Webappendix

Webtable 1. Patient characteristics in public-sector HIV treatment programmes with and without routine viral load monitoring in the Southern Africa IeDEA cohort.

Variable	Viral load sites				Non-viral load sites	
	Themba Lethu	Tygerberg	Gugulethu	Khayelitsha	Lighthouse	CIDRZ
Women (%)	4758 (63.8%)	885 (65.0%)	1806 (68.0%)	4842 (67.0%)	5582 (58.1%)	44454 (62.3%)
Median age [IQR] (years)	36 (31-42)	35 (29-41)	33 (29-39)	33 (29-39)	36 (30-43)	35 (30-42)
Clinical stage (%)						
Stage available	7457 (100%)	1017 (74.2%)	2656 (99.9%)	7229 (100%)	8277 (86.2%)	69295 (97.1%)
Advanced *	1897 (25.4%)	729 (71.7%)	2028 (76.4%)	5947 (82.3%)	7736 (93.5%)	47142 (68.0%)
CD4 cell count (cells/μL)						
CD4 count available	3684	937	2206	5053	5311	54628
Median [IQR]	87 (33-156)	113 (48-171)	101 (48-159)	90 (38-157)	130 (59-213)	132 (67-202)
HIV-1 viral load (copies/ml)						
Viral load available (%)	1188 (15.9%)	721 (53.0%)	2196 (82.6%)	3078 (42.6%)	5 (0.1%)	834 (1.2%)
Median log viral load [IQR]	5.0 (4.3-5.6)	5.3 (4.9-5.8)	4.9 (4.4-5.3)	5.1 (4.6-5.6)	0 (0-2.6)	5.2 (4.7-5.6)
≤ 10,000	225 (18.9%)	38 (5.3%)	261 (11.9%)	281 (9.1%)	5 (100%)	93 (11.2%)
10,001-100,000	352 (29.6%)	181 (25.1%)	996 (45.4%)	1097 (35.6%)	0	228 (27.3%)
First-line regimens (%)						
3TC d4T EFV	6499 (87.1%)	747 (54.9%)	1778 (66.9%)	3207 (44.4%)	56 (0.6%)	4914 (6.9%)
3TC ZDV EFV	215 (2.9%)	59 (4.3%)	88 (3.3%)	592 (8.2%)	20 (0.2%)	2736 (3.8%)
3TC d4T NVP	648 (8.7%)	374 (27.5%)	528 (19.9%)	2654 (36.7%)	9452 (98.4%)	37488 (52.6%)
3TC ZDV NVP	39 (0.5%)	147 (10.8%)	262 (9.9%)	769 (10.6%)	76 (0.8%)	25343 (35.5%)
Other	56 (0.8%)	34 (2.5%)	2 (0.1%)	8 (0.1%)	0 (0%)	852 (1.2%)
Second-line regimens (%)						
TNV FTC LPV/r	2 (0.5%)	1 (0.9%)	0 (0%)	4 (1.9%)	0 (0%	817 (63.1%)
AZT ddI LPV/r	326 (73.8%)	88 (83.0%)	97 (69.8%)	146 (68.9%)	0 (0%)	4 (0.3%)
ABC ddI LPV/r	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	231 (17.8%)
3TC AZT LPV/r	63 (14.3%)	9 (8.5%)	0 (0%)	9 (4.3%)	5 (6.8%)	52 (4.0%)
3TC AZT LPV/r TNV	1 (0.2%)	0 (0%)	0 (0%)	1 (0.5%)	59 (79.7%)	53 (4.1%)
3TC AZT EFV LPV/r	0 (0%)	0 (0%)	33 (23.7%)	0 (0%)	0 (0%)	0
Other	50 (11.3%)	8 (7.5%)	9 (6.5%)	52 (24.5%)	10 (13.5%)	138 (10.7%)

Interquartile ranges (IQR) are shown in square brackets and percentages in brackets. ABC, abacavir; ddI, didanosine; EFV, efavirenz; d4T, stavudine; FTC, emtricitabin; LPV, lopinavir; NVP, nevirapine; RTV: boost of ritonavir; 3TC, lamivudine; ZDV, zidovudine * US Centers for Disease Control and Prevention (CDC) stage C, or World Health Organization (WHO) stages III or IV.

