Published in final edited form as:
S Afr Med J. 2009 September ; 99(9): 653–660.

Monitoring the South African National Antiretroviral Treatment Programme, 2003 – 2007: The IeDEA Southern Africa Collaboration

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Conflict of interest. The authors declare that they have no conflict of interest.

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for the International epidemiologic Databases to Evaluate AIDS Southern Africa (IeDEA-SA) Collaboration

Abstract

Objectives—To introduce the combined South African cohorts of the International epidemiologic Databases to Evaluate AIDS Southern Africa (IeDEA-SA) collaboration as reflecting the South African national antiretroviral treatment (ART) programme; to characterise patients accessing these services; and to describe changes in services and patients from 2003 to 2007.

Design and setting—Multi-cohort study of 11 ART programmes in Gauteng, Western Cape, Free State and KwaZulu-Natal.

Subjects—Adults and children (<16 years old) who initiated ART with ≥3 antiretroviral drugs before 2008.

Results—Most sites were offering free treatment to adults and children in the public sector, ranging from 264 to 17 835 patients per site. Among 45 383 adults and 6 198 children combined, median age (interquartile range) was 35.0 years (29.8 – 41.4) and 42.5 months (14.7 – 82.5), respectively. Of adults, 68% were female. The median CD4 cell count was 102 cells/μl (44 – 164) and was lower among males than females (86, 34 – 150 v. 110, 50 – 169, $p<0.001$). Median CD4% among children was 12% (7 – 17.7). Between 2003 and 2007, enrolment increased 11-fold in adults and 3-fold in children. Median CD4 count at enrolment increased for all adults (67 – 111 cells/μl, $p<0.001$) and for those in stage IV (39 – 89 cells/μl, $p<0.001$). Among children <5 years, baseline CD4% increased over time (11.5 – 16.0%, $p<0.001$).

Conclusions—IeDEA-SA provides a unique opportunity to report on the national ART programme. The study describes dramatically increased enrolment over time. Late diagnosis and ART initiation, especially of men and children, need attention. Investment in sentinel sites will ensure good individual-level data while freeing most sites to continue with simplified reporting.

The World Health Organization (WHO) estimated that in 2007, 9.7 million people in low- and middle-income countries needed antiretroviral treatment (ART),1 9% of whom were living in South Africa.2 By the end of 2007, the South African National Department of Health (DoH) reported that 371 731 people had initiated highly active antiretroviral therapy (HAART),2 making it the largest ART programme in the world.1 As the public health system has only provided ART since 2004, this has involved a massive scale-up of services within a comparatively short space of time.

In the context of such an ambitious undertaking, trends in enrolment and key outcomes must be understood in order to plan for the changing needs of health services and patients.[1] Monitoring is a major challenge to effective delivery of ART at a national level,[2] and it becomes increasingly important as the continued scale-up of ART creates a tension between service provision and collecting good data.

The International epidemiologic Databases to Evaluate AIDS (IeDEA) Southern Africa collaboration (IeDEA-SA) has assembled a collaborative individualised dataset of children and adults starting ART at sites in South Africa. Numerically the collaboration represents 20% of all children and 10% of all adults entering the public sector roll-out programme. This provides a unique opportunity to report in detail, based on individual patient data, on a subset of the national ART programme.

This paper aims to introduce the South African cohorts participating in IeDEA as a collaboration that reflects the South African national ART programme, to characterise the children and adults accessing these services, and to describe changes in services and patients over the past 5 years.

Background and setting

The IeDEA collaboration

IeDEA is an international collaboration of seven regional data centres funded by the National Institutes of Health (NIH). It was established to pool data across numerous cohorts of patients on ART, creating large datasets to address research questions that cannot be answered within single cohorts.

IeDEA Southern Africa

IeDEA-SA is the regional cohort collaboration of southern Africa. Since its establishment in 2006, 22 sites have joined the collaboration. The current database includes cohorts from South Africa, Zimbabwe, Mozambique, Zambia, Malawi and Botswana. Some countries have more than one cohort participating, providing an opportunity to describe characteristics and outcomes at a national level, in the absence of good routine national monitoring systems. In South Africa, 11 large sites from 4 provinces have joined the collaboration.

