at birth	0%*	30%; 60%; 90%
Infant testing at 6 weeks	60%	30%; 90%
General population HCT	60%	30%; 90%
Testing of pregnant women	90%	30%; 60%
Testing of adolescents	30%	60%; 90%

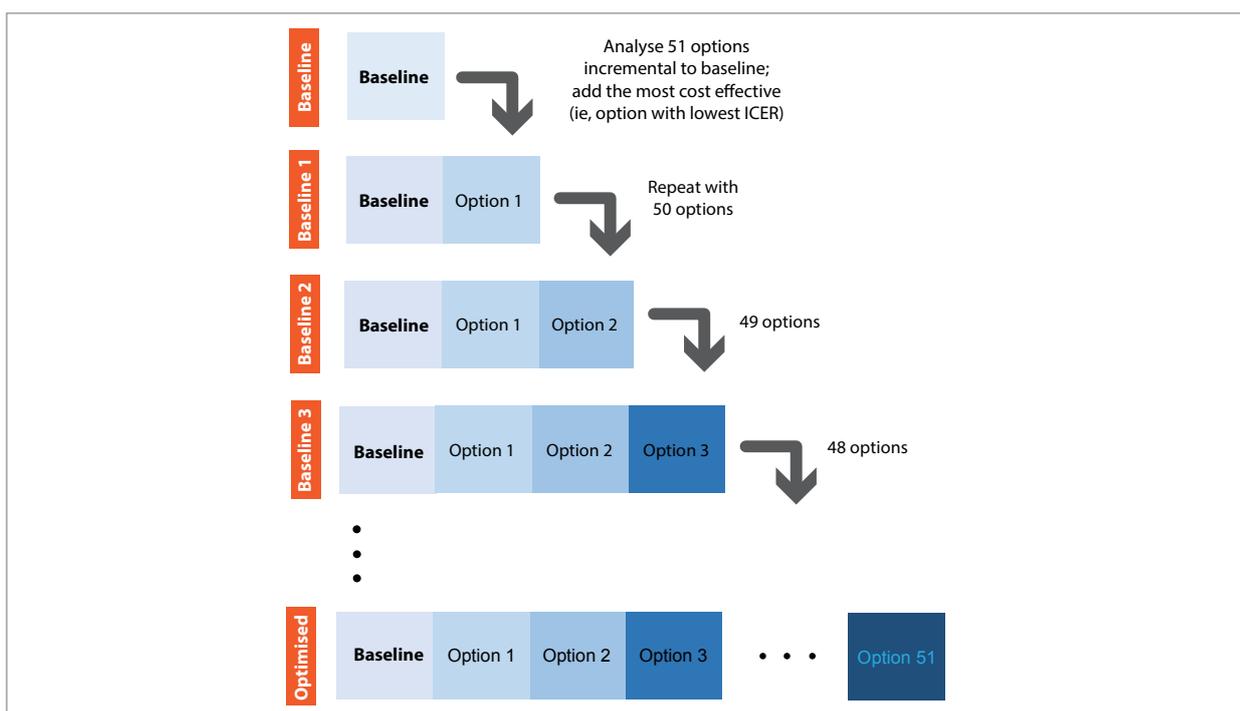
Intervention	Baseline coverage level used in model	Coverage levels modelled (coverage in 2019)
SBCC campaign 1	30%	60%; 90%
SBCC campaign 2	90%	30%; 60%
SBCC campaign 3	60%	30%; 90%
PrEP for discordant couples	0%*	30%; 60%; 90%
PrEP for adolescents	0%*	30%; 60%; 90%
Microbicides	0%*	30%; 60%; 90%

The optimisation analysis calculated the ICERs of each intervention at each coverage level over the baseline scenario, resulting in 50 separate ICERs (Figure 22).

To take into account effects arising from interactions between interventions, the baseline was modified to include the most cost-effective intervention, i.e. the intervention with the lowest ICER, and the modelling team evaluated the incremental cost-effectiveness of all interventions relative to this new baseline. Thus, for a highly cost-effective prevention intervention, it would also be important to evaluate the impact that adding any of the other interventions would have to the ultimate impact of the prevention intervention. Taking account of these synergistic effects, other interventions were evaluated relative to the new baseline instead of the initial baseline.

Rules were adopted to deal with negative ICERs, which can either represent cost savings (positive impact on effectiveness, negative impact on cost) or harmful interventions (negative impact on effectiveness, positive impact on cost). After excluding interventions in the latter category, the team evaluated the remaining cost-saving interventions by ranking them by both life-year-saved and incremental cost, in descending order and ascending order respectively. The intervention with the lowest combined rank was selected, representing the most effective and cost saving intervention in aggregate.

Figure 22: Optimisation routine and decision rules



The team repeated this procedure iteratively until the entire list of options was exhausted. At each iteration, the analysis considered reverting to the previous baseline as an option. As a result, some options were eliminated when the model suggested that the more cost-effective option was not to implement this intervention at the particular level of coverage^r. Each intervention was only given one chance of reverting, in the run immediately after which it was implemented; if an intervention was robust to reversion (in other words, if it was more cost effective to implement it at the coverage level that was higher (or lower) than its baseline coverage), it was included without further evaluation; if no robust effect over baseline was seen, it was definitively excluded from the analysis altogether. Finally, for interventions that were mutually exclusive, such as ART at current guidelines and UTT, or for different coverage levels for the same intervention, for the final package of care resulting from this scenario the option that was selected later by the optimisation routine was chosen instead of the option that was selected earlier, provided that it withstood the test of reversion to the previous baseline explained above. For those interventions for which several coverage levels were chosen, options representing higher coverage were selected for the final package.

For the final package of interventions, the team calculated the total impact on life-years saved and HIV infections averted as well as the total cost of this scenario, with results used to compare across the different scenarios.

Optimisation scenario with budget constraint (Scenario 4)

Scenario 4 examined how many of the interventions selected in the previous scenario would be affordable under the planned budget for the current mid-term expenditure framework (MTEF) period (2014/15 to 2016/17) and whether the priorities would change in light of budget limitations. To undertake this analysis, the team repeated the procedure for Scenario 3 while comparing the total cost after the addition of every new option to the constrained budget^s.

All planned HIV-related contributions from all government sources over these years (including the comprehensive HIV/AIDS conditional grant as well as direct national and provincial HIV spending) were reviewed, based on documents from the National Treasury. These documents included the Estimates of Provincial Expenditure and Estimates of National Expenditure, the Medium Term Budget Policy Statements, Budget Reviews and the Division of Revenue Bills/Acts) as well as planned expenditure from PEPFAR (based on PFIP committed amounts) and a forecast of annual budgeted amounts from the GF. (Note that although data from the latter two sources were available through 2017/18, it was determined to restrict the analysis to the South African government MTEF period, as the government contributed by far the largest amounts.) While there are a number of other donors who traditionally contribute funds to the South African HIV programme, these are much smaller in comparison to these three funding sources and will not likely have an impact on the ranking and inclusions of interventions in this scenario.

^r In cases where two interventions at different coverage levels had an identical ICER, we deferred to the higher coverage level option due to a preference for a greater epidemiological impact.

^s For this specific procedure, we excluded the cost of inpatient care from the total cost of the package since inpatient care is not funded under the HIV funding envelope we constructed.

Table 20: Assumed HIV budget constraint for 2014/15 to 2016/17, based on planned budgets from the South African government, PEPFAR and GFATM

Totals (ZAR millions)	2014/15	2015/16	2016/17	Source
South African government	14,698	16,425	18,358 ^t	Estimates of Provincial Expenditure; Estimates of National Expenditure; Medium Term Budget Policy Statements; Budget Reviews; Division of Revenue Bills/ Acts.
PEPFAR	3,670	3,300	2,800	PFIP
GFATM	1,246	1,400	541 ^u	Forecast of annual budgeted amounts
Total funding envelope	19,613	21,125	21,699	

In the final constrained optimisation scenario, some budget remained unspent after adding as many full interventions as were affordable under the budget constraints. To account for this remaining budget, the next most cost-effective intervention was scaled to as high a coverage as possible before hitting the budget limit.

90-90-90 scenario

Although informative for national policy-making and resource allocation, neither the package of interventions included in the full unconstrained optimisation nor the budget constrained scenario necessarily corresponded to political realities. Accordingly, the team consulted with relevant stakeholders and the steering committee to ascertain the most pertinent policy questions and epidemiological targets were. These informants noted that the Minister of Health had endorsed the 90-90-90 coverage targets (Table 21) prescribed by UNAIDS as “ambitious treatment targets to help end the AIDS epidemic” [10]. These are now widely accepted as policy-relevant aspirational coverage targets for South Africa.

Table 21: The 90-90-90 coverage targets specified by UNAIDS

90-90-90 targets (in 2020)	Target
% of all people living with HIV who know their status	90%
% of all people diagnosed with HIV who receive sustained antiretroviral therapy	90%
% of people receiving antiretroviral therapy who have viral suppression	90%

Accordingly, the team repeated the optimisation procedure described above, while comparing model outputs on coverage against the targets specified by UNAIDS at each stage. The final 90-90-90 scenario includes the minimum package of interventions required to meet these targets in 2020.

Sensitivity analysis

Sensitivity analysis on epidemiological, cost, and cost-effectiveness estimates were undertaken to provide an estimate of the uncertainty regarding key results. First, the team conducted probabilistic sensitivity analysis regarding key effectiveness parameters in Thembisa^v. Table 22 lists the effectiveness parameters included in the sensitivity analysis, as well as the characteristics of the distributions used for the sampling. The team conducted 1000 simulations, sampling collectively across the three parameters in this analysis, for each of the IC scenarios^w.

^t In cases where two interventions at different coverage levels had an identical ICER, we deferred to the higher coverage level option due to a preference for a greater epidemiological impact.

^u For this specific procedure, we excluded the cost of inpatient care from the total cost of the package since inpatient care is not funded under the HIV funding envelope we constructed.

^v The methods used for this analysis are similar to those used and outlined in separate analysis conducted using the Thembisa model.

^w Note that we excluded the government targets scenario (Scenario 2) from our sensitivity analysis since the purpose of the scenario was to examine the epidemiological impact, cost and cost effectiveness if the precise government targets were achieved.

Table 22: List of effectiveness parameters included in sensitivity analysis

Parameter	Distribution	Mean	Standard deviation
Infectiousness after ART initiation, relative to pre-ART	Beta	0.2	0.093
Multiplicative factor on mortality on ART	Gamma	1	0.257
Reduction in the proportion of sex acts that are unprotected after HIV diagnosis	Beta	0.31	0.269

For each of the scenarios, the level of uncertainty for the key epidemiological outputs were informed directly by the 95% confidence intervals of the 1000 simulations generated in Thembisa, calculated using the 2.5th and 97.5th percentiles from the model estimates. The epidemiological results were then entered into the cost model, where variation in the costing populations across simulations informed the uncertainty regarding the total cost of each scenario. Although there is uncertainty regarding the unit costs of each intervention, the team was unable to take this into consideration under the current analysis.

Implementation of scenarios in key populations analysis

The Goals model was used to estimate the cost, impact and cost-effectiveness of scaling up HIV interventions targeting each of the key high-risk populations. In keeping with the main analysis, a baseline scenario was modelled for each high-risk group, maintaining the current coverage for all interventions at constant 2014 levels. The analysis then scaled up the entire intervention package for each key population in a linear manner from 2015 to a target coverage of 30%, 60% or 90% by 2019, calculating the incremental cost-effectiveness of the package over the baseline scenario. As in the main analysis, cost-effectiveness for key population packages was expressed as incremental cost per life-year saved over a 20-year time span. Results from these separate analyses (Thembisa and Goals) were not combined in order avoid double-counting of costs and impact, as a number of the interventions for young women and sex workers are also part of the main analysis. In addition, Thembisa and Goals have different underlying assumptions, making a simple combination of results from these two models inappropriate.

3.2.2 Methods of the TB Investment Case

The TB Investment Case aimed to establish whether implementation of a combination package of prevention, diagnosis, and treatment of TB would achieve global targets for the elimination of TB. In contrast to the HIV Investment Case, an additional optimisation of interventions was not possible at this stage of the Investment Case but is planned for Phase 3.

TB epidemiological model

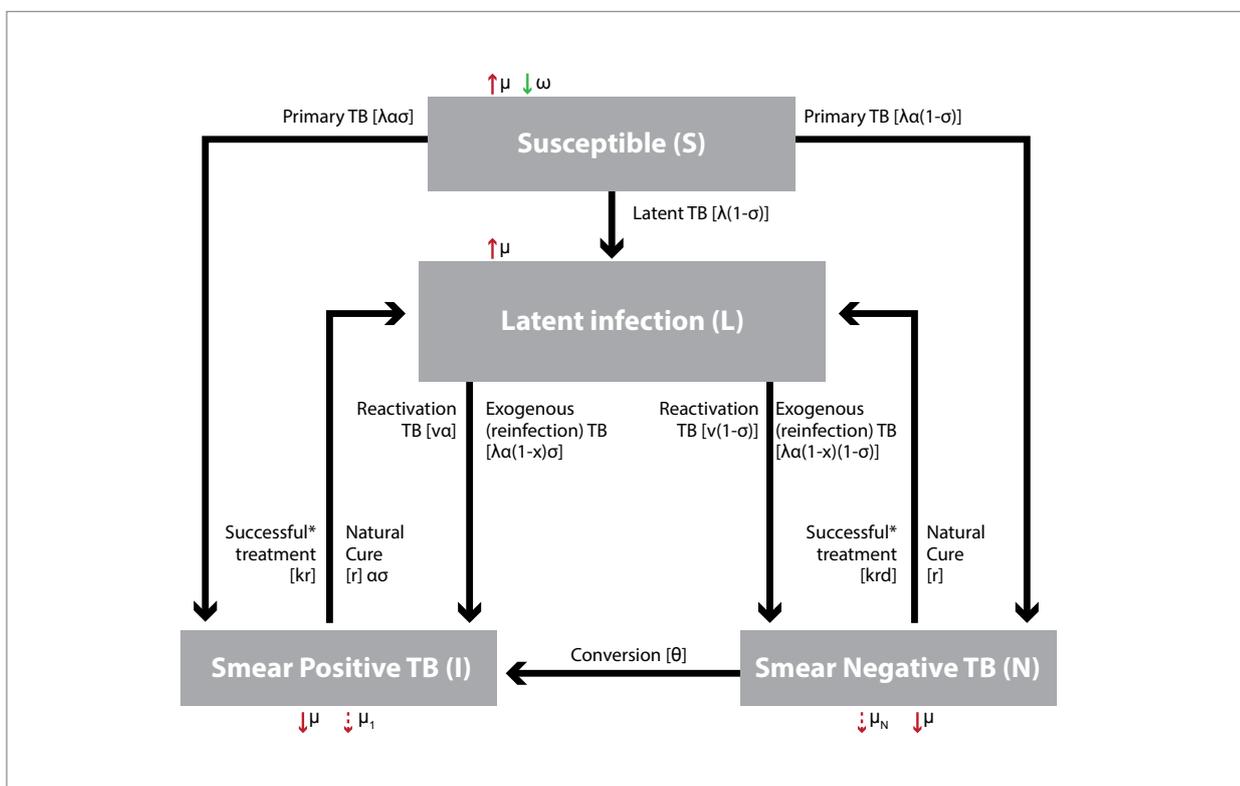
The results of the different HIV scenarios (see Section 3.2.1) served as the starting point for the TB IC. The AIM model in Spectrum, which was used estimate the impact of TB interventions on TB incidence and mortality, includes the TB Impact Model and Estimates (TIME), which uses HIV information directly from AIM. This information includes the distribution of the age-structured population by HIV, ART status and CD4 category. The HIV sub-model in TIME has the same population structure as AIM, as well as the same progression rates with or without ART. After new HIV infections are input directly in AIM, TIME uses the estimate of new HIV infections from AIM. HIV program statistics (ART and PMTCT figures) are also entered directly to AIM. These data input mechanisms made it possible to map the HIV scenarios as produced by the HIV IC into TIME, including those estimated by the Thembisa model.

TIME is a dynamic compartmental TB model developed by the TB Modelling and Analysis Consortium (TB MAC) in the version calibrated to the South African TB epidemic. The model version is the same as that used by the Stop TB

Partnership to develop the new TB Global Plan. It includes all essential TB processes: primary infection, latent infection, reactivation, re-infection, the presence of a general MDR strain (with a fitness and acquisition rate that are different to that of drug-susceptible TB), mortality from TB and the impact of HIV on TB incidence and mortality. The model allows users to investigate the impact of scaling up key TB interventions, such as active case finding, diagnosis via Xpert^x, improving treatment success and others, on measurable indicators such as TB incidence and notification rates, and to cost the scale-up of such activities.

The TIME model was developed through a collaboration between the WHO Global TB Programme, UNAIDS, TB MAC, the Stop TB Partnership, and Avenir Health under the auspices of the UNAIDS Reference Group on Estimates, Modelling and Projections [13]. The model has more than 1000 compartments: two for sex, 17 for age (5 year bins), two for MDR TB status, seven for TB status, five for ART status and eight for CD4 category. The structure of the model is shown in Figure 23.

Figure 23: Core TIME structure and population flows



(The structure is repeated for MDR status, HIV and ART status, different CD4 categories, ages and sex. Black arrows represent transitions between TB states, green arrows represent births, and red solid arrows represent background deaths)

Parameters for TIME were developed through a separate process of systematic review and model calibration. Further information on the development of the TIME model, including systematic reviews informing the selection of single parameter values, can be found elsewhere [14-25].

x As explained by WHO: "Xpert MTB/RIF is an automated, cartridge-based nucleic amplification assay for the simultaneous detection of TB and rifampicin resistance directly from sputum in under two hours."

TB cost model

The TB IC used an newly developed TB cost model, the Stop TB Global Plan (TB GP) costing workbook, which was parameterised with relevant South African data regarding the unit costs of TB screening (active case finding and intensive case finding), diagnosis, and treatment of susceptible and resistant strains at the outpatient and, where necessary, inpatient level treatment. A software routine was developed to update the target population and coverage for each of the HIV and TB scenarios within the TB GP costing workbook in order to calculate the costs of each scenario.

Several specific methods were used in the TB GP costing tool. The general formula for the calculating the costs of delivering an intervention was:

Target population(t) x PIN (t) x Coverage(t) x Level(t) x Unit cost(t)

where:

- **(t)** is the model year, i.e. the target population at time (t)
- **Target population(t)** is the population who should or have received an intervention, e.g. the projected number of TB patients that should be or have been tested for drug resistance.
- **PIN (t)** is the percentage of the target population eligible for the intervention based on guidelines, which may expand to more cases; e.g. isoniazid preventive therapy (IPT) for HIV-infected patients on ART who are tuberculin skin test (TST) positive.
- **Level(t)** is used to track at which 'level' of the overall programme the service is provided, e.g. community, primary health care clinic, district, or provincial. For example, XDR TB treatment is largely centralised at the provincial level in South Africa, while access to Xpert MTB/RIF sputum testing is available through the primary health care clinic. Intervention coverage by level of delivery is specified for 2015 and at 2020.
- **Unit cost(t)** is a time-dependent unit cost, e.g. reflecting a gradual move to cheaper diagnostic methods.

Unit costs were sourced from published and unpublished research of costs in South Africa (see Section 4.3).

Case finding in high-risk populations and the TB screening campaign

The method in the costing workbook for active case finding (ACF) was not able to correct the yearly percentage of TB found in the high-risk groups. TIME did not specify the mix of active, intensive, and passive case finding. As these two approaches – passive case finding (free – wait for the patient to present) and active case finding (symptom screen people wherever they are in the community) – differ in the resources they require, a mix of case finding methodologies were added into the cost model; optimisation of this case finding mix was not done in Phase 1.

On World TB Day, 24 March 2015, Health Minister Aaron Motsoaledi and Deputy President Cyril Ramaphosa pledged to launch a massive TB campaign. Costs associated with the campaign were estimated and added to the overall interventions described above. This multi-phase massive TB screening campaign is one of the specific activities that planned for achieving the 90-90-90 targets.

The national campaign involves three phases:

Phase 1: Persons living in six identified peri-mining communities will be reached through a combination of intensified case finding (ensuring that all attendees at primary health care facilities are symptom-screened for TB) and active case finding (using symptom screening in poor communities to reach people who did not know to or were not able to access the primary health care centres).

Phase 2: While intensified case finding continues in the peri-mining communities, active case finding with field workers and community events will focus on the informal, poor, and at-risk communities in the 10 municipalities in South Africa that account for the highest burden of TB cases.

Phase 3: While intensified case finding continues at clinics in all high-risk communities, active case finding will focus on informal, poor, and at risk communities not previously reached within the four provinces that account for the highest burden of TB cases in South Africa.

In total, 8.5 million people who are at increased risk of TB will be reached through active TB case finding during the campaign.

TB Investment Case interventions

As noted in Section 3.1, preliminary results of the TB MAC exercise for South Africa were presented at the World Lung Conference in Barcelona, November 2014. Informed by these results (described below), Minister Motsoaledi announced the 90-90-90 TB targets scenario at the same conference. Accordingly, the TB IC case was informed by two scenarios: one maintaining current coverage and the other achieving the 90-90-90 TB targets (Table 23).

Table 23: List of scenarios analysed under the TB Investment Case

Scenario	Description
Baseline	The baseline for the incremental analysis. This scenario keeps the coverage of all interventions constant at current (2014) coverage levels throughout the 20-year projection period.
90-90-90	Calculates the costs and impact of screening 90% of those most vulnerable to TB, diagnosing and initiating on treatment 90% of the prevalent cases of active TB, and ensuring that 90% of those on treatment are successfully treated.

Baseline coverage levels for the TB MAC exercise were those reported in 2014, projected forward across 20 years. To undertake this scenario modelling, the model was calibrated to the South African TB epidemic. Baseline coverage for TB interventions and outcomes is outlined in Table 24.

Table 24: Coverage levels with TB interventions under baseline and 90-90-90 scenarios.

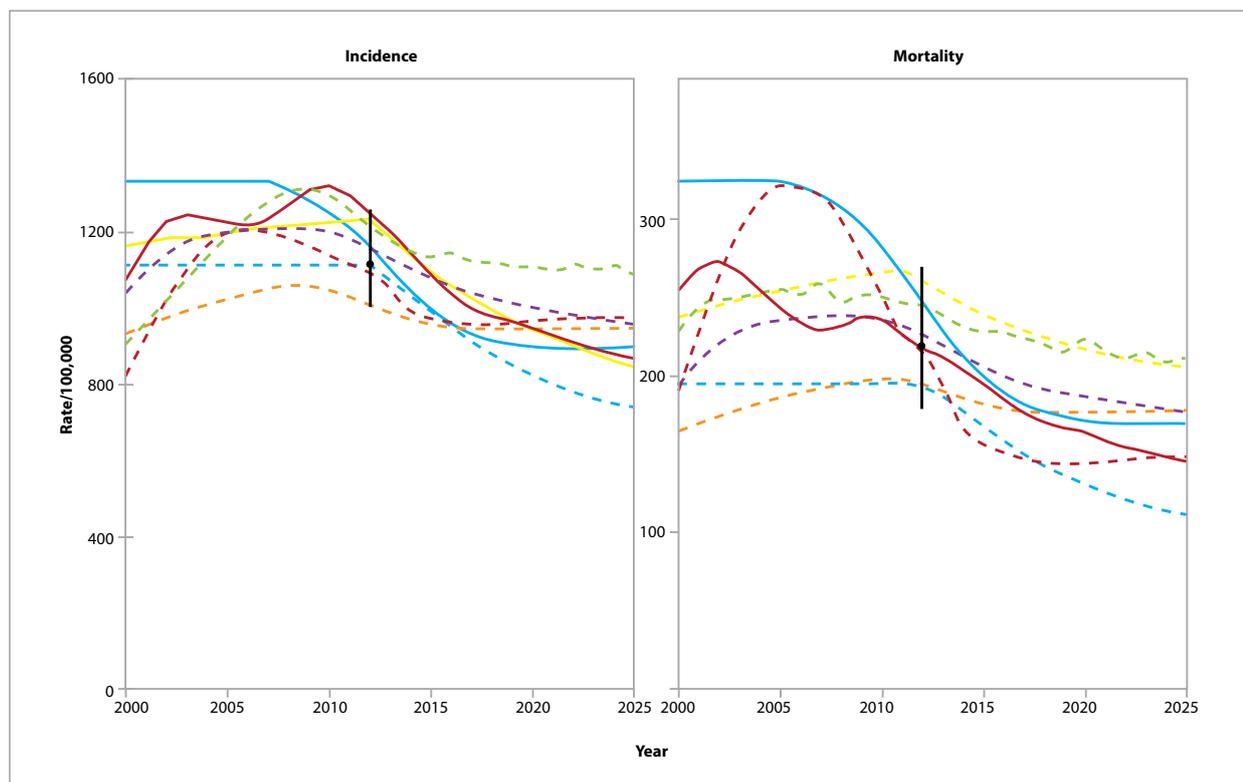
Aim	Intervention	Baseline (2014)	90-90-90 (2020)
1. Screen vulnerable populations for TB	Proportion of high risk groups symptom screened for TB: intensified case finding in clinics and other health facilities	20%	90%
	Proportion of high risk groups symptom screened for TB: active case finding in communities, schools, correctional facilities, workplaces, etc.	5%	90%
	If no active TB and eligible for IPT, initiate on IPT	5%	100%
2. Diagnose and treat TB	Proportion of estimated TB cases diagnosed and initiated on treatment	57%	90%
	If HIV co-infection, appropriate treatment includes ART	66%	100%
3. Successfully treat TB	Proportion of drug sensitive TB cases treated successfully	76%	90%
	RIF resistant TB, successful outcome	45%	70%

Rationale for a combination package of interventions

The TB IC began with the premise that a combination of TB interventions would be required and that no single intervention would achieve the required global targets. This starting point resulted from the TB MAC Targets modelling exercise, a multi-model exercise designed to answer operational questions about the potential impact of a set of defined TB interventions on reaching WHO's 2025 TB targets of a 50% reduction in TB incidence and a 75% reduction in TB deaths.

To undertake this multi-model exercise, the team calculated baseline coverage levels using data from the South African National TB Programme (SA NTP), the WHO Global TB database, the Institute for Health Metrics and Evaluation's Global Burden of Disease study and UN Population Division estimates. Models were calibrated to the TB incidence, mortality, and population size values reported in 2012. As a result, the baseline scenario indicates declining trends in both TB incidence and mortality. Figure 24 below shows the modelled TB incidence and mortality produced by the eight participating models. The black dot and vertical black line are the 2012 point estimate and uncertainty range used for calibration, respectively. Each of the eight models projected a continued decline in TB incidence and mortality as the baseline scenario.

Figure 24: Modelled baseline trends in TB incidence and mortality, 2000 to 2025



Source: P. Hippner, 2015 [25]

Six intervention packages, each comprising those existing TB tools or interventions which extensive reviews of the evidence had suggested would potentially be effective in reducing TB incidence and/or mortality, were defined and applied to three TB contexts: South Africa, India and China. A seventh scenario combined the effect of all of the interventions. Several modelling groups prepared results for the each of the interventions individually and in combination, using different models. Two sets of potential coverage levels or targets for each intervention were sourced: a) 'Country experts' based upon the SA NTP targets at end 2014 and b) 'Advocates' based upon input from Stop TB. The interventions in the TB MAC Targets exercise were strongly aligned to interventions suggested during the stakeholder review process of evidence, and thus were used as the preliminary step for the TB IC model.

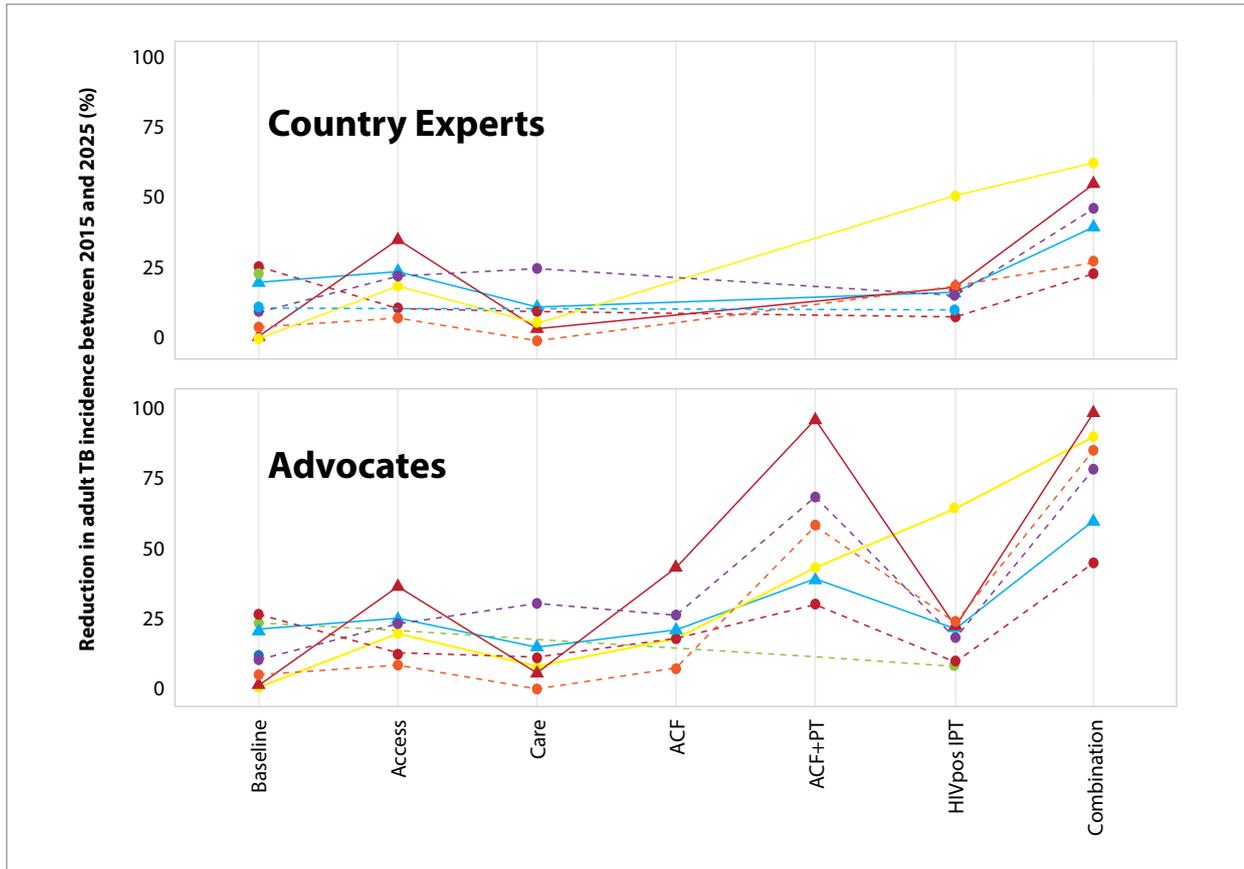
Interventions in the TB MAC Targets exercise

The modelling exercise focused on the following interventions:

1. Increase the average diagnostic rate (i.e., case detection rate) by screening all primary health care clinic attendees for TB symptoms, a method of intensified TB case finding (ICF).
2. Increase linkage into care, for drug-sensitive and drug-resistant (DR) TB cases (reduced pre-treatment loss-to follow up). The diagnostic rate in the model is multiplied by 1-(initial default) to determine the rate at which individuals enter the treatment pathway.
3. Improve treatment success for drug-sensitive and DR TB. All individuals starting treatment move to the “previously treated” strata of the model, with the proportion successfully treated moving to the latent state and the remainder remaining in the active disease states.
4. Replace smear microscopy with Xpert MTB/RIF as first-line diagnostic method for TB. South Africa had achieved full Xpert roll-out at baseline (2014/2015); Xpert sensitivity for diagnosing smear-negative TB and DR TB were maintained from baseline.
5. Provide lifelong isoniazid preventive therapy (IPT) for HIV-infected persons on ART who are TST positive for latent TB infection.
6. IPT for persons with latent TB infection and no active TB disease identified through the biannual general population ACF indicated above. Because ACF in the general population was not modelled, IPT follow-up after ACF was also not modelled.
7. Combined effects of the above interventions (if included), a comprehensive package of TB prevention, case finding, diagnosis, and treatment.

Biannual active case finding (ACF) in the general population through community-based outreach was not included in the package of interventions for South Africa. Although ACF among high-risk groups is planned for South Africa, the models participating in the TB MAC Targets exercise did not have separate compartments for high-risk groups (e.g. miners or prisoners). While ACF and IPT for the general population was proposed by the international advocates, country experts did not regard it as feasible to provide IPT to the millions of persons who are HIV-negative and not at high risk for active TB disease in the context of South Africa.

Figure 25 displays the impact on TB incidence in South Africa between 2015 and 2025 for each of the modelled interventions, using either the country expert or advocates coverage levels. Each of the different coloured lines represents a different model and modelling group’s estimates, while each of the points represents an estimate of the percent reduction in TB incidence for a specific intervention. Among interventions (excluding ACF + IPT), only the combination of all interventions achieved the overall target of 50% reduction in TB incidence, providing the basis for use of a combination package approach by the TB IC.

Figure 25: % reduction in TB incidence achieved with each intervention individually or in combination

Different TB MAC participating models. Source: P. Hippner, 2015 [25]

3.2.3 Integration of HIV and TB interventions

The SA IC concerns itself with both HIV and TB, and a considerable fraction of the patient population will need both HIV and TB services. To take this into account, the modelling team took care to avoid double-counting the costs of services rendered to the same person. The exercise further assumed that services for HIV and TB would be fully integrated, e.g., by assuming that separate visits would not be needed for TB screening or diagnosis in people living with HIV but that these would be part of a standard testing event or ART initiation visit. TB screening was costed as part of HCT under the HIV IC, and IPT for people living with HIV as part of the TB IC.

Table 25 summarises these interventions.

Table 25: TB/ HIV interventions included in the HIV or TB Investment Case

In the HIV model

ART for TB patients
Co-trimoxazole prophylaxis (CPT)
HCT for TB cases (costs of HCT)
TB symptom screening (ICF) at HCT, regardless of HIV result (costs of symptom screening)
TB symptom screening during HIV care (on ART) (costs of symptom screening)

In the TB model

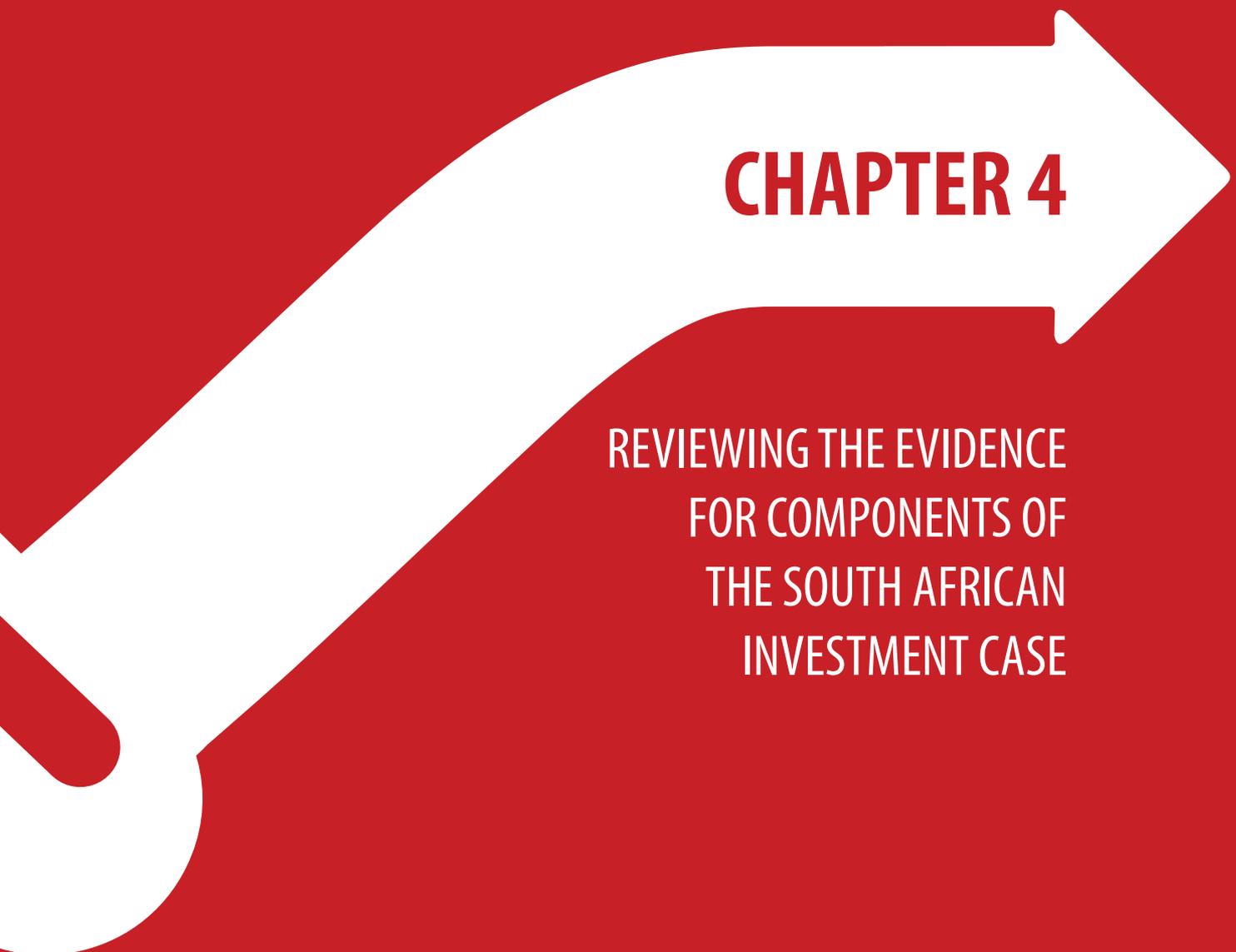
IPT for HIV positives (drug costs only, costs of clinic visit ART clinic visit cost)
TB symptom screening (ICF) at HCT, regardless of HIV result (costs of diagnostic tests for symptomatics)
TB symptom screening during HIV care (on ART) (costs of diagnostic tests for symptomatics)

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CHAPTER 4

REVIEWING THE EVIDENCE
FOR COMPONENTS OF
THE SOUTH AFRICAN
INVESTMENT CASE

This section describes in detail the basic programmes included in the intervention packages that we modelled to inform development of the SA IC case. As the Investment Framework recognizes, efficacious interventions are neither delivered nor taken up in a vacuum. Critical enablers (both social and programme enablers) and development synergies are often vital to building demand for services, overcoming deterrents to uptake and extending the reach and impact of basic programmatic activities; as a result, these too were taken into account in scenario modelling and are also described below.

(Note that due to the large number of references in this review chapter, references can be found at the end of each section rather than at the end of the chapter.)

4.1 BASIC PROGRAMMES

Basic programmes are the core programmatic interventions used to prevent new infections, illness and death related to HIV and TB.

4.1.1 FOCUSED INTERVENTIONS FOR KEY POPULATIONS AT HIGHER RISK

The IC took into account packages of interventions designed for selected key populations.

Stakeholder consultation and synthesis of the evidence

Drawing on the expertise of the SANAC-led National Key Populations Task Team, a small group of representatives of key populations collaborated to prepare a national stakeholder consultation in Pretoria on 30-31 July 2014. In pre-consultation meetings, this group prepared a draft list of high-impact interventions and TE factors for consideration at the larger, national meeting. Where feasible, unit costs of such interventions were also collected from partner organizations.

The national stakeholder consultation included about 40 public health practitioners, academics, government officials and representatives from international and donor organizations. The group was diverse, representing SWs, MSM, PWID, orphans and vulnerable children (OVC) and people with disabilities (PWD).

The national stakeholder consultation first focused on defining key populations before discussing effective interventions. Roles and responsibilities were agreed, and a consensus reached on criteria for collecting and synthesising evidence.

Although the current NSP identifies several groups as key populations [1], WHO defines key populations as defined groups who are at increased risk of HIV infection and onward transmission due to high-risk sexual behaviors, and who often have legal and social issues related to their behaviours [2]. The criminalization of sex work and drug use (as well as homosexuality in many African countries) increases the vulnerability of key populations and impedes the ability of these groups to access essential health services. Due to deterrents experienced by many key populations to accessing mainstream services, tailored HIV testing, prevention, treatment and care programs are required to meet the needs of hard-to-reach and marginalized populations [3, 4]. These criteria, combined with the high HIV prevalence among concentrated HIV sub-epidemics in the generalized setting, resulted in agreement on five key populations for the IC exercise: inmates, MSM, PWID, SWs and transgender people.

Description of final list of interventions

For the groups categorised as key populations, the consultation collected evidence published in peer-reviewed journals, as well as South African government policy. This evidence review found elevated HIV risk and vulnerability among the key populations, although little reliable data were found for inmates and transgendered people. Of the approximate 170 000 SWs in South Africa [5], studies have detected HIV prevalence ranging from 35% to 60% [1], it is estimated that MSM represent 750 000 to 1.2 million men in South Africa [6], with studies in three urban areas finding HIV prevalence of 22% to 48% in this population [7]. Although data is scarce regarding PWID, it is estimated that 67 000 people in South Africa inject drugs and that 14% of these are living with HIV [8].

Although the HIV burden among key populations in South Africa is clearly severe, data on key populations in the country are limited, largely due to the early focus on preventing mother-to-child transmission and prevention of heterosexual HIV transmission.

Several interventions and TE factors were identified for key populations, although evidence specific to key populations is sometimes scarce.

PrEP

Oral preexposure prophylaxis (PrEP) is an evidence-based biomedical prevention intervention indicated for MSM, men and women who have a high number of sex partners or who engage in sex work, PWID, and serodiscordant couples [2, 9]. Several trials have demonstrated that the efficacy of PrEP ranges from 48% and 84%. PrEP is in its infancy as an approved biomedical intervention, which may explain why the group's review found no evidence-based technical efficiencies associated with this intervention. However, as several guidelines emphasize the important effect that adherence to prescribed PrEP regimens has on efficacy, patients should be encouraged and enabled to use PrEP in combination with other effective prevention methods. CDC guidelines recommend follow-up visits every three months for PrEP users to provide HIV testing, medication adherence counseling, behavioural risk reduction support, side effect assessment, STI symptom assessment risk-reduction counselling, and adherence support [9].

Condoms

Condom use and promotion with FSWs is an essential part of government policy, including the National Strategic Plan for HIV Prevention, Care and Treatment for Sex Workers (NSWP) [10] and the NSP [1]. A meta-analysis identified *community empowerment* as a technical efficiency for condom programming for FSWs, with eight studies finding increased condom use and reductions in HIV and STIs among FSWs [11]. Ample evidence also indicates that exposure to *peer educator* and *outreach* was associated with increased consistent condom use among male and female sex workers, particularly with clients, as well as among MSM [12-14].

Availability and accessibility of condoms were also deemed evidence-based interventions for key populations. A meta-analysis of promotion of female and male condoms found a reduction in HIV and STI incidence at three-month follow-up assessment. Significantly, the meta-analyses provided evidence that interventions that promote the use of female and male condoms increase consistent use, compared to promotion of male condoms alone [15]. Another systematic review revealed that structural-level condom distribution interventions reduced HIV risk behaviors and STIs, increased condom use, increased condom acquisition/condom carrying, delayed sexual initiation among youth, and reduced incident STIs [16].

Dolan et al. [17] found that the presence of condom vending machines in prisons reduced HIV incidence among prison inmates. Nearly a third (28%) of respondents in the study reported using condom vending machines, and of these, nearly half (40%) reported using condoms for sex within the correctional facility.

HIV counselling and testing

HCT is a critical first step in linking people to prevention, treatment and care services, but technical efficiencies play an important role with respect to HCT promotion for key populations. Evidence indicates that mass media, internet-based services, and mobile or venue-based HCT all increase acceptability and accessibility of HCT among MSM, PWID, and inmates [18-20].

Behavioural interventions

Although behavioural interventions such as community empowerment, one-on-one counselling, peer interventions, support groups, social and mass media marketing and other risk reduction strategies are recommended by WHO for all key populations [2], there is little evidence clearly linking these approaches to reductions in HIV incidence or prevalence. Luchters et al. [21] offer evidence that, over a five-year period, FSWs' exposure to peer interventions was associated with an increase consistent use of condoms with casual sex partners, as well as increased awareness of HIV status.

As previously noted, empowerment and community mobilization play a central role in HIV prevention interventions for FSWs, particularly to enable them to negotiate condom use and access health services. A behavioural-biological survey conducted in 2008 and 2011 in India provides some evidence that empowered FSWs are more likely to use condoms and get tested for HIV and are less likely to engage in risk behaviours for the transmission of STIs [22].

Screening for and treatment of sexually transmitted infections

WHO recommends regular STI symptomatic screening for FSWs, as well as the offer of periodic presumptive treatment (PPT) for asymptomatic STIs [23]. It should be noted, however, that PPT is a short-term measure, only used in high STI prevalence settings. PPT may reduce prevalence of gonorrhoea, chlamydia and ulcerative STIs among sex workers in whom prevalence is high, but sustained STI reductions occur only when interventions are coupled with peer interventions and condom promotion [24]. STI management and PPT may theoretically reduce transmission of STIs at a population level, but this has yet to be demonstrated.

Interventions for people with intravenous drug use

WHO and PEPFAR recommend 10 critical interventions for PWID, including HCT, ART, needle and syringe programs (NSP) and medicated assisted therapy (MAT). Although widespread distribution of clean needles and syringes are effective in reducing HIV prevalence over time [25], TE factors enhance the efficacy of the intervention. For example, widespread needle and syringe distribution is particularly effective among injecting FSWs if it is accompanied by one-on-one counselling by peers [26].

A study of the administration and clinical follow-up of MAT among a cohort of HIV-positive PWID on ART also show a strong protective benefit against ART discontinuation and was also associated with a significant increase in plasma HIV RNA suppression among HIV-infected opioid-dependent drug users [27].

Antiretroviral treatment

Although antiretroviral treatment and management for key populations were listed as interventions, these were moved to and addressed in the treatment section as these are not exclusive to the needs of key populations.

Table 26 summarises the quality of the evidence base and grading for the interventions discussed in this section.

Table 26: Summary of quality of the evidence base and grading for interventions for key populations

Intervention	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
PrEP and PEP						
PrEP	MSM & Transgender women	Cohort	HIV incidence/ person years	44% reduction in incidence; 4.7 infections per 100 person years	[28]	1 ^a , 2 ^b
PEP or PrEP	MSM	Cohort	HIV transmission	0.0% transmission	[29]	1, 2
PreP - Oral TDF	PWID women & FSW	Cohort	HIV incidence	48.9% reduction (CI 9.6-72.2)	[30]	1
PrEP	FSWs	RCT	HIV transmission	Protective from 64%to 84%	[31]	1
Condoms						
Condom promotion with <i>community empowerment</i>	FSWs	Meta-analysis	Increased use of condoms and decrease in HIV and STIs.	RCT showed improved condom use (p=0.002); another reported increased consistent condom use (OR 1.9, 95% CI 1.1 to 3.3), at 30 days follow-up.	[1, 10, 32]	1, 2, 3 ^c
Condom promotion with <i>peer education</i>	FSWs	Randomized control trial	Significant decrease in STIs	Chlamydia OR 0.7 (95% CI 0.4-1.0) Gonorrhoea OR 0.7 (95% CI 0.5-1.0) Trichomoniasis OR 0.8 (95% CI 0.6 -1.2)	[10]	1
Condom promotion with <i>peer education</i>	Male SWs	Pre-post text time-venue sampling	Exposure to peer educators had a protective effect	aOR=1.97 (95% CI 1.29-3.02)	[13]	1, 2
Condom promotion with peer education, small groups, campaigns	MSM	RCT	Reduction in unprotected anal intercourse (UAI)	27% reduction in UAI 45% reduction with non-primary partners 2% reduction with intimate partners	[14]	1,2

a Good evidence (included)

b Exclude because this cannot be modelled

c Government policy

Intervention	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Male and female condom promotion and distribution	FSWs	Meta-analysis of 13 trials	Availability and accessibility of both male and female condoms led to increased consistent use and reduction of HIV and STI incidence	Reduced HIV incidence at 3 month: RR 0.07, 95% CI 0.00-1.38 Social cognitive interventions and promotion of female and male condoms significantly reduced STI incidence (RR 0.57, 95% CI 0.34 to 0.96)	[10, 15]	1
Male and female condom promotion and distribution	Inmates	Meta-analyses	Condom vending machines reduce HIV infections in prisons	54% reduction in HIV infection (RR-0.46; 95% CI 0.32-0.67)	[17]	2
Male and female condom promotion and distribution	All populations	Systematic review, 21 studies	Structural condom distribution has a positive effect on HIV risk behaviors	OR=1.81 (95% CI 1.51-2.17)	[16]	1
HIV counselling and testing						
HCT plus TE of targeted communication, especially multi-media campaigns	MSM and TG women	Meta-analyses	Uptake of HCT more likely	OR 1.58; (95% CI 1.40 - 1.77)	[20]	1, 2, 3
HCT plus TE of mass media	MSM	Meta-analyses	Uptake of HCT	Est. mean uptake 4.447 (95% CI 0.188--0.082)	[33]	1, 2, 3
HCT plus TE of venue/mobile HCT	MSM, PWID	Prevention study	Uptake of HCT	98% of PWID and 97% of MSM approached accepted HCT in a venue-based setting	[19]	2, 3
HCT	Inmates	Modelling	Cost-effectiveness	HCT offered to 10,000 inmates resulted in 50 new infections, and 4 averted; Cost of %125,000, but a savings of \$550,000	[18]	2, 3

Intervention	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Behavioural interventions						
Peer educators to enable HCT and condom use	FSWs	Time-lapse survey	HCT; Condom use	40.2% increase in HCT 22.2% increase in condom use	[21]	1
Community mobilization/empowerment	FSWs	BBS	Condom use; STI infection, HCT	Condom use aOR 4.74 (95%CI 2.17-10.37) HCT aOR 25.13 (95% CI 13.07-48.34) STI infection aOR 0.53 (95% CI 0.37 - 0.87)	[22]	1
Behavioural interventions (multiple)	MSM	Meta-analyses	HIV incidence	RR=0.07 (95% CI 0.0-1.38)	[34]	2
Sexually transmitted infections						
Periodic presumptive treatment & TE of peer education and condom promotion	FSW	Meta-analyses	STI reduction	significant reductions of gonorrhoea RR 0.46, 95% CI 0.31-0.68] and chlamydia RR 0.38, 95%CI 0.26-0.57	[24]	1, 4 ^d
STI Syndromic management	General population	Cross sectional	HIV incidence reduction	38% HIV incidence reduction	[35]	1, 4
Interventions for PWID						
NSP plus TE of motivational interviewing and peer support	PWID, FSW	RCT	HIV incidence reduction	RR 0.38 (95% CI 0.16-0.89) and RR 0.44 (95% CI 0.19-0.99)	[26]	1, 2
NSP	PWID	Serial cross sectional studies	HIV prevalence	33% HIV reduction over 12 years	[25]	1, 2
NSP plus TE peer educators	PWID	Meta-analyses	HIV prevalence	8.4 to 2.5 per 100 person years	[36]	1, 2
ART retention with TE of MAT	PWID	Cohort	MAT improved ART retention	Adjusted Relative Hazard = 0.67 (95% CI 0.54-0.83); p < 0.001	[27]	1, 2

d STI cofactors are not modelled, but costs may be modelled

Although the studies summarised in the table indicate that numerous interventions have been validated for some key populations, the scarcity of available information on effective interventions for all key populations is an important limitation, as is uncertainties regarding the size of these populations. A recent expansion of evidence-based and rights-based policies and programmes for key populations, with a number of donor-driven surveillance and size estimations, will expand the evidence base for key populations.

Limitations of this chapter

A continuously changing group representing and leading the key populations working group led to gaps in continuity in the process of assessing evidence for the effectiveness of interventions for key populations. This may have impeded effective and comprehensive retrieval of data, and may also have influenced the final selection of interventions to be modelled.

Four of the five key populations listed above could not be included in the main analysis as they are not misrepresented in the Thembisa model. (All key populations however were included in the separate key population analysis using the Goals model, see Sections 3.2.1 and 5.1.4.) This limitation may have led to a misrepresentation of key populations and their needs in South Africa. Indeed, these groups have long been under-prioritised in the national response, a failing that may unfortunately be perpetuated in their under-representation in the modelling for the SA IC.

An important reason why data on key populations are so limited is that few interventions have been focused on key populations in the South African and the broader African regional context. In addition, data collection is often particularly difficult for key populations, as they are often “hidden” (frequently due to fears created by criminalisation) and may live clandestine lives.

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4.1.2 ELIMINATION OF NEW HIV INFECTIONS AMONG CHILDREN

Summary of evidence synthesis process

Remarkable progress has been made in the area of eliminating new HIV infections in children since the initiation of the Prevention of Mother to Child Transmission (PMTCT) programme in South Africa in early 2000 [1]. The 2010 South African PMTCT Evaluation (SAPMTCTE) [2, 3] showed that “South Africa has managed to reduce MTCT from between 20% to 30% (in the absence of any PMTCT intervention) to 2.7% by 6 weeks post-delivery [2,3]. This represents a reduction in MTCT from 70 000 to less than 10 000 babies born HIV positive, per year, over the past 10 years.” [4] This is a significant finding in light of the country’s commitment to achieving its millennium development goals (MDGs) and *the Global Plan towards the Elimination of New HIV Infections among Children by 2015 and Keeping Their Mothers Alive* [5].

In 2014, the South African PMTCT programme data indicates national MTCT rates below 2% at 6 weeks post-delivery [6,7]. The data on MTCT from the SAPMTCTE cohort shows transmission rate as low as 2.6% in 2012 [1]. It is therefore critical for South Africa to focus on the ‘last mile’ in eliminating new HIV infections in children, with specific key interventions to continue on the trajectory towards further reduction in MTCT rates. The discussions during the Investment case process was focused on key interventions and technical efficiency factors towards the last mile for eliminating new HIV infections in children in South Africa, towards targets that translate to <2% transmission at 6 weeks and <5% transmission at 18 months post delivery [8].

From the outset of the development of the South African Investment Case, technical expertise in the area of EMTCT (eliminating mother-to-child-transmission of HIV) and paediatric and adolescent HIV was drawn from existing national structures. These structures were used to understand the current status of implementation of interventions and to determine an initial list of key interventions and technical efficiency factors for inclusion in the South African Investment Case. These structures included the PMTCT Technical Working Group (TWG), PMTCT Steering Committee; and the Paediatric and Adolescent HIV and TB Technical Working Group (TWG) under the leadership of the National Department of Health. The members include key stakeholders working within the area of eliminating new HIV infections among children who have played an integral role in providing technical oversight, direction and inputs into the PMTCT programme. In order to solicit engagement from the TWG, a background presentation on the investment case was made during the TWG’s April 2014 meeting. An initial list of interventions and technical efficiency factors was then generated and a rapid data review of all on the list was conducted. Thereafter, the list of interventions and technical efficiency factors was shared with members of the TWG and feedback incorporated both virtually and during face-to-face opportunities. This initial list of interventions and technical efficiency factors formed the basis of the discussions at the national stakeholders’ consultation.

The national Stakeholders Consultation took place on 30-31 July, 2014 in Pretoria. Stakeholders included representation from national government; development partners; academia; clinicians and non-government organisations (NGOs). Approximately 14 stakeholders participated in the discussion around eliminating new HIV infections in children on the first day of the stakeholder consultation and 11 stakeholders, including the national PMTCT programme manager (NDoH) participated in the second day of the consultation. The discussions during the stakeholder consultation were two-fold that included a review of the current status and progress of the PMTCT programme and discussions on interventions and specific programmatic inputs needed to ensure elimination of new infections in children. In addition, the four-pronged approach to PMTCT (discussed in section 5.1.2.2 below) allowed the group to identify key interventions for inclusion. In conclusion of the discussions and presentation to the larger stakeholder group, it was evident that the list of the evidence suggested in support of interventions further documented the bottlenecks rather than provided evidence for interventions to address the bottlenecks and ensure elimination of new infections in children. In order to refine the list of interventions and technical efficiency factors following the stakeholder consultation, the list was re-examined and refined. The refined list was shared with the stakeholders, the PMTCT TWG and the representatives from the national PMTCT programme.

Description of final list of interventions and TE factors

HIV is one of the leading causes of death for women of reproductive age and a major contributor to infant mortality worldwide. PMTCT interventions are the most effective way of reducing new HIV infections in children. PMTCT is a gateway for HIV prevention, treatment, care, and support services for the whole family. The Four-Pronged Approach to PMTCT Strategy is a programme model developed by the U.N. Interagency Group for HIV/AIDS in 2001 [9]. Each of the four “prongs” represents a stage at which program services work to 1) prevent HIV in women of reproductive age (primary prevention), 2) prevent unintended pregnancy in women with HIV, 3) prevent HIV transmission from mother to child, and 4) provide ongoing care and support to mothers, their children, and families. Within the third stage-preventing HIV transmission from mother to child- the PMTCT Continuum of Care Services include critical antenatal, intrapartum, and postpartum/ postnatal health services to both mothers and infants. South Africa has made significant strides in addressing prong 3, however in order to eliminate new HIV infections in children, more focus needs to be directed towards prongs 1 and 2 and 4, while continuing to address any bottlenecks and achieving maximal coverage with quality services to provide prophylaxis, and linkages to treatment, care and support for all women.

In addressing the 4 “prongs” of PMTCT, South Africa released new clinical guidelines for PMTCT on 1 April 2010 [10]. These guidelines were further updated in March 2013. In 2015, the guidelines were further updated to ensure that all HIV positive pregnant women initiate lifelong HAART regardless CD4 count, ensuring that HIV positive mothers no longer stop treatment after pregnancy and breastfeeding (PMTCT Option B+) [11].

Further to the clinical guidelines, in 2011 South Africa developed an action framework entitled *‘No child born with HIV by 2015 and improving the health and wellbeing of mothers, partners and babies in South Africa* [5]. The framework strives for integration at all levels to achieve coverage, access, quality and availability of services including PMTCT, MCH, integrated management of childhood illnesses (IMCI), expanded programme on immunisation (EPI), nutrition, HCT, ART, care and support, early childhood development, school health, youth services, child support and social services, HIV prevention and FP services. The national framework was built up from districts and provincial frameworks and aims to identify and deal with bottlenecks at all levels of service delivery including community level to allow for continuous improvement. A small number of key MNCH indicators included in a 15-indicator dashboard for easy monitoring containing key PMTCT indicators are used to monitor integration and track progress on a quarterly basis through the Data for Action reports at national, provincial and district levels [5,12].

While significant progress is seen towards the achievement of the targets set out in the framework, a number of programmatic bottlenecks need ongoing attention [13]. These programmatic bottlenecks and constraints were highlighted in the National Joint HIV, TB and PMTCT Programmatic Review that was conducted in 2013, as well as in the mid-year stock taking exercise conducted in June 2014. Programmatic bottlenecks to eliminating new infections in children as highlighted in the Joint Review include the following [13,14].

- Data across the specific points in the PMTCT cascade are lacking, and the MTCT rate at 18 months is not known. Follow up in the post-partum period of the mother-baby pair is sub-optimal and retention in care presents a challenge.
- Tools such as registers and tally sheets are not aligned with the new guidelines leading to difficulties in monitoring policy changes.
- There is a low couple year protection rate (CYPR) measuring protection from unwanted pregnancies and a need for training and mentorship towards improved family planning provision and usage. All health care workers should be trained in family planning which should be well integrated into the both antenatal care and postnatal care programmes.

