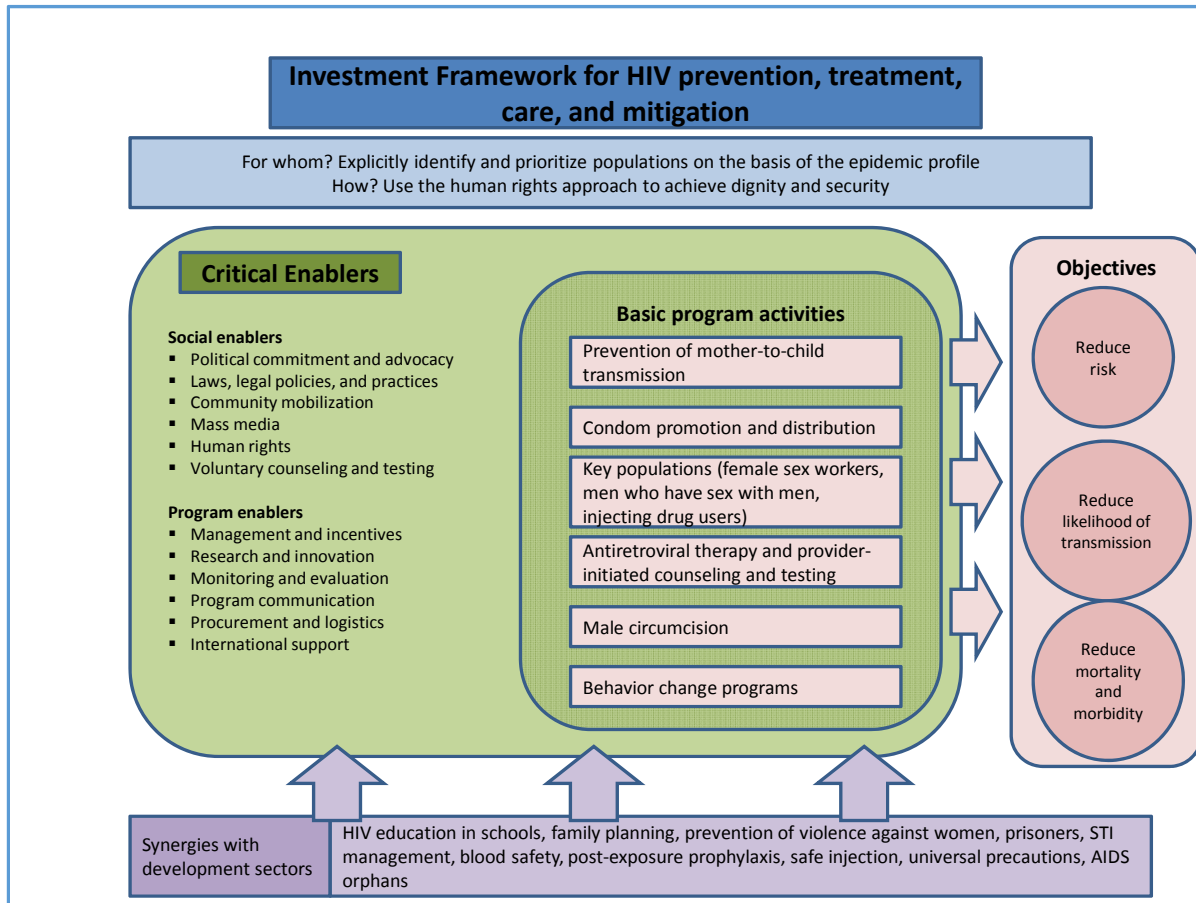
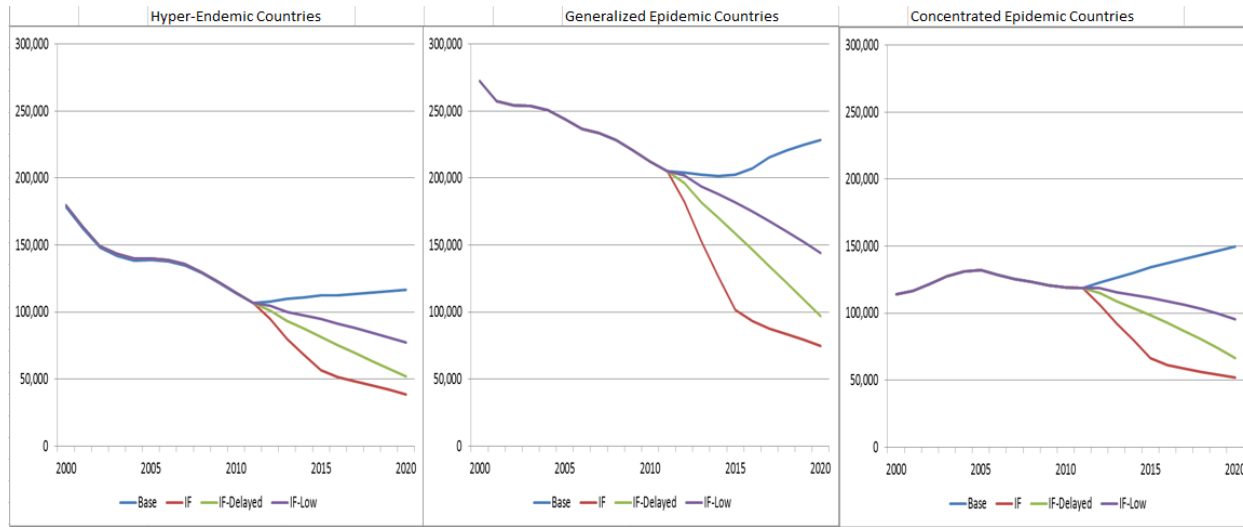