The South African ART programme

Since the start of the national ART roll-out programme in 2004, the South African guidelines for initiation of ART3 have recommended treatment for adults with CD4 cell counts <200 cells/μl or WHO stage IV illness except for extrapulmonary tuberculosis, who are assessed to be willing and ready to take and adhere to ART. Before this, most sites offering ART followed similar criteria, based on the 2002 WHO guidelines.[4] First-line therapy in ART-naïve adults, unless contraindicated, is stavudine (d4T), lamivudine (3TC) and efavirenz (EFV) or nevirapine (NVP). Women of child-bearing age who are unable to guarantee reliable contraception should receive NVP instead of EFV. Patients receive monthly medication and are seen by a doctor at 4, 8 and 12 weeks and 3-monthly thereafter if well. CD4 count and viral load are measured 6-monthly. Patients with a detectable viral load (>400 copies/μl) receive a stepped-up adherence package. If their viral load persistently exceeds 5 000 copies/μl despite adherence support, they may be switched to second-line therapy. Second-line therapy comprises zidovudine (AZT), didanosine (ddI) and lopinavir/ritonavir (LPV/r). Drug substitutions are also made if patients experience toxicity on first-line therapy.

The 2004 South African paediatric guidelines[3] recommend ART initiation based on a confirmed HIV diagnosis (HIV DNA polymerase chain reaction (PCR) testing if the child is <18 months of age) and one of the following criteria: (*i*) recurrent hospitalisations (>2 admissions/year) or prolonged hospitalisation (>4 weeks) for HIV-related illness; (*ii*) WHO stage III/IV disease; or (*iii*) CD4 <20% if under 18 months or <15% for older children. Based on the new WHO staging,[5] most paediatric sites changed from the 3- to the 4-stage system towards the end of 2004, which may have impacted to some extent on the paediatric staging

data in this dataset. Paediatric first-line ART for children from 6 months to 3 years is d4T, 3TC and LPV/r. For children >3 years and >10 kg, EFV replaces LPV/r.

Methods

Study population

Most participating 'sites' comprise single clinics in urban or peri-urban areas. The definition of site is broad: one site encompasses 3 clinics, and another includes all the facilities within an entire province, from primary to tertiary level. The study included data on all adults and children (<16 years old) with documented age, gender and ART start date who initiated ART with at least 3 antiretrovirals before 2008.

Data collection and management

The study utilised data that are routinely collected by sites. All sites have current ethics committee approval for contribution of their data to IeDEA analyses. The data were all anonymised before transfer to the data centre. Sites submitted data during the course of 2007 and early 2008. Data on programme-level characteristics were collected through site assessment questionnaires.

Data analysis

Cleaning, coding and analysis of data were done in Intercooled STATA 10.0 for Windows (STATA Corporation, College Station, TX). Continuous variables were described by medians and interquartile ranges and categorical variables as proportions. Temporal trends were tested using the Kruskal-Wallis test (continuous variables) and the chi-square test (categorical variables).

Results

Programme-level characteristics

Seven of the sites offer services to children and adults, either in separate or combined clinics (Table I); 1 site treats children and pregnant women and the other sites treat children or adults exclusively. Nine sites are public programmes funded largely by the DoH with strong research partnerships. One site is funded entirely by donor funding and another is a not-for-profit hospital that receives a DoH subsidy and external funding for research projects. The study utilised data on adult patients from 8 sites, contributing between 642 and17 835 patients. Seven sites contributed data on paediatric patients, contributing between 264 and 2 226 patients.

Treatment was free to all patients except those attending the state-subsidised hospital, who were charged a small inclusive monthly co-payment. Although most sites reported active follow-up of patients, follow-up of defaulting patients was generally limited owing to resource constraints. Patients were referred for treatment primarily from clinics, hospital wards and other medical facilities. Treatment readiness and patient preparation was fairly consistent across sites, involving a baseline psychosocial assessment and 3 individual or group education sessions over 3 consecutive weeks. This process could be fast-tracked if the patient was pregnant or required immediate treatment for medical reasons. Patients were encouraged to disclose their HIV status and to have 'treatment buddies', and were referred to support groups where available.