- There is a low baby ART initiation rate. NIMART-trained nurses often do not feel confident to initiate infants, highlighting a need for mentorship and strengthening of Integrated Management of Childhood Illnesses (IMCI).
- Awareness and use of data for planning and quality improvement actions needs to be strengthened to meet targets at the facility level.
- Although there is universal access to PCR testing, specimen rejection rates are unacceptably high in some facilities.
- There is a lack of focused programmes to reach sexually active adolescents and young people, as well as young people before they become sexually active. Adolescent friendly services are limited because they are not well understood by health care workers.
- Late booking for antenatal care, and even presenting for the first time during labour, remains a problem. Some of the reasons identified for this include health care workers sending back women who present early, and cultural beliefs around not visiting facilities until 16 weeks.

Programmatic bottlenecks to eliminating new infections in children as highlighted in the 2014 mid-year stock taking exercise [13] included the following (Table 27):

Table 27: Bottlenecks to eliminating new HIV infections in children

Key area	Key Findings/ gaps
Early antenatal care (visit before 20 weeks)	Cultural beliefs preventing women from seeking antenatal care early High teenage pregnancies, facilities not friendly to this age group and teenagers hiding their pregnancies Lack of integration into broader SRH and other common services leading to missed opportunities for identifying pregnant women early
ART initiation (and retention on treatment) for HIV infected and breastfeeding women and children	Lack of standard data collection tools following the PMTCT guideline changes in 2013, leading to misunderstanding of data elements and inaccurate data recording Non-functional of systems for tracing / follow up eligible mothers but not on ART
HIV re-testing during pregnancy, labour and delivery and breastfeeding period	Non adherence or poor understanding of the retesting guidelines leading to missed opportunities to identify new HIV infections during pregnancy and breastfeeding Existing data tools not capturing the new retesting guidelines (three monthly re-testing vs retest at 32 weeks)
Contraceptive use	Low contraceptive coverage – long term methods not well marketed, i.e. , IUCD, sterilization, implant
HIV testing of children at 18 months	Poor postnatal follow-up systems and integration within child survival services leading to missed opportunities for testing at 18 months Lack of guidance on data collection regarding universal testing at 18 months (unclear denominators leading to outliers)

Based on the bottlenecks documented above, interventions and technical efficiency factors for inclusion in the investment case and closing of the “last mile” in eliminating new infections in children should ensure the following: a) primary prevention of HIV, especially among women of childbearing age; b) integration of PMTC interventions with basic antenatal care, sexual and reproductive health, Child and Adolescent Health, CCMT and TB services, c) strengthen postnatal care for mother-baby pair; d) provision of an expanded package of PMTCT services that extends beyond the drug regimens, e) integrating PMTCT into the continuum of care and management of the woman and child from pre-pregnancy (family planning and other services) through pregnancy, delivery, postnatal care and the first 18 months of life, and f) strengthens infant feeding practices with the emphasis on exclusive breastfeeding for the first 6 months of life.

This translates into the following list of key interventions and technical efficiency factors:

Improve early antenatal care bookings

Specific interventions include routine pregnancy screening of all adolescent girls and women of reproductive age (15-49) who seek health services, as well as community-based pregnancy screening by community health care workers [15]. While this intervention targets all women of reproductive age, it will ensure that adolescents and young mothers, who account for a high number of unintended pregnancies, are not missed. Inclusion of pregnancy screening within adolescent-specific health services will facilitate early identification of adolescents who are pregnant, ensuring they are able to seek services early. Anecdotal evidence suggests that the effectiveness of both community-based pregnancy testing and facility-based pregnancy testing on the impact of PMTCT. According to Wabiri, 46% of pregnancies in South Africa are unplanned. Many of these women are unaware that they are pregnant, therefore are missed opportunities for PMTCT interventions [16].

Expansion of pregnancy testing for women of reproductive age can reduce the missed opportunities for early pregnancy identification and enrollment in antenatal care services and PMTCT programmes. Further to this, Anderson et al [17], Languza et al [18] make a strong case for community pregnancy screening and improved outcomes with respect to early antenatal care bookings. [17,18]. In addition to the evidence presented, there are a number of pilot projects being implemented in KZN, where anecdotal evidence suggests community-based pregnancy testing and facility-based pregnancy testing for women of reproductive age are identifying a large number of unintended pregnancies, and ensuring that these women receive the appropriate services [6].

Preconception services/ fertility planning for HIV affected couples

HIV positive women have the same desires for pregnancy and children as their HIV negative counterparts [19]. In addition, many HIV-infected adults are sexually active. In advanced HIV infection, fertility is reduced, but the incidence of pregnancy increases with ART initiation [20]. South Africa has an estimated 1 million births annually, and an estimated 29% of these occur in women living with HIV. A substantial proportion of these pregnancies are unplanned, despite effective contraception being a critical component of the prevention of mother-to-child transmission (PMTCT) of HIV/AIDS programme. However, many HIV-infected women and men want to have children, either immediately or at some time in the future. In this context, dealing with issues of fertility and childbearing should be seen as part of routine HIV care.

The pregnancy rate for HIV positive women in South Africa is 7.8 per 100 women [20]. According to Schwartz et al [21], 30% of women who tested HIV positive desired to be pregnant in the future. According to Westreich et al, women between the ages of 18-25 had a 13.2 times higher pregnancy rate after initiation of ART [22]. Experiences in implementing preconception services in Witkoppen, South Africa, also showed that ART initiation was associated with higher pregnancy intentions. For this reason, preconception services and fertility planning for HIV affected couples is essential to ensuring that the last mile of PMTCT is covered. However, despite the need for interventions of this type, there is limited evidence on the effectiveness of preconception services for HIV affected couples. An evaluation of the Mothers2Mothers (M2M) programme found evidence of increased postpartum contraception use in women who had participated in M2M compared to non-M2M participant mothers [23].

PMTCT option B+

Option B+ provides the same triple ARV drugs as option B to all HIV-infected pregnant women beginning in the antenatal clinics but ensures that ART is continued for life. Important advantages of Option B+ include: further simplification of service delivery and harmonization with ART programmes, protection against mother-to-child transmission in future pregnancies, a continuing prevention benefit against sexual transmission to HIV negative partners, and avoiding stopping and starting of ARV drugs. According to Schouten et al. providing universal, lifelong ART to HIV infected pregnant women will play a significant role in the potential elimination of vertical transmission. In addition it will improve both coverage and adherence [23]. The evidence in support of option B+ is strong [25,26,27] suggesting that the implementation of option B+ will reduce MTCT rates <1% of life births [25,26,27,28]. The South African government has decided that as of January 1, 2015 PMTCT option B+ will be national policy and this is currently being implemented

Birth HIV testing

Early Infant Diagnosis (EID) is an essential component of the PMTCT programme and ensures early access to treatment for HIV infected children, thus reducing mortality. However, the Children with HIV Early Antiretroviral Therapy (CHER) study demonstrated the importance of early initiation of ART for children at a median age of 7 weeks to reduce infant morbidity and mortality [29]. Based on the findings of the CHER study, it is evident that EID should be implemented as early as possible in a child's life to ensure optimal infant outcomes [29]. Lilian et al [30] found that six week testing delayed antiretroviral therapy initiation beyond the time of early HIV-related infant mortality and missed one-fifth of perinatally HIV-infected infants in a routine HIV service in Johannesburg, South Africa. Earlier diagnosis and improved retention in care are required to reduce infant mortality and accurately measure elimination of mother-to-child transmission [30]. There is strong evidence to suggest that birth HIV testing for HIV exposed infants would ensure early identification of HIV infected children and initiation on ART, hence further reducing infant morbidity and mortality.

Infant testing at 9 months linked to EPI

While measurement of PMTCT effectiveness and transmission rates at 6 weeks are well documented [31,32,2,33], late transmission or transmission occurring as a result of breastfeeding is difficult to monitor. This is primarily a result of the high loss to follow up before the standard follow-up HIV test when the child is 18 months old. While it is important to strengthen systems to conduct and track ELISA testing at 18 months, there is strong evidence that HIV ELISA tests can be used from as early as 7 months to provide an accurate result of infant HIV status [30]. Integration of HIV testing into routine 9-month EPI services would therefore ensure better follow-up of infants [31]. This intervention would therefore ensure that when HIV exposed infants visit the health facility for their 9 month EPI visit, they not only receive immunization and well-baby visit, but also HIV ELISA testing with linkages to treatment, care and support services as needed are also conducted. There is strong evidence to suggest that integration of EPI services and HIV testing services for infants leads to better long term health outcomes.

It is important to point out that as the South African ART programme matures and expands to include initiation of all adolescents and adults with CD4 counts below 500 cells/microl, in accordance to the current adult treatment guidelines, significantly more women will be entering pregnancy not only aware of their HIV status, but already on life-long ART. This will require a substantial shift in the delivery and monitoring of the PMTCT programme and strengthening of the linkages between antenatal care, labour/ delivery services and ART programmes, as well as postnatal and well-baby services. More importantly, family planning and contraceptive services for all women are critical to ensure planned pregnancies.

Table 28 summarises the evidence base and grading for interventions and TE factors discussed in this section.

Table 28: Summary of quality of the evidence base and grading for PMTCT

Intervention/ TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
PMTCT option B+	All pregnant women	WHO policy documents	MTCT	<1%	[24,26]	1
Nurse quality mentor programmes (TE)	Health care workers	Observational	MTCT	<1%	[34]	1
Preconception Services/ Fertility Planning	Women of reproductive age (15-49); adolescents; discordant couples	Lack of evidence; assumptions made based on improved FP services postpartum with mentoring	MTCT	<1%	[22]	1
Early ANC booking	Women of reproductive age (15-44)	Observational	% coverage	85-95%	PHC in Western Cape	1
Health education (TE)	Women of reproductive age	No evidence	% coverage	85-95%	[36,37]	2
Facility-based pregnancy screening (TE)	Women of reproductive age (15-44)	Anecdotal evidence (pilot underway)	% coverage	85-95%	KZN implementers	1
Community-based pregnancy screening (TE)	Women of reproductive age (15-44)	Observational	% coverage	85-95%	[16,36]	1
Birth testing	All HIV exposed newborns (at birth)	Trial	Child survival EID/ child survival	9-13 IMR	[17]	1
Home birth attendant training	Health care workers	No evidence on effectiveness	Child survival	9-13 IMR	[18,38]	2
Infant testing at 9 months linked to EPI	All 9 month old infants attending immunization clinic for 9 month immunisations	Trial	Child survival	IMR 9-13	[30,38]	1

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4.1.3 SOCIAL AND BEHAVIOUR CHANGE COMMUNICATION

Among the earliest of all HIV prevention interventions, social and behaviour change communication (SBCC) remains a core prevention activity. The Investment Framework includes SBCC as a basic programme activity.

Summary of evidence synthesis process including discussion during stakeholder consultation

A working group reviewed evidence regarding the effectiveness of SBCC. Working group included members from SANAC, National Department of Health, UNAIDS, loveLife, Soul City, Johns Hopkins Health and Education in South Africa, CDC, AIDS Consortium, SANAC Youth Sector, Gauteng Department of Health and City of Tshwane.

The working focused on several topics, including: i) the definition SBCC; ii) how SBCC works; iii) the difficulties in evaluating SBCC and; iv) how SBCC should be treated within the Investment Case. The working group grappled substantively with the complexity of SBCC interventions in relation to the needs of the IC to identify evidence that could be linked into existing models. As below described, the agreed approach has certain limitations, and interpretation of modelling results need to bear these limitations in mind.

Members agreed that SBCC encompasses a broad range of activities and approaches that focus on the individual, community, and environmental influences on behaviour and social change. It was also agreed that SBCC occurs and is most effective at multiple levels of a socio-ecological system including: intrapersonal (e.g., emotion, cognition, and decision-making), interpersonal (e.g., social relationships), networks and organisations (e.g., norms and social structures), and societal (e.g., broad social systems, policies, law and culture) [1, 2]. The group acknowledged that outside of the field many people think of communication as messages or materials (e.g., a pamphlet), rather than a social process [1]. Members agreed that SBCC comprises a number of different approaches and that the exact mix appropriate in any given situation or for a particular target audience is determined by communication theory. Key SBCC approaches include mass media, interpersonal communication (e.g., face to face counselling; support groups; peer support and counselling), advocacy, community mobilisation (e.g., community dialogues in which participants are encouraged to take action, social action groups) and social marketing. The working group acknowledged that interventions are more likely to succeed when they use multiple coordinated approaches to reach people with consistent, high-quality messages through a variety of channels (e.g., media, peer networks, and provider contact) and in a variety of forms (e.g., print, verbal, broadcast, informational, and entertaining, debates and dialogues) [1].

Having defined SBCC, the working group worked to understand how SBCC works, agreeing that the theory of change used for any particular SBCC is critical in evaluating the effectiveness of the approach. The working group discussed the different communications theories that purport to describe the mechanisms of action for SBCC. SBCC does not act directly on HIV but instead seeks to influence intermediate factors that “affect if and when the virus is transmitted, where and when testing and/or care is sought, how care is delivered, and how well adherence to ART is maintained” [1]. In other words, SBCC affects behaviours, the determinants of behaviours and the environment that enables these behaviours, which in turn influences health outcomes (e.g. condom use, partner reduction etc.) through intermediary factors (e.g., increasing people’s knowledge and behavioural skills and motivations). Determinants of behaviour may include knowledge, beliefs, social norms, access to products (such as condoms) etc.

SBCC practitioners use numerous models to describe how communications works to exert this indirect effect on health outcomes. The working group’s consensus was that the common elements of “best practice” models involve an ecological approach in which the individual’s behaviours are influenced by a range of determinants that include social and structural factors. Recognition of the importance of an ecological approach has been recognized internationally, as reflected by

the shift from an emphasis on designing interventions targeting individuals alone (e.g., traditional behaviour change communication of information, education and communication) to the prevailing paradigm of SBCC. As SBCC programmes aim to take account of the environment, they are unlikely to be effective if the environment does not include meaningful access to essential services and commodities. Thus, an SBCC programme that aims to increase condom use will not achieve its optimal impact if condoms are not readily available. This may frustrate efforts to evaluate SBCC programmes, as evaluations may draw the erroneous conclusion that SBCC is ineffective when the underlying problem has to do with environmental conditions rather than the efficacy of the intervention itself.

In some respects, SBCC is a misnomer, as SBCC does not always seek to change behaviour but may instead focus on reinforcing healthy behaviour and encouraging people who are behaving safely to continue to do so. SBCC may also remind people who have stopped practicing a given behaviour to resume doing so.

After clarifying how SBCC works, the working group turned to examination of the evidence for the effectiveness of SBCC. Health communicators are increasingly being asked to demonstrate that SBCC affects population-based health outcomes and to use rigorous evaluation methodologies, particularly randomised controlled trials (RCTs). Echoing arguments from the literature [3, 4], the working group determined that alternative study designs are needed to evaluate full-coverage SBCC campaigns. RCTs, the working group found, often cannot be generalised to the broader population [5] and are frequently better at assessing individual effects rather than assessing impacts that occur as a result of social processes. As it is difficult to assign complex social networks to treatment and control groups, RCTs may be better at detecting quick, large effects than slow and small changes [6]. In the case of an RCT of a high-coverage SBCC campaign (e.g., national mass media campaign), it may be difficult to keep control groups uncontaminated, as the effects of SBCC are often experienced through discussion with family, friends and communities. As a result of its finding that RCTs may not always be the most appropriate mechanism for evaluating SBCC campaigns, the working group proposed using data for the IC generated using other research methods, such as quasi-experimental studies where statistical means are used to construct a comparison group (propensity score matching [5, 7, 8] and multi-variate causal attribution [9-11]).

The working group also examined evidence regarding the cost-effectiveness of SBCC programmes, although few studies have actually examined the cost-effectiveness holistic communication campaigns. Most of the few available studies have focused on the mass media component. However, it was deemed inappropriate to compare cost-effectiveness of different components of SBCC, e.g., the cost-effectiveness of mass media vs community mobilisation, as the premise behind using different approaches is for each one to reinforce the other.

The working group examined how SBCC should be treated in the Investment Case. In other countries, SBCC has been included as a social enabler in that it influences a number of different programmatic areas. However, for the South African Investment Case, it was determined that SBCC would be treated as a stand-alone intervention, as it has direct effects, e.g. reduction of sexual partners, that are independent of other programme areas.

After the stakeholder consultation, members of the working group provided relevant evidence for SBCC in line with the discussions described above. All studies were reviewed in terms of their effectiveness, i.e. HIV infections averted, life-years gained, and/ or other, more programmatic or intermediate outcomes, e.g. condom use or reduction in sexual partners. The working group evaluated the strength of the evidence and documented where each study was conducted.

Description of final list of interventions and TE factors

The section summarises the evidence for the effectiveness of different types of SBCC interventions, taking into account systemic reviews, RCTs, quasi-experimental studies and modelling studies, before discussing the evidence used in the Investment Case.

Evidence for advocacy interventions

Effective advocacy campaigns have helped reshape the HIV response from South Africa. For example, the Treatment Action Campaign mobilised members at a grassroots level and successfully advocated for the provision of antiretroviral drugs (ARVs) [12]. Soul City also took an advocacy approach, with the aim of securing the speedy and effective implementation of the Domestic Violence Act (DVA) which although passed into law, was not being implemented due to lack of political will, lack of police training and other factors. Independent evaluation shows that the fast tracking of the implementation process was a direct result of the advocacy campaign [13] (see also section 4.2.1).

Evidence for community mobilisation interventions

Salam and colleagues (2014) reviewed 39 community-based interventions (CBIs) targeting HIV knowledge, attitudes and transmission, finding that CBIs increase HIV awareness and risk reduction and improve knowledge, attitudes, and practice outcomes. In particular, CBIs increase knowledge scores for HIV (SMD: 0.66, 95% CI: 0.25, 1.07), protected sexual encounters (RR: 1.19, 95% CI: 1.13, 1.25), and condom use (SMD: 0.96, 95% CI: 0.03, 1.58), while reducing the frequency of sexual intercourse (RR: 0.76, 95% CI: 0.61, 0.96). CBIs were not found to have any significant impact on scores for self-efficacy and communication [14].

South Africa provides numerous examples of effective community mobilisation interventions. Stepping Stones, for example, is a 50-hour programme designed to improve sexual health by using participatory learning approaches to build knowledge, risk awareness, and communication skills and to stimulate critical reflection [15]. Although an RCT found no evidence that Stepping Stones lowered the incidence of HIV (adjusted incidence rate ratio 0.95, 95% confidence interval 0.67 to 1.35), programme was associated with a reduction of about 33% in the incidence of HSV-2 (0.67, 0.46 to 0.97; $P=0.036$) [15]. Jewkes and colleagues (2008) also found that a lower proportion of men reported perpetration of intimate partner violence across two years of follow-up after exposure to Stepping Stones and less transactional sex and problem drinking at 12 months [15].

A drama-based intervention to promote HCT services in a peri-urban community in South Africa was found by Middelkoop and colleagues (2006) to be associated with a 172% increase in the uptake of HCT services in the intervention community [16].

An evaluation of South Africa's national government HIV communication programme, Khomanani, which included community action in 27 sites, found that around 10% of the population had been exposed to the intervention [17]. Statistical analysis determined that exposure to community action was responsible for 4% increase in uptake of HCT in past 12 months, with exposure also responsible for 5% increase in testing with a sex partners and a 7% increase in condom use at last sex [17].

An evaluation of Soul Buddyz Clubs in South Africa found that those aged 16-24 years who were exposed to the intervention were 5% more likely to practice safer sexual behaviour (measured using a safer sex index) than those who were unexposed [18].

Evidence for mass media interventions

Globally, several systematic reviews have found that mass media interventions affect a number of HIV-related outcomes. A meta-analysis by LaCroix and colleagues (2014) of HIV prevention mass media interventions between 1986 and 2013 found that media campaigns were associated with an increase in condom use ($d+ = 0.25$, 95% confidence interval, CI = 0.18 to 0.21), transmission knowledge ($d+ = 0.30$, 95% CI = 0.18 to 0.41), and prevention knowledge ($d+ = 0.39$, 95% CI = 0.25 to 0.52) [19]. A 10-year systematic review by Noar and colleagues (2009) found that the majority of HIV mass media communications campaigns which used strong study designs had favourable effects on behaviour change or behavioural intentions [20]. A review Vidanapathirana and colleagues (2009) determined that mass media interventions

have immediate and overall effects in promoting HIV testing although no long-term effects were seen [21]. A systematic review of mass communications programmes for behaviour change by Bertrand and colleagues (2006) found mixed results, with half of the studies showing a positive impact of mass media on knowledge of HIV transmission and reduction in risky sexual behaviour [4]. However, it is important to note that these reviews only cover mass media interventions. The working group found no systematic review of holistic SBCC programmes of which mass media was but one component.

In South Africa, an RCT found that *Talk to Me*, a component of Takalani Sesame, was effective in increasing dialogue between caregivers and young children about HIV. Caregivers who were exposed to the programme were found to be around 2.5 times more likely (OR 2.45, 95% CI 1.14; 5.32) to have communicated with their children than those in the control group (unexposed to the programme) [22].

In South Africa, the First National HIV Communication Survey (NCS), using propensity score matching, found that the more communication programmes respondents were exposed to, the more likely they were to have used a condom at last sex [23].

Kincaid and Parker (2008) found that 701,495 infections were averted/ delayed in 2005 because 64.2% or 16.7 million sexually active South Africans practiced some form of HIV prevention behaviour, with HIV communication programmes having an indirect effect on HIV status through its direct positive effect on several prevention behaviours [24]. To reach this conclusion, Kincaid and Parker explored the 2005 HSRC survey, using multi-variate causal attribution comprising structural equation modelling, bioprobit regression and propensity score matching to identify the effect of sexual risk reduction and the impact of HIV communications programmes.

Johnson et al (2012), fitting dynamic mathematical models to age-specific HIV prevalence data from national antenatal and household surveys, found that adult HIV incidence in South Africa has declined significantly since the year 2000. The models suggested that most of this decline can be attributed to the effect of increased condom usage, and that some of the decline may be attributable to the impact of ART on the infectiousness of individuals with advanced HIV [25]. The assumed increases in condom usage are consistent with the timing of increases in the distribution of male condoms in the South African public health sector as well as the timing of behaviour change interventions [25].

The Third National HIV Communication Survey (NCS), undertaken in 2012, assessed the impact of a number of HIV communication programmes (HCPs) and their components, which total to 19 communication interventions. Using multiple causal attribution analysis, researchers found that people exposed to HCPs were 3% more likely to report testing in the past 12 months (AOR 1.03), and 10% more likely to report condom use with one or more of one's three most recent sex partners (AOR 1.10) [26]. Men exposed to HCPs were 16% more likely to have been circumcised and to have high intention to get circumcised in the next year (AOR 1.16) [26]. The NCS also demonstrated a dose response relationship, i.e. the more programmes people were exposed to, the more likely they were to practice HIV prevention behaviours.

The individual impact of each large, national multi-level SBCC campaign was measured as part of the NCS. It was decided that the results of these impact evaluations would be included in the modelling. Anonymity of these campaigns was maintained so as not to influence funding decisions in relation to individual campaigns.

However, there are a number of important limitations to using NCS data which need to be considered when interpreting these results. First, although the campaigns evaluated comprised a variety of different approaches i.e. mass media, community mobilisation and advocacy, the design of the NCS only allowed the authors to measure the impact of the mass media components of SBCC efforts. Due to this limitation, other aspects of SBCC, e.g., advocacy and certain community mobilisation programmes, have been included in the section on Social Enablers and Development Synergies.

In addition, the NCS was conducted when the various campaigns were in different stages of roll out. Accordingly, a finding from the NCS that Campaign A had greater impact/effect than Campaign B may simply have reflected that roll-out of Campaign A was incomplete. Accordingly, NCS results should not be used to determine that one campaign is more effective than another.

Third, the NCS did not measure the impact of these campaigns on a number of important social outcomes, such as the impact on gender norms, HIV related stigma, gender-based violence and social cohesion.

Finally, the models used could not accommodate some of the intermediate factors which SBCC aims, such as knowledge, social norms and self-efficacy.

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4.1.4 COMPREHENSIVE CONDOM PROGRAMMING

Summary of evidence synthesis process

The review and synthesis of evidence for the Comprehensive Condom Programming (CCP) programme area was undertaken in three phases: The first phase involved a review of literature and identification of effective interventions by Leonard Kamugisha (UNFPA), the working group co-chair. The list of interventions identified in phase one – seven interventions and 12 TE factors – was shared with the other co-chair of the working group, Thato Chidarikire (NDoH), for inputs. Subsequently, experts working in this programme area were identified and engaged on the development of interventions to be included in the analysis. The interventions and TE factors were subsequently presented by UNFPA at a scheduled national condom coordination meeting, consisting of representatives of the National Department of Health (NDoH), Society for Family Health (SFH), Sexual HIV Prevention Programme (SHIPP). During the next Investment Case Task Team meeting, both these lists were discussed, with no additional interventions identified.

The second phase involved consultations and inputs at the national stakeholder workshop. The workshop was attended by 24 individuals representing 11 organisations, including national and provincial departments of health (Northern Cape and Mpumalanga), implementing partners, and organisations such as UNFPA, SANAC, SHIPP, Johns Hopkins Health and Education in South Africa (JHHESA), Maternal Adolescent and Child Health (MatCH), and CDC. Prior to the stakeholder workshop, all working group participants were provided with the list of interventions and TE factors, asked to submit documentation of their effectiveness, and invited to suggest additional interventions. The working group co-chairs additionally searched for and reviewed evidence for each suggested intervention. During day one of the consultation, co-chairs reviewed the list of interventions and TE factors with participants. Some interventions and TE factors were added during this discussion. During the subsequent market place session held on day 2 of the consultation, the team received additional information on available data from members of other working groups.

The third and last phase involved the compilation and review of all the evidence generated from the discussions and literature search, by Mary O'Grady (Consultant).

Description of final list of interventions and TE factors

Interventions

The impact of consistent condom use on reducing HIV infections is well documented, with a systematic review finding that consistent use of condoms reduces HIV incidence by 80%. In this review, consistent use was defined as using a condom for all acts of penetrative vaginal intercourse [1].

The condom working group explored various interventions designed to increase condom use. One intervention among married women in Zimbabwe, which provided education and the offer of free male and female condoms and HIV testing, significantly increased condom use between baseline and follow-up [2].

Peltzer et al (2012) found that young South Africans who discussed condom use with their partner in the past 12 months were less likely to report being HIV-positive (AOR 0.09, 95% CI 0.01 – 0.58). The study also found that those who reported difficulty accessing condoms were more likely to report being HIV-positive (AOR 2.75, 95% CI 1.09 – 6.88) [3].

A study among MSM in South Africa found that those who used condoms inconsistently were 2.3 times more likely to be HIV-positive [4]. Hoke and colleagues (2007) followed 1,000 FSW in Madagascar for 18 months and found that introduction of female condoms among FSWs reduced the likelihood STI prevalence (AOR 0.71, 95% CI 0.58 - 0.86) [5].

Mass media campaigns to increase condom use in South Africa have also been evaluated. Using rigorous data analysis techniques, the National HIV Communication Survey found that those exposed to 19 different communication programmes were 10% more likely to report using a condom at last sex (AOR 1.10) [6]. A SBCC campaign aimed at increasing condom use in men was responsible for an increase in condom self-efficacy – or one's belief in one's ability to be able to use a condom (AOR 1.03) [7]. In turn, those with high self-efficacy for condom use were 51% more likely to use a condom at last sex (AOR 1.51) [7]. Young people exposed to a youth-focused national communication campaign were 3% more likely to have positive attitudes about condom use (AOR: 1.03), and young people having more positive attitudes towards condoms were 48% more likely to use a condom at last sex (AOR 1.48) [7]. The same evaluation found those exposed to the campaign were 1.05 times more likely to have high self-efficacy for condom use, and those with high self-efficacy for condom use were 1.49 times more likely to actually use condoms [7]. Persons exposed to a TV drama to promote HIV prevention behaviours demonstrated similar findings were more likely to have positive attitudes regarding condom use and have higher self-efficacy for condom use, and those displaying these attributes were then more likely to report condom use at last sex [8]. As described in the earlier SBCC discussion, Kincaid and Parker (2008) modelled the impact of combined exposure to communication programmes on condom use using multivariate causal attribution analysis, finding that some 701,495 infections were averted as a result of condom use [9].

A study from Zambia found that those exposed to radio and television programmes about family planning and HIV were more likely to have ever used a condom (OR = 1.16 for men and 1.06 for women) [10].

Technical efficiency factors

The CCP working group also identified various TE factors, including factors related to barriers to condom use, condom distribution and factors related to condom characteristics and perceptions thereof.

Literature tended to describe barriers to condom use rather than reporting on the extent to which these affected condom uptake. Some of the barriers to condom availability noted in the literature included the opening and closing times of government clinics, hostile attitudes of providers and the cost of condoms in shops [11]. Tanser (2006) explains that travel time to clinics to collect condoms is a substantial barrier to accessing condoms [12].

Another TE factor was condom distribution, such as condom distribution in schools [13] and expanding condom distribution to non-traditional outlets such as hotels and shops [14]. However, no data was found regarding the effectiveness of these strategies in increasing condom uptake.

Mulwo and colleagues reported that many people have a negative perception of public sector condoms, with people complaining about their odour and reporting that public sector condoms have lower status than commercially available condoms [15]. It has also been reported that 'fit and feel' is a critical determinant of condom use [16] and that people would like to have different types and sizes of condoms available [17].

Table 29: Summary of quality of the evidence base and grading for comprehensive condom programming

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Intervention						
Consistent condom use	Serodiscordant sexually active heterosexual couples	Systematic review	Reduction in HIV incidence	80%	[1]	1
Male and female condom education	Sexually active women of reproductive age	2 phase study	Condom use ever	58.8% vs 98.9%, p≤0.001	[2]	1
			Consistent condom use, part 2 months	0.25% vs 48.5%, p≤0.001		
			Condom use at last sex	10.1% vs 87.0%, p≤0.001		
Discussion of condom use	Young people 18-24 years	Cross-sectional population-based household survey	Self-reported positive HIV status	AOR 0.09 (95% CI 0.01 – 0.58)	[3]	4a - SBCC
Difficulty in getting condoms	Young people 18-24 years	Cross-sectional population-based household survey	Self-reported positive HIV status	AOR 2.75 (95% CI 1.09 – 6.88)	[3]	3c
Inconsistent use of male condoms	MSM in peri-urban townships	Venue-based cross-sectional	HIV status	AOR 2.3 (95% CI 1.0 - 5.4)	[4]	3c
Introduction of female condoms	Female sex workers	Cohort	STI prevalence	AOR 0.71 (95% CI 0.58 - 0.86)	[5]	4a - Key populations
National mass media programmes	General population	Cross sectional	Condom use at last sex	AOR 1.10	[6]	4a - SBCC
National mass media programmes	General population	Cross sectional, multivariate causal attribution analysis	HIV infections averted as a result of condom use	701,495	[18]	4a - SBCC
National mass media programme	Men	Cross sectional, structural equation modelling	Condom self-efficacy	AOR 1.03	[17,18]	4a - SBCC

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
National mass media programme	Youth	Cross sectional, structural equation modelling	Condom attitudes	AOR 1.03	[17,18]	4a - SBCC
			Condom self-efficacy	AOR 1.05		
Mass media programmes	Men and women	Demographic and Health Survey	Condom use ever	OR = 1.16 for men and 1.06 for women	[10]	4a - SBCC
Community health workers	Sexually active males and females ages 15-49 years	Systematic review	ART treatment pick-up rate	95% compared to those without CHW adherence support	[19]	4a -ART
Technical efficiency factors						
Condom distribution in schools						5
Expand distribution to non-traditional outlets						5
PEPFAR limitation on distribution of condoms in schools						5
Rebrand Choice condoms to increase uptake						5
Negative perception of public sector condoms						5
Availability of and preference for other types of condoms						5
Fit and feel						5
Barriers to condom use						5

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4.1.5 TREATMENT, CARE AND SUPPORT FOR PEOPLE LIVING WITH HIV

Summary of evidence synthesis process

The co-chairs of the care and treatment working group, Gesine Meyer-Rath from HE²RO/ Boston University and Augustin Ntilivamunda from WHO, and their Department of Health (DoH) counterpart, Letta Seshoka from the HIV/AIDS Unit, drafted an initial list of interventions for inclusion in the IC. This initial list consisted of six interventions and 16 TE factors. The co-chairs also identified potential working group members from within the DoH, NHLS, and the country offices of donor organisations and international organisations. During the next Investment Case Task Team meeting, both these lists were discussed and additional interventions and working group members identified. Sixteen people were invited to the first working group meeting, of which ten were from the DoH. The working group met once before the stakeholder workshop; the meeting resulted in 2 more interventions and a total of 18 TE factors.

For the stakeholder workshop, invitations were sent to 40 individuals representing about 30 organisations, including national and provincial departments of health, academic institutions, implementing partners, medical aid organisations, and a diverse number of bodies such as SANAC, Treatment Action Campaign (TAC), the Southern African HIV Clinicians Society, the Networking HIV AIDS Community of South Africa (NACOSA), the Pharmacy Council, and the US Centers for Disease Control. Before the stakeholder workshop, all participants allocated to the care and treatment working group were provided with the list of interventions, asked to submit documentation regarding the effectiveness of any interventions, and invited to recommend additional interventions. Two institutions submitted materials before the workshop. The working group searched for and reviewed evidence for each suggested intervention.

During day 1 of the workshop, participants reviewed the list of interventions and TE factors twice, and were asked to add to and/or discuss the evidence supporting each intervention on the initial intervention list. A number of interventions and TE factors were added during this meeting, which also included a lively debate regarding the merits of different proposed TE factors and the state of published and unpublished evidence pertinent to the list of interventions and TE factors. The full list of the 12 interventions and 35 TE factors identified before or during the workshop can be found in Table 30; notes from the meeting are available on request to gesine@bu.edu. As part of the “Marketplace” on day 2 of the workshop, additional information and pertinent data were also suggested by members of other working groups.

During the remainder of the workshop and in the days immediately afterwards, materials were received from 18 institutions, including TAC, Wits Reproductive Health & HIV Institute, Kheth’Impilo, iTech, National Institute of Communicable Diseases, NDoH, MSF, Right to Care, Aurum, Broadreach, Clinton Health Access Initiative, Foundation for Professional Development, the Southern African HIV Clinicians Society, the Hospice Palliative Care Association, WHO and iACT, all of which (with the exception of i-ACT, Aurum and MSF) were represented on the working group. In reviewing the evidence, the working group followed up with a number of the authors of studies directly whenever additional data or information was needed.

The working group reviewed all published and unpublished data it received to assess its relevance to the interventions and TE factors under consideration (see Table 30). This assessment also determined whether the evidence came from South Africa and whether it was of high quality, using IC Data Template and grading instructions.

Description of final list of interventions and TE factors

The programme area covered by the care and treatment working group included care for HIV-positive people before the initiation of ART, ART, and palliative care. Costs of both outpatient and inpatient care were included in the working group’s analysis.

Palliative care

The cost of hospice-based palliative care to every person dying of AIDS was incorporated in the model. This is most likely an overestimate since coverage with palliative care, even though hard to estimate given current data, is likely much smaller. Costs associated with palliative care were derived from a recent analysis of 44 hospices run by NGOs, taking account of results for 16,550 patients (Alain Lolliot, personal communication).

Inpatient care before and after ART initiation

The modelling team also modelled the cost of inpatient care of patients not yet on ART (both for those who were eligible but not yet initiated or lost to initiation, and those who were not yet eligible in any given scenario of ART eligibility). This analysis was based on the frequency and cost of inpatient care of patients on and off ART in two hospitals, one in rural Mpumalanga and one in Soweto [1]. For this analysis, data on the frequency and length of stay was re-analysed according to the CD4 cell count categories used in Thembisa, and cost was adjusted for inflation from 2009 to 2014. The same data and adjustment was used for the cost of inpatient care for patients on ART.

Outpatient care before ART initiation

For pre-ART care, many of the papers reviewed focussed on a description of loss to care after testing or loss to initiation of people eligible for ART after uptake of pre-ART care [2-10]. However, little literature was found evaluating interventions to reduce this loss or improve other patient outcomes during this pre-ART period. (It should be noted that the relevance of pre-ART care will decrease as the new eligibility guidelines take hold, where the majority of people presenting for ART will be eligible for initiation, and certainly under Universal Test and Treat, where all people will be eligible.)

During the stakeholder workshop, four specific interventions to address the pre-ART period were suggested: (1) same-day ART initiation, (2) pre-ART care and ART initiation at primary health clinic (instead of specialised ART clinics), (3) IPT for the prevention of TB alone, and (4) cotrimoxazole for the prevention of TB and other OIs. One ongoing randomised clinical trial is evaluating same-day ART, with results from the first six months after enrolment expected in February 2015; the working group graded the evidence for this intervention as 3a. No data was available for the second proposed intervention (pre-ART care and ART initiation at primary health clinic), and it was unclear how this would differ from other attempts at integrating care at the PHC level; this was graded 3c. Prevention of OIs with cotrimoxazole is a well-established intervention, although recent data from South Africa regarding its effectiveness is scarce. Data from a longitudinal study in a PHC clinic in Johannesburg found a hazard ratio of 16 for ART initiation at 12 months between patients who took cotrimoxazole as prescribed and those who did not (personal communication based on Clouse 2012 [11]). IPT was judged as falling into the remit of the TB programme area and was therefore graded 4c.

Outpatient care after ART initiation: Interventions

Care and treatment interventions following ART initiation generally consisted of interventions that expand ART eligibility and interventions that aim to increase the demand for ART in specific populations. For the former, five non-mutually exclusive eligibility criteria were considered: (1) Patients with CD4<500 and PMTCT Option B+, (2) HIV-positive persons in serodiscordant relationships, (3) Universal test and treat (UTT) for adults, (4) early paediatric treatment for children ages 6-13, and (5) Expanding access to third-line treatment. Existing models have well-parametrised inbuilt mechanisms [12] that assessed the effectiveness of the first three interventions in this category, to which the team deferred after cross checking central model assumptions against existing evidence. Intervention (4) regarding children ages 6-13 was graded 3c; no evidence was available supporting the intervention, and the consensus from the stakeholder consultation was that expanding ART eligibility to children ages 6-13 unconditionally was ineffective in terms of increasing survival. Given the small population on third-line treatment in South Africa (about 300 patients, personal communication F. Venter), the lack of evidence suggesting additional benefits from third-line treatment over that of standard first- or second line treatment, intervention (5) was graded 5. as 6, taking into account the impact on cost only.

Men, older children, and farmworkers were highlighted as populations requiring specific demand creation interventions in order to access ART. Establishing teen- and adolescent-friendly clinics was suggested as a means of targeting older children. However, as the only such intervention with available effectiveness data reported only an impact on the uptake of testing of children, not treatment, the intervention 4a and transferred it to the HCT programme area to prevent overlap. The provision of ART in the workplace was suggested as a means of targeting men, but the only evidence provided [13] lacked a comparator, and the intervention was therefore graded 3c. Despite a long discussion of the importance of increasing ART coverage in farmworkers, the working group was unable to find evidence demonstrating the effectiveness of any specific intervention, making this an important question for future research, hence 3b.

Outpatient care after ART initiation: TE factors

Broadly speaking, the TE factors considered may be divided into three main categories: (1) task shifting and down referral, (2) interventions to improve ART adherence and retention in care, and (3) technological innovations to improve care and treatment.

Task shifting and down referral

Task shifting, ie, the provision of services by lower cadres of staff than originally planned, and down referral, ie, the referral of patients on ART to lower levels of clinics, represent important strategies for improving the technical efficiency of ART. These two strategies aim to ease the ever increasing burden on an overstretched health system facing a shortage of medical practitioners, while potentially also reducing cost and freeing up budgetary capacity to extend care and treatment to more of those in need. According to a review of the evidence, technical efficiency is improved increasing the initiation and management of ART by nurses instead of medical doctors (NIMART) and various ways of improving NIMART through training and mentorship, as well as patient down referral to general practitioners.

In their respective matched cohort analyses, Long et al. and Brennan et al. examined treatment outcomes among stable HIV patients down-referred from a doctor-managed, hospital-based ART clinic to a nurse-managed primary health care facility in Johannesburg, South Africa [14] [15]. Both found treatment outcomes among the down-referred cohort to be at least as good as the outcomes of similar patients who are maintained at a hospital-based ART clinic. The finding of non-inferiority is echoed in a separate randomised trial at two South African primary care clinics that were part of the Comprehensive International Program for Research in AIDS in South Africa [16]. However, all three studies focused on nurse management of ART, rather than nurse initiation and management of ART, which limits their generalizability to the effectiveness of NIMART overall.

Regarding the full spectrum of NIMART, several studies evaluated the Streamlining Tasks and Roles to Expand Treatment and Care for HIV (STRETCH) programme, a randomised control trial in 31 primary care clinics in Free State Province, South Africa, that included nurse initiation in addition to nurse-management of ART. Both Fairall et al. and Barton et al. demonstrated the non-inferiority of NIMART compared to standard of care, the latter citing a 0.42% reduction in mortality (with the 95% confidence interval encompassing 0) which we interpreted as an indication of non-inferiority [17] [18].

Providing training and mentorship to nurses responsible for NIMART also appears to improve treatment outcomes, mainly by improving patients' ART adherence. In a before-after cross-sectional study conducted on nurses completing a Médecins Sans Frontières (MSF) mentorship programme in Khayelitsha, South Africa, Green et al. found a 27.5% improvement in the number of patients with adherence assessed and documented [19]. Similarly, Workneh et al. found a 39.5% improvement in the documentation of pill counts after nurses participated in a clinical mentoring programme at four sites in Botswana [20]. Both of these studies reported process indicators that could not be translated into the intermediate measures used in the models; moreover, the latter study was based on paediatric HIV care in Botswana and was hence of limited relevance to the general South African population.

During the stakeholder workshop, there additional suggestions were made regarding ways to improve NIMART: (1) expanding NIMART to include lower cadres of nurses, specifically to staff nurses, (2) introducing final assessments of

NIMART-trained nurses by their mentor, and (3) integrating NIMART into IMCI sites. As no evidence was found regarding the effectiveness of either of the interventions, each was graded 3c.

Task shifting was similarly found to be effective in pharmacies. In a retrospective cohort study using routinely collected electronic individual-level patient data from 10 sites in Cape Town, Monteith et al. found that treatment outcomes were equivalent between those treated under the Indirectly Supervised Pharmacist Assistant model and those treated in the standard of care (adjusted hazard ratio of 1.03)[21].

With respect to down-referral, referring stable patients from specialised ART clinics to general practitioners also appeared to improve technical efficiency. In a cohort study of a down-referral programme involving 72 private practitioners in South Africa, Innes et al. suggested that general practitioners (GPs) achieved comparable results to public sector clinics, citing 58%-64% retention at 12 month rate and 82%-85% virological suppression at 6 months in the GP treated cohort [22]. However, the study lacked a comparator cohort, which prevented the working group from isolating the impact of the intervention. Going one step further, Leisegang et al. used a health-state transition model to compare the costs and outcomes of a private care and a public care ART program in South Africa, and found the private care program less costly but similar in terms of treatment outcomes (a difference in 0.1 life years gained over a patient's lifetime) [23]. However, the primary data used in the analysis seemed to suggest higher mortality and loss to follow-up in the private cohort, in contrast to the model results. On the other hand, in a retrospective cohort study that compared the public-private partnership (PPP) model and the standard of care, Navario found the PPP model to be more costly but also beneficial in terms of improving patient retention on ART (19% improvement under the PPP model) [24]. In face of the competing evidence, the working group gave preference to the empirical data from Navario et al over the modelled estimates in Leisegang et al.

Improving ART adherence and patient retention

Interventions that aim to improve patients' adherence and retention in care constitute a second major category of outpatient TE factors after ART initiation. This cluster of factors can be further divided into innovative models of care to bring services closer to patients, initiatives improving counselling and support, and interventions using novel technology to improve the monitoring of adherence and defaulting from care.

Amongst the innovative models of care, facility-based adherence clubs have ample literature documenting their effectiveness due to their relatively long history, having been piloted from 2007 onwards, and MSF's sustained efforts to evaluate them. In short, adherence clubs reduce the duration of clinic visits as well as the workload of clinical staff by allowing a large number of stable patients to be seen by a lay counsellor in a group session that includes the issuing of pre-packed medication as well as weight monitoring and screening of side effects. Only those patients with weight loss or side effects are referred up to a full review by a clinician. In a cohort study of the MSF adherence clubs in a large urban ART clinic in Khayelitsha, South Africa, Luque-Fernandez et al. found that club participation reduced loss-to-care by 57% when compared to standard care (hazard ratio 0.43) [25]. This finding is cited and endorsed by a subsequent cost-effectiveness analysis conducted at the same site [26]. The next logical step in the development of these clubs is to take them into other venues in the community that might be closer to patients' homes, or into these homes directly. Even though these models are currently being piloted in a number of places, no evidence regarding the effectiveness of these types of adherence clubs is available yet.

Community ART groups (CAG) are a second model of care proposed to improve adherence, with strong evidence on effectiveness from multiple settings. In this model of care, patients on ART from a single community that doesn't have a local clinic take turns to travel to the nearest ART clinic to collect medication for all members of the group, allowing them to pool transport money and time. Evaluating an MSF pilot of such a group in Tete, Mozambique, Decroo et al. found an extremely high patient retention rate of 97.5% amongst CAG members after a median follow-up of 12.9 months [27, 28]. This finding is supported by a retrospective cohort study in Nazareth, Lesotho, that found that CAG participation reduced attrition risk (adjusted hazard ratio of 0.18 over 12 months, from 90.2% to 98.7%) [29]. The working group selected the

evidence from Vandendyck et al. since the data was more recent and Decroo et al.'s finding lacked a relevant baseline comparator. However, it remains unclear how applicable CAGs will be in the South African context – CAGs were designed for settings with scarce treatment facilities, where patients must travel long distances for services, which might not apply to South Africa which has a dense network of primary health care clinics, the majority of which already offer ART.

A number of studies discussed the merits of home-based care as another means of improving retention. In a cluster-randomised equivalence trial in Jinja, Uganda, Jaffer et al. found home-based care to be less costly but equivalent in terms of treatment outcomes (adjusted rate ratio of 1.04 for virological failure) [30]. In a randomised controlled clinical trial in western Kenya, Selke et al. reached similar conclusions, finding that community-based care (equivalent to what is termed home-based care in Jaffer et al.) resulted in similar clinical outcomes but a reduction by half in the number of clinic visits [31]. Two studies from Uganda additionally suggest that home-based care improved treatment outcomes [32] [33] – although Marseille et al. use no ART at all as the baseline comparator, thereby exaggerating the effects of home-based care. As none of the studies were conducted in South Africa, the working group determined to err on the conservative side, grading home-based care as 6 – similar in terms of treatment outcomes but cost saving.

Of the initiatives improving counselling and support, two specific programmes were suggested: (1) the Integrated Access to Care and Treatment programme (iACT), whose key objective is to promote early recruitment and retention of newly diagnosed people living with HIV in care and support programmes, thus bridging the time between testing and treatment initiation and reducing loss to initiation, and (2) community-based adherence supporters. At the time of our review there was no quantitative evidence demonstrating the effectiveness of the iACT programme, but the working group was subsequently informed that evaluations were ongoing; the intervention was graded as 3a. Concerning community-based adherence supporters, the working group reviewed three complementary evaluations, different population groups, of a patient advocate programme conducted at 57 public ART sites across South Africa. These multicentre cohort studies found a reduction in loss to follow up over standard care (adjusted hazard ratios of 0.57 and 0.63 for adults and children respectively) as a result of community-based adherence support [34] [35] [36].

Several interventions using novel technology to improve the monitoring of adherence and defaulting from care were suggested, including: (1) defaulter tracers, (2) SMS reminders, and (3) real-time adherence monitoring using pill-cap devices and similar methods. With respect to defaulter tracers, an evaluation of a pilot intervention in South Africa found that 4% (23 out of 493) of previously lost patients returned to care as a result of being contacted by a defaulter tracer [37]. Some also suggested that further training of defaulter tracers would improve technical efficiency, but the working group found no evidence support this claim; the intervention was graded as 3c. Two studies [38] [39] found that SMS reminders had a positive effect on ART adherence, though with different results regarding the magnitude of the effect. This result was later confirmed in a meta-analysis on the subject which included these two studies. Since neither study was conducted in South Africa, the working group relied on the evidence from the meta-analysis (relative risk of ART adherence at 48-52 weeks of 0.82) [40]. As for real-time adherence monitoring, the only available evidence were preliminary data from the only two trials of such real-time adherence monitoring devices that included clinical outcomes beyond adherence, one of which was from South Africa. Since neither of these showed an effect, the intervention was assigned a grade of 3c.

Technological innovations

During the stakeholder workshop, many technological innovations to improve care and treatment more generally were suggested, but overall evidence for their effectiveness was scarce.

Point of care (POC) technology for the measurement of CD4 cell count, viral load and creatinine was suggested as a potential means of improving technical efficiency. In terms of CD4 POC tests, one study evaluated a pilot programme in South Africa using the PIMA analyser, finding an improvement in linkage to care (relative risk of completing the referral visit for HIV care of 1.25) [41]. However, as no evidence for the effectiveness of POC testing for either viral load or creatinine could be found, both were graded as 3c.

As NDoH has a national strategy for drug resistance (NDoH 2014b), the working group reviewed evidence for a number of resistance prevention strategies, namely genotype testing, drug resistance surveillance and the uses of non-laboratory early warning indicators for virological failure. The use of genotype testing was suggested for two specific instances: (1) for children with suspected first-line failure, and (2) for all patients suspected of second-line failure. Although three modelled studies in the genotyping literature were identified, none directly addressed children with suspected first-line failure. (Levison et al. and Rosen et al. modelled genotype testing at first-line failure for the general population, instead of just children [42].) With respect to genotype testing for all patients suspected of second-line failure, Lorenzana et al. found a 25% increase in 5-year survival rates [43]; this intervention was graded 1. Drug resistance surveillance and the use of early warning indicators for virological failure did not have any evidence supporting their effectiveness; the only available literature described the respective programme as envisaged by the NDoH (NDoH 2014b), and a number of clinic-level implementations, respectively. Since both are existing government policies, they were assigned a grade of 2.

With respect to a second government programme – new NDoH pharmacovigilance policy – the working group found only implementation plans but no evidence of clinical impact. This programme focuses on strengthening feedback loops and management of side effects associated with drugs for chronic conditions, with a focus on HIV and TB drugs. Again, this intervention was graded as 2.

The working group also examined evidence regarding the monitoring of drug levels in plasma as a tool for establishing treatment adherence. Two pertinent studies were found [44, 45], but these focused on the feasibility, rather than the effectiveness, of the technology, possibly because the technology was too new to be evaluated in a clinical setting. The working group assigned a grade of 3b to technological intervention.

Other suggestions that lacked evidence regarding their effectiveness included: (1) Analysis of drug levels in hair as screening for first-line resistance before genotyping; (2) Increasing the use of viral load monitoring, and (3) pharmacy automation. Hair screening and enhanced viral load monitoring were graded as 3c, whilst pharmacy automation was graded as 3a since an analysis of the effectiveness of this intervention is forthcoming.

Table 30: Summary of quality of the evidence base and grading for treatment, care and support

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Interventions						
Pre-ART care						
Pre-ART care and ART initiation at primary health clinic	HIV+ children and adults	-	-	-	-	3c
Isoniazid preventive therapy	HIV+ people	-	-	-	-	4a (TB)
Cotrimoxazole	HIV+ people with CD4 cell counts <350 cells/microl	Observational study	Increase in ART initiation over 12 mts	16%	Clouse 2012 [11]	1
Same day ART initiation	HIV+ children and adults	-	-	-	-	3a
ART care						
ART (Current guidelines) ^e	ART eligible patients	N/A	N/A	N/A	Model assumptions	1

CHAPTER 4

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
ART for discordant couples	HIV+ partners of HIV-adults	N/A	N/A	N/A	Model assumptions	1
Universal test and treat	HIV+ children and adults	N/A	N/A	N/A	Model assumptions	1
Early paediatric treatment for children from 6-13	HIV+ children from 6-13	-	-	-	-	3c
Third line treatment	Adults and children who have failed second-line ART	-	-	-	Model assumptions	6
Teen and adolescent friendly clinics	ART eligible children and adolescents	-	-	-	-	4a (HCT)
Workplace ART	HIV+ employees	Cohort study	% of patients with suppressed viral loads at 12 months	72	Charalambous (2007) [13]	3c
Increase ART coverage in farmworkers	Farmworkers	-	-	-	-	3b
TE factors						
NIMART	ART patients	Randomised controlled trial	% reduction in deaths (for ART naïve patients with CD4 \geq 350)	0.42	Barton (2013) [18]	6
- NIMART (Nurse management only)	ART patients	Observational study	Hazard ratio (likelihood of loss to follow-up, LTFU)	0.3	Brennan (2011) [15]	6
- NIMART by staff nurses	ART patients	-	-	-	-	3c
- Improved mentorship for NIMART	ART patients	Before-after cross-sectional study	% improvement in number of patients with adherence assessed and documented	27.5	Green (2014) [19]	1
- Final assessment of NIMART nurse by mentor	ART patients	-	-	-	-	3c

e Note this refers to guidelines effective in January 2015, specifically eligibility at CD4<500 and PMTCT Option B+

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
- Improved training and mentorship for paediatric NIMART	ART patients	Retrospective chart review	% improvement in documentation of pill count	39.5	Workneh (2013) [20]	1
- Integration of NIMART into IMCI sites	ART patients	-	-	-	-	3c
Indirectly supervised pharmacy assistants (ISPA)	ART patients	Retrospective cohort study	Adjusted hazard ratio (mortality at ISPA vs pharmacist sites)	1.03	Monteith (2011) [21]	6
Incentives for all chronic care patients	Chronic care patients	-	-	-	-	4b
GP down referral	ART patients	Retrospective cohort study	Difference in % of patients retention on ART	19	Navario (2009) [24]	1
- GP initiation and management of ART	ART patients	Cohort study	% retention (alive and in care) after 12 months (2005 cohort)	63	Innes (2012) [22]	3b
Home-based ART	ART patients	Cluster randomised equivalence trial	Adjusted rate ratio (virological failure)	1.04	Jaffar (2009) [30]	6
Community-based adherence support	Adults on ART	Observational multicohort study	Adjusted hazard ratio (attrition)	0.57	Fatti (2012) [34]	1
Community-based adherence support	Children on ART	Multicentre cohort study	Adjusted hazard ratio (LTFU)	0.63	Grimwood (2012) [35]	1
Community ART groups	ART patients	Retrospective cohort study	Adjusted hazard ratio of attrition risk (CAG vs Non-CAG)	0.19	Vandendyck (2014) [29]	1
i-ACT	ART patients	-	-	-	-	3a
Adherence clubs	ART patients	Cohort study	% reduction in loss to care	57	Luque-Fernandez Adherence (2013) [25]	1

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Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Defaulter tracers	ART patients	Observational study	Number of patients returned to care (out of 260 reached, out of 493 lost patients)	23	Rosen (2010) [37]	1
Training of defaulter tracers	ART patients	-	-	-	-	3c
SMS reminders	ART patients	Meta-analysis	Relative risk of ART adherence at 48-52 weeks	0.82	Horvath (2012) [40]	1
Real-time adherence monitoring	ART patients	-	-	-	-	3c
More adherence counsellors	ART patients	-	-	-	-	3c
Analysis of drug levels in hair	ART patients	-	-	-	-	3c
Pharmacy automation	-	-	-	-	-	3b
Analysis of drug levels in plasma	ART patients	Cohort study	Adjusted hazard ratio of viral load >400 copies (children with lopinavir <1mg/l vs >1mg/l)	2.3	Moholisa (2014) [44]	3b
Point of care CD4 testing	-	Observational study	Relative risk of completing the referral visit for HIV care	1.25	Larson (2012) [41]	1
Point of care viral load testing	ART patients	-	-	-	-	3a
Point of care creatinine clearance testing	ART patients	-	-	-	-	3a
Increase use of viral load monitoring	ART patients	-	-	-	-	3c
Follow up on unsuppressed viral loads by NHLS	ART patients with unsuppressed viral loads	-	-	-	-	3c
Reminder in Tier. net register and mentorship	-	-	-	-	-	3c
Early warning indicators for viral failure	-	-	-	-	-	2

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Drug resistance surveillance	-	-	-	-	-	2
Use of genotype testing at suspected first line failure	Children suspected of first line failure	-	-	-	-	3c
Use of genotype testing at suspected second line failure	ART patients suspected of second line failure	Modelling study	% increase in 5-year survival	25	Lorenzana (2012) [43]	1
Pharmacovigilance	All patients (not just ART)					4b ^f
Improving the drug supply chain	All patients (not just ART)					4b

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^f 4b: Programme enabler

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4.1.6 MEDICAL MALE CIRCUMCISION^g

Summary of evidence synthesis process

The working group for Medical Male Circumcision (MMC) used a collaborative process to arrive at a list of interventions and TE factors included in the IC modelling. The MMC working group consisted of experts representing the government of South Africa, donors, implementers, and civil society with an advisory mandate.

Beginning its work in June 2014, the working group formulated an initial list of interventions and TE factors based on non-systematic literature reviews, consultation with outside consultants, and personal expertise. At this stage, the group began to note estimates of effectiveness and cost for many of the interventions and TE factors proposed.

On 30-31 July 2014, the working group and other stakeholders met as part of the IC consultation workshop to vet the initial list of proposed interventions and TE factors. Table 31 and Table 32 present all interventions and TE factors considered. The group reviewed the evidence available for each intervention and identified plans to compile additional evidence in the days following the workshop. The evidence available for each was measured against the criteria established by the Task Team.

Following the stakeholder consultations, the MMC working group compiled data identified during the workshop. The group submitted a matrix of interventions and TE factors, along with supporting literature, to the modeling group on Aug 20.

The MMC working group classified Voluntary Medical Male Circumcision (VMMC) and Early Infant Male Circumcision (EIMC) as interventions due to the fact that these have the clearest and most direct effect on reductions in HIV infection. All other factors influence effectiveness indirectly through either: (1) reducing cost; (2) increasing demand; (3) improving targeting; or (4) improving quality of MCC.

In September, the working group graded the evidence for each intervention and TE factor. The grades included input from the modeling group. At this stage, VMMC and EIMC were judged to have sufficient data for inclusion in the model.

Description of final list of interventions and TE factors

Interventions included

Voluntary Medical Male Circumcision (VMMC)

VMMC is defined as male circumcision performed after infancy (i.e., more than 60 days after birth) in a formal medical setting on a voluntary basis. In accordance with the stakeholder consultation workshop, this definition does not include circumcision performed by traditional authorities, as the removal of foreskin in traditional settings can vary from the medical procedure and the efficacy of protection is not known in cases of partial removal.

Wamai *et al* [1] summarise the state of evidence for VMMC and report that VMMC reduces men's risk of acquiring HIV through heterosexual intercourse by approximately 60% (95% CI: 32 – 76). The estimate is based primarily on three RCTs. The confidence interval is based on one of the three RCTs, Auvert *et al* [2]. VMMC also indirectly protects men's sexual partners from HIV, because HIV-negative men cannot infect their female sexual partners. However, for HIV-positive men, VMMC does not reduce their risk of transmitting HIV to their sexual partners.

^g We use the term "MMC" to refer to medical circumcisions performed at any age. "EIMC" is used for MMC performed during infancy (0 – 60 days after birth) while "VMMC" is used for cases after infancy.