Supplemental Digital Content

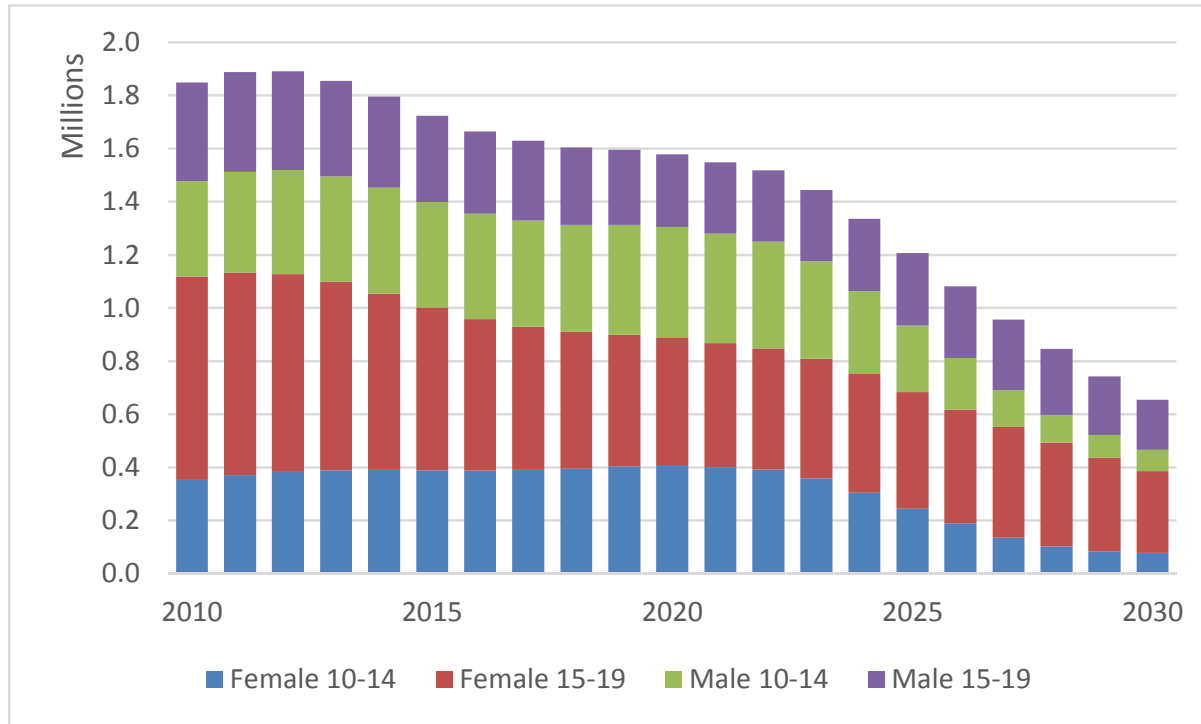
Supplemental Digital Content Figure 1. The Investment Framework