Characteristics of patients

The analysis included 45 383 adults and 6 198 children. The median age among adults was 35 years (interquartile range (IQR) 29.8 – 41.4) and among children 42.5 months (IQR 14.7 –

82.5) (Table II). Of children, 21.2% (*N*=1 315) and 38.9% (*N*=2 411) were aged <1 year and ≥5 years, respectively. Adult patients were predominantly female (67.6%, *N*=30 684). In contrast, the gender balance of children was even.

Among adults, the median CD4 cell count was 102 cells/μl (IQR 44 – 164). The median CD4 count was lower among adult males than females (86 v. 110 cells/μl, $p<0.001$). Among patients with baseline CD4 counts, the majority (89.4%, *N*=30 105) commenced therapy with CD4 cell counts below 200/μl. A total of 9 363 adult patients (27.8%) initiated ART with CD4 counts <50 cells/μl.

Among children, the median CD4% was 12.0% (IQR 7.0 – 17.7), and 64.6% of paediatric patients (*N*=3 004) initiated therapy with CD4% <15%. In cohorts reporting WHO staging (28.1% of adults, *N*=12 763 and 66.5% of children, *N*=4 120) most patients had advanced HIV disease (WHO stage III or IV).

In line with the national protocol, the majority of adult patients (87.7%, *N*=31 852) started on a regimen containing d4T and 3TC as the two nucleoside reverse transcriptase inhibitors (NRTIs); 68% (*N*=24 734) of adults and 53% (*N*=2 846) of children started on a regimen containing EFV. Data on previous ART and prevention of mother-to-child (PMTCT) exposure were limited. Where previous ART exposure was recorded, most adults (93%, *N*=22 062) and children (96%, *N*=4 100) were reportedly ART-naïve. In cohorts that reported PMTCT exposure, 13% (*N*=696) of women and 25% of children (*N*=617) were known to have been exposed. Reliable data on tuberculosis (TB) at ART initiation were available from 2 adult and 2 paediatric cohorts. Among these adult patients, 3 722 (21%) had TB, while the proportion among children was slightly higher (32%, *N*=1 052). Of the 3 adult cohorts that provided pregnancy data (*N*=8 828 female patients), 7% of female patients (*N*=633) were pregnant at ART initiation. In these cohorts, median CD4 count was higher among pregnant women than those who were not pregnant (150 v. 104, $p<0.001$) and higher among non-pregnant women than men (104 v. 80, $p<0.001$).

Temporal trends

Table III shows temporal trends in enrolment, absolute and percentage CD4 and WHO stage. Over 5 years, patient numbers increased nearly 11-fold among adults (from 1 462 to 15 628), and 3-fold among children (from 376 to 1 139). The majority of adults in this analysis (63%, *N*=28 643) started treatment in 2006 – 2007. Although paediatric enrolment appeared to drop substantially in 2007, this is probably because data from one of the largest paediatric cohorts were not available for the second half of 2007.

There was an increase in overall adult baseline CD4 count, from a median of 67 cells/μl (IQR 23 – 134) in 2003 to 111 cells/μl (IQR 49 – 171; $p<0.001$) in 2007, although the rate of increase declined over the years. Of all the paediatric patients, 3 787 (61%) were <5 years of age. Among these patients, baseline CD4% was available for 76% (*N*=2 884) and median CD4% increased from 11.5% (IQR 7.1 – 18) in 2004 to 16.0% (11.0 – 22.8; $p<0.001$) in 2007. In cohorts that provided data on staging, the proportion of adult patients in stage IV at enrolment fell from 50.3% (*N*=494) in 2003 to 26.9% (*N*=800) in 2007 ($p<0.001$). This was mirrored by an increase in median CD4 count in this group from 39 cells/μl (IQR 13 – 93) in 2003 to 89 cells/μl (IQR 40 – 162; $p<0.001$) in 2007. Over time, the availability of baseline CD4 cell counts decreased from 72.2% to 64.8%.

Variation between sites

Table IV and Table V demonstrate some degree of heterogeneity in patient characteristics between sites. Median adult age at enrolment ranged from 32 to 36 years. Baseline median

CD4 cell count ranged from 85 to 121 cells/μl. Within the paediatric sites, patients at two exclusively tertiary paediatric hospitals were younger, with a greater proportion <1 year, than those from other sites.