Wamai *et al* [1] also summarise 15 observational studies of VMMC effectiveness, adjusting for confounders. These studies found a protective effect of 65%. This data was not explicitly included in the model as it is effectively indistinguishable from the RCTs' conclusions.

All men aged 10-49 constitute the target population for VMMC. The working group considered age-specific targeting to be a TE factor.

During the stakeholder consultation workshop, the VMMC group estimated that the cost to perform one circumcision ranges from 1060 to 1802 ZAR. This estimate is based primarily on USAID competitive procurements, where the budgets of bidders are based on an average forecasted cost per circumcision. However, the price per circumcision that USAID pays is not necessarily what a circumcision costs in full. Therefore, the working group made an upward adjustment for inputs not covered by the USAID contract and instead provided by public clinics in kind, such as facility operating costs. Downward adjustments for implementer profit and as a result of operation at higher scale were also considered. Efforts to improve the cost estimate were underway at the time of this study (discussed below).

Early Infant Male Circumcision (EIMC)

EIMC is defined as circumcision performed during infancy (0 to 60 days after birth). The target population is male infants. Both EIMC and VMMC are defined as complete removal of foreskin, with the only difference being the age of the client. The physical result achieved is identical and the effectiveness is therefore assumed identical as well.

TE factors included

Prioritisation by site type (impact on effectiveness: cost reduction)

Resources for VMMC may be prioritized to fixed sites, outreach sites, mobile sites, or some combination of these modalities. Fixed sites are permanent structures—often located near or within existing health care facilities—that offer VMMC on a continuous basis. Outreach sites are generally small sites that provide VMMC services for a temporary time period in rural areas and in areas that are hard to reach. Outreach sites are often supplied by a fixed site on a daily or weekly basis. Mobile sites, including the commodities and staff, regularly move, following demand and/or supplementing existing services. Mobile sites are usually temporary structures, often tents and prefabricated structures and sometimes vehicles.

The TWG noted that cost per VMMC and percent of target population reached vary across sites. Bollinger *et al* [3] compiled cost per VMMC from 99 facilities across six countries in a variety of settings. The study observes a cost increase of 106 ZAR at outreach sites compared to fixed sites across the full sample (not controlling for other factors). The TWG did not have estimates for the percentage of target population reached by site type. The feasibility of significantly expanding the outreach and mobile models may be limited by human resource constraints. Specifically, under current guidelines, a physician must be involved in the removal of the foreskin, which may limit more decentralized approaches.

This TE Factor was not included in the model due to lack of adequate outcome data and estimation techniques. Cost data for outreach and mobile sites are available from other countries but are of questionable relevance to the South Africa context. Additionally, modeling the trade-off between site types is difficult; marginal demand and cost associated with each site type will vary depending on local conditions. Finally, the relevance of modeling prioritization by site type is unclear, as local implementers are likely best positioned to identify the low cost/high demand option.

Alternative staffing model (impact on effectiveness: cost reduction)

Multiple alternative models for revising staff arrangements and deployment for VMMC have been proposed, generally involving a reduction of physician time and an increase in nurse time.

The TWG noted that the feasibility of alternative staffing models may be limited by human resource constraints. As noted, current guidelines require that a physician must be involved in the removal of the foreskin. Alternative models would not be viable if they violated these guidelines.

Cost per VMMC varies by staffing model. Tumwesigye *et al* [4] report a 31.16 ZAR reduction in cost per VMMC when medical officers are used in place of surgeons in Uganda. Rech *et al* [5] report a 257-second reduction in time required of the primary physician with an increase in time required of other, less costly staff resulting in a net savings.

High intensity campaigns (impact on effectiveness: demand increase)

High intensity campaigns are defined as communication over a short period of time and corresponding increase in VMMC capacity to generate a large number of VMMC's from a specific locality. These may be aligned with traditional seasonal timing of circumcisions to benefit from pre-existing cultural practices, which may enhance efficiency.

In the case of such campaigns, the TWG noted that cost per VMMC and demand will vary from the standard clinic based model. Bollinger *et al* [3] observe 265 ZAR greater cost for high intensity campaigns compared to baseline conditions.

Media and work place campaigns (impact on effectiveness: demand creation)

Effective use of communication strategies and channels may increase coverage rates (probability of circumcision) by building demand for VMMC. Both media and work place campaigns are included in this category.

Bertrand *et al* [6] attempt to estimate the costs of demand creation for VMMC scale-up in 13 countries of eastern and southern Africa. They note, "Costing demand creation presents a greater methodological challenge than costing service delivery, in part because there is no straight line 'dose-response' relationship (i.e., the delivery of a given amount of communication does not yield a predictable uptake in VMMC services). For example, it is possible to estimate the service delivery costs to provide 1,000 VMMC procedures in a given location with fair accuracy. However, one cannot predict with the same accuracy the increase in service uptake that will be generated by a given level of demand creation activity" [6].

The cost of demand creation is implicitly included in the overall PEPFAR-based estimate of the cost per VMMC, as PEPFAR partners regularly employ demand creation activities. For the reasons noted by Bertrand, the TWG was not able to isolate the demand creation effect.

Collaboration with traditional male circumcision system (impact on effectiveness: demand increase)

Various interventions leverage the traditional circumcision system to generate demand for medical male circumcision. For example, professional staff may be available on-site during traditional ceremonies to perform the circumcision. This TE factor does not include traditional circumcision as protective, as the benefits of partial removal of the foreskin is low.

No data was provided to the working group to permit a reliable estimate of the effectiveness or cost of this TE factor, although participants noted during the stakeholder consultation workshop that administrative data exists. Commenters during the consultation emphasized that this TE factor should only be included under circumstances where the collaboration with the traditional system led to a *medical* circumcision; as noted above, the effectiveness of a traditional circumcision is not equivalent.

Prepex™ (impact on effectiveness: demand increase)

Prepex™ is a device that achieves non-surgical circumcision by stopping the flow of blood and oxygen to the foreskin, with the foreskin naturally detaching after about seven days; a scalpel is not required.

It is hypothesised that, with *Prepex™*, demand may vary from the currently used circumcision method. For example, clients might prefer *Prepex™* to avoid the use of scalpels or the injections required with the scalpel method. However, no data yet substantiate the increased demand hypothesis.

Effectiveness of circumcisions conducted using *Prepex™* is assumed equivalent to current surgical methods as the physical result is identical. Njeuhmeli *et al* [7] report a 53 ZAR greater cost using *Prepex™* compared to baseline VMMC. Additional cost studies were underway at the time of this study.

Private sector providers (impact on effectiveness: demand increase)

Engagement of private sector providers has the potential to increase the volume of VMMC provided by diversifying the source of circumcisions. Public promotion of VMMC might increase the volume of circumcisions performed by private providers with the procedures covered by private medical aid. However, studies estimating the potential increase in demand are not yet available. Additionally, the cost of performing male circumcision in private facilities is likely to differ from the cost in public facilities.

Geographical targeting (impact on effectiveness: improved targeting)

Geographical targeting is defined as prioritizing resources for VMMC along a geographic dimension such as urban/rural or by province.

Population-wide effectiveness of geographical targeted will vary by geographic region due to differing HIV prevalence and incidence and the corresponding variance in exposure to HIV during future sexual encounters. Kripke (manuscript in preparation) shows that there is some variation in cost-effectiveness across provinces, based on differences in HIV incidence in the different provinces. Anderson *et al* [8] also demonstrate the benefit of geographical targeting in Kenya for a large set of HIV interventions, including VMMC.

Key population targeting (impact on effectiveness: improved targeting)

The effectiveness of enhanced targeting of VMMC services for key populations will vary depending on the group's different exposure to HIV through future sexual encounters.

During the consultative process, it was noted that it may be difficult to target VMMC by key populations due to the assumed additional cost of targeting hard-to-reach populations and potential stigmatization associated with targeting these key populations. Furthermore, to date, research does not exist to suggest that MMC reduces the acquisition of HIV through anal sex - the primary mode of infection among MSM. Other key populations such as PWID are likely to have limited benefits given that sexual intercourse is not their primary mode of infection.

Age group targeting (impact on effectiveness: improved targeting)

Age group targeting is defined as prioritizing resources for VMMC within a particular age group before performing VMMC for other ages. Effectiveness of this intervention varies by age group as a result of the age distribution of HIV incidence. Effectiveness therefore is a function of model parameters such as age, age distribution, sexual behavior, and HIV incidence. In the model, age groups were defined as 10-14, 15-19, 20-24, and 25-49.

Kripke (manuscript in preparation) using the Decision Makers' Program Planning Tool (DMPPT 2.0) models the effects of age targeting VMMC in South Africa and demonstrates the potential decrease in HIV incidence when compared to an un-targeted approach. The investment case model does not explicitly use the results of DMPPT but rather replicated the approach based on previously defined model parameters

Continuous quality improvement (impact on effectiveness: improved quality)

Continuous quality improvement is defined as technical assistance to improve operations at sites providing VMMC. This may result in improved communication to clients for follow-up, design of optimal data collection tools, improved documentation of client consent, modification of procedures to include screening for sexually transmitted infections, and improved documentation of adverse events.

Byabagambi *et al* [9] document several improvements associated with Continuous Quality Improvement: 1) 50 percentage point increase in clients returning for follow-up within 48 hours of circumcision; 2) 31 percentage point increase in clients attending VMMC health education with their partners; 3) 60 percentage point increase in sites collecting data on adverse events; and more. However, evidence that would allow conversion of these outcomes to parameters in the model was not

available. Additionally, the applicability of Ugandan conditions to South Africa was questioned. South Africa specific data is expected from University Research Council in 2015 and should allow conversion to model parameters.

Table 31: Summary of male medical circumcision interventions/ TE factors with evidence regarding both effectiveness and costs

Intervention/ TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Medical male circumcision	All males, after infancy	RCT	Protection efficacy	60%	[1]	1
Early infant male circumcision	All males, during infancy	--	Protection efficacy	60%	Inferred from [1]	1

Table 32: Summary of male medical circumcision interventions/TE factors with indirect impacts on effectiveness

TE Factor	Potential impact on effectiveness	Source(s) considered	Grading
Prioritisation by site type	Cost reduction (, demand creation)	[3]	3a
Alternative staffing model	Cost reduction	[4]	3
High intensity campaigns	Demand increase	[3]	3
Media and work place campaigns	Demand increase	[6]	3a
Collaboration with traditional male circumcision system	Demand increase	--	3
Prepex	Demand increase	--	3a
Private sector providers	Demand increase	--	3a
Geographical targeting	Improved targeting	Kripke, in progress	3a
Key population targeting	Improved targeting	--	3c
Continuous quality improvement	Improved quality	[9]	5

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4.1.7 HIV COUNSELLING AND TESTING

Summary of evidence synthesis process

The HIV counselling and testing (HCT) sub-working group co-chairs, Eva Kiwango, UNAIDS South Africa, and Thato Chidarikire, DoH, drafted an initial list of interventions and TE factors to be included in the synthesis of evidence for this programme area. A working group was constituted drawing members from NDoH, Foundation for Professional Development (FPD), CDC, and SFH, among others. The HCT sub-working group reviewed the proposed list of interventions and TE factors, and the IC Task Team and Steering Committee also reviewed and confirmed members who had been nominated to the sub-working group. The sub-working group met twice before the national stakeholder workshop in July 2014.

In preparation for the national stakeholder consultation, members of the HCT sub working group and other key stakeholders were provided with the list of interventions and TE factors that the sub-working group co-leads had compiled. Participants were asked to meet within their organisations and discuss the draft list of HCT interventions and efficiency factors, critical enablers and development synergies that would guide the synthesis of HCT evidence. They were also requested to submit documentation of evidence regarding the effectiveness of any interventions or TE factors that they wished to see included for HCT. Prior to the workshop, the sub-working group reviewed and compiled evidence for each proposed intervention and TE factor.

During the stakeholder workshop, approximately 30 participants joined the HCT sub-working group. On the first day, the participants reviewed the proposed list of HCT interventions and current and future TE factors again and also discussed existing published and unpublished evidence regarding the effectiveness of each intervention in terms of HIV and/ or TB infections averted, life-years gained, and/ or other more programmatic or intermediary parameters.

Participants either provided references to these materials during the workshop, or indicated who would be responsible for submitting the evidence following the workshop. Participants of other working groups added to this information during the “Marketplace” on day 2 of the workshop. Shortly after the national consultation, participants were reminded to provide the suggested evidence.

The sub-working group received information from the following institutions: NDoH, SANAC, MSF, CDC, USAID, Children’s Right Centre, South African Business Coalition on HIV and AIDS (SABCOHA), NACOSA, Agri SA, SFH, SHOUT it Now, Right to Care, ANOVA, AURUM, HE2RO, Broadreach, Clinton Health Access Initiative, FPD, Higher Education and Training HIV/ AIDS Programme (HEAIDS), International Organization for Migration (IOM), International Labour Organization (ILO), UNICEF, WHO and UNAIDS.

The sub-working group reviewed all studies provided for evidence of effectiveness of various HCT-related interventions in terms of HIV infections averted, life-years gained, and/ or other, more programmatic or intermediate outcomes. The strength of the evidence was evaluated, as well as where each study was conducted.

Description of final list of interventions and TE factors

HCT has been promoted as a key component in preventing HIV acquisition and/ or transmission in low resource settings, promoting behaviour change and linking people who test HIV-positive to care and treatment services.

Interventions

Testing of the general population

A number of studies have assessed the impact of HCT on infections averted as well as on risky sexual behaviours. Sweat

and colleagues (2000) undertook a multisite trial of HCT to assess its impact, cost, and cost-effectiveness in Kenya and Tanzania, concluding that HCT averted 1,104 HIV infections in Kenya and 895 in Tanzania over one year [1]. According to Sweat and colleagues, the cost per infection averted was US\$249 and US\$346, respectively, and the cost per disability adjusted life year (DALY) saved was US\$12.77 and US\$17.78 [1]. The intervention was found to be most cost-effective for people infected with HIV and those who tested as a couple [1].

Research has demonstrated that HCT is more effective than provision of health information alone in terms of encouraging behaviour change. The Voluntary HIV-1 Counseling and Testing Efficacy Study Group found that HCT was associated with a greater reduction in unprotected sex with non-primary partners among those who received HCT compared to those who received health information only [2].

Studies have demonstrated variable impact of HCT on risky sexual behaviour depending on the HIV status of the individual receiving HIV testing services. For example, a study from Tanzania found moderate associations between uptake of HCT and reduction in some sexual risk behaviours in those testing HIV negative, yet the same study found no impact among HIV-positive individuals in a context of low overall HCT uptake [3]. However, as Scott-Sheldon and colleagues (2013) point out, HIV testing benefits those who test positive, allowing them to receive treatment, but the benefits for those who test negative remain unclear [4]. The South African study by Scott-Sheldon and colleagues found that for men, "HIV testing may increase knowledge and lead to reductions in sexual risk even when results are negative" [4].

A systematic review examining the efficacy of HCT in changing HIV-related risk behaviours in developing countries found that the odds of reporting increased number of sexual partners were lower among individuals receiving HCT compared to those who did not (unadjusted random effects pooled odds ratio (OR) = 0.69 (95% CI: 0.53-0.90, p=0.007). [5]. When stratified by serostatus, reductions in risky sexual behaviour remained significant only for those who tested HIV-positive. The study found an insignificant increase in the odds of condom use/ protected sex among participants who received HCT compared to those who did not, with an unadjusted random effects pooled OR of 1.39 (95% CI: 0.97-1.99, p=0.076). When stratified by HIV status, this effect became significant among HIV-positive participants (random effects pooled OR= 3.24, 95% CI: 2.29-4.58, p<0.001) [5].

Technical efficiency factors

Broadly speaking, the TE factors considered can be divided into eight main categories: (1) Provider initiated counselling and testing; (2) Community-based HCT approaches; (3) Targeting key populations and geographic locations; (4) Task shifting; (5) Multi-disease screening; (6) Pre-and post-test counselling interventions; (7) Mass media and (8) Other. Most of these factors increase the uptake of testing, often among a specific sub-population, while some also increase the effectiveness of counselling or reduce stigma. Yield, ie, the number of people who need to be tested to identify a single case of HIV infection, differs greatly between various TE factors.

Provider initiated counselling and testing

Provider initiated counselling and testing (PICT) involves the routine offer of counselling and testing to persons attending health facilities as a standard component of care. A number of studies have demonstrated this strategy's effectiveness in increasing uptake of HCT in different populations, including adults [6], STI patients [7, 8] and pregnant women attending antenatal clinics [9].

A study in South Africa found that PICT increased the uptake of HIV testing compared with referral to onsite voluntary counselling and testing (VCT) [10]. McNaughton and colleagues (2013) undertook a cluster-randomised trial of HCT interventions to determine which of three HCT models implemented in outpatient departments increased HIV testing [11]. The percentage of patients testing positive for each HCT model was as follows: i) Providers referring patients to HCT after outpatient department (OPD) consultation (11.9%, 95%CI 6.2, 17.7) ii) Providers offering testing to patients during OPD consultation (11.2%, 95%CI 7.3, 15.0) and iii) Counsellors offering testing to patients before OPD consultation

(10.2%, 95% CI 7.0, 13.3). The study found that all models resulted in high testing rates, but the highest percentage of patients receiving HIV testing occurred when counsellors offered testing to patients before OPD consultation [11].

Mutanga and colleagues (2012) found that institutional PICT was a feasible strategy for increasing access to paediatric HIV care and suggest that effects are especially pronounced in countries with generalised epidemics [12].

Community based HCT approaches

There is strong evidence that community-based approaches improve uptake of HCT. Menzies and colleagues (2009) conducted a retrospective cohort study of 84,323 individuals who received HCT at one of four Ugandan HCT programmes between June 2003 and September 2005: stand-alone HCT; hospital-based HCT; household-member HCT; and door-to-door HCT [13]. The study concluded that all testing strategies had relatively low per client costs. Hospital-based HCT most readily identified HIV-infected individuals eligible for treatment, whereas home-based strategies more efficiently reached populations with low rates of prior testing and HIV-infected people with higher CD4 cell counts [13].

A meta-analysis of community-based HCT approaches from 2013 included: (a) door-to-door testing, (b) mobile testing for the general population, (c) index testing, (d) mobile testing for men who have sex with men, (e) mobile testing for people who inject drugs, (f) mobile testing for female sex workers, (g) mobile testing for adolescents, (h) self-testing, (i) workplace HCT, (j) church-based HCT, and (k) school-based HCT. The authors concluded that community-based HCT achieves high rates of HCT uptake, reaches people with high CD4 counts, and links people to care. Further research is needed to further improve acceptability of community-based HCT for key populations [14].

Door-to-door testing/ home-based counselling and testing

Evidence indicates that door-to-door testing, or systematically offering HCT to homes in a catchment area, is effective at increasing uptake of HCT, reducing high risk behaviours and decreasing stigma [15]. A systematic review and meta-analysis of home-based testing (HBT) in sub-Saharan Africa concluded that HBT substantially increases awareness of HIV status in previously undiagnosed people, with over three-quarters of the studies in this review reporting 70% uptake [16]. Among studies reviewed, HIV prevalence ranged from 2.9% to 36.5%, and new HIV diagnosis following HBT ranged from 40% to 79% of those testing positive [16]. In South Africa, a cluster RCT found that door-to-door HCT increased uptake of couple counselling and testing and reduced risky sexual behaviour [17]. Home-based testing also appears to be acceptable in South Africa [18].

To assess the ability of HBT to link individuals to HIV care and treatment, Van Rooyen et al (2013) piloted home-based HCT with point-of-care (POC) CD4 count testing and follow-up lay counsellor visits [19]. This study found that this integrated intervention resulted in very high uptake of HIV testing with 91% of adults getting tested for HIV. Some 30% were HIV-infected, of which 36% were new diagnoses. The authors conclude that POC CD4 testing and lay counsellor follow-up achieved almost universal linkage to HIV care and ART initiation in line with South African guidelines [19].

Studies have concluded that home-based counselling and testing (HBCT) programmes are cost-effective [13] and should be considered for implementation, especially in areas where access to HCT is low [15]. However, it is important for these programmes to consider community context and to tailor messages and services to meet the needs of different groups [18].

HBCT has been demonstrated not only to increase uptake of HCT but also to reduce stigma. A study in Zambia found that being tested for HIV was associated with a reduction in stigma ($\beta = -0.57$, $p = 0.030$), and there was a trend towards HBCT having a larger impact on reducing stigma than other testing approaches ($\beta = -0.78$, $p = 0.080$ vs. $\beta = -0.37$, $p = 0.551$). This is possibly explained by a strong focus on counselling and the safe environment of the home [20].

Mobile testing for the general population

Substantial data support the use of mobile services to increase uptake of HCT. For example, Maheswaran and colleagues (2012), comparing users of home and mobile HCT services in KZN, found that a higher percentage of participants offered HCT agreed to be tested with mobile testing than with home testing (96.6% vs. 91.8%; $p < 0.001$) [21]. HIV prevalence among clients of the two services was comparable. Both services tested more clients per day than the local primary health care clinics, but had similar testing numbers to the local hospital. The authors concluded that “both modalities have an important role to play, especially in rural communities where cost of transport may be a deterrent” [21].

Other authors have also suggested that mobile services are particularly important in serving populations that may not access facility-based testing. For example, those who test at mobile services are more likely to be male, first-time testers, and in the earlier stages of diseases, and they also tend to consider themselves at low risk for HIV [22, 23]. Mobile testing is also a feasible method for reaching rural populations with HCT and has a high level of user acceptability in South Africa [24].

In general, men are more difficult than women to reach with testing services. Nglazi et al. (2012) compared facility based testing, mobile testing without incentives and incentivised mobile testing in hard-to-reach men. Incentivised mobile testing resulted in more men testing for the first time and more men testing with advanced disease compared to men testing at non-incentivised sites. [25]. Kranzer and colleagues (2012), comparing the yields of newly diagnosed cases of HIV infection a mobile HCT service and voluntary routine testing, found that mobile HCT, combined with incentives, doubled the yield of newly diagnosed HIV infections and increased the yield almost four-fold among individuals needing ART [26].

Two studies examined the cost of mobile testing services. Shrestha et al. 2008 report on the cost per person treated with mobile services in the United States [27], while Bassett and colleagues (2014) examined the cost-effectiveness of adding a mobile screening unit to current medical facility-based HIV testing in Cape Town, South Africa [28]. The South Africa study concluded that adding mobile HIV screening to current testing programmes could improve survival and be highly cost-effective in South Africa and other resource-limited settings [28].

Self-testing

HIV self-testing offers an approach to scaling up testing that could be high impact, low cost, confidential, and empowering for users [29]. Empirical research on self-testing is limited, resulting in a limited evidence base upon which to base policy recommendations.

Self-testing is receiving increasing attention as a means to help achieve universal HCT. A systematic review concluded that “both supervised and unsupervised testing strategies were highly acceptable, preferred, and more likely to result in partner self-testing” [30]. Dong and colleagues (2014) report that participants in a cross-sectional study in KZN, who tested themselves using a specially developed kit, revealed that, when packaged with illustrated instructions and a helpline number, the test was highly accurate when performed by laypersons [31]. Study participants were also able to accurately interpret the results and understand the next steps based on their results [31].

One important deterrent to testing utilization, widely reported in the public health literature, is that people often know the health care providers administering the test – a barrier not present in self-testing. A study in Malawi, examining the potential of supervised oral HIV self-testing, found that the approach was well accepted and accurate, although small errors were common, highlighting the need for supervisory support [32]. They concluded that this option has potential for high uptake at local community level if it can be supervised and safely linked to counselling and care [32].

Spielberg and colleagues (2003) undertook a survey with clients of a needle exchange, people attending an STI clinic, and sex venues for MSM in Seattle, United States. Aiming to identify strategies to overcome barriers to HIV testing, they found that promising options for encouraging higher risk individuals to learn their status included: expanding options for

rapid testing, urine testing, and home self-testing; providing alternatives to venipuncture; making pre- test counselling optional; and allowing telephone results disclosure [33].

Workplace HCT

As highlighted in South Africa's most recent national seroprevalence survey, the provision of HCT in non-traditional settings, such as workplace, is needed to increase HIV testing [34]. There are a number of examples of successful workplace HCT programmes in southern Africa [35]. For example, a programme at Heineken Breweries, Rwanda, showed high uptake of HCT in employees (72.9%), spouses (61.7%), children (6.5%), and retired staff (2.0%), with 2 595 eligible individuals tested and 109 cases of HIV infection identified [36]. In South Africa, a national workplace programme for a leading coal mining company found that that 7,203 of 18,353 employees tested between 2009 and 2013 (39.2%) had never been tested for HIV [37]. Rifkin et al (2014) report that there was a higher HIV positivity rate in first time testers vs repeat testers (13.6% vs. 19.8%, $p < 0.05$) for South Africa's national workplace programme [37]. The authors concluded that a decrease in the percentage of first time testers over time indicates that the programme was effective in reaching miners with repeat testing [37].

A review of workplace HIV interventions found that uptake of HCT increased to 51% when testing was provided at the workplace compared to receiving a voucher for HCT (RR=14.0 (95% CI 11.8 to 16.7)). The same study found that self-reported STIs decreased (RR = 0.10 (95% CI 0.01 to 0.73)) with workplace HCT but no change was found in HIV (RR=1.4 (95% CI 0.7 to 2.7)) and unprotected sex (RR=0.71 (0.48 to 1.06)) [38].

In a cluster RCT, Corbett and colleagues (2006) found that uptake of HCT among workers was higher for on-site workplace testing than for referral to offsite location (51.1% vs. 19.2%). The study concluded that workplace HCT offers the potential for high uptake when offered on-site and linked to basic HIV care [39].

School-based HCT

In Zimbabwe, Bandason et al. (2013) evaluated school-linked HIV counselling and testing (HCT) for pupils, finding that uptake of diagnostic HIV testing by pupils was low, with only 47 of 4 386 (1%) pupils undergoing HCT. [40]. Among children under 15 years who underwent HIV testing in this study, 6.8% were HIV-positive [40]. The main barrier to testing was caregiver fear of their children experiencing stigma and of unmasking their own HIV status should the child test HIV-positive [40].

In a systematic review and meta-analysis, Suthar and colleagues (2013) suggest that school-linked HCT shows promise for increasing testing in adolescents, although additional research is needed to support operationalization of this approach [14].

Targetting

Pregnant women

The sub-working group on HCT examined several strategies for pregnant women. PICT appeared to be an effective strategy to increase HCT among pregnant women. For example, Creek and colleagues (2007) found that after introduction of routine but non-compulsory testing in pregnant women in Botswana, the percentage of all HIV-infected women delivering in the regional hospital who knew their HIV status increased from 47% to 78% and the percentage receiving PMTCT interventions increased from 29% to 56% [41]. Chandisarewa et al (2008) reported a similar increase in Zimbabwe: of the 4 551 women presenting for antenatal care during the first six months of routine HIV testing, 4 547 (99.9%) were tested for HIV compared with 3,058 (65%) of 4700 women during the last 6 months of the opt-in testing ($p < 0.001$) [42]. HIV prevalence was lower in the opt-in group than in the opt-out group (16.8% vs 20.4%, $p < 0.001$).

Children

Taking account of the multiple factors that diminish knowledge of HIV status among children, the sub-working group

explored various testing strategies for children. The importance of timely knowledge of HIV status among HIV-exposed children is underscored by evidence demonstrating that early paediatric treatment dramatically reduces deaths from HIV in young children [43].

Rollins and colleagues (2009), assessing the acceptability and feasibility of universal HIV testing of 6-week-old infants attending immunisation clinics, found that the majority (90.4%) of mothers agreed to HIV testing of their infant and over half (56.8%) subsequently returned for results [44]. Most mothers interviewed said they were comfortable with testing of their infant at immunisation clinics and would recommend it to others, leading the authors to conclude that testing of all infants at immunisation clinics is acceptable and feasible as a means for early identification of HIV-infected infants and referral for ART [44].

Another strategy to target children is the provision of routine paediatric HIV testing in outpatient clinics. Evaluating the feasibility and acceptability of routine paediatric HIV testing in an urban, fee-for-service, outpatient clinic in Durban, Ramirez-Avila et al (2013) found that of 124 patients who underwent testing on physician referral over five months, 21 (17%, 95% CI: 11-25%) were HIV infected. Based on the results of this study, the authors argue that targeted and symptom-based testing referral identifies an equivalent number of HIV-infected children as routine HIV testing. It is a feasible and moderately acceptable strategy in an outpatient clinic in a high prevalence area [45].

Early childhood development (ECD) playcentres, which provide providing multiple health and social services for orphans and vulnerable children (OVC) under 5 years, may also serve as an entry point for HIV testing and for linkage to care and treatment, especially for HIV-exposed children who are missed by PMTCT programmes or those who are exposed to HIV during breastfeeding. As Patel et al (2012) explain, 58.8% of the 697 children attending 16 rural community-based, community-run ECD playcentres in Zimbabwe were tested for HIV, with 18% tested positive. This community-based playcentre model strengthens comprehensive care (improving emotional, cognitive and physical development) for OVC younger than 5 years and provides opportunities for caregivers to access HCT, care and treatment for children exposed to, affected by and infected with HIV in a secure and supportive environment [46].

Another strategy suggested by the sub-working group was routine counselling and offers of antibody testing to paediatric inpatients. In a study of routine HIV counselling and testing for hospitalised paediatric patients in Zambia, Kankasa and colleagues (2009) found that 13 239 (84.5%) of children <18 months of age/parent units received counselling and 11 571 (84%) of those counselled were tested with polymerase chain reaction (PCR) testing [47]. Overall, 3 373 (29.2%) of those tested were seropositive. The authors concluded that routine counselling and antibody testing of paediatric inpatients can identify large numbers of HIV-seropositive children in high prevalence settings [47].

The KidzAlive programme aims to find and test children with undiagnosed HIV and link these children to care and treatment programmes. One way that this is done is through the provision of age-appropriate, child-focused testing, care and support services in child-friendly spaces [48]. The KidzAlive model has been shown to: increase the willingness of primary caregivers to bring children for testing; increase health care provider confidence and skill in providing age-appropriate, child-centred counselling and testing; increase uptake of HCT among children 4-11 years; increase levels of disclosure in children; increase numbers of facilities with child-friendly spaces; increase adherence support for children; and establish a case for the effectiveness of mentorship in improving service delivery [48].

Couples

Couples counselling and testing is another strategy for delivering HCT. In a study in Rwanda, discordant couples watched an educational video, participated in a discussion, underwent testing and were encouraged to receive their results together. In the Rwanda study, Allen and colleagues (1992) found that "confidential HIV serotesting with counselling caused a large increase in condom use and was associated with a lower rate of new HIV infections" [49]. Conkling et al. (2010) assessed an intervention consisting of same-day individual HCT and weekend couples testing, finding that

couples testing was beneficial in terms of reducing loss to follow-up [50]. Among women attending a Nairobi antenatal clinic who were encouraged to return with partners for voluntary HCT and offered individual or couple post-test counselling, Farquhar et al. (2004) concluded that antenatal couple counselling may be a useful strategy to promote HIV prevention interventions [51].

One study described targeting male partners of pregnant women. In a South African RCT, the intervention group of pregnant women were provided with a written invitation to HCT for their partners while the control group attended pregnancy information sessions. The authors found that the written letters increased male participation in antenatal care and uptake of couples counselling and testing where community sensitisation was conducted and ART was available [52].

Key populations

The working group suggested targetting key populations including MSM, PWID and FSW.

With respect to MSM, Zou et al. (2013) found that one out of every four men that were recruited through instant messaging actually went for HIV testing, while the recruitment yields for online gay chat rooms, mobile phone contact, and email were 1:6, 1:10, and 1:140, respectively [53]. The authors concluded that outreach through instant messaging was a promising way to encourage MSM to test, especially for MSM who were younger, never tested for HIV, or who tested less often [53].

In a Kenya study of venue-based testing, approximately 98% of PWID and 97% of MSM agreed to HCT, providing evidence that populations with little access to services and whose behaviours are stigmatised and/or considered illegal in their countries may still be reached with needed HIV prevention services [54].

Also in Kenya, Luchters and colleagues (2008) explored the impact of peer-mediated interventions for FSWs on various outcomes, including awareness of HIV serostatus. Peer mediated interventions were associated with an increase in awareness of HIV status among FSWs [55].

Closed settings including prisons and detention centres

The sub-working group explored provision of HCT in closed settings such as among inmates, in detention centres and in prisons. Varghese and Peterman (2001) found that cost of testing among soon-to-be-released inmates in the United States differed by HIV status (US\$78.17 in those testing HIV positive vs. US\$24.63 in those testing HIV negative). The study concluded that compared to no HCT, offering HCT to 10 000 inmates detected 50 new or previously undiagnosed infections and averted four future cases of HIV at a cost of US\$125,000 to prison systems. The savings to society at large were estimated to be much greater: over US\$550 000 [56].

Geographic areas

As per government policy, farms, townships/ informal settlements and mines were highlighted as areas that require specific HCT interventions. However, no studies describing the results of targeting HCT in these areas were found.

Trucking routes were also suggested as important areas for provision of HCT. In a study from Nigeria, Aniebue and Aniebue (2011) found that over half (54.8%) of truck drivers in the study were willing to undergo HIV screening test if offered freely and that 43.7% had previously been screened [57].

Task shifting

One of the main ways to improve technical efficiency is to implement task shifting, whereby tasks are conducted by a lower level of staff than previously, as a way of compensating for shortages of more highly skilled staff. One study found that task shifting from physicians to nurses was effective in increasing access to paediatric HIV care while only marginally

increasing operational costs [58]. Another study examined the outcomes of task shifting from physicians to nurses on ART, finding that task shifting does not compromise patient outcomes in first 2 years of ART [59]; this study was not directly relevant to HCT.

Multi-disease screening

In low-resource settings, integrated disease prevention initiatives have been found to increase coverage, equity and efficiency in controlling high-burden infectious diseases. As part of an integrated campaign for HIV testing, safe water, and malaria control in Western Kenya, respondents were offered HCT, male condoms, insecticide-treated bednets, a water filter, or HIV-infected individuals cotrimoxazole prophylaxis and referral for ongoing care [60, 61]. Lugada and colleagues (2010) found that 96% of respondents took up the multi-disease preventive package. Of these, 99.7% were tested for HIV. Some 80% had never tested before [60]. The authors concluded that "Through integrated campaigns it is feasible to efficiently cover large proportions of eligible adults in rural underserved communities with multiple disease preventive services" [60]. Kahn and colleagues (2011) modelled the potential cost-effectiveness of this mass, rapidly implemented campaign and found that it appears economically attractive [61].

Pre-and post-test counselling interventions

Pre-test counselling interventions

In the United States, Calderon et al (2011) compared a youth-friendly, pre-test HIV video vs in-person counselling and found that youth who watched the video were 3.6 times more likely (OR:3.6, 95% CI: 1.8 –7.2) to get tested than those who had the counsellor intervention [62].

Post-test counselling interventions

In the United States, Calderon et al (2009) examined the impact of an educational, post-test educational video on HIV knowledge, finding that this intervention was as successful as post-test counselling in terms of instilling knowledge but was likely to be more cost-effective [63].

A number of studies have demonstrated the effectiveness of telephonic post-test counselling on ensuring clients received their results and the counselling itself [64–66]. For example, in a meta-analysis of the evidence regarding alternative HIV counselling and testing methods, Hutchinson and colleagues (2006) found that clients are substantially more likely to receive their HIV test results with telephonic testing compared with conventional HCT (RR, 1.38. 95% CI, 1.24–1.47) [65]. Another study found that telephonic post-test counselling was an effective method of increasing access for low-risk clients attending STI clinics and concluded that this strategy may be especially useful for those who are otherwise unlikely to obtain post-test counselling [66].

Mass media campaigns

A number of different mass media campaigns have aimed to increase condom use in South Africa. The National HIV Communication Survey reported that those exposed to 19 different communication programmes were 3% more likely to report testing in the past 12 months (AOR 1.03) [67]. An SBCC campaign was found to be responsible for an increase in discussing getting tested with a sex partner (AOR 1.1), while in turn those who had discussed testing were 3.63 times more likely to get tested in the past 12 months [68]. Respondents exposed to the same campaign were more likely to think that people in their community were getting tested for HIV (AOR 1.1), and those who thought that people in their community were likely to test were 1.28 times more likely to get tested in the past 12 months [68].

Another study found that those exposed to an SBCC campaign targeted at changing male norms and behaviour in South Africa were 8% more likely to report get tested for HIV [69]. The same study found that those exposed to this campaign were more likely to discuss getting tested (AOR: 1.07), and those who discussed HCT were 3.57 times more likely to have been tested in past 12 months (AOR 3.57) [69].

An evaluation of an SBCC campaign directed at South African youth found a direct impact on uptake of HCT in the past 12 months (AOR 1.04). This study found that those exposed to the campaign had high self-efficacy for testing i.e. felt able to get tested (AOR: 1.03), and those who had high self-efficacy for HCT were 1.27 times more likely to have been tested in past 12 months (AOR 1.27).

These studies were deemed more relevant to SBCC and were referred to the SBCC working group.

Other TE factors

Mobile technology for early infant diagnosis

A Zambian study found that mobile phone texting can overcome the logistical and distance barriers that can impede the early diagnosis of HIV infection in infants, particularly in rural area [70]. An automated SMS allowed the results of PCR testing of infant dried blood samples to be reported to the relevant point-of-care health facility or infant caregivers much faster than would have been possible using a courier to deliver the results on paper to the relevant health facility. In addition, the results delivered through SMS texting were highly accurate in comparison to the results recorded on paper [70].

Dried blood spots

In China, Su and colleagues (2014) suggest improvement in antibody testing strategies with dried blood spots (DBSs) for early infant diagnosis through analysis of anti-HIV seroconversion of infants. Using this method, the authors concluded that HIV infection can be determined as early as 3 months of age and excluded as early as 6 months of age [71].

Screening infants with rapid HIV tests before DNA-PCR

Menzies and colleagues explored the cost-effectiveness of incorporating initial screening with rapid HIV tests into the conventional testing algorithm to screen out HIV-uninfected infants, thereby reducing the need for costly virologic testing in Uganda [72]. The authors conclude that screening infants with rapid HIV tests before DNA-PCR is cost-effective in infants three months old or older. Incorporating rapid HIV tests into early infant testing programmes could improve cost-effectiveness and reduce programme costs [72].

Table 33: Summary of quality of the evidence base and grading for HIV testing and counselling

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Interventions						
Testing of general population	Adults	Multisite trial	Infections averted (Kenya)	1,104	[1]	1
			Infections averted (Tanzania)	895		
			Cost per infection averted (Kenya)	\$249		
			Cost per infection averted (Tanzania)	\$346		
Testing of general population	Adults	RCT	Reduction in unprotected sex with non-primary partners (men)	35% reduction with HCT vs 13% reduction with health information	[2]	1
			Reduction in unprotected sex with non-primary partners (women)	39% reduction with HCT vs 17% reduction with health information		
Testing of general population	Adults	HIV serologic surveillance rounds (Seros 4,5,6)	Reduction in the number of sexual partners in the last year (HIV negative)	aRR Seros 4-5: 1.42, 95% CI 1.07-1.88; aRR Seros 5-6: 1.68, 95% CI 1.25-2.26	[3]	1
Testing of general population	Men	Cross-sectional survey	Fewer sexual partners	IRR = 0.91, 95% CI = 0.84, 0.98)	[4]	1
			Fewer unprotected anal sex events	IRR = 0.81, 95% CI = 0.66, 1.00		
		Systematic review				

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
TE factors						
PICT						1
PICT	Adults	Testing registers linked to patient records from	Increase in HIV testing rates	4% in 2001 to 20% in 2006 (p<0.001)	[6]	
			Decrease in yield of first-time testers	47% in 2001 to 28% in 2006		
PICT	STI patients	Cross sectional study	Uptake of testing among those provided with education, information and offered HIV testing	43.5%	[7]	
PICT	STI patients	Cluster-controlled trial	% of new STI patients tested for HIV	56.4% intervention versus 42.6% control, p = 0.037	[8]	
PICT	Pregnant women	Systematic review	Pre vs post-intervention testing uptake	Pre: 5.5% to 78.7%; post: 9.9% to 65.6%	[9]	
			Linkage to ARVs for PMTCT	53.7% to 77.2%		
PICT	General outpatient clinic patients, 18–49 years	Pre-intervention/post-intervention	Increase in uptake of HIV testing	OR 2.85, 95% CI 1.71, 4.76	[10]	
PICT for children	Children	Retrospective case study	Uptake of testing	40.8% before introduction of PICT vs. 98.2% afterwards	[12]	

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Community based HCT approaches						1
Community based HCT relative to facility-based HCT	Various	Systematic review and meta-analysis	Increased uptake of HCT	RR 10.65, 95% CI 6.27-18.08),	[14]	
			Increased proportion of first time testers	RR 1.23, 95% CI 1.06-1.42		
			Increased proportion of participants with CD4 counts above 350 cells/microl	RR 1.42, 95% CI 1.16-1.74		
			Decreased positivity rate	RR 0.59, 95% CI 0.37-0.96		
Door-to-door	Adults	Serial cross-sectional studies	Increase in proportion ever tested	18.6% to 62% (p<0.001)	[15]	
			Increase in sharing HIV test result with a sexual partner	41% to 57% (p<0.001)		
			Decrease in proportion of persons who wanted infection status of a family member not to be revealed	68% to 57% (p<0.001)		
Door-to-door	-	Systematic review and meta-analysis	Pooled proportion of people who accepted HCT	83.3% (95% CI: 80.4%–86.1%)	[16]	
Door-to door	Adults and adolescents 14-17 years	Cluster randomised controlled trial	HIV testing	Results 69% in home based HCT arm vs 47% in control arm (prevalence ratio 1.54, 95% CI 1.32 - 1.81).	[17]	
Door-to-door	Adults	Cross-sectional survey	Uptake of HCT	75.27%	[18]	

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
HBCT and POC CD4 testing, lay counsellor follow-up	Household members 18+ years	Cross-sectional	HIV testing	≈91%	[19]	
			Linkage to care	≈90%		
Door-to door	-	Nested study within a pair-matched cluster-randomised trial	Reduction in stigma	7%	[20]	
Mobile testing for the general population						1
Mobile HIV screening	General population	Cross-sectional	HIV testing	Mobile testing vs home testing (96.6% vs. 91.8%;; p < 0.001)	[21]	
Mobile HCT vs clinic and hospital settings	Adults	Prospective observational cross-sectional study	HIV prevalence	5.9% (Mobile); 18.0% (Clinic); 23.3% (Hospital)	[22]	
Clinic-based, urban mobile, rural mobile, and stand-alone	Adults	Cross sectional	Highest proportion of male clients	52% (urban mobile)	[23]	
			Highest proportion of clients with no prior HCT	61% (rural mobile)		
			Highest proportion of clients reporting no perceived HIV risk	64% (rural mobile)		
Mobile HCT	Adults	Pilot studies	Younger participants	Median 22 years (rural compared to urban; p < 0.001)	[24]	
			Young people more likely to be first time testers	p = 0.01 in rural area, p < 0.001 in urban area		
			Men more likely to be first time testers than women	p = 0.01 in Vulindlela, p < 0.001 in Soweto		

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Incentivised mobile HCT	Adult men	Retrospective analysis of HCT data	HIV prevalence	16.6% (incentivised mobile testing); 5.5% (non-incentivised mobile); 10.2% (clinic-based services)	[25]	
			Percentage of first time testers	(60.1% (incentivised mobile testing) vs. 42.0% (non-incentivised mobile testing))		
			Yield of newly diagnosed HIV infections (incentivised mobile testing vs. non-incentivised mobile testing)	RR 2.33, 95% CI 2.03 – 2.57; p<0.001		
Mobile HIV screening		Cost Effectiveness of Preventing AIDS Complications International model	Five year survival	69% in medical facility compared to 73% in mobile unit	[28]	
Self testing						1
Self-testing	-	Systematic review	Acceptability	range: 74%–96%	[30]	
			Partner self-testing	range: 80%–97%		
Self-testing	Adults 18 + years	Cross-sectional	Obtained valid self-test result	99.1%	[73]	
Oral supervised self-testing	Adults 16+ years	Cross-sectional, self-testing	Accuracy	99.2%	[32]	
			Rated test “not hard at all to do”	98.5%		
			Made small procedural errors	10.0%		

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Workplace HCT						1
Workplace HIV programme	Employees and their dependents	-	HIV prevalence among those tested	3.8%	[35]	
			Annual average uptake of testing among eligible persons	15-32%		
Workplace HIV programme	Employees, spouses and children	Programme review	Number of HIV positive individuals identified	109	[36]	
Workplace HCT	Employees in mining sector	Programme review	Percentage of first time testers	38.2%	[37]	
			HIV positivity rate among first-time testers vs repeat testers	13.6% vs 10.8%, p<0.05		
Behavioural interventions in occupational settings	-	Systematic review	Increase in HCT uptake (workplace compared to voucher for HCT)	RR = 14.0, 95% CI 11.8-16.7	[38]	
			Decrease in self-reported STIs	RR = 0.10 (95% CI 0.01 to 0.73)		
Rapid HIV testing in the workplace	Employees	Cluster-randomised trial	Mean uptake of HCT	51.1% (onsite-testing) vs 19.2% (vouchers for clinic) RR 2.8, 95% 1.8 to 3.8 (onsite vs voucher)	[39]	
School-based HCT						1
School-linked HCT	Primary school children	HIV prevalence survey	Provision of specimens for anonymous testing	73%	[40]	
			HIV prevalence	2.7%, 95% CI: 2.2-3.1)		
			Uptake of diagnostic HIV testing	1%		

CHAPTER 4

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Targeting children - school linked HIV testing	Children	Systematic review and meta-analysis	Pooled estimate of HCT	62.1 (39.6–84.5)	[14]	
Targeting						1
<i>Pregnant women</i>						
Routine antenatal HIV testing	Pregnant women	Routine data collection	Percentage of all HIV-infected women delivering in the regional hospital who knew their HIV status	Increase to 78% from 47%	[41]	
Routine antenatal HIV testing	Pregnant women presenting for antenatal care	Routine data collection	Tested for HIV during routine testing vs. tested for HIV during opt-in testing	99.9% vs 65%	[42]	
<i>Children</i>						1
Universal HIV testing	6-week-old infants attending immunisation clinics	Observational cohort with intervention	Percentage mothers who agreed to HIV testing of their infants	90.4%	[44]	
			Percentage mothers who returned for their infants' results	56.8%		
			Percentage mothers and infants with HIV status confirmed/ reaffirmed by time infant was 3 months old	51.4%		
			Percentage samples positive for HIV DNA by PCR among all infants tested	9.2%		
Routine paediatric HIV testing	Paediatric patients	Baseline and follow-up	Increase in average number of HIV tests (routine vs baseline testing)	49 versus 25 tests/month, p = 0.001	[45]	

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Community-based early childhood development play centres	Orphans and vulnerable children	-	Uptake of testing	58.8%	[46]	
			Tested HIV positive and initiated on antibiotic prophylaxis	18%		
Routine offering of HIV testing	Hospitalised paediatric patient		Percentage received counselling	84.5%	[47]	
			Percentage tested of those counselled	87.4%		
			Percentage HIV positive of those tested	29.2%		
<i>Couples</i>						1
Couples counselling and testing	Discordant couples	Prospective study	Condom use	16% in control group vs 57% in intervention group	[49]	
Couples counselling and testing	Pregnant women	Prospective cohort study	Have a record in delivery i.e. less likely to be lost to follow-up	OR 1.28	[50]	
Antenatal couple counselling	Pregnant women and partners	-	Percentage HIV positive women who came with their partners for HCT	10% (these women were 3-fold more likely to return for nevirapine (P = 0.02) and to report administering nevirapine at delivery (P = 0.009)).	[51]	
			Nevirapine use among HIV infected women	88% of HIV-infected women who were couple counseled, 67% whose partners came but were not couple counseled, and 45% whose partners did not present for VCT (P for trend = 0.006)		

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Demand creation for couples HCT	-	-	Most frequently reported promotion strategy	80% mentioned influence agents	[74]	
Targeting men – HCT invitations for pregnancy partners	Male pregnancy partners	RCT	HIV testing	32% in intervention group vs 11% in the control arm (RR 2.82, 95% CI 2.14–3.72, P < 0.001)	[52]	
<i>Key populations</i>						
Internet outreach to encourage testing	MSM	-	Recruitment yield i.e. actually went for testing	1 out of 4 (instant messaging); 1:6 (online gay chat rooms); 1:10 (mobile phone contact); 1:140 (email)	[53]	
HCT	MSM, injecting drug users and general population	-	Uptake of HCT	98% of IDUs; 97% of MSM	[54]	
Peer-mediated interventions	Female sex workers	Pre-post study design	Awareness of own HIV status	Increased from 5.2% in 2000 to 40.2% in 2005	[55]	
<i>Closed settings</i>	Soon-to-be-released inmates in US prisons	Cost-effectiveness study	Marginal costs of HCT	\$78.17 (infected); \$24.63 (uninfected)	[56]	4a-KP
<i>Geographic areas</i>						
Targeting farms	-	-	-	-	-	3b
Targeting townships/ informal settlements	-	-	-	-	-	3b
Targeting mines	-	-	-	-	-	3b
Targeting trucking routes	Men	Cross sectional	Percentage awareness of HIV amongst the drivers	94.9%	[57]	3b

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Task shifting						1 & 6
Task shifting routine inpatient paediatric HIV testing	Paediatric inpatients	Retrospective observational study	Offered HIV test	19.9% in traditional model vs. 43.1% in task shifting model	[58]	
Task shifting to nurses for ART	ART-naive patients starting treatment	Cohort study	Consultant ratio was not significantly associated with virological success	OR 1.00, 95% CI: 0.59 to 1.72, P = 0.990	[59]	
Multi-disease screening						4c
Integrated Large-Scale HIV Counselling and Testing, Malaria, and Diarrhoea Prevention Campaign	15-49 year olds	Modelling	Uptake of HCT	99.7% (87% in the target 15-49 age group)	[60]	
Integrated HIV Testing, Malaria, and Diarrhoea Prevention Campaign	Adults	Modelling	Estimated deaths averted	16.3 deaths per 1,000 participants	[61]	
			Estimated DALYs averted	359 DALYs per 1,000 participants		
Pre-and post-test counselling interventions						
Pre-test counselling						1
Youth-friendly HIV video vs in-person counselling	Sexually active 15-21 year olds	2-armed, randomised controlled trial	Uptake of HCT	OR:3.6, 95% CI: 1.8 –7.2	[62]	
Post-test counselling						1
Rapid HIV post-test counselling video	Patients, 18 + years	2-armed, randomised trial	Mean knowledge scores	76.20% vs 69.3%; 90% CI for the difference, 2.8, 11.2	[63]	

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Telephone vs. face-to-face notification of HIV results	High-risk youth	Randomised study	Likelihood of receiving their results than those required to have face-to-face notification	OR: 2.301	[64]	
Telephone post-test counselling	-	Meta-analysis	Increase in likelihood of receiving HCT results	RR, 1.38. 95% CI, 1.24–1.47	[65]	
Telephone post-test counselling	Patients attending STI clinics	Clinical audit	Obtained post-test counselling	OR 1.75 (95% CI 1.50-2.06)	[66]	
POC CD4 testing and telephonic follow-up	Patients testing HIV positive at mobile HCT site	Pilot	Successful follow-up after 8 weeks of testing	62.7%	[75]	
			Completed referral visit	RR 1.25 (95% CI 1.00-1.57)		
Mass media programmes						4a - SBCC
National mass media programmes	General population	Cross sectional	Discussion of HCT	AOR 1.03	[76]	
National mass media programme	General population	Cross sectional, structural equation modelling	Discussion of HCT	AOR 1.1	[77,78]	
			Think people in their community are getting tested	AOR 1.1		
National mass media programme	Males	Cross sectional, structural equation modelling	Uptake of HCT in the past 12 months	AOR 1.08		
			Discussion of HCT	AOR: 1.07		
National mass media programme	Males	Cross sectional, structural equation modelling	Uptake of HCT in the past 12 months	AOR 1.04		
			Self-efficacy for HCT	AOR 1.03		

Intervention or TE factor	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Other TE factors						
Mobile technology for early infant diagnosis	Infants	Baseline evaluations	Decrease in mean turnaround time for result notification to a health facility	44.2 days pre-implementation to 26.7 days post-implementation	[70]	4c
Dried blood spot	Infants	Cross sectional survey	Differentiate infected from uninfected infants	Sensitivity as 100% and specificity >= 94.2%	[71]	3c
Screening infants with RHT before DNA-PCR	Infants	Retrospective cohort	Identification of HIV infected infants	Conventional algorithm - 94.3% (91.8%-94.7%) Modified algorithm using RHT - 87.8% (79.4%-90.5%)	[72]	3c

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4.1.8 OTHER BIOMEDICAL PREVENTION METHODS

Summary of evidence synthesis process including discussion during stakeholder consultation

To assess the evidence base for other biomedical prevention methods, a team of experts, chaired by Dr. Alfred Bere, was selected within the field of biomedical sciences, epidemiology, public health practice, and clinical research. The team gathered all the evidence taken into account, with the chair playing a key role in synthesizing the information in the required data template. The team met in person on one occasion, the stakeholder consultation, and thereafter conducted all meetings by phone and via email.

The list of four key interventions was derived by group consensus. Certain other biomedical prevention interventions, such as VMMC, were already represented by other sections of the investment case. Other interventions such as prevention of HIV transmission by medical staff including blood safety and injection safety were considered for inclusion but instead were dealt with as programme enablers within the investment case.

It should be noted that the discussions that shaped this section were based on data available as of the end of January 2015. More recent developments in this rapidly evolving field were not taken into account in this analysis, but may be considered in Phase 2 or 3.

One of the critical discussions in the early phase of the work revolved around the distinction between an intervention and a TE factor, as instructions provided to the group were not always clear in this regard. In particular, the working group found that the distinction between the definition of an intervention (i.e., the “what” of delivering this service) and the TE factor (i.e., the “how”) often invited considerable ambiguity. In an effort to overcome confusion regarding the distinction, the working group determined that an intervention should be classified as any act that will directly decrease mortality or prevent the transmission of HIV, while a TE factor indirectly contributes to the effectiveness of these interventions. For example, routine monitoring of the HIV status of PrEP users, which was first presented as an intervention, was eventually considered to be a TE factor because screening alone does not directly have an impact on aversion of HIV infections.

Following a literature search, the team reviewed approximately 140 documents, including at least 20 background articles and documents that presented the evidence of its impact, different modalities and technical approaches for each intervention. The working group also collected and reviewed documents concerning the cost of the interventions.

An initial document other biomedical prevention approaches was derived from the IC stakeholder consultation. The working group chair then elaborated on this initial document, expanding it to include interventions, TE factors, types and measures of impact, costing information and additional variables. This initial draft served as the foundational document from which data elements were extracted for the data template spreadsheet.

The process allowed working group participants to efficiently analyse evidence for the effectiveness of each intervention. Effectiveness is described as measures of association that demonstrate improved survival of HIV patients or reduced HIV or STI infection. Other impact measures, such as increased adherence to medication or increased number of protected sexual acts, have also been accounted for in this analysis.

The quality of the evidence was then graded per intervention based on review of the evidence collated by the working group. In the absence of direct measures of impact, interventions included in South African government policies were not excluded, but were downgraded if no other evidence of impact existed. Interventions with weak evidence were excluded from the initial round of modelling, either awaiting more evidence for phase 3, deemed an important question for future research or excluded altogether.

The location of the study was an important factor in the working group's assessment of the evidence for other biomedical interventions. Studies performed in South Africa were generally preferred over others, but exceptions were made for studies performed in countries of similar economic structure.

There was limited evidence that was deemed sufficient for modelling for most of the other biomedical prevention methods. Data was often not available that was local, or within the appropriate target groups, and data was not always derived from an RCT or other approach that lends itself to modelling methods.

After applying the evidence review criteria, syndromic management of STIs was excluded from the final IC, although the evidence is presented in the summary table in the anticipation that it might be included in later phases. The two remaining interventions, pre-exposure prophylaxis and microbicides, were as of January 2015 considered to have sufficient evidence for inclusion in the investment case.

Description of final list of interventions and TE factors

In this section, we describe each intervention in turn, together with the TE factors that could increase uptake or technical efficiency of the intervention and any information we could find on the cost of the intervention.

Pre-exposure prophylaxis

Pre-exposure prophylaxis (PrEP) involves administration of antiretroviral medicines to uninfected individuals prior to contact with HIV, with the aim of preventing HIV acquisition. The most frequently used form of PrEP is a combination of tenofovir and emtricitabine. PrEP is significantly less effective if not taken regularly, and requires users to see their health-care provider for follow-up every three months. Since PrEP is not 100% effective, it should always be combined with other methods of HIV prevention [1].

PrEP offers a method to prevent HIV transmission with a reasonable degree of certainty. PrEP greatly reduces the risk of acquiring HIV among those who are sexually active with HIV-positive partners or with partners of unknown HIV status. PrEP is of particular importance for HIV-negative people who are in danger of coming into contact with HIV regularly. This includes anyone in a sexual relationship with an HIV-positive partner. Populations targeted for PrEP include gay or bisexual men who are not in a mutually monogamous relationship with an HIV-negative partner, and have been sexually active without a condom or have been diagnosed with an STI within the past six months. Other potential PrEP populations include heterosexual men or women who are not in a mutually monogamous relationship with an HIV-negative partner, and who do not always use condoms when having sex with partners known to be at risk for HIV (e.g. injecting drug users or bisexual male partners of unknown HIV status). Other populations at risk of HIV acquisition, such as persons who have injected illicit drugs and shared equipment or been in a treatment program for injection drug use within the past six months, could also benefit from the HIV prevention effect of PrEP [1].

The evidence for the effectiveness of PrEP is strong. Six studies, three of them RCTs, have found a strong decrease in HIV incidence among people receiving PrEP, ranging between 44% and 75% [2]. Another study in Kenya and Uganda in 2012 compared effects of two different forms of PrEP with a placebo on prevention of HIV-transmission, finding that both were effective in preventing HIV acquisition, although PrEP containing both tenofovir and emtricitabine (75% reduction) was shown to be more effective than a form of PrEP using only tenofovir (67% reduction) [3].

Despite these promising results, two PrEP studies found no significant decrease in HIV incidence in their intervention groups. One of these, a study by van Damme et al. in 2012, evaluated a form of PrEP requiring a daily dose to be taken. According to the author, low adherence by test subjects is the most likely cause for the lack of effect of PrEP in this study [4].

The second study that failed to find a significant protective benefit from PrEP was performed by the Vaginal and Oral Interventions to Control the Epidemic (VOICE) in 2011. This study was discontinued due to demonstrated lack of efficacy for HIV protection, but this result only related to a new form of PrEP containing tenofovir but lacking emtricitabine. The more commonly found form of PrEP containing both tenofovir and emtricitabine was not reported to have shown a lack of efficacy [5].

TE factors

Prescription regimen

Evidence available as of January 2015 indicated that daily administration of PrEP was needed to offer protection from HIV [3]. However, evidence suggests that adherence to such a *prescription regimen* is low in the South African population [6]. Accordingly, several TE factors for PrEP aim to increase adherence among PrEP users.

Counselling: education about PrEP, adherence counseling

Educating PrEP users about the importance of adherence is a crucial step to increase the efficacy of the treatment. Haberer et al. found that counselling during treatment led to an increase in PrEP efficacy to 100%. Intensive counselling had the added benefit of reducing risk-taking behaviour and increasing condom use in the target demographic [7]. Education of health care workers to properly manage the decision-making process will lead to better guidance of PrEP users, thereby increasing the likelihood that users adhere to the regimen [1].