Supplemental Digital Content Figure 2: New HIV infections among adolescents under four scenarios by epidemic type



Supplemental Digital Content Figure 3: HIV-positive population 10-19 under the Investment Framework scenario



Supplemental Digital Content Table 1. Description of the Intervention in the Investment Framework

Intervention	Description
Basic Programs	
PMTCT	Prevention of mother-to-child transmission of HIV. This includes: <ul style="list-style-type: none"> • Family planning for HIV+ women • Screening of pregnant women for HIV infection • CD4 testing for HIV+ pregnant women • ARV prophylaxis: Option A or B for women with CD4 counts > 350 cells/μl and ART for those with lower CD4 counts • Early infant diagnosis • Cotrimoxazole prophylaxis
Condom promotion and distribution	Programs to increase the correct and consistent use of male and female condoms, including procurement and distribution and demand generation activities such as social marketing, awareness raising and communication programs.
Male circumcision	Refers to the removal of the prepuce or foreskin covering the tip of the penis for the purpose of reducing the risk of HIV infection. The costs include the medical procedure, promotion, training, supervision and counseling and testing
Key populations	Interventions for female and male sex workers, MSM and IDU are based on a peer outreach model. These interventions combine one-on-one or small group awareness, group education, and access to commodities and services
Commercial sex workers	Programs to promote risk-reduction measures among commercial sex workers and their clients. Includes STI treatment, peer outreach and counseling, condom promotion, removing stigma and discrimination, elimination of gender-based violence, programs addressing clients, HIV testing and treatment.
Men who have sex with men	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 counseling and testing, and initiatives to ensure that these groups are able to access these services.
Injecting drug users	Initiatives directed at injecting drug users to reduce the risk of spreading HIV and to mitigate other harmful effects of drug use. This can involve harm reduction programs, such as sterile needle and syringe programs, as well as opioid substitution and peer outreach.
Behavior change programs	Behavioral change programs for AIDS includes the strategic use of an integrated program of advocacy, communication, and social mobilization to systematically facilitate and accelerate behavior change and social change to the underlying drivers of HIV risk, vulnerability, and impact. Programs include both interpersonal communication and media communication. The model uses the cost of workplace behavior change programs a proxy to arrive at a plausible overall estimate of resource needs for the behavior change programs included in the basic program activities category.
ART	Treatment, care, and support includes antiretroviral therapy, routine counseling and testing; treatment and care of opportunistic infections; essential illness prevention interventions for people living with HIV (PLHIV); nutrition supplements for those on ART; treatment for tuberculosis; and palliative care.
PITC	Provider initiated counseling and testing for HIV-infected clients
Critical Enablers	
Social enablers	
Voluntary counseling and testing	Stand-alone centers that offer counseling and testing for those who seek the service

Community mobilization	Community mobilization can include group discussions, community forums, outreach, and establishing community networks. Community mobilization tries to ensure that people most affected by HIV (including people living with HIV) can play an active and influential role in shaping an effective response to it.
Mass media	Radio, television, billboards and other information campaigns aimed at the general population.
Workplace	Prevention programs in the workplace. These typically include health education, condom distribution and STI treatment.
Advocacy	Advocacy is the combined effort of a group of individuals or organizations to persuade influential individuals, groups and/or organizations to adopt an effective approach to AIDS as quickly as possible. Advocacy efforts have diverse targets of change: policies, laws, regulations, guidelines, additional funding, and/or programmatic or institutional change. Advocates use a wide variety of organizational techniques and communication channels to bring about political change, including letters, meetings, social networking and internet campaigning, face-to-face interactions, media campaigns, forums and newspaper articles.
Legal	A supportive legal environment entails having laws in place that protect people living with HIV and key populations from discrimination and having policies that facilitate all populations having access to the HIV programs and services they require. It also involves removing punitive laws, regulations, and policies that block effective HIV responses. HIV-related legal services include legal information and referral, legal advice, and legal representation.
Human rights and stigma reduction	HIV-related stigma refers to negative beliefs, feelings, and attitudes towards people living with HIV or associated with HIV. Stigma has been addressed through multi-component programs that include mass communication, participatory education, mobilization of community leaders and a variety of community interaction techniques. Other stigma programs address health workers.
Program enablers	
Management	Management of HIV/AIDS programs, including quality and availability of staff, training, organizational capacity, clarity of objectives, decision-making structures etc.
Research	Research on strategies for HIV prevention and treatment.
Monitoring and evaluation	Monitoring and evaluation
Program communication	Activities that inform and create awareness among the general public or specific populations about HIV, and empowering people to take action.
Logistics	Activities to ensure the proper functioning of the supply chain for the hundreds of HIV/AIDS commodities.
International	Support from international organizations such as UNAIDS, WHO, etc.
Development Synergies	
HIV education in schools	Costs of training teachers in AIDS education.
STIs	Prevention and treatment of sexually transmitted infections
Family planning	Family planning for those living with HIV
Prevention of violence against women	Programs to prevent violence against women
Prisoners	HIV prevention programs for prisoners
Blood safety	Screening of donated blood and programs to recruit low-risk donors.
Post-exposure prophylaxis	Post-exposure prophylaxis with ARVs for those who might have been exposed to HIV
Safe Injection	Safe medical injection including disposable syringes
Universal precautions	Universal precautions to avoid transmission in health care settings
OVC	Support for children orphaned by AIDS