Discussion

IeDEA-SA: the South African collaborative cohort

This paper introduces the South African sites of IeDEA-SA, a dynamic collaboration that offers an excellent opportunity to provide information on the South African ART programme. It describes the baseline characteristics and temporal trends of the largest national cohort yet assembled of adults and children starting ART. The collaborative cohort is representative of patients accessing ART through the national programme in large urban centres, which constitute the largest part of this programme. It is constrained by the absence of cohorts from some provinces and by limited participation from rural sites. Many of the sites linked to research programmes may also have more capacity for monitoring than other sites in the national programme. The cohorts included in this collaboration have dramatically increased enrolment in line with the national roll-out of treatment, and demonstrate the same uniformity of clinical practice and patient preparation recommended in national guidelines.

Evidence of national scale-up

The massive increase in enrolment over time, especially over the last 2 years, provides strong evidence of the successful scale-up of ART in South Africa. Patients are enrolling with less advanced disease in urban sites: among patients with a baseline CD4 count, there has been a trend towards higher CD4 count at initiation, and the proportion of patients in stage IV has decreased.

Late diagnosis and initiation of treatment

Patients in this combined cohort were still being diagnosed and started on ART later than recommended in national and international guidelines, increasing their risk of early mortality on treatment.[6] In our collaborative cohort, more than 25% of patients started with a CD4 count <50 cells/μl, and similarly with stage IV disease. Earlier diagnosis and initiation of ART would reduce the risk of morbidity and mortality among these patients, especially for men, who present with more advanced HIV disease and appear to be disadvantaged in their access to treatment.[7,8]

Children

The paediatric component of this collaboration is to our knowledge the largest national cohort of children on ART in the world. While the successful enrolment of so many children on ART is encouraging, limited success in preventing vertical transmission of HIV remains a major concern.

In addition, children also started ART later than is now internationally recommended.[9] South African data have demonstrated the high risk of disease progression and mortality in the first year of life.[10,11] The low proportion enrolled in the first year of life in this cohort, and high numbers of children with advanced disease, suggest massive under-diagnosis and missed treatment opportunities, and an enormous hidden burden of morbidity and mortality among children.

First-line regimen

Unlike many countries in southern Africa, in which the first-line regimen is a fixed-dose combination of d4T, 3TC and NVP, EFV use predominates in adults on treatment in South

Africa in spite of the higher cost of EFV-based regimens. Analyses in South Africa have, however, reported inferior virological outcomes in patients on NVP-containing compared with EFV-containing regimens.12,[13] For many adults starting ART, concomitant TB at the time of starting ART precludes the use of NVP. In addition, the greater toxicity profile of NVP compared with EFV has discouraged many clinicians from using it as first-line treatment. The use of protease inhibitors (PIs) versus non-nucleoside reverse transcriptase inhibitors (NNRTIs) in children in this analysis is in line with the proportions of children starting ART above and below 3 years of age.

Data challenges and the need for sentinel surveillance

Although South Africa has implemented the largest treatment programme in the world, the ability to monitor the programme closely has not kept pace with this expansion.[2] The lack of complete data on baseline characteristics in these cohorts – among the best-monitored ART programmes nationally – provides insight into the pressures facing the public health system.

Numerous challenges face cohort analysis of ART programmes in developing countries, chiefly the need to balance service provision and the collection of good-quality data in the face of rapidly increasing patient numbers. An 11-fold increase in patients over 5 years is bound to result in a corresponding decrease in data quality unless substantial resources are provided to support monitoring systems. For health care workers, providing access to clinical care is – and should be – the priority. It is therefore essential to find ways to avoid overwhelming health care providers and prioritising monitoring over service provision.[14] Establishing selected, representative sentinel surveillance sites may facilitate the collection of good-quality individual data on a subset of patients in the national programme, thus freeing most government sites to continue with simplified aggregate reporting.[15]

Conclusion

The South African cohorts participating in IeDEA-SA provide a unique opportunity to undertake analyses of the national ART programme based on individual patient data, to complement routine monitoring. This analysis demonstrates the massive scale-up in recent years and the improvement in the level of disease severity at ART initiation. Earlier diagnosis and enrolment of patients, particularly children and men, need to be prioritised. A solid investment in representative sentinel surveillance could support a context-appropriate national ART monitoring system.

