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Rapid scaling-up of antiretroviral therapy in 10,000 adults in Côte d'Ivoire: two-year outcomes and determinants

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Abstract

Objective—To assess the rates and determinants of mortality, loss-to-follow-up (LTFU) and immunological failure in a non governmental organization implemented program of access to antiretroviral treatment (ART) in Côte d'Ivoire.

Methods—In each new treatment center, professionals were trained in HIV care, and a computerized data system was implemented. Individual patient and program level determinants of survival, LTFU and immunological failure were assessed by multivariate analysis.

Results—Between May 2004 and February 2007, 10,211 patients started ART in 19 clinics (median pre-ART CD4 count 123/mm^3, initial regimen ZDV-3TC-EFV 20%, d4T-3TC-EFV 22%, d4T-3TC-NVP 52%). At 18 months on ART, the median gain in CD4 cells was +202/mm^3, the probability of death was 0.15 and the probability of being LTFU was 0.21. In addition to the commonly reported determinants of impaired outcomes (low CD4 count, low body mass index, low hemoglobin, advanced clinical stage, older age and poor adherence), two factors were also shown to independently jeopardize prognosis: (i) male sex (men *vs.* women: hazard ratio [HR]=1.52 for death, HR=1.27 for LTFU, HR=1.31 for immunological failure); and (ii) attending a recently opened clinic (unexperienced *vs.* experienced centres: HR=1.40 for death, HR=1.58 for LTFU). None of the three outcomes was associated with the drug regimen.

Discussion—In this rapidly scaling-up programme: survival and immune reconstitution were good; women and patients followed-up in centres with longer experience had better outcomes; outcomes were similar in ZDV/d4t-based regimens and in EFV/NVP-based regimens. Decreasing the rate of LTFU should now be the top priority in ART roll-out.

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Conflict of interest

None

Contributors

S Toure, F Dabis, C Grundmann, B Kouadio, R Marlink and C Seyler sought funding for the study. S Toure and X Anglaret were responsible for overall study coordination. B Kouadio was the program administrator. M Traore and S Karcher were the data managers. J Duvignac was the study statistician. N Dakoury-Dogbo and N Diakite were the study monitors. S Toure and X Anglaret drafted the manuscript, which all authors subsequently reviewed, edited and approved.

Keywords

adults; sub-Saharan Africa; antiretroviral treatment; outcomes; determinants

Introduction

At the end of 2006, the World Health Organization (WHO) and UNAIDS estimated that 28 millions people were living with HIV/AIDS in sub-Saharan Africa, including almost one million in Côte d'Ivoire, one of the most affected countries in West Africa. Between 2002 and 2007, the number of HIV-infected patients receiving antiretroviral therapy (ART) increased from 100,000 to more than two million in sub-Saharan Africa and from 3000 to 30,000 in Côte d'Ivoire. These figures are expected to triple within five years [1].

Most of these African patients start ART in primary care centres with limited facilities. Patients who start ART need to continue on treatment for the course of their lives, all the while maintaining maximal adherence. At individual patient level, health care teams who are in charge have to be able to detect treatment failures as soon as possible in order to reinforce adherence or to change the failing ART regimens where appropriate. At a public health level, program managers, drug suppliers and donors are looking for real time data and indicators, including the exact numbers of patients lost to the program and of those remaining in care together with key indicators of ART efficacy. To reinforce the efficacy of the programme, they will also need to know the determinants of the main treatment outcomes of patients in the programme.

In February 2007, we estimated these indicators and outcomes and their determinants in a three-year HIV care and treatment program in Côte d'Ivoire, West Africa.

Methods

Patients

Between 1996 to 2003, 723 HIV-infected adults were followed in the ANRS 1203 Cotrame cohort study in Abidjan [2]. At the end of the study, health professionals associated with the project created a non-governmental association, Aconda [3]. In June 2004, Aconda, in partnership with the Institute of Public Health, Epidemiology and Development (ISPED, Bordeaux, France), launched a five-year program of access to HIV care and treatment. This program was funded by the United States President's Emergency Plan for AIDS Relief (PEPFAR), through the Elizabeth Glaser Pediatric AIDS Foundation (EGPAF, Washington DC, USA).

The Aconda program relies on two types of HIV care centres: (i) the CePReF clinic, formerly the Cotrame study center, now directly administered by Aconda and entirely dedicated to HIV care; (ii) a number of public and private health care facilities, not entirely dedicated to HIV care and not directly administered by Aconda. In these centres, the Aconda program trained personnel in standardized procedures of HIV care and treatment, and implemented a computerized data management system. Clinical training consisted of an initial one-week didactic course, followed by one-week of work experience in the CePReF centre, and then in a long term continuing education through repeated visits to each centre by Aconda staff members. In each centre, one staff member was identified to be responsible for the data management system. This person received specific training and was supported on site and online by the central Aconda data management team.

