Individual and healthcare supply-related barriers to treatment initiation in HIV-positive patients enrolled in the Cameroonian antiretroviral treatment access programme

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Conflict of interest statement

The authors have no conflicts of interest to declare.

Keywords: HIV, Cameroon, Time to ART initiation, healthcare supply-related factors

ABSTRACT

Increasing demand for antiretroviral treatment (ART) together with a reduction in international funding during the last decade may jeopardize access to ART. Using data from a cross-sectional survey conducted in 2014 in 19 HIV services in the Centre and Littoral regions in Cameroon, we investigated the role of healthcare supply-related factors in time to ART initiation, after adjustment for individual factors, in HIV-positive patients eligible for ART at HIV diagnosis.

HIV service profiles were built using cluster analysis. Factors associated with time to ART initiation were identified using a multi-level Cox model.

The study population included 847 HIV-positive patients (women 72%, median age: 39 years). Median [interquartile range] time to ART initiation was 1.6 [0.5-4.3] months. Four HIV service profiles were identified: 1) small services with a limited staff practising partial task-shifting (n=4); 2) experienced and well-equipped services practising task-shifting and involving HIV community-based organisations (n=5); 3) small services with limited resources and activities (n=6); 4) small services providing a large range of activities using task-shifting and involving HIV community-based organisations (n=4). The multivariable model showed that HIV-positive patients over 39 years old (Hazard Ratio: 1.26 [95% Confidence Interval] [1.09-1.45], p=0.002), those with disease symptoms (1.21 [1.04-1.41], p=0.015), and those with hepatitis B co-infection (2.31 [1.15-4.66], p=0.019) were all more likely to initiate ART early. However, patients in the first profile were less likely to initiate ART early (HR [95% CI]: 0.80 [0.65-0.99], p=0.049) than those in the second profile, as were patients in the third profile (association only significant at the 10% level; HR [95% CI]: 0.86 [0.72-1.02], p=0.090).

Our findings provide a better understanding of the role played by healthcare supply-related factors in ART initiation. In HIV services with limited capacity, task-shifting and support from community-based organisations may improve treatment access. Additional funding is required to relieve healthcare supply-related barriers and achieve the goal of universal ART access.

1. Introduction

The implementation of national antiretroviral treatment (ART) programmes over the last two decades in low- and middle-income countries (LMIC) led to approximately 20 million people living with HIV (PLWHIV) receiving ART by the end of 2016, compared with only 300,000 in 2000 (1). This progress was made possible thanks to the commitment of both national governments and international health agencies which supported free access to ART, the installation of HIV equipment in healthcare facility laboratories, and procedure simplification to facilitate treatment initiation (2). In recent years, ART scale-up has also been driven by the progressive widening of ART eligibility criteria in the World Health Organization's (WHO) recommendations. More specifically, based on evidence that early ART initiation dramatically reduces HIV-related mortality and morbidity, as well as HIV transmission risk (3–6), CD4 count criteria for ART initiation evolved from ≤350 cells/mm^3 in 2010 (7) to ≤500 cells/mm^3 in 2013 (8), and finally to initiation irrespective of CD4 count in 2015 (9). In addition, to optimize treatment benefits and hasten the end of the HIV epidemic, UNAIDS launched the "90-90-90" targets in 2014 with the aim of diagnosing HIV infection in 90% of PLWHIV, initiating ART in 90% of those diagnosed with HIV, and achieving viral suppression in 90% of those treated with ART, all by 2020 (10).

However, acute challenges to health systems in LMIC - especially to healthcare supply, which suffers from a lack of equipment and human resources (11) - hamper efforts to meet UNAIDS targets. Achieving the second of the "90-90-90" targets is still some way off in LMIC, especially in West and Central Africa where 60% of PLWHIV (2.5 million people) remained untreated as of 2017 (12). In addition, despite growing needs for ART, a slowdown in international financial support for HIV has continued since the early 2010s (13). Western and Central African countries have been particularly affected by this reduced funding, and are not offset by increased national resources (14). This situation may jeopardize the quality and the sustainability of the region's already fragile HIV services.

Growing attention is being given to monitoring timely ART initiation, as it reflects the capacity of national programmes to respond to the second "90" UNAIDS target and constitutes an important indicator of HIV care service quality (15). The literature suggests that late ART initiation might be explained by many factors, including individual characteristics, HIV testing and treatment behaviours, as well as healthcare supply-related factors (16–18). A literature review focusing on 18 Sub-Saharan African countries highlighted that limited staff, heavy workloads and long waiting times in HIV services were all associated with lower rates of ART

initiation (19). However, studies to date only assessed a limited number of HIV care service characteristics whose effects on ART initiation were investigated separately, without considering the complexity of the organization of HIV services as a whole, including dimensions such as available resources and working processes. In addition, the role of healthcare supply-related factors on ART initiation needs further investigation in Sub-Saharan Africa where resources are increasingly limited, while the number of PLWHIV needing ART is rapidly growing.

The objective of this study was therefore: i) to describe the available resources, activities and working processes of HIV services in the Cameroonian ART programme, ii) to document the time from HIV diagnosis to ART initiation in PLWHIV linked to care, and iii) to investigate the role of healthcare supply-related factors on ART initiation delay, after adjustment for individual factors.

2. Materials and methods

2.1. Setting: the national Cameroonian ART programme

Cameroon is a LMIC in Central Africa with a yearly gross domestic product (GDP) of 1354 USD per capita in 2015 (20) and a human development index of 0.55 in 2018, which ranked the country 151 out of 188 (21). The health system is mainly funded by private health expenditures through out-of-pocket payments which represent approximately two-thirds of total health expenditures (22). The country is one of the most affected by the HIV epidemic in the West and Central Africa with an estimated mean HIV prevalence of 3.6% in the adult population (aged 15-49 years) in 2018 and large disparities according to gender, region and urban area (23). The highest prevalence rates are reported in women (5.6%), in the South (7.2%) and East regions (6.3%) and in the country's two main cities (6.3% and 4.6% in Yaoundé and Douala, respectively) (24). Initiated in 2001, the national ART programme relies on the pre-existing decentralized framework of the Cameroonian health system to deliver HIV care and ART at the district level (25). Starting in 2001-2002, Accredited Treatment Centres were set up in the national reference hospitals of Yaoundé and Douala, and then in each regional hospital of the country's eight other regions. From 2005 onwards, the diffusion of ART delivery services was extended to district hospitals with the implementation of HIV Management Units. Additionally, to facilitate access to ART and remove financial barriers, ART has been provided for free since 2007, and both biological tests for HIV initiation and follow-up have been

simplified and subsidized (25). Thanks to this strategy, a total of 210,000 PLWHIV received ART in 2016 *versus* only 15,000 in 2004 (26–28).