Table 2. Adolescent markup score: Investment Framework interventions, by program element and whether costs might be the same (=), higher (+), or lower (-) for adolescent versus adult programming

Intervention	Program Element										Markup Score	Markup	
	Service Delivery			System Support									
	Drugs / Supplies	Labor	Equipment	IEC	Training	Supervision	Logistics	Management	Infrastructure	M&E			
Basic Programs													
Prevention of mother-to-child transmission												4.4	25%
Screening	=	+	=	+	+	+	=	+	+	+		7	
Family Planning	=	+	=	+	+	+	+	+	+	+		8	
CD4 Testing	=	=	=									0	
Prophylaxis for HIV infected pregnant women (Option A)	=	+	=	+	+	+	+	+	=	+		7	
Prophylaxis for HIV infected pregnant women (Option B)	=	+	=	+	+	+	+	+	=	+		7	
ART for mothers who need it for their own health	=	+	=	+	+	+	=	+	=	+		6	
Early infant diagnosis	=	=	=									0	
Cotrimoxazole Prophylaxis	=											0	
Condom promotion and distribution	=	+	=	+	+	+	+	+	=	+		7	40%
Male circumcision												3	25%
Procedure	=	=	=				+	=	=	+		2	
Promotion				+								1	
Training, including counseling and supervision					+	+						2	
Counseling and testing	=	=	=	+	+	+	+	+	+	+		7	
Key populations													
Female sex workers												5.6	25%
STI treatment	=	=	=	+	+	+	=	+	+	+		6	
Peer outreach and counseling	=	+	=	+	+	+	=	+	=	+		6	
Condom promotion	=	+	=	+	+	+	+	+	=	+		7	
Removing stigma and discrimination	=	=	=	=	=	=	=	=	=	=		0	
Elimination of gender-based violence	=	+	=	+	+	+	=	+	=	+		6	
Programs addressing clients	=	+	=	+	+	+	=	+	+	+		7	

Intervention	Program Element										Markup Score	Markup
	Service Delivery			System Support								
	Drugs / Supplies	Labor	Equipment	IEC	Training	Supervision	Logistics	Management	Infrastructure	M&E		
HIV testing and treatment	=	+	=	+	+	+	=	+	+	+	7	
Men who have sex with men											7.3	40%
Risk reduction activities	=	+	=	+	+	+	+	+	=	+	7	
Outreach	=	+	=	+	+	+	+	+	=	+	7	
Prevention of sexual transmission of HIV (including condom)	=	+	=	+	+	+	+	+	+	+	8	
Injecting drug users											7.5	40%
Outreach and needle/syringe exchange	=	+	=	+	+	+	+	+	=	+	7	
Opioid substitution therapy	=	+	=	+	+	+	+	+	+	+	8	
Behavior change programs				+	+	+	+	+	+	+	7	40%
Provider-initiated counseling and testing	=	=	=	+	+	+	+	+	+	+	7	40%
Antiretroviral therapy	=	+	=	+	+	+	+	+	+	+	8	40%
Critical Enablers												
Voluntary counseling and testing	=	=	=	+	+	+	+	+	+	+	7	40%
Community Mobilization	=	+	=	+	+	+	=	+	=	=	5	25%
Mass media	=	=	=	+	+	+	=	+	=	+	5	25%
Development Synergies												
HIV education in schools											0	0%
STI treatment	=	=	=	+	+	+	=	+	=	+	5	25%
Family Planning	=	+	=	+	+	+	+	+	+	+	8	40%
Prevention of violence against women	=	+	=	+	+	+	=	+	=	+	6	25%
Prisoners	=	=	=	+	+	=	=	=	=	=	2	10%
Blood safety	=	=	=	=	=	=	=	=	=	=	0	0%
Post-exposure prophylaxis	=	=	=	+	+	+	=	+	=	+	5	25%
Safe Injection	=	+	=	+	+	+	+	+	=	+	7	40%
Universal precautions	=	=	=	=	=	=	=	=	=	=	0	0%
Orphans and vulnerable children programs	=	=	=	=	=	=	=	=	=	=	0	0%