Preference for administering method

Adherence can also be increased by altering the method of administration to better suit the patient's needs and desires. For instance, a study by Minnis et al. in 2013 found that women in the United States prefer tablets over gel, while this distinction could not be found in African sites [6]. This preference for an administering method – or lack thereof – can influence adherence and could be taken into account when prescribing PrEP.

Clinical eligibility

Other efficiency factors are designed to prevent misuse of PrEP. For instance, if a patient is found to have renal damage, PrEP should not be administered, as the intervention may possibly aggravate the condition. By testing for *clinical eligibility* such dangers can be avoided. Additionally, as resistance to the drugs included in PrEP regimens is an important public health concern, PrEP should not be administered to those already infected with HIV. *Routine monitoring* of the HIV status of PrEP users improves the chance of diagnosing an HIV infection early, allowing physicians to terminate PrEP and start a more suitable treatment regimen [1].

Targeting risk groups

Specific targeting of PrEP to a certain risk group or geographical location can be used to increase the efficiency of the intervention [8].

Costs

PrEP in general is estimated to cost US\$12 500 to US\$20 000 per averted infection. Specific costs depend on the level of ART coverage in a particular setting and the baseline incidence [9].

Pretorius et al. [9] assumed intervention costs for PrEP, including serum creatinine testing and HIV counselling and testing, of US\$150 per person per year in South Africa. A different study by Long et al. assumed annual costs per person to be US \$100 in South Africa, and translated HIV infections averted into QALYs (quality-adjusted life years) which is a measure of how many years of healthy living can be gained by an intervention. Long et al. found that PrEP would cost \$9,000 per QALY gained [10].

Microbicides

Microbicides are specially formulated products that are applied topically (vaginally or rectally) to reduce their risk of acquiring HIV and possibly other STIs. They are a type of PrEP and can take the form of a cream, gel, ring or film, and are designed to be administered before each possible contact with HIV or to deliver the agent over a longer period of time, as in the case with intravaginal rings [11]. Unlike condoms, microbicides are solely under the control of those using them, and do not require the cooperation or even knowledge of the partner. Such a method to prevent transmission of HIV could further empower women to influence the result of their sexual encounters [12].

Vaginal microbicides are still under development, but results at the time of the evidence review (before February 2015) were promising. One of the most promising of these was a study on a tenofovir-containing vaginal microbicide, performed in South Africa by the Centre for the AIDS Programme of Research in South Africa (CAPRISA) in 2010. In this CAPRISA 004 trial, an overall decrease in HIV incidence of 39% was found, and a 54% decrease was found in women who consistently use microbicides [13].

Another study (HPTN 035), evaluating the safety and effectiveness of two microbicide gels (BufferGel and 0.5% PRO2000), was a phase II/IIb, randomized, placebo-controlled, double-blinded study. The 0.5% PRO 2000 gel showed a 30% reduction in HIV infections, but the results were not statistically significant [14]. The authors of this study note that most hope can be found in the topical use of ARV agents, specifically tenofovir gel [14].

A tenofovir-containing form of microbicide has been considered the best option available because tenofovir has a long tissue half-life, meaning that the drug will remain active for prolonged periods after application [15]. However, in February 2015, results of the FACTS 001 trial found no reduction in HIV incidence among women assigned to the study arm using tenofovir gel. Sub-optimal adherence was believed responsible for the disappointing findings.

A review by Shattock et al. discussing recent and future developments for microbicides states that a number of phase III trials of microbicides are currently underway. Researchers are optimistic that the efficacy of microbicides can be increased further in the future, thereby making it possible to introduce them as part of a comprehensive, multicomponent prevention strategy [11].

TE factors

Acceptance and appropriate use

As the CAPRISA and FACTS 001 trials indicate, increasing adherence is essential to the effectiveness of microbicides. Most TE factors focus on this challenge. To maximise adherence, the *acceptance and appropriate use* of the medicine by the patient is crucial. Bentley et al. found in a four-country phased clinical trial in Malawi, Zimbabwe, India, and Thailand that the acceptability of a vaginal microbicide was high, with a 73% approval rate in all sites [16]. Participants reported minor side effects, but none could be linked to the use of the microbicide gel [16]. Women reported a willingness to use this product if it was proven to be effective and if they perceived they were at risk of contracting an STI. However, both men and women suggested that keeping microbicide use secret from one's partner could undermine trust within the relationship.

Acceptability and preference differ geographically. For example, while most women in the United States preferred tablets (72%), African women were evenly split between gel (42%) and tablets (40%) [6]. Geographical and cultural differences should be considered in intervention strategies.

Monitor adherence and safety

Because the overriding importance of adherence, it is logical to *monitor adherence and safety* in patients. An acceptability and safety study of a cervical barrier and gel delivery system in Zimbabwe concluded that most women were very

comfortable with using microbicides continuously (86.3%) and inserting it before sexual contact (92.8%) [17]. No serious adverse effects were found in this study, with 57 of 90 participants reporting events that were classified as mild or moderate.

Educate users of microbicides and their partners

A third method to increase adherence is to educate users of microbicides and their partners. This could be done by developing materials for education and counselling of users and their partners, or by creating informative and understandable instructions to go along with the medicines.

Costs

The costs for microbicides specifically were estimated based on the CAPRISA 004 trial in a study by Williams et al [22]. In this South African trial researchers calculated that the cost per infection averted is US\$1 701 for 90% coverage (coverage is defined as the proportion of all sexual encounters that are protected by the use of the gel). For 25% coverage, unit costs were US\$2 392. The cost per DALY averted was US\$74 (90% coverage) and US\$104 (25% coverage).

In another study it was found that a tenofovir-based vaginal microbicide was highly cost-effective and bordered on cost saving. Decreasing the costs of the product and programme by 50% would further increase the cost savings [18].

Table 34: Summary of quality of the evidence base and grading for other biomedical prevention interventions

Intervention or TE factor	Target population	Type of evidence	Metric	Value	Source	Grading
Pre-exposure prophylaxis (PrEP)						
Counseling: education about PrEP, adherence counseling	KP; Discordant couples;	Randomized clinical trial	Risk reduction, adherence	92%	[19]	1
	Discordant couples	Clinical Trial	Adherence to PrEP	83.7-100%	[18]	
Clinical eligibility: HIV Testing, renal function, Hep B individual education and counseling	KP; Discordant couples;	Southern African guidelines	Clinical eligibility for PrEP, guidelines for PrEP for MSM		[20]	1
Prescription regimen: daily dosing, ≤90 day supply (renewable only after HIV testing confirms that patient remains HIV-uninfected)	KP; Discordant couples;	Randomized clinical trial	PrEP among at risk groups, PrEP efficacy reduction in HIV incidence reduction in intervention compared to control arm	44%	[19]	1

Intervention or TE factor	Target population	Type of evidence	Metric	Value	Source	Grading
	heterosexual men and women	Randomized clinical trial	PrEP efficacy in HIV incidence	67% (TDF); 75% (TDF/FTC)	[3]	
Educating health workers on PrEP	KP; Discordant couples;	CDC Guidelines on PrEP 2014	Increase in uptake of PrEP			1
Target risk groups	Heterosexual women and men, Sex workers, pregnant women, adolescents	Randomized controlled trials	PrEP and HIV Prevention in high risk groups	RR 0.51	[8]	1
Geographic target: High Transmission Areas (HTA)	KP; Discordant couples;					1
Support services	KP; Discordant couples;	Randomized cross-over trial	Testing for differences in adherence, evaluation of product acceptability	Most women in the U.S. (72 %) favoured tablets over gel; while preferences varied at the African sites (42 % preferred gel and 40 % 1 tablets).	[6]	1
Drug resistance survey	KP; Discordant couples	MModel	drug resistance	9.2 % over 10 years	[21]	1
Microbicides (vaginal/ rectal gels, vaginal rings)						
				PrEP can avert 30% of new infections in targeted age groups of women in highest risk of infection.	[11]	
Acceptability and appropriate Use	HIV- women	A double-blind, randomized controlled trial	% reduction in incidence	39%	[13]	1
Monitoring adherence	HIV- women					1
Safety monitoring	HIV- women	A double-blind, randomized controlled trial	Monitoring adherence	CAPRISA 004 showed 39% effectiveness, but could be as high as 54% with higher adherence.	[13]	1

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4.1.9 TUBERCULOSIS

Summary of evidence synthesis process including discussion during stakeholder consultation

The TB working group of the investment case was established in 2014 under the joint chairmanship of the Drs Lindiwe Mvusi (NDOH) and Alasdair Reid (UNAIDS). Once appointed the two co-chairs drove TB investment case process described in this chapter.

The co-chairs of the TB working group compiled an initial list of interventions, critical programme and social enablers as well as technical efficiency factors based on current TB control activities in South Africa. A sub-group of the TB working group met on the 24th July 2014 and expanded on the initial list to come up with a more comprehensive list of interventions containing 37 interventions, critical enablers and technical efficiency factors for presentation and discussion at the stakeholder consultation workshop.

The co-chairs also compiled an initial list of stakeholders and individuals working on different aspects of TB control in the country, who could be invited to take part in a stakeholder consultation. The group who attended the 24th July 2014 meeting was asked to identify additional people who could be invited for the stakeholder consultation workshop. In total 47 individuals representing a variety institutions and organisations were invited; 19 individuals attended the two day TB stakeholder consultation workshop.

During the stakeholder consultation process, participants discussed the list of interventions, critical enablers and technical efficiency factors and any evidence for efficacy, impact or cost they had. The participants also suggested or provided references to literature with the evidence on the efficacy, impact or cost of interventions, social or program enablers and technical efficiency factors in the list. Preference was given from evidence from South Africa followed by that from Sub-Saharan Africa and the rest of the world. Participants were also welcome to suggest additional interventions if there were not included in the original list of interventions and were invited to send the corresponding evidence for them. In total, more than different interventions, technical efficiency factors and social or programmes enablers were discussed by stakeholders during the consultation process. A list of interventions, technical efficiency factors and social or programmes enablers for which there was no evidence available was also compiled in order to identify areas where gaps existed and further research was needed.

Initial synthesis, review and grading of evidence.

Once the evidence (research articles, reviews, articles, abstracts, posters, presentations and unpublished reports) was received from stakeholders, it was reviewed by the TB sub-working group resource persons and then summarised in an Excel template. The Excel template allowed the evidence received to be summarised according to whether the intervention had any impact on TB incidence, mortality and what the cost effectiveness of the intervention per case prevented or per disability life years saved. Summarising the evidence in this Excel template also allowed the evidence to be graded using the set grading criteria. Also available for review were EVISAT systematic reviews and the Joint HIV, TB and PMTCT review report. After this review and synthesis process there was a final list of 116 interventions for which there was some evidence which could be graded.

Review of final list of interventions

A series of meetings were conducted to review the final list of interventions which were sent to the modellers to include in the model. The first meeting the lists of interventions were presented to the TB working group chairs and the NDOH TB programme managers. In the second meeting the list of interventions were presented to the TB investment case task team. In both instances feedback was received and taken into account in finalising the list of interventions sent to the modellers. In compiling the final list of interventions the TB resource persons took into account the following:

- Availability of good quality evidence for the intervention
- Interventions which were already national policy and were included in national guidelines or other policy documents
- The capacity of the model to evaluate the intervention. This meant that some interventions could not be included on the list of interventions as the model could not evaluate them directly.

Description of final list of interventions, TE factors or enablers

Included interventions

Minister Motsoaledi announced the 90-90-90 TB targets scenario at the World Lung Conference in Barcelona, Spain in November 2014.

1. In line with the evidence of increased risk for certain population groups in South Africa, 90% of high risk and vulnerable groups should be screened for TB.
2. 90% of persons with active TB need to be diagnosed and initiated on effective treatment, before TB transmission, morbidity and mortality.
3. Loss to treatment needs to be reduced and more effective treatment for RR TB introduced so that 90% of TB cases have successful outcomes.

Although prevention of TB is not explicit in the TB 90-90-90 strategy, it is implicit and was included in the modelled interventions. Lifelong IPT for persons on ART with confirmed latent TB infection was assumed to result in a 35% reduction in risk of active TB. ART was assumed to reduce the risk of TB disease between 30% - 65% depending on the period of time on ART and to reduce the risk of TB mortality by 50% - 70%. BCG vaccine was assumed to have 40% effectiveness in reducing primary TB, progression to TB and mortality.

Excluded interventions, technical efficiency factors, and critical enablers

Although the scenarios, interventions and TE factors included in Phase 1 of the TB Investment Case were limited, the review of the evidence and available tools for addressing TB was extensive. This work will continue to inform the future phases of the TB Investment Case as well as implementation within the SA NTP.

Targeting high-risk groups

Targeting high-risk groups with TB interventions was repeatedly identified as important to improving the allocative efficiency and overall effectiveness of the South African National TB Programme (SA NTP); however, the available models do not yet include TB risk groups. As a result, the impact or costs of interventions targeted at these groups could not be estimated yet. Table 35 summarises the excluded targeted interventions.

Table 35: Excluded interventions targeted at groups at high risk for TB disease

<p>Decrease of non-access to TB screening and diagnosis for high risk groups:</p> <ul style="list-style-type: none"> • Informal settlements and peri-mining communities • Correctional facilities • Proportion low quality TB services for selected groups upgraded • Screening of all PHC attendees • Screening at rehabilitation facilities, homes for the elderly • Screening within schools • Screening of ANC, MNCH
<p>High quality TB diagnosis:</p> <ul style="list-style-type: none"> • Improved diagnosis of paediatric TB
<p>Active case finding in high risk populations:</p> <ul style="list-style-type: none"> • Contacts of TB • Inmates and correctional services officers • Miners and mine workers • Health care workers • Peri-mining communities
<p>Preventive therapy for HIV-negative, high risk populations:</p> <ul style="list-style-type: none"> • Correctional services • Child contacts • Health care workers • People with silicosis
<p>Infection control in high risk areas:</p> <ul style="list-style-type: none"> • Public buildings, taxis • Household infection • Workplaces • Mines • Correctional services • Healthcare settings

Technical efficiency (TE) factors

TE factors were excluded from the TB model because the current model did not address the 'how' of reaching the targets. Instead, one basic description of the intervention was used, for example, the cost of MDR-TB treatment in 2021 is based on a regimen including bedaquiline and linezolid. Table 36 summarises the TE factors that had been suggested during the stakeholder workshop but had to be excluded because of this. For Phase 2 or 3, inclusion and comparison of alternative TE factors will be essential to refining the guidance provided to the SA NTP in terms of implementation. This has been noted as especially important for the implementation of the mass TB screening campaign.

Table 36: Excluded TE factors for TB services

<p>Intensified case finding in PHC:</p> <ul style="list-style-type: none"> • Different symptom screening algorithms • Targeted at pregnant women, children <5, diabetics • Once per annum or once per visit • Recording and reporting systems • Lay worker or nurses • Cough triage • Screening of all persons at clinics (e.g. accompanying persons) • Screening at all hospitals
<p>Improve high quality TB services (post diagnosis):</p> <ul style="list-style-type: none"> • Centralised (inpatient/specialist unit) • Decentralised DR TB to the PHC or community level • Bedaquiline, delamanid, pretomanid and other new drugs • New treatment regimens for drug-sensitive TB • Incentives to initiate TB treatment • Incentives to remain on TB treatment • Adherence support (basic TB, RR TB) • Social grants, food parcels, transport vouchers
<p>High quality TB diagnosis:</p> <ul style="list-style-type: none"> • EPTB diagnosis with Xpert • EPTB diagnosis with LAM • Increased screening, awareness for EPTB • Increased sample collection for paed • Nebulizers at PHC for paed • Diagnostic algorithm for Xpert negative
<p>Active case finding:</p> <ul style="list-style-type: none"> • Door-to-door • Community activation events • Mobile Xpert MTB/RIF • Mobile x-rays • Culture, Xpert MTB/RIF, or ultra Xpert as first line diagnostic
<p>Preventative therapy:</p> <ul style="list-style-type: none"> • TST positive or all eligible • Other tests for latent TB infection • HIV+ on ART or all HIV+ • Health care workers, regardless HIV status • Miners, regardless HIV status or silicosis status • Once-a-month dosing • Rifampicin regimens • PT for DR TB

Interventions needing further definition

For some known risk factors of TB, the intervention has not been defined sufficiently in terms of its effect on the population. Table 37 summarises those interventions that were excluded because evidence of association or risk could not be translated into model parameters.

Table 37: TB interventions excluded and needing further definition

Intervention	Reason for exclusion
Infection control	No evidence of population-level effects found. Evidence supported that infection control measures could be implemented. There was also evidence supporting that non-sociocomal transmission of TB takes places, especially within DR TB hospitals. However, the models required a measurement of effect and population in need.
TB vaccine	There was not sufficient evidence that the BCG vaccine available would have an effect if persons had booster doses or repeated vaccination. No other effective TB vaccine is currently available.
Reduction of indoor air pollution	No evidence of population-level effects found. Evidence supporting that indoor air pollution increases the risk of lung disease, including TB was found. However, interventions to reduce indoor air pollution were poorly defined and researched; only one example of switching cooking fuel for South African households could be found for this setting. However, the models required a measurement of effect of an intervention and population in need.
Nutritional support to prevent TB	While persons with TB disease often have lower body mass index (BMI) than the general population, systematic reviews had not found evidence of nutritional supplementation to prevent TB disease. That being said, if a person has TB and is malnourished, treatment guidelines indicate nutritional supplementation is appropriate.

HIV and TB interventions

Most combined HIV/TB interventions are captured either within the HIV Investment Case or the TB Investment Case; care was taken to exclude it from the respective other Investment Case to avoid duplication of costs or impact (see Table 38).

Table 38: TB and HIV interventions included components in HIV and TB models

<p>Within the HIV model:</p> <ul style="list-style-type: none"> • ART for TB patients • Co-trimoxazole prophylaxis (CPT) • HCT for TB cases (costs of HCT) • TB symptom screening (ICF) at HCT, regardless of HIV result (costs of symptom screening) • TB symptom screening during HIV care (on ART) (costs of symptom screening)
<p>Within the TB model:</p> <ul style="list-style-type: none"> • IPT for HIV positives (drug costs only, costs of clinic visit ART clinic visit cost) • TB symptom screening (ICF) at HCT, regardless of HIV result (costs of diagnostic tests for symptomatics) • TB symptom screening during HIV care (on ART) (costs of diagnostic tests for symptomatics)

Critical enablers

Critical enablers were excluded because they often affect more than one disease and could not be modelled within the TB-specific models (see Table 39).

Table 39: Identified but excluded TB critical enablers

<p>Programme communication:</p> <ul style="list-style-type: none"> • Kick TB/HIV activations in high burden settings
<p>Management & incentives:</p> <ul style="list-style-type: none"> • Service providers
<p>Research & innovation:</p> <ul style="list-style-type: none"> • TB surveillance • National prevalence survey
<p>Monitoring:</p> <ul style="list-style-type: none"> • Recording, reporting and analysis of programme data • Provincial, district & facility supervision visits • Surveillance in health care workers, prisoners & prison officials
<p>Laws, policies & practices:</p> <ul style="list-style-type: none"> • Smoking cessation • Alcohol control • Accelerated justice & alternative sentencing to reduce overcrowding in correctional services • Adequate infection control in the design of public buildings
<p>Community mobilization:</p> <ul style="list-style-type: none"> • Better case finding • Earlier presentation with possible TB symptoms • Adherence support for friends and family

4.2 CRITICAL ENABLERS AND DEVELOPMENT SYNERGIES

4.2.1 SOCIAL ENABLERS AND DEVELOPMENT SYNERGIES

Summary of evidence synthesis process

The process of deciding which social enablers and developmental synergies to review and include in the investment case commenced with the stakeholders workshop on the 30 / 31st July 2014. The co-chairs of this group, Lebo Ramafoko (Soul City) and Saul Johnson (Anansi Health Consulting) were only appointed in the days before the workshop, and did not have time to meet in person. Nonetheless invitations were sent out to various stakeholders who were thought to be able to contribute to this area, and a table with the various potential interventions and TE factors was circulated to this group before the workshop, with instructions to come prepared with supporting documents.

The group met over the 2 days of the workshop. About 15 people attended, although the number fluctuated greatly over the 2 days. No-one arrived with documents. The group went through the social enablers and development synergies listed in the Investment Framework guidance document from UNAIDS, and for each one discussed possible evidence relevant to South Africa. This was filled into a table while the group was in session. In many cases participants mentioned programmes being run, but were unsure whether evidence of effectiveness existed, or where this evidence could be sourced. There was a sense that the number of factors and TE factors was quite overwhelming, while in many cases evidence seemed to be scanty.

At the end of the workshop the conclusion made was that consultant support would be valuable, to source evidence for the interventions discussed, and to document and summarise this evidence.

After the workshop, a number of decisions were made during the initial scan of the literature provided by the working group:

- Instead of having community mobilisation as a separate intervention under social enablers, community mobilisation interventions were included in different sections depending on the content they addressed. For example, the SASA! Intervention, a community mobilisation intervention to prevent violence and reduce HIV-risk behaviours [1], was included under the gender-based violence (GBV) section.
- Mass media was initially listed as a stand-alone intention under social enablers. It was agreed that mass media was one component of social and behaviour change communication and fitted better within this section.
- Social protection and poverty reduction were combined into one section.
- No relevant data on legal reform was found so this enabler was excluded from the review.

We reviewed all published and unpublished literature and prepared a draft summary describing the social enablers, development synergies and effectiveness data. Content experts were asked to comment on the draft and to suggest additional helpful literature to be included in the overall analysis. Table 40 below shows the experts who provided feedback by intervention.

Table 40: Experts consulted for social enablers and development synergies

Social enabler or development synergy	Experts who provided feedback
Political commitment and advocacy	N/ A
Laws, policies and practices	Nkhensani Mathabathe
Stigma reduction	Rentia Agenbag Nkhensani Mathabathe
Social protection	Lucie Cluver Andrew Gibbs Audrey Pettifor Jason Wolfe
Education	Lucie Cluver Saadhna Panday Audrey Pettifor
Alcohol	Charles Parry
Gender-based violence	Andrew Gibbs Nkhensani Mathabathe Gesine Meyer-Rath Samantha Willan

The next section summarises the decisions taken with regards to whether the data spoke to the enabler in the form that had been suggested, whether the evidence was from South Africa, and whether it was of high quality using the Investment Case data template and grading instructions.

Description of final list of enablers

Some of the interventions described in this section may differ substantially from each other in how the pathways through which change happens are understood. However, the purpose of this section is to describe the social enablers and development synergies proposed by the working group and which members thought should be included.

Political commitment and advocacy

Literature quantifying the impact of political commitment and advocacy on the HIV epidemic is scarce but case studies suggest that political commitment and advocacy may impact on the HIV epidemic. This impact tends to be indirect through creating an enabling environment for social and behaviour change and/ or uptake of services.

One of the best examples of the importance of political support and community and religious engagement in the HIV response is from Uganda [2]. It is estimated that HIV prevalence in Uganda was about 15% in 1991. This had fallen to 5% ten years later [3]. It has been suggested that Uganda's decline in HIV prevalence was not due to a 'natural die-off syndrome', but rather to a number of behavioural changes, especially a reduction in multiple sexual partners [2, 3]. Two key factors created an enabling and supportive environment. These were: i) high level political support with multi-sectoral response and ii) early and active involvement of the religious sector in the HIV response [2, 3].

There are a number of examples of effective advocacy campaigns that helped reshape the HIV-response from South Africa. For example:

- The Treatment Action Campaign mobilised members at a grassroots level and successfully advocated for the provision of antiretroviral drugs (ARVs) [4].
- Soul City took an advocacy approach, the goal of which was to secure the speedy and effective implementation of the Domestic Violence Act (DVA) which although passed into Law, was not being implemented due to a range of factors including lack of political will and barriers related to the lack of police training. Independent evaluation shows that the fast tracking of the implementation process was a direct result of the advocacy campaign [5].

Laws, policies and practices

There does not appear to be much literature which quantifies the impact of laws, policies and practices on various HIV related outcomes, although globally, there is clear consensus of the negative impact of the criminalisation of behaviour and unsupportive legal environments for the realisation of human rights.

Laws pertaining to sex work have been examined. One study modelled the impact of decriminalisation on new HIV infections. Shannon et al. (2015) estimated that decriminalising sex work could prevent between 33-46% of global HIV infections in sex workers and their clients in the next ten years [6]. Decker and colleagues (2014) reviewed evidence from more than 800 studies and reports on the burden and HIV implications of human rights violations against sex workers worldwide. The study shows that these violations directly and indirectly increase HIV susceptibility, and undermine effective HIV-prevention and intervention efforts [7].

Gruskin et al (2013) evaluated the impact of legal empowerment programmes on health and human rights in Kenya. This study determined that trained clients appeared to have greater awareness of how and where to access legal services to safeguard their rights. Clients also developed greater access to legal and non-legal resources and reported feeling more empowered [8].

Stigma reduction

Stigma is considered a barrier to effective HIV prevention and treatment programmes and stigma reduction remains an important component of the HIV response. A review of HIV and stigma in South Africa concluded that stigma can affect many different components of the HIV response including condom use, HIV counselling and testing (HCT), antiretroviral therapy (ART) and prevention of mother-to-child transmission of HIV (PMTCT) [9]. In this section, the impact of stigma on different components of the HIV response is summarised.

Stigma can result in risky sexual behaviour. For example, in South Africa, Simbayi et al. (2007) found that people who live with HIV (PLHIV) who experienced stigma or discrimination were less likely to disclose their HIV status to their sexual partner. Those who had not disclosed were more likely to have unprotected vaginal intercourse with concordant partners (odds ratio, OR: 4.7; 95% confidence interval, CI, 3.3 to 6.5, $p < 0.01$) [10]. Skinner and Mfecane (2012) state that “many youth in South Africa are scared to use condoms due to the felt implications” [9].

Literature also reveals the relationship between stigma and lack of testing. In Botswana, a survey of patients receiving ART found that 40% had delayed getting tested for HIV, mostly due to stigma [11]. Health care workers interviewed in South Africa cited stigma as the most important reason why people in their communities do not get tested [12]. Skinner and Mfecane (2012) report that stigma results in delayed diagnosis and therefore also delayed entry into care and treatment [9]. A systematic review and meta-synthesis found that worldwide, HIV-related stigma also compromised patients' adherence to ARVs [13].

Testing and treatment appears to be accompanied by particular stigma among pregnant women. Bond et al (2002) report that in Zambia, stigma is one of the main reasons women do not want to test for HIV [14]. In South Africa, Varga et al (2005) found that pregnant women may avoid participating in PMTCT programmes due to fear of stigma, discrimination, and violence, particularly from partners when disclosing their HIV status [15].

A number of HIV vaccine acceptability studies revealed fear of vaccine induced HIV infection and concerns about being stigmatised based on receiving the vaccine [16-19]. Although these studies are from outside of southern Africa, the findings are still worth consideration. Little literature on stigma in relation to other biomedical interventions was found.

As is evident from the summary above, the majority of the literature on stigma describes the nature of the problem rather than the effectiveness of interventions which address stigma. However, there is evidence to from South Africa and Uganda to suggest that support groups for PLHIV have been effective in tackling stigma [20, 21].

Description of final list of development synergies

Social protection

Social protection is a wide term comprising a number of different components suggested by the working group and including poverty reduction. Cash payments to improve health outcomes have been used for many years, however, their use for HIV prevention is new and the impact not yet well understood [22]. In this section, the impact of various social protection interventions including, among others, cash transfers, "cash plus care" interventions and village loan and saving schemes on various outcomes (ideational factors - which encompass cognitive, emotional, and social determinants of behaviour -, risky sexual behaviour, biological outcomes, GBV, uptake of services, poverty and nutrition) is described.

Various studies have reported on the association to social protection interventions and ideational factors in relation to HIV. A programme for girls in Uganda which aimed to enable girls to establish small-scale enterprises and was combined with social empowerment components resulted in an increase in both HIV and pregnancy knowledge, as well as an increase in self-reported condom use and a near elimination of experiences of sexual violence ($p < 0.01$) [23]. Dunbar et al (2014) found that exposure to the SHAZ! project, which combined vocational training and social empowerment also resulted in an increase in HIV knowledge, a reduction in GBV and a reduction in transactional sex among adolescent female orphans in Zimbabwe [24]. Other studies from Uganda show that integrated interventions were associated with improved HIV prevention attitudes [25] and with intentions to engage in safer sexual behaviour [26].

The majority of cash transfer studies – where cash is transferred to a carer to improve the child's well-being - have been conducted with adolescents in developing countries and payments are focused on addressing structural risk factors such as poverty. Most have seen promising reductions in sexual behaviour [22]. In Kenya, Handa et al. (2014) found that receiving cash transfers was associated with a 31% reduction in the odds of sexual debut [27]. Studies from South Africa and Zimbabwe have demonstrated a relationship between social protection interventions and transactional sex in young women [28, 29]. For example, Cluver et al (2013), found that receipt of cash transfers was associated with significant reductions incidence of transactional sex for girls (OR 0.49, 95% CI 0.26–0.93; $p = 0.028$) in South Africa. The same study found that girls whose families received a grant were less likely to engage in age-disparate sex (OR 0.29, 95% CI 0.13–0.67; $p = 0.004$) [28]. There were no consistent effects for any of the behaviours among boys [28].

Social protection interventions are associated with increased condom use [23, 29] in young women. Condom use also increased among female sex workers (FSWs) exposed to a micro-enterprise intervention in Kenya [30]. The same study found that self-reported weekly mean number of all sexual partners changed from 3.26 (SD 2.45) at baseline to 1.84 (SD 2.15) at end-line survey ($p < 0.001$) [30].

In South Africa, Cluver et al (2014) found that cash alone was associated with reduced HIV risk for girls (OR 0.63; 95% CI 0.44–0.91, $p=0.02$) but not for boys. Integrated cash plus care was associated with halved HIV-risk behaviour incidence for both sexes (girls OR 0.55; 95% CI 0.35–0.85, $p=0.007$; boys OR 0.50; 95% CI 0.31–0.82, $p=0.005$), compared with no support and controlling for confounders [31].

Few randomised controlled trials (RCTs) have assessed behavioural interventions with biological outcomes. However, an RCT in Malawi found that a cash transfer programme that was tied to school attendance can lead to meaningful reductions in HIV and HSV-2 infections in girls aged 13–22 years who were enrolled in school at baseline [32]. A study in Uganda found a decrease in child-bearing incidence among girls receiving life skills and vocational training enabling them to establish small-scale enterprises [23].

Kohler and Thornton (2011) make an important point saying, “[Conditional cash transfer] Programs that aim to motivate safe sexual behavior in Africa should take into account that money given in the present may have much stronger effects than rewards offered in the future” [33]. This study, which evaluated the effect of conditional cash transfers on maintenance of HIV status over a year, found no effect on HIV status or on reported sexual behaviour [33]. However, the authors report that shortly after receiving the reward, men who received the cash transfer were 9 percentage points more likely and women were 6.7 percentage points less likely to engage in risky sexual behaviour [33]. However, these approaches are very different to social protection models that have shown no similar impact on short-term risk behaviours.

There are demonstrable relationships between social protection interventions and GBV, with strong evidence coming from South Africa [34, 35]. The IMAGE study, which evaluated the impact of a structural intervention that combined a microfinance programme with a gender and HIV training curriculum on intimate partner violence (IPV) and HIV, found that those exposed to the programme were less likely to report IPV (adjusted risk ratio [aRR] 0.45, 95% CI 0.23–0.91; adjusted risk difference –7.3%, 95% CI 16.2 to 1.5) [34]. In their study of a combined structural and behavioural intervention designed to address gender inequalities and livelihood insecurity simultaneously in South Africa, Jewkes and Gibbs (2014) report that there was a 37% reduction in sexual and/ or physical IPV in the past three months among women between baseline and follow-up [35]. In Côte d’Ivoire, women attending >75% of groups addressing group savings and gender dialogues were less likely to report physical IPV (adjusted odds ratio (aOR): 0.45; 95% CI: 0.21, 0.94, $p=0.04$) [36]. Bandiera et al (2012) found that there was a 17.1 percentage point decrease in girls reporting having sex unwillingly [23].

Cash transfers can increase willingness to, and actual uptake of, services. A study among men who have sex with men (MSM) in Mexico showed that those receiving conditional economic incentives were more willing to attend HIV prevention talks and to get tested for STIs [37]. In South Africa, Brahmhatt’s (2014) pilot study of unconditional and conditional cash transfers found that youth in the clinic condition were twice as likely to have attended a clinic or hospital over the study period than youth in the other arms (64% in the clinic condition compared to 26% in the unconditional cohort and 24% in the school condition cohort) [38]. In Ethiopia, PLHIV receiving a comprehensive intervention comprising a savings group, mentoring and support, and nutritional counselling and support, were more likely to adhere to ARVs (97% among participants vs 84% among controls) [39].

Social protection has been shown to be effective with regards to nutritional outcomes in PLHIV. An Ethiopian study found a 36% reduction in severe hunger after a comprehensive intervention [39].

Education

This section describes the effect of several important education-related interventions on reducing the risk of HIV transmission. We looked at both interventions which focus on the intrinsic benefit of schooling as well as ones which are delivered in school.

Education has been shown to have an important relationship with HIV status. Barnighausen et al. (2007) found that for each additional year of education participants in a South African study were 7% less likely to seroconvert (adjusted hazard rate, aHR:0.93, $p = 0.022$) [40]. Pettifor and colleagues (2008) found that young South African women who had not completed high school were more likely to be infected with HIV compared with those that had completed high school (AOR 3.75; 95% CI 1.34-10.46) [41].

Different types of education interventions have demonstrated effectiveness in keeping girl children in school. A study in Kenya found that school dropout was lower in the experimental group compared with the control group (4% vs. 12%, $p = 0.05$). The intervention included: school fees, uniforms, and a “community visitor” who monitored school attendance and helped to resolve problems [42]. In Zimbabwe, Hallfors et al. (2011) found that control participants had higher odds of dropping out of school (OR 8.5, 95% CI 3.6, 19.8; $p < 0.001$) and nearly 3 times the odds of getting married (OR 2.92; 95% CI 1.0, 8.3, $p = 0.02$) [43].

Education interventions also have demonstrable impact on risky sexual behaviours. In Uganda, Ssewamala et al. (2010) found that orphans receiving a comprehensive intervention including child savings accounts, workshops, and mentorship (in addition to counselling and school supplies) in Uganda were more likely to report intending to practice safer sexual behaviour [26]. In Kenya, prevalence of sexual debut was lower among girls receiving the intervention (19%) vs. the control group (33%) ($p = 0.07$) [42]. Another Kenyan study found that boys receiving the school-based HIV intervention reported an increase in having ever used a condom [44]. A South African study demonstrated that those receiving a school-based HIV/ STI risk reduction intervention were less likely to have unprotected sex (OR 0.51, 95% CI 0.30-0.85, $p = 0.01$) and multiple sexual partners (OR 0.50, 95% CI 0.28-0.89, $p = 0.02$) [45].

A new study from South Africa, where respondents were asked retrospectively whether they received various interventions, shows promising results for both young men and women [46]. Young men who received free schooling and books were 33% less likely to have engaged in “careless” sex, defined as unprotected sex, sex whilst using substances, multiple sexual partners, or casual sex. Young women were 37% less likely to report careless sex if they received school feeding. Young women who received free schooling and books were 59% less likely to have engaged in transactional or age-disparate sex [46].

There do not seem to be many studies which make use of biological outcomes to measure the effectiveness of education programmes.

Interventions against alcohol abuse

A number of studies have reported on the relationship between alcohol and HIV sero-positivity in sub-Saharan Africa [47-49]. Kalichman et al (2007) found that any alcohol use as well as greater quantities of alcohol use were strongly associated with the risk of HIV transmission in sub-Saharan Africa [50]. A systematic review of the association between HIV infection and alcohol use found that even when all other factors were taken into account, alcohol users had a 57% greater likelihood of being HIV positive than non-drinkers [51].

The explanation for the relationship between alcohol use and the transmission of HIV in sub-Saharan countries is increasingly being recognised as indirect. Alcohol use has been found to contribute to risky sexual behaviour [52] such as having multiple sexual partners and inconsistent condom use.

A modelling study from Kenya has estimated that an alcohol reduction programme with 45% reduction in unhealthy alcohol consumption could avert around 70,000 HIV infections [53]. Experts have concluded that designing and implementing interventions to promote safer drinking practises together with interventions to reduce risky sexual behaviour may have the potential to reduce HIV transmission in South Africa [53, 54]. This section describes the evidence for various alcohol interventions on risky sexual behaviour.

A number of studies undertaken in South Africa have demonstrated the effectiveness of alcohol and HIV risk reduction programmes on both risky drinking and risky sexual behaviour. Participants in an empowerment-based HIV intervention to reduce sexual risk, substance use, and victimisation among at-risk and underserved women reported a reduction in mean days of alcohol use in the past month [55]. Black women in the study reported an increase in protection at last vaginal sex [55]. Kalichman et al (2007) found that sexually transmitted infection (STI) patients who participated in a 60-minute HIV and alcohol risk reduction behavioural skills intervention had fewer mean acts of unprotected vaginal sex than their control group counterparts [56]. Another study undertaken in shebeens used a brief single-session HIV-alcohol risk-reduction intervention [57]. Results show an increase in consistent condom use at 3 months among lighter drinkers [57].

Studies from elsewhere in the world have also evaluated methods for reducing alcohol use and risky sex. Popular opinion leaders have been successfully utilised to address unprotected sex in MSM in the United States [58]. A bar-based, peer-led community-level intervention to promote sexual health was effective in increasing the likelihood of HCT and of condom use among gay men in Scotland [59].

Interventions against gender-based violence

GBV is a risk factor for HIV transmission [60, 61]. A number of interventions which address different types of violence and gender norms have been developed and implemented. This section describes the impact of these interventions on violence, risk factors for HIV transmission, uptake of services and partner support.

A variety of different interventions designed to address gender and violence specifically or containing elements which address these factors have shown to be effective in reducing different forms of violence. South African studies found that among women who volunteered to take part in a structural intervention combining a microfinance programme with a gender and HIV training curriculum, experience of IPV was decreased by 55% [34, 62]. Similarly, exposure to Stepping Stones and Creating Futures, a combined structural and behavioural intervention designed to address gender inequalities and livelihood insecurity simultaneously, resulted in a reduction in sexual and/ or physical IPV in the past three months among women [35].

In Uganda, women who were highly exposed to the SASA! community mobilisation intervention experienced lower levels of physical and sexual IPV. Non-polygamous men exposed to the intervention were less likely to report concurrent sexual partners in the past year (aRR 0.57; 95%CI 0.36 to 0.91) [21]. A study from Côte d'Ivoire found that women who regularly attended (>75%) gender dialogue groups with their partners and were involved in group savings were less likely to report physical IPV than the control group (savings only) [36].

A male norms initiative in Ethiopia using group-based sessions with men and community mobilisation also showed success in reducing physical, sexual or psychological violence [63]. Jewkes et al (2008) report that two years after participating in the Stepping Stones programme, a lower proportion of men in Eastern Cape, South Africa, reported perpetration of IPV [61]. This study also found some evidence that a lower proportion of men in the Stepping Stones reported raping or attempting rape at 12 months [61]. A Kenyan study found that after attending a gender-transformative programme, there was an increase in the percentage of men who were classified as 'gender equitable men' and a decline in the percentage who reported 'touching her buttocks or breast without her permission' [64].

Interventions which address gender and violence also have demonstrable impact on risky sexual behaviour. The One Man Can Campaign (OMC), which aimed to change gender norms in South Africa, was effective in improving condom use among both men and women. Two-thirds of participants (67%) reported an increase in condom use after OMC workshops [65]. After one year, men who participated in Stepping Stones were more likely to report using a condom at last sex (AOR 1.26, (95 % CI 0.92, 1.74) [61]. A Kenyan study found that after attending a gender-transformative programme, more sexually active boys reported always using a condom [64]. Men who attended sessions which examined the personal and

community consequences of gender based violence and HIV were nearly twice as likely as controls to use a condom at one month follow-up (AOR 1.7, 95% CI: 1.1, 2.7) [66]. A South African study found that relative to women in the comparison group, women participating in SISTA South Africa reduced the frequency of unprotected vaginal intercourse acts [67].

Interventions addressing gender and violence have also addressed other risky sexual behaviours such as transactional sex among men [61] and sexual concurrency in the past year among men [21]. Another risk behaviour which has been addressed is risky drinking. Wechsberg and Myers (2014) report that men in the Couples Health Coop study arm were 2 to 3 times less likely to drink heavily than men in the other two study arms at the 6-month follow-up [68]. Men in the Couples Health Coop arm were more than 4 times as likely to report protected sex than men in another study arm at the 6-month follow-up [68].

A few studies have shown that those exposed to interventions addressing violence and gender had a higher likelihood of accessing health services. For example, 27% of participants who attended OMC interventions reported going to get tested for HIV [65]. South African men who attended Phaphama Men sessions were also more likely to have tested for HIV in the past month [66]. In South Africa, people highly exposed to Soul City Series 4 which, together with the National Network on Violence Against Women, aimed to address domestic violence, were more likely to have made contact with violence against women services/ organisations during the evaluation period [69]. While men who participated in the Stepping Stones/ Creating Futures intervention were also significantly more likely to test [35].

Men who were part of gender-related interventions were more likely to support their partners. In South Africa, Ditlopo et al. (2007) found that men exposed to the Men as Partners programme were more likely to encourage their partner to attend antenatal clinics (ANC), to accompany their partners to ANC and to support their partner's choice of infant feeding [70]. Exposure to the programme also resulted in an increase in the percentage of men who tested for HIV with their partner – from 7% to 15% [70].

Table 41: Summary of quality of the evidence base and grading for social enablers and development synergies

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Social protection						
Cash incentives	Men and women	-	HIV status	No effect	[33]	1
State-provided child-focused cash transfers	Adolescents	Case-control study	Incidence of transactional sex in girls	OR: 0.49	[28]	2
Unconditional cash transfers	Poor families with at least one orphan and vulnerable child	Cluster-randomised experimental Design	Sexual debut	OR:0.69	[27]	1
Conditional economic incentives	MSM	Survey experiment	Percentage willing to attend monthly HIV prevention talk Percentage willing to get tested for STIs	71.4% 71.4%	[37]	1
Unconditioned, school conditioned, clinic conditioned	Adolescents living in urban environments	Follow-up	Percentage been to clinic in the past six months	Clinic CT: 64.1%; School: 24.2%; Unconditional 26.3%	[38]	1
Structural intervention that combined a microfinance programme with a gender and HIV training curriculum	-	Cluster randomised controlled trial	Experience of IPV in past 12 months	Adjusted risk ratio: 0.45	[34]	1
“Cash” vs “cash plus care”	10-18 year olds	Prospective observational study	Reduction in incidence of HIV risk behaviour among girls	Compared to no support - Cash: OR 0.63; 95% CI 0.44–0.91; Cash plus care: OR 0.55; 95% CI 0.35–0.85	[31]	1

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Life-skills-based HIV education, business training and mentorship, and access to microcredit loans for business development	Adolescent female orphans	Pre-post design	Increase in HIV knowledge	16% at baseline to 38% at follow-up	[24]	1
Mentorship, financial education, and an economic asset ownership Opportunity	AIDS-orphaned adolescents	Cluster-randomised experimental design	Intention to engage in risky sexual behaviour	9.84 (8.64, 11.04) in control group vs. 7.74 (6.96, 8.52) in treatment group (p<0.1)	[26]	1
Family economic intervention, which included a Child/ Youth Development Account and six 2-hour classes on career planning, career goals, microfinance, and financial well-being	AIDS-orphaned adolescents	Randomised controlled trial	Increase in HIV prevention attitude scores	17.2 at baseline to 18.5 at follow-up	[25]	1
Life skills and vocational training	Adolescent girls	Randomised controlled trial	Increase in HIV knowledge	46.5 pp	[23]	1
			Increase in pregnancy knowledge	6.3pp		
			Decrease in child-bearing incidence	2.7pp		
			Increase in "always" uses a condom (if sexually active)	12.6pp		
			Decrease in reporting having had sex unwillingly	17.1pp		
Group savings plus gender dialogue groups	Women and their male partner	Two-armed, non-blinded randomised-controlled trial	Physical interpersonal violence in the past year	aOR: 0.45; 95% CI: 0.21, 0.94	[36]	1

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Combined intervention package including life-skills and health education, vocational training, micro-grants and social supports	Adolescent women	Randomised controlled trial	Lower risk of transactional sex	IOR=0.64, 95% CI (0.50, 0.83)	[29]	1
			Higher likelihood of using a condom with their current partner	IOR=1.79, 95% CI (1.23, 2.62)		
Combined structural and behavioural intervention	Young people	Interrupted time-series design	Decrease in sexual or physical IPV in the past three months among women	37%	[35]	1
			Decrease in sexual IPV	7.5%		
Micro-enterprise services added to a peer-mediated HIV intervention	FSWs	Pre-post without control	Weekly mean number of all sexual partners	3.26 (SD 2.45) at baseline to 1.84 (SD 2.15) at end-line	[30]	1
			Weekly mean number of regular partners	1.96 (SD 1.86) at baseline to 0.73 (SD 0.98) at end-line		
Nutritional assessment, counselling and support + savings groups + mentoring and peer support	PLHIV	-	Increase in ART adherence	97% among participants vs 84% among controls	[39]	1

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Cash plus different types of care	Adolescents	-	Careless sex in males	OR 0.607 if receiving free schooling and books	[46]	1
			Careless sex in males	OR 0.496 if monitored		
			Economic sex in males	OR 0.099 if monitored		
			Careless sex in females	OR 0.668 if receiving medical care		
			Careless sex in females	OR 0.633 if receiving school feeding		
			Pregnancy sex in females	OR 0.245 if receiving school feeding		
			Economic sex in females	OR 0.479 if receiving child grant		
			Careless sex in females	OR 0.411 if free school and books		
Education						
One additional year of education	-	Longitudinal population-based HIV surveillance	Hazard of HIV seroconversion	aHR:0.93	[40]	1
Supporting Adolescent Orphan Girls to Stay in School as HIV Risk Prevention	Adolescent orphans	Randomised controlled trial	Sexual debut	19% in intervention vs. 33% in control	[42]	1
			School drop-out	12% in control group vs 4% in experimental group		

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Three school-based HIV/ AIDS interventions in Kenya: 1) training teachers in the Kenyan Government's HIV/ AIDS-education curriculum; 2) encouraging students to debate the role of condoms and to write essays on how to protect themselves against HIV/ AIDS; and 3) reducing the cost of education	Adolescents	Randomised evaluation	Increase in condom use EVER among boys	Teacher training: 7% or 6.1 percentage points	[44]	1
			Increase in condom use at last sex among boys	Condom debates and essays: 20% or 5.6 percentage points		
School-based HIV/ STI risk reduction intervention	Adolescents	Randomised controlled trial	Unprotected vaginal intercourse	OR: 0.51 (95% CI 0.30-0.85)	[45]	1
			Multiple sexual partners	OR: 0.50 (95% CI 0.28-0.89)		
Fees, uniforms, and a school-based helper to monitor attendance and resolve problems (plus daily feeding)	Orphan girls	Randomised controlled trial	School drop-out	OR: 8.5 in control group	[43]	1
			Marriage	OR: 2.92 in control group		
Interventions against alcohol abuse						
School-based HIV/ AIDS and alcohol abuse educational programme	Adolescents	-	Communication in females	4	[71]	1
			Efficacy in females	2.73		
Alcohol intervention with 45% effectiveness	-	Modelling	Reduction in AIDS deaths over 20 years	17,824	[53]	1

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Popular opinion leaders	MSM	Randomised community-level field design	Increase in the mean percentage of occasions of anal intercourse protected by condoms	Baseline 44.7%; follow-up 66.8%	[58]	1
Brief single-session HIV–alcohol risk-reduction intervention	Men and women who drink at shebeens	Randomised community field trial	Consistent condom use	In lighter drinkers: 31% at baseline and 67% at 3 months.	[57]	1
Bar-based, peer-led community-level intervention to promote sexual health	MSM	Quasi-experimental, repeat cross-sectional design	HIV testing	OR: 1.38 (95%CI: 1.04±1.84)	[59]	1
			Unprotected anal intercourse casual	OR: 0.67 (95%CI: 0.39±1.15)		
Empowerment-based HIV intervention designed to reduce sexual risk, substance use, and victimisation	At-risk and underserved women	Cross-sectional	Reduction in mean days of alcohol use in the past month	6.23 days for the Black sample and 3.14 days for the Coloured sample	[55]	1
			Increase in protection at last vaginal sex among Black women	16%		
School-based alcohol/ HIV prevention curriculum	Grade 9 learners	Pretest–posttest field trial	Intention to use a condom every time they have sex during the next 3 months among those who had had sex	0.77	[72]	1
HIV and alcohol risk reduction behavioural skills intervention	STI patients	Randomised intervention trial	Mean unprotected vaginal intercourse occasions	3.6 at baseline vs 6 months later: 1.3	[56]	1
			Percentage condom use	64.8% at baseline vs 87.8% 6 months later		

CHAPTER 4

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Interventions against gender-based violence						
Structural intervention that combined a microfinance programme with a gender and HIV training curriculum	-	Cluster randomised controlled trial	Experience of IPV in past 12 months	Adjusted risk ratio: 0.45	[34]	1
SASA! Community mobilisation intervention to prevent violence and reduce HIV-risk behaviours	Men and women	Cluster randomised controlled trial	Lower levels of past year experience of physical IPV among women	aRR: 0.48; 95%CI 0.16 - 1.39	[1]	1
			Lower levels of past year experience of sexual IPV	aRR 0.76, 95% CI 0.33 to 1.72		
			Lower past year sexual concurrency among men	aRR: 0.57, 95% CI 0.36 to 0.91		
Soul City series 4 and partnership with the National Network on Violence Against Women	General population	Pre-post survey	Made contact with VAW organisations/ services	0% among those with no/ low exposure; 4% among those with high exposure	[69]	1
One Man Can (Sonke Gender Justice)	Men and boys	Telephonic survey	HCT after OMC intervention	27%	[65]	1
			Condom use after OMC intervention	67%		
Combined structural and behavioural intervention	Young people	Interrupted time-series design	Decrease in sexual or physical IPV in the past three months among women	37%	[35]	1
			Decrease in sexual IPV	7.5%		

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Men as Partners	Men and women	Pre-post survey	Increase in support for a female partner / wife's choice of feeding option	52% vs 71%	[70]	1
			Increase in % of men who encouraged their partner to access ANC	26% vs 37%		
			Increase in % of men who accompanied partner to ANC	22% vs 31%		
			Increase in % of partners who accessed HCT for PMTCT	19% vs 30%		
			Increase in % of men who accessed HCT with their partners	7% vs 15%		
Phaphama Men	Adult men	Quasi-experimental field trial	Proportion of sex acts with condoms at one month follow-up	OR: 1.7 (95% CI: 1.1, 2.7)	[66]	1
			Tested for HIV in past month among men not tested at baseline	OR: 0.4 (95% CI: 0.2-0.8)		
			Increase in HCT in the last month at three months follow-up (amongst men not previously tested)	OR: 0.5 (95% CI: 0.3-0.9)		
			Hit a sex partner in the past month at 6 month follow-up	OR: 0.3 (95% CI: 0.2-0.4)		

CHAPTER 4

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Male norms initiative	Young men	Quasi-experimental study	Reduced physical or sexual violence	Reduced in both intervention arms ($p < 0.05$) Arm 1: 36% to 16% Arm 2: 36% to 18%	[63]	1
			Reduced physical or sexual or psychological violence	Reduced in both intervention arms ($p < 0.05$); Arm 1: 53% to 38%; Arm 2: 60% to 37%		
Stepping Stones	Men and women 15-26 years	Cluster randomised controlled trial	Increase in condom use at last sex (without error or breakage) at 12 months follow-up	AOR: 1.26 (95% CI 0.92, 1.74)	[61]	1
			Decrease in transactional sex at 12 months			
Breaking Gender Barriers: Changing Gender Norms of Boys and Men	Boy and girl scouts	Baseline and endline	Increase in proportion of sexually active boys who reported always using a condom	34% to 47%	[64]	1
			Decline in those reporting "Touched her buttocks or breast without her permission"	11% to 4%		
			Increase in percentage of men classified as high equity men	39% to 70%		
Group savings plus gender dialogue groups	Women and their male partner	Two-armed, non-blinded randomised-controlled trial	Physical interpersonal violence in the past year	aOR: 0.45; 95% CI: 0.21, 0.94	[36]	1

Enabler	Target population	Type of evidence	Final effectiveness measure		Source(s)	Grading
			Metric	Value		
Couples Health CoOp	Couples	Clustered randomised field experiment	Heavy drinking in men	Men in the CHC arm were 2 to 3 times less likely to drink heavily than men in the other two study arms at the 6-month follow-up	[68]	1
			Protected sex in men	Men in the CHC arm were more than 4 times as likely to report protected sex than men in the WHC arm at the 6-month follow-up		
SISTA South Africa	Women	Randomised controlled trial	Frequency of unprotected vaginal intercourse	Adjusted mean difference = 1.06; p = .02	[67]	1

After the grading exercise described above, some 71 social enablers had been evaluated as having good evidence.

After the grading, a meeting was held with working group members to review the methodology and results for the critical enablers, to define target populations for each enabler and to agree on a method of allocating the cost of enablers across HIV and non-HIV budgets and between government departments for the Budget scenario. The table below shows the enablers which could be included in the model as well as the target population which the working group agreed on.

Table 42: Social enablers and development energies included in the model: Impact and target population

Enabler	Source	Impact	Target population
SASA! community-based GBV intervention	[1]	Multiple sexual partners (MSP)	Intense intervention to adults 18-35 + community outreach; in HTA only
Life skills and vocational training for out-of-school adolescent girls	[23]	Condom use	All adolescents aged 16-25 who aren't in education or employment
- Alcohol and substance users	[56]	Condom use	Alcohol and substance using adults
- Substance users	[55]	Condom use	Meth- and cannabis-using women 15+
- School children	[45]	MSP, condom use	Combine with life skills
Teacher support	Cluver (personal communication)	MSP	Adolescents in informal settlements and rural areas (with >28% ANC prevalence)
Parental monitoring		MSP, condom use	
Positive parenting		Condom use	
School feeding		MSP	
Supporting adolescent orphan girls to stay in school	[42]	Delay in age of sexual debut	Adolescent orphan girls
State-provided child-focused cash transfers	[28]	Reduction in age disparate sex	Prioritise for low-income schools

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4.2.2 PROGRAMME ENABLERS AND DEVELOPMENT SYNERGIES

Summary of evidence synthesis process

Programme enablers are initiatives that support the effectiveness and efficiency of interventions to address HIV and TB. A SANAC-convened consultative workshop – involving representatives of civil society organizations, NGOs, government departments, public and private health services, and development partners – on 30-31 July 2014 identified an initial list of programme enablers. Many of the initiatives identified reflected the knowledge and experience of participants as well as new or pilot programmes within the public health setting. A summary report of the outcomes of this workshop was prepared to inform the collection of evidence for the different programme enablers.

A preliminary review found there was often little evidence available on which to base conclusions regarding the impact of these interventions. Thus, it was often not possible to straightforwardly include specific initiatives in the final evidence for modelling. Instead, the list of programme enablers was reviewed and re-organised to better reflect available studies. At all times the list of programme enablers reflected the specific concerns and observations of stakeholders involved in the consultative process. Box 1 lists the revised programme enablers as structured to inform a review of available evidence as presented in this chapter.

A second round of evidence review identified 31 original studies and six review articles for presentation as evidence for the modeling exercise. Of these studies, 22 were conducted in South Africa. The original studies include both RCTs and observational studies published in peer-reviewed journals. Although the evidence from programme enablers is considerable, it is far from comprehensive, as there were significant evidence gaps for certain enablers. Moreover, as the implementation of programme enablers varies substantially across different geographical regions and health districts, one could reasonably expect the impact of specific programme enablers to vary in different contexts depending on the mode of implementation – an effect that was not taken into account in the modelling here. Finally, it was not always easy to distinguish programme enablers from TE factors, which meant that some enablers had already been reviewed and included as TE factors by other programme areas (for example, point-of-care laboratory tests, task-shifting, and workplace testing). Where the approach was previously included elsewhere as a TE factor, the enabler was removed from this review.

Table 43: Revised programme enablers and development synergies aligned with available evidence

Programme enabler	Sub-categories and examples
Blood safety	Centralised model of transfusion services
Clinical governance and primary health care integration	<ul style="list-style-type: none"> Sound management and procedures (for example: financial management, cost centre management/ contracting out) Standardisation of care and improved compliance with treatment guidelines Integration of services (for example, PMTCT with maternal and child health services) Task shifting –doctor-led to nurse-led treatment
Community centred design and delivery	<ul style="list-style-type: none"> Collaboration and partnerships (for example, between community organizations such as churches, NGOs and between sectors) Outreach services: Community Health Care workers, Local programme champions, home- and community-based care
Employer practices	<ul style="list-style-type: none"> On-site workplace and mobile health services Extending benefits to families and communities Guidance documentation for business

Programme enabler	Sub-categories and examples
Human resources	Nurses Positive Practice Environments Continuing Professional Development Human Resource occupation specific dispensation (OSD) incentives and non-financial benefits Training other Cadres CHWs and other community based lay workers Mid-level workers (Clinical Associates) Scaling up International Training and Education Centre for Health (I-TECH) initiatives Management capacity
Laboratories (diagnostic services)	Point of care (PoC) technologies in PHC facilities Xpert MTB/RIF test for TB PoC HIV rapid test PoC CD4 test PoC viral load test
Monitoring, evaluation (M+E) and reporting	Electronic and other data collection Three tier M+E system Other databases such as logistic management and information system (LMIS) Cellphone technologies Patient complaints and queries National call centres – AIDS helpline
Patient identification and mobile technology	Unique Patient Identifier E-health or mobile health technology
Supply chain management processes and infrastructure	Supply Chain Reforms: Direct Delivery model of distribution (Limpopo & Gauteng) Central Chronic Medicine Dispensing and Distribution Programme (CCMDD) Improved networks and systems to facilitate bi-directional data flow for procurement related data Cross docking Direct purchasing End-to-end visibility and electronic data interchanges (eg mobile networking at clinics) National control tower and provincial medicine procurement unit Stop Stock Outs Consortium Condom supply chain management Logistic management and information system (LMIS) ROWA (Pilot technology to improve dispensing of drugs)

Final list of programme enablers and development synergies

In general, each programme enabler is characterized by one or more central themes about which there is some evidence. Table X lists the studies presented for consideration for modeling.

Blood safety

WHO's Blood Safety Unit in Geneva has long advocated that countries develop nationally coordinated blood services, which are community-based and reliant on non-remunerated volunteer blood donors. South Africa is one of the fewer than 20% of countries in sub-Saharan Africa that has developed this model. As a unit of blood from a centralized system costs about three times as much as one from the hospital-based replacement system, much of the literature focuses on the cost-effectiveness and efficiency of models of blood collection and screening, including the value of a centralized model of transfusion services for blood safety and the value (both cost and health gains) of improving HIV screening of donated blood [1]. Blood safety is a critical prevention measure, as the risk of being infected with HIV through contaminated blood and blood products is exceptionally high compared to other common routes of exposure. Earlier in the epidemic, it was estimated that contaminated blood transfusions accounted for 5%-10% of HIV transmission in Africa [1] [2], although recent estimates regarding the role of blood transfusion in incident infections in the region are not available.

In South Africa, blood is screened for a range of transfusion-transmitted infections, such as HIV, hepatitis B and C, and syphilis. WHO established a goal of ensuring regional blood safety by 2012 through improved organization and management; blood donor recruitment and collection; testing of donor blood; and appropriate clinical use of blood [3].