ART scale-up through the national programme has been largely supported by international funding, which represented more than 80% of the country's HIV budget in 2015 (13). However, the programme has been strongly affected by the slowdown of international financial support since 2010 (29). In particular, national expenditures allocated to HIV/AIDS decreased by nearly 30% from approximately USD 60 million in 2009 to USD 44 million in 2012 (30). Thanks to the Round 10 grants of the Global Fund and the involvement of bilateral partners such as PEPFAR funds, resources dedicated for the HIV epidemic increased in 2013 to USD 53 million but remained below the level recorded in 2009 (30).

2.2. Study design and data collection

EVOLCam (ANRS-12288) is a cross-sectional mixed-methods survey conducted in 19 HIV services in the Centre and Littoral regions of Cameroon between April and December 2014 to study evolutions in the national ART programme through a comparison with the ANRS-12116 EVAL survey conducted in 2006-2007 (31,32). Eligibility criteria included being aged at least 21 years, diagnosed HIV-positive for at least three months and attending one of the 19 participating HIV services.

For eligible outpatients consulting in each service, a random selection procedure similar to that implemented in the ANRS-12116 EVAL was used (31). After being informed about the study, patients who agreed to participate provided written informed consent. At the end of their consultation, they were referred to trained independent interviewers to answer a standardized face-to-face questionnaire which gathered information on socioeconomic characteristics, HIV infection, hepatitis B and tuberculosis co-infection (testing, treatment and history), and access to HIV services.

After the interview, blood samples were collected for viral load and CD4 cell count measurements and transported to a reference laboratory in Yaoundé the same day to assess virological suppression and immunological status at the time of the study (33,34). Clinical data obtained from patient examinations and retrospective medical files were recorded by healthcare providers in a standardized medical questionnaire and included the following: date of HIV diagnosis, date of ART initiation, CD4 count at ART initiation, WHO clinical stage of HIV infection at ART initiation and at time of the survey, drug regimen at time of the survey, body

mass index, and any history of tuberculosis and hepatitis B co-infection and related diagnosis dates.

In addition, the characteristics of the 19 participating HIV services were collected through interviews with hospital staff, *in situ* observations and cross-validation with data recorded in service activity reports.

The survey protocol was approved by the Ministry of Public Health in Cameroon and the Cameroonian National Ethics Committee.

2.3. Study population

The population for the present study included EVOLCam's participants who were diagnosed HIV-positive between January 2011 and September 2014 and were eligible for ART at HIV diagnosis.

Patients diagnosed HIV positive before 2011 were excluded for two reasons: i) we wished to study time to ART initiation in a relatively 'homogenous' population and over a recent time period, with unchanged ART initiation guidelines, ii) patients diagnosed HIV for a long time had poor quality data.

According to national Cameroonian guidelines in the period 2011-2014, patients were eligible for ART if they met at least one of the following criteria: CD4<350 cells/mm^3, or tuberculosis co-infection, or hepatitis B co-infection, or pregnancy (25). To assess ART eligibility at HIV diagnosis, CD4 count at diagnosis was estimated using a retrospective imputation method previously used by Ndawinz et al. (35).

2.4. Outcome variable

The study outcome was time to ART initiation, which was calculated as the time in months from the HIV diagnosis date to the date of first ART prescription.

2.5. Explanatory variables

2.5.1. Individual-related variables

Individual-related variables considered in the analyses included:

- Socio-demographic and socioeconomic characteristics at the time of survey: age, gender, having a partner (yes, the same partner since HIV diagnosis; yes, a new partner since HIV diagnosis; no), education level (secondary school and lower *versus* higher than secondary school), having an economic activity, and living below the absolute poverty threshold (i.e., household monthly income ≤28,310 FCFA (approximately 51 USD in 2020)) (36).
- HIV testing experience and accessibility to the HIV service: HIV testing initiative (on patient's own initiative; on a healthcare provider's initiative with informed consent; on the partner's initiative; without being informed), HIV testing performed on the occasion of a pregnancy or delivery, having disease symptoms at HIV diagnosis, living in the city where the HIV service providing ART treatment was located.
- Clinical characteristics: hepatitis B and tuberculosis co-infection at the time of HIV diagnosis, CD4 cell count at ART initiation (<100 *versus* ≥100 cells/mm^3) and WHO clinical stage at ART initiation (1 or 2 *versus* 3 or 4).

2.5.2. HIV-services variables

The following healthcare supply-related characteristics were used to build an HIV service profiles variable (cf. Statistical analysis section), which was used as explanatory variable in the models:

(1) Hospital's general characteristics: location (Littoral *versus* Centre region), opening date (before or in 2001 *versus* after 2001), legal status (public *versus* private), type of HIV service (HIV Management Units *versus* Accredited Treatment Centres), and number of beds (dichotomized using the median: >100 *versus* ≤100).

(2) Human resources: number of healthcare providers according to category (physicians, nurses, psychologists, nursing assistants and social workers).

(3) Activity: number of ART-treated patients (dichotomized using the median: >1803 *versus* ≤1803) and available services (subsidized biological check-up, educational, nutritional and financial support, HIV community-based organisations' involvement).

(4) Organisation: specific ART storage, stock management, and task-shifting from physicians to nurses for i) clinical follow-up consultations for patients on ART or ii) ART prescription renewals.

