Web Appendix

First Population-level Effectiveness Evaluation of a National Programme to Prevent HIV Transmission from Mother to Child, South Africa



- 1. Web Appendix 1: PMTCT policy timeline
- 2. Web Appendix 2: Sample size calculation
- 3. Web Appendix 3: Number of facilities needed by Province
- 4. Web Appendix 4: Construction of socio economic status variable
- 5. Web Appendix 5: Imputations for gestational age and CD4 cell count
- 6. Web Appendix 6: MTCT by province, 2010

Web Appendix 1: PMTCT policy time-line

FIGURE 1: SUMMARY OF WHO AND SOUTH AFRICAN PMTCT GUIDELINES: 2000-2013

WHO GUIDELINES BY YEAR										
2000 ¹	February 2006 ³	June 2010⁵		April 2012 ⁷						
Prophylaxis:	Treatment:	Treatment:		Treatment:						
AZT, AZT+3TC or sdnvp* or combinations (as HAART)	Mother: ART [AZT+3TC+NVP (or EFV) for stage III or IV disease, or stages I and II disease with CD4 cell count <200 cells/ul.	Mother: ART if CD4 ≤350 cells/ul or stage III or IV disease [AZT + 3TC + NVP or AZT + 3TC + EFV].		Mother: ART if CD4 ≤350 cells/ul or stage III or IV disease [AZT + 3TC + NVP or AZT + 3TC + EFV].						
Choice should consider feasibility, efficacy and cost.	Infant: AZT x 7 days	Infant: daily nvp or AZT x 4-6 weeks		Infant: daily nvp or AZT x 4-6 weeks						
	Prophylaxis	Prophylaxis:		Prophylaxis:						
	<i>Mother</i> : Antepartum: AZT from 28 weeks gestation; Intrapartum: Sd-NVP + AZT/3TC; Postpartum: AZT/3TC × 7 days	Option A: <i>Mother:</i> Antepartum AZT 14 weeks gestation, Intrapartum: sdnvp and AZT+3TC. Postpartum: AZT+3TC x7 days		Option A or Option B or Option B+: <i>Mother:</i> ART from 14 weeks' gestation and taken for life.						
	Infant: Sd-NVP + AZT × 7 days (or 28 days if no maternal prophylaxis)	Infant: daily sd nvp for six weeks in non BF infants or until 1 week after all BF has stopped		Infant: Daily infant nvp x 6 weeks						
		Option B:								
		Mother: ART throughout BF								
		Infant: daily nyp or AZT x6 weeks								

SUUIM AFRIGAN GUIDELINES BY YEAK										
2001 ²		February 2008⁴		April 2010 to end March 2013 ⁶		April 2013 to date ⁸				
Mother: Single dose nevi-		Treatment:		Option A:		Treatment:				
rapine at onset of labour		Mother: ART if CD4 cell count ≤200 cell/ul or stage IV		Treatment: <i>Mother</i> : ART (Tenofovir (TDF) + 3TC/Emtricit- abine (FTC) + NVP or AZT + 3TC + NVP (with renal disease) if WHO clinical stage III/IV or CD4 count ≤350/µI		All mothers regardless of CD4 cell count: Option B: Start FDC (TDF, FTC/3TC, EFV) same day unless renal or psychiatric disease. If CD4>350/ μ l stop FDC 1 week after breastfeed- ing stops. If CD4≤350/ μ l continue FDC for life				
Baby: single dose nevirap- ine during the first 72 hours of delivery		Infant: Sd-NVP + AZT x7 days (or 28 days if ARV exposure < 4 weeks)		Infant: daily nvp prophylaxis for 6 weeks		Infant: 6 weeks NVP unless mother on prophy- laxis only – see below.				
,		Prophylaxis: <i>Mother:</i> Antepartum AZT from 28 weeks. Intrapartum: sd NVP + AZT 3hrly		Prophylaxis – women not on ART Mother: AZT from 14 weeks AND		Prophylaxis: only if maternal ART contraindi- cated. Infant NVP from birth until one week after breastfeeding stops only if mother not on ART				
		Infant: sd-NVP + AZT x7 days (or 28 days if ARV exposure<4 weeks)		Infant: NVP prophylaxis for six weeks (if on HAART or if no breastfeeding) or continuing throughout the breastfeeding period.						