All papers reporting on the cost-effectiveness of post-donation HIV antibody screening in sub-Saharan Africa conclude that HIV screening results in health gains and cost savings. New HIV infections prevented by HIV antibody screening ranged from 150 to 1 400 per 10 000 donations. The number of new HIV infections prevented depends heavily on the HIV prevalence among blood donors and the prevalence of HIV infection in transfusion recipients [4]. One review determined that the strategies implemented by South African National Blood Service (SANBS) in 1999 to mitigate HIV transfusion risk have resulted in a dramatic drop of HIV risk from blood transfusion. Almost 10 years ago, WHO reported that South Africa had reduced HIV prevalence to 0.46% among first-time blood donors and 0.03% among regular blood donors. HIV prevalence (%) in all donors fluctuated between 0.18% and 0.24% during April 2011 – March 2013. With the exception of Northern Zone (Limpopo), all zones experienced an increase in HIV prevalence in all donors during the last quarter of 2013 [5].

Challenged for a discriminatory approach to the selection of blood donors, SANBS in 2005 responded with implementation of concurrent HIV RNA nucleic acid testing (NAT) and serology-based screening to allow more equitable blood collection in South Africa without compromising recipient safety. HIV NAT affords added protection by identifying infected donors in the pre-seroconversion “window period.” This, however, is an expensive system of blood screening and not thought to be viable in many other African contexts [6]. October 2012 marked eight years of state-of-the-art screening in South Africa, and over these eight years not one HIV infection through blood transfusion has been reported.

In 2012, in an effort to assess the magnitude of blood wasted, SANBS implemented a system in Gauteng to collect data from the 14 major hospitals on blood ordered but not transfused to patients. On average approximately 6% of blood issued to hospitals is not being transfused. SANBS will be implementing further monitoring and education programmes in 2013-2014 to reduce this wastage.

Clinical governance and integration

This programme enabler, organized into three main sub-categories or themes, encapsulates a vast array of actions and strategies to improve coverage and the quality of services delivered: 1) sound management and procedure; 2) integration of services; and 3) task shifting. Only evidence from the last two sub-categories had available data that could be used for modelling.

However, there are many aspects of the sub-category 'sound management and procedure' that are important for health system functioning. For example, involving the private sector in the delivery of public health services has proved promising in many parts of Africa. There are various ways of doing this, including fee for service; leveraged (or donor-sponsored) provider networks; decentralised national ART programmes (in which government provides ARVs to the private sector); output-based aid (i.e., donors purchase outputs to be provided by the private or public sector); insurance company sponsored clinics; workplace initiatives; and regional business coalitions [7]. An example of a leveraged provider network is the down-referral model implemented by BroadReach in the North West province. In this model patients start treatment at a public care facility, are stabilized for six months, and are then down referred to a private sector clinician. The programme has resulted in a patient retention rate of 97.3% and a viral load suppression rate of 96% (see also Chapter 4.1.5).

Integration of services

There is a growing body of evidence regarding the benefits of service integration, although the evidence base is difficult to summarise as it addresses a broad range of opportunities for integration (e.g., HIV/TB and information systems, PMTCT and maternal and child health services, HIV risk reduction and PMTCT, family planning and HIV care and treatment). However, the evidence is convincing that service integration, where feasible and appropriate, often increases health impact. For example, the PartnerPlus intervention pilot study in rural Mpumalanga, South Africa, which integrated HIV risk reduction interventions for both women and men into existing PMTCT services during and following pregnancy, was associated with increased and sustained rates of consistent condom use (from 27% at baseline to 60% post intervention), while similar improvements were not achieved among participants in the enhanced standard of care (21% to 20%) [8].

Other studies in Eastern and Southern Africa demonstrate that integration can also be cost-efficient and cost-effective. In a cluster-randomized trial study of 12 health facilities in Kenya, researchers found that the integration of family planning services into HIV care and treatment clinics is feasible, inexpensive to implement, and cost-efficient in the Kenyan setting [9]. A multi-country study (involving 274 public health facilities in Kenya, Lesotho, Mozambique, Rwanda and Tanzania, concluded that expansion of paediatric services to public health facilities increased the number of children receiving ART, with early findings suggesting lower loss to follow-up and mortality [10].

Task shifting

In African countries with a high disease burden and a shortage of doctors, evidence now supports the benefits of shifting certain HIV-related clinical tasks from physicians to nurses. In a review of pertinent research articles between January 2009 and August 2012, seven of eight studies found no difference in mortality between task-shifting and non-task-shifting sites, while five found better retention and lower client loss to follow-up in nurse-managed groups [11]. Another study found that the expansion of primary care nurses' roles to include ART initiation and re-prescription can be done safely and improve health outcomes and quality of care, but may not reduce the time to be initiated on ART or mortality [12]. A Cape Town study that compared patient outcomes between a doctor-managed clinic and a nurse-managed down-referral site found that there was no difference in the risk of mortality by the nurse model of care [13].

A review of 10 African studies, including four RCTs, had similar results. RCT data indicates no difference in death at one year unadjusted risk ratio was 0.96 (95% CI 0.82 to 1) when nurses initiated and provided follow-up HIV therapy. One trial, reporting on the time to initiation of antiretroviral therapy, found no clear evidence of a difference between groups but did find that nurse-initiated care was associated with an increase in the number of TB diagnoses made [14].

(See also chapter 4.1.5 for a discussion of task-shifting as a technical efficiency factor for ART provision.)

Community-centred design and delivery

Community design and delivery interventions aim to extend outreach into rural areas and hard-to-reach communities; build partnerships between different sectors, such as Operation Sukuma Sakhe in KwaZulu-Natal; build partnerships

between local organisations; and strengthen capacity for a local-level response. Such interventions also often aim to take services to key populations such as sex workers, truckers and migrant labourers. Often considered a soft intervention, the benefits of community centred design and delivery are supported by an extensive body of qualitative evidence, which indicates that these community-centred approaches reinforce and support biomedical interventions [15].

As some of the evidence for community centred design and delivery was incorporated into other sections of the modelling exercise (e.g., HCT, PMTCT, ART), these studies are therefore not referenced here. A meta-analysis identified nine studies reporting statistically significant improvements in PMTCT outcomes when community groups were used. Strong associative evidence for increased condom use and reduced risk behaviours (Kenya and Zimbabwe), increased testing for women (Zimbabwe), increased use of PMTCT services (Zimbabwe), and increased home based care (Zimbabwe) was found [16].

Outreach lay community workers (e.g., CHWs, CCWs, patient advocates) have long been part of the architecture of primary health care at the local level and are a pillar of the re-engineered approach to primary care in South Africa. A Malawi study found that case management and support by dedicated CHWs resulted in an increase in the proportion of HIV-infected children enrolled on ART from 39.4% to 76.7%, leading researchers to conclude that case management and support by dedicated CHWs may help create a continuum of longitudinal care in the PMTCT cascade and improve health outcomes [17]. A study in four South African provinces found that community-based adherence support (CBAS) to caregivers resulted in higher rates of virological suppression (65.6% (95% confidence interval [CI]: 62.7-68.4%)) compared to non-CBAS children (55.5% (95% CI: 54.1-57.0%)) at any time-point on treatment ($P < 0.0001$). The effect of CBAS increased in magnitude with increasing duration of ART, and CBAS particularly improved virological suppression in a higher-risk subgroup (children younger than two years, aOR 2.47 [95% CI: 1.59-3.84]) [18]. Positive associations are found when CHWs were involved with supporting TB, HIV and PMTCT programming services [19] and in MCH interventions targeted to reach mothers in the first six months of a child's life [20] or when a child is a newborn [21].

Positive outcomes in a range of community-centred approaches are described in Table X, and these outcomes were taken into account in the IC modelling. (See also chapter 4.1.5 for a discussion of community-centred design and delivery as a technical efficiency factor for ART provision.)

Employer practices

Workplace HIV and AIDS programmes have been an important component of the South African response to the epidemic. The commitment of workers and employees has strengthened the multisectoral nature of the national AIDS response. Worldwide best practice in workplace programming is often cited from South Africa, and although there is evidence supporting the involvement of big business in the AIDS response, there is less evidence supporting the involvement of organised labour [22].

While big business in South Africa has warmly embraced comprehensive programming for HIV and TB, some businesses, notably the gold and platinum mining sector, continue to experience high incidence of both diseases. In 2014, the National Institute of Communicable Diseases reported gold mining in South Africa to have the highest incidence of TB in the world, with cases ranging from 3,000 to 7,000 per 100,000 miners per year; by way of comparison, WHO declares a health emergency when TB incidence reaches 250 per 100,000 per year [23].

High HIV and TB incidence in the mining sector also fuels broader regional epidemics. The mine labour sending area of Lesotho, for example, has the fourth highest TB incidence in the world, and tuberculosis is responsible for 15% of all deaths in the country. The relationship between the South African mining sector and the TB epidemic in Lesotho is unambiguous, with a recent study finding that close to 40% of adult male TB patients in three of Maseru's main hospitals were working, or had formerly worked, in South African mines [24]. At least 25% of the drug-resistant TB cases treated in Lesotho since August 2007 have a history of mine work or were referred directly from mines in South Africa. It is clear

that the public health threat of TB in Lesotho cannot be adequately addressed without dealing with the issues around TB control amongst migrant Basotho miners and their families – on the mines in South Africa, across the border, and in their communities in Lesotho.

The evidence presented in the investment case focuses on three approaches to employee health: on-site workplace and mobile services that link HCT and TB screening to care; the benefit of extending HIV and TB services to employees' families and communities; and the limitations of guidance documents for business.

Screening and linkage to care

In 2003, the AngloGold Ashanti medical team, adopting digital X-ray technology on a large scale, increased the detection rate for TB by about 3.8%. The technology could also be used in mobile facilities that allowed testing for TB on site. The AngloGold approach of integrating technology into the control of TB at its South African operations has over a period of some 11 years played a significant role in reducing TB incidence by about 60% [25].

As a 2003/4 cluster-randomised trial of two HCT strategies, one offered on site and the other off-site to small- and medium-sized businesses in Harare, Zimbabwe, found that workplace-based initiatives have the potential to expand HIV care at little cost to government. HCT at the workplace offers the potential for high uptake when offered on-site and linked to basic HIV care. Convenience and accessibility appear to play critical roles in the acceptability of community-based HCT [26].

Bophelo! – a public private partnership between Pharm Access Namibia, the Namibian Business Coalition on AIDS and the Namibian Institute of Pathology – began in 2009 operating began using two mobile testing vans travel to employment sites and later to remote farms and tourist lodges. The programme, which charged participating companies a fee, tested employees for HIV, cholesterol, blood glucose and haemoglobin levels, hepatitis B, syphilis, and hypertension, and questions were also asked regarding TB. The study demonstrated the advantages for governments of both mobile multi-disease screening and a strong public-private partnership, as Bophelo! proved to be an especially effective way for reaching men in need of health screening, in part due to the convenience of testing at work and also because the programme did not focus on a single disease. Over half of persons (50.6%) tested had at least one of the nine health conditions for which screening was provided [27].

Seasonal, migrant and informal workers, such as those in the agriculture, fisheries and forestry sectors, are vulnerable populations involved with work that is often precarious. Mobile health services offered through non-governmental support have proven effective in extending services into these working communities [28].

Extending workplace programmes to families and communities

Corporate social responsibility is motivating an increasing number of companies to extend HIV and other health programmes to the families of workers and to the communities in which businesses are located. According to the International Finance Corporation/Global Business Coalition, companies that have invested in more broad-based community health interventions have reaped benefits, including increased performance and motivation among employees and improved reputation. An example of a workplace-plus model of business engagement is the Thuso (meaning “help”) HIV/AIDS Workplace Program, established in 2004, which reached all of Telkom's more than 30 000 employees and their families [29].

Guidance for workplace policies

An analysis of 14 recognised codes and guidelines for workplace HIV programming found that usage of the codes was low. Although large companies in South Africa may recognise certain interventions as examples of best practice, it appears these are not being readily implemented, in part because the cost-benefit of a recommended intervention is not immediately apparent or conclusive. In addition, there is evidence that the concept of best practice with respect to

workplace HIV interventions is not yet fully accepted [30].

Human resources

Interventions pertaining to human resources are difficult to capture as a single programme enabler due to the variation in the number, quality and skills of available cadres of health care workers. In general, as the prices of ARVs have sharply declined in recent years, inadequate human resources may represent the single most important barrier to achieving universal access to HIV treatment in Africa. Treatment as prevention strategies will require considerable additional financial and human resources commitments, as new evidence indicates that early initiation of ART is associated with clear therapeutic, as well as preventive, benefits. One study estimated that the move from the very early threshold for treatment initiation of 200 CD4 cells/ μ l (per 2004 WHO guidelines) to CD4 cell count of ≤ 350 cells/ μ l (per the 2010 WHO guidelines) increased the number of needed health care workers by 2 200 nurses, 3 800 counselors, and 300 physicians, at an additional annual salary cost of R929 million (equivalent to US\$ 141 million). For universal treatment ('treatment as prevention') an additional 6 000 nurses, 11 000 counselors, and 800 doctors will be required at an additional annual salary cost of R2.6 billion [31].

Although the number and quality of human resources is an important programme enabler, there is little evidence from well-designed studies suitable for incorporation in the modelling exercise. For example, a relationship of trust between patients and health care providers is widely recognised as an important component of ART programmes, but this difficult to measure or to model in the investment case. A meta-analysis of 207 studies of predictors and correlates for ART adherence found that trust/satisfaction with the HIV healthcare provider had a stronger positive effect on adherence in countries with a low or medium human development index than in countries with a high HDI [32].

What follows is primarily a description of the importance of human resources as identified in the Investment Case consultative workshop under three headings: nurses, other cadres of health worker, and scaling up.

Nurses

Nurses are the backbone of re-engineered primary health care (PHC), and task shifting to nurses is widely supported as a critical mechanism for sustaining the growing the ART programme. South Africa has suffered an exodus of nurses over the past decade, both to countries abroad and to other professions locally. The Department of Health Strategic Plan for Nurse Education, Training and Practice 2012/13 – 2016/17 [33] is candid regarding the sea change needed to ensure a robust supply of nurses. Taken as a whole, the strategy describes a revamp of the complete system of nursing recruitment, training and professionalization in South Africa. An important feature of this is the "positive practice environment," addressing nursing shortages, unrealistic workloads, poorly equipped facilities, unsafe working conditions and perceived unfair compensation as some of the factors affecting the work life and performance of nurses and midwives. The loss of essential nurses due to such factors jeopardizes that quality of patient care and therefore the potential health outcomes of patients.

Both continuing professional development (CPD) and occupational specific dispensation (OSD) are essential components of a positive practice environment for nurses. CPD promotes staff development and improves competence and skills development, thereby contributing to better staff morale and motivation, while OSD may help attract nurses who have previously left the health sector, strengthen recruitment of young adults to the nursing profession, and improve nurse retention. However, as the Strategic Plan for Nurse Education, Training and Practice acknowledges, OSD implementation in 2010 was characterized by inadequate planning, weak managerial practices, and uneven and inconsistent interpretation of the agreement, causing disgruntlement and worsening the motivation among nurses in the public health sector. More recent non-financial incentives include revitalization of hospitals, nurses' colleges and nurses' homes. The Strategy Plan states that OSD should be revised to eliminate inequalities and also accommodate career-pathing to retain advanced practitioners in clinical settings. In addition, consideration should be given to nurses allowances; currently, only nurses working in psychiatric hospitals receive a *danger allowance*, and consideration should be given to provide for nurses working in high-risk settings such as MDR/XDR TB hospitals.

Other cadres

Community health workers (CHWs) are an important component of the South African health care system, and these workers should be accredited and receive appropriate training. CHWs extend the outreach of biomedical interventions into communities. Evidence indicates that a broad range of community care givers (CHWs, home and community based care givers) may be successfully trained to improve outreach and access to HIV related services (as noted above in the discussion of community-centred enabling interventions).

International experience suggests that mid-level health workers such as clinical officers, a cadre somewhere between nurses and medical doctors in terms of duration and depth of training, remuneration and experience, have played an important role in addressing human resource shortages and improving health care access and equity, especially in low- and middle-income countries. In South Africa, the creation of this new cadre forms part of a broader strategy to strengthen district health systems and extend health care coverage by dealing with South Africa's human resource shortages. Doherty et al argue that these shortages are considerable when compared to other middle-income countries, with 60 000 additional doctors required to reach ratios equivalent to those in Brazil. Mid-level health care workers are useful not only in low- and middle-income countries, but they routinely play a variety of key roles in developed countries, from augmenting the work of doctors to independent practice. They are present in large numbers in Southeast Asia and are the backbone of the primary care system in East Africa, with more than 10 000 clinical officers trained in Uganda, Tanzania, and Kenya alone. They are being introduced or having their roles expanded in the United Kingdom, Canada, and Australia [34].

Presently, it is unclear whether national-level support for the clinical associate will be sustained. The NDoH is currently absorbed in implementing two far-reaching and challenging reforms (i.e. primary health care re-engineering and national health insurance) and policy-makers and planners have largely not highlighted the part that clinical associates could play in realizing the objectives of these reforms. Clinical associates in South Africa are thus very few, and nationally the strategy is still in its infancy.

Scaling up human resources

Within NDoH, the International Training & Education Centre for Health (I-TECH) administers a number of donor-initiated programmes to support human resources for health. These initiatives include improved data collection regarding human resources, standardised training of health care and community health workers, and management and leadership support. Scaling up services will require more local management capacity, as will the withdrawal of donor funding for HIV and TB services. According to one study conducted in rural KwaZulu-Natal, up-skilling community care workers (CCWs) has potential for enhancing TB/HIV case finding, TB contact tracing and linkages to care [35].

Laboratories (diagnostic services)

Participants in the consultative workshop expressed concerns regarding the slow turn-around-time of the diagnostic services required by PHC facilities. Point of Care (POC) diagnostics have the potential to greatly reduce inappropriate prescribing, LTFU and other challenges associated with delayed diagnosis.

Universal access to HIV counselling and testing and TB screening, as an entry point for diagnosis and HIV and TB treatment, care and support, is fundamental to achievement of objectives outlined in the NSP. As the NSP notes, special attention will be required to ensure that people from key populations know their HIV and TB status. Evidence the potential of POC technologies to improve service delivery to key populations is extremely promising [36, 37].

POC technologies for monitoring viral load also have a potentially important role to play in the long-term management of people receiving ART [38]. PoC tests need to be supported by a decentralized laboratory service, additional or altered human resource capacity, continuous training, and a sustainable supply chain.

Likewise, POC technologies have the potential to improve management of TB drug resistance. The current TB POC test, GeneXpert, can diagnose resistance to the drug rifampicin, which allows the diagnosing clinician to choose the appropriate treatment at the initial visit. If performed at the point of care, the Xpert MTB/RIF test for diagnosing smear-negative TB is cost saving for both patients and the provider, primarily due to reduced transportation costs for patients and reduced clinic fees (where applicable) when test results are made available on the day of the clinic visit [39]. This finding is somewhat outdated, as Xpert is now used as a first-line test for all TB suspects in South Africa, regardless of smear status, and POC is more costly than laboratory-based placement of Xpert tests, due to the additional investment in training, security, and maintenance necessary for every instrument placed at a clinic [40].

Monitoring, evaluation & reporting

Monitoring, evaluation and reporting involves the collection of information that provides insight into health system functioning, enabling sound and timely decision making. The South African public health sector has limited network infrastructure and electronic data management systems; where systems exist, they normally operate in silos. As a result, accessing and sharing data is typically labour-intensive and administratively costly, and the difficulty in accessing strategic information undermines rigorous monitoring and sound decision-making. A cross-sectional survey of 51 public health service managers in two South African provinces, completed in 2012, found that inefficiencies in HIV monitoring and evaluation risk undermining policies to strengthen health system planning and management [41].

The introduction of the three-tier monitoring system in facilities offering ARV, piloted in the Western Cape, is seen as an important intervention with respect to Internet connectivity in the health system. Each tier produces the same nationally required monthly enrolment and quarterly cohort reports, allowing outputs from the three tiers to be aggregated into the health management information system (HMIS) at any level of the health system. In this system, individual health facilities are able to collect data on standardized templates at a level of technology appropriate to the setting: paper based, off-line electronic or on-line electronic database. After the successful 2010 pilot [42], in 2011 NDoH commenced implementing the three tiered ART monitoring system with a strong emphasis on the second tier, a non-networked monitoring system referred to as TIER.Net. By November 22, 2013, 967 facilities had fully implemented TIER.Net, with a further 1 582 facilities in process of implementing the software. As a result, clinical outcome data was centrally collated to the HMIS and cohort outcomes available for over 500 000 patients [43].

Other innovations to monitor service delivery include the use of cell phones by CHWs. One sub-district in the North West province explored the development of a cell phone-based and paper-based M&E system to support the work of the CHWs. By the fifth month, all CHWs achieved a correspondence of 90% or above between phone and paper data. The small study indicated that although mobile technology can be successfully used, any monitoring system requires reinforcement and quality control by supervisors [44].

Similarly, without access to real-time data and a functional Logistics Management Information System (LMIS), it is exceptionally difficult to mitigate routine operational challenges in the supply chain such as medicine shortages (see below for a fuller discussion of supply-chain management solutions).

The National AIDS Helpline presently receives calls on a variety of health-related queries, including reporting medicine stock outs, although Helpline counsellors are not equipped to deal the full range of queries they receive. This suggests the need for an appropriately advertised 'one-stop-shop', with respondents who are trained in fielding various health-related questions. Information generated at such a platform could be used to monitor system responsiveness and health care quality over time. For example, medicine stock-outs reported to the Stop Stock Outs Consortium are automatically escalated to provincial authorities immediately upon receipt, reducing response time and negative patient impact [45].

Patient identification & mobile technology

Network connectivity, patient identification and improved patient communication are likely to have increasing impact on society and service delivery in the next 20 years.

Unique patient identification codes are essential for managing a coordinated care package for individual patients, especially across a number of service providers and clinical settings. Non-governmental participants in the consultative workshop cited the need for appropriate patient registers to facilitate working linkages between the government and other organisations. Currently, however, patients are often registered at a number of different facilities and across multiple civil society organisations, resulting in duplication of effort and double-counting of results. From the standpoint of the government, the current system makes it difficult to ensure that patients' care is uninterrupted, or to link specific interventions to patient outcomes. All participants highlighted the need for a unique identifier [28], but only within a context of information security and confidentiality. Western Cape has a provincial Patient Master Index, on which an estimated 80%-90% of the uninsured population is already registered. Gauteng province is implementing an Electronic Health Record System. The implementation of a national Unique Patient Identifier system is underway that will use ID numbers. From January 2015 this identifier system will be mandatory for all laboratory tests, and there is currently a national project (700 NHI facilities) that will roll out more fully from May [46]. It is also being implemented in the MomConnect Programme for pregnant women, with nearly 100 000 women registered using ID numbers [47].

Although phone ownership is ubiquitous among health workers and patients, the real potential and institutionalisation of phone technologies to improve health outcomes has yet to be properly established. Many studies, currently ongoing, seek to establish an evidence base for this, although such approaches confront important difficulties that will need to be addressed, such as the risk of disclosure of HIV status with SMS messaging. Kenyan studies indicate that SMS messaging can help promote patient adherence, with one study finding that 53% of participants receiving weekly SMS reminders achieved adherence of at least 90% during the 48 weeks of the study, compared with 40% of participants in the control group ($P=0.03$) [48, 49]. Mobile health technology has been used to communicate successfully with CHWs, improving follow-ups at home [50], and this approach is presently underpinning a pilot programme in KwaZulu-Natal to improve the referral of patients to local clinics for further care (refer to the programme enabler: laboratories).

Supply chain management processes and infrastructure

Although supply chain concerns typically focus on medicines, there is actually a much broader range of centrally procured commodities of importance on HIV/TB programming.

Currently, several pilots are underway across South Africa for reforms to existing supply chain approaches for drugs and other commodities used in the public sector (listed in the sub-categories in Table 43 above). Data regarding efficiency and impact of these reforms to the country's evolving procurement strategies were not available at the time of publication, as several pilots were started only in 2014. However, the modelling analysis included anticipated costs for three of the pilot projects.

The inefficiency of the present supply chain poses substantial health risks. There are shocking reports of supply chain failure in the Eastern Cape [51], although this is not the only area of the country where there are significant problems. Better access to real-time information, such as through the use of mobile phones (presently piloted in KZN) and/or LMIS, should enable informed medicine supply management decision making, which in turn can save the lives of people who depend on uninterrupted access to life-saving commodities. The value of electronic dispensing tools has been shown in Namibia, where better data regarding the dispensing of drugs does have been clearly linked with enhanced supply chain management and improved health outcomes [52].

Supply chain management is an important cost component in the delivery of services. A study of VMMC in Swaziland found that supply chain and waste management add approximately US\$60 per circumcision, nearly doubling the total per procedure cost [53]. The supply chain is also critical to support correct procedures, infection control, safe injections, and health care waste management - all of which have a bearing on HIV and TB service delivery and outcomes.

Table 44: Summary of quality of the evidence base and grading for programme enablers and development synergies

Programme enabler	Intervention	Potential impact on programme area(s)	Type of evidence	Final effectiveness measure		Source	Grading
				Metric	Value		
Patient identification & mobile technology							
E-health or mobile health technology	Short message service (SMS) reminders on adherence to ART (4 interventions: daily short, daily long, weekly short, weekly long)	ART	Randomized controlled trial	% with >90% adherence	Intervention weekly: 53% (p=0.03) Intervention daily: 41% (p=0.92) Control: 40%	[48]	1
	Short message service (SMS) reminders (weekly reminder)	ART	Randomized controlled trial	Relative risk for non-adherence (<95% in last 30 days at 6 and 12 mo) to ART (intervention vs control)	RR 0.81; 95% CI 0.69–0.94; p=0.006	[49]	1
	Mobile technology for community health care workers (CHW) for clinical guidance, referral system and data collection	ART, TB , PMTCT	Step-wedged cluster randomized controlled trial	% of home visits complete via SMS message to CHW	74%	[50]	1
	Implementation of mobile monitoring and evaluation (M&E) system	Data quality, patient referral	Observational study	% of correspondence between phone and paper data	~52% to ~92% improvement on accuracy between phone and paper	[44]	1

Programme enabler	Intervention	Potential impact on programme area(s)	Type of evidence	Final effectiveness measure		Source	Grading
				Metric	Value		
Community-centered design and delivery							
Outreach services: Community Health Care workers, Local programme champions	PMTCT cascade intervention (WHO guidelines)	ART, PMTCT	Observational study	% of HIV infected infants enrolled on ART	Baseline 39.4%; Follow-up 76.7%	[17]	1
	Community-based adherence support (CBAS) on virological outcomes amongst children receiving ART	PMTCT, ART	Observational study	Adjusted odds ratio for virological suppression for children receiving CBAS	OR 1.60; 95% CI 1.35-1.89; p<0.0001	[18]	1
	Training of CHW, structural adjustment, harmonisation of scope of practice and stipend of CHW, enhanced supervision of CHW	TB, PMTCT, ART, VCT	Cluster randomized trial	% uptake of HIV testing	Baseline: 55%; Followup: 78%	[19]	1
	Integrated home visit package delivered to mothers by CHW	PMTCT, ART	Observational study	% of mothers who completed referrals by CHWs	87% - 95%	[21]	1
	Effect of home visits by CHW on maternal and infant well-being from pregnancy through the first six months of life for women living with HIV	PMTCT, PREV	Cluster randomized controlled trial	Odds ratio for consistent condom use in intervention group	OR 1.52; 95% CI 1.16-1.99; p=0.002	[20]	1
	Effect of home visits by CHW on maternal and infant well-being from pregnancy through the first six months of life for women living with HIV	PMTCT	Cluster randomized controlled trial	Odds ratio for adherence to PMTCT tasks in intervention group	OR 1.95; 95% CI 1.36-2.79; p<0.001		1
	Effect of home visits by CHW on maternal and infant well-being from pregnancy through the first six months of life for women living with HIV	PMTCT	Cluster randomized controlled trial	Odds ratio for exclusive breast feeding tasks in intervention group	OR 3.59; 95% CI 1.91-6.75; p<0.001		1

Programme enabler	Intervention	Potential impact on programme area(s)	Type of evidence	Final effectiveness measure		Source	Grading
				Metric	Value		
Clinical governance and PHC integration							
Sound management and procedure	Down-referral model	ART	Observational study	Patient retention rate and viral suppression rate	97% and 96%, respectively	[7]	1
Integration of services	Integrated family planning into HIV care and treatment	PREV	Cluster Randomized trial	% increase in use of effective family planning within integrated sites	19.9% (from 16.7% to 36.6%)	[9]	1
	Comprehensive couples-based PMTCT behavioural intervention (PartnerPlus)	PMTCT, CCP	Cluster Randomized trial	% consistent condom use among pregnant couples	Baseline: 27%; Post-intervention: 60%	[8]	1
	Impact of primary health facility (PHF) and secondary/ tertiary health facilities (SHFs) on trends in ART initiation of children.	ART, PREV	Observational study	% of children initiated on ART in PHF	Baseline:17% Follow-up:44%	[10]	1
	Integrated ART in antenatal care (ANC) clinics compared to standard referral approach	ART, PMTCT, PREV	Stepped wedge cluster trial design	% of eligible pregnant enrolled within 60 days of HIV diagnosis (integrated service vs. referral service)	Intervention: 44.4%, Control: 25.3%	[54]	1
	Integrated nurse-midwife provided ART care within ANC clinics compared to standard referral approach	ART, PMTCT, PREV	Review	% of ART-eligible women initiating ART within pregnancy	Intervention: 86% Control: 12%	[55]	1
	Impact of primary health facility (PHF) and secondary/ tertiary health facilities (SHFs) on loss-to-follow-up rates	ART	Observational study	Adjusted rate ratio for lower LTFU (primary vs. secondary health facilities)	RR 0.55; p=0.022	[10]	1

Programme enabler	Intervention	Potential impact on programme area(s)	Type of evidence	Final effectiveness measure		Source	Grading
				Metric	Value		
Integration of services	Impact of primary health facility (PHF) and secondary/tertiary health facilities (SHFs) on mortality	ART	Observational study	Adjusted rate ratio for lower mortality (primary vs. secondary health facilities)	RR 0.66; p=0.028		1
	Immediate vs. early integration of ART during TB treatment and impact on mortality	ART	Randomized controlled trial	% with AIDS or death by 48 weeks	With CD4<50: 15.5% (immediate) vs 26.6% (early) With CD4>50: 11.5% (immediate) vs 10.3% (early)	[56]	1
Task shifting	Nurse Initiated Management of Antiretroviral Treatment (NIMART) compared to doctor-led management in patients initiating ART	ART	Cluster randomized controlled trial	Incremental cost-effectiveness ratio	US\$24 500/ death averted	[57]	1
	NIMART and decentralised care	ART	Cluster randomized controlled trial	Adjusted hazard ratio for mortality (NIMART vs. standard of care)	Primary: HR 0.92; 95%CI 0.76–1.12; p=0.401 CD4 201-350 cells/µl: HR 0.70; 95%CI 0.52–0.95; p=0.020 CD4 ≤200 cells/µl: 0.94; 95%CI 0.77–1.16; p=0.577	[12]	1
	Nurse-managed down-referral site vs doctor-managed clinic	ART, PMTCT, PREV	Observational study	Adjusted hazard ratio for mortality risk between doctor-led and nurse-led site	HR 1.51; 95% CI 0.90-2.55(no difference)	[13]	1
	Task shifting of HIV management from doctors to nurses	ART, PMTCT, PREV	Review	Mortality	no difference	[11]	1

Programme enabler	Intervention	Potential impact on programme area(s)	Type of evidence	Final effectiveness measure		Source	Grading
				Metric	Value		
	Nurse-led vs. doctor-led management of ART care for HIV infected patients	ART, PREV, PMTCT	Randomized control trial	Hazard ratio for composite failure (mortality, LTFU, virological/toxicity failure, withdrawn consent, defaulting, disease progression)	HR 1.09; 95%CI 0.89-1.33; p=0.42	[58]	1
Laboratories (diagnostic services)							
Point of care (PoC) technologies in PHC facilities	GeneXpert MTB/RIF test compared to sputum smear microscopy	ART, PREV, TB	Randomized controlled trial	% of same-day diagnosis (MTB/RIF group vs microscopy group)	24% vs 13%; p<0.001	[59]	1
	GeneXpert MTB/RIF test compared to sputum smear microscopy	ART, PREV, TB	Randomized controlled trial	% of drop-out (MTB/RIF group vs microscopy group)	8% vs 15%; p=0.0302	[59]	1
	Home-based HIV counselling and testing vs. VCT at local clinics	PREV, ART	Randomized controlled trial	% testing uptake	69% intervention vs 47% control arm;	[34]	1
	Home-based HIV counselling and testing vs. VCT at local clinics	PREV	Randomized controlled trial	% with multiple partners	3% intervention vs 6% control arm (55% reduction)		1
	Home-based HIV counselling and testing vs. VCT at local clinics	PREV	Randomized controlled trial	% with casual sexual partners	5% intervention vs 8% control arm (45% reduction);		1
	CD4 PoC	ART, PREV	Review	Pooled odds ratio of achieving the next step in the treatment cascade comparing PoC CD4 testing against standard of care	HIV testing to CD4 testing: 4.1; CD4 testing to receipt of result: 2.8; CD4 testing to ART initiation: 1.8	[36]	1

Programme enabler	Intervention	Potential impact on programme area(s)	Type of evidence	Final effectiveness measure		Source	Grading
				Metric	Value		
Blood safety							
Centralised model of transfusion services	No intervention	PREV		HIV prevalence among all donors 2012-2013	0.2%	[5]	
	No intervention	PREV		% of issued blood not being transfused (wasted)	6%		
	HIV antibody screening of donated blood	PREV	Review	No. of new HIV infections prevented by antibody screening/ 10,000 donations	150 to 1400	[4]	1
Human resources							
Training other cadres	Integration and training of community care workers (CCWs) to enhance collaborative TB/HIV/PMTCT/ home-based HCT activities	TB, PREV	Cluster randomized trial	% uptake of TB and STI symptoms screening services	Intervention: 44% (32%) for TB (STI) symptom screening; control: 10% (7%)	[35]	1
Monitoring, evaluation & reporting							
Electronic and other data collection	No intervention	ART	Observational study	Facility level data collation on ART using TIER.Net & EKAPA	87% facilities offering ART reported cohort outcomes for inclusion in the presented data	[42]	1
	No intervention	ART, PMTCT, PREV	Observational study	Odds ratio of horizontal vs vertical managers	Authority over HIV data collation: OR 7.26; 95%CI 1.9-27.4 Authority over HIV data use: OR 0.19; 95% CI 0.05-0.84	[41]	1

Programme enabler	Intervention	Potential impact on programme area(s)	Type of evidence	Final effectiveness measure		Source	Grading
				Metric	Value		
Employer practices							
On-site workplace services	Digital X-ray technology for TB screening	TB	Observational study	% decrease in incidence of occupational TB	60% (increase in detection rate 3.8%)	[25]	1
	On-site VCT testing at occupation clinic vs off-site VCT at free-standing clinics	ART, PREV	Cluster randomized controlled trial	Adjusted risk ratio for uptake of HIV testing (on-site compared to off-site)	RR 12.5 (95%CI 8.2 - 16.8)	[26]	1
	Mobile screening program	ART, PREV	Observational study	% diagnosed positive for one of the tested diseases (HIV, Hepatitis B, Syphilis, hypertension)	50.6%	[27]	1
Extending benefits to families and communities	Workplace voluntary testing and counselling program	ART, PMTCT	Observational study	Number of employees and families covered by Thuso HIV/AIDS Workplace Program	100% (over 30,000)	[29]	1
	Workplace voluntary testing and counselling program	ART, PREV	Observational study	% of spouses and partners of employees who have taken HIV test and know their status	65%		1
	Workplace voluntary testing and counselling program	ART, PREV	Observational study	Reduction of the average number of sick leave days/employee/year	from 25-40 days to 5-6 days		1

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4.3 UNIT COSTS

4.3.1 METHODS

The IC exercise defined a unit cost as the cost per unit of output delivered by an intervention, TE factor or enabler. The output unit may be a person, test, visit, patient year or an entire programme, but most often it will be a person reached by the particular intervention.

As mentioned in section 3.2.1, the project used a number of methods to establish the unit cost for each intervention:

First, the project team reviewed available estimates of the cost of each intervention and TE factor from both published and unpublished sources. The team gave greater weight to South African data over evidence from other countries, to data from cost analyses over data based on expenditure or budgets, and to bottom-up cost analyses over ingredient-based analyses^e. Care was also taken to include only those results of cost analyses that represented implementation of the intervention under the most recent guidelines, for the target population in question and at the relevant level of care.

Second, wherever necessary, the project team updated published unit cost estimates to represent more recent input costs, such as staff salaries and drug costs, while maintaining information on the types and quantities of inputs required for the intervention.

Third, where no unit cost could be found in the literature, cost was established using ingredient costing based on published data regarding the type and number of resources used in the intervention, and input costs from government commodity tenders, public servant remuneration documentation, retail advertisements, government programme costings and budgets from South Africa's current and past portfolio of GF grants. Finally, for selected interventions for which no published data on either unit cost or ingredients was available, information from budgets or expenditure records was used; in particular, this method was used to estimate units costs of male medical circumcision for the general population, for the three social behaviour change communication campaigns included in the analysis, and for a number of programme enablers.

The total cost of each intervention, TE factor or enabler was then calculated by multiplying the population covered by this intervention in a given year (an output of the epidemiological models) by the unit cost of this intervention.

4.3.2 RESULTS

Table 45 below gives an overview of the method used in arriving at the unit cost of each intervention, TE factor and enabler included in the South African HIV and TB Investment Case, the sources of all data, and the resulting unit cost.

^e For the purpose of this analysis, 'bottom-up costing' denotes the collection of resource use data (quantities) in a sample of people covered by an intervention or service and the collection of cost data (prices) in the same intervention or service. 'Ingredient-based costing' is the calculation of costs based on quantities and prices collected from or assumed based a number of sources.

Table 45: Summary of methods and sources used in calculating unit costs

Intervention/ Technical efficiency factor/ Enabler	Programme area	Unit cost	Cost value	Source	Notes
1a. HIV interventions					
Cotrimoxazole	ART	R 93.72	per patient year	[1]	
ART (Adults)	ART	R 3,292	per patient year	[2]	Cost reported is for 2014/15 only
ART (Paediatric)	ART	R 3,422	per patient year	[2]	Cost reported is for 2014/15 only
Male medical circumcision	MMC	R 1,210.19	per circumcision	CHAI (public sector sites) PEPFAR (NGO sites); both PC	Weighted average of public sector and NGO services
Early infant male circumcision	MMC	R 605.10	per circumcision	Based on above	Assumed to be 50% of adult MMC cost
MMC age group targeting	MMC	R 1,322.90	per circumcision	From ingredients	MMC cost augmented with outreach and community mobilisation costs
Condom use	CCP	R 0.68	per condom	From ingredients	Weighted average of male and female condoms, including distribution costs
Male and female condom education	CCP	R 45.46	per person educated	From ingredients, based on [3]	
PMTCT (mother not on any ART)	PMTCT	R 62.38	per mother-baby pair	[2]	
PMTCT B (mother not on lifelong ART)	PMTCT	R 2,260.03	per mother-baby pair		
Infant testing at birth	PMTCT	R 389.49	per patient year	From ingredients	
Infant testing at 6 weeks	PMTCT	R 369.11	per patient year		
HCT (negative result)	HCT	R 81.65	per test		
HCT (positive result)	HCT	R 89.98	per test		
Testing of pregnant women (negative result)	HCT	R 81.60	per test		
Testing of pregnant women (positive result)	HCT	R 89.93	per test		
Testing of adolescents	HCT	R 234.13	per test		

Intervention/ Technical efficiency factor/ Enabler	Programme area	Unit cost	Cost value	Source	Notes	
SBCC Campaign 1 (Message: testing, multiple partners)	SBCC	R 9.78	per person reached	Expenditure records from implementing agencies		
SBCC Campaign 2 (Message: condom usage and self- efficacy)	SBCC	R 5.00	per person reached			
SBCC Campaign 3 (Message: testing, condom usage and self-efficacy, MMC)	SBCC	R 2.74	per person reached			
Post-Exposure Prophylaxis (PEP)	other	R 615.61	per patient year	From ingredients		
Pre-Exposure Prophylaxis (PrEP)	PREV	R 1,009.73	per patient year			
Microbicides	PREV	R 404.28	per patient year			
Palliative care	other	R 767.41	per patient	Lolliot (PC)		
Inpatient care	other					
pre-ART, <200 cells/microl		R 1,292.20	per patient year	[4]		
pre-ART, 200-349 cells/microl		R 754.56				
pre-ART, 350-500 cells/microl		R 616.76				
pre-ART, >500 cells/ microl		R 299.87				
ART, <200 cells/ microl		R 1,586.16				
ART, 200-349 cells/ microl		R 1,266.10				
ART, 350-500 cells/ microl		R 649.87				
ART, >500 cells/ microl		R 577.18				
1b. TB interventions						
Flourescent smear microscopy (for new and retreatment patients, and RR TB treatment monitoring)	TB	R 123.05	per test		Cunnama (PC)	
Liquid culture (as diagnostic test for Xpert-, EPTB; RR TB treatment monitoring)	TB	R 185.14	per test	Cunnama (PC)		

CHAPTER 4

Intervention/ Technical efficiency factor/ Enabler	Programme area	Unit cost	Cost value	Source	Notes
Xpert MTB/RIF (as first line diagnostic test)	TB	R 226.54	per test	Cunnama (PC)	
Symptom screening by lay worker based in health facility	TB	R 6.55	per test	Foster (PC)	
Line probe assay (as genotypic resistance testing)	TB	R 351.89	per test	Cunnama (PC)	
X-rays (as screening for high risk groups)	TB	R 103.50	per test	Cunnama (PC)	
First-line TB drugs (adults)	TB	R 379.49	per treatment course	Vassall (PC)	
First-line TB drugs (children)	TB	R 321.99	per treatment course	Vassall (PC)	
Second-line TB drugs (MDR and RR TB)	TB	R 22,389.63	per treatment course	based on [5]	
Second-line TB drugs (XDR TB)	TB	R 57,497.77	per treatment course	based on [5]	
Hospitalisation					
First line patients	TB	R 5,764.38	per stay	From ingredients	
MDR and RR TB	TB	R 105,404.91	per stay	based on [5]	
XDR TB	TB	R 105,404.91	per stay	based on [5]	
Outpatient clinic utilization (MDR and RR TB)	TB	R 14,213.45	per stay	based on [5]	
Preventive therapy (IPT)	TB	R 229.99	per patient year	From ingredients	
2. Technical efficiency factors (HIV only)					
GP down referral	ART	R 4,810.28	per patient year	[6] [2]	Full cost of ART under GP down referral Cost reported is for 2014/15 only
Community based adherence supporters (Adults)	ART	R 445.49	per patient year	[7] Kheth'Impilo (PC)	

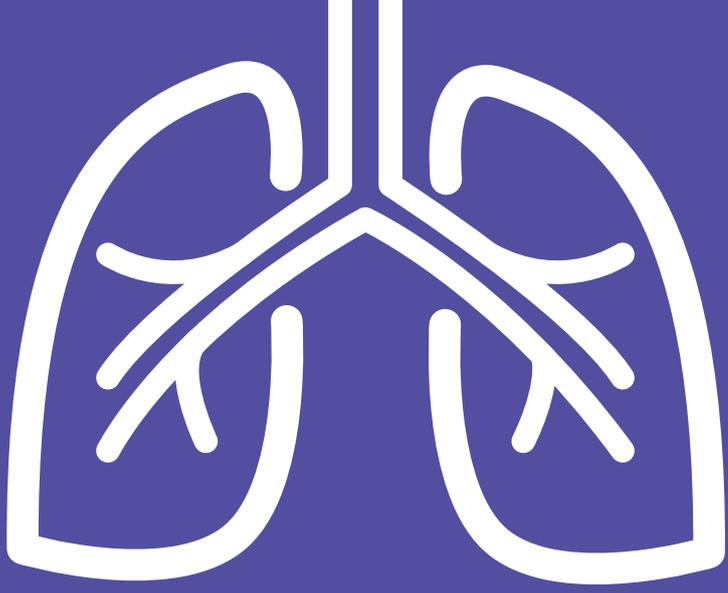
Intervention/ Technical efficiency factor/ Enabler	Programme area	Unit cost	Cost value	Source	Notes
Adherence clubs	ART	R 3,661.08	per patient year	[2] adjusted based on [8]	Full cost of ART under adherence clubs Cost reported is for 2014/15 only
Point-of-care CD4	ART	R 218.45	per test	[9]	
Provider initiated counselling and testing (negative result)	HCT	R 85.91	per test	[10]	
Provider initiated counselling and testing (positive result)	HCT	R 128.40	per test	[10]	
Mobile HCT (negative result)	HCT	R 92.69	per test		
Mobile HCT (positive result)	HCT	R 120.59	per test	Personal communication based on [11]	
Home based HCT (negative result)	HCT	R 114.46	per test		
Home based HCT (positive result)	HCT	R 145.32	per test		
Workplace HCT	HCT	R 153.84	per test	From ingredients	
HCT invitations to partners of pregnant women (negative result)	HCT	R 85.14	per test	From ingredients	
HCT invitations to partners of pregnant women (positive result)	HCT	R 95.47	per test	From ingredients	
3. Critical enablers					
Teacher support	ENB	R 136.00	per student reached	Mudekunye (PC)	
SASA! Community based gender-based violence intervention	ENB	R 245.78	per person reached	Michaels-Igbokwe (PC)	
Life skills and vocational training for adolescent girls	ENB	R 207.44	per person reached	From ingredients, based on [12]	
School based HIV/STI risk reduction intervention	ENB	R 658.11	per person reached	From ingredients, based on [13]	

Intervention/ Technical efficiency factor/ Enabler	Programme area	Unit cost	Cost value	Source	Notes
Parental monitoring	ENB	R 1,061.78	per parent monitored	Expenditure records from implementing agency	
Positive parenting	ENB	R 1,061.78	per parent trained		
Risk reduction counselling for alcohol in STI clinics	ENB	R 186.51	per participant	From ingredients, based on [14]	
Supporting adolescent orphan girls to stay in school	ENB	R 2,706.00	per child supported	From ingredients, based on [15]	
State-provided child-focused cash transfers	ENB	R 400.78	per child supported	From ingredients, based on [16]	

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CHAPTER 5

DESIGNING AN OPTIMAL
HIV AND TB RESPONSE
FOR MAXIMUM IMPACT

5.1 RESULTS OF THE HIV INVESTMENT CASE: THE OPTIMAL HIV RESPONSE

This chapter summarises the findings of the Investment Case modelling exercise aiming to identify the optimal mix of interventions for maximum impact on the HIV epidemic in South Africa. We report all results in two separate time periods- five years, including the current and the next four financial years (2014/15 to 2018/19), and 20 years, including the current and the next 19 financial years (2014/15 to 2033/34). This allows us to compare the cost and the impact of changes in policy over the short- as well as the long-term, and whether or not this impact changes depending on the time period. It also allows us to compare the results of those scenarios which we have projected over 20 years with the government scenario which we ran only for as many years as there were government targets available (until 2018/19). Please also note that for the optimisation scenarios we report the results of optimising interventions by cost per life year saved (rather than by cost per HIV infection averted), for reasons discussed in Section 3.2.1.

5.1.1 Results at current levels of technical efficiency

As set out in Section 3.2.1, we analysed all scenarios (including the baseline scenario) at a) current and b) optimal levels of technical efficiency of each intervention. While we assume we can reach high coverage levels (90%) under both, only the second set of results fully incorporates the cost and impact of the additional factors (termed technical efficiency or TE factors) as well as additional social and programme enablers and development synergies required to reach these levels.

This section presents the results for each of the scenarios at *current* levels of technical efficiency- in other words, this section examines what the impact would be of scaling up interventions further without improving the way they are being implemented or taking enablers or synergies outside the health sector into account.

Packages of care and coverage

Before looking at the impact on cost and outcomes, this section explains what interventions were included at what level of coverage in each of the scenarios. (Note that for the analysis of scenarios at current level of technical efficiency, no technical efficiency factors, enablers or synergies were included.)

Baseline and government target scenarios

The packages of care for the baseline and government target scenarios were introduced in chapter 4 and are summarised again in Table 46; they are based on available government documentation of achieved coverage by 2013/14 and planned targets for 2014/15 to 2018/19, respectively.

Table 46: Coverage under baseline and government target scenarios

Intervention	Baseline	Government targets
Cotrimoxazole	90%	90%
ART under current guidelines	60%	90%
Universal test and treat	0%	-
Medical male circumcision (MMC)	30%	>90%
MMC age group targeting	-	-
Early infant male circumcision	10.5%	10.5%

Intervention	Baseline	Government targets
Condom availability	60%	90%
Condom education	30%	30%
PrEP for sex workers	0%	0%
PMTCT	80%	90%
Infant testing at birth	0%	0%
Infant testing at 6 weeks	60%	60%
General population HCT	60%	60-90%
Testing of pregnant women	90%	90%
Testing of adolescents	30%	30%
SBCC campaign 1	30%	30%
SBCC campaign 2	90%	90%
SBCC campaign 3	60%	60%
PrEP for discordant couples	0%	0%
PrEP for adolescents	0%	0%
Microbicides	0%	0%

Optimisation without constraint

For the optimisation scenario without budget constraint, we ranked options by their incremental cost-effectiveness over a shifting baseline including the original baseline as well as all previously selected options, while disregarding any option that had both higher cost and lower effectiveness.^a (For more details on the optimisation routine, see Chapter 3.2.1.) This resulted in 21 interventions with coverage levels that were deemed more effective and/or more cost-effective than the baseline coverage with the same intervention (Table 47). Amongst these interventions, increasing condom availability to 90% was the most cost-effective, followed by increasing the reach of Sexual Behaviour Change Communication (SBCC) campaign 1 to 90% of the general population (with a message encouraging testing and discouraging multiple partners, aimed at the general population), and offering all Medical Male Circumcision (MMC) interventions that we analysed to 90% of the respective target population, with the exception of Early infant male circumcision. Within the MMC interventions, the most cost-effective option was providing MMC to all highly sexually active men regardless of age. After this had been rolled out, targeting the remaining boys and men in all other age group was the next cost-effective option.

Amongst the HIV Counselling and Testing (HCT) interventions, testing infants at 6 weeks was the most cost-effective intervention. The next most cost-effective intervention was providing ART at current guidelines (including eligibility at 500 cells/microl and PMTCT B+) at 90% coverage. This was also the most effective intervention in terms of saving life years- 16 million over 20 years, an order of magnitude higher than everything else.

The next increase in ART coverage, to 90% of all HIV positives as part of Universal Test and Treat (UTT) is quite a lot less cost effective than increasing access to ART at current guidelines to 90% coverage, and there are a number of interventions that rank between the two, namely increasing HCT coverage to 90% and scaling up SBCC campaign 3 (with a message of increasing HIV testing, condom usage, and MMC uptake). Note that after all interventions ahead of it in the list, including UTT, are implemented, testing 90% of adolescents becomes cost saving- the only cost saving option to appear in the second half of the list.

Amongst the remaining prevention interventions, PrEP for sex workers was the most cost-effective, followed by microbicides for the general female population at 90%^b, PrEP for the HIV-negative partner in discordant couples, and

^a Specifically, this excluded only one intervention - reducing condom availability to 30% - from our analysis.

condom education (modelled on an intervention limited to married couples), all at 90% coverage. Scaling up Early Infant Male Circumcision (EIMC) to 90% was the least cost-effective intervention of all those included, but this was largely due to the 20-year time horizon of the analysis which meant that the absolute majority of the impact of this intervention would fall in the period beyond 20 years, ie, after sexual debut of the circumcised infants.

Table 47: Ranking of options^c in Optimisation without constraint scenario

Intervention (coverage)	Life years saved ^d	Incremental cost	Incremental cost effectiveness ratio
Condom availability (90%)	2,438,320	-15,014	Cost saving
MMC (90%)	1,196,860	-2,515	Cost saving
SBCC 1 (90%)	791,200	-1,406	Cost saving
MMC targeting 15-19	266,260	-510	Cost saving
MMC targeting 25-49	209,610	-476	Cost saving
MMC targeting 20-24	170,960	-344	Cost saving
MMC targeting 10-14	5,980	-1	Cost saving
Infant testing at 6 weeks (90%)	352,450	264	749
ART at current guidelines (90%)	16,104,650	16,793	1,043
PMTCT ^e (60%)	-271,900	-799	2,940
HCT (90%)	1,684,450	10,070	5,978
SBCC 3 (90%)	104,490	1,370	13,111
UTT (90%)	2,461,308	36,043	14,644
Testing of adolescents (90%)	66,873	-927	15,303
Infant testing at birth (90%)	214,338	7,868	36,710
Sex worker PrEP (90%)	9,654	1,028	106,452
Microbicides (90%)	806,584	156,414	193,922
Adolescent PrEP (90%)	42,372	12,914	304,776
Discordant couple PrEP (90%)	2,624	1,864	710,421
Condom education (90%)	3,073	17,766	5,781,471
EIMC (90%)	7	2,067	295,239,305

While the coverage with most interventions was scaled up in the final set of options, only one intervention was scaled down- the initiation of pregnant women on ART (termed PMTCT), which was less effective, and as a result, less cost-effective than the combination of ART at 500 CD4 cells/microl and PMTCT B+ at 90% coverage which had been selected ahead of it (see Table 47).

b As noted in Chapters 3.1 and 3.2.1, microbicides were included as an intervention because at the time of the evidence review (until 31 Jan 2015), the available evidence suggested that they might be effective.

c All other options remain at baseline coverage, e.g. cotrimoxazole at 90%, etc.

d Life years saved and cost are calculated incremental to *baseline + all options further up in the list*.

e This refers to the initiation of pregnant women on ART only; continuation of ART for life (PMTCT B+) is covered under "ART at current guidelines".

Optimisation with budget constraint

As explained in Section 3.2.1, for this scenario we re-ran the optimisation of options by their incremental cost-effectiveness over the shifting baseline until the total cost of the package was above the currently committed funding envelope for HIV for 2014/15 to 2016/17 from the three main sources for such funding, the South African government, the US President's Emergency Plan for AIDS Relief (PEPFAR), and the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM). This reduced the number of options included from 19 to 8 (Table 48). The package included all interventions that were cost-saving over 20 years as well as ART under current guidelines at 90%, though the coverage with ART in 2018/19 had to be reduced from 90% to 85% to still be affordable.

Table 48: Final set of options included in Optimisation with budget constraint scenario

Intervention
Condom availability (90%)
MMC (90%)
SBCC 1 (90%)
MMC targeting (10-14, 15-19, 20-24, 25-49)
Infant testing at 6 weeks (90%)
ART under current guidelines (at 85%)

Optimisation towards 90-90-90 targets

As explained in Section 3.2.1, for this scenario we re-ran the optimisation of options by their incremental cost-effectiveness over the shifting baseline until the 90-90-90 targets adopted by UNAIDS in 2014 [1], and confirmed as a target for South Africa by the South African Minister of Health during his budget speech in July 2014, were reached [2]. These targets include ensuring that 90% of HIV positive people know their HIV status, that 90% of those tested HIV positive initiate ART, and that 90% of those ever initiated on ART are virally suppressed [1].

In order to reach the 90-90-90 targets by 2020, one has to move further down the list of interventions ranked by cost effectiveness under the Unconstrained optimisation scenario and implement increasingly less cost effective interventions (Table 49). These include scaling up HCT and SBCC Campaign 3 (with a message of increasing HCT, condom use, condom self-efficacy, and MMC), increasing HIV testing to 90%, and improving linkage to care and escalating initiation under a policy of universal test and treat (UTT).

Table 49: Final set of options included in Optimisation towards 90-90-90 targets scenario

Intervention (coverage)	Life years saved ^f	Incremental cost	Incremental cost effectiveness ratio
Condom availability (90%)	2,438,320	-15,014	Cost saving
MMC (90%)	1,196,860	-2,515	Cost saving
SBCC 1 (90%)	791,200	-1,406	Cost saving
MMC targeting 15-19	266,260	-510	Cost saving
MMC targeting 25-49	209,610	-476	Cost saving
MMC targeting 20-24	170,960	-344	Cost saving

^f Life years saved and cost are calculated incremental to *baseline + all options further up in the list*.

Intervention (coverage)	Life years saved ^f	Incremental cost	Incremental cost effectiveness ratio
MMC targeting 10-14	5,980	-1	Cost saving
Infant testing at 6 weeks (90%)	352,450	264	749
ART at current guidelines (90%)	16,104,650	16,793	1,043
PMTCT ^g (60%)	-271,900	-799	2,940
HCT (90%)	1,684,450	10,070	5,978
SBCC 3 (90%)	104,490	1,370	13,111
UTT (90%)	2,461,308	36,043	14,644

Programme coverage under each scenario

Based on the difference in ART coverage described above, the total number of patients on ART differed drastically between scenarios. From a baseline of 3.4 million in 2015, both the unconstrained optimisation and 90-90-90 scenarios contained a rapid scale up of ART in the immediate future to 6 million patients on ART by 2017 before flattening out for the rest of the projection period. This is a result of implementing universal test and treat and achieving 90% ART coverage by 2020.

On the other hand, the government targets and constrained optimisation scenarios (which track each other quite closely) implied a slower, more moderate scale up of ART, reaching 6 million only by 2022 and flattening out for the rest of the projection period. Most notably, all scenarios cross the baseline during our modelling period, implying a year on year reduction in the number of patients on ART ever afterward. The key difference and central policy question lies in when that turning point is reached.

The total number of HIV tests performed ranges from 10 to 13 million per year under both the baseline and the constrained optimisation scenarios, 33 to 44 million per year under the 90-90-90 scenario, and 40 to 94 million in the unconstrained optimisation scenario. The large scale-up under the unconstrained scenario reflects not only the scale up of HCT in the general population, but also PrEP and microbicides that include HIV testing four times a year.