In this study we analyze data from all HIV-infected adults who started ART under the Aconda program from May 27th 2004 (the start of the program) through February 1st 2007.

Data management system

The Aconda data management system was directly derived from the ANRS 1203 Cotrame cohort study information system [2], and approved by the National Ethics Committee of Côte d'Ivoire. It has been recently presented at a PEPFAR meeting [4]. In summary, standardized forms are used at all program sites to record the following variables: *initial visit*: date sex, date of birth (or age), height, weight, type of HIV positivity (HIV-1, HIV-2 or dual); *subsequent visits*: date, weight; *at ART initiation*: date, WHO clinical stage, weight; *for each drug prescription (either ARV or non ARV)*: date, name and quantity of drugs delivered; *at each CD4 count and blood cell count measurement*: date, CD4 number, CD4 percentage, hemoglobin level, platelet, granulocyte and leukocyte counts; each time a patient is contacted by phone or through home visits, and for each death reported to the care centre team, the date of death or, for patients not known to be dead, the date the last time the patient was known to be alive. The CePReF ACONDA-managed HIV care centre collects further variables, not included in this analysis. [4]

Standardized follow-up procedures

In Cote d'Ivoire, the standard serologic testing algorithm for primary care centres consists in a serie of two rapid HIV assays, the Determine® HIV-1/2 (Abbott Diagnostics, Abbott Park, Illinois, USA), followed by the Geni II® HIV1/HIV2 (Bio Rad laboratories, Marne-La-Coquette, France)[5]. During the study period, all HIV-infected adults followed either off-ART or on-ART in the Aconda program had bi-annual CD4 cell count measurements. ART was started when the following criteria were met: WHO clinical stage 4, CD4 count <200/mm^3 or WHO stage 3 and CD4 count at 200–350/mm^3. Antiretroviral drugs and biannual CD4 measurements were provided under a monthly package price to the patient of 2 US$. For all non-antiretroviral drugs, patients were required to pay an additional package price of 1 US$ per drug prescription, irrespective of the number and type of drugs prescribed. Antiretroviral drugs were provided on a monthly basis. Cotrimoxazole prophylaxis was prescribed in all HIV infected patients with a CD4 count <500/mm^3. For patients who did not keep their monthly scheduled appointment, telephone calls or home visits were made by a community-based team, composed of experienced social workers and members of associations of people living with HIV/AIDS [6]. A patient was defined as lost-to-follow-up if his last contact with the care centre was ≥ 3 months (patients who ever started ART) or ≥ 6 months (patients who never started ART) while he was not known to be dead or transferred out.

Statistical analysis

For all patients who started ART, we considered three outcomes: death, loss-to-follow-up (when time since last contact with program was ≥3 months on February 1st 2007, in a patient not known to be dead before this date), and immunological failure of ART at month-6 (defined as a difference between the baseline and the 6-months CD4 counts lower than +50/mm^3). Baseline was the date of ART initiation. Data were censored on February 1st 2007 for patients who were still alive, on the date of death for patients who died before February 1st 2007 or on the date of last contact with the care centre for patients whose last contact was before February 1st 2007 and who were not known to be dead. We used multivariate Cox proportional hazard regression models to analyze the association between death or loss-to-follow-up and the following determinants: (i) characteristic on ART initiation: sex, age, WHO clinical stage, haemoglobin level, body mass index, CD4 count, type of HIV seropositivity (HIV-1, HIV-2 or dual); (ii) the initial ART regimen; (iii) the type of care

clinic (CePReF dedicated HIV care center, *vs*. all other care centers); (iv) the medication possession ratio (MPR), defined as the number of days of treatment actually given to the patient at the pharmacy during the study period divided by the follow-up time between ART initiation and last visit at the care center (or February 1st 2007 if last visit was posterior to this date). Finally, all patients who were still alive and actually followed-up at month-6 were included in a multivariate logistic regression model to analyze the association between immunological failure at month-6 and the explanatory variables listed above. Analyses were conducted using the SAS software, version 8.2.

Role of the funding source

The sponsor of the study had no role in study design, data collection, data analysis, data interpretation or writing of the report

Results

Patients

From program initiation through February 1st 2007, 20,474 HIV-infected adults (72% women) had at least one contact with one of the 19 centers participating in the Aconda program (17 urban centers in Abidjan and 2 rural centers)(figure 1). Of these patients, 1018 had already started ART prior to their first contact, and 19,456 were not on ART at their first contact with the program. Of the latter, 10,211 had started ART before the end of the study period, 968 had died before ART initiation, 218 had been transferred to another care center before ART initiation, 2612 had been lost-to-follow-up before ART initiation (last contact with program ≥ 6 months), and 5,447 were still followed up without ART (last contact with program < 6 months) at the end of the study period. Among the 5,447 latter, the last available CD4 count was < 200/mm^3 in 772 patients, between 200 and 350/mm^3 in 1048, > 350/mm^3 in 2431, and non available in 1196 patients. During the overall study period, the 6-months probability of starting ART in patients off ART with a CD4 count lower than 200/mm^3 was estimated at 0.94 (95%CI 0.93–0.95).