(5) Technical resources: functional medical imaging equipment (electrocardiography, echography, radiology and scanner), CD4 count machine, ART stock-outs for at least one of the three most prescribed ART regimens (TDF+3TC+EFV; AZT+3TC+NVP; and TDF+3TC+NVP). A regimen was considered out of stock during the previous year if i) the 3-molecule combination was unavailable for a minimum of three consecutive days and ii) reconstituting the combination using separate single molecules was impossible.

2.6. Statistical analysis

First, we identified HIV services which had a similar profile in terms of the above healthcare supply-related characteristics. To do this, we performed a multiple correspondence analysis (MCA) combined with a hierarchical cluster analysis (37), using the Stata commands 'mca' and 'cluster'. More specifically, the MCA allowed us to combine healthcare supply-related correlated variables to create continuous factors, which were then used in a classification procedure to identify service profiles (clusters), hereafter called "HIV-service profiles" (HSP) (38,39). The choice of the number of factors (dimensions) in the MCA was based on the principal inertia values and the total explained variance. We used hierarchical cluster analysis with the Ward's linkage clustering method and the Duda–Hart stopping rule (Duda et al., section 10.10) to determine the optimal number of clusters (i.e., HSP) (40). A descriptive analysis was then performed to describe all HSP in terms of the healthcare supply-related characteristics.

Second, variability in time to ART initiation – overall across all 19 HIV services, and according to both HSP and each HIV service – was evaluated using descriptive statistics (mean (Standard Deviation (SD)) and median [Interquartile Range (IQR)]). We also computed the proportions of PLWHIV who initiated ART within one month and within 6 months of diagnosis (41).

Third, we investigated the relationships between HSP and time to ART initiation using a multilevel Cox proportional-hazards regression model which allowed us to assess whether our outcome variability depended on individual characteristics (level 1) and/or on structural characteristics, i.e. healthcare supply-related factors which are summarized by the HSP variable (level 2) (42). The pertinence of using a multilevel model was tested by using a likelihood-ratio (LR) test by comparing a null 1-level Cox model (assuming that time to ART initiation

variability was caused only by individual heterogeneity) with a 2-level null model (assuming that variability was caused by both individual and structural heterogeneity).

Based on the modelling strategy for multilevel models (43), individual-related factors in the level-1 model were selected using the "augmented backward elimination" approach (44). To do this, significant variables with a p-value <0.05 were first retained using a backward elimination approach (except gender and CD4 cell count, which were maintained in the model irrespective of their p-values, in order to control for demographic and clinical characteristics) (44). The possible presence of confounding factors was then evaluated by testing each non-significant variable, and noting the effect on the coefficients of the other explanatory variables. If at least one of these coefficients changed by more than 25%, the variable being tested was considered to be a confounder and was reintroduced into the model irrespective of its p-value. Finally, we introduced the HSP variable as a level 2 variable to obtain the final multilevel model.

Analyses were performed using R software (version 3.4.0) and Stata/SE version 14.2 (College Station, Texas, United States).

3. Results

3.1. Characteristics of HIV services and HIV service profiles

As shown in the Supplementary Figure 1, three dimensions (factors) were retained in the MCA based on the principal inertia values, corresponding to a total explained variance of 69.5% (the percentage of explained variance for the 3 factors was 43.7%, 17.2% and 8.7%, respectively). The hierarchical cluster analysis led to the identification of 4 distinct HSP (see Supplementary Figure 2). More details on the results of the MCA and the hierarchical cluster analysis are provided in the Supplementary Materials.

Characteristics of the 19 participating HIV services and of the 4 HSP identified are described in detail in Table 1, while Figure 1 summarizes the main features of each HSP. Participating HIV services included 11 HIV Management Units and 8 Accredited Treatment Centres. Eleven (58%) were located in the Centre region and 13 (68%) were public.

In the first profile (HSP1), all the HIV services (n=4) were HIV Management Units located in small district hospitals (i.e., <100 beds) in the Littoral region. They provided ART to a large number of patients (>1803) but were understaffed: all had more than 2 nurses but 2/4 had fewer than 5 physicians and just one had psychosocial workers (3/4 had no psychologist or social

worker). The majority (3/4) practiced task-shifting for consultation but not for ART prescription, and none involved HIV community-based organisations in their activities. In addition, technical resources were poor (2/4 had no CD4 count machine and none had medical imaging equipment). Conversely, in the second profile (HSP2), all HIV services (n=5) were experienced Accredited Treatment Centres dealing with a high number of ART-treated patients (>1803) located in large (>100 beds) and relatively well-equipped healthcare facilities. They had highly qualified staff: 4/5 had more than 4 physicians and more than 1 social worker, and 3/5 had more than 2 nurses and at least one psychologist. Most practiced task-shifting for both consultation and ART prescription and provided educational and nutritional counselling with the support of HIV community-based organisations. In the third profile (HSP3), 5/6 HIV services were recent, and 4/6 were located in small district hospitals in the Centre region. They followed a smaller number of ART-treated patients (≤1803) but had very few human resources (most (5/6) had fewer than 5 physicians and fewer than 3 nurses). Task-shifting for consultation and prescription was limited in HSP3, as were available services and collaboration with HIV community-based organisations. Furthermore, technical resources were particularly poor. The majority of these HIV services had no CD4 count machine (4/6) or medical imaging equipment (5/6), and 5/6 reported ART stock-outs. In the fourth profile (HSP4), HIV services had similar general characteristics: they were all HIV Management Units located in small district hospitals, with a number of ART-treated patients ≤1803, and had few technical and human resources. Moreover, all implemented task-shifting both for consultation and prescription and proposed a larger range of services than other profiles. Most (3/4) involved HIV community-based organisations in their activities.