Webtable 2. Availability of diagnostic examinations in the six antiretroviral treatment programmes from the Republic of South Africa, Malawi and Zambia in the Southern Africa IeDEA cohort

	Viral load sites				Non-viral load sites	
	Themba Lethu	**Tygerberg**	**Gugulethu**	**Khayelitsha**	**Lighthouse**	**CIDRZ**
Imaging						
X-ray	On site	On site	On site	On site	Off site	On-site at some facilities, off-site at others
CT scan	On site, within a day	On site, within a day	Off site, within a week	Off site, within one week	Off site, not generally available	Off site, not generally available
Bacteriology						
Culture of *M. tuberculosis*	On site	On site	Off site	Off site	Off site	Limited availability
Mycobacterial species identification	On site	On site	On site	On site	Not available	Not available
Parasitology						
CSF cryptococcal antigen test	On site	On site	On site	On site	Not generally available	Limited availability
CSF culture for *Cryptococcus neoformans*	On site	On site	On site	On site	Not generally available	Not available
Other examinations						
Lumbar puncture procedure	On site	On site	On site	Off site	On site	Off site, not often done
Blood culture	On site	On site	On site	Off site	On site	Limited availability
Resistance testing	As part of research studies or after second-line failure				Not available	Not available

CSF, cerebrospinal fluid

Webtable 3. Cumulative percentages (95% confidence intervals) of treatment outcomes from 6 months after starting ART initiation in sites with and without routine viral load monitoring in the Southern Africa IeDEA cohort.

Time since ART start (years)		0.5	1	1.5	2	2.5	3
Viral load sites							
On first line	%	100.0 (100-100)	93.9 (93.5-94.3)	88.0 (87.4-88.6)	83.1 (82.4-83.9)	78.9 (78.1-79.8)	75.4 (74.4-76.4)
Failed first-line	%	0	0.5 (0.4-0.6)	1.1 (0.9-1.3)	1.5 (1.3-1.8)	1.6 (1.3-1.9)	1.3 (0.9-1.6)
Switched to second-line	%	0	1.4 (1.2-1.6)	3.3 (3.0-3.7)	5.4 (4.9-5.8)	7.6 (7.1-8.2)	9.8 (9.1-10.5)
Lost to follow-up	%	0	2.7 (2.5-3.0)	5.1 (4.7-5.5)	6.8 (6.3-7.3)	8.1 (7.6-8.7)	9.2 (8.5-9.8)
Died	%	0	1.5 (1.3-1.7)	2.5 (2.2-2.7)	3.1 (2.8-3.5)	3.7 (3.3-4.1)	4.3 (3.9-4.8)
Non-viral load sites							
On first line	%	100.0 (100-100)	92.9 (92.5-92.9)	85.9 (85.7-86.2)	80.4 (80.1-80.7)	76.1 (75.7-76.5)	72.6 (72.2-73.0)
Failed first-line	%	0	0.6 (0.6-0.7)	1.6 (1.5-1.7)	2.3 (2.2-2.4)	3.1 (2.9-3.3)	3.7 (3.6-3.9)
Switched to second-line	%	0	0.2 (0.2-0.2)	0.5 (0.5-0.6)	0.9 (0.8-1.0)	1.4 (1.3-1.6)	2.1 (2.0-2.3)
Lost to follow-up	%	0	4.4 (4.2-4.5)	8.5 (8.3-8.7)	11.7 (11.5-12.0)	13.9 (13.6-14.2)	15.3 (15.0-15.7)
Died	%	0	2.1 (2.0-2.2)	3.5 (3.4-3.7)	4.7 (4.5-4.8)	5.5 (5.3-5.7)	6.1 (5.9-6.4)

Webtable 4. Adjusted hazard ratios for treatment outcomes comparing programmes with and without (reference group) routine viral load monitoring from sensitivity analyses excluding one cohort at a time.