NVP - nevirapine, sdNVP - single dose nevirapine; BF - breastfeeding, EBF - exclusive breastfeeding, FF - formula feeding

1 UNFPA, UNICEF, WHO, UNAID on behalf of the Inter-Agency Task Team. New Data on the Prevention of Mother-To-Child Transmission of HIV and their Policy Implications. Conclusions and Recommendations. WHO Technical Consultation, 11-13 October 2000. Available from: http://whqlibdoc.who.int/hq/2001/WHO_RHR_01.28.pdf. Accessed 27 August 2012

2 National Department of Health SA. National Department of Health. Protocol for providing a comprehensive package of care for the prevention of mother to child transmission of HIV (PMTCT) in South Africa. 2001

3 World Health Organisation. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access. Recommendations for a public health approach (2006 revision). Available from: http://www.who.int/hiv/pub/mtct/arv_guidelines_mtct.pdf. Accessed 27 August 2012

4 Policy and Guidelines for the Implementation of the PMTCT programme [database on the Internet]2008 [cited 1 October 2009]. Available from: www.doh.gov.za.

5 World Health Organisation. Antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: towards universal access. Recommendations for a public health approach (2010 revision). Available from http://whylibdoc.who.int/publications/2009/9789241598934_eng.pdf 6 National Department of Health and SANAC. Clinical Guidelines: PMTCT (Prevention of Mother-to-Child Transmission). Available from http://www.doh.gov.za/docs/policy/2008/pmtct.pdf. Accessed 25August 2012 7 World Health Organisation. Programmatic update: Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants: http://www.doh.gov.za/docs/policy/2008/pmtct.pdf. Accessed 25August 2012 7 World Health Organisation. Programmatic update: Use of antiretroviral drugs for treating pregnant women and preventing HIV infection in infants. April 2012. Available from: http://www.doh.gov.za/docs/policy/2008/pmtct.pdf. Accessed 25August 2012 8 The South African Antiretroviral Treatment Guidelines: PMTCT Guidelines revised March 2013. Available from http://www.hst.org.za/publications/pmtct-guidelines-2013. Accessed 9 April 2013.

of **21**

Web Appendix 2: Sample Size Calculation by Province

To determine the sample size for each province, HIV prevalence was calculated based on the provincial antenatal survey prevalence and coverage of antiretroviral interventions to prevent mother to child transmission of HIV (PMTCT) (Table 1). Estimates of transmission rates for single dose nevirapine (sdNVP) and no treatment are taken from Rollins[1] while the transmission rate for dual therapy came from Horwood et.al.[2], which was reported prior to publication. Given these estimates we then deliberated on the relevant precision required. The first sample size calculations were based on a fixed relative precision of 30% across all provinces. The Western Cape Province (WC) had the lowest estimated prevalence at 6 weeks of 1.9%. Specifying a 30% relative precision leads to a sample size of nearly 4000 infants for this province alone. The numbers for the other provinces are also indicated in the table and this approach leads to an imbalance in field work effort required. The biggest effort would be required in the province with the lowest expected prevalence. We felt that given the low prevalence a larger relative precision would be acceptable. For the WC we felt that a 1% precision would be adequate for public health purposes. The upper limit of the 95% confidence interval will be around 3% and this equates a relative precision of 51%.

For the provinces with a higher expected prevalence we want a reasonable precision. In Gauteng Province (GP) the incidence is estimated at 8.2% and therefore a higher precision of 2% is required to monitor this transmission. We argue that a 2% precision will be reasonable. The precision required and specified for the nine provinces thus vary from 1% to 2%. In general provinces with a higher prevalence will have a lower (better) relative precision. The relative precision implemented in each province is indicated in the table. The benefit of this is that better equity in sample size is achieved between provinces. Using this approach the largest sample in a province is 1800 (Gauteng Province) and the smallest 700 (Northern Cape Province) with a total sample size of 12,200 across all provinces (Web Appendix Table 1).