Table 1 shows the main pre-ART characteristics of the 10,211 treatment-naïve patients who started ART in the program. Their median pre-ART CD4 count was 123/mm^3, 26% of them had a CD4 count <50 /mm^3, their median body mass index was 19.1 kg/m^2 and 81% of them were at WHO stage 3 or 4, including 470 (4.6%) with a past history of successfully treated tuberculosis and 556 (5.5%) with an ongoing episode of active tuberculosis when ART was started. The three most frequently prescribed HAART regimens were ZDV-3TC-EFV (20%), d4T-3TC-EFV (22%), and d4T-3TC-NVP (52%).

ART regimens

Figure 2A illustrates the changing importance of each ART regimen during the 2.5 year study period. The monthly number of patients who started ART increased from around 100 in June 2004 to more than 400 at the beginning of 2007. During the first months, the two most frequently prescribed ART regimens were ZDV-3TC-EFV and d4T-3TC-EFV. From May 2005 onwards, d4T-3TC-NVP became the first regimen, accounting approximately for two-thirds of the new ART regimens prescribed. During follow-up, 1410 patients (14%) experienced 2006 changes in their ART regimen, including 307 patients (16%) with 467 changes among those whose initial regimen was ZDV-3TC-EFV, 345 patients (16%) with 465 changes among those whose initial regimen was d4T-3TC-EFV and 558 patients (11%) with 733 changes among those whose initial regimen was d4T 3TC NVP. Among the 9592 patients who started one of the three most frequent regimens, the most frequent reasons for the 1665 changes were toxicity (55%), pregnancy (11%), tuberculosis (12%) and treatment failure (3%). Among the 595 HIV-2 and HIV dually reactive patients, the initial regimens

were 2 nucleoside reverse transcriptase inhibitors (NRTIs) + 1 protease inhibitor (PI) in 301 patients (50%), 3 NRTIs in 69 patients (12%), and 1 NNRTI in 225 patients (38%). Among the latter, 53 (24%) switched toward PI-based or 3 NRTIs regimens during follow-up, and the remaining 172 (76%) remained on NNTI until the study closing date.

Follow-up on ART

Patients were followed for a median of 7.7 months after ART initiation (IQR 2.6–15.5). During the overall study period, the median medical possession ratio (MPR) was 0.98 (IQR 0.78–1.00) and 5,402 (53%) of patients had a MPR <100%, including 44% with a MPR <95%, 37% with a MPR <90%, 26% with a MPR <80%, 16% with a MPR <65% and 9% with a MPR <50%. At the end of the study period, 1,385 (14%) of patients who initiated ART during the study period were lost-to-follow-up, 1,140 (11%) were known to be dead, 304 (3%) had been transferred to another HIV care program, and 7,382 (72%) were still receiving ART in the program. Of the latter, 5681 patients (77%) had renewed their last prescription of ARV drugs as scheduled, and 1701 (23%) were late renewing their supply of drugs. Figure 2B shows the temporal evolution of the proportion of patients dead, lost to follow-up and still actively followed up on ART.

Outcomes on ART

Overall, the 18-month probability of death regardless of baseline CD4 count was estimated at 0.15 and the 18-month probability of being lost to follow-up was at 0.21.

Figure 3A shows the probability of survival by baseline CD4 count. Survival estimates were systematically lower with lower pre-ART CD4 count, with a 15–17% crude difference in survival at the three time points between those patients starting ART at <50 CD4 cells/mm^3 and those starting at >150 CD4 cells/mm^3. Overall, the median time between ART initiation and death was 1.9 months (IQR 0.7–4.6).

Figure 3B shows the probability of being lost to follow-up over time, by type of care center, with much lower figures at all time points in the most-experienced center, the CePReF clinic, compared to those opened in the course of the program. The median gain in CD4 cells since ART initiation was +136/mm^3 (IQR +71; +218), +166/mm^3 (+84; +249) and +202/mm^3 (+107; +314) at 6, 12 and 18 months, respectively for patients with adequate follow-up and repeated measurements. At 6 months, 645 (19%) patients had a gain in CD4 <50 cells/mm^3.

As shown in table 2 the risk of mortality, the risk of being lost to follow-up, and the risk that the CD4 gain at 6 months would be <50 cells/mm^3 were higher in men and in patients with low haemoglobin level. Older age, low CD4 count, advanced clinical stage and low BMI were associated with a higher risk of death only. The risk of death and the risk of loss to follow-up were lower in the CePReF clinic compared to the other less experienced centers. A low MPR (<80%) was associated with a higher risk of loss to follow-up and a higher risk of immunological failure. The risk of loss to follow-up was independent of the CD4 count. Importantly, none of the three outcomes was associated with the initial ART regimen. Finally, the risk of immunological failure was higher in patients infected with HIV-2 or dually reactive than in those infected with HIV-1 only.