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Acknowledgments

We thank the children and adults whose data were used in this analysis, and the staff who provide their care. Thanks to all staff at participating sites for collection and preparation of data contributed to IeDEA-Southern Africa and Mar Pujades and Olivia Keiser for their comments on the manuscript. We acknowledge all those who died without access to ART.

Funding. This study was supported by the National Institute of Allergy and Infectious Diseases and by the Eunice Kennedy Shriver National Institute of Child Health and Human Development (grant 1 U01 AI069924-01). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Table I

Characteristics of IeDEA-SA sites providing paediatric and adult ART in South Africa

Cohort	Level of care	No. of patients in dataset	Type of site	Patients	1st year ART provision	Cost to patient	Tracing of patients LTFU	Main sources of referral to site
Empilweni Clinic, Johannesburg	All levels	1 088 children	Public & research	Children & pregnant women	2002	Free	No	Hospital wards
Free State provincial roll-out programme	All levels	17 835 adults	Public	Adults & children, mostly in combined clinics	2003	Free	Active tracing* in smaller facilities	Clinics: primary health care, TB, antenatal
Gugulethu, Cape Town	Primary	2 924 adults 264 children	Public & research	Adults & children, separate clinics	2002	Free	Active tracing	Other medical facilities; clinics: PMTCT, TB
Harriet Shezi clinic, Johannesburg	All levels	2 226 children	Public & research	Children only	2002	Free	Active tracing	Hospital wards
Khayelitsha, Cape Town	Primary	8 119 adults 662 children	Public & research	Adults & children, combined clinic	2001	Free	Phone call only	Clinics: PMTCT, TB; other medical facilities
Masiphumelele, Cape Town	Primary	642 adults	Public & research	Adults & children	2003	Free	Active tracing	Clinics: PMTCT, STIs, TB; other medical facilities
McCord Hospital, Durban	Secondary	3 575 adults 415 children	Government-subsidised, not-for-profit hospital	Adults & children, combined clinic	1999 (drug trial); 2000 (fee-paying); 2004 onwards (PEPFAR funding)	Small co-payment	Active tracing	Clinics: PMTCT, TB; other medical facilities
Perinatal HIV Research Unit, Johannesburg	Tertiary	948 adults	Research	Adults & children, combined clinics	2004 with some trials <2004	Free	Active tracing	Wellness programme for people with HIV in unit
Red Cross Children's Hospital, Cape Town	Tertiary	859 children	Public & research	Children only	2001	Free	Active tracing	Hospital wards
Themba Lethu, Johannesburg	Tertiary	9 250 adults	Public & research	Adults	2004	Free	Active tracing	Other medical facilities
Tygerberg Hospital, Cape Town	Tertiary	1 504 adults 684 children	Public & research	Adults & children, separate clinics	2004, with some trials <2004	Free	Active tracing	Other medical facilities; clinics: PMTCT, TB

* Active tracing implies dedicated resources to undertake one or more of the following: telephone call, home follow-up, physician's report and/or data linkage.

LTFU = lost to follow-up; PMTCT = prevention of mother-to-child-transmission programme; TB = tuberculosis; STIs: sexually transmitted infections.

Table II

IeDEA South African cohort, patient characteristics at ART initiation: 45 383 adults and 6 198 children followed up in 11 IeDEA-SA sites in South Africa, 2003 – 2007