ART = antiretroviral therapy, STI = sexually transmitted infections

Supplemental Digital Content Table 3: Current coverage of interventions and Investment framework coverage targets for 2015

Intervention	Epidemic type (by country)			
	Hyper-endemic	Generalized	Concentrated	Low prevalence
General Population				
Mass media	80%	80%	20%	20%
Community mobilization	16%/70%	11%/70%	6%/6%	1%/1%
Counseling and testing	17%/17%	5%/5%	7%/7%	9%/9%
Condoms: discordant couples	41%/60%	31%/60%	20%/60%	9%/60%
Vulnerable populations				
Youth in school	54%/100%	47%/100%	30%/30%	35%/35%
Outreach to most-at-risk-populations	36%/60%	51%/60%	59%/60%	60%/60%
IDU needle exchange	13%/60%	15%/60%	19%/60%	17%/60%
IDU drug substitution	0%/0%	2%/2%	7%/40%	8%/40%
Workplace	26%/50%	10%/50%	0%	0%
Condoms: high risk populations	34%/50%	49%/50%	57%/57%	58%/58%
Condoms: medium risk populations	41%/60%	31%/60%	20%/20%	9%/20%
Medical services				
PMTCT	80%/90%	48%/90%	52%/90%	36%/90%
Male circumcision (2020)	28%/80%	54%/80%	0%	0%
ART (2025)	69%/90%	47%/90%	43%/90%	42%/90%
STI management	36%/100%	36%/100%	35%/100%	22%/100%
PITC	80%	80%	80%	80%
Blood safety	99%/100%	99%/100%	98%/100%	97%/100%

Note: The first number shows current coverage where available and the number after the “/” shows the Investment Framework target. If only one number is shown then no estimate of current coverage is available. For male circumcision and ART the coverage goals refer to 2020 and 2025 respectively. IDU = Injecting drug users. PMTCT = prevention of mother-to-child transmission, ART = antiretroviral therapy, STI = sexually transmitted diseases, PITC = provider initiated counseling and testing

Supplemental Digital Content Table 4. Effects of Exposure to Behavior Change Interventions on Key Behaviors by Risk Group

Intervention	Impact on key risky behavior											
	Reduction in condom nonuse					Reduction in number of partners					Increase in age at first sex	Reduction in needle sharing
	Risk group					Risk group					Risk group	
	High	Medium	Low	MSM	PWID	High	Medium	Low	MSM	PWID	Medium	
Mass media		3/11/20	17				0/4/6				0	
VCT	34	5/16/19	2/18/30			60	2					
Community mobilization		8/18/18					3/10/15				-0.3	
Sex worker outreach	12/36/60					26/38/49						
Youth in school		7/13/13					15/22/33					
Youth out of school		9/33/40					15/22/33					
Workplace programs		19/23/27	23				3/10/15					
Social marketing		33	22								0.1125	
Condoms	76	12/19/26	12/24/35				0					
IDU outreach										0		25/39/51
Needle & syringe exchange					27							24
Drug substitution for IDU										46		54/63/71
MSM outreach				9/25/34								

Note: This table summarizes the literature on the impact of interventions on these key risky behaviors. The risk groups are High (sex workers and clients), medium (heterosexual contact with casual partners), low (stable heterosexual couples), MSM (men who have sex with men, and PWID (people who inject drugs.) When three numbers are presented, such as 3/11/20, they represent the lower, median, and upper quartile of impacts from the literature. Single values are used when there are not enough studies to develop a range. This study used the median impacts for all scenarios except the pessimistic scenario intended to indicate poor implementation, which used the low values. Impact refers to the percent reduction in the risky behavior after exposure to the intervention. VCT = voluntary counseling and testing, IDU = injecting drug users.