Web Appendix Table 1: SAMPLE SIZE CALCULATION

								30% relative precision in each province			in each	Varying re	Varying relative precision across provinces			
	ANC HIV Prev. 2008	% ANC HIV test	% babies on PMTCT	Estimated Coverage (%tested X %admin to baby)	No PMTCT coverage	MTCT in exposed assuming sd NVP =15% & untreated=29% (Rollins)*	Overall Pop. Prev.	Error margin with 30% relative precision (RP)	RP	SS for 30% RP	Sample size for design effect (DE)** of 2 & RP 30%	Error margin with RP	Varying RP by province	Sample size using varying RP without DE	Sample size using varying RP with DE** of 2	
ZA	29	67	47	31.5%		24.6%	7.1%	2.1	30	575	1150					
EC	24	73	35	25.6%	74.5%	25.4%	6.1%	1.8	30	680	1360	1.8	30%	700	1400	
FS	29	70	52	36.4%	63.6%	23.9%	6.9%	2.1	30	560	1120	2.0	29%	617	1300	
GP	31	65	27	17.6%	82.5%	26.5%	8.2%	2.5	30	463	926	2.0	24%	723	1800	
KZN*	37	66	52	34.3%	65.7%	21.4%	7.9%	2.4	30	485	970	2.0	25%	699	1400	
LP	20	74	54	40.0%	60.0%	23.4%	4.7%	1.4	30	878	1756	1.5	32%	703	1400	
MP	34	56	36	20.2%	79.8%	26.2%	8.9%	2.7	30	428	856	2.0	22%	779	1600	
NC	14	81	70	56.7%	43.3%	21.1%	2.9%	0.9	30	1336	2672	1.8	60%	350	700	
NW	29.9	86	50	43.0%	57.0%	23.0%	6.9%	2.1	30	560	1119	2.0	29%	601	1200	
WC*	15	97	75	72.8%	27.3%	13.0%	1.9%	0.6	30	1989	3978	1.0	51%	716	1400	
TOTAL										7379	14758				12200	

Footnote: EC - Eastern Cape Province; FS - Free State Province; GP = Gauteng Province; KZN = Kwa-Zulu Natal Province; LP - Limpopo Province; MP - Mpumalanga Province; NW - North West Province;
NC - Northern Cape Province; WC - Western Cape Province. Prev. - prevalence ANC = antenatal clinicRP = relative precisionsdNVP = single dose nevirapinePop. = populationRP = relativeprecisionDE = design effect

ANC HIV seroprevalence from the 2008 antenatal survey, published in 2009 and immunisation coverage data from the 2007 District Health Information system (DHIS)

*WC and KZN assume full coverage dual therapy - Rollins KZN Study is 7%

** Design Effect = 1+(100-1)*(ICC=.01)=2

Web Appendix 3: Number of facilities needed per province

Each province was divided into 3 strata:

- Stratum 1 is clinics and community health centres (CHCs) that have annual Diphtheria Tetanus Pertussis – 1st dose (DTP1) 130-300 based on the 2007 District Health Information System (DHIS) data
- Stratum 2 are clinics and CHCs with ≥300 DTP1 and HIV prevalence below the national (<29%) rate based on the 2007 DHIS data and the 2008 antenatal survey data (published 2009) respectively
- Stratum 3 are clinics and CHCs with ≥300 DTP1st dose (based on the 2007 DHIS data) and HIV prevalence above the national rate based on 2008 antenatal survey data

Small facilities were excluded for issues relating to feasibility and cost-efficiency of data collection

Provinces that did not have a third stratum

Western Cape Province (WC), Limpopo Province(LP) and Northern Cape Province (NC) have no third stratum because there is no district with \geq 29% HIV prevalence and high delivery rate (>300 Immunization) in the province. However, for WC, sub district level data from the antenatal clinics HIV sero-prevalence survey (ANC survey) was available, which indicated that Khayelitsha sub-district has \geq 29% HIV prevalence. Thus the third stratum was created from large clinics in Khayelitsha. We were unable to do the same for Limpopo and NC, as we didn't have sub-district level HIV prevalence data (from the ANC survey) for these two provinces.

Web Appendix Tables 2-10 show the number of clinics that needed to be randomly selected in each stratum within each province, given the uptake of six weeks immunisation in DHIS 2007 (multistage probability proportional to size sampling).