3.2. Selection of the study population

Overall, 2130 HIV-positive patients were enrolled in the EVOLCam survey. Of these, 1150 were excluded from the present study because they were diagnosed with HIV before January 2011. Among the remaining individuals, 41 were secondarily excluded as they were not eligible for ART treatment at HIV diagnosis based on the Cameroonian national guidelines in the period 2011-2014 (i.e., CD4 ≥350 cells/mm^3 without tuberculosis or hepatitis B co-infection and no pregnancy for women). Ninety-two others were also excluded as their ART eligibility status at HIV diagnosis was unknown due to missing data for some of the study eligibility criteria. The study population therefore included 847 patients. In order to identify potential selection bias resulting from missing data for some of the eligibility criteria, we compared the main

characteristics of the study population (n=847) with those of the excluded population (n=92). No significant difference was observed in terms of demographic, socioeconomic, HIV testing and clinical characteristics (data not shown).

3.3. Study population characteristics

The majority of patients were women (72%). Forty-two percent had the same partner since HIV diagnosis and median [IQR] age was 39 [33-46] years (Table 2). Most had low socioeconomic status: only 8% had an educational level higher than secondary school, 61% declared having an economic activity and 15% reported a monthly household income below the absolute poverty threshold. Twenty-seven percent decided to be HIV tested on their own initiative, and 69% on a healthcare provider's initiative. The majority (69%) reported being diagnosed following disease symptoms, and a minority (9% overall, 13% of women) upon becoming pregnancy or at childbirth. Clinical characteristics showed that 1% and 23% of patients were co-infected with hepatitis B and tuberculosis at HIV diagnosis, respectively. In addition, at ART initiation, a quarter had <100 CD4 cells/mm^3 (23%) while half were at WHO clinical stage 3 or 4. Although all patients initiated ART after HIV diagnosis, at the time of survey, 4% had interrupted their treatment.

3.4. Descriptive analysis of time to ART initiation

The period from the earliest HIV diagnosis (2011-01-01) to the last ART initiation date (2014-12-01) was 46.9 months (i.e. 3.9 years). Overall, the median [IQR] time from HIV diagnosis to ART initiation was 1.6 [0.5-4.3] months (Table 3). Specifically, more than one third (35%) of the study population initiated ART within one month of diagnosis and one-fifth more than six months after diagnosis. Large variability was also observed across HIV services with minimum and maximum medians of 0.5 and 2.6 months, respectively, and proportions of patients initiating ART within one month ranging from 6% to 62%.

When considering time to ART initiation according to HSP, the shortest times were found in HSP2 and HSP4 (median [IQR] times = 1.5 [0.6-3.2] and 1.0 [0.2-3.5] months, respectively), while the longest times were observed in HSP1 and HSP3 (median [IQR] times = 2.0 [1.1-5.9] and 1.9 [0.8-5.9] months, respectively). HSP4 and HSP1 had the highest (52%) and lowest (21%) proportions of PLWHIV initiating ART within one month of diagnosis, respectively. The highest proportions of PLWHIV not having initiated ART 6 months after diagnosis were

observed in HSP1 and HSP4 (24%). The cumulative probability of initiating ART was higher for ART-eligible patients in HSP2 and HSP4 than for those in the other two HSP (log-rank test, p<0.001).

3.5. Factors associated with time to ART initiation

Factors associated with time to ART initiation in univariate and multivariable analyses are presented in Table 2. After adjustment for gender and CD4 cell count at ART initiation, the final model showed that HIV-positive patients who were over 39 years old (Hazard Ratio (HR) [95% Confidence Interval (CI)]: 1.26 [1.09-1.45], p=0.002), those with disease symptoms at HIV diagnosis (HR [95% CI]: 1.21 [1.04-1.41], p=0.015), and those co-infected with hepatitis B at HIV diagnosis (HR [95% CI]: 2.31 [1.15-4.66], p=0.019) were all more likely to initiate ART early. However, patients in HSP1 were less likely to initiate ART early (HR [95% CI]: 0.80 [0.65-0.99], p=0.049) than those in HSP2 as were patients in HSP3 (association only significant at the 10% level; HR [95% CI]: 0.86 [0.72-1.02], p=0.090). No such association was found for HSP4 compared with HSP2 (HR [95% CI]: 1.10 [0.90-1.34], p=0.36).

The value of the LR test statistics (4.81) was significant at the 5% level (χ^2=3.84 for 1 degree of freedom; p=0.04), confirming the better performance of the 2-level model specification than the 1-level model specification, and therefore the pertinence of using the multilevel Cox model.

4. Discussion

This study investigated the relationships between healthcare supply characteristics and time to ART initiation in PLWHIV who were eligible for ART in 19 HIV services in the Centre and Littoral regions in Cameroon.

Time to ART initiation and variability across HIV services

The median time from HIV diagnosis to ART initiation was estimated at 1.6 months but large differences were observed across HIV services, with the median time to initiation varying from less than one month to approximately 3 months. Comparison of our results with those from other studies is difficult as various definitions for time to ART initiation have been used in the literature, such as time from eligibility to ART initiation (35,45–47), time from CD4 test to ART initiation (18,48) and time from enrolment in HIV care to ART initiation (49). In a review

of 6 studies conducted in Sub-Saharan Africa, the authors examined, just as we did, the whole period from HIV diagnosis to ART initiation, and found that the median time to initiation ranged from a few weeks to more than 6 months (50). In another study conducted in the specific setting of Cameroon, the median time from HIV diagnosis to ART initiation was estimated in 2011/2012 at 3 months in 3 HIV services in the city of Douala in the Littoral region (51). While this is longer than the overall median time to initiation in our study, it is comparable with the values for the 8 participating HIV services in the Littoral region, which had median delays of two to three months.

Role of HIV service characteristics in ART initiation

Using detailed information on resource allocation, activities and organisational characteristics in the 19 participating HIV services, our study highlighted four HIV service profiles (HSP1 to HSP4) with different performance in terms of delays to ART initiation. HSP2 and HSP4 had the smallest delays and HSP1 and HSP3 the longest. These results were confirmed in the multivariable analysis where HSP1 and HSP3 patients were significantly (only at 10% level for HSP3) less likely to initiate ART than HSP2 patients. No such difference was found for HSP4 patients. A description of each profile's characteristics enabled us to identify healthcare supply-related factors which may explain these different levels of performance. In HSP2, HIV services were large, experienced, well-staffed (i.e., most had more than 4 physicians, 2 nurses, 1 social worker and at least 1 psychologist), and adequately equipped (especially with a CD4 count machine). Conversely, the three other profiles were small district hospitals with few qualified staff, little technical equipment (including CD4 count machines) and more frequent ARV stock-outs, especially in HSP3.