Supplemental Digital Content Table 5. Number of Adolescents in Need of Services

Intervention	Adolescents in need of services	Notes
Basic Programs		
PMTCT	8%	Percent of births to mothers < 20 years of age
Condom promotion	17%	Adolescents as % of sexually active adults
CSW and clients	15%	Average from surveys on age distribution
MSM	15%	Average from surveys on age distribution
IDU	15%	Average from surveys on age distribution
ART (minus ART in PMTCT program)	7%	Need for ART by age
OI treatment (included in ART)	7%	Need for ART by age
Provider initiated C&T	26%	Adolescents as % of adult population
Male circumcision	67%	Most MC targeted to 10-24 yr old males
Workplace (proxy for BC programs)	26%	Adolescents as % of adult population
Critical Enablers		
SOCIAL ENABLERS		
Voluntary counseling and testing	26%	Adolescents as % of adult population
Community mobilization	26%	Adolescents as % of adult population
Mass media	26%	Adolescents as % of adult population
Political commitment and advocacy	1%	Calculated as a percent of direct service delivery costs. The same as for all adults.
Laws, legal policies and practices	1%	Calculated as a percent of direct service delivery costs. The same as for all adults.
Human rights	1%	Calculated as a percent of direct service delivery costs. The same as for all adults.
PROGRAM ENABLERS		
Management and incentives	3%	Calculated as a percent of direct service delivery costs. The same as for all adults.
Research and innovation	1%	Calculated as a percent of direct service delivery costs. The same as for all adults.
Monitoring and evaluation	1%	Calculated as a percent of direct service delivery costs. The same as for all adults.
Programme communications	2%	Calculated as a percent of direct service delivery costs. The same as for all adults.
Procurement and logistics	1%	Calculated as a percent of direct service delivery costs. The same as for all adults.
International Support	3%	Calculated as a percent of direct service delivery costs.

Intervention	Adolescents in need of services	Notes
		The same as for all adults.
Synergies with Development Sectors		
Youth in school	100%	All are adolescents
Family planning	17%	Adolescents as % of sexually active adults
Gender based violence	26%	Adolescents as % of adult population
Prisoners	13%	Half of adolescent % of all adults
STI management	17%	Adolescents as % of sexually active adults
Blood safety	26%	Adolescents as % of adult population
Post-exposure prophylaxis	26%	Adolescents as % of adult population
Safe injections	26%	Adolescents as % of adult population
Universal precautions	26%	Adolescents as % of adult population
AIDS Orphans	56%	Orphans ages 10-17 as % of total

PMTCT = prevention of mother-to-child transmission, CSW = commercial sex worker, IDU = injecting drug user, ART =antiretroviral therapy, OI = opportunistic infection, C&T = counselling and testing, BC = behaviour change, STI = sexually transmitted diseases

Supplemental Digital Content. The Goals Model

Goals is a model that simulates an HIV epidemic based on population behaviors and intervention coverage. It has been used for global analysis (for example, to estimate the impact of the Investment Framework) and has been used by 20 countries in the preparation of their HIV strategic plans. It can be used to estimate the need for services and the impact of scaling up those services. 10 of the 26 countries included in this modeling exercise, have used the Goals model to inform their national strategic plans. The models for the 156 countries included in the analysis were updated with the latest coverage information from the national 2010 UNGASS reports and with unit costs from the latest round of country estimates from the UNAIDS regional Resource Needs workshops and from the AIDS2031 activities. Estimates of new HIV infections and AIDS deaths were extracted for the 26 countries and scaled up to obtain global estimates, matching the 2011 UNAIDS estimates.