Exclusion of	Adjusted* HR (95% CI)	P
CIDRZ		
All-cause mortality	0.71 (0.54-0.93)	0.02
Loss to follow-up	0.61 (0.50-0.73)	<0.001
Switch to second-line ART	3.52 (2.46-5.05)	<0.001
Lighthouse		
All-cause mortality	0.57 (0.50-0.65)	<0.001
Loss to follow-up	0.53 (0.48-0.58)	<0.001
Switch to second-line ART	4.21 (3.61-4.91)	<0.001
Khayelitsha		
All-cause mortality	0.50 (0.42-0.60)	<0.001
Loss to follow-up	0.77 (0.69-0.86)	<0.001
Switch to second-line ART	7.21 (6.00-8.66)	<0.001
Gugulethu		
All-cause mortality	0.57 (0.49-0.66)	<0.001
Loss to follow-up	0.58 (0.53-0.63)	<0.001
Switch to second-line ART	4.18 (3.56-4.90)	<0.001
Tygerberg		
All-cause mortality	0.56 (0.49-0.65)	<0.001
Loss to follow-up	0.44 (0.40-0.49)	<0.001
Switch to second-line ART	3.96 (3.37-4.64)	<0.001
Themba Lethu		
All-cause mortality	0.66 (0.57-0.77)	<0.001
Loss to follow-up	0.42 (0.38-0.48)	<0.001
Switch to second-line ART	3.17 (2.65-3.79)	<0.001

* Adjusted for age, sex and CD4 cell count at 6 months.

Webtable 5. Adjusted hazard ratios for treatment outcomes comparing programmes with and without routine viral load monitoring from complete case analysis.

Outcome	Adjusted* HR (95% CI)	P
From start of ART to 6 months		
All-cause mortality	0.79 (0.70-0.88)	<0.001
Loss to follow-up	0.95 (0.84-1.07)	0.42
From 6 months to end of follow-up		
All-cause mortality	0.75 (0.63-0.89)	<0.001
Loss to follow-up	0.80 (0.71-0.91)	<0.001
Switch to second-line ART	2.96 (2.50-3.51)	<0.001

* Adjusted for age, sex, first-line regimen, CD4 cell count and clinical stage at start of first line therapy and for age, sex and CD4 cell count at 6 months.

Webtable 6. Observed and expected death rates (per 100 person years) assuming same non-HIV-related death rate in sites with and without routine viral load monitoring (months 7 to 36).

Setting	**Observed mortality rate**	**Non-HIV related death rate[a]**	**Expected mortality assuming identical non-HIV related mortality[b]**	**Expected mortality assuming identical non-HIV related mortality[c]**
RSA	2.12 (1.93-2.34)	0.62 (0.52-0.75)	2.12 (1.93-2.34)	2.31 (2.10-2.53)
Malawi/Zambia	3.10 (2.99-3.20)	0.80 (0.75-0.85)	2.92 (2.82-3.02)	3.10 (2.99-3.20)
Rate ratio	0.68 (0.62-0.76)		0.73 (0.65-0.81)	0.75 (0.68-0.82)
Rate difference	0.0097 (0.0074- 0.0120)		0.0079 (0.0056-0.0102)	0.0079 (0.0055-0.0103)

RSA, Republic of South Africa
[a] Using data from the global burden of disease project from the World Health organisation (WHO).
[b] Based on South African rates
[c] Based on Malawian and Zambian rates

Webfigure 1. Sensitivity analysis of evolution of CD4 cell counts from start of antiretroviral therapy (ART) up to three years after start of ART in sites with (blue) and without (red) routine viral load monitoring. Lines represent the mean fit of the mixed effect model. Dots show the moving averages of the observed data. The excluded cohort is labelled.