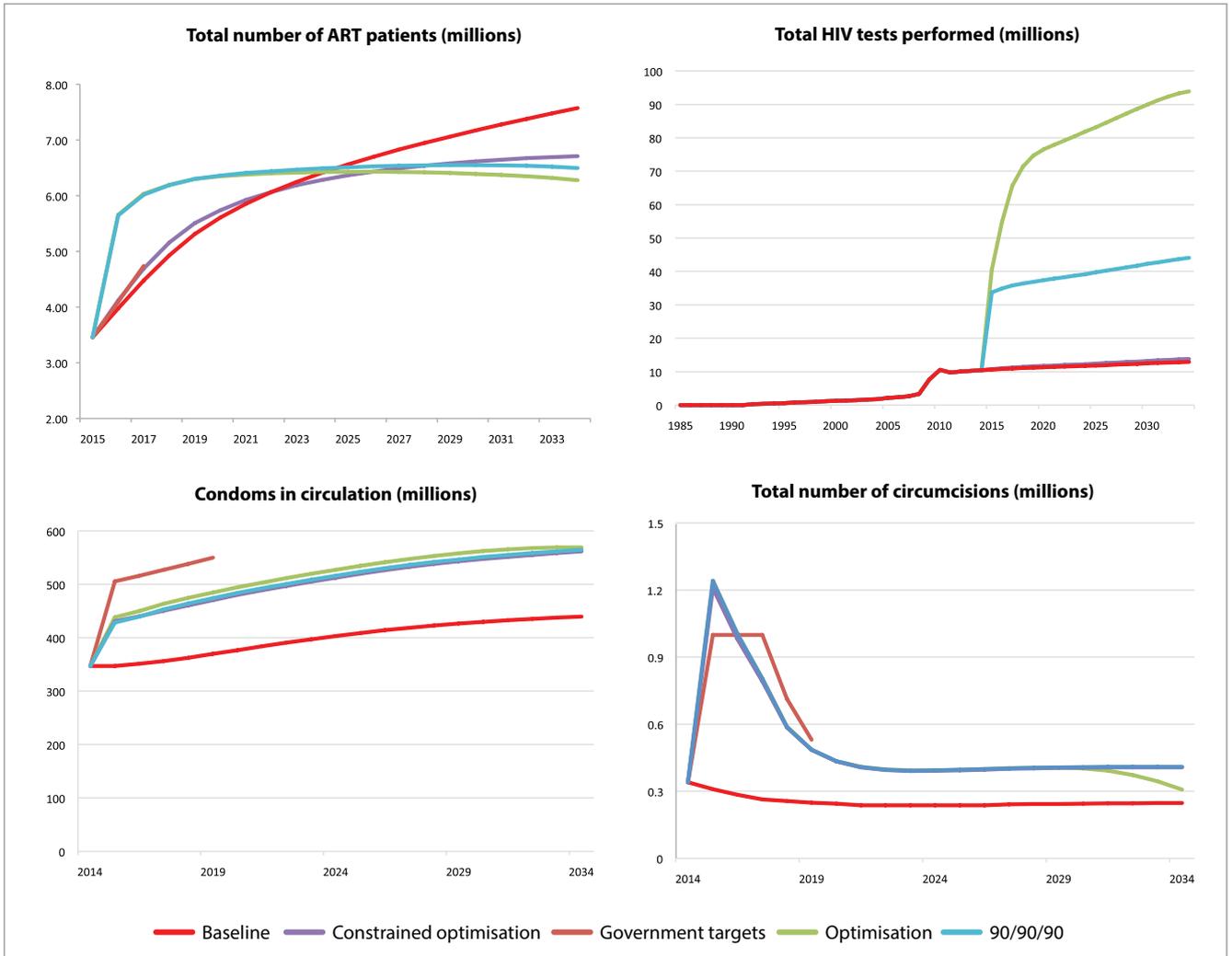
The number of circumcisions performed is relatively similar between the constrained optimisation, government targets, and 90-90-90 scenarios, as MMC is scaled up rapidly in each of the scenarios. Note that optimisation includes even more circumcisions due to the scale up of early infant male circumcision. Most noteworthy is the fact that all scenarios experienced a massive dip in the number of circumcisions shortly after scale up. The model reached a saturation of circumcisions, given inherent assumptions about the limited number of men willing to undergo circumcision, suggesting that current government targets of 1 million per year may be unsustainable.

The difference in the number of condoms in circulation between scenarios also raises questions about the sustainability of government targets. Whilst current policy recommends the distribution of 1 billion condoms each year, the model results indicated that these numbers are too high. Given realistic assumptions about the nature of condom usage and current sexual behaviour, the model suggested that distributing between 300,000 to 600,000 condoms a year will be sufficient to cover the number of protected sex acts that occur each year, even allowing for a liberal assumption of condom wastage (where only one in three distributed are used in the first place).

Figure 26 summarises several key output indicators that highlight the main differences between the scenarios.

^g This refers to the initiation of pregnant women on ART only; continuation of ART for life (PMTCT B+) is covered under "ART at current guidelines".

Figure 26: Key HIV output indicators by scenario



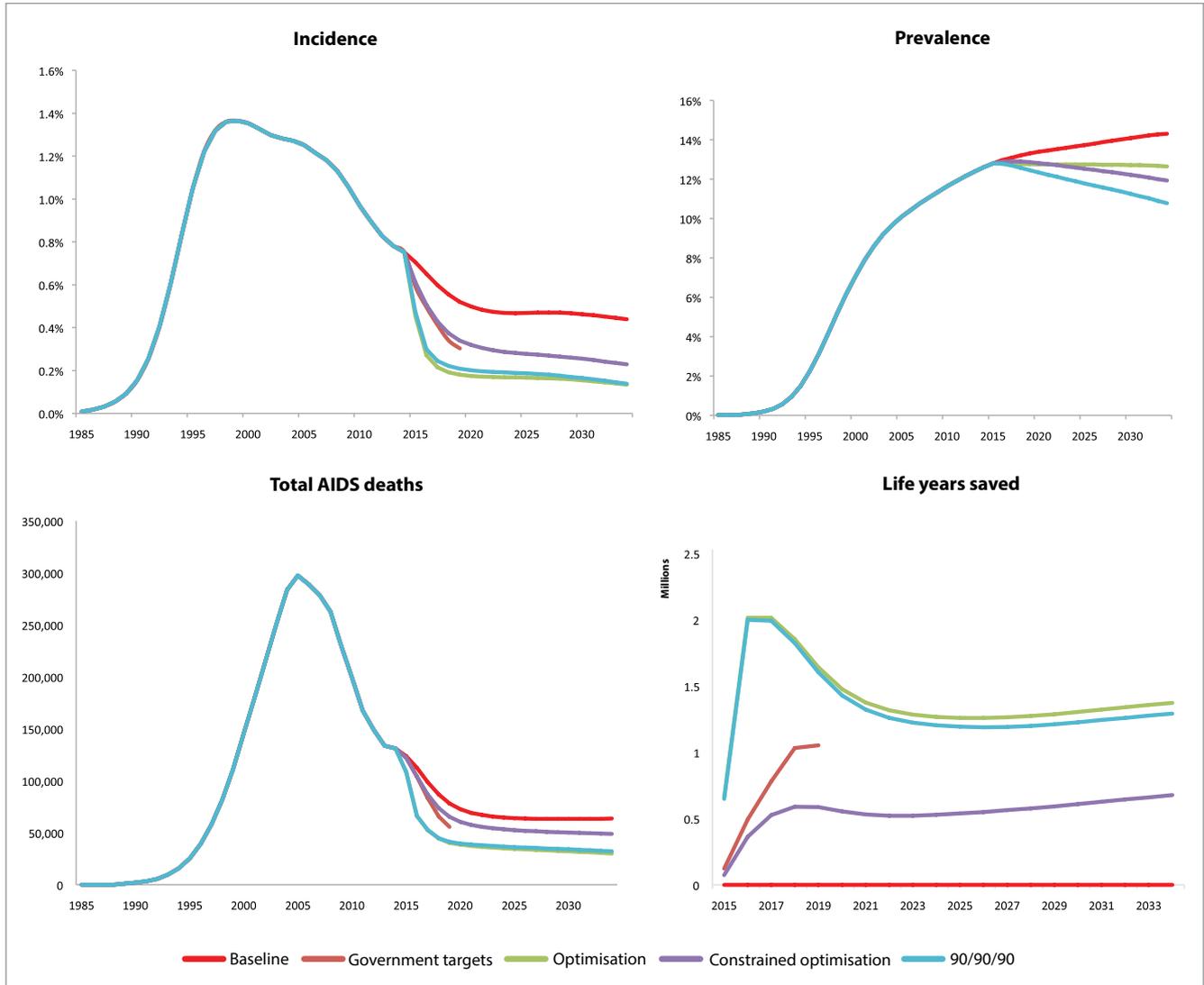
Epidemiological impact

After summarising the packages of care defined by intervention coverage and key output indicators for each of the five scenarios of analysis in the previous sections, this section reviews the impact of each scenario on the development of the HIV epidemic in South Africa over the next 20 years.

Incidence, total deaths from AIDS and prevalence

Until 2013/14, all scenarios followed the same development of the HIV epidemic as the baseline scenario, with HIV incidence peaking at 1.365% in 1998, then decreasing- first slowly, then, from the start of the national ART roll-out in 2004 onwards, more rapidly, AIDS deaths peaking at 297,368 per year in 2004, then steadily reducing to 133,626 in 2013, and HIV prevalence increasing rapidly to 10% in 2004, then rising somewhat slower, to 12.4% in 2013 (Figure 27).

Figure 27: HIV incidence, prevalence, life years saved and total AIDS deaths, by scenario



Under the baseline scenario, from 2014/15 onwards incidence continued to decrease at about the same pace until 2019, then stabilised at 0.47% to 0.44% over the remaining 15 years. Under all other scenarios, incidence dropped dramatically from 2014/15 onwards, with the largest reductions in the unconstrained optimisation scenario (with the 90-90-90 scenario coming in at a close second), and the government targets and constrained optimisation scenarios following an almost identical path. The constrained optimisation scenario reduced incidence by half when compared to the baseline scenario, to 0.22% by 2033/34; the unconstrained optimisation scenario reduced it even further, to 0.13%. Of note is that none of the scenarios managed to reduce incidence to below 0.1%, the level proposed necessary for ‘virtual elimination’ of HIV by Granich et al [3].

Total AIDS deaths followed a similar pattern, with a decline seen in all scenarios- with the largest decrease, to 30,115 deaths per year in 2034/35, in the unconstrained optimisation scenario and the 90-90-90 scenarios, the constrained optimisation scenario still decreasing to 48,938 deaths per year, and the government scenario following a very similar path to the first five years of the constrained optimisation scenario.

As a result of the development of incidence and mortality, prevalence in the baseline scenario continued to increase, to a maximum of 14.3% in 2034/35, and declined in all other scenarios, to 12.6% in the unconstrained and to 11.9% in

the constrained optimisation scenario. Whilst it is difficult to determine how much each intervention in the package contributed to the overall impact, increasing ART coverage likely played a significant role, not only because it differed most significantly between scenarios (Figure 26), but also because the ART scale up options contributed the greatest amount of life years saved in their respective baselines (Table 47).

Table 50 reports the progress towards two health targets laid out in the National Development Plan by 2030 and the UNAIDS 90-90-90 targets by 2020. The scenarios did not differ drastically when compared to the NDP targets. None of the scenarios reached a life expectancy of 70 years, or eradicated HIV amongst under 20 year olds, although all scenarios came close on both accounts. In terms of the 90-90-90 targets, only the 90-90-90 and unconstrained optimisation scenarios allowed us to reach the targets, the former by design, and the latter since it included the 90-90-90 mix of interventions and more. This suggests that South Africa needs to indeed further scale up its response, dramatically so over the next years, if it is to reach the UNAIDS targets by 2020.

Table 50: Progress towards government and UNAIDS targets under each HIV scenario

	Current (2015)	Target	Baseline	Unconstrained optimisation	Constrained optimisation	90-90-90
NDP targets (by 2030)						
Life expectancy	62.02	70	67.18	68.14	67.66	68.17
Generation free of HIV						
- Prevalence <20 year olds	3.6%	0	1.9%	1.6%	1.4%	1.1%
- Incidence < 20 year olds	1.0%	0	0.7%	0.2%	0.3%	0.2%
90-90-90 targets (by 2020)						
% of all people living with HIV who know their status	85%	90%	92%	99%	94%	98%
% of all people diagnosed with HIV who receive sustained antiretroviral therapy	60%	90%	81%	94%	85%	94%
% of people receiving antiretroviral therapy who have viral suppression ^h	N/A	90%	N/A	N/A	N/A	N/A

New HIV infections

In the baseline scenario, if interventions continued to be delivered at the current (i.e., 2013 or 2014) level of coverage, a total of 1,439,654 HIV infections would occur over five years, and 5,115,877 infections over 20 years (Table 51). The government scenario reduced the number of HIV infections over the next five years to 1,017,880- a reduction by 421,774 infections, or 29%. The optimisation scenarios, despite being set up to optimise interventions by their impact on life years lost, not infections averted, reduced this number by 57% and 66% without budget constraint, by 25% and 37% with budget constraint, and by 52% and 59% under the 90-90-90 targets, over 5 and 20 years, respectively.

AIDS deaths and life years lost due to AIDS

Under the baseline scenario, more than 500,000 will die of AIDS over 5 years, and 1.5 million over 20 years. This results in over 5 years more than 20 million life years and almost 60 million life years being lost to AIDS over 5 and 20 years, respectively, when compared to perfect life expectancy in an HIV-free cohort (Table 51). Under the government scenario, 14% of AIDS deaths would be averted and 3,484,160 or 16% of life years lost to AIDS would be saved over 5 years.

^h Note that we are unable to report on progress towards this target since viral suppression is not explicitly modelled in Thembisa.

The optimisation scenarios would save 38% and 47% of lost life years without constraint, 10% and 18% with budget constraint, and 37% and 45% under the 90-90-90 targets, over the next 5 and 20 years, respectively, with very similar percentages for AIDS deaths averted.

Table 51: Summary of epidemiological results by scenario (Total numbers and % change on baseline)

	Baseline	Government targets	Optimisation without constraint	Optimisation with constraint	Optimisation towards 90-90-90
Total new HIV infections					
2014/15 - 2018/19	1,439,654	1,017,880	618,311	1,074,311	688,680
2014/15 - 2033/34	5,115,877	-	1,754,570	3,234,578	2,112,296
HIV infections averted (% change on baseline)					
2014/15 - 2018/19	-	421,774 (-29%)	821,344 (-57%)	365,343 (-25%)	750,974 (-52%)
2014/15 - 2033/34	-	-	3,361,307 (-66%)	1,881,299 (-37%)	3,003,581 (-59%)
Total AIDS deaths					
2014/15 - 2018/19	499,584	430,137	311,483	452,135	313,499
2014/15 - 2033/34	1,473,686	-	818,433	1,238,994	845,794
AIDS deaths averted (% change on baseline)					
2014/15 - 2018/19	-	69,447 (-14%)	188,101 (-38%)	47,449 (-9%)	186,085 (-37%)
2014/15 - 2033/34	-	-	655,252 (-44%)	234,692 (-16%)	627,892 (-43%)
Total life years lost due to AIDS					
2014/15 - 2018/19	21,711,080	18,226,920	13,527,710	19,571,480	13,642,710
2014/15 - 2033/34	59,425,080	-	31,475,398	48,585,710	32,634,462
Life years saved (% change on baseline)					
2014/15 - 2018/19	-	3,484,160 (-16%)	8,183,370 (-38%)	2,139,600 (-10%)	8,068,370 (-37%)
2014/15 - 2033/34	-	-	27,949,682 (-47%)	10,839,370 (-18%)	26,790,618 (-45%)

As with HIV infections averted, the unconstrained optimisation scenario was the most effective, very closely followed by the 90-90-90 scenario- saving more than three times as many life years as the constrained optimisation scenario, and more than twice times as many as the government scenario, as a result of scaling up almost all available interventions to maximum coverage. This of course however comes at a cost.

Cost and cost-effectiveness

After looking at the epidemiological impact of each scenario, the following section describes the cost and cost-effectiveness of each scenario, in total and incremental to the baseline scenario.

Cost by programme area

When looking at the contribution of each of the programme areas to total cost, the distribution amongst areas differed somewhat between the scenarios (Table 52). As in previous cost analyses of the South African HIV programme, the cost

of the ART component of the Care and Treatment programme area was by far the largest contributor, with between 56% and 77% of total cost. The second largest component in all but the unconstrained optimisation scenario was the palliative and inpatient care component of the Care and Treatment programme area, with between 10% and 16% of total cost. Each of the remaining programme areas contributed less than 5% to total cost in any given scenario, with the exception of HCT which made up 14% of the total cost of the unconstrained optimisation scenario, rendering it the second most expensive programme component after ART in that scenario. The lowest share of total cost, again in all but the unconstrained optimisation scenario, was contributed by the Other Biomedical Prevention programme area; this is due to the fact that two of the three interventions included in this programme area, PrEP and microbicides, have not yet been rolled out in the public sector in South Africa, and no published targets are available for them yet, resulting in 0% coverage and zero cost at baseline and in the government target scenario for these interventions. In the optimisation scenarios these interventions ranked low in terms of cost effectiveness, resulting in them not being selected under the budget constraint in the constrained budget scenario.

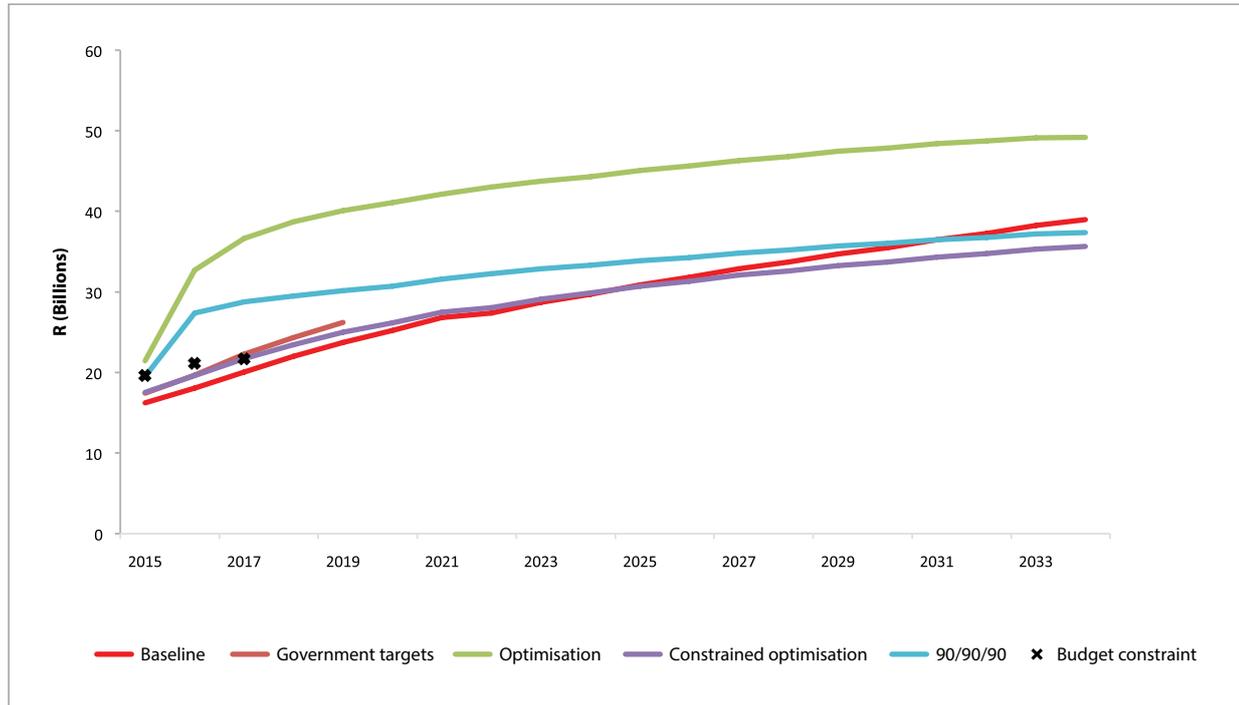
Table 52: Distribution of cost between programme areas, by scenario

Intervention	Baseline	Government targets	Optimisation without constraint	Optimisation with constraint	90-90-90
Care and treatment					
- ART	77%	68%	56%	76%	73%
- Inpatient care	15%	16%	9%	14%	12%
- Palliative care	1%	2%	0.8%	1%	1%
Medical male circumcision	0.9%	4%	2%	2%	2%
Condom comprehensive programming	2%	4%	4%	2%	2%
Prevention of mother to child transmission	0.3%	0.4%	0.4%	0.2%	0.2%
HIV counselling and testing	3%	4%	14%	3%	9%
Social behaviour change communication	1%	1%	0.9%	1%	1%
Other biomedical prevention	0.1%	0.1%	13%	0.1%	0.1%

Development of cost over time

In terms of the development of cost over time, Figure 28 shows that while all other scenarios were more expensive than the baseline scenario during the first ten years, by 2025 the constrained optimisation scenario became less expensive by year than the baseline scenario, with increasing savings over baseline every year thereafter. The unconstrained optimisation scenario however continued being more expensive throughout the projection period, by roughly the same amount year on year. The 90-90-90 scenario fell between the two, following the same trajectory of the unconstrained optimisation scenario but peaking at significantly lower cost and crossing the baseline by 2032.

Figure 28: Total cost of HIV programme



Note that even though we included the cost of inpatient care in order to compute the cost-effectiveness of interventions, it is excluded here since the HIV budget does not cover it.

As with many of the results presented above, the government scenario closely followed the path of the first five years of the constrained optimisation scenario. Given that the two had similar epidemiological impacts, and that the government targets scenario was more effective than the constrained optimisation scenario as measured by life years saved over 5 years, the current mix of interventions under government policy is relatively cost effective, and therefore allocatively efficient at the current budget constraint. However, it is important to note that questions remain over the feasibility of the government scenario – most notably, the government targets scenario includes far higher levels of condom distribution, and slightly higher levels of medical male circumcision, than the model suggests is possible.

Regardless of scenario, it is important to note the impending budgetary shortfall beyond the short term (the duration of the MTEF, 2014/15 to 2016/17- see Section 2.3). The unconstrained optimisation and 90-90-90 scenarios, whilst containing the greatest epidemiological impact, far exceeded the potential future HIV budget (based on a crude extrapolation of current budgetary data), and continued to increase in cost year on year throughout the projection period. This result suggests that, unlike what was shown in other countries' Investment Cases, frontloading the HIV response in South Africa will not lead to a reduction in total cost year on year in the near future. Although front-loading certainly leads to a greater epidemiological impact, the nature of South Africa's large scale generalised epidemic and higher cost of ART provision suggests that HIV is more persistent and the total cost remains high given the large number of people remaining on treatment over a life time. Even under the constrained optimisation and baseline scenarios, the total cost exceeds the current HIV budget from 2016/17 onwards. This reinforces the need for renewed (and expanded) financial commitment from the South African Government if the HIV response is to be sustained in the future.

Total and incremental cost

Under the baseline scenario, the HIV programme would cost R122 billion and R688 billion over 5 and 20 years, respectively (Table 53); the government targets scenario would cost only marginally more (8%) over 5 years. Optimisation without budget constraint, while being very effective, would increase the cost of the baseline scenario by 57% and 38% over 5 and 20 years, respectively- meaning that the largest cost increases would be at the beginning of the programme, during the period of fastest scale-up of, in particular, the most costly interventions such as ART. The constrained optimisation scenario would increase cost only marginally when compared to the baseline scenario, by 6%, over the first five years; over the longer term it would in fact be cost-saving, though only just- saving R14 billion, or 2% of total cost, over 20 years. The 90-90-90 scenario, even though being as effective as the unconstrained optimisation scenario, comes at a much lower cost; it would increase cost by only 29% over 5 years, and be only marginally more expensive over 20 years (an increase by 8%), mostly as a result of the cost-savings brought about by rapidly increasing ART access by 2020.

Table 53: Summary of cost by scenario

	Baseline	Government targets	Optimisation without constraint	Optimisation with constraint	Optimisation towards 90-90-90
Total cost [billion 2014 ZAR]					
2014/15 - 2018/19	122	131	191	129	157
2014/15 - 2033/34	688	-	947	675	743
Incremental cost [billion 2014 ZAR] (% change on baseline)					
2014/15 - 2018/19	-	10 (8%)	70 (57%)	7 (6%)	35 (29%)
2014/15 - 2033/34	-	-	259 (38%)	-14 (-2%)	55 (8%)

Cost effectiveness

We summarised the impact of each scenario on effectiveness and cost of the HIV programme in a single metric, the incremental cost effectiveness over the baseline scenario (Table 54). (Note that because cost effectiveness is calculated incremental to the cost and effectiveness of the baseline scenario, here we present results for the four non-baseline scenarios only.) When taking cost per life year saved into account, the constrained optimisation scenario was the most cost effective over both the 5 and the 20 year projection period, becoming cost saving over 20 years. When looking at cost per HIV infection averted, the government scenario was the most cost effective over the 5 year time horizon for which targets were available. The discrepancy between these two results is explained by the fact that the optimisation scenarios selected interventions and coverage levels on the basis of their incremental cost by life year saved, thereby optimising this metric of programme effectiveness. It should be noted however that the constrained optimisation scenario is cost-saving under either metric over the 20-year period. Given that the 90-90-90 scenario reached similar epidemiological outcomes at a significantly lower cost than unconstrained optimisation (8% rather than 38% more expensive than baseline), it is the more cost effective option amongst the two, echoed by the lower ICER found (R 2,055 vs R9,250 per life year saved, Table 54).

Table 54: Summary of cost effectiveness by scenario

	Baseline	Government targets	Optimisation without constraint	Optimisation with constraint	Optimisation towards 90-90-90
Incremental cost [ZAR] per life year saved					
2014/15 - 2018/19	-	2,742	8,506	3,250	4,381
2014/15 - 2033/34	-	-	9,250	-1,251	2,055
Incremental cost [ZAR] per HIV infection averted					
2014/15 - 2018/19	-	22,650	84,749	19,035	47,069
2014/15 - 2033/34	-	-	76,915	-7,206	18,329

5.1.2 Results at *optimal* levels of technical efficiency

This section presents the cost results of the modelling exercise and compares cost with epidemiological impact for each of the scenarios at optimal levels of technical efficiency- in other words, this section examines what the impact would be of scaling up interventions while also improving the way they are being implemented and taking enablers or synergies outside the health sector into account.

Packages of care and coverage

As explained in Section 3.2.1, we added only those TE factors and enablers for which evidence was available and whose cost effectiveness was of the same order of magnitude as that of the least cost effective scenario at current levels of technical efficiency. This meant we only included TE factors for both ART and HCT, as these were the only programme areas for which our review of TE factors found evidence of high enough quality, and only one enabler, teacher support, as the others were a lot less cost effective than the standard scenarios.

Table 55 summarises the assumptions regarding coverage with the TE factors and enabler as well as the relative impact on the cost and effectiveness of the total HIV programme. As can be seen, though the impact on effectiveness is small for each factor and the enabler, the largest potential impacts are gained by those that reduce the loss to follow-up between HIV testing and ART initiation (point-of-care CD4 testing and provider-initiated testing). The only TE factor or enabler that is cost saving is adherence clubs for ART which reduce the average cost of ART provision per person on ART as well as the total cost of the HIV programme.

Table 55: Target population, coverage and impact on total cost and effectiveness for TE factors and enablers included in the 'optimal technical efficiency' scenarios

Program area	TE factor/ enabler	Target population	Coverage	% change in	
				total life years lost	total cost
ART	Adherence clubs	All adults currently on ART	2015: 10%	5%	-1%
			2016: 10%		
			2017: 20%		
			2018: 30%		
			2019: 40%		
			2020: 50%		
			2021: 60%		

Program area	TE factor/ enabler	Target population	Coverage	% change in	
				total life years lost	total cost
	Point-of-care CD4 testing		100%	8%	1%
HCT ⁱ	Provider initiated HCT	All adults undergoing testing	25% of tests	8%	1%
	Mobile HCT		25% of tests	5%	3%
	Home-based HCT		14% of tests	3%	2%
	HCT invitations to pregnancy partners		1% of tests ^j	6%	5%
2. Critical enabler					
	Teacher support	Adolescents in informal settlements and rural areas with >28% ANC prevalence		1%	0.2%

5.1.3 Sensitivity analysis

Our sensitivity analysis showed that when varying the impact of the three main epidemiological parameters, the impact of higher eligibility on mortality on ART, the impact of ART on infectivity (and hence onwards transmission of HIV), as well as the reduction in the proportion of sex acts that are unprotected after HIV diagnosis, along wide ranges, the findings about the cost and effectiveness of each scenario hold, though the resulting 95% ranges overlap widely, weakening the difference between them. In scenarios where budget constraints are not taken into account (i.e. optimisation without constraints and optimisation towards 90-90-90), the life years lost results in the sensitivity analysis are substantially larger than the estimates in the main analysis. This is likely due to the increased variation of mortality on ART, leading to increased life years lost for especially those scenarios in which have large numbers of people are initiated on ART.

Table 56: Results of sensitivity analysis^k

	Baseline	Optimisation without constraint	Optimisation with constraint	Optimisation towards 90-90-90
Results of main analysis, 2015-2034				
Life years lost [millions]	59.43	31.48	48.59	32.63
Life years saved [millions] (% change on baseline)	-	27.95 (-47%)	10.84 (-18%)	26.79 (-45%)
Total cost [billion 2014 ZAR]	688	947	675	743
Incremental cost [billion 2014 ZAR] (% change on baseline)		259 (38%)	-14 (-2%)	55 (8%)
Results of sensitivity analysis (medians and 2.5%-97.5% percentiles from 1,000 model runs), 2015-2034				

ⁱ The impact and cost for the HCT TE factors was calculated assuming that 100% of tests were done using this TE factor, by way of normalising results.

^j The remaining 36% of tests are assumed to be done through traditional stand-alone, clinic-based, non-targeted HCT.

^k Note that we left the government target scenario out of the sensitivity analysis.

	Baseline	Optimisation without constraint	Optimisation with constraint	Optimisation towards 90-90-90
Life years lost [millions] (95% ranges)	60.90 (44.75 - 83.74)	33.12 (22.96 - 46.52)	50.15 (36.05 - 69.32)	34.25 (23.97 - 48.05)
Life years saved [millions] (% change on baseline)	-	27.78 (-46%)	10.75 (-18%)	26.66 (-44%)
Total cost [billion 2014 ZAR] (95% ranges)	683 (618 - 754)	938 (899 - 1011)	669 (620 - 732)	734 (688 - 820)
Incremental cost [billion 2014 ZAR] (% change on baseline)	-	255 (37%)	-14 (-2%)	51 (7%)

5.1.4 Results for key populations

The results of the key populations sub-analysis based on the Goals model are summarised in Table 58. Note that while Table 58 summarises cost effectiveness results in terms of cost per life-year saved in order to facilitate comparison with the remainder of the results in this analysis, the text below also gives the cost per infection averted results.

Baseline scenario

In the Goals baseline scenario, the model predicts 1.18 million new HIV infections within 5 years and 5.31 million new HIV infections within 20 years. The total cost is R122 billion within 5 years and R591 billion within 20 years, with the somewhat lower total cost in comparison to those calculated by the Thembisa model (see Table 56) reflecting the limited number of interventions included in the Goals model in comparison to the Thembisa model.

Package of care for young women aged 15-24

The package of care for young women was based on the DREAMS initiative and included PrEP, cash transfers, condom promotion and provision, HIV testing and counselling, school-based HIV and violence prevention, as well as community mobilisation.

Compared to the baseline scenario, within a 5-year time span, scaling up this package of interventions for young women averted 6% to 15% of new HIV infections, with a cost per infection averted ranging from R87,351 to 112,301. Within a 20-year time span, scaling up these interventions for young women averted 9% to 17% of new HIV infections, with a cost per life-year saved ranging from R82,042 to R104,568.

Package of care for commercial sex workers (CSW)

The package of care for CSW included STI treatment, peer outreach and counselling, condom promotion, removing stigma and discrimination, elimination of gender-based violence, HIV testing and treatment, and programmes addressing clients.

Compared to the baseline scenario, within a 5-year time span, scaling up the CSW intervention package averted 0.2% to 0.8% of new HIV infections, with a cost per infection averted ranging from R18,767 to R19,901. Within a 20-year time span, scaling up these interventions averted 0.42% to 1.35% of new HIV infections, with a cost per life-year saved ranging from R12,321 to R13,213.

Package of care for intravenous drug users (IDU)

The package of care for IDU included harm reduction programmes, such as sterile needle and syringe programmes, as well as opioid substitution and peer outreach.

Compared to the baseline scenario, within a 5-year time span, scaling up the IDU intervention package averted 0.7% to 1.7% of new HIV infections, with a cost per infection averted ranging from R7,425 to R8,981. Within a 20-year time span, scaling up these interventions averted 1.2% to 3.3% of new HIV infections, with a cost per infection averted ranging from R5,506 to R5,943.

Package of care for men who have sex with men (MSM)

The package of care for MSM included risk-reduction activities, outreach (including by peers), prevention of sexual transmission of HIV (including condom use, prevention and treatment of STIs), voluntary and confidential HIV counselling and testing, and initiatives to ensure that these groups are able to access these services.

Compared to the baseline scenario, within a 5-year time span, scaling up the MSM intervention package averted 0.02% to 0.06% of new HIV infections, with a cost per infection averted ranging from R775,626 to R789,240. Within a 20-year time span, scaling up these interventions averted 0.05% to 0.16% of new HIV infections, with a cost per infection averted ranging from R376,028 to R395,296.

Summary of key populations analysis

With the exception of young women (who were not defined as a key population in the context of this Investment Case, see Section 4.1.1), each of the packages for key populations had a limited impact on total infections averted and life-years saved compared to the baseline scenario of keeping coverage constant at 2014 levels. The package of care with the largest impact in terms of infections averted is the package for young women; the one with the largest impact in terms of life-years saved is those for MSM and CSW; and the most cost-effective package is that for IDU, while the MSM package was the least cost effective. Bearing in mind the limitations of this stand-alone analysis that starts from a different baseline to our main analysis and does not take into account the impact of scaling up any interventions in the general population, the incremental cost-effectiveness ratio of each package over 20 years would have been below the cost-effectiveness threshold of R100,000 per life-year saved that we used for TE factors and enablers in the Budget scenario.

Table 57: Results of key populations sub-analysis

Key population	Young women			IDU			MSM			CSW		
	Coverage	30%	60%	90%	30%	60%	90%	30%	60%	90%	30%	60%
HIV infections averted (% change on baseline)												
2015-2019	6.41%	11.31%	14.95%	0.69%	1.25%	1.72%	0.02%	0.04%	0.06%	0.25%	0.54%	0.81%
2015-2034	9.31%	16.51%	21.92%	1.17%	2.27%	3.29%	0.05%	0.11%	0.16%	0.52%	1.11%	1.65%
Life-year saved												
2015-2019	112,428	198,224	262,121	15,427	28,666	40,618	35,484,008	35,483,638	35,483,335	35,478,955	35,472,422	35,466,051
2015-2034	9,079,059	16,060,182	21,285,312	1,046,949	2,004,860	2,838,302	184,300,159	184,261,900	184,225,253	183,891,737	183,384,266	182,913,182

CHAPTER 5

Key population	Young women			30%	60%	90%	30%	60%	90%	30%	60%	90%
	Coverage	30%	60%									
Incremental cost of HIV programme (% change on baseline)												
2015-2019	5.44%	10.88%	16.32%	0.05%	0.10%	0.15%	0.15%	0.29%	0.44%	0.05%	0.10%	0.16%
2015-2034	6.88%	13.76%	20.64%	0.06%	0.12%	0.18%	0.18%	0.37%	0.55%	0.06%	0.13%	0.20%
Cost per life-year saved												
2015-2019	R40,249	R45,592	R51,711	R2,438	R2,553	R2,743	R271,489	R253,167	R250,667	R6,668	R6,908	R7,052
2015-2034	R3,076	R3,478	R3,936	R205	R216	R231	R14,172	R14,480	R14,780	R504	R522	R542

5.2 RESULTS OF THE TB INVESTMENT CASE

The TB Investment Case modelling used the TIME model, using results from the HIV scenarios (above). In all figures in this section, dotted lines represent TB baseline (i.e., continuing current efforts), while solid lines reflect the impact of implementing the TB 90-90-90 strategy. In each figure, the relevant WHO targets are also noted.

5.2.1 Reduction in TB mortality

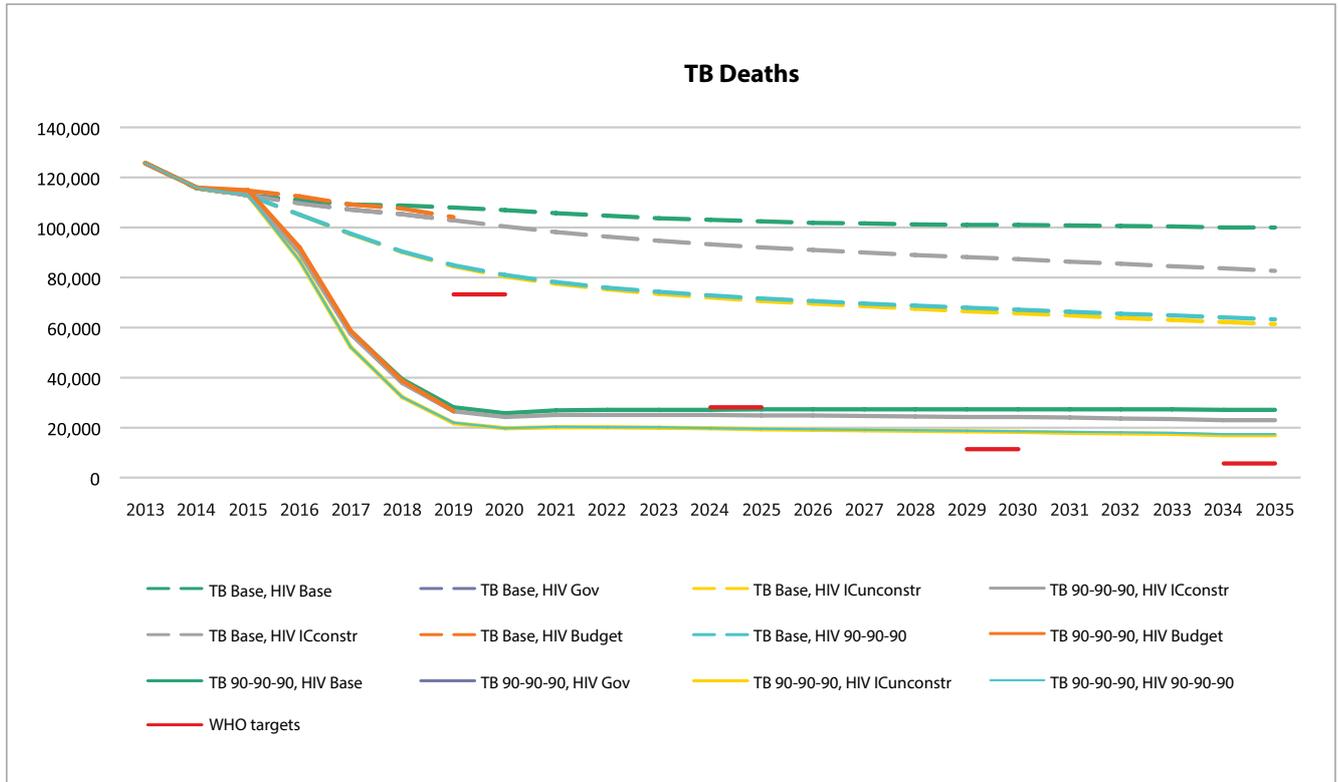
WHO targets for percent reduction from deaths due to TB are: 35% reduction from 2015 levels by 2020; 75% reduction by 2025; and 95% reduction by 2035.

Figure 30 presents the impact on deaths from TB, both for HIV-infected and HIV-negative people, of implement the TB 90-90-90 strategy, compared against TB baseline for each of the HIV scenarios. The baseline scenario estimates that 89 000 persons (range: 62,000 to 121,000) died from TB in South Africa in 2013, including both HIV-positive and -negative TB cases. Under both baseline HIV and baseline TB scenario, 2.1 million TB-related deaths are anticipated over the next 20 years (2014/15 to 2033/34). The number of TB deaths per 100 000 population would drop from a rate of 196 in 2015 to 149 in 2035.

Implementation of the HIV 90-90-90 scenario against the baseline TB scenario would achieve the targeted 35% reduction in TB deaths after the target date of 2020 and eventually plateau at the level of 35% reduction. With achievement of the HIV 90-90-90 scenario, there would still be 1.6 million TB deaths over the next 20 years, or 93 TB deaths per 100,000 population – a reduction of 24% compared to baseline.

If the TB 90-90-90 and HIV 90-90-90 scenarios are implemented together, the reduction in TB mortality will be considerably greater. The TB 90-90-90 scenario for South Africa reaches the 2025 WHO target for 75% reduction in TB deaths; however, further interventions or new tools would be necessary to bring down TB mortality to the 2035 WHO target of a 95% reduction. Under the TB 90-90-90 and HIV 90-90-90 scenario, an estimated 690 000 TB deaths would occur over the next 20 years, effectively averting 67% of the estimated TB deaths under baseline scenario. With this combined 90-90-90 scenario, in 2035, the TB death rate would be 26 per 100,000 population (down from 196 in 2015).

Figure 29: TB deaths by scenario 2013 to 2035



5.2.2 Reduction in TB disease incidence

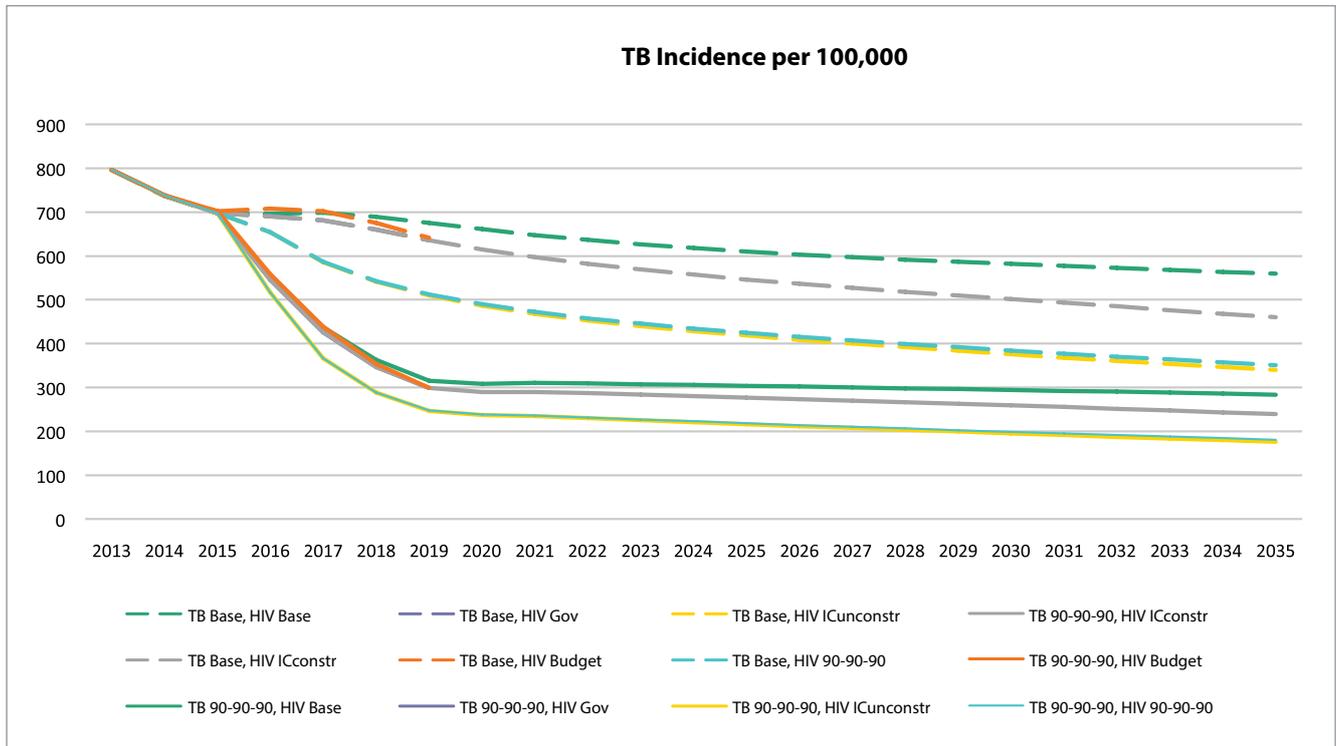
WHO targets for reduction in TB incidence are: 20% reduction from 2015 levels by 2020; 50% reduction by 2025; and 90% reduction by 2035.

As South Africa is now implementing a TB prevalence survey, it is currently relying on modelled estimates from WHO. WHO estimates that there were 450 000 incident TB cases in 2013 and 380 000 prevalent cases. Under the baseline TB and HIV scenario, there would be 7.8 million incident TB cases over the next 20 years (2014/15 to 2033/34). While the 2035 estimated number of incident cases (374,350) is below that of 2015 (400,306), the reduction is minor and does not mean a meaningful advance the overall aim of eliminating TB. The TB incidence rate is estimated at 697 per 100 000 population in 2015 and only drops to 560 per 100 000 population in the baseline scenario that continues current efforts.

Implementation of the HIV 90-90-90 scenario achieves the WHO 2020 target for reduction in TB incidence, largely due to the impact of rapid expansion of ART, which greatly reduces the risk of TB disease for people living with HIV (PLWH). However, if only HIV interventions were scaled up while TB interventions were kept at baseline, TB incidence plateaus far above the 2025 WHO targets even by 2035. The projected TB incidence rate of 351 per 100,000 population in 2035 would still exceed the threshold for classification of TB as an 'emergency' in South Africa.

Figure 31 demonstrates that WHO's 2025 targets can be achieved through the TB 90-90-90 strategy with the currently available tools, even while keeping HIV interventions at baseline. Combined implementation of the HIV and TB 90-90-90 scenarios would avert 54% of incident TB cases averted over the next 20 years, with a projected TB incidence rate of 181 per 100 000 population in 2035.

Figure 30: TB disease incidence by scenario, 2013 to 2035



Even with combined aggressive strategies for TB and HIV, the 2030 and 2035 WHO targets will be missed, with TB incidence plateauing around 2020 with the achievement of the current strategy. Additional reductions in incidence will require new tools for prevention and diagnosis in particular. Because efforts at prevention in the 90-90-90 strategies currently focus on persons living with HIV, it is likely that further improvements will require tools for reducing the incidence of TB among persons who are HIV-negative.

5.2.3 Reduction in TB case registration

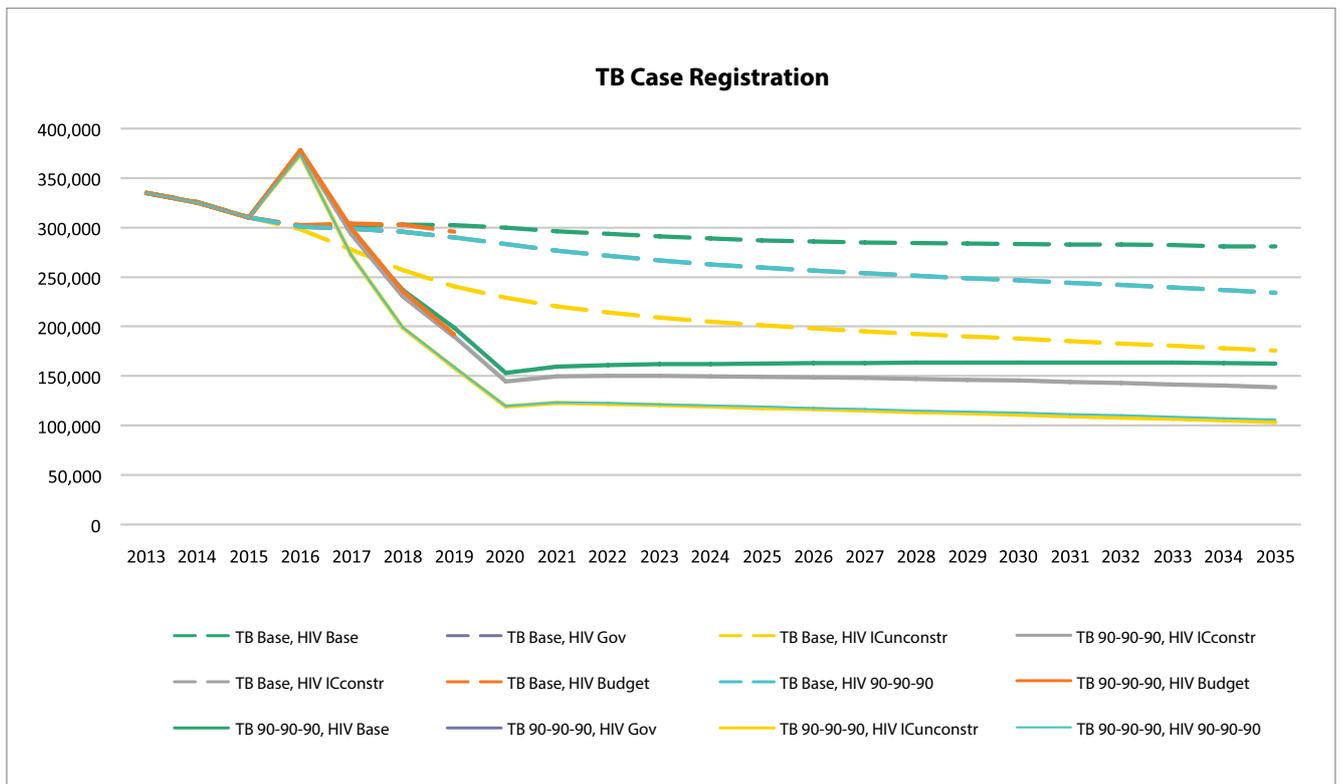
Figure 32 depicts the impact of the modelled strategy on TB case notifications, ie, the number of TB cases registered with the National TB Programme each year. WHO estimates that only 69% of prevalent TB cases are currently found and diagnosed in South Africa. Moreover, loss to follow-up once diagnosed is also high; for example, only 41% of rifampicin-resistant (RR) TB cases diagnosed in South Africa in 2013 were initiated on RR TB treatment.

Annual case registration in South Africa has declined since peaking around 2009 - 2011. The model projects that in 2015, there will be 310 298 cases registered. Under the combined TB and HIV baseline scenario, registered cases will drop to 280 875 in 2035. TB prevalence rate per 100,000 in 2015 is estimated at 622 and would drop to 493 in 2035 under the baseline scenario. Under this scenario, 5.9 million TB cases would be detected and initiated on treatment (registered) over the next 20 years.

Diagnosing at least 90% of all prevalent TB cases and initiating treatment for these cases will increase case notifications in South Africa. Annual TB case registrations would peak again in 2016 at 373 684 but then drop sharply to 119 872 per year in 2020 and 106 024 TB cases on treatment in 2035. Although the spike from 2015-2018 is marked, it is below the number of TB cases registered and treated by the South African National TB Programme from 2009 to 2011, when case registrations exceeded 400 000 per annum. Implementation of both the TB and HIV 90-90-90 scenarios could avert 44%

of TB case registrations against baseline. The TB prevalence rate is projected to drop to 87 cases per 100 000 in 2035 compared to a peak of 993 per 100 000 in 2011. Reducing the number of TB cases requiring treatment could save the SA NTP substantial money, which could then be invested in prevention and early case detection.

Figure 31: TB notifications by scenario, 2013 to 2035



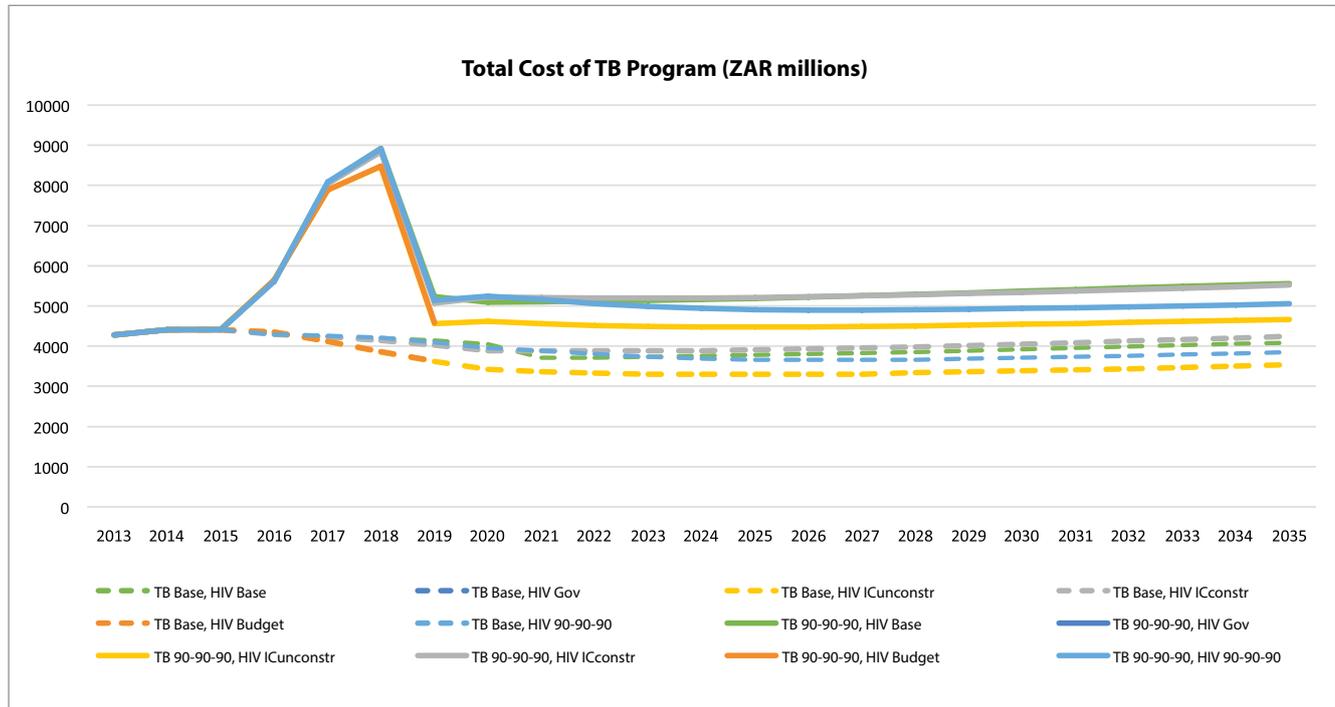
5.2.4 Costs and cost-effectiveness

Implementing improved case finding, prevention, treatment, and care will require additional investment, specifically in TB interventions. While the decrease in the number of cases of active TB will lower treatment costs over time, funding for case finding and prevention will need to be sustained at higher levels than currently.

Figure 33 depicts the estimated cost curves for the various scenarios. The baseline costs depicted and estimated from 2013 to 2015 exceed those reported as expenditures for the SA NTP due to underreporting of TB expenditure in terms of health facilities and services utilization.

The combined TB 90-90-90 and HIV 90-90-90 scenario intersects with the baseline scenario cost curve at 2035, suggesting the cost in the years beyond this will be lower than what would need to be paid were the HIV and TB programmes continued at the current level of coverage. The TB 90-90-90 scenario, combined with the unconstrained HIV scenario, would bring costs lower than baseline somewhat earlier (2030) and be cost saving beyond that; however, this does not factor in the high incremental costs of an unconstrained optimisation approach to the HIV programme (see Section 5.1).

Figure 32: Total cost of TB programme, ZAR millions, 2013 to 2035



At its peak in 2020/21, the TB 90-90-90 strategy would require double the annual TB expenditure required by the baseline scenario. Over the first five years (from the base year 2015/16 to 2020/21), implementation of the TB 90-90-90 strategy would demand a 46% budget increase, including costs associated with a mass TB screening campaign. Over 20 years, a 22% budget increase will be needed to implement the TB 90-90-90 strategy.

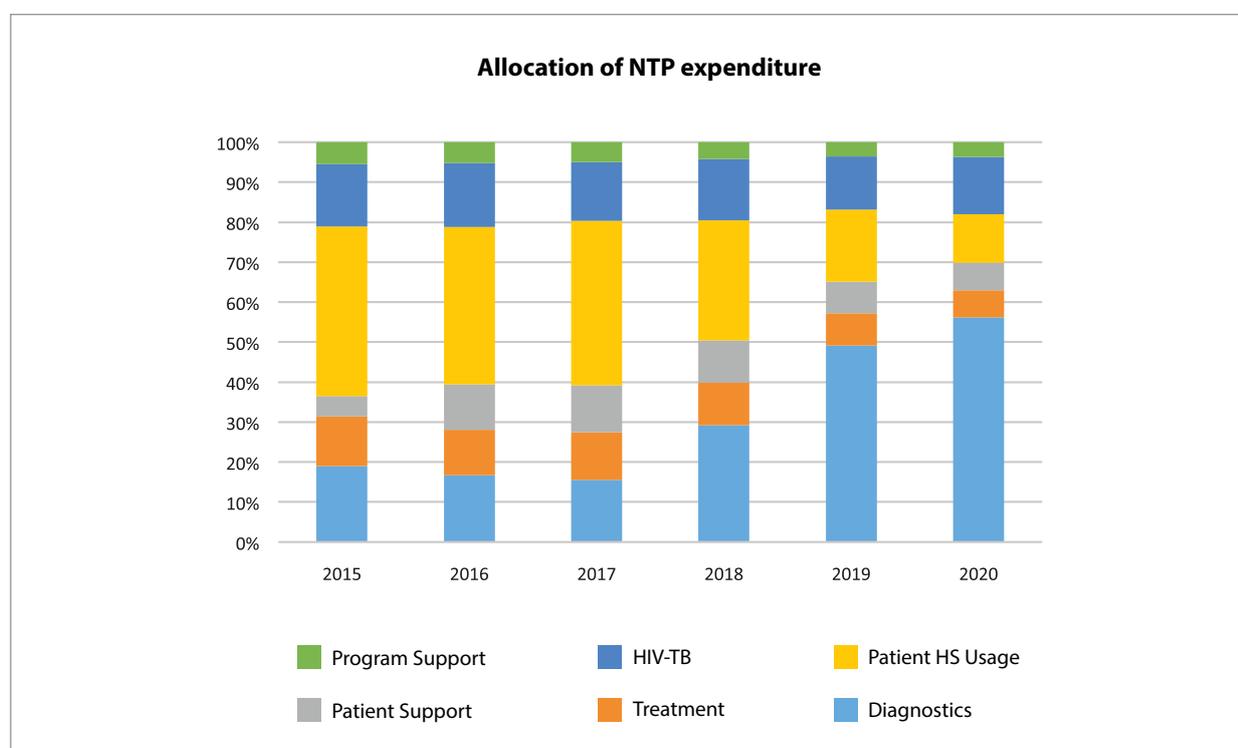
Table 58: Costs to the South African National TB Programme, ZAR millions 2015 to 2020

Cost component	2015/16	2016/17	2017/18	2018/19	2019/20	2020/21
Diagnostics	814	785	829	1,931	4,136	4,737
Smears	96	95	106	100	82	65
Culture	245	237	261	237	190	145
Xpert	430	414	421	1,395	3,233	3,659
LPA	8	5	6	8	8	7
X-rays	35	34	36	193	623	862
Treatment	529	539	628	701	672	577
Drug sensitive TB	111	108	115	102	80	62
MDR and XDR TB	418	432	513	599	592	515
Patient support	220	539	628	701	672	577
Patient health service usage	1,810	1,856	2,186	1,981	1,519	1,020

Cost component	2015/16	2016/17	2017/18	2018/19	2019/20	2020/21
Non-MDR	181	175	186	165	130	101
MDR	1,629	1,682	2,000	1,817	1,389	919
HIV-TB	669	749	782	1,008	1,118	1,208
Program support	236	250	265	281	298	316
Program management	22	24	25	26	28	30
Service delivery	169	180	190	202	214	227
Health and community workforce	35	37	40	42	44	47
Community systems strengthening	9	10	10	11	12	12
Total costs	4,278	4,720	5,318	6,603	8,415	8,435

The allocation of the expenditure across TB cost categories also changes over time with implementation of the TB 90-90-90 strategy. The biggest shift is a reduction in the health services utilization by MDR TB patients, from a peak of ZAR 1.6 billion per year to less than ZAR 1 billion in 2020/21 through further decentralization and ambulatory treatment of MDR TB patients under the policy adopted in 2011. Health services utilization for drug-sensitive TB treatment also drops over time, as the total number of TB cases requiring treatment declines over time. Although the costs of ART, HCT, co-trimoxazole prophylaxis, and health care visits for IPT are included under the HIV Investment Case and not duplicated here, the proportion of NTP expenses for HIV/TB increases over the period (from a base of ZAR 669 million to ZAR 1.2 billion) because of increased coverage of IPT (drug costs) for persons receiving ART.