Web Appendix - Tables 2-10: Number of facilities needed to be sampled from each province to collect data within 3wks (4 weeks for Northern Cape) duration from each facility. Note DTP1 = 1^{st} DTP at six weeks post-delivery

Web Appendix Table 2: EASTERN CAPE

Strata	Total Annual DTP1 for the province	Percentage	Adjusted Percentage (Column D)	Sample size proportional	Sample size adjusted proportional	Median yearly clinic DTP1 number	Median 3 week clinic DTP1 number	number of facilities need to be visited	number of facilities need to be visited based on adjusted distribution (Column J)
Small clinics (<130 DTP1#)	25862							20	20
Medium size clinics (130-300 annual DTP1#)	41620	36.38%	30%	509	420	186.5	11	47	39
large size (Annual DTP1 #>300) but low HIV prevalence	41646	36.40%	43%	510	602	459	26	19	23
large size (Annual DTP1 #>300) but high HIV prevalence	31141	27%	27%	381	378	402	23	16	16
Over all Total	114407	100%	100%	1400	1400			83	78 (or 98 if small facilities are included)

Web Appendix Table 3: FREE STATE

Strata	Total Annual DTP for the province	Percentage	Sample size proportional	Median yearly clinic DTP1 number	Median 3 week clinic DTP1 number	number of facilities need to be visited
Small clinics (<130 DTP1#)	4880					20
Medium size clinics (130- 300 annual DTP1#)	14418	27.34%	355	201	12	31
large size (Annual DTP1 #>300) but high HIV prevalence	38326	72.66%	945	404	23	41
Overall Total	52744	100%	1300			72 (or 92 if small facilities are included)

In Free state, we have only two strata - we grouped the last two strata as one stratum: The second strata (large and low HIV prevalence) in Free state had only 0.74% weighting which translates to sampling only 1 facility from the second stratum. Since sampling cannot be done for one facility, the second stratum is combined with the third stratum and thus we have only two strata for Free state.

Web AppendixTable 4: GAUTENG

Strata	Total Annual DTP for the province	Percentage	Sample size	Median yearly clinic DTP1 number	Median 3 week clinic DTP1 number	number of facilities need to be visited
Small clinics (<130 DTP1#)	1926		F- 0F 0- 100-100			20
Medium size clinics (130- 300 annual DTP1#)	15359	8.95%	161	237.5	14	12
large size (Annual DTP1 #>300) but low HIV prevalence	33023	19.25%	347	549	32	11
large size (Annual DTP1 #>300) but high HIV prevalence	123199	71.80%	1292	629	36	36
Over all Total	171581	100%	1800			59 (or 79 if small facilities are included)

Web Appendix Table 5: KWA-ZULU NATAL

Strata	Total Annual DTP for the province	Percentage	Sample size proportional	Median yearly clinic DTP1 number	Median 3 week clinic DTP1 number	number of facilities need to be visited
Small clinics (<130 DTP1#)	7365					20
Medium size clinics (130- 300 annual DTP1#)	40070	20.84%	292	209	12	24
large size (Annual DTP1 #>300) but low HIV prevalence	6505	3.38%	47	536.5	31	2
large size (Annual DTP1 #>300) but high HIV prevalences	145661	75.77%	1061	483	28	38
Over all Total	192236	100%	1400			64 (or 84 if small facilities are included)

Web Appendix Table 6: LIMPOPO

Strata	Total Annual DTP for the province	Percentage	Sample size proportional	Median yearly clinic DTP1 number	Median 3 week clinic DTP1 number	number of facilities need to be visited
Small clinics (<130						
DTP1#)	7166					20
Medium size clinics (130-						
300 annual DTP1#)	41027	33.89%	474	206	12	40
large size (Annual DTP1						
#>300) but low HIV						
prevalence	80048	66.11%	926	470.5	27	34
large size (Annual DTP1						
#>300) but high HIV						
prevalence	0	0.00%	0		0	0
						74 (or 94 if small facilities are
Over all Total	121075	100%	1400			included)