Discussion

This routinely collected data from an NGO-implemented HIV care program in West Africa provide encouraging information and raise several concerns.

On one hand, in only three years, 19 care centers, mostly primary health care units, of which 18 had no previous experience in HIV care, could be mobilized to initiate ART in more than 10,000 adult patients. An easy-to-manage computerised data monitoring system could be implemented in each site, providing real-time indicators for the number of patients in care and for treatment effectiveness. At 18 months, the estimates of survival and immune reconstitution were as good as in industrialized countries [7], as previously shown in several other large programs throughout Eastern and Southern Africa.[8–11].

On the other hand, these good clinical indicators were achieved despite a worrying rate of patients lost to the program in the background. Any definition of loss to follow-up can be seen as arbitrary as a patient who is late can never be considered as definitively lost unless he is reported as being dead. However it is crucial that any report of program indicators include the proportion of patients who have lost contact for a significant period of time. This is for two reasons: first, some of these patients are likely to be dead, and the rate of loss to program reflects to a certain extent the degree of underestimation of mortality [6]; and second, even if the proportion of dead patients among patients lost to follow-up is unknown, loss to program can undoubtedly be seen as a program failure indicator. In our study, the overall 18-months probability that the time interval since last contact exceeded three months was estimated at 21%. This is equivalent [12] or lower [13] than previously reported in some pilot programs, but recent reports of home-based programs have clearly shown that a lower rate of loss to follow up can be achieved [14]. Assessing the determinants of prolonged treatment interruption in low-resource settings should be a top priority in the near future at international level.

A major strength of our study was its power to investigate the determinants of major outcomes.

First, we found in a single large data base a series of determinants that were previously separately shown to be associated with impaired outcomes in sub-Saharan Africa: low CD4 count, low BMI, advanced WHO stage, and low haemoglobin [9–11,13,15–25]. These variables mostly reflect advanced immunosupression, suggesting that mortality could be substantially decreased by starting ART earlier. More than half of the documented deaths occurred within the first two months of treatment, a period of time during which the hazard ratio of mortality has been shown to be higher in low-resource settings than in industrialized countries [16]. In the African context, many patients start ART with a CD4 count much lower than currently recommended by WHO, even in settings where access to antiretroviral drugs has become easier in the past three years [9–11,14–16,20,21,23,26–28].

Second, in our study, older age was independently associated with a higher risk of death. Though most studies previously done in Africa have failed to show a significant association between age and prognosis [9–11,16,18,19,22,23], our finding is probably due to a higher statistical power to demonstrate this association and is consistent with reports from industrialized countries [7].

Third, we found a strong association between male gender and impaired outcomes. Some previous studies in sub-Saharan Africa had already reported a significant association between male gender and a higher risk of mortality [9–11,22] or between male gender and a higher risk of withdrawal from programs [8]. Other studies did not find any association between gender and prognosis [13,16,23,26]. In South Africa, men have been reported to have poorer adherence to ART than women [12]. The fact that, in our study, male gender was associated not only with immunological failure and mortality but also with the rate of withdrawal from program might suggest that the association between gender and treatment failure may have been mediated by adherence.

Fourth, in our program, we did not measure adherence. However, we calculated the medication possession ratio by dividing the number of patient-days of treatment actually given to the patients by the number of days of follow-up. A low MPR has been previously shown to predict treatment failure in Uganda [14]. In South Africa, a low rate of pharmacy claims, another type of pharmacy-based indicator, has been shown to predict mortality in adults on ART[12]. These pharmacy-based indicators are easy to monitor. In our experience, the strong association between a low MPR and poor outcomes confirms that the MPR is a valuable key indicator both at the individual and program level. A good MPR does not exempt physicians from looking for symptoms of bad adherence. But a poor MPR always reflects a failure in accessing to drugs.

Fifth, in our study, the rate of lost to program and the mortality were dramatically lower in the HIV care center with the most extensive experience. In industrialized countries, the positive impact of sites and physicians experience on HIV-infected patients outcomes has been reported for quite a long time but has leveled off over time [29,30]. However, these findings are also thought-provocative in terms of ART effectiveness, as a lot of economical, managerial, logistical and organizational characteristics may make a given care center different from another. Cost-effectiveness analyses should take up the challenge of identifying the characteristics that make an HIV care center more efficient than others, in order to generalize the best practices [31].