However, two main factors may explain why, unlike HSP1 and HSP3, the delay to ART initiation in HSP4's small HIV services was similar to that in the well-equipped and staffed HIV services of HSP2. The first is the large amount of task-shifting for prescriptions and patient consultations. Several studies conducted in Sub-Saharan Africa have shown that task-shifting may lead to substantial benefits in the various steps of the HIV care cascade (52–55). In Cameroon, two previous studies conducted in nine district hospitals in the STRATALL ANRS-12110 trial highlighted that task-shifting from physician to nurses improved patient quality of life and did not compromise treatment outcomes such as virological success, CD4 recovery and survival (56,57). The second factor is the participation of HIV community-based organisations in patient support activities. In both HSP2 and HSP4, almost all HIV services (9/10) involved

community-based organisations in their activities. This contrasts with HSP1 and HSP3, where only two out of 10 HIV services involved such organisations. Several studies have shown that the participation of community-based organisations delivering adherence support, peer-education and outreach programmes is an effective strategy for reducing time to ART initiation (58,59).

Public health policy recommendations

Overall, median time to ART initiation was quite short in HIV-positive patients initiating ART in the 19 study sites. However, one-fifth of the patients had delays of over 6 months. Our results also suggest that a substantial number of HIV-positive patients were diagnosed late, which together with suboptimal time to ART initiation, may sharply reduce both treatment effectiveness at the individual level, and public health benefits in terms of HIV transmission (60).

Although our study was conducted in 2014, it is likely that the situation of the national HIV programme in Cameroon has not improved over recent years. Indeed, from 2014 to 2018, financial resources allocated to the fight against HIV infection did not significantly increase (13). Furthermore, WHO treatment guidelines were extended to recommend universal treatment (9), most probably increasing the burden on ART access. In Cameroon, the number of patients on ART in 2018 was estimated at 332,000 while the total number of PLWHIV was approximately 540,000. This translates into treatment coverage of only 48% or approximately 210,000 PLWHIV who still needed treatment (23). This poor coverage may be partly explained by patient-level factors that influence the decision to initiate ART, such as fear of HIV-related stigma, not being ready to start treatment, and concerns about side effects (61–63) as well as substantial resource shortfalls resulting in insufficient capacity of HIV services (14).

Our findings suggest that two key strategies may help HIV services foster earlier ART initiation: task-shifting for prescriptions and patient consultations, and involvement of HIV community-based organisations. Although both these strategies were recommended in national guidelines at the time of the study and in the country's 2014-2017 strategic plan for HIV/AIDS (25,64), they were not yet implemented in all HIV services. Additional innovative approaches which are less human resource-intensive, are also required to allocate more time to patients initiating ART and decongest HIV services. These could include less frequent clinic attendance for stable patients on treatment, three-monthly drug prescriptions and/or drug pick-up points

managed by community-based organizations with the supervision of HIV services (65). The latter approach has been successfully experimented with in the Cameroonian ART programme since 2016 (66,67). Further research is needed however to assess the efficiency of these strategies on the time to ART initiation, and to identify the best strategies to optimize the allocation of resources in HIV services, with the aim of achieving universal treatment.

However, the large number of patients in Cameroon who still need ART suggests that without additional funding, implementing such strategies will not be enough. According to the latest UNAIDS estimates (23), HIV funding for Western and Central Africa needs to double if the UNAIDS objectives are to be met. More visibility is also required regarding the sustainability of international funding over the long term.

Study limitations

This study has several limitations. First, the ANRS-12288 EVOLCam survey was conducted in only 2 of Cameroon's 10 regions and is therefore not representative of the whole population of PLWHIV followed in the Cameroonian ART programme. However, we selected a representative sample of HIV services in the two regions with some of the highest HIV prevalence rates and largest patient populations. Furthermore, we used a random selection procedure for participant inclusion. Our survey therefore provides quite a comprehensive picture of the HIV-positive population linked to care and treated with ART in the Centre and Littoral regions in 2014.

Second, our study was performed using data obtained from a cross-sectional survey. Accordingly, we were not able to consider potential changes over time in healthcare supply. However, field observations and interviews indicated that changes in staffing levels and equipment allocation occurred relatively slowly. This was also suggested by the comparison of the characteristics of the 9 HIV services which participated in both this survey and the previous EVAL ANRS-12116 survey conducted in 2006-2007.

Third, patient responses regarding their past experience of HIV diagnosis and entry into care may have suffered from recall bias. To limit this bias, clinical information at the time of HIV diagnosis and ART initiation were obtained through medical files and cross-checked with information provided by patients. In addition, we did not have some information which may have affected time to ART initiation, for example the sites where patients had their first HIV positive test, and HIV status disclosure to one's partner after diagnosis. We cannot therefore

completely exclude the risk of omitted variable bias (i.e., the bias due to the omission of potential relevant covariates) in the estimations of the parameters of the multivariable Cox model.

Fourth, our study was conducted in 2014 when national guidelines recommended ART initiation for PLWHIV with CD4 count $\leq 350/mm^3$ while current WHO guidelines recommend treatment initiation irrespective of CD4 count (9). These simplified treatment initiation criteria have led to a large increase in the number of ART-eligible and ART-treated patients, which constitutes a great burden for healthcare systems, especially in terms of human resources (68,69). As Cameroon is still confronted with severe resource shortfalls (14), it is likely that time to ART initiation has not improved in recent years, and that the health system challenges highlighted in our study are still a reality today, something also suggested by the currently low treatment coverage in the country (48% in 2018) (23).

Finally, HIV services participating in the EVOLCam survey were mainly provided in hospitals (national reference level, regional-level and district-level) which limits the generalisability of our results to other settings (mainly southern Africa), where HIV services including ART delivery are decentralized in primary healthcare facilities (70,71). However, our findings may be relevant for other West and Central African countries where HIV prevalence is low (<1%) to medium (1-5%), and where ART delivery is similarly decentralized at the district level (72).