Figure 4. The Goals Model

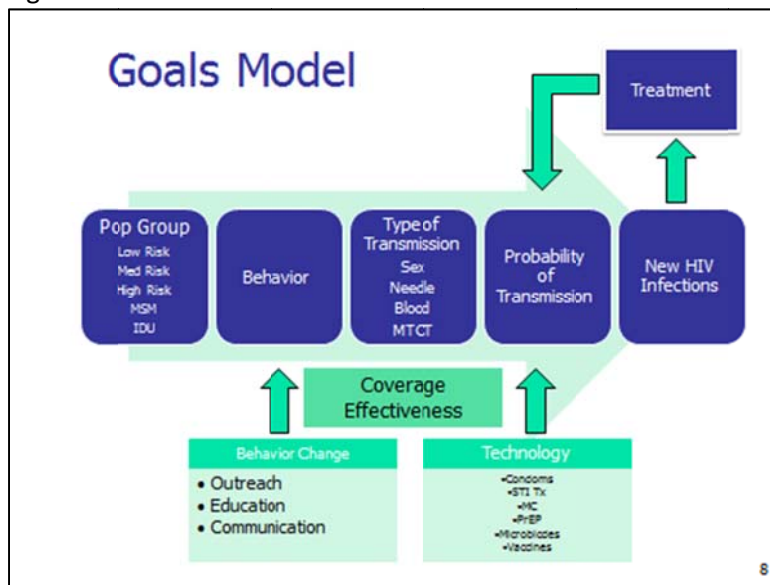


Table 6. Countries where we conducted detailed modeling, by type of epidemic

Hyper-Endemic	Generalized	Concentrated
Botswana	Cameroon	Brazil
Lesotho	Côte d’Ivoire	Cambodia
Mozambique	Ethiopia	China
South Africa	Kenya	India

Swaziland	Malawi	Indonesia
Zambia	Nigeria	Mexico
Zimbabwe	Rwanda	Russia
	Tanzania	Thailand
	Uganda	Ukraine
		Viet Nam

Table 7. Key Parameter Values Used in the Goals Model

Parameter	Value	Source
Transmission of HIV per act (female to male)	0.0011	Baggaley <i>et al.</i> ⁱ , Gray <i>et al.</i>
Multiplier on transmission per act for		
- Male to female	1.0	Galvin and Cohen ⁱⁱ , 2.2-11.3 Powers <i>et al.</i> ⁱⁱⁱ . 5.1-8.2 Vittinghoff <i>et al.</i> ^{iv} .
- Presence of STI	8	
- MSM contacts	2.6	
Relative infectiousness by stage of infection		
- Primary infection	9 – 40	Boily <i>et al.</i> ^v . 9.17 (4.47-18.81) Pinkerton ^{vi}
- Asymptomatic	1	Reference stage
- Symptomatic	7	Boily <i>et al.</i> ⁶ . 7.27 (4.45-11.88)
- On ART	0.04 – 0.08	Cohen <i>et al.</i> ^{vii} Attia <i>et al.</i> ^{viii}
Efficacy in reducing HIV transmission		
- Condom use	0.8	Weller and Davis ^{ix}
- Male circumcision	0.6	Auvert <i>et al.</i> ^k , Gray <i>et al.</i> (2007) ^{xi} , Bailey <i>et al.</i> ^{xii}
- PrEP	0.55 – 0.73	Grant <i>et al.</i> ^{xiii} Partners PrEP Study
- Microbicide	0.6	Abdool Karim <i>et al.</i> ^{xiv}

'Reference stage' means that the relative infectiousness of all other stages is specified with reference to the asymptomatic stage.

Supplemental Digital Content. Estimating the Adolescent Markup

To estimate unit costs for serving adolescents, we took an approach that determines the extent to which unit costs might differ for adolescent versus adult programming. For each intervention, we assessed 10 service delivery and system support elements and judged whether serving adolescents versus adults requires additional, the same, or fewer resources. This assessment produced a score that determined the cost of serving adolescents compared to serving adults (expressed as a percentage markup over adult unit cost). We classified each intervention according to whether there would be no markup, or a low (10%), medium (25%), or high (40%) markup. We set the upper bound of the markup at 40 percent based on recent work costing a package of adolescent health services (Deogan et al 2012).