Figure 33: Allocation of cost to National TB Programme by category, 2015 to 2020



5.2.5 Summary of TB IC results

It is clear that an ambitious expansion of the TB services will be required to achieve the WHO TB targets. Even with no expansion of the HIV program, i.e. if the HIV scenario remains at baseline (red lines), an expansion of the TB program as defined by the government targets scenario will achieve the WHO TB epidemiological impact targets for 2020. Focusing only on a massive expansion of the HIV programme, without also expanding the TB programme, will not reach TB targets, as gains from the HIV-focused approach stabilize after 2025. Combining the expansion of the TB programme with the unconstrained expansion HIV program will reach the 2025 WHO TB impact targets.

In expanding the TB programme, the results also point towards the importance of focusing TB interventions not only on reducing HIV incidence but also for reducing TB-related deaths. An ambitious TB control expansion program is thus as critical to averting TB-related deaths as expanding ART coverage for HIV-positive TB cases will be. Results also reinforce the importance of collaborative HIV/TB programmes, as ART expansion could serve as a platform to strengthen monitoring and linkage of patients at high risk of developing active TB.

Table 59: Summary of impact, cost and cost effectiveness results from the TB Investment Case

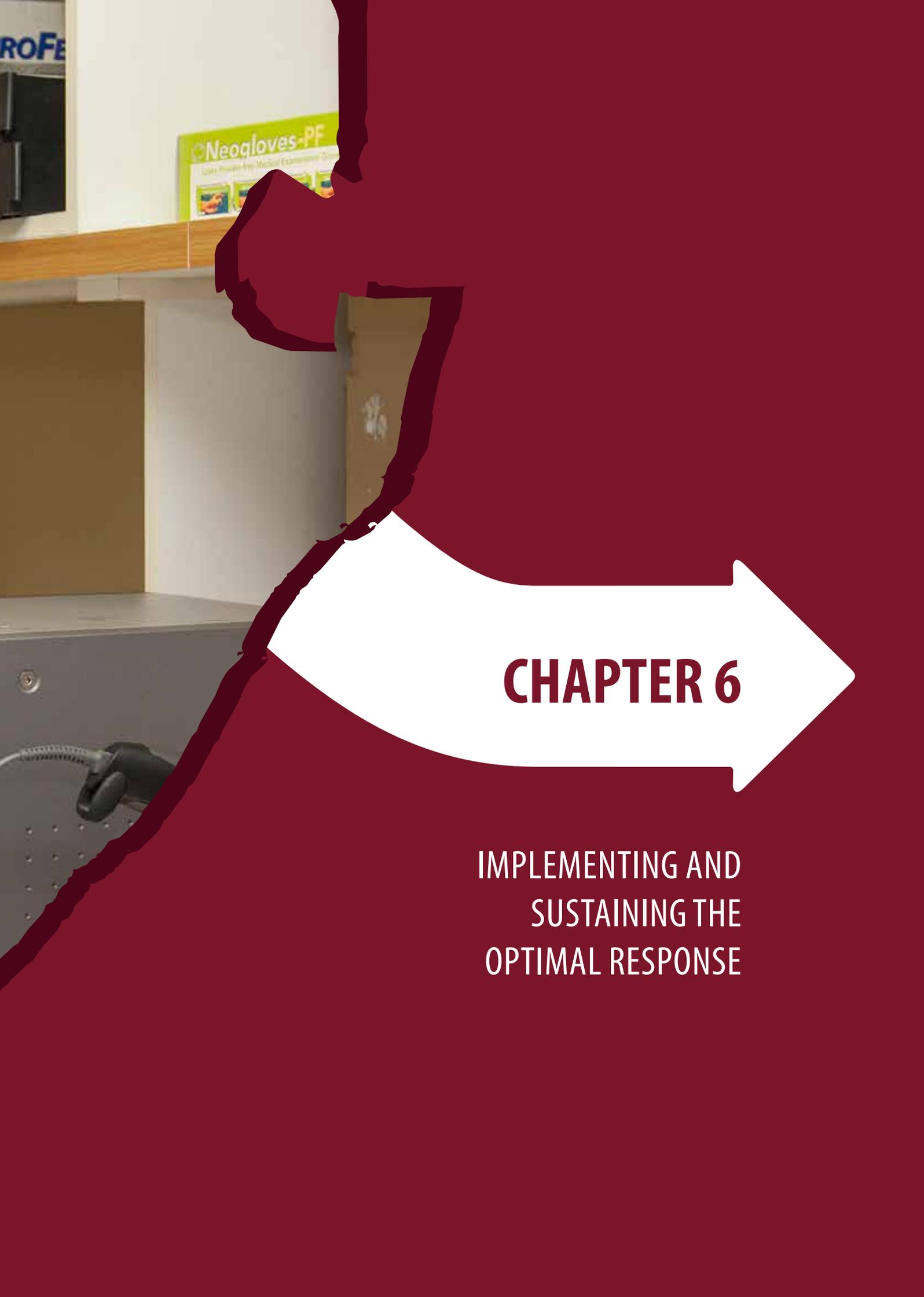
	TB baseline	TB 90-90-90				
	HIV baseline	HIV baseline	HIV government targets	HIV unconstrained optimisation	HIV constrained optimisation	HIV 90-90-90
Total TB cases						
2014/2015 - 2018/2019	2 037 638	1 607 755	1 589 770	1 504 086	1 589 644	1 505 082
2014/2015 - 2033/2034	7 799 005	4 455 779	-	3 527 617	4 172 090	3 552 587
TB cases averted (% change on baseline)						
2014/2015 - 2018/2019		-21.1%	-22.0%	-26.2%	-22.0%	-26.1%
2014/2015 - 2033/2034		-42.9%	-	-54.8%	-46.5%	-54.4%
Total life years lost due to TB & HIV						
2014/2015 - 2018/2019	158 236 193	156 743 515	156 410 936	153 848 942	156 391 357	153 865 591
2014/2015 - 2033/2034	672 347 357	594 455 548	-	590 882 007	597 050 181	590 007 327
Total life years saved due to TB & HIV interventions						
2014/2015 - 2018/2019		-0.9%	-1.2%	-2.8%	-1.2%	-2.8%
2014/2015 - 2033/2034		-11.6%	-	-12.1%	-11.2%	-12.2%
Incremental cost to TB programme (ZAR millions)						
2014/2015 - 2018/2019		45.76%	45.15%	42.92%	45.21%	45.65%
2014/2015 - 2033/2034		35.62%	-	13.80%	26.96%	22.49%
Total cost to TB Programs (ZAR millions)						
2014/2015 - 2018/2019	21 570	31 440	31 310	30 828	31 320	31 416
2014/2015 - 2033/2034	86 840	117 771	-	98 827	110 256	106 373

	TB baseline	TB 90-90-90				
	HIV baseline	HIV baseline	HIV government targets	HIV unconstrained optimisation	HIV constrained optimisation	HIV 90-90-90
Cost per TB infection averted (ZAR)						
2014/2015 - 2018/2019		22 960	238 129	1 280 687	204 681	651 304
2014/2015 - 2033/2034		9 252	-	712 886	cost saving	154 376
Cost per life year saved (ZAR)						
2014/2015 - 2018/2019		6 612	58 430	155 750	49 704	79 361
2014/2015 - 2033/2034		397	-	37 378	cost saving	7 961

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CHAPTER 6

IMPLEMENTING AND
SUSTAINING THE
OPTIMAL RESPONSE

With the aim of aiding decision-makers in optimizing the HIV and TB response in South Africa, this chapter summarises recommendations arising from the Investment Case, with particular attention to priority actions to ensure the sustainability of the response.

6.1 IMPLEMENTING THE OPTIMAL RESPONSE

This section summarises the recommendations arising out of the optimisation exercise for the HIV Investment Case and out of the TB Investment Case, and details how the results of the HIV Investment Case were used to construct a sixth scenario to inform the Department of Health's budget bid to Treasury for the Comprehensive HIV/AIDS Conditional Grant 2016/17 to 2028/19.

6.1.1 Recommendations for the HIV programme

The Investment Case results point to an optimal package of HIV services over the next 20 years.

Allocative efficiency

Current government policy appears to be relatively efficient from an allocative perspective, although it should be noted that the Thembisa model could not replicate the national government's targets for condoms in circulation (1 billion per year) and the number of circumcision procedures (1 million each year over five years). This suggests that there may be insufficient numbers of sex acts or sexually active men to warrant these targets. At the time of the Investment Case analysis, government policy did not take account of some of the interventions considered by the IC, such as universal test and treat.

To maximize allocative efficiency, the HIV response in South Africa should first scale up interventions that are cost-saving, in that they prevent HIV infections and reduce future needs for antiretroviral therapy. These include

- increasing condom availability to a maximum of about 570 million per year;
- increasing access to male medical circumcision, including for adolescents who are not currently targeted by the intervention (even though our results did not support prioritisation of one age group over another) to a maximum of 4 100 000 over the next five years, and
- social behaviour change communication that focuses on increasing HIV testing uptake in adolescents and discouraging them from having multiple sexual partners.

Using the money saved, the next cost-effective intervention would be to scale up ART to the greatest degree possible. As the current government response (where feasible) is already largely efficient from an allocative point of view, the potential gains from changing the mix of interventions are limited.

Budgetary impact

In part as a result of the success of South Africa's HIV programme to date, the results of the South African HIV Investment Case differ from those of other countries that have undertaken this exercise in two important aspects: First, the South African HIV Investment Case does not result in a programme of interventions that will "bend the curve" of HIV incidence and mortality, as these curves have already been altered, in large parts by the successful roll-out of ART since 2004. Again

in contrast to other countries' Investment Cases, this Case also does not identify ways to save money by "front-loading" the investment over a short period of time. In all scenarios examined, the total annual cost of the HIV programme would be above that of the baseline scenario until between 2025 and 2032. Under all scenarios, responding to HIV will remain costly in South Africa for many years to come.

However, this finding highlights the important decisions that must be made. Even though the total cost of the HIV programme will increase regardless of the mix of interventions chosen, it is in the government's hands of government to decide *when* total costs will begin to decrease. If the government chooses to spend more later, it will spend more in total. If government spends more now, the impact over 20 years will also be greater.

Recommendations by intervention

Using the incremental cost-effectiveness of the 90-90-90 scenario as the benchmark, the IC team grouped all interventions into three categories of cost-effectiveness. Table 61 summarises these categories as well as the recommendation for each intervention.

Table 60: Recommendation by intervention

Intervention	ICER (Cost per life year saved, ZAR)	Recommendation
1. Cost-effective		
Condom availability	Cost saving	Scale up, as this is the most cost-effective intervention amongst the list considered. However, since the number of protected sex acts is limited, it is not necessary to oversaturate the country with condoms as per current government targets.
MMC	Cost saving	Scale up as much as possible. However, the intervention will reach a saturation point, as there is a limit to the number of men willing to undergo circumcision even after taking into account demand creation efforts.
SBCC 1	Cost saving	Scale up
MMC targeting	Cost saving	Scale up as much as possible, and extend age targeting to younger age groups (aged 10-17) that are not covered under current policy. (Note that targeting each of the age groups is equally cost-effective.)
Testing at 6 weeks	749	Scale up
ART		
- Current guidelines	1,043	Scale up ART as much as possible. Increasing coverage under current guidelines is more cost-effective than extending the eligibility criteria to UTT, but the latter is necessary if achieving UNAIDS' 90-90-90 targets is a priority.
- Universal Test and Treat (UTT)	14,644	
HCT	5,978	Scale up. As the entry point in the treatment cascade, scaling up HCT is a prerequisite to scaling up ART.
SBCC 3	13,111	Scale up.
2. Neutral		
PMTCT (Initiation of ART in pregnancy)	2,940	Although the model suggests scaling down the initiation of ART in pregnancy, this is primarily a result of PMTCT being made redundant once very high levels of ART coverage have been achieved. The IC does not recommend scaling down PMTCT under the status quo.

CHAPTER 6

Intervention	ICER (Cost per life year saved, ZAR)	Recommendation
SBCC 2	N/A	The model is indifferent between scaling down and maintaining the high baseline levels of SBCC 2.
Testing of pregnant women	N/A	The model is indifferent between scaling down and maintaining the high baseline levels of testing of pregnant women.
3. Not cost-effective compared to cost-effectiveness of UTT, and once all of the above have been scaled up		
Testing of adolescents (15-19)	15,303	None of these interventions should be prioritised before universal testing and treatment (UTT) coverage has been achieved, as each is less cost-effective than UTT. For PrEP and microbicides in particular, this result hinges on the cost of the intervention; the likely public sector costs of these interventions remains unknown, requiring the IC modelling team to use assumptions.
Birth testing	36,710	
PrEP		
- for sex workers	106,452	
- for adolescents	304,776	
- for discordant couples	710,321	
Microbicides	304,776	
Condom education	5,781,471	
EIMC	295,239,305	

6.1.2 Recommendations for the TB programme

The current national and global incidence and mortality targets for 2025 are obtainable with interventions that are currently available. However, finding and successfully treating TB will require an additional investment. Over the next 20 years implementing the required package of comprehensive intensified case finding, diagnosis and high quality treatment, requires an increase of 22-36% over the estimated baseline TB expenditure, depending on the HIV scenario implemented. Most of this investment is required in the first five years (46% increase in the 5-year budget; with the annual budget for TB nearly doubling at the peak of the campaign), to implement the massive case finding campaign to screen high risk groups, find the TB cases and reduce the force of TB infection in the community. The overall impact of finding TB in communities and clinics will reduce the burden of disease in terms of incidence and death and reduce the costs of treating TB in the future.

6.1.3 Summary

HIV programme

HIV policy in South Africa is already, in general, allocatively efficient. Some current government targets (regarding medical male circumcision and condoms in particular) will be difficult, if not impossible, to achieve. Under the currently assigned budget from the three major funding sources, ART can only be scaled up to 85% of coverage under guidelines that were in place when the IC analysis was conducted, underscoring that changes in government policy (specifically, rolling out universal test and treat) will be needed if South Africa hopes to reach the UNAIDS 90-90-90 targets by 2020. Assuming adoption of universal test and treat to reach the 90-90-90 target, the annual cost of the programme will continue to increase until 2032, but these costs will be cheaper than the baseline scenario (i.e. maintaining current coverage) every year from 2032 on.

Based on this analysis, the recommended policy actions that flow from the IC fall into two main categories:

1. Interventions that are part of current government policy and that should be scaled up further:
 - ART (including universal testing and treatment)
 - MMC (including to 10-17 year olds, but with downward-adjusted overall targets)
 - Condoms (albeit with downward adjusted targets)
 - SBCC campaign 1
 - Infant testing at 6 weeks
 - HIV counselling and testing
 - SBCC campaign 3

2. Interventions that are not currently part of current government policy that should not be introduced until UTT has been introduced:
 - Testing of adolescents
 - PrEP to discordant couples, sex workers, or adolescents
 - Microbicides
 - Infant testing at birth
 - Condom education
 - Early infant male circumcision

TB programme

While the national and global TB incidence and mortality targets in 2025 are obtainable with current interventions available, these targets will not be reached by HIV prevention and treatment alone. A comprehensive combination package of TB and HIV prevention, intensified case finding, diagnosis and high quality treatment is required, which in turn will demand additional funding.

6.1.4 HIV Budget scenario

Why a sixth HIV scenario?

In order to take into account issues of implementation and sustainability, the IC team further adapted the 90-90-90 scenario into a more budget-relevant scenario. Whilst the three optimisation scenarios were designed for comparative analysis, where issues of feasibility were secondary to determining the theoretical allocatively efficient mix of interventions, the 90-90-90 budget scenario places a strong emphasis on feasibility by making three key changes to the 90-90-90 scenario.

First, the 90-90-90 budget scenario started implementation of all scale-up of interventions in the current financial year (2015/16) rather than 2014/15. This allowed for a realistic time frame for the transition from research into policy implementation, and put the results of the Investment Case in a better position to influence budgetary decisions for the MTEF.

Second, the 90-90-90 budget scenario involved refitting the rate of ART scale-up to provide more realistic, feasible targets. Whilst the original 90-90-90 scenario involved extending eligibility guidelines to universal test and treat (UTT) as early as 2014/15 and the rapid scale-up to 90% coverage of all HIV infected people by 2017/18, the 90-90-90 budget scenario delayed the implementation of UTT eligibility guidelines until 2016/17 to account for uncertainty regarding the timing of the policy change, and further smoothed the scale-up in a way that was less ambitious but still guaranteed achieving the first two 90-90-90 targets by June 2021.

Additional TE factors and enablers

In another difference with the optimisation scenarios, the budget scenario took account of a number of interventions and enablers that had been suggested by the enabler working groups and were current government policy but had not been included in the optimisation routine because their effectiveness could not be established during the evidence review process (see Table 62). This involved making the conservative assumption of no effect on the epidemiological side, but adding a cost impact to inform budgets.

This adaptation takes into account two limitations regarding the optimisation scenarios. First, the strictly evidence-based screening process used for the selection of interventions has certain inherent limitations. Evidence of effectiveness may exist but have escaped the evidence review process, and certain interventions may be effective but not appear so under the narrow definitions of effectiveness used.

Second, the budget scenario recognises that certain government policies regarding HIV are likely to continue regardless of whether or not the IC team demonstrate their effectiveness or cost-effectiveness. As such, a realistic scenario used for budgetary planning ought to take these expenditures into consideration.

Lastly, adding these enablers based on the recommendations of the group of experts working on social and programme enablers convened during the IC process takes into account some of the criticism that the initial list of modelled interventions attracted. In particular, questions were raised regarding the feasibility of achieving very high levels of coverage for testing, treatment and other interventions based solely on existing, facility-based models of treatment delivery.

Table 61: Technical efficiency (TE) factors, social and programme enablers and synergies that were part of the HIV Budget scenario

TE factors	Social enablers and synergies	Programme enablers and synergies
1. ART TE factors	Teacher support and school feeding	Pharmacovigilance
Adherence clubs	Community-based GBV intervention (SASA!)	Supply chain reforms
Home-based ART	Vocational training for adolescent girls	
POC CD4	HIV prevention for alcohol and drug users	

TE factors	Social enablers and synergies	Programme enablers and synergies
2. HCT TE factors	School based HIV/STI risk reduction	
Mobile HCT	Positive parenting and parental monitoring	
Home-based HCT	Alcohol counselling in STI clinics	
PICT	Supporting orphan girls to stay in school	
HCT invitations to pregnancy partners	State-provided child-focused cash transfers	

Given the uncertainty regarding cost estimates, especially with regard to these newly included interventions and enablers, and the greater need for precision in the case of budgetary projections, cost projections for the budget scenario were limited to the time period until 2018/19 (but we continued to project the epidemiological model until 2034/35). This outer year was chosen based on the need to inform the district implementation plans which run until 2018/19 (see Section 6.2.1).

Results of the Budget scenario

Packages of care and coverage

The package of care included in the Budget scenario is the same as for the 90-90-90 scenario, with the above-mentioned TE factors, enablers and synergies added. However, the key outputs in terms of number of HIV tests performed, number of people on ART, condoms and circumcisions, etc, change as a result of shifting the roll-out of services by a year, from 2014/15 to 2015/16, and of UTT by two years, from 2014/15 to 2016/17. Table 63 summarises these outputs in terms of the population reached by each intervention or enabler. (Please note that the ART and HCT TE factors are applied to subsets of the ART and HCT populations, and that the target population for each enabler is given as only that proportion of the total population that is assumed to be covered by the HIV budget of any of the involved government departments, NDOH, DSD or DBE.)

As can be seen, the number of people tested for HIV needs to almost double between 2015/16 and 2016/17, to more than 18 million tests per year, and the number of people initiating ART must stay at the current levels of 500,000 to 600,000 people for years to come, in order to reach the 90-90-90 targets by 2019/20. To reach the high MMC coverage modelled in the optimisation scenarios, 800,000 circumcisions have to be performed in 2016/17, lower than the current target of 1 million- and the targets can be reduced quickly thereafter. Similarly, as mentioned previously, the number of condoms that need to be circulated are, at 348 to 850 million per year, far lower than the current government target of 1 billion. Finally, coverage with both the mass media campaigns included under SBCC and with community mobilisation and other enablers need to increase massively.

Table 62: Populations reached by each intervention and enabler included in Budget scenario

	2015/16	2016/17	2017/18	2018/19	2019/20
Interventions: Population reached by programme area					
ART (public sector only)					
Total number of patients on ART	3,537,146	3,975,517	4,450,097	4,910,419	5,358,735
Number of people starting ART	447,253	534,712	579,242	566,576	555,367

CHAPTER 6

		2015/16	2016/17	2017/18	2018/19	2019/20
MMC						
Total number of circumcisions		370,092	800,000	650,000	650,000	397,836
Condoms						
Number of condoms distributed		348,160,200	700,000,000	800,000,100	850,000,000	469,972,800
HCT						
Total HIV tests performed at ages 10+		10,784,400	14,206,600	18,288,300	18,241,000	18,126,667
PMTCT for mothers not on ART (NB, PMTCT for mothers on ART, PMTCT B+, is covered under ART)						
Mothers not on lifelong ART (PMTCT B)		12,703	10,982	9,875	8,364	6,516
Mothers not on any ART (PMTCT)		42,442	39,597	35,580	29,359	22,388
Key populations						
Commercial sex workers reached with combination prevention package and outreach		103,029	106,281	109,732	113,339	116,974
Social behaviour change communication						
Number of people reached by SBCC campaign 1		1,678,651	1,669,834	1,653,556	1,629,348	1,608,428
Number of people reached by SBCC campaign 2		41,074,033	41,657,000	42,222,796	42,776,426	43,319,122
Number of people reached by SBCC campaign 3		32,005,740	32,460,000	32,900,880	33,332,280	33,755,160
Enablers: Target population covered by HIV budget						
% covered by HIV budget						
SASA! GBV intervention	20% (DOH) ^a	1,834,540	1,859,484	1,884,011	1,908,077	1,931,597
Supporting adolescent orphan girls to stay in school	50% (DBE)	383,646	377,677	371,999	370,928	375,294

a The brackets denote the government department whose HIV budgets will most likely cover each enabler, based on the recommendations of the social enablers working group (DOH: Department of Health, DBE: Department of Basic Education; DSD: Department of Social Development).

		2015/16	2016/17	2017/18	2018/19	2019/20
School based HIV/STI risk reduction intervention	100% (DBE)	4,664,390	4,591,820	4,522,780	4,509,760	4,562,840
Empowerment based HIV intervention for alcohol and substance abuse users	50% (DOH)	948,817	962,677	975,491	987,961	1,001,236
Risk reduction counselling for alcohol in STI clinics	50% (DOH)	218,505	221,527	224,332	227,263	230,479
Life skills and vocational training for adolescent girls out of school	100% (DBE)	2,609,857	2,589,715	2,552,726	2,512,710	2,480,753
School feeding	20% (DBE)	192,453	189,458	186,610	186,073	188,263
Parental monitoring	20% (DSD)	292,843	288,287	283,953	283,135	286,467
Teacher support	10% (DBE)	146,421	144,143	141,976	141,567	143,234
Positive parenting	20% (DSD)	292,843	288,287	283,952	283,135	286,467

Cost and cost-effectiveness

Cost and impact by intervention

Table 64 summarises the assumptions regarding coverage with TE factors and enablers as well as the relative impact on the cost and effectiveness of the total HIV programme. There are two caveats to bear in mind when comparing these numbers:

1. The impact and cost for the HCT TE factors was calculated assuming that 100% of tests were done using this TE factor, by way of normalising results.
2. The impact and cost for enablers was calculated using full impacts and full costs, not just those paid for under the HIV budget.

As discussed in Section 5.1, the largest potential impacts are gained by TE factors that reduce the loss to follow-up between HIV testing and ART initiation (point-of-care CD4 testing and provider-initiated testing). The only TE factor or enabler that is cost saving is adherence clubs for ART, which reduce the average cost of ART provision per patient as well as the total cost of the HIV programme. Generally, critical enablers and development synergies do not have a considerable impact on life-years saved from preventing HIV infections and deaths. The enabler with the greatest impact is the community-based GBV intervention based on the SASA! intervention in Uganda, through its reported impact on a reduction of multiple sexual partners.

Table 63: Target population, coverage and impact on total cost and effectiveness for TE factors and enablers included in the Budget scenario

TE factor/ enabler	Target population	Coverage	% change in	
			total life years lost	total cost
1. TE factors				
a. for ART				
Adherence clubs	All adults currently on ART	2015: 10% 2016: 10% 2017: 20% 2018: 30% 2019: 40% 2020: 50% 2021: 60%	5%	-1%
Home-based ART ^b	All adults currently on ART	2015: 0% 2016: 0% 2017: 3% 2018: 7% 2019: 10% 2020: 13% 2021: 17%	-	?
Point-of-care CD4 testing			8%	1%
b. for HCT				
Provider initiated HCT		25% of tests	5%	3%
Mobile HCT		25% of tests	3%	2%
Home-based HCT	All adults undergoing testing	15% of tests ^c	3%	2%
HCT invitations to pregnancy partners			6%	5%
2. Critical enablers				
SASA! Community-based gender-based-violence intervention	Intense intervention to adults 18-35 + community outreach; in HTA ^d only		3%	6%
Life skills and vocational training for adolescent girls	All adolescents aged 16-25 who aren't in education or employment		1%	1%
Risk reduction for alcohol and substance users	Alcohol and substance using adults		0.2%	1%

b We did not assess the cost impact of this TE factor in isolation. We know that home-based care reduces the cost of first-line adult ART by 6%, but this likely doesn't translate into a saving in total cost.

c The remaining 36% of tests are assumed to be done through traditional stand-alone, clinic-based, non-targeted HCT.

d HTA: high transmission area

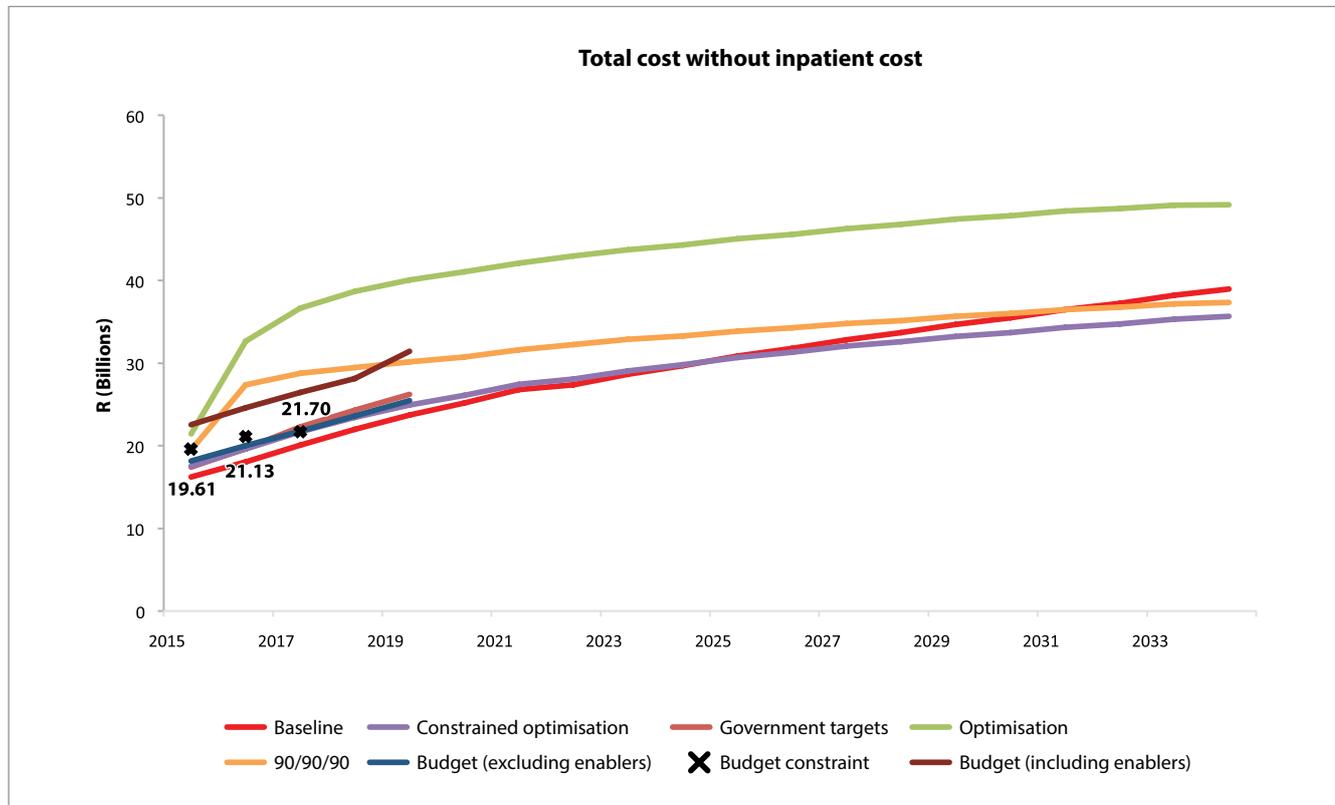
TE factor/ enabler	Target population	Coverage	% change in	
			total life years lost	total cost
Risk reduction for substance users	Meth- and cannabis-using women 15+		0.1%	0.3%
School-based HIV/STI risk reduction	Same as Life skills curriculum ^e		2%	8%
Teacher support	Adolescents in informal settlements and rural areas with >28% ANC prevalence		1%	0.2%
Parental monitoring			2%	4%
School feeding			0.2%	2%
Positive parenting	High schools in low-income districts		1%	5%
Supporting adolescent orphan girls to stay in school			0.2%	6%
State-provided child-focused cash transfers	Adolescent orphan girls		0.01%	2%

Total cost

The Budget scenario is limited to the three years of the MTEF, which means we were unable to project the epidemiological impact over 5 or 20 years in order to compare with the main scenarios described in Sections 5.1.1 and 5.1.2. In terms of total cost over those three years, the budget scenario will increase the currently allocated HIV budget for the mid-term expenditure framework (2015/16 to 2017/18) by 23% with enablers, reduce it by 4% without enablers, and require, like all other scenarios, additional funding year-on-year for foreseeable future. However, as with the 90-90-90 and constrained optimisation scenarios, annual cost is likely to decrease below baseline in 15-20 years (Figure 36).

^e These values are based on covering all adolescents, not only those covered by the life skills curriculum.

Figure 34: Total cost without inpatient care for all scenarios including the Budget scenario (including and excluding the cost of enablers)



6.2 SUSTAINING THE OPTIMAL RESPONSE

To sustain the long-term implementation of the recommendations of the HIV and TB Investment Cases, the South African government will need to take key steps. First, the HIV and TB District Implementation Plans will use the results of the HIV budget scenario to inform targets and budgets at the district level for the years 2015/16 to 2020/21. These inputs will be updated at the end of Phase 3, once results are available at the sub-provincial level. Additionally, the results of the evidence review will inform parts of the mid-term review of the National Strategic Plan on HIV, STIs and TB 2012-2016. On the part of external funders, the results are presently being used to inform the gap analysis for the concept note for the country’s next GFATM proposal that is currently being drafted.

6.2.1 90-90-90 HIV and TB District Implementation Plans

Resources for HIV activities have traditionally been allocated to provinces and districts on the basis of last year’s budget and demographics, rather than on the basis of need and yield. In early 2015, NDOH embarked on a process to elevate the role of South Africa’s 52 districts and municipalities in setting targets and implementing public sector HIV and TB policies, in order to support reaching the 90-90-90 targets. This includes the development of costed and prioritised District Implementation Plans (DIP) for all districts.

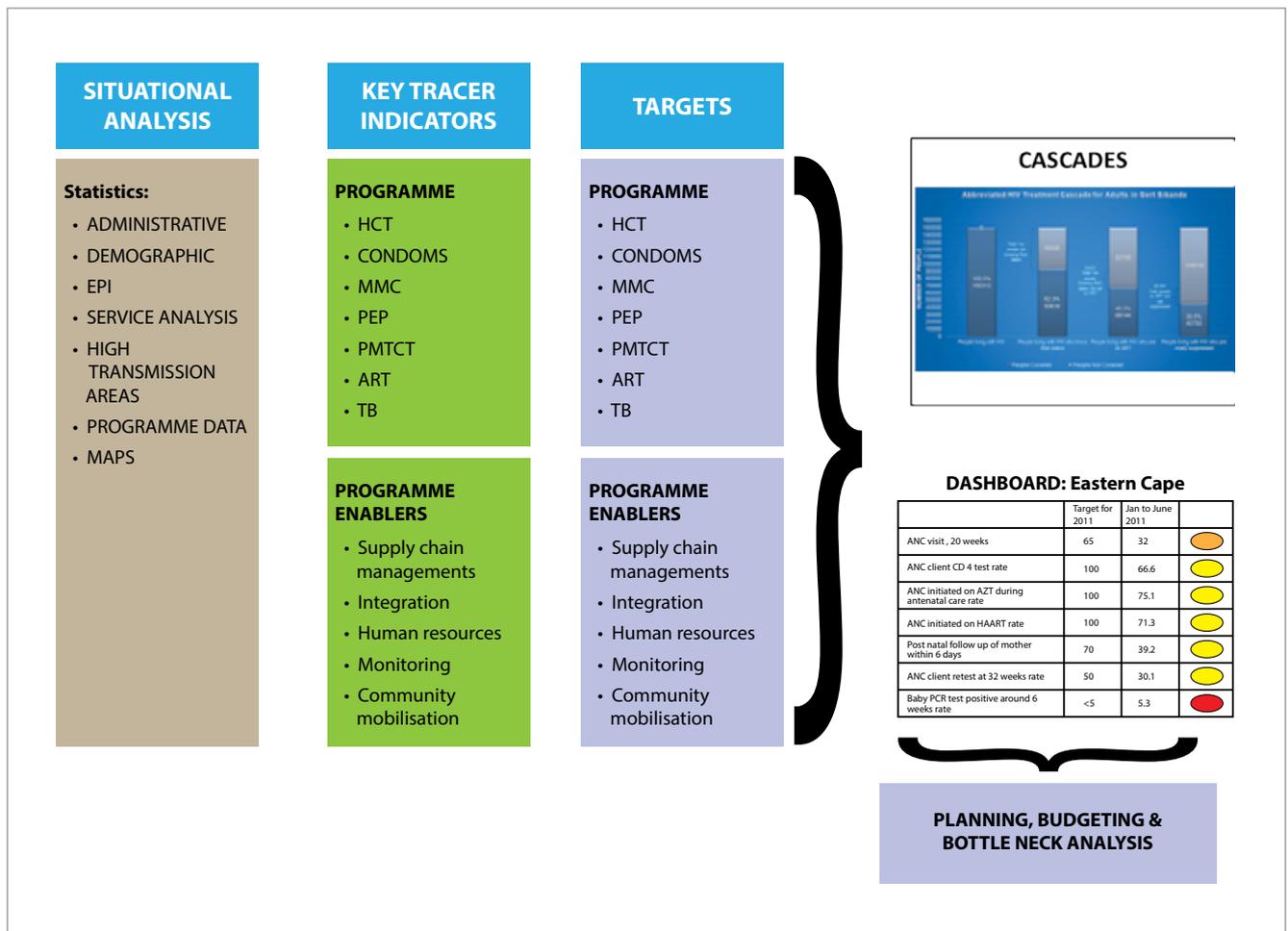
For these, districts were issued templates allowing them to choose their own priority interventions from a set menu, establish targets for each of them, and calculate budgets for the package of care. At the beginning of the 2015/16 financial year, the template was piloted in the West Rand District Municipality. The template includes information on the national-level targets for the HIV budget scenario and the HIV and TB unit costs collected during the IC process.

Through the DIP process the NDOH aims to ensure that:

- South Africa takes steps to ensure that it is on track to achieve the 90-90-90 targets for TB and HIV by 2020;
- financial resources are available and are allocated on the basis of greatest need and directed towards the evidence-informed interventions shown to have greatest impact in the HIV and TB investment case; and
- efforts to meet the new targets will be fully integrated into the existing health system at primary health care level, potentially leading to decongestion and increased efficiency of the health service.

Progress against the 90-90-90 targets will be closely monitored monthly through a sub-set of tracer indicators, district and facility level targets and dashboards. This protocol is modelled on South Africa’s highly successful approach to achieve the Global Plan for eMTCT (Elimination of Mother to Child Transmission). In addition to programme indicators the plans will include actions to address critical enablers such as human resources, community mobilization, and procurement and supply management (see Figure 37).

Figure 35: Tools for developing and monitoring the District Implementation Plans



6.2.2 NSP mid-term review

The end of September 2014 marked the mid-term of the implementation of the country's current National Strategic Plan on HIV, STIs and TB 2012-2016. Accordingly, in early 2015 SANAC initiated a mid-term review of the NSP. The mid-term review included an assessment of the impact of existing interventions (biomedical and other) currently rolled out under the NSP. The NSP review process will be realigned to take into account the evidence review undertaken for Phase 1 of the Investment Case, wherever relevant (see Chapter 4).

6.2.3 GF concept note

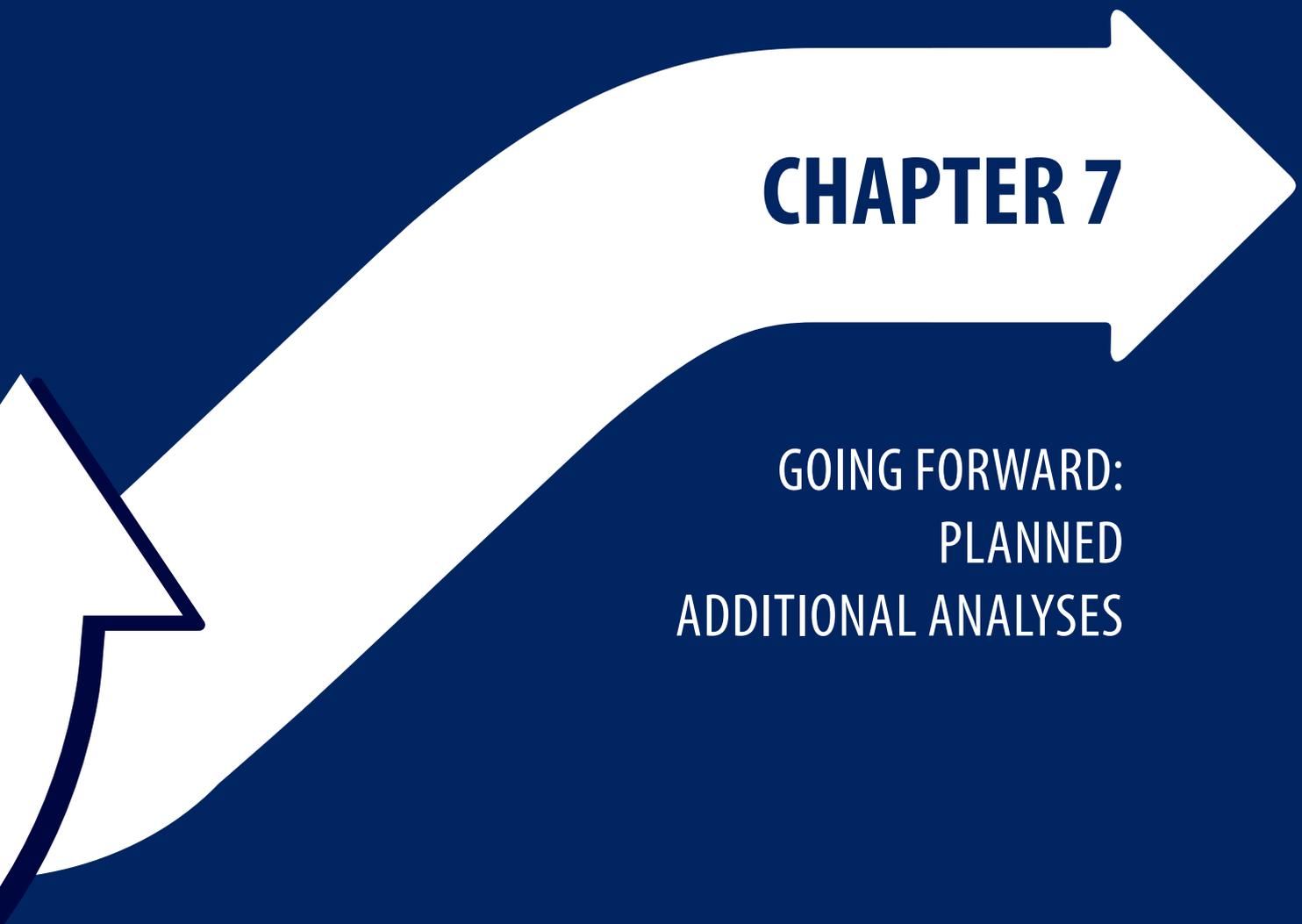
Since the beginning of 2015, SANAC has also been leading the development of a new proposal for funding from the GF. The Investment Case provides the backdrop for the GF concept note as well the landscape for which the concept note is developed. The grant implementation period for this proposal will be from 1 April 2016 to 31 March 2019.

The proposal will focus on high-impact areas to support the implementation of the 90-90-90 strategy chosen by the GF Country Coordinating Mechanism, informed by the work of the Investment Case. Under the GF's New Funding Model, this proposal must be accompanied by a concept note that makes the economic case for a recipient country's entire HIV response (not just the part that is funded by the GF, which, as seen in Section 2.3, is rather small in the case of South Africa). The format of the IC lends itself well to inform this concept note, in particular by creating the data necessary for the analysis of the gap in current and future funding. The results will also be used to support the choice of priority interventions and, likewise, of those areas where additional research is needed, such as with regards to the effectiveness of non-biomedical or behavioural interventions, TE factors and enablers/ synergies. Furthermore, the IC provides information on unit costs and will serve as a guide for the estimation of target population groups for specific interventions.

6.2.4 PEPFAR's "Focus for Impact"

Lastly, from Phase 2 and 3 onwards, the results of the IC will be used to update the "Focus for Impact" programme initiated by PEPFAR in 2015. Under this programme, PEPFAR South Africa sought to geo-prioritise their support to those districts with the highest number of people in need of both HIV prevention and treatment. Even though decisions with regards to which districts to include have already been made for the year 2015/16, they might be re-evaluated based on sub-provincial level results from the HIV and TB IC once they become available.





CHAPTER 7

GOING FORWARD:
PLANNED
ADDITIONAL ANALYSES

Work on the South African IC is meant to be iterative, with additional rounds of evidence collection, synthesis, and analysis planned in the coming years, as new data become available and as the models used in this analysis evolve.

This report covers Phase 1, which ended in March 2016, producing national-level results. Phase 2 (April to July 2016) will bring these results to the provincial level. Phase 3 (July to December 2016) aims to incorporate geospatial data as well as district-level data into the optimisation exercise to answer the question whether resources should be targeted to specific districts or sub-districts.

7.1 PLANNED ANALYSES FOR HIV

7.1.1 Phase 2: Provincial-level optimisation and budgets

In Phase 2, the IC exercise will undertake the optimisation at the provincial level, using versions of Thembisa parameterised to the nine provinces in South Africa and the same unit costs as in Phase 1 (as scant data on the variation of costs between provinces are available). This will enable decision-makers and other stakeholders to assess whether the order in which interventions should be scaled up changes between provinces, especially those with very different epidemics.

7.1.2 Phase 3: Geo-spatial analysis

Currently a number of strategic exercises focus on the district (as opposed to national or provincial) level of HIV planning and programming. For the mainstay of HIV funding, the South African Government's Comprehensive HIV/AIDS Conditional Grant, planning and budgeting is increasingly performed at the district level, with the first set of district-level HIV business plans due in September 2015. PEPFAR, contributing about 15% of current public-sector HIV expenditure, recently undertook a district planning exercise (called "Focus for Impact") to inform the planned geographical prioritisation of PEPFAR programme support, which is planned to start in the coming months. The GF, contributing about 5% of current public-sector HIV expenditure, also suggested geographical targeting as a part of the concept note for the country's 2015 funding application. (For more information on any of these analyses, see also Chapter 6.)

The increasing interest in a geographical targeting strategy for the country's HIV response is juxtaposed by a number of recent modelling exercises using sub-national level data from a number of different sources, either for South Africa or for other sub-Saharan African countries. As the current modelling framework does not allow for sub-provincial level analysis, the IC project Phase 3 will convene a working group composed of analysts involved in these modelling exercises to discuss whether the results of these analyses may be used to inform policy, and how they can be improved by the best use of available South African data and advanced triangulation techniques.

This geospatial analysis will aim to help the South African government to:

- (a) Understand the magnitude of current HIV infections by district (estimates of current district-level prevalence and incidence);
- (b) Predict the likely magnitude of future HIV infections by district (estimates of future district-level incidence);
- (c) Use this information to plan interventions, including, if necessary, the geospatial targeting of prevention and/or treatment interventions to specific districts (potential impact of geographic targeting).

The process will involve two steps:

1. Review and, where necessary, update the results of existing analyses and determine whether and how they can be used to inform a geographical focus for prevention and treatment services in South Africa.
2. Review, and where necessary, facilitate access to, the best data sources to further improve on the geographical accuracy of existing or new models, with the aim of improving a geographical focus for prevention and treatment services in South Africa.

7.2 PLANNED ANALYSES FOR TB

7.2.1 Phase 2: Improved model functionality

TB transmission model

The version of the models which was used to project the epidemiological and cost impact of the interventions had a number of key limitations. These included:

- Inability of the epidemiological model (TIME, largely a transmission model) to take account of the impact of extra-pulmonary TB. Extra-pulmonary TB accounted for 13% of all TB cases in 2013 and is associated with higher mortality. As patients with extra-pulmonary TB are often hospitalised and must undergo multiple tests to confirm the diagnosis, the condition is associated with substantial costs.
- Inability of the models to disaggregate high-risk groups either with respect to their contribution to the TB burden or regarding the impact of interventions on specific groups.
- Inability to model the impact of specific interventions required achieving the given targets. TIME had the capacity to assess the impact of the interventions if scaled up from a baseline to a given target but could not contribute meaningful information as to how to reach these targets. As an example, the model was able to estimate the epidemiological impact of screening a particular percentage of primary care clinic attendees, but could not describe the interventions required to achieve this target.

The current version of the model therefore needs to be revised and its functionality improved in order to take into the account these limitations.

Defining and incorporating key populations

Several key populations have been defined in the current version of the NSP. These include household contacts of people with TB, miners, health care workers, correctional services officers and inmates, children, diabetics, people living with HIV, people who live in informal settlements and migrants. The sizes of some of these key populations, the burden of TB among them and the contribution they make to the overall burden of TB in South Africa is not well defined. The EVISAT reviews attempted to do this but were also limited by the lack of pertinent evidence. There is therefore an urgent need to define these key populations and their contribution to the TB burden in South Africa.

7.1.2 Phase 2: Extended cost model

Phase 2 will make use of a new cost model developed TB-MAC to estimate the costs of reaching the global TB Targets. As part of this exercise, a cost model was developed for South Africa that can generate estimates of the costs of different combinations of TB interventions implemented at different levels of coverage. The cost model takes a societal perspective and includes costs incurred by patients as well as service providers. As for Phase 1, the model draws on data from a number of on-going TB services costing studies from South Africa to generate estimates for a range of interventions from intensified case finding to improving the quality of MDR-TB treatment. Working with the NDOH, in Phase 2 the cost model will be expanded to include the 90-90-90 interventions.

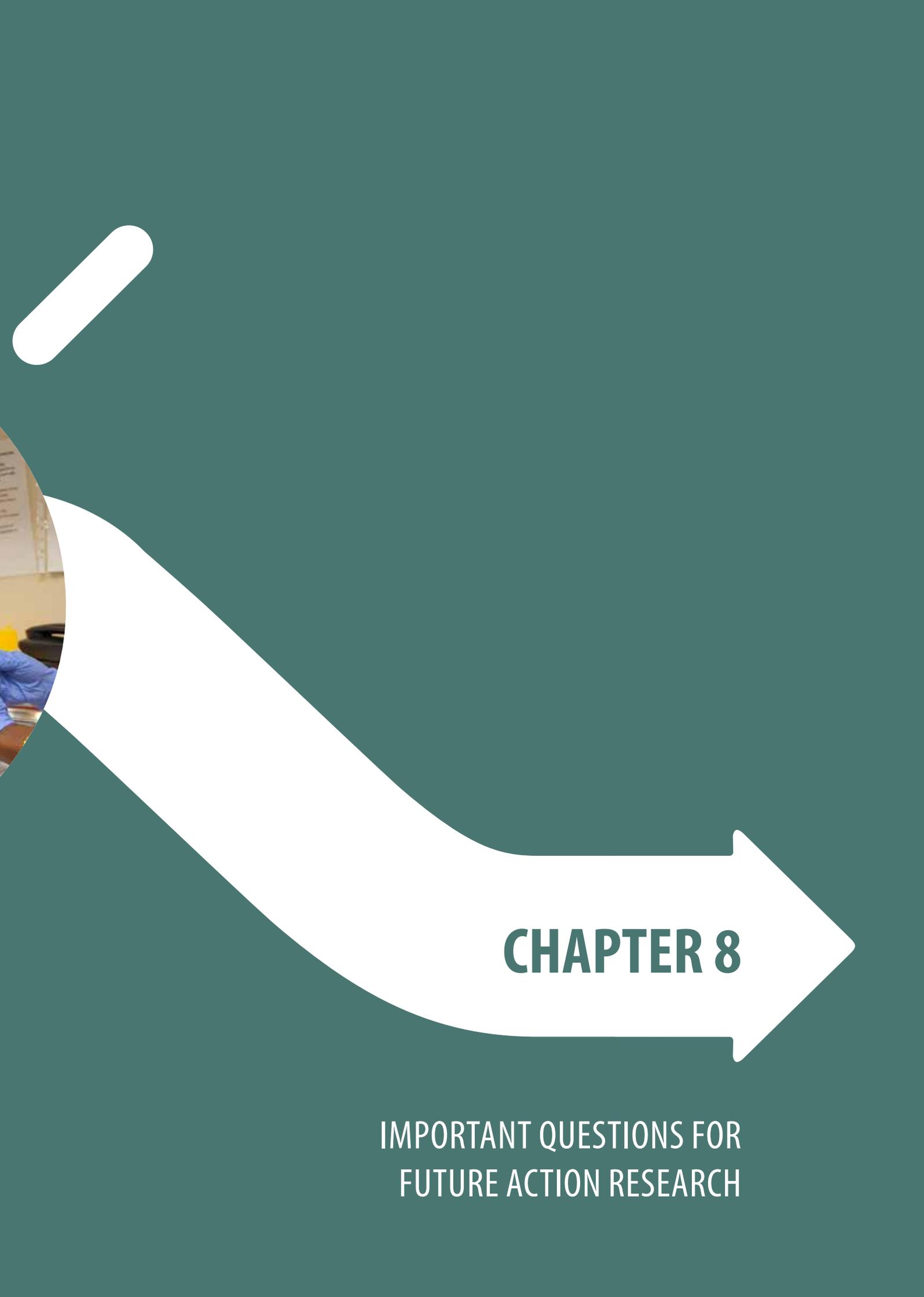
7.1.3 Phase 2: Provincial-level analysis

With funding by the Bill & Melinda Gates Foundation, a user-friendly version of the cost model will be made available for use by the NDOH. The model will be simplified for use at the provincial level to support cost estimation of different TB control strategies.

7.1.4 Phase 2: Technical efficiency factors

During Phase 1 of the Investment Case, the team developing the cost model worked to define the 'how' of reaching the targets. The new TB cost model is built to additionally answer questions on the allocative efficiency (can we invest in better strategies?), scale efficiency (what is the optimal level of coverage?), as well as technical efficiency (can we improve implementation?) of TB investment strategies. Most of the technical efficiency factors that were excluded from Phase 1 due to a lack of detail on the structure of the interventions modelled (see Section 3.2.2) will be included in Phase 2.





CHAPTER 8

IMPORTANT QUESTIONS FOR
FUTURE ACTION RESEARCH

An important purpose of the Investment Case was to take stock of available evidence. As previously noted, the absence of evidence for effectiveness does not mean that a particular intervention is not effective, although it does limit the ability of decision-makers to use an evidence-based approach to optimise the national response to HIV and TB. Out of desire to ensure a sound evidence basis for its recommendations, the IC exercise excluded a number of interventions, TE factors and enablers due to the absence of clear evidence, even though the members of sub-working groups were convinced that they are, in fact, effective.

With the aim of guiding future research efforts to close some of these important evidence gaps, sub-working groups identified gaps in the evidence currently available. It is hoped that these gaps will soon be filled, in order to inform future iterations of the IC.

8.1 KEY POPULATIONS

Several surveys are currently underway to determine the size, biological and behavioural characteristics of a number of key populations. Demonstration projects and evaluations of interventions are being conducted, and it is anticipated that these can supply some of the evidence that is sorely lacking on optimal responses for high-burden groups.

Although biomedical interventions such as PrEP have been shown to be effective, uptake and adherence are critical technical efficiencies, and evidence regarding these factors, particularly among sex workers and PWID, are sparse.

Behavioural interventions are widely used among key populations, and are strongly recommended by WHO, SWEAT, SANAC and the NDOH. However, little data link these interventions to survival or reductions in new HIV and STI infections. Finally, hard-to-reach populations are often reluctant to visit health facilities for fear of stigmatization, and successful models are urgently need for taking health services to key populations, or ensuring that facilities are health workers are competent to address health issues specific to these target populations are important and need to be further investigated.

8.2 PMTCT

Although PMTCT was one of the first HIV interventions broadly implemented in South Africa, the bulk of available evidence focuses on the clinical components of the programme. This is quite surprising, as one would have expected there to be a significant body of evidence around all programme effectiveness components of the programme beyond “prongs” 3 and 4. There is limited evidence on the impact of “prongs” 1 and 2 (primary HIV prevention for women and girls, and reducing unmet need for family planning) on the impact of MTCT outcomes; maternal and child survival. Further to this, measuring the impact of community-driven approaches is also limited.

Several key questions need to be addressed to ensure that PMTCT efforts cross the final mile and reach the ultimate goal of ending new infections among children and keeping their mothers alive. Answers to these research questions will enable interventions to become more evidence base, hence strengthening the implementation.

Key PMTCT-related research questions that need to be addressed include:

1. What are best practices for integrated services at different levels of health care delivery (eg, primary, community, hospital), and which types of integrated service will ensure the best results with respect to fewer new infections in children and improved child and maternal survival?

2. How best may male involvement in MCH services in the South African context be enhanced?
3. What is the impact of preconception and fertility planning on PMTCT outcomes?
4. What is the best approach to providing optimal postnatal care services that strengthen referrals and linkages with ART services and EPI/well-baby services?
5. What are the best models of facility-community linkages and referral pathways that simultaneously strengthen the delivery of PMTCT services, the linkage with treatment, care and support services as well as linkage to services delivered post delivery through the first 18 months of the infant's life.
6. What are the barriers and facilitators for young adolescent women in accessing services related to family planning/contraception as well as ANC, and how do these barriers link to the gaps in PMTCT services for young mothers.
7. What is the impact on child survival of birth PCR testing and repeat testing at different intervals (10 weeks/14 weeks and 9 months/18 months)?

8.3 SOCIAL AND BEHAVIOUR CHANGE COMMUNICATION

As explained in Section 4.1.3, there remain a number of gaps in the evidence for SBBC that need to be addressed by research:

- **Few evaluations of holistic /comprehensive communication programmes.** The majority of rigorous impact evaluations have focused on mass media. Far fewer studies have evaluated community mobilisation programmes, and even fewer have assessed integrated campaigns comprising mass media, social mobilisation and advocacy. As the majority of campaigns are designed using all of these approaches, this is a major gap in the evidence.
- **Evaluations focus on whether communication programmes work rather than how they work.** Traditionally meta-reviews of communication programmes have sought to answer whether communication programmes reduce risky behaviour [354]. It may be more useful for programme designers to understand how these programmes have worked and which “intervention content dimensions might be related to success” [20].
- **The majority of studies focus on behaviour change as an outcome.** Many programmes, however, focus on sustaining a behaviour rather than changing it. For example, while it may not be feasible to increase the age of sexual debut further in South Africa, communications programmes will need to continue promoting delayed sexual debut in order to prevent further increases in early sexual debut.
- **Context matters.** A communication programme is instituted in a particular place and time. With respect to desired outcomes, this context may be neutral, supportive or negative. An example is a condom campaign among young people where the school and adult environment opposes sex of any kind, protected or unprotected; a campaign in this context is likely to be less successful than a comparable campaign undertaken in a context where condoms are freely available to young people. Likewise, a gender equity campaign may struggle for traction in a broader media environment that actively supports gender stereotyping and inequality. Measuring the context is not easy and rarely done, although it is important for programme planners and implementers.

- **There are few cohort studies.** Studies of SBCC interventions often report only short-term outcomes (3-12 months). However, changing behaviour is a complex process and takes time. One or more cohort studies that measure exposure, behaviours and biological end-points over time would add value to the field.
- **Many evaluations are not published in peer-reviewed journals.** Peer reviewed journals are not always interested in publishing project evaluations. As grey literature is often not included in systematic reviews, the findings may be skewed towards the notion that communication is not as effective an intervention as other interventions for HIV.

8.4 COMPREHENSIVE CONDOM PROGRAMMING

Many of the studies initially suggested by the working group on comprehensive condom programming described either the predictors of condom use or the intervention without an evaluation of its effectiveness. In addition, many studies, particularly for the TE factors, were qualitative and were not able to be included in the model. Literature tended to describe barriers to condom use rather than reporting on the extent to which these affected the uptake of condoms. Some of the studies evaluated interventions for populations such as MSM, who were not included in the primary model. The evidence review also struggle to find adequate effectiveness data for condom demonstration interventions, a potentially important shortcoming, as the CCP working group stressed that not knowing how to use a condom is a potential barrier to condom use, especially among youth.

8.5 CARE AND TREATMENT

Most of the gaps identified by the care and treatment working group fell into two areas: pre-ART care, and improving the health system more generally.

8.5.1 Pre-ART care

Surprisingly, given extensive documentation of the extent of loss at each stage of the HIV care continuum, the evidence review failed to find a single published study evaluating interventions aimed at reducing loss from pre-ART care, or loss to ART initiation. Studies were identified covering interventions to improve linkage from testing to the establishment of ART eligibility (ie, CD4 cell count test, see the HCT discussion, Section 4.1.7), but none evaluating linkage to ART initiation once ART eligibility has been established. The single such study found, of same-day ART initiation after HIV testing, had not finalised analysis of follow-up data by the time of the project's data lock in the end of January 2015.

8.5.2 ART

In terms of ART, the working group agreed that the next frontier would not so much be another increase in eligibility (from a threshold of 500 CD4 cells/ microl to treat-and-treat) but rather improving the health system, which affects the quality of all care, including ART. In particular, evidence gaps impeded the modelling team's ability to take account of **programme enablers**.- Potential enablers include a unique identifier to trace people receiving ART across facilities and provinces; decreasing drug stock outs across all provinces, by improving quantification systems from clinics to pharmacies to sub-depots to depots to district to national (tenders), using direct delivery vouchers and/ or tracer stock; fully integrating ART with all other chronic health care at the primary health care level; and, finally, combatting treatment fatigue of the

growing cohort of people who have been for ART for up to a decade, and are still expected to spend a day every three months queuing at a health facility simply to get their prescriptions refilled. Some of the ART-specific approaches to improve longstanding patients' experience were included in the IC analysis, such as adherence clubs, but many more need to be piloted and evaluated, including those that could improve integration with other NDOH initiatives, such as having community health workers issue adult patients with pre-packaged ARV prescriptions as part of the primary healthcare re-engineering initiative. Also needed are evaluations of approaches with the potential to improve adherence to any chronic medication, such as the planned Central Chronic Medicine Distribution and Dispensing (CCMD) programme.