Characteristic	Adults (≥16 yrs) *N*=45 383	Children *N*=6 198
Age	*N*=45 383 (100%)	*N*=6 198 (100%)
Adults (yrs), median (IQR)	35.0 (29.8 – 41.4)	
Children (mo.), median (IQR)		42.5 (14.7 – 82.5)
Age categories, *N*(%)		
<12 mo.		1 315 (21.2)
12 – 23 mo.		891 (14.4)
24 – 59 mo.		1 581 (25.5)
≥60 mo.		2 411 (38.9)
Gender	*N*=45 383 (100%)	*N*=6 198 (100%)
Female, *N* (%)	30 684 (67.6)	3 051 (49.2)
Absolute CD4 cell count (cells/μl)	*N*=33 672 (75.2%)*	*N*=4 900 (79.1%)
All adults, median (IQR)	102 (44 – 164)	
Men	86 (34 – 150)	
Women	110 (50 – 169)	
CD4 cell count categories, *N*(%)		
<50	9 363 (27.8)	
50 – 199	20 742 (61.6)	
≥200	3 567 (10.6)	
All children, median (IQR)		391 (172 – 730)
CD4%	N/A	*N*=4 648 (75.0)†
Median (IQR)		12.0 (7.0 – 17.7)
CD4% categories, *N* (%)		
<15%		3 004 (64.6)
15 – 19%		760 (16.4)
≥20%		884 (19.0)
WHO stage, *N* (%)	*N*=12 763 (28.1)‡	*N*=4 120 (66.5)§
I	1 134 (8.9)	270 (6.5)
II	1 512 (11.9)	752 (18.3)
III	6 118 (47.9)	
IV	3 999 (31.3)	3 098 (75.2)¶
HIV RNA level (log_{10} copies/ml)	*N*=14 955 (33.0)□	*N*=4 116 (66.4)
Median (IQR)	4.89 (4.34 – 5.41)	5.3 (4.7 – 5.9)
1st-line ART regimen used, *N*(%)	*N*=36 319 (81.1)**	*N*=5 331 (86.0)
d4T+3TC+EFV	23 568 (64.9)	2 692 (50.5)

Characteristic	**Adults (≥16 yrs) *N*=45 383**	**Children *N*=6 198**
d4T+3TC+NVP	8 284 (22.8)	93 (1.7)
AZT+3TC+NVP	1 350 (3.7)	74 (1.4)
AZT+3TC+EFV	1 166 (3.2)	154 (2.9)
d4T+3TC+KLT[††]		1 343 (25.2)
d4T+3TC+RTV		268 (5.0)
Other	1 951 (5.4)	707 (13.3)
Previous ART exposure, *N*(%)	*N*=23 735 (53.0)[‡‡]	*N*=4 262 (68.8)
ART exposure	1 673 (7.1)	162 (3.8)
PMTCT exposure, *N* (%)	*N*=5 526 (12.3)[§§]	*N*=2 430 (39.2)[¶¶]
Known exposed women/children	696 (12.6)	617 (25.4)
TB at ART initiation, *N*(%)	*N*=17 369 (38.8)[□□]	*N*=3 305 (53.3)
Yes	3 722 (21.4)	1 052 (31.8)
Pregnant at ART initiation, *N*(%)	*N*=8 828[***]	N/A[†††]
Yes	633 (7.2)	

[*] Data from all cohorts; CD4 not always provided in dataset.

[†] Data from 6 paediatric cohorts.

[‡] Includes data from 4 cohorts.

[§] Data from all cohorts; WHO stage not always provided in dataset.

[¶] Stages III & IV combined for children.

[□] Data from all cohorts; viral load not always provided in dataset.

[**] Only listed those regimens prescribed to >4% of adult patients.

[††] Includes 209 children on ritonavir and Kaletra.

[‡‡] Data from 3 cohorts.

[§§] Data from 2 cohorts.

[¶¶] Data from 4 cohorts.

[□□] Data from 2 cohorts.

[***] Data on female patients from 3 cohorts.

[†††] Data not provided in paediatric datasets.

IQR = interquartile range; TB = tuberculosis.