Web Appendix Table 7: MPUMALANGA

Strata	Total Annual DTP for the province	Percentage	Adjusted percentage (Column D)	Sample size proportional	Sample size adjusted proportional	Median yearly clinic DTPDTP1 number	Median 3 week clinic DTPDTP1 number	number of facilities need to be visited	number of facilities need to be visited based on adjusted distribution (Column J)
Small clinics (<130 DTP1#)	4545							20	
Medium size clinics (130- 300 annual DTP1#) large size (Annual DTP1 #>300) but low HIV	20858	26.73%	20%	428	320	225	13	33	25
prevalences	0	0.00%		0	0	0	0	0	0
large size (Annual DTP1 #>300) but high HIV prevalence	57172	73.27%	80%	1172	1280	439	25	46	51
Over all Total	78030	100%	100%	1600	1600			79	76

Web Appendix Table 8: NORTHERN CAPE

Strata	Total Annual DTP for the province	Percentage	Sample size proportional	Median yearly clinic DTP1 number	Median 4 week clinic DTP1 number	number of facilities need to be visited
Small clinics (<130 DTP1#)	2475					20
Medium size clinics (130- 300 annual DTP1#)	7766	51.82%	363	207.5	16	23
large size (Annual DTP1 #>300) but low HIV prevalence	7221	48.18%	337	400	32	11
large size (Annual DTP1 #>300) but high HIV prevalence	0	0.00%	0		0	
Over all Total	14987	100%	700			34 (or 54 if small facilities are included)

Sample size in Northern Cape

Northern Cape had 96 facilities to be sampled which was not an achievable target, given the vastness of the province, within the allocated time. A decision was taken to reduce the number of facilities that need to be visited to 53. Because the facilities are very far apart it was logistically not feasible to visit 53 facilities; thus we increased the duration of field work per facility to 4 weeks and reduced the number of facilities to 34. All small facilities were excluded from this 34

Web Appendix Table 9: NORTH WEST

Strata	Total Annual DTP	Domonto do	Sample size	Median yearly clinic	Median 3 week clinic	number of facilities need to be
	for the province	rercentage	proportional	DIFI number	DIFI humber	visited
DTP1#)	8758					20
Medium size clinics (130-						
300 annual DTP1#)	22925	34.26%	411	204.5	12	35
large size (Annual DTP1 #>300) but low HIV prevalence	24100	36.02%	432	413	24	18
large size (Annual DTP1 #>300) but high HIV prevalence	19887	29 72%	357	432.5	25	14
prevalence	17007	23.1270	331	452.5	23	14 67 (or 97 if small facilities are
Over all Total	66912	100%	1200			included)

Web Appendix Table 10: WESTERN CAPE

Strata Small clinics (<130	Total Annual DTPDTP#	Percentage	Sample size proportional	Median yearly clinic DTP1 number	Median 3 week clinic DTP1 number	number of facilities need to be visited
DTPDTP1#)	4537					20
Medium size clinics (130- 300 annual DTPDTP1#) large size (Annual DTPDTP1 #-300) but low	15953	17.85%	250	192	11	23
HIV prevalence	62884	70.38%	985	535	31	32
large size (Annual DTPDTP1 #>300) but						
high HIV prevalence	10517	11.77%	165	857	49	3
Overall Total	89354	100%	1400			58 (or 78 if small facilities are included)

Adjusting weighting for Mpumalanga and Eastern Cape

The number of facilities needed to be sampled for Mpumalanga (MP) and Eastern Cape (EC) was 79 and 83 respectively. Most of the facilities were from the medium-sized clinic stratum. It was realised that sample size might be difficult to achieve with the available logistics capacity; thus we have slightly shifted the weighting to the large clinics (see column D) and hence the number of facilities need to be sampled from medium facilities decreased from 47 to 39 for EC and from 33 to 25 for MP (see column J). This was considered to be logistocally feasible.