5. Conclusions

Our findings provide a better understanding of the role played by healthcare supply-related factors on ART initiation. They suggest that in HIV services suffering from shortfalls in technical and human resources, the development of task-shifting and the involvement of HIV community-based organisations could foster greater and quicker access to treatment. As international HIV funding for Cameroon is decreasing, the question of how to optimize the organisation of HIV services needs to be addressed by the Cameroonian ART programme. However, without additional long-term funding, the country will probably not be able to meet the needs of the ever-growing number of PLWHIV who require prompt ART initiation.

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Table 1.

Characteristics of the 19 HIV services and the four HIV service profiles (EVOLCam survey, ANRS 12288).

	Total n=19 n (%)	HSP 1 n=4 n (%)	HSP 2 n=5 n (%)	HSP 3 n=6 n (%)	HSP 4 n=4 n (%)
Hospital's general characteristics					
Location (region)					
Centre	11 (58)	0 (0)	3 (60)	4 (67)	4 (100)
Littoral	8 (42)	4 (100)	2 (40)	2 (33)	0 (0)
Date of opening					
≤2001	7 (37)	1 (25)	5 (100)	1 (17)	0 (0)
>2001	12 (63)	3 (75)	0 (0)	5 (83)	4 (100)
Legal status					
Public	13 (68)	3 (75)	4 (80)	4 (67)	2 (50)
Private	6 (32)	1 (25)	1 (20)	2 (33)	2 (50)
Type of HIV service					
HMU	11 (58)	4 (100)	0 (0)	3 (50)	4 (100)
ATC	8 (42)	0 (0)	5 (100)	3 (50)	0 (0)
Number of beds					
≤100	12 (63)	4 (100)	0 (0)	4 (67)	4 (100)
>100	7 (37)	0 (0)	5 (100)	2 (33)	0 (0)
Number of healthcare providers					
Number of physicians					
≤4	12 (63)	2 (50)	1 (20)	5 (83)	4 (100)
>4	7 (37)	2 (50)	4 (80)	1 (17)	0 (0)
Number of nurses					
≤2	11 (58)	0 (0)	2 (40)	5 (83)	4 (100)
>2	8 (42)	4 (100)	3 (60)	1 (17)	0 (0)
Number of nursing assistants					
0	11 (58)	1 (25)	3 (60)	6 (100)	1 (25)
≥1	8 (42)	3 (75)	2 (40)	0 (0)	3 (75)
Number of psychologists					
0	12 (63)	3 (75)	2 (40)	3 (50)	4 (100)
≥1	7 (37)	1 (25)	3 (60)	3 (50)	0 (0)
Number of social workers					
≤1	9 (47)	3 (75)	1 (20)	3 (50)	2 (50)
>1	10 (53)	1 (25)	4 (80)	3 (50)	2 (50)
Services available					
Number of ART-treated patients					
≤1803	10 (53)	0 (0)	0 (0)	6 (100)	4 (100)
>1803	9 (47)	4 (100)	5 (100)	0 (0)	0 (0)
Subsidized biological check-up					
No	13 (68)	4 (100)	3 (60)	5 (83)	1 (25)
Yes	6 (32)	0 (0)	2 (40)	1 (17)	3 (75)
Educational support					
No	11 (58)	1 (25)	2 (40)	6 (100)	2 (50)
Yes	8 (42)	3 (75)	3 (60)	0 (0)	2 (50)
Nutritional support					
No	6 (32)	3 (75)	0 (0)	3 (50)	0 (0)
Yes	13 (68)	1 (25)	5 (100)	3 (50)	4 (100)
Financial support					
No	13 (68)	3 (75)	4 (80)	2 (33)	4 (100)
Yes	6 (32)	1 (25)	1 (20)	4 (67)	0 (0)
Organisation					
Task-shifting for consultation and medical follow-up					
No	7 (37)	1 (25)	2 (40)	4 (67)	0 (0)

Yes	12 (63)	3 (75)	3 (60)	2 (33)	4 (100)
Task-shifting for prescription					
No	8 (42)	3 (75)	2 (40)	3 (50)	0 (0)
Yes	11 (58)	1 (25)	3 (60)	3 (50)	4 (100)
HIV community-based organisations' involvement					
No	9 (47)	4 (100)	0 (0)	4 (67)	1 (25)
Yes	10 (53)	0 (0)	5 (100)	2 (33)	3 (75)
Specific ART management					
No	5 (26)	1 (25)	0 (0)	2 (33)	2 (50)
Yes	14 (74)	3 (75)	5 (100)	4 (67)	2 (50)
Technical capacities					
Medical imaging equipment					
No	14 (74)	4 (100)	1 (20)	5 (83)	4 (100)
Yes	5 (26)	0 (0)	4 (80)	1 (17)	0 (0)
Availability of CD4 count machine					
No	10 (53)	2 (50)	2 (40)	4 (67)	2 (50)
Yes	9 (47)	2 (50)	3 (60)	2 (33)	2 (50)
ARV stock-out					
No	9 (47)	3 (75)	3 (60)	1 (17)	2 (50)
Yes	10 (53)	1 (25)	2 (40)	5 (83)	2 (50)

Abbreviations: HSP: HIV service profile; HMU: Management Units; ATC: Accredited Treatment Centres; ARV: Antiretroviral drugs; ART: Antiretroviral treatment.

Table 2.

Individual factors and HIV-service profiles associated with time to ART initiation: multi-level Cox model (EVOLCam survey, ANRS 12288).