The IC review clearly indicates that the only way forward for ART is complete integration of the intervention with all other healthcare services, notably TB, and that ART should be integrated with the planned scale-up of the National Health Insurance System, including the need for facilities to meet national core standards. Affected families should be able to seen together at the same appointment by the same staff. Finally, it was equally clear to the care and treatment working group that additional research is needed on concrete interventions improving health care workers' conditions, such as improved staffing levels, infrastructure, and information systems (including the new DHIS module, standardised paediatric stationery, and the full roll-out of Tier.net).

8.6 MMC

During the consultative workshop, the working group on MMC expressed interest in including all TE factors in the model once high-quality data becomes available. An ongoing study planned by NDOH and the Health Policy Project (HPP) and sponsored by USAID will provide data on differences between various models of VMMC. The same analysis will provide information regarding the cost of demand creation.

Other data gaps noted include:

8.6.1 Alternative staffing model

Commenters noted that an alternative staffing model could result in sizable cost savings and is a high priority for future iterations of the analysis. In particular, the decision that savings from other parts of Africa were not applicable to the South Africa context was questioned.

8.6.2 Demand creation

Although some data on demand creation for MMC is available, more analysis is needed to estimate the impact of different interventions on actual demand for services. For example, data made available to the MMC sub-working group did not present a counterfactual for how many of the circumcised individuals would have likely received the procedure regardless of the additional demand creation. Studies should also be designed to allow generalization across the country.

A new study on demand creation from Johns Hopkins Health and Education in South Africa (JHHESA) is expected in 2015.

8.6.3 Prepex™

The Centre for HIV and AIDS Prevention Studies (CHAPS), Aurum Institute and the Perinatal HIV Research Unit (PHRU), in collaboration with Society for Family Health (SFH), are all working on studies of *Prepex*™. Once these are complete, it may be possible to include *Prepex*™ in the model, particularly if the study allows an estimation of the device's impact on both cost and increased demand.

8.6.4 Private sector providers

While some information is available for assessing cost and increased demand through private sector providers, additional analysis is necessary. The HPP study noted above will also provide cost data regarding private sector providers.

8.6.5 Collaboration with traditional healers

Several participants in the consultative workshop expressed a strong interest in including collaboration with traditional healers in the model. Data for the total number of traditional circumcisions performed is reportedly available, and cost data may be available from NGOs implementing these interventions. However, analysis is required to process this data and estimate the cost and increased demand associated with this approach. For any circumcisions to be included in this category, full removal of the foreskin would need to be verified, as the protective benefits of partial removal of the foreskin has not been shown.

8.7 HCT

Although a wealth of data regarding HCT was examined by the sub-working group, little was in a form that was usable in the IC. For example:

- Some studies did not describe an intervention
- There was no quantitative result in many studies.
- The context of some studies was inappropriate for South Africa e.g. studies from China and the United States
- The interventions for some populations cannot be targeted in the models e.g. OVC, MSM, PWID.

Some potential research gaps include:

- In terms of self-testing, no studies evaluated post-test linkage with counselling and treatment outcomes, and reporting quality was poor. Controlled, high-quality trials in diverse settings are warranted to confirm and extend these findings. There was little evidence on feasibility, acceptability, ethics and effectiveness of self-testing in South Africa.
- The impact of couples HCT on concurrent partnerships, including potential reduction in new infections among concordant HIV-negative couples, remains undocumented.

- More evidence is needed regarding the potential risks of adverse social and psychological consequences of couples HCT, such as those affecting quality of life, marital relationships or the risk of violence, including emotional abuse and GBV.
- Other topics warranting additional research include barriers to accessing couples HCT; ways to generate demand and increase utilisation of community-based HTC (CHTC); and the range of acceptable and effective models for CHCT, including models of community based services.

8.8 OTHER BIOMEDICAL PREVENTION INTERVENTIONS

Several studies are currently underway to determine the efficacy of a range of prevention methods, including PEP and syndromic STI management. Demonstration projects and evaluations of interventions currently underway will strengthen the evidence base on other biomedical prevention interventions and likely enable future iterations of the IC to take account of important prevention methods that were not modeled here.

While biomedical interventions such as PrEP have proven efficacious, successful implementation relies on a number of technical efficiencies, particularly on consistent use and availability. Evidence regarding these factors, as well as regarding their use in key populations, is sparse.

8.9 TB

The TB IC identified several gaps and questions for further research.

8.9.1 Unit costs and costs of implementation

The IC took account of the costs of diagnostics and drug treatments, but there was limited information available on costs for other key interventions. More work is needed to determine the costs of key TB interventions such as household contact tracing and screening PHC attendees.

8.9.2 Evidence of efficacy or effectiveness of TB interventions

A number of interventions were excluded because of lack of evidence of effect. Table 10.X lists the main evidence gaps identified in the review and synthesis of evidence.

Table 64: Summary of gaps in the evidence for TB interventions and TE factors

Area	Gaps in evidence/ Questions for further research
Infection control	Effectiveness of TB infection control interventions in reducing transmission, incidence of TB disease, mortality from TB disease and cost effectiveness of such interventions
TB preventive therapy	<p>Effectiveness of interventions to improve uptake, reporting and recording of TB preventive therapy among HIV negative eligible for IPT i.e. child contacts of TB patients , HIV negative adults with silicosis is needed.</p> <p>Effectiveness of IPT in reducing TB incidence in other high risk groups or key populations such as HIV negative taxi drivers, miners and health care workers need to be explored in studies.</p> <p>Evaluations of alternative TB preventive therapy regimens among HIV positives and high risk HIV negatives are also recommended.</p> <p>The ideal preventive therapy regimens for contacts of drug resistant TB patients need to be identified.</p>
TB vaccines	Identification and evaluation of TB vaccine candidates are needed.
Active case finding in high risk population	<p>Studies are needed to determine the affect of case finding on TB transmission, morbidity and mortality.</p> <p>The cost-effectiveness of ICF interventions should be evaluated.</p>
TB diagnostics	Use of Xpert MTB/Rif or similar tools for monitoring response to treatment should be evaluated.
Decentralised MDR treatment	Evaluation of decentralised care and its effect on MDR TB transmission, incidence or mortality is needed.
New drugs	Effectiveness of new TB drugs and TB regimens on TB treatment outcomes for both DR TB and DS TB needs to be assessed.
Adherence support including m-Health	<p>Studies are needed to evaluate the effectiveness of SMS reminders in improving TB treatment completion in programme settings and its impact TB treatment outcomes, including mortality.</p> <p>Evaluation of m-Health technologies in reducing initial loss to follow up.</p> <p>Evaluation of interventions to reduce initial loss to follow-up among patients with both drug-resistant TB and drug-sensitive TB is needed.</p>
TB/HIV integration	<p>Development of validated tools to measure TB/HIV integration is needed.</p> <p>Studies should compare different models of integrating TB and HIV and assess their effect on TB and HIV outcomes</p>
Management and supervision	Evaluation of interventions to improve the management and supervision of staff at primary care clinics is needed.
TB surveillance	Implementation of a pharmacovigilance programme to track adverse events within the TB programme is needed.
Smoking cessation	Studies should evaluate tobacco smoking cessation interventions on TB transmission, incidence or mortality.
TB advocacy, communication and community mobilisation (ACSM) practices	Evaluation of ACSM interventions on TB knowledge and practices is needed.

8.10 SOCIAL ENABLERS

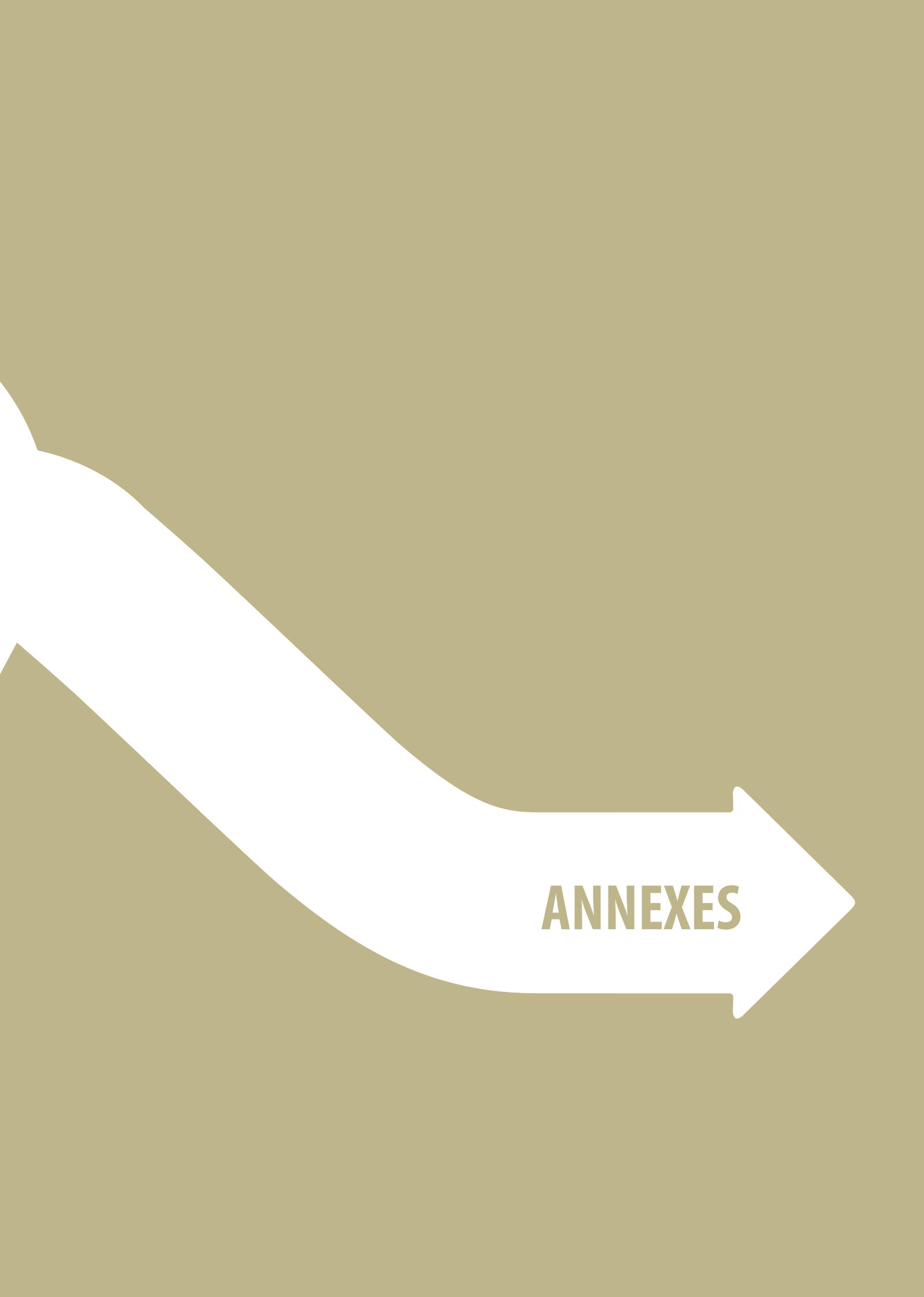
Compared to other components of the Investment Case, evidence was especially sparse for social enablers. Some of the problems encountered in the evidence review included:

- The study did not describe an intervention e.g. longitudinal studies describing the problem, not the intervention.
- There was no baseline comparator, e.g. GBV intervention that increases HCT uptake data by x% with no baseline.
- No quantitative result was available in many studies.
- There was no immediate HIV-relevant outcome e.g. impacts on GBV, school attendance, etc.
- The context of the intervention was inappropriate for South Africa.
- The impact could not be modelled in Thembisa, e.g. increased knowledge of HIV, intention to engage in risky sex.
- The interventions for some populations could not be modelled in Thembisa e.g. adolescents, OVC, MSM.

There is a fair amount of literature describing the impact of development synergies on intermediate outcomes such as risky sexual behaviour. However, relatively few studies examine and report biological endpoints.

Future studies will also need to determine the impact of social enablers and development synergies on newer prevention and treatment interventions, such as PrEP and UTT.



A large, white, stylized arrow pointing to the right, set against a solid gold background. The arrow has a curved tail on the left side. The word "ANNEXES" is written in a bold, gold, sans-serif font inside the arrow's shaft.

ANNEXES

ANNEX 1: SUMMARY OF GRADING OF EVIDENCE FOR EACH INTERVENTION, TE FACTOR OR ENABLER

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Them-bisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
1. Key populations								
PrEP and PEP								
- PrEP for MSM and transgender women	Grant (2014)	1, 2	5	PrEP for MSM and transgender women cannot be modelled	-	-	-	-
- PEP or PrEP for MSM	O'Neal (2014)	1, 2	5	PrEP for MSM cannot be modelled	-	-	-	-
- Oral TDF PrEP for female sex workers and women who inject drugs	Choopanya (2013)	1	5	PrEP for sex workers included	✓	✓	-	-
- PrEP for sex workers	Murnane (2013)	1	1		✓	✓	-	-
Condoms								
Condom promotion with community empowerment for female sex workers	SANAC NSP (2011)	1	1				✓ (CSW)	
	SANAC NSP for sex workers (2013)	2	1				✓ (CSW)	
	Kerrigan (2014)	2	1				✓ (CSW)	
Condom promotion with peer education for female sex workers	SANAC NSP for sex workers (2013)	1	2				✓ (CSW)	✓

a 1: IN (good evidence); 2: IN (government policy); 3: OUT (weak evidence); 3a: Likely more data by Phase 2; 3b: Important research question; 3c: Exclude; 4: OUT (transfer elsewhere); 4a: Other programme area; 4b: Social enablers; 4c: Programme enablers; 5: OUT (can't be modelled); 6: IN (cost only).

b Packages of care for young women (YW), commercial sex workers (CSW), intravenous drug users (IDU), men having sex with men (MSM)

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Themisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
	Feldblum (2005)	1	3c	No impact on HIV. The paper only reports on an impact on STIs	-	-	-	-
Condom promotion with peer education for male sex workers	Geibel (2012)	1,2	5		-	-	✓ (CSW)	
Male and female condom promotion and distribution for sex workers	SANAC NSP for sex workers (2013)	1	2			✓	✓ (CSW)	
	Wariki (2012)	1						
Male and female condom promotion and distribution for inmates	Dolan (2004)	2	5	Inmates are not part of the key populations considered in the Investment Case	-	-	-	-
Male and female condom promotion and distribution for all populations	Charania (2011)	1	4a-CCP		✓	✓	-	-
HIV counselling and testing								
HCT plus TE of targeted communication, especially multi-media campaigns for MSM and transgender women	Wei (2011)	1,2,3	1		-	-	✓ (MSM)	
HCT plus TE of mass media for MSM	Vidanapathirana (2005)	1,2,3	1		-	-	✓ (MSM)	
HCT plus TE of venue/mobile HCT for MSM and people who inject drugs	Sing (2012)	2,3	2		-	-	✓ (IDU)	
HCT for inmates	Varghese (2001)	2,3	5	Inmates are not part of the key populations considered in the Investment Case	-	-	-	-
Behavioural interventions								
Peer educators to enable HCT and condom use for female sex workers	Luchters (2008)	1	1		-	-	✓ (CSW)	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Community mobilization/empowerment for female sex workers	Beattie (2014)	1	1		-	-	✓ (CSW)	
Behavioural interventions for MSM	Johnson (2008)	2	2		-	-	✓ (MSM)	
Sexually transmitted infections								
Periodic presumptive treatment & TE of peer education and condom promotion for female sex workers	Steen (2012)	1,4	3c	No HIV outcome. Impact on STIs only	-	-	✓ (CSW)	
STI syndromic management for the general population	Grosskurth (2000)	1,4	3c	No HIV outcome. Impact on STIs only	-	-	-	
Interventions for people who inject drugs (PWID)								
NSP plus TE of motivational interviewing and peer support for PWID and female sex workers	Strathdee (2013)	1,2	1		-	-	✓ (IDU)	
NSP for PWID	Des Jarlais (2013)	1,2	1		-	-	✓ (IDU)	
NSP plus TE peer educators for PWID	WHO (2004)	1,2	1		-	-	✓ (IDU)	
ART retention with TE of MAT for PWID	Reddon (2013)	1,2	5	Could not be included under current IDU package in Spectrum. To be revisited in Phase 2	-	-	-	
2. PMTCT								
PMTCT Option B+	Black 2013							
WHO guidelines	1	1		✓	✓			
Nurse quality mentor programs	Grimwood	1	4a – ART		-	-	-	
Preconception services and fertility planning	M2M Impact Report	1	3c	No direct HIV impact found in the study	-	-	-	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembeisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Early ANC booking	PHC in Western Cape	1	3c	No source provided	-	-	-	
Health education for women of reproductive age		2	5	No evidence provided. The intervention cannot be modelled even if it were part of government policy	-	-	-	
Facility based pregnancy screening	KZN Implementers	1	3c	Anecdotal evidence; cannot be quantified in a way that can be modelled	-	-	-	
Community based pregnancy screening	Anderson et al.	1	3c	No HIV end point. All evidence refers to uptake of services	-	-	-	
Infant testing at birth	Human et al.							
Langanza et al.	2	1		✓	✓	-	-	
Home birth attendant training	Lillian (2013)	1	3c	Source refers to infant testing at 6 weeks, not home birth attendant training	-	-	-	
Universal infant testing at 9 months	Lilian (2013)	1	3c	Source refers to infant testing at 6 weeks, which has been included in place of infant testing at 9 months suggested by working group	-	-	-	
3.SBCC								
SBCC campaign 1 (encouraging testing and discouraging multiple partners)	Programme data	1	1		✓	✓	✓	
SBCC campaign 2 (increasing condom usage)	Programme data	1	1		✓	✓	-	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
SBCB campaign 3 (increasing HIV testing, condom usage and MMC uptake)	Programme data	1	1		✓	✓	✓	-
4. Comprehensive condom programming								
Consistent condom use	Weller and Davis-Beatty (2002)	1	1		✓	✓	✓	-
Male and female condom education	Callegari (2008)	1	1		✓	✓	✓	-
Discussion of condom use	Peltzer (2012)	4a-SBCC	4a-SBCC		✓	✓	✓	-
Difficulty getting condoms	Peltzer (2012)	3c	3c	No intervention				-
Inconsistent use of male condoms amongst MSM in peri-urban townships	Baral (2011)	3c	3c	No intervention				
Introduction of female condoms for female sex workers	Hoke (2007)	4a-KP	4a-KP				✓	✓ (FSW)
National mass media programmes for the general population	Johnson (2013)	4a-SBCC	4a-SBCC		✓	✓	✓	-
	Kincaid and Parker (2008)	4a-SBCC	4a-SBCC		✓	✓	✓	-
National mass media programmes for men	Kincaid and Figueroa (2012)	4a-SBCC	4a-SBCC		✓	✓	✓	-
National mass media programmes for youth	Kincaid and Figueroa (2012)	4a-SBCC	4a-SBCC		✓	✓	✓	-
Mass media programmes for men and women	Van Rossem and Meekers, 2007	4a-SBCC	4a-SBCC		✓	✓	✓	-
Community health workers	Mwai et al (2013)	4a-ART	4a-ART		✓	✓	✓	-

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Condom distribution in schools	None	5	3c	These interventions were excluded because of a lack of evidence on their effectiveness rather than an inability to model them				
	-	-	-	-				
Expand distribution to non-traditional outlets	None	5	3c		-	-	-	-
PEPFAR limitation on distribution of condoms in schools	None	5	3c		-	-	-	-
Rebrand Choice condoms to increase uptake	None	5	3c		-	-	-	-
Negative perception of public sector condoms	None	5	3c		-	-	-	-
Availability of and preference for other types of condoms	None	5	3c		-	-	-	-
Fit and feel	None	5	3c		-	-	-	-
Barriers to condom use	None	5	3c		-	-	-	-
5. ART								
<i>Pre-ART care</i>								
Pre-ART care and ART initiation at primary health clinic	None	3c	3c		-	-	-	-
Isoniazid preventive therapy	None	4a-TB	4a-TB		-	-	-	-
Cotrimoxazole	Clouse 2012	1	1		✓	✓	✓	-

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Same day ART initiation	None	3a	3a		-	-	-	
ART care								
ART (Current guidelines)	Model assumptions	1	1		✓	✓	✓	
ART for discordant couples	Model assumptions	1	5	Discordant couples are not a separate population in the model and could not be targeted	-	-	-	
Universal test and treat	Model assumptions	1	1		✓	✓	✓	
Early paediatric treatment for children from 6-13	None	3c	3c		-	-	-	
Third line treatment	Model assumptions	6	6	Third-line ART was included as a cost increase in the NACM	✓	✓	✓	
Teen and adolescent friendly clinics	None	4a-HCT	4a-HCT		-	-	-	
Workplace ART	Charalambous (2007)	3c	3c		-	-	-	
Increase ART coverage in farmworkers	None	3b	3b		-	-	-	
NIMART	Barton (2013)	6	6	60-80% NIMART coverage is included in all scenarios, incl. baseline	✓	✓	✓	
NIMART (Nurse management only)	Brennan (2011)	6	5	Since NIMART was modelled as part of baseline, it was not possible to model specific changes to the NIMART package. This will be added in Phase 2	-	-	-	
Improved mentorship for NIMART	Green (2014)	1	5		-	-	-	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembeisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Improved training and mentorship for paediatric NIMART	Workneh (2013)	1	1		-	-	-	
Integration of NIMART into IMCI sites	Barton (2013)	6	5		-	-	-	
6. MMC								
Medical male circumcision	Watami (2014)	1	1		✓	✓	-	
Early infant male circumcision	VMMC RCTs	1	1		✓	✓	-	
Prioritization by site type	Bollinger (2014)	3a	3a	Excluded due to lack of adequate outcome data and estimation techniques	-	-	-	
Alternative staffing model	Tumwesigye 2013	3	5	Could not be modelled since changing the staff ingredients in the MMC unit cost was not feasible as a detailed breakdown by cost ingredients was not available	-	-	-	
High intensity campaigns	Bollinger 2014	3	3	Excluded due to lack of adequate data ^c	-	-	-	
Media and work place campaigns	Bertrand 2011	3a	3a	Partially included from the cost side as part of demand creation ^d	✓	✓	-	
Collaboration with traditional male circumcision system	None	3	3	No effectiveness data available	-	-	-	
Prepex	None	3a	3a	Excluded due to lack of data on demand for PrePEX.	-	-	-	

^c PEPAR reports that data is available to determine the total number of individuals reached through campaigns to date; however, a projection of the percent of target population that could be reached was not readily available. The cost data for outreach sites are of questionable relevance given that many of the observations come from outside South Africa.

^d Commenters during the consultation also noted that this TE Factor should only be included under circumstances where the collaboration with the traditional system led to a medical circumcision

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Private sector providers	None	3a	3a	Studies estimating the potential increase in demand are not yet available ^e	-	-	-	-
Geographical targeting	Kripke, in progress	3a	5	Geographical targeting cannot be modelled currently. This will be addressed in Phase 2	-	-	-	-
Key population targeting	None	3c	3c	No effectiveness data available	-	-	-	-
Continuous quality improvement	Byabagambi 2014	5	5	Evidence that would allow conversion of the reported outcomes to parameters in the model was not available. Additionally, the applicability of Ugandan conditions in to South Africa was questioned.	-	-	-	-
7. HCT								
Rapid HIV post-test counselling video	Calderon et al (2009)	1	5	Differences in mean HIV knowledge scores could not be modelled	-	-	-	-
Youth-friendly HIV video	Calderon et al (2011)	1	3c	The study setting (adolescent patients of an urban emergency department in the Bronx, New York City) was not applicable to South Africa	-	-	-	-
PICT integration into standard HIV care	Leon et al (2010)	1	1		-	✓	✓	-

^e Additionally, the cost of performing male circumcision in private facilities is likely to differ from the cost in public facilities. However, since the extent of this variation remains unknown, it was not included in the model.

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Them-bisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
PICT	Dalal et al. (2011)	1						-
Mobile HIV screening	Basset et al. (2011)	1	1		-	✓	✓	-
Mobile HIV screening	Maheswaran et al. 2012	1						-
Door-to-door/ home-based HCT	Doherty et al. 2013	1	1		-	✓	✓	-
Home-based HCT and point of care CD4	Van Rooyen et al. 2013	1						-
Self-testing	Dong et al. 2014	1	3c	Evidence focused on the acceptability and feasibility of self-testing, rather than increases in uptake	-	-	-	-
Self-testing	Pai et al. 2013	1	3c		-	-	-	-
Oral supervised self-testing	Choko et al. 2011	1	3c		-	-	-	-
Routine antenatal HIV testing	Creek et al. 2007	2	4a-PMTCT		✓	✓	✓	-
Routine antenatal HIV testing	Chandisarewa et al. 2008	2	4a-PMTCT		✓	✓	✓	-
Targeting men – invitations to male pregnancy partners	Mohlala et al. 2011	1	1		-	✓	✓	-
Couples counselling and testing	Allen et al. 1992	?	3c	The evidence was from 1988, so somewhat outdated	-	-	-	-
Couples counselling and testing	Conkling et al. 2010	?	3c	No HIV outcome	-	-	-	-
PICT for children	Mutanga et al. 2012	1	5	The model could not model increase in HCT uptake amongst children, only in infants and adolescents	-	-	-	-

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
School linked HIV testing	Suthar et al. 2013	1	5		-	-	-	
Non-targeted rapid HIV screening, opt-out for emergency department patients	Haukoos et al (2013)	3c	3c		-	-	-	
8. Oher biomedical prevention								
<i>Pre-exposure prophylaxis (PrEP)</i>								
Counseling: education about PrEP, adherence counseling for discordant couples	Grant et al. (2010). Haberer et al. (2013).	1	1	PrEP for discordant couples was modelled as an intervention	✓	✓	-	✓ (YW)
Clinical eligibility: HIV testing, renal function, Hep B individual education and counseling	Scheibe, A. (2012).	1	1		✓	✓	-	✓ (YW)
Prescription regimen: daily dosing, <90 day supply (renewable only after HIV testing confirms that patient remains HIV-uninfected)	Grant et al. (2010). Baeten et al. (2012).	1	1	Included in all scenarios that include PrEP	✓	✓	-	✓ (YW)
Educating health workers on PrEP	CDC Guidelines on PrEP (2014)	1	1		✓	✓	-	✓ (YW)
Support services for PrEP	Minnis et al.(2013).	1	1		✓	✓	-	
Drug resistance survey for PrEP	Abbas et al. (2011).	1	1		✓	✓	-	
Target risk groups with PrEP	Okwundu et al.	1	1	PrEP for sex workers and adolescents were both modelled as interventions	✓	✓	-	
Geographic targeting of PrEP: High Transmission Areas (HTA)	None	1	3c	No data on effectiveness available	-	-	-	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Microbicides								
Microbicides (vaginal/ rectal gels, vaginal rings)	Shattock (2012)	1	1		✓	✓		
Acceptability and appropriate use of microbicides	Abdool Karim et al., 2010	1	1	Included in all scenarios that include microbicides	✓	✓		
Monitoring adherence to microbicides	None	1	3c		✓	✓		
Safety monitoring of microbicides	Abdool Karim et al., 2010	1	1		✓	✓		
9.Social enablers								
Social protection								
Cash incentives	Kohler and Thornton 2011	1	3c	Evidence of no effect	-	-	✓ (YW)	
State-provided child-focused cash transfers	Cluver et al. 2013	2	2		-	✓	✓ (YW)	
Unconditional cash transfers to defer sexual debut	Handa et al. 2014	1	3c	The study setting is not applicable to South Africa. Sexual debut in the context of Kenya is different from that in South Africa	-	-	-	
Conditional economic incentives for MSM	Galárraga et al. 2014	1	3c	No HIV outcomes	-	-	-	
Unconditioned, school conditioned, clinic conditioned	Brahmbhatt. 2014	1	3c	The paper explicitly states no change in sexual behaviour. School attendance and clinic visits are not direct HIV outcomes	-	-	-	
Structural intervention that combined a microfinance programme with a gender and HIV training curriculum	Pronyk et al. 2006	1	3c	No direct HIV impact	-	-	-	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
"Cash" vs "cash plus care"	Cluver et al. 2014	1	1	"Cash plus care" was further broken down into four different interventions for the Investment Case, based on communication with the first author: teacher support, parental monitoring, positive parenting, and school feeding	-	✓	-	
Life-skills-based HIV education, business training and mentorship, and access to microcredit loans for business development	Dunbar et al. 2010	1	3c	Small sample, and HIV knowledge cannot be modelled	-	-	-	
Mentorship, financial education, and an economic asset ownership opportunity	Ssewamala et al. 2010	1	3c	Intention to engage in risk sexual behaviour cannot be modelled	-	-	-	
Family economic intervention, which included a Child/Youth Development Account and six 2-hour classes on career planning, career goals, microfinance, and financial well-being	Ssewamala et al. 2008	1	3c	HIV attitudes survey score is a poor effectiveness measure and cannot be modelled regardless	-	-	-	
Life skills and vocational training	Bandiera et al. 2012	1						
Combined intervention package including life-skills and health education, vocational training, micro-grants and social supports	Dunbar et al. 2014	1	1		-	✓	✓ (YW)	
Group savings plus gender dialogue groups	Gupta et al. 2013	1	3c	No direct HIV impact	-	-	-	
Combined structural and behavioural intervention	Gibbs and Jewkes. 2014	1	3c	No direct HIV impact	-	-	-	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Micro-enterprise services added to a peer-mediated HIV intervention for FSW	Odek et al. 2009	1	5	Number of regular partners for female sex workers cannot be modelled. Might be possible to add in Phase 2	-	-	-	-
Nutritional assessment, counselling and support + savings groups + mentoring and peer support	Birx, 2014	1	3c	Ethiopian context is not applicable to South Africa	-	-	-	-
Intervention comprising: 1) Village Savings and Loan Associations (VSLAs) and the provision of entrepreneurship and financial literacy education and 2) Healing Families and Communities discussion sessions	Annan et al. 2013	1	3c	No direct HIV impact	-	-	-	-
Savings and credit groups	Barber. 2011 [361]	1	3c	No direct HIV impact	-	-	-	-
Savings groups	Gash and Odell. 2013	1	3c	No direct HIV impact	-	-	-	-
Cash plus different types of care	Cluver et al. 2015	1	1		-	✓	✓	✓ (YW)
Education								
One additional year of education	Barnighausen et al. 2007	1	3c	Not an evaluation of an intervention	-	-	-	-
Supporting Adolescent Orphan Girls to Stay in School as HIV Risk Prevention	Cho et al. 2011	1	1			✓	✓	-

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Three school-based HIV/AIDS interventions in Kenya: 1) training teachers in the Kenyan Government's HIV/AIDS-education curriculum; 2) encouraging students to debate the role of condoms and to write essays on how to protect themselves against HIV/AIDS; and 3) reducing the cost of education	Duflo et al. 2006			Authors explicitly state that effects on HIV are unclear	-	-	-	-
School-based HIV/STI risk reduction intervention	Jemmott et al. 2010	1	1		-	✓	✓	✓ (YW)
Fees, uniforms, and a school-based helper to monitor attendance and resolve problems (plus daily feeding)	Hallfors et al. 2011	1	3c	Evidence shows a reduction in marriage which is harmful according to the model if long term relationships are substituted with short term relationships	-	-	-	-
Interventions against alcohol abuse								
School-based HIV/AIDS and alcohol abuse educational programme	Chhabra et al. 2010	1	3	"Self-efficacy" and "Communication" cannot be modelled. The coefficient for risk taking is negative (questionable statistical significance)	-	-	-	-
Alcohol intervention with 45% effectiveness	Braithwaite et al. 2014	1	3c	Evidence is based on a modelled study with underlying assumptions that differ from this exercise	-	-	-	-
Popular opinion leaders	Kelley et al. 1997	1	3c	Study setting is not applicable to South Africa – MSM in the US in 1991-94	-	-	-	-

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Them-bisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Brief single-session HIV–alcohol risk-reduction intervention	Kalichman et al. 2008	1	1		✓	✓	-	
Bar-based, peer-led community-level intervention to promote sexual health	Flowers et al. 2002	1	3c	Study setting is not applicable to South Africa – MSM in Scotland in 1999				
Empowerment-based HIV intervention designed to reduce sexual risk, substance use, and victimisation	Wechsberg et al. 2008	1	1					
School-based alcohol/ HIV prevention curriculum	Karnell et al. 2006	1	3c	Weak evidence since all condom usage measures but one are not statistically significant	-	-	-	
HIV and alcohol risk reduction behavioural skills intervention	Kalichman et al. 2007	1	1		✓	✓	-	
Interventions against gender-based violence								
Structural intervention that combined a microfinance programme with a gender and HIV training curriculum	Pronyk et al. 2006	1	3c	No direct HIV impact	-	-	-	
SASA! Community mobilisation intervention to prevent violence and reduce HIV-risk behaviours	Abramsky et al. 2014	1	1		✓	✓	-	
Soul City series 4 and partnership with the National Network on Violence Against Women	Usdin et al. 2005	1	3c	No direct HIV impact	-	-	-	
One Man Can (Sonke Gender Justice)	Colvin and Peacock. 2009	1	3c	Weak evidence. HCT has no baseline comparator, condom use has no quantitative impact measure	-	-	-	
Combined structural and behavioural intervention	Gibbs and Jewkes. 2014	1	3c	No direct HIV impact	-	-	-	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Men as Partners	Ditlopo et al. 2007	1	3c	No direct HIV impact	-	-	-	
Phaphama Men	Kalichman et al. 2009	1	3c	Positive effects on condom usage and HCT after 1 month but not in the longer term	-	-	-	
Male norms initiative	Pulerwitz et al. 2010	1	3c	No direct HIV impact	-	-	-	
Stepping Stones	Jewkes et al. 2008	1	3c	Effectiveness measures are not statistically significant	-	-	-	
Group savings plus gender dialogue groups	Gupta et al. 2013	1	3c	No direct HIV impact	-	-	-	
10. Programme enablers								
<i>Patient identification and mobile technology</i>								
Short message service (SMS) reminders on adherence to ART (4 interventions: daily short, daily long, weekly short, weekly long)	Pop-Eleches C et al 2011	1	4a- ART	Included in all scenarios, incl. baseline	✓	✓	-	
Short message service (SMS) reminders (weekly reminder)	Lester RT et al 2010	1	4a- ART				-	
Mobile technology for community health care workers (CHW) for clinical guidance, referral system and data collection	Schuttner L et al 2014	1	3c	No HIV outcomes	-	-	-	
Implementation of mobile monitoring and evaluation (M&E) system	Neupane S 2014	1	3c	No HIV outcomes	-	-	-	
Community-centred design & delivery								
PMTCT cascade intervention (WHO guidelines)	Kim MH et al 2012	1	4a - PMTCT	Will be included in Phase 2	-	-	-	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembeisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Community-based adherence support (CBAS) on virological outcomes amongst children receiving ART	Fatti G et al 2014	1	5	Impacts on retention could not be modelled for children specifically	-	-	-	
Training of CHW, structural adjustment, harmonisation of scope of practice and stipend of CHW, enhanced supervision of CHW	Uwimana J et al 2013	1	3	No HIV impact. Only TB and STI outcomes reported	-	-	-	
Integrated home visit package delivered to mothers by CHW	Nsibandwe D et al 2013	1	4a - PMTCT	No paper available	-	-	-	
Effect of home visits by CHW on maternal and infant well-being from pregnancy through the first six months of life for women living with HIV	Le Roux et al 2013	1	4a - PMTCT	No paper available	-	-	-	
Clinical governance and PHC integration								
Down-referral model	Sargent et al 2009	1	4a - ART		-	-	-	
Integrated family planning into HIV care and treatment	Shade SB et al 2013	1	3c	No HIV endpoints	-	-	-	
Comprehensive couples-based PMTCT behavioural intervention (PartnerPlus)	Villar-Loubet OM et al 2013	1	5	Condom usage in pregnant women cannot currently be targeted in the model. Might be included in Phase 2	-	-	-	
Impact of primary health facility (PHF) and secondary/tertiary health facilities (SHFs) on trends in ART initiation of children.	Fayorsey RN et al 2013	1	4a - ART	No paper available	-	-	-	
Integrated ART in antenatal care (ANC) clinics compared to standard referral approach	AIDS Star One-Review 2012	1	4a - PMTCT	Inappropriate context. The intervention described in Zambia is similar to the South African standard of care	-	-	-	

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembiisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Integrated nurse-midwife provided ART care within ANC clinics compared to standard referral approach	Chi BH et al- Review 2013	1	4a - PMTCT	Will be included in Phase 2	-	-	-	-
Immediate vs. early integration of ART during TB treatment and impact on mortality	Havlir D. V et al 2011	1	3c	Not relevant under current guidelines	-	-	-	-
Nurse Initiated Management of Antiretroviral Treatment (NIMART) compared to doctor-led management in patients initiating ART	Barton GR et al 2013	1	4a - ART		-	-	-	-
NIMART and decentralised care	Fairall L et al 2012	1	4a - ART		-	-	-	-
Nurse-managed down-referral site vs doctor-managed clinic	Grimrud A et al 2014	1	4a - ART	Included in all scenarios incl. baseline	-	-	-	-
Task shifting of HIV management from doctors to nurses	Iwu EN et al- Review 2014	1	4a - ART		-	-	-	-
Nurse-led vs. doctor-led management of ART care for HIV infected patients	Sanne I et al 2010	1	4a - ART		✓	✓	✓	-
Laboratories (diagnostic services)								
GeneXpert MTB/RIF test compared to sputum smear microscopy	Grant T et al 2014	1	4a - TB	Included in all TB scenarios incl. baseline	N/A	N/A	✓	✓
Home-based HIV counselling and testing vs. VCT at local clinics	Doherty et al 2013	1	4a - HCT		-	✓	✓	-
CD4 PoC	Wynberg E et al Review 2014		4a - ART		-	✓	✓	-
PoC CD4, receipt of written information, standard of care (CD4 collection after 1 week) – impact on ART initiation	Faal M et al 2011	1	4a - ART		-	✓	✓	-

Intervention, TE factor or enabler	Source	Grading by working group ^a	Final grading by modellers	Rationale for final grading	Thembeisa-based analyses			Spectrum-based analysis ^b
					Scenarios at		Budget scenario	
					current level of technical efficiency	optimal level of technical efficiency		
Blood safety								
HIV antibody screening of donated blood	Van Hulst M et al 2010	1	6	Will be included in Phase 2	-	-	-	
Human resources								
Integration and training of community care workers (CCWs) to enhance collaborative TB/HIV/PMCT/home-based HCT activities	Uwimana et al 2012	1	1	Included in all scenarios incl. baseline	✓	✓	✓	
Employer practices								
Digital X-ray technology for TB screening	http://www.anglogoldashanti.com	1	3c	Very small increase in detection rate	-	-	-	
On-site VCT testing at occupation clinic vs off-site VCT at free-standing clinics	Corbett et al 2006	1	4a - HCT		-	✓	-	
Mobile screening program	Feeley F et al 2010		4a - HCT		-	✓	-	
Workplace voluntary testing and counselling program	Fighting Hiv/ Aids In The Workplace-A Company Management Guide	1	3c	No quantifiable HIV impact measure. Only discusses the number of employees covered by the programme rather than testing uptake	-	-	-	

ANNEX 2: DETAILS OF HIV AND TB EXPENDITURE ANALYSIS

Annex 2.1: The common BAS categories applied to all public HIV and TB spending

BAS Common Categories for HIV and TB Activities

ART

Blood bank

CE Political commitment (non-BAS)

CE Stigma reduction (non-BAS)

CHBC

Condoms

DCS Inmates HIV/TB programmes

HCT (or VCT)

HIV (not disaggregated)

HIV Treatment (not disaggregated)

HTA

Key pop prevention

Key pop prevention (not disaggregated)

Key pop prevention other (not elsewhere classified)

M&E

Mass media/ social mobilisation

MMC

OVC (DSD HIV support)

Palliative/ hospice care

PEP/ OPEP/ NOPEP (occupational or non-occupational)

PM

PMTCT

Policy and systems development

Prevention (not disaggregated)

SDC

STI

TB control

TB (not disaggregated)

TB treatment (clinics or outpatient)

TB treatment (hospitals)

TB treatment not disaggregated

TB XDR/MDR treatment

TB/HIV (Integration)

Training

Uniformed HIV services (DOD/SAPS)

Workplace prevention

Youth services (not disaggregated)

Annex 2.2: The crosswalk between the four expenditure classification systems

SA IC categories	BAS Common Codes	EA Program Areas	NASA Categories
1. Interventions			
1.1-3. ART (incl. pre-ART, HB treatment, NIMART)	ART Treatment	Facility Based Care, Treatment, & Support (75%)	ASC.02.01.03.98 Antiretroviral therapy not disaggregatedregated neither by age nor by line of treatment
1.4. Treatment Adherence	Adherence (non-BAS)	Adherence (non EA category)	ASC.02.01.07 Psychological treatment and support services
1.nec ^a . SDC (non SA IC)	SDC	Community Based Care, Treatment, & Support (50%)	ASC.02.01.09 Home-based care
1.nec. CHBC (non SA IC)	CHBC	Community Based Care, Treatment, & Support (50%)	ASC.02.01.09 Home-based care
1.nec. Palliative Care (non SA IC)	Palliative / hospice care	Palliative care (Non EA category)	ASC.02.02.02 Inpatient palliative care & ASC.02.01.08 Outpatient palliative care
1.nd ^b . C&T not disaggregatedreg	HIV Treatment not disaggregated	C&T not disaggregatedreg (non-EA)	ASC.02.98 Care and treatment services not disaggregatedregated by intervention
2. MMC	MMC	Voluntary Medical Male Circumcision	ASC.01.18 Male circumcision
3. Comprehensive Condom Programming	Condoms	Condoms	ASC.01.13 Public and commercial sector male condom provision
4.1. Key pops: CSWs	HTA (CSW & clients)	Sexual and Other Risk Prevention - Key Populations (CSWs)	ASC.01.08.01-.98 Programmatic interventions for sex workers and their clients not disaggregatedregated by type
4.2. Key pops: MSM	Key Pop MSM (non-BAS)	Sexual and Other Risk Prevention - Key Populations (MSM)	ASC.01.09.01-.98 Programmatic interventions for MSM not disaggregatedregated by type
4.3. Key pops: Inmates	DCS Inmates HIV/TB programmes	Key Pops Inmates (non EA category)	ASC.01.04.99 Other programmatic interventions for vulnerable and accessible populations not elsewhere classified (n.e.c.)
4.nec. Other Key Pops.	Key Pop Other (non-BAS)	Sexual and Other Risk Prevention - Key Populations (Other)	ASC.01.04.99 Other Programmatic interventions for vulnerable and accessible population not elsewhere classified
4.nd. Key Pop not disaggregatedreg.	Key pop prevention n.d.	Sexual and Other Risk Prevention - Key Populations	ASC.01.04.98 Programmatic interventions for vulnerable and accessible population not disaggregatedregated by type

SA IC categories	BAS Common Codes	EA Program Areas	NASA Categories
4.nec. Other Key Pops: IDUs	Key Pop IDU (non-BAS)	Sexual and Other Risk Prevention - Key Populations (IDUs)	ASC.01.10.01-.98 Programmatic interventions for IDUs not disaggregated by type
4.nec. Other Key Pops.	Key pop prevention other nec.	Sexual and Other Risk Prevention - Key Populations (Other)	ASC.01.04.98 Programmatic interventions for vulnerable and accessible population not disaggregated by type
4.nec. Other Key Pops: Youth	Youth services (not disaggregated)	DS: Youth (non EA)	ASC.01.05 Prevention – youth in school & ASC.01.06 Prevention – youth out-of-school
5. PMTCT	PMTCT	Prevention of Mother to Child Transmission	ASC.01.17.98 PMTCT not disaggregated by intervention
6. HCT	HCT (or VCT)	HIV Counseling & Testing	ASC.01.03 Voluntary counselling and testing (VCT) & ASC.02.01.01 Provider- initiated testing and counselling (PITC)
7. SBCC	Mass media/ soc.mob	Sexual and Other Risk Prevention - General Populations (certain sub-areas)	ASC.01.01.98 Communication for Social and behavioural change not disaggregated by type
8.1. Prevention: PEP	PEP/ OPEP/ NOPEP	PEP	ASC.01.22.01-.99 Post-exposure prophylaxis
8.2. Prevention: PrEP	PrEP (Non-BAS)	Other prevention: PrEP (non EA category)	PrEP: Non NASA
8.3. STI syndromic management	STI	Other prevention: STI (non EA category)	ASC.01.16 Prevention, diagnosis and treatment of sexually transmitted infections (STI)
8.4. Prevention: Microbicides	Other Prevention (non-BAS)	Other prevention (non EA category)	ASC.01.15 Microbicides
8.nec. Other Prevention (Non SA IC)	Other Prevention (non-BAS)	Infection Control	ASC.01.99 Prevention activities n.e.c.
8.nd. Prevention not disaggregated (Non SA IC)	Prevention not disaggregated	Other prevention (non EA category)	ASC.01.98 Prevention activities not disaggregated by intervention
9.1. TB treatment services	TB treatment (clinics or outpatient)	TB (non EA)	ASC.02.01.02.02 OI outpatient treatment
9.1. TB treatment services	TB treatment (hospitals)	TB (non EA)	ASC.02.01.02.02 OI outpatient treatment

a n.e.c.: not elsewhere classified

b n. d.: not disaggregated

SA IC categories	BAS Common Codes	EA Program Areas	NASA Categories
9.1. TB treatment services	TB treatment not disaggregated	FBCT (25%)	ASC.02.01.02.02 OI outpatient treatment
9.2. TB post treatment, MDR treatment	TB XDR/MDR treatment	TB (non EA)	ASC.02.01.02.02 OI outpatient treatment
9.3-4. TB diagnosis, TB case finding	TB Diagnosis (non-BAS)	TB (non EA)	TB diagnosis (non NASA)
9.5-6. TB Preventive therapy, IPT	TB prevention (IPT, etc) (Non-BAS)	TB (non EA)	ASC.02.01.02.01 OI outpatient prophylaxis
9.7. TB Control	TB control/management/surveys	TB (non EA)	TB control (non NASA)
9.nec. TB/HIV Integration (non SA IC)	TB/HIV (Integration)	TB (non EA)	TB/HIV Integration (non NASA)
9.nd. TB not disaggregated	TB not disaggregated	TB (non EA)	ASC.02.01.02.98 OI outpatient prophylaxis and treatment not disaggregated by type
2. Social enablers			
SE.1. Political commitment and advocacy	CE Political commitment (non-BAS)	CE Other (non EA)	ASC.07.01-.99 Enabling environment
SE.2. Laws, policies and practices	Policy and systems development	Health Systems Strengthening	ASC.04.01 Planning, coordination and programme management
SE.3. Stigma reduction	CE Stigma reduction (non-BAS)	CE Other (non EA)	ASC.07.01-.99 Enabling environment
SE.4. Social protection	DSD: Social Grants	DS: Poverty alleviation (non EA)	ASC.06.01-.99 Social protection services and social services
SE.5. Education	Youth in school	DS: Youth (non EA)	ASC.01.05 Prevention – youth in school & ASC.01.06 Prevention – youth out-of-school
SE.6. Alcohol reduction programmes	Alcohol reduction (non-BAS)	CE Other (non EA)	ASC.07.01-.99 Enabling environment
SE.9. Gender equality/GBV	GBV / gender equality (non-BAS)	CE Other (non EA)	ASC.07.05 Programmes to reduce Gender Based Violence
SE.10. Poverty reduction	DS: Poverty alleviation (non-BAS)	DS: Poverty alleviation (non EA)	ASC.06.01-.99 Social protection services and social services
SE.11. OVC	OVC (DSD HIV support)	Orphans and Vulnerable Children	ASC.03.01-.99 OVC services
3. Programme enablers			
PE.1. Network connectivity and information systems	M&E	Strategic Information	ASC.04.03 Monitoring and evaluation
PE.1. Network connectivity and information systems	M&E	Surveillance	ASC.04.03 Monitoring and evaluation

ANNEXES

SA IC categories	BAS Common Codes	EA Program Areas	NASA Categories
PE.1. Network connectivity and information systems	PE. Pharmacovigilance (non-BAS)	Pharmacovigilance	ASC.04.05 Serological-surveillance (serosurveillance)
PE.1. Network connectivity and information systems	PE: Lab (non-BAS)	M&E	ASC.04.05 Serological-surveillance (serosurveillance)
PE.1. Network connectivity and information systems	PE: Other (non-BAS)	PE other (non EA)	ASC.04.99 Programme management and administration n.e.c
PE.2. Community-Centered design & delivery	PE: Building comm. Capacity/ Inst. strengthening (non-BAS)	PE other (non EA)	ASC.07.03 AIDS-specific institutional development
PE.3. Management and incentives	PM	Program Management	ASC.04.01 Planning, coordination and programme management
PE.4. Research & innovation	PE. Research (non-BAS)	Research (non EA)	ASC.08.01-.99 HIV and AIDS-related research activities
PE.5. Blood safety	Blood bank	Blood Safety	ASC.01.19 Blood safety
PE.6. Integration	PE: Other (non-BAS)	PE other (non EA)	ASC.04.99 Programme management and administration n.e.c
PE.10. Employer practices	Workplace prevention	Other prevention (non EA category)	ASC.01.11.01-.99 Programmatic interventions in the workplace
PE.nec. Workforce (non SA IC)	PE: Workforce (non-BAS)	PE other (non EA)	ASC.05.99 Human resources n.e.c.
PE.nec. Training (non SA IC)	Training	Training (non EA)	ASC.05.03 Training
4. Development synergies (non SA IC)			
DS: Uniformed/ Armed HIV services (non SA IC)	Uniformed HIV services (DOD/SAPS)	DS: Uniformed/ Armed HIV services (non EA)	ASC.01.04.98 Programmatic interventions for vulnerable and accessible population not disaggregated by type
All other HIV not disaggregated	HIV not disaggregated	All other EA categories not above	ASC.98 HIV not disaggregated

ANNEX 3: DEFINITION OF KEY TERMINOLOGY

What is the Investment Approach?

The HIV strategic investment approach was developed in 2011 by an international group of experts, including from UNAIDS, the Global Fund, the Bill & Melinda Gates Foundation, civil society organizations (CSOs), the World Bank, the WHO, UNICEF and PEPFAR to increase the impact of HIV funding and to assist countries in planning and prioritizing different elements of an effective, efficient and sustainable AIDS response. The investment approach is a process that can be used by countries to focus efforts on reaching the 2015 global AIDS targets and beyond and to ensure an optimized and sustainable HIV response by applying a long-term outlook (typically 10+ years). It is underpinned by meticulous analysis of empirical evidence, a realistic appraisal of existing resources, and quantification of the returns of HIV investments. It shifts the focus from costs and expenditures to investments that deliver optimal returns [Schwartländer B, Stover J, Hallett T, et al. Towards an investment approach for an effective response to HIV/AIDS. *Lancet*. 2011; 377:2031–2041. (2011) [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(11\)60702-2/fulltext#article_upsell](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60702-2/fulltext#article_upsell)]

What is an Investment Case?

Applying the investment approach sometimes culminates in the development of an Investment Case. The Investment case is a document that makes the case for optimized HIV investments. At its core is a description of returns on investment in a country's optimized HIV response over the long-term (typically 10+ years). It summarises the state of the epidemic and the response, describes the prioritized interventions, populations, and geographic areas to be implemented to achieve the greatest impact over the long term and the resources required. It also outlines the main access, delivery, quality and efficiency issues to be addressed to improve HIV services and describes what will be done to address these issues. It includes an analysis of, and plan for, realistic and more sustainable financing of the HIV response, including increases in domestic financing where relevant. (Global Fund Information Note: Strategic Investments for HIV Programs (2014) www.theglobalfund.org/documents/core/infonotes/Core_HIV_InfoNote_en)

What is the objective of the South Africa HIV and TB investment Case?

The South Africa Investment Case aims to establish the most cost-effective mix of interventions to address HIV and TB for South Africa over the next 20 years, taking into account both current and future levels of technical efficiency. Cost effectiveness will be measured as cost per HIV or TB infection averted, as well as number of life years saved, by the entire programme of interventions.

How will the South Africa Investment Case be used?

The South Africa Investment Case will inform the country's HIV and TB policy going forward; funding for the HIV and TB programmes under the HIV/AIDS Conditional Grant, Equitable Share, and other sector Medium Term Expenditure Frameworks; the midterm review of the National Strategic Plan on HIV, STIs and TB (2012 -2016) as well as the next 5-year National Strategic Plan; and resource mobilization for additional domestic or external financing. A robust investment case will also form the basis of Global Fund concept note, the principal means to request funding under the new Global Fund funding model.

What is the linkage between the Investment Case and the NSP?

Countries are encouraged to use the investment approach whenever a rigorous examination of the HIV response is required, especially in the development and review of their national disease strategic plans (NSPs) and/or investment cases for HIV. While there is significant overlap between robust NSPs and investment cases in the sense that investment cases are also evidence-based documents providing essential information on the epidemiological context, the current response, and other key areas, a sound investment case differs in that it explicitly quantifies the returns on HIV investments. Many NSPs often do not include such an assessment, but in an ideal case would do. Investment cases have a longer-term perspective (typically 10+ years), which is crucial, as returns of investments often occur beyond the 5-year horizon of a NSP.

Who are the key stakeholders in the development of the South Africa Investment Case?

The South Africa Investment Case was developed through an intensified national dialogue about investment choices and priority setting involving all key national partners, including civil society groups at all stages. Appropriate forums for this dialogue include existing multi-stakeholder structures and processes such as SANAC structures and other governance bodies and partnership forums. In particular, the Investment Case facilitated an intensified dialogue between HIV and TB programmes and between funding, planning and development authorities responsible for steering broad national development programmes.

Who are the users of an Investment Case?

The target audience for the South Africa investment case includes: cabinet; SANAC; premiers; provincial, district and local AIDS councils and their civil society chairs; national Treasury; national departments – NDOH, DBE, DSD others; the Global Fund (joint concept note for HIV & TB); civil society; the private sector; and development partners.

What are the core components of South African HIV and TB Investment Case?

The South Africa Investment Case laid out three categories of investments essential to the HIV and TB response, namely basic program activities that have high impact, critical enablers, and development synergies.

What are basic programmes in the Investment Case?

Basic program activities are high impact interventions that have a direct impact on HIV and/ or TB risk, transmission, morbidity and mortality. High impact interventions are essential to an adequate HIV or TB response and should be delivered at scale according to the size and geographical location of the relevant population in need. High impact interventions directly reduce HIV or TB transmission and keep people alive, healthy and productive. They are evidence based and evidence informed interventions, which when implemented together at scale, can change the course of epidemics.

Which basic programmes does the South African Investment Case include?

The South African Investment Case includes nine basic programmes, namely:

1. Focused interventions for key populations at higher risk
2. Elimination of new HIV infections among children
3. Social and behaviour change programmes
4. Comprehensive condom promotion and distribution
5. Treatment, care and support for people living with HIV
6. Voluntary medical male circumcision
7. HIV counseling and testing
8. Tuberculosis screening, diagnosis and treatment
9. Other biomedical prevention

What are the critical enablers?

Critical enablers are “activities that are necessary to support the effectiveness and efficiency’ of basic programme activities”. Critical enablers tend to be more HIV-specific. One of their primary purposes is to contribute to HIV-related outcomes. That means critical enabler programmes should be primarily assessed in terms of their effectiveness in increasing the uptake, equitable coverage, rights-based delivery and quality of basic programme activities. Critical enablers are defined in two categories – social enablers such as community mobilisation, changing laws and stigma reduction. The second category of critical enablers are programme enablers, or efforts to make programmes work, such as community centred design and delivery, communication, management, procurement and research and innovation.

What are social enablers?

Social enablers make environments conducive for rational HIV and TB responses possible and programme enablers that create demand for and help improve the performance of key interventions. Social enablers consist of outreach for HIV testing and HIV treatment literacy, stigma reduction, advocacy to protect human rights, and monitoring of the equity and quality of programme access and results and mass communication designed to raise awareness and support change in social norms.

What are programme enablers?

Programme enablers include incentives for programme participation, methods to improve retention of patients on antiretroviral therapy, capacity building for development of community-based organisations, strategic planning, communications infrastructure, information dissemination, and efforts to improve service integration and linkages from testing to care.

What are development synergies?

Development synergies are investments in other sectors that can have a positive effect on HIV and TB outcomes. The Investment approach identifies a few key development sectors that present opportunities for synergies in multiple contexts: social protection, education, legal reform, gender equality, poverty reduction, gender-based violence, health systems (including STI treatment and blood safety), community systems and employment practices. Development synergies are less HIV-specific. They tend to have a broader range of impacts across health and development sectors. Although development synergies can have a profound impact on HIV and TB outcomes, their reason for being is not typically for HIV or TB. The South Africa Investment Case addressed synergies with the broader health and development programmes.

Why are critical enablers and development synergies important?

Critical enablers and development synergies are essential to the South Africa HIV and TB response for five main reasons. They

- support and increase the effectiveness, efficiency, equity and reach of basic programme activities;
- can act directly to reduce (or exacerbate) risk to HIV and TB;
- can help to protect and promote human rights and human rights principles: participation, accountability, inclusion, non-discrimination and informed consent;
- can result in a multitude of positive development and health outcomes across the Millennium Development Goals; and
- encourage the sustainability of the HIV and TB response.

What key questions does the South African investment Case answer?

The South Africa Investment Case provides answers in the following areas:

Technical efficiency: The Investment Case analysed the cost and cost effectiveness of the current mix of interventions against HIV and TB over the next 20 years, *at current coverage targets* and (a) current levels of technical efficiency and (b) optimal levels of technical efficiency. This analysis allowed us to see what the *current* programme does, and could, achieve. It also served as the baseline for the calculations of incremental cost and cost effectiveness.

Technical and allocative efficiency: The Investment Case analysed the full and incremental cost and cost effectiveness of the most efficient mix of interventions against HIV and TB, with efficiency measured in number of HIV infections averted, number of TB cases averted, and number of live years saved, over the next 20 years, *at optimal coverage targets* and (a) current levels of technical efficiency and (b) optimal levels of technical efficiency. This analysis allowed us to see what the *optimal* programme could achieve- both if we don't change technical efficiency and if we change both technical and allocative efficiency.

Economic efficiency: By holding the current or a future planned funding envelope constant and analysing the most efficient mix of interventions *at this level of funding* and (a) current levels of technical efficiency and (b) optimal levels of technical, we proposed ways to improve economic efficiency.

What data was required to develop the South Africa Investment Case?

The South Africa Investment Case used the following data for each intervention and, where relevant, each technical efficiency factor:

1. Target population: Definition and size of the target population
2. Current government targets (e.g., NSP on HIV, STIs and TB; ministerial performance agreements)
3. Effectiveness of each intervention in terms of HIV and/ or TB infections averted and/or other, more programmatic or intermediary parameters,
4. Unit cost(s) or cost ingredients if a full unit cost is not available

How did the Investment Case team address missing data on unit costs?

Where no unit cost could be found, or no unit cost from South Africa or based on a cost analysis, the cost of an intervention, TE factor, enabler or synergy was established using ingredient costing based on expert opinion or literature on resources used or to be used in the intervention.

What are the key success factors for a strong Investment Case?

The key success factors for a strong Investment Case are clear objectives, proper process design and management, stakeholder engagement and leadership, effective prioritisation of effective interventions, data availability, appropriate focus on enablers and development synergies to counteract a potential bias towards biomedical interventions alone; and a consideration of cost effectiveness and coverage, not just cost reduction.