To score the markup, we broke each of the investment framework interventions into its service delivery and system support elements, as the table below shows. Under service delivery is included drugs and supplies, labor, and equipment. System support includes information, education and communication (IEC), training, supervision, logistics, management, infrastructure, and monitoring and evaluation. Next, for each program element we judged whether we could make a case that additional (+), the same (=), or fewer (-) resources would be needed to serve adolescents versus older adults. For each element where we judged that additional resources would be needed we added one point to the markup score. Where we judged fewer resources might be needed we subtracted one point from the score. Where no additional resources were needed, zero points were awarded. Shaded cells indicate that, for that intervention, a program element is not applicable. We calculated the total markup score by adding the total points. We did no weighting of elements.

For example, for the screening component of PMTCT as defined by the Investment Framework, we judged that there would be an increase in labor cost, IEC, training, supervision, management, infrastructure, and monitoring and evaluation. Thus we assigned a score of 7 to the screening component. For multi-component package interventions such as PMTCT, we scored each individual component (screening, family planning, CD4 testing, etc.) and then assigned an overall score calculated as simple average of the scores for each component. We assigned the percentage markup based on the score:

- An intervention scoring 0 (or below) got a 0% markup.
- An intervention score between 0 and 2 got a 10% markup
- An intervention score between 2 and 6 got a 25% markup
- An intervention score greater than 6 got a 40% markup (the maximum)

The authors did an initial scoring of the markup, then received comments from a group of reviewers with expertise in adolescent programming, then revised the scoring based on those comments.

-
- ⁱ Baggaley RF, Fraser C. Modelling sexual transmission of HIV: testing the assumptions, validating the predictions. *Curr Opin HIV AIDS*. 2010; **5**(4): 269-76.
- ⁱⁱ Galvin and Cohen, "The Role of Sexually Transmitted Diseases in HIV Transmission" *Nature Reviews Microbiology* Volume 3, January 2004, pps. 33-42.
- ⁱⁱⁱ Powers KA, Poole C, Pettifor AE, Cohen MS Rethinking the heterosexual infectivity of HIV-1: a systematic review and meta-analysis *The Lancet* Published on line August 5, 2008 DOI:10.1016/S1273-3099(08)70156-7.
- ^{iv} Vittinghoff E, Douglas J, Judson F, McKirnan D, MacQueen K, Buchbinder SP. Per-Contact Risk of Human Immunodeficiency Virus Transmission between Male Sexual Partners *Am J Epidemiol* (1999)150:3;306-31 suggests 0.0016/0.0011.
- ^v Boily MC, Baggaley RF, Wang L, Masse B, White RG, Hayes RJ, Alary M. Heterosexual risk of HIV-1 infection per sexual act: systematic review and meta-analysis of observational studies *Lancet Infect Dis* 2009; **9**: 118-29.
- ^{vi} Pinkerton SD. Probability of HIV transmission during acute infection in Rakai, Uganda. *AIDS Behav*. 2008; **12**(5): 677-84.
- ^{vii} Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, *et al*. Prevention of HIV-1 Infection with Early Antiretroviral Therapy *N Engl J Med* 2011; 10.1056/NEJMoa1105243.
- ^{viii} Attia S, Egger M, Muller M, Zwahlen M, Low N. Sexual transmission of HIV according to viral load and antiretroviral therapy: systematic review and meta-analysis. *AIDS* 2009, **23**:1-8.
- ^{ix} Weller S, Davis, K. Condom effectiveness in reducing heterosexual HIV transmission (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2004. Chichester, UK: John Wiley & Sons, Ltd.
- ^x Auvert B, Puren A, Taljaard D, Lagarde E, JoëlleTambekou-Sobngwi, RémiSitta. The impact of male circumcision on the female-to-male transmission of HIV : Results of the intervention trial : ANRS 1265. IAS 2005: INSERM, France; 2005.
- ^{xi} Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, *et al*. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet*. 2007; **369**(9562): 643-56.
- ^{xii} Bailey RC, Moses S, Parker CB, Agot K, Maclean I, Krieger JN, *et al*. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet*. 2007; **369**(9562): 643-56.
- ^{xiii} Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L. Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men *New Engl J Med* 2010, 10.1056/NEJMoa1011205.
- ^{xiv} Karim QA, Karim SSA, Frohlich J, Grobler AC, Baxter C, Mansoor LE, *et al*. Effectiveness and Safety of Tenofovir Gel, an Antoretroviral Microbicide, for the Prevention of HIV Infection in Women. *Science* **329**; 1168-1174 (September 2010).