	Total (n=847)	Time to ART initiation (in months)	Univariate analyses (n=847)		Multivariable analyses (n=819)	
	n (%)	Mean (SD)	HR [95% CI]	p-value	HR [95% CI]	p-value
Socio-demographic and economic characteristics						
Age						
≤39 years	458 (54)	4.54 (6.49)	1		1	
>39 years	389 (46)	3.28 (5.00)	1.27 [1.10-1.46]	<0.001	1.26 [1.09-1.45]	0.002
Gender						
Male	236 (28)	4.16 (5.83)	1		1	
Female	611 (72)	3.87 (5.89)	1.01 [0.86-1.18]	0.930	1.04 [0.89-1.22]	0.580
Having a partner (missing data=26)						
Yes, the same partner since HIV diagnosis	365 (43)	3.88 (5.35)	1			
Yes, a new partner since HIV diagnosis	104 (12)	4.45 (6.22)	0.88 [0.70-1.09]	0.260		
No	352 (42)	3.98 (6.42)	1.00 [0.86-1.16]	0.950		
Education						
Secondary school or less	778 (92)	3.90 (5.71)	1			
Higher than secondary school	69 (8)	4.52 (7.45)	0.90 [0.70-1.16]	0.430		
Living below the absolute poverty line[1] (missing data=100)						
Yes	127 (15)	3.87 (5.63)	1			
No	620 (73)	4.10 (5.98)	0.99 [0.84; 1.17]	0.940		
Having an economic activity						
No	330 (39)	3.82 (5.67)	1			
Yes	517 (61)	4.04 (6.00)	0.97 [0.84-1.12]	0.700		
HIV testing experience and HIV services accessibility						
HIV testing initiative (missing data=1)						
On patient's own initiative	225 (27)	4.50 (7.06)	1			
On a healthcare provider's initiative with informed consent	588 (69)	3.59 (5.07)	1.17 [1.00-1.37]	0.053		
On the partner's initiative	18 (2)	7.38 (10.58)	0.71 [0.43-1.15]	0.160		
Without being informed	15 (2)	5.91 (6.05)	0.82 [0.48-1.41]	0.480		
HIV testing performed on the occasion of a pregnancy or delivery (missing data=61)						
No	715 (84)	3.78 (5.71)	1			
Yes	71 (8)	4.81 (6.04)	0.84 [0.65-1.08]	0.170		
Disease symptoms at HIV diagnosis (missing data=1)						
No	260 (31)	5.04 (7.20)	1		1	
Yes	586 (69)	3.48 (5.12)	1.29 [1.11-1.51]	0.001	1.21 [1.04-1.41]	0.015

Living in the city where the HIV service was located						
Yes	333 (39)	3.83 (5.50)	1			
No	514 (61)	4.11 (6.19)	0.96 [0.83; 1.12]	0.610		
Clinical and ART-related characteristics						
Hepatitis B co-infection at HIV diagnosis						
No	839 (99)	3.98 (5.89)	1			
Yes	8 (1)	1.03 (0.90)	2.25 [1.11; 4.56]	0.024	2.31 [1.15-4.66]	0.019
Tuberculosis co-infection at HIV diagnosis (missing data=8)						
No	648 (77)	4.04 (6.07)	1			
Yes	191 (23)	3.75 (5.17)	1.04 [0.88; 1.24]	0.640		
CD4 cell count at ART initiation (missing data=21)						
≥100 cells/mm^3	627 (74)	4.18 (6.13)	1		1	
<100 cells/mm^3	199 (23)	3.24 (4.91)	1.17 [1.00-1.38]	0.057	1.16 [0.98-1.36]	0.087
WHO clinical stage at ART initiation (missing data=123)						
Stage 1 or 2	288 (34)	4.39 (6.32)	1			
Stage 3 or 4	436 (51)	3.66 (5.50)	1.12 [0.95-1.33]	0.140		
Healthcare supply-related characteristics						
HIV service profiles						
HSP 2 (n=5)	249 (29)	3.37 (5.44)	1		1	
HSP 3 (n=6)	279 (33)	4.28 (5.72)	0.84 [0.71-1.00]	0.055	0.86 [0.72-1.02]	0.090
HSP 4 (n=4)	180 (21)	3.34 (5.69)	1.03 [0.85-1.26]	0.730	1.10 [0.90-1.34]	0.360
HSP 1 (n=4)	139 (16)	4.96 (6.91)	0.74 [0.60-0.92]	0.006	0.80 [0.65-0.99]	0.049

Abbreviations: SD: Standard Deviation; HR: Hazard ratio; [95%CI]: 95% Confidence Interval; ART: Antiretroviral treatment; HSP: HIV service profile

[1] Household monthly income <28310 FCFA i.e. 51 USD.

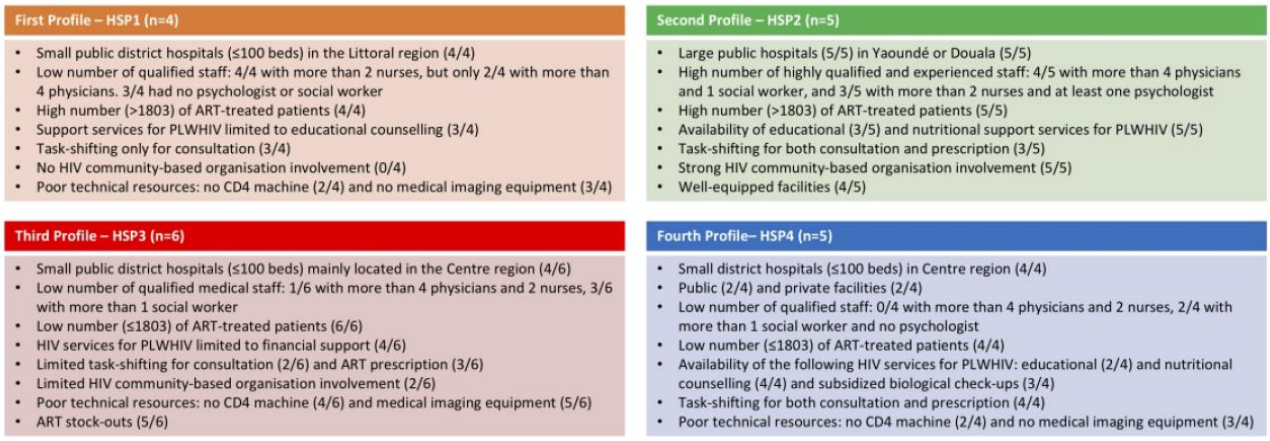
Table 3.