Table III

IeDEA South African cohort: temporal changes

Year of ART initiation		≤2003	2004	2005	2006	2007	*p* -value for trend	Combined
Patients enrolled, *N* (%)								
Adults		1 462 (3.2)	5 340 (11.8)	9 938 (21.9)	13 015 (28.7)	15 628 (34.4)		45 383 (100)
Children		376 (6.0)	1 094 (17.7)	1 849 (29.8)	1 740 (28.1)	1 139 (18.4)		6 198 (100)
Baseline CD4 (cells/μl)								
All adults	*N*	1 055	4 597	8 476	9 417	10 127		33 672
	Med. (IQR)	67 (23 – 134)	86 (38 – 147)	101 (43 – 159)	105 (45 – 168)	111 (49 – 171)	<0.001	102 (44 – 164)
Men	*N*	341	1 433	2 726	3 177	3 397		11 074
	Med. (IQR)	54 (18 – 123)	74 (33 – 138)	87 (33 – 149)	88 (34 – 154)	93 (36 – 154)	<0.001	86 (34 – 150)
Women	*N*	714	3 164	5 750	6 240	6 730		22 598
	Med. (IQR)	74 (26 – 138)	91 (41 – 150)	107 (48 – 164)	115 (52 – 174)	120 (56 – 179)	<0.001	110 (50 – 169)
Children <5 yrs	*N*		638*	1 160	1 091	684		3 787
CD4%	Med. (IQR)		11.5 (7.1 – 18)	12.2 (8.1 – 17.6)	14.0 (9.4 – 20)	16.0 (11.0 – 22.8)	<0.001	13.0 (8.7 – 19)
Adults in stage IV	*N* (%)	494 (50.3)	708 (38.5)	998 (31.3)	999 (26.5)	800 (26.9)		3 999 (33.3)
	Med. CD4, cells/μl (IQR)	39 (13 – 93)	54 (20 – 115)	68 (24 – 138)	74 (29 – 147)	89 (40 – 162)	<0.001	66 (25 – 236)
Availability of laboratory tests at baseline	CD4 cell count	72.2%	86.1%	85.3%	72.4%	64.8%		74.2%
	CD4% <5 yrs		74.9%	77.2%	78.6%	71.9%		76.2%

* In this table, all children <5 yrs before 2004 were combined owing to low numbers and erratic enrolment in different research sites.

Med. = median; IQR = interquartile range.

Table IV

Adult patient characteristics by cohort

Cohort	Free State province	Gugulethu	Khayelitsha	Masiphumelele	McCord	PHRU	Themba Lethu	Tygerberg
Adults enrolled, *N* (%)	17 835 (39.3)	2 924 (6.4)	8 119 (17.9)	642 (1.4)	3 575 (7.9)	948 (2.1)	9 836 (21.7)	1 504 (3.3)
Age (yrs), med. (IQR)	36 (31 – 43)	33 (29 – 39)	33 (28 – 39)	32 (27 – 37)	35 (30 – 41)	34 (30 – 40)	35 (30 – 41)	34 (29 – 41)
CD4 cell count (cells/μl), med. (IQR)	114 (55 – 167)	101 (48 – 158)	101 (45 – 165)	121 (46 – 193)	85 (31 – 152)	108 (43 – 171)	88 (32 – 158)	116 (52 – 174)
Patients with CD4 <50 cells/μl, *N* (%)	2 175 (22.1)	631 (25.4)	1 932 (27.3)	152 (25.8)	1 025 (35.1)	197 (25.7)	2 966 (33.7)	284 (23.9)

med. = median; IQR = interquartile range.

Table V

Paediatric patient characteristics by cohort

Cohort	Empilweni	Gugulethu	Harriet Shezi	Khayelitsha	McCord	Red Cross	Tygerberg
Children enrolled, *N* (%)	1 088 (17.5)	264 (4.3)	2 226 (35.9)	662 (10.7)	415 (6.7)	859 (13.9)	684 (11.0)
Age (mo.), med. (IQR)	44 (16 – 85)	47 (19 – 82)	56 (22 – 90)	42 (20 – 74)	72 (33 – 109)	16 (6 – 50)	22 (9 – 57)
Children <1 yr, *N* (%)	216 (20)	42 (16)	331 (15)	97 (15)	31 (7)	361 (42)	237 (35)
Children <5 yrs, CD4%, med. (IQR)	14 (9 – 19)	-	12 (7 – 17)	14 (10 – 20)	13 (9 – 17)	14 (9 – 21)	16 (11 – 23)
Children <5 yrs with CD4 <15%, *N* (%)	243 (54)	-	707 (66)	145 (52)	30 (58)	367 (56)	168 (44)

med. = median; IQR = interquartile range.