Finally, in an intent-to-treat multivariate analysis, we did not find any difference in terms of outcomes between ZDV and d4T-based regimens on one hand, or between NVP and EFV-based regimens on the other hand. Regarding the latter, these findings are consistent with comparisons performed between NVP and EFV-based regimens in the 2NN international trial [32]. A limitation however is that we did not measure virological outcomes, and NVP-based regimens have been shown to be independently associated with higher rates of virological failure [33]. Moreover, in the ART-CC collaboration based on 12 cohorts from industrialized countries, clinical outcomes were poorer in NVP-based regimens compared with EFV-based regimens and in d4T-based regimens compared to ZDV-based regimens [34]. Though our findings may be globally interpreted as reassuring from a programmatic point of view, they cannot prove that all these ART regimens are equivalent at the individual level.

In conclusion, our report documents the efforts to expand a national ART program from a clinically experienced, pre-existing program of care and treatment in one location. Two concerns were raised by the available data collected on the first 10,000 patients starting ART: treatment initiation occurs late in general and opportunities to save lives are clearly missed; once in the program, too many patients are subsequently lost at relatively early phases, leading again to missed opportunities. Individual patient characteristics may explain some of the losses to program but it is likely also that program characteristics and organization contribute greatly to this phenomenon that impairs the true success story of ART introduction in sub-Saharan Africa.

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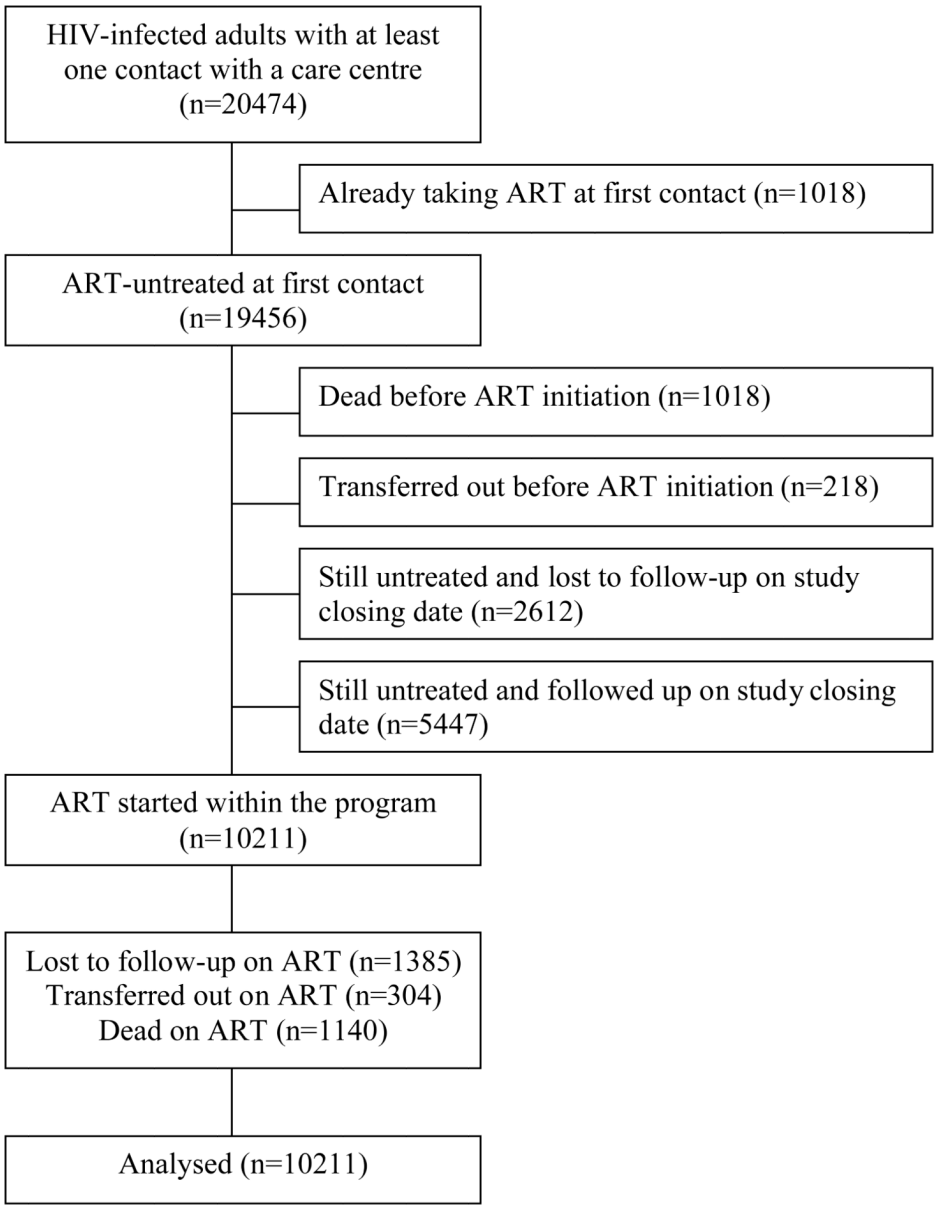


Figure 1.
Flow diagram of enrollment and retention,
Study closing date: February 1st 2007
Lost-to follow-up: patients not known to be dead or transferred out and whose last contact with the care centre was ≥ 3 months (patients who ever started ART) or ≥ 6 months (patients who never started ART) on study closing date.
ART: antiretroviral therapy

Figure 2A.