Web Appendix 4: Construction of Socio-economic status variable

The SES variable was constructed using a clustering algorithm (Spath, H. (1980), *Cluster Analysis Algorithms*, Chichester, Eng.: Ellis Horwood.; Hartigan, J. A. (1985), "Statistical Theory in Clustering," *Journal of Classification*, 2, 63–76. SAS STAT 9.2 Documentation.) that considered 10 interview items that measured a spectrum of socioeconomic indicators, and used the distance between an observations value on each of these variables and the overall mean for that variable to create three SES levels for the population. Web Appendix Table 11 shows the distribution of these variables across the 3 levels of our calculated SES variable for the entire study sample. The largest differences between the lower and lowest SES groups were the availability of electricity or gas for cooking, and access to home amenities such as a stove, radio, television or telephone. There was not a significant difference between the lower and lowest SES groups in terms of reported food scarcity, however, women in the lowest SES group were less likely to receive support from a male partner and more likely to receive a Child support grant from the South African government. (http://www.services.gov.za/services/content/Home/ServicesForPeople/Socialbenefits/childsupportgrant/en ZA ;

http://www.info.gov.za/view/DownloadFileAction?id=90553

Web Appendix Table 11: Distribution of individual variables that contributed to the overall socio-economic status (SES) score levels of average, lower than average and lowest SES.

Variable		SES Category						
		Average	Lower	Lowest				
	Included in	the SES factor analysis						
Home Material	Brick	88.2 (86.8-89.7)	0.0	91.7(89.8-93.5)				
	Informal material/corrugated iron/wood	11.8 (10.3-13.2)	51.0 (45.1-56.9)	8.3 (6.5-10.1)				
	Traditional/Mud	0.0	49.0 (43.0-54.9)	0.0				
Water Source)Piped vs. not	Piped	91.8 (90.5-93.0)	32.5 (27.6-37.4)	41.0 (36.5-45.5)				
piped								
Toilet Type	Flush	73.1 (71.0-75.3)	6.5(5.2-7.9)	12.5 (9.4-15.6)				
	Pit Latrine	26.8 (24.6-29.0)	84.0(80.8-87.2)	76.9 (73.6-80.3)				
	None/Other	0.0	9.4(6.5-12.4)	10.6 (7.9-13.2)				
Cooking Fuel	Electricity/Gas	98.2 (97.7-98.6)	88.3 (79.7-86.8)	74.8 (71.2-78.5)				
	Wood/coal	1.8(1.3-2.2)	16.1(12.6-19.6)	24.8 (21.1-28.4)				
Household owns	Refrigerator	86.4 (85.3-87.7)	23.5(20.2-26.9)	46.7 (42.7-50.7)				
	Radio	86.4(85.5-87.4)	63.0 (59.9-66.0)	46.5 (42.7-50.3)				
	Television	93.5(92.8-94.3)	42.1(38.4-45.9)	27.3(24.4-30.2)				
Household owns cont/	Stove	98.4 (98.0-98.7)	86.2(83.1-89.3)	40.1(35.8-44.4)				
	Landline Telephone / Cell phone	90.9(89.9-91.8)	80.7(77.6-83.7)	50.6(46.0-55.2)				
	Car	18.3(16.9-19.7)	2.8 (1.9-3.7)	3.1(2.0-4.1)				
	Variables expected to be associated with socio-econo	mic status used to test the face validi	ty of the clustering procedure.					
In the last year was there a time	when the family ran out of food and had to ask for	13.1 (11.5-14.8)	25.4(21.5-29.2)	20.1(17.2-23.0)				
help? (Yes)								
Source of maternal income								
	Mother's employment	20.3 (19.1-21.6)	10.1(8.3-11.8)	10.3 (8.8-11.9)				
	Partner/Husband/Ex-husband	65.2 (63.4-67.0)	61.7 (58.7-64.6)	41.8 (38.7-44.9)				
	Child Support grant	11.5(10.2-12.7)	16.5 (13.8-19.1)	27.5 (24.4-30.7)				