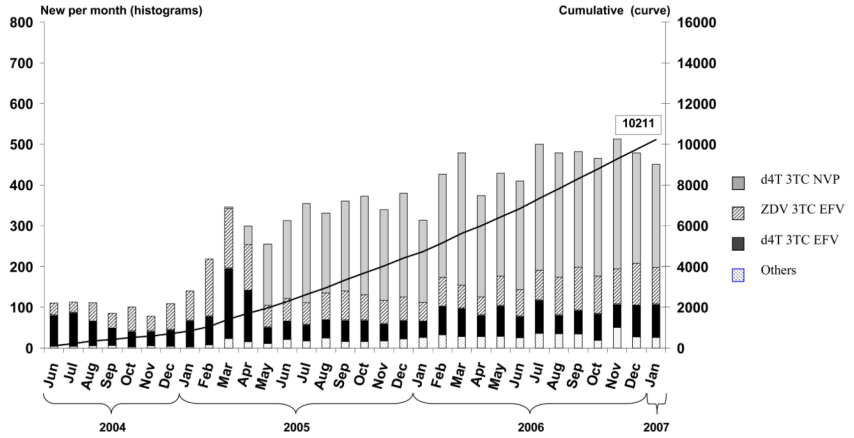


Figure 2B.

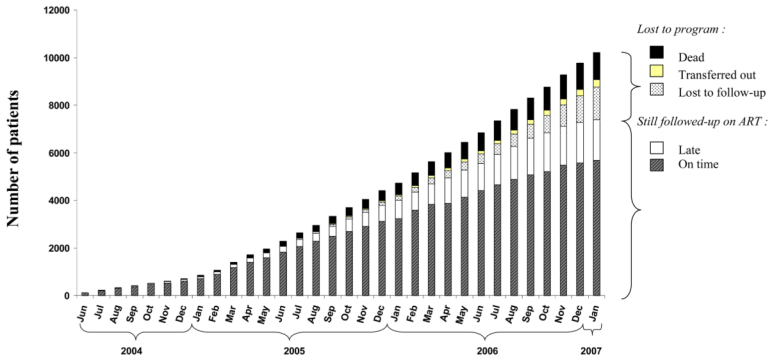


Figure 2.

Figure 2A. Number of patients who started ART over time, by initial ART regimen.

ZDV: zidovudine

d4T: *stavudine*

EFV: efavirenz

ART: antiretroviral therapy

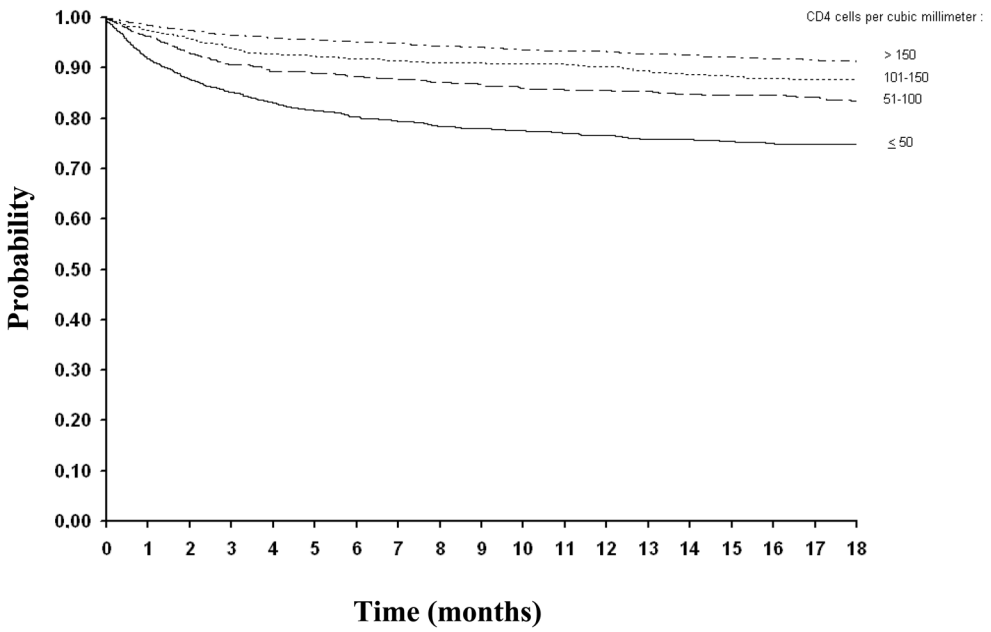
Figure 2B. On-ART patients status at the end of each month between the date when the program was launched and the study closing date.