Web Appendix 5: Multiple Imputations

In order to impute missing CD4 count data for HIV-infected mothers only, we created dummy values for mothers that had reported a negative HIV test result during their current pregnancy (n=7050) that were designed to represent a normally distributed range of CD4 counts for healthy South Africans with mean 650 and standard deviation of 360.[3, 4] This resulted in a need to impute CD4 for only 1408 women, representing 13.8% of the total sample but 47% of all infected women (Web Appendix Table 12). Thus while imputed CD4 was used for imputing gestational age at first antenatal clinic (ANC) visit for the entire sample, we did not include the imputed CD4 variable as potential confounder in analyses limited to HIV-infected mothers as we felt that too large a percentage of the data was missing to allow for reliable inference in this sub-population. After filling in cd4 counts for the part of the population for which these data were not relevant, roughly 20% of the sample was missing data for at least one variable of interest (Supplemental Table 13). Missing data were imputed to a monotone missing pattern using Marcov Chain Monte Carlo imputation of 5 replicates of the original data (See Web Appendix Table 13 for the monotone missing data patterns). The remaining missing values of birthweight, CD4 count for HIV infected mothers, gestational age at birth and then gestational age of the infant at first ANC visit were imputed using regression techniques that used imputation models which included all exposures of interest (ARV status of the mother, breastfeeding status, and type of delivery) and potential confounders (SES strata, mothers age, education and marital status and whether or not the pregnancy was planned) of the analytic models described in the main text. The majority of those with any missing data to impute (13.4% of the total study sample) were missing data on gestational age of the infant at birth, an additional 4.5% were missing data on both gestational age of the infant at birth and at the mother's first ANC visit. As expected and evidenced by the similarities of the data in Web Appendix Tables 12 and 14, the imputation did not change the distribution of values in the overall sample, with similar mean, median and standard deviation for variables of interest in all categories of HIV test results in the complete case and imputation data sets. The final model reported in Table 2 of the main text was developed using methods for analysis of imputed data because the data contained 1944 imputed values of gestational age at first ANC visit for the entire sample, including data for 620 of 3088 (20%) with infants categorized as exposed to HIV. In this model there were also 157 (5%) of values imputed for birthweight as a continuous variable prior to categorization of this variable into the dichotomous values of \geq 2.5kg and <2.5kg.

Mothers self- reported HIV test result during this pregnancy	HIV antibody test result of infant	Variable	Number with valid values	Number with missing values	Mean ^a	Median ^a	Std Dev ^a
Unknown	Non-reactive	cd4 count	0	282			
		Week ^b first ANC	33	249	16.8484848	16.0000000	9.8714272
		Week ^b of birth	201	81	38.2736318	39.0000000	2.1259707
	Reactive	cd4 count	0	135			
		Week first ANC	19	116	21.2631579	22.0000000	7.7232845
		Week of birth	89	46	38.4494382	40.0000000	2.1320671
Positive	Non-reactive	cd4 count	32	57	444.6250000	358.0000000	273.0943061
		Week first ANC	67	22	18.2686567	18.0000000	7.3269575
		Week of birth	69	20	38.0289855	40.0000000	3.2583423
	Reactive	cd4 count	1686	934	391.2781732	351.0000000	262.2071808
		Week first ANC	2174	446	18.4001840	20.0000000	7.3512192
		Week of birth	2111	509	38.3908100	39.0000000	2.2860158
Negative	Non-Reactive	cd4 count ^c	6700	0	660.2199949	647.1804199	349.6981996
Ũ		Week first ANC	5654	1046	17.9349133	20.0000000	7.4632426
		Week of birth	5470	1230	38.4104205	39.0000000	2.2237110
	Reactive	cd4 count ^c	350	0	650.1553387	660.2065430	334.8463837
		Week first ANC	285	65	18.9263158	20.0000000	7.7417500
		Week of birth	243	107	37.8436214	38.0000000	2.7424258

Web Appendix Table 12: Mean and Standard Deviation of CD4 count and weeks of gestational age in the study sample prior to data imputation

a) Of non-missing values

b) Gestational age

c) These values were included as placeholders for women who reported an HIV negative test result during their current pregnancy. Values were intended to be (and are approximately) normally distributed with mean 650 and standard deviation of 360.

Missing Data Patterns													
Group	Ses Strata	Mother's Age	Marital Status	Planned Pregnancy	Delivery Type	Breast Feeding	Rx Regimen	Birth weight	CD4 count	Gestag e at first ANC	Gest. Age at birth	Count	Percent of Total
1	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х	43160	80.41
2	Х	Х	Х	Х	Х	Х	Х	Х	Х	Х		7165	13.35
3	Х	Х	Х	Х	Х	Х	Х	Х	Х			2315	4.31
4	Х	Х	Х	Х	Х	Х	Х	Х				805	1.50
5	Х	Х	Х	Х	Х	Х	Х					230	0.43