Late: patients who where late renewing their supply of ARV drugs but who were not considered as lost-to-follow-up.

Lost to follow-up: patients whose last contact with the care centre was ≥ 3 months and who were not known to be dead or transferred out.

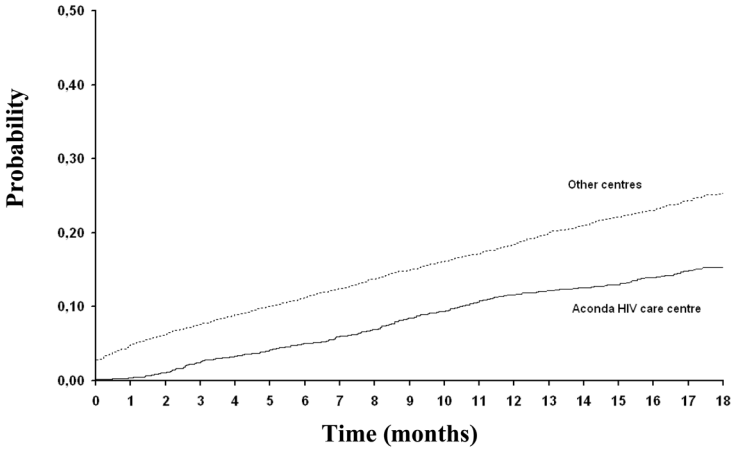
ART: antiretroviral therapy

Figure 3A.



Probability (95% CI) at :	Baseline CD4 count			
	≤ 50	51-100	101-150	> 150
Month-6	0.81 (0.79; 0.83)	0.89 (0.87; 0.91)	0.92 (0.90; 0.94)	0.96 (0.94; 0.97)
Month-12	0.77 (0.75; 0.80)	0.86 (0.84; 0.89)	0.91 (0.89; 0.93)	0.94 (0.92; 0.95)
Month-18	0.76 (0.73; 0.78)	0.84 (0.82; 0.87)	0.88 (0.86; 0.91)	0.92 (0.90; 0.93)

Figure 3B.



Probability (95% CI) at :	Type of care centre		
	Aconda care centre (CePReF care centre, exclusively dedicated to HIV care)	Other centres (recently opened, and non exclusively dedicated to HIV care)	Overall
Month-6	0.05 (0.04 ; 0.06)	0.11 (0.10 ; 0.12)	0.09 (0.08 ; 0.11)
Month-12	0.11 (0.09 ; 0.13)	0.18 (0.16 ; 0.20)	0.16 (0.16 ; 0.18)
Month-18	0.15 (0.13 ; 0.17)	0.25 (0.23 ; 0.27)	0.21 (0.21 ; 0.23)

Figure 3.

Figure 3A. Survival after ART initiation, by pre-ART CD4 count.
CI: confidence interval
Figure 3B. Probability of being lost to follow-up after ART initiation, by type of care centre.
Lost to follow-up: patients whose last contact with the care centre was ≥ 3 months and who were not known to be dead or transferred out.
CI: confidence interval

Table 1

Pre-ART characteristics and follow-up characteristics (*patients who started ART within the Aconda program, Côte d'Ivoire, May 2004 – January 2007, n = 10211*)

Pre-ART characteristics		
Time since first contact with program, months, median (IQR)	9.6	(3.9;17.2)
Sex male, number (%)	3024	(30%)
Age, years, median (IQR)	36	(30; 42)
Body mass index, kg/m^2, median (IQR)	19.1	(17.1; 21.4)
Time since last weight measurement†, months, median (IQR)	0.0	(−0.2; 0.0)
Type of HIV seropositivity, number (%)		
HIV-1	9117	(94%)
HIV-2	214	(2%)
Dual	381	(4%)
WHO clinical stage, number (%)		
Stage 1 or 2	1714	(19%)
Stade 3	6222	(69%)
Stade 4	1163	(12%)
Last available CD4+ cells count /mm^3, median (IQR)	123	(47; 207)
Time since last CD4 measurement††, months, median (IQR)	−0.4	(−0.8;− 0.2)
Haemoglobin level, g/L, median (IQR)	9.4	(8.2; 10.7)
Initial ART regimen, number (%)		
ZDV-3TC-EFV	2024	(20%)
d4T-3TC-EFV	2226	(22%)
d4T-3TC-NVP	5343	(52%)
Other	618	(6%)
Follow-up after ART initiation		
Follow-up time		
Cumulative, person-years	8157	-
Median (IQR), months	7.7	(2.6 – 15.5)
Medication possession ratio during follow-up*		
median (IQR)	0.98	(0.78 – 1.00)
< 80%, number (%)	2704	(26%)

†Time between last available weight measurement and ART initiation. Only weights measured the day when ART was started or within the preceding 15 days were taken into account.

††Time between last available CD4 count and ART initiation. Only CD4 counts performed the day when ART was started or within the preceding 3 months were taken into account.

*Medication possession ratio: number of days of treatment given to the patient divided by number of days from ART initiation to last visit at the care centre (or to February 1st 2007 if last visit posterior to this date)

Missing values: type of HIV seropositivity (n=499), body mass index (n=2787), CD4 count (n=488), WHO clinical stage (n=1112), haemoglobin (n=696).

ART: Antiretroviral therapy

IQR: Interquartile range

WHO: World Heath Organization

3TC: Lamivudine

d4T: Stavudine

EFV: Efavirenz

NVP: Nevirapine

ZDV: Zidovudine

Table 2

Factors associated with death, loss to follow-up, and CD4 count evolution on ART (multivariate analysis). *Patients who started ART within the Aconda program, Côte d'Ivoire, May 2004 – January 2007.*

	Death			Loss to follow-up†			Gain in CD4 < 50/mm³ at 6 months††		
	HR	95%CI	p	HR	95%CI	p	OR	95%CI	p
Sex male (ref: women)	1.52	1.29 – 1.80	<.0001	1.27	1.09 – 1.48	0.002	1.31	1.03 – 1.65	0.02
Age (for one year older)	1.01	1.00 – 1.02	0.02	0.99	0.98 – 1.01	0.08	1.00	0.99 – 1.02	0.47
CD4 count (ref > 150/mm^3)			<.0001			0.74			<.0001
101–150/mm^3	1.32	1.01 – 1.72		1.10	0.91 – 1.33		0.60	0.45 – 0.81	
51–100/mm^3	1.63	1.29 – 2.07		1.00	0.83 – 1.21		0.63	0.47 – 0.84	
≤ 50/mm^3	2.72	2.23 – 3.32		1.01	0.85 – 1.20		0.45	0.33 – 0.60	
WHO clinical stage 3 or 4 (ref 1 or 2)	1.61	1.32 – 1.96	<.0001	1.25	1.01 – 1.55	0.03	1.01	0.69 – 1.47	0.95
ART regimen (ref ZDV 3TC EFV)			0.88			0.28			0.07
d4T 3TC EFV	1.03	0.82 – 1.30		1.00	0.82 – 1.22		0.89	0.66 – 1.18	
d4T 3TC NVP	1.15	0.92 – 1.43		1.14	0.95 – 1.36		0.72	0.56 – 0.93	
Others	1.11	0.65 – 1.86		1.20	0.79 – 1.80		1.00	0.56 – 1.79	
Type of HIV seropositivity (ref HIV-1)			0.50			0.40			0.03
HIV-2	0.87	0.45 – 1.72		0.78	0.41 – 1.35		2.06	0.97 – 4.37	
Dual	0.91	0.59 – 1.40		1.11	0.79 – 1.56		1.79	1.08 – 2.95	
Haemoglobin level (for 10 g/L lower)	1.22	1.14 – 1.29	<.0001	1.07	1.03 – 1.13	0.0006	1.08	1.01 – 1.16	0.02
Body mass index (ref > 25.0 kg/m^2)			<.0001			0.05			0.08
18.5–25 kg/m^2	0.93	0.59 – 1.46		0.93	0.69 – 1.25		1.22	0.82 – 1.82	
< 18.5 kg/m^2	1.93	1.23 – 3.02		1.11	0.82 – 1.50		0.96	0.62 – 1.48	
Type care centre (ref CePReF)*	1.40	1.18 – 1.67	<.0001	1.58	1.36 – 1.84	<.0001	1.15	0.93 – 1.41	0.19
Medication possession ratio ** < 80%	0.87	0.73 – 1.04	0.12	1.19	1.03 – 1.38	0.01	2.11	1.66 – 2.67	<.0001

* CePReF: The HEART program relies on two types of care centres: (i) the CePReF clinic, formerly the Cotrame study center between 1996 and 2003, now directly administered by the NGO Aconda and entirely dedicated to HIV care; (ii) a number of public and private health care facilities, not entirely dedicated to HIV care, and not directly administered by Aconda.

** Medication possession ratio: number of days of treatment actually given to the patient divided by number of days from ART initiation to last visit at the care centre (or to February 1st 2007 if last visit posterior to this date).

† Loss to follow up: patient were defined as lost-to-follow-up when their last contact with the care centre was ≥ 3 months on February 1st 2007 if they were not known to be dead or transferred out before this date.

†† Gain in CD4 at 6 months: difference between the pre-ART CD4 count and the CD4 count measured 6 months after ART was started.

Ref: Reference

HR: Hazard ratio (Cox proportional hazard model)

OR: Odds Ratio (Logistic regression)

CI: confidence interval

WHO: World Heath Organization

3TC: Lamivudine

d4T: Stavudine

EFV: Efavirenz

NVP: Nevirapine

ZDV: Zidovudine

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