Web Appendix Table 13: Missing data patterns for imputation after Markov Chain Monte Carlo

imputation to create 5 replicate datasets with a monotone missing data pattern

Mothers self reported HIV Status	HIV antibody results of the infant	Variable	Number of observations ^a	Missing data	Mean	Median	Standard Deviation
Unknown	Negative	cd4 count	1410	0	681.1248227	672.0000000	341.2960686
		Week ^b first ANC	1410	0	17.2829787	17.0000000	8.1222076
		Week ^b of birth	1410	0	38.2156028	38.0000000	2.1223166
	Positive	cd4 count	675	0	656.2814815	646.0000000	342.9423966
		Week first ANC	675	0	15.8059259	16.0000000	8.8884929
		Week of birth	675	0	38.3377778	39.0000000	2.1867509
Positive	Negative	cd4 count	445	0	450.3865169	384.0000000	291.1589668
		Week first ANC	445	0	18.2022472	18.0000000	7.5309867
		Week of birth	445	0	38.1910112	40.0000000	3.0346216
	Positive	cd4 count	13100	0	416.4175573	372.0000000	279.2226348
		Week first ANC	13100	0	18.4049618	20.0000000	7.3709509
		Week of birth	13100	0	38.3758779	39.0000000	2.2887447
Negative	Negative	cd4 count ^c	33500	0	660.2235821	647.0000000	349.6868243
0	0	Week first ANC	33500	0	17.9696418	20.0000000	7.4491663
		Week of birth	33500	0	38.3952836	39.0000000	2.2203710
	Positive	cd4 count ^c	1750	0	650.1714286	660.5000000	334.4629845
		Week first ANC	1750	0	18.8777143	20.0000000	7.7032524
		Week of birth	1750	0	37.8668571	38.0000000	2.5939166

Web Appendix Table 14: Mean and Standard Deviation of CD4 count and weeks of gestational age in the study sample after data imputation

a) In 5 imputed datasets representing copies of the original data to which the imputed data were added.

b) Of Gestation

c) These values for CD4 count were not imputed but were set to a standard normal distribution with mean 650 and standard deviation 360.

Web Appendix 6: MTCT by province

Web Appendix Table 15: HIV exposure and MTCT by province

Province	Infant HIV exposure % (95% CI)	MTCT (%) 95% CI
Fastern Cane*	30 5 (26 9-34 2)	47(2470)
Free State	31.3 (29.1-33.5)	5.9 (3.8-8.0)
Gauteng	30.4 (27.9-33.0)	2.5 (1.5-3.6)
KwaZulu-Natal	44.3 (40.2-48.4)	2.9 (1.7-4.0)
Limpopo	23.9 (21.8-25.9)	3.6 (1.4-5.8)
Mpumalanga	37.0 (34.3-39.7)	5.7 (4.1-7.3)
Northern Cape*	16.0 (13.7-18.3)	1.4 (0.1-3.4)
Northwest	31.3 (29.0-33.5)	4.4 (2.9-5.9)
Western Cape	21.0 (17.0-25.0)	3.9 (1.9-5.8)
South Africa	32.0 (30.7-33.3)	3.5 (2.9-4.1)

REFERENCES

- 1. Rollins N, Little K, Mzoloa S, Horwood C, Newell M-L: Surveillance of mother-to-child transmission prevention programmes at immunization clinics: the case for universal screening. *AIDS* 2007, 21:1341-1347.
- 2. Horwood C, Vermaak K, Butler L, Haskins L, Phakathia S, Rollins N: Elimination of paediatric HIV in KwaZulu-Natal, South Africa: large-scale assessment of interventions for the prevention of mother-to-child transmission. *Bulletin of the World Health Organisation* 2012, 90:168-175.
- 3. Zaidi J, Grapsa E, Tanser F, Newell M, Bärnighausen T: Dramatic increases in HIV prevalence after scale-up of antiretroviral treatment: a longitudinal population-based HIV surveillance study in rural kwazulu-natal. *AIDS* 2013.
- 4. Vinnard C, Wileyto E, Bisson G, Winston C: First Use of Multiple Imputation with the National Tuberculosis Surveillance System. *Epidemiology Research Int* 2013.