Time to ART initiation and proportions of PLWHIV who initiated ART within 1 month of diagnosis and more than 6 months after diagnosis, according to HIV service profiles (EVOLCam survey, ANRS 12288, n=847).

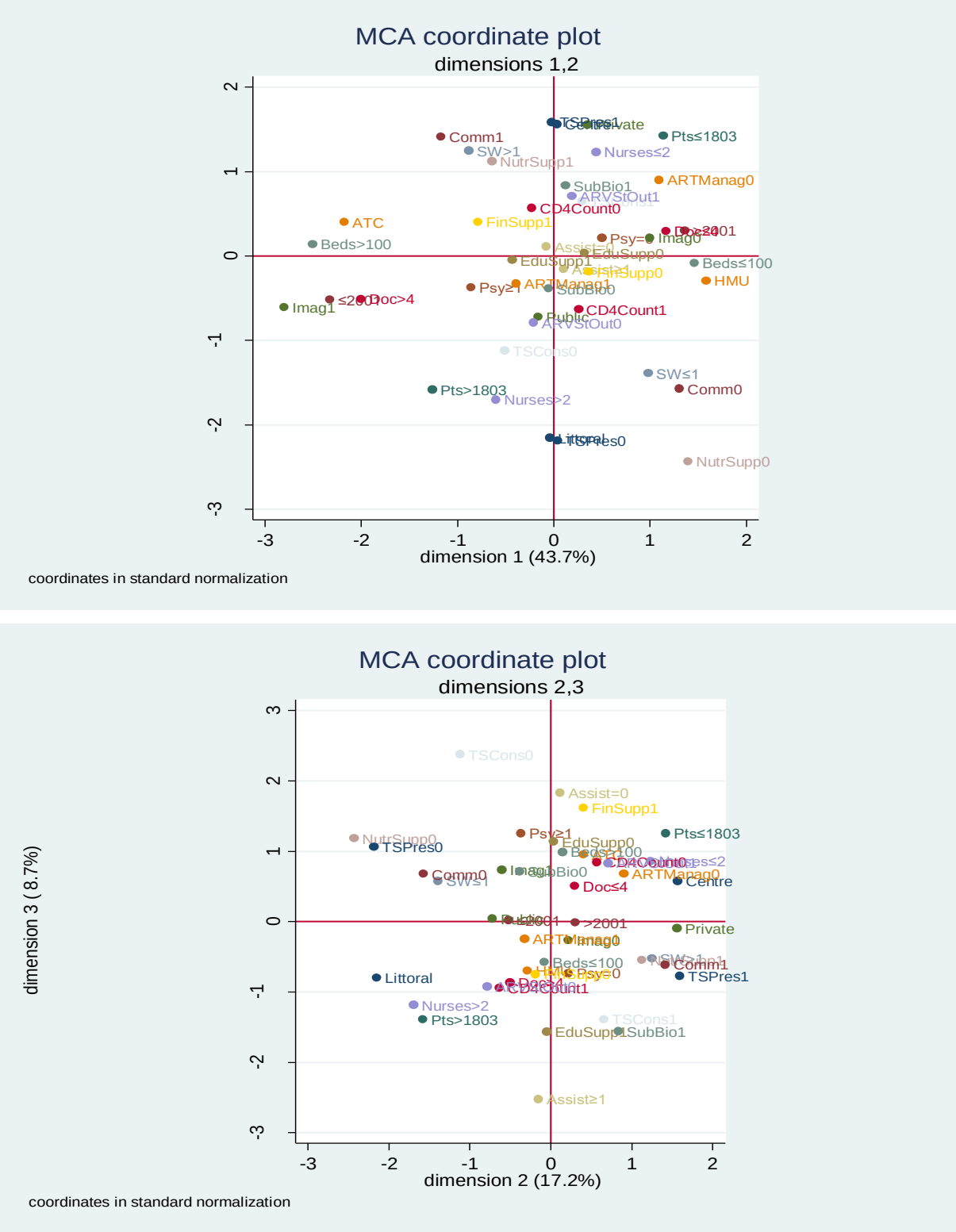
HIV service profiles (HSP)	Number of PLWHIV	Time to ART initiation		Number of PLWHIV	
		Mean time (months)	Median time (months)	ART initiation <1 month	ART initiation >6 months
	n (%)	(SD)	[IQR]	n (%)	n (%)
HSP1	139 (16)	5 (6.9)	2.0 [1.1 - 5.9]	29 (21)	33 (24)
S1	45 (5)	6.3 (8.6)	1.9 [1.0 - 11.7]	10 (22)	13 (29)
S2	35 (4)	5.2 (7.6)	2.6 [1.1 - 6.4]	8 (23)	10 (29)
S3	28 (3)	3 (3.4)	1.6 [0.9 – 4.0]	9 (32)	4 (14)
S4	31 (4)	4.4 (5.1)	2.6 [1.5 - 5.2]	2 (6)	6 (19)
HSP2	249 (29)	3.4 (5.4)	1.5 [0.6 - 3.2]	92 (37)	37 (15)
S5	18 (2)	3.2 (4.5)	1.0 [0.5 - 4.2]	8 (44)	3 (17)
S6	14 (2)	3.6 (5.2)	1.4 [0.3 – 2.0]	7 (50)	3 (21)
S7	86 (10)	2.9 (4.5)	1.3 [0.5 - 2.9]	34 (39)	10 (12)
S8	60 (7)	4.2 (7.2)	1.3 [0.3 – 3.0]	25 (42)	11 (18)
S9	71 (8)	3.3 (5.1)	1.7 [0.9 - 3.5]	18 (25)	10 (14)
HSP3	279 (33)	4.3 (5.7)	1.9 [0.8 - 5.9]	84 (30)	67 (24)
S10	41 (5)	3.6 (4.3)	2.1 [1.0 – 4.0]	9 (22)	8 (19)
S11	72 (9)	5.5 (7.7)	1.7 [0.2 - 9.9]	27 (37)	22 (31)
S12	30 (4)	2.2 (3.3)	0.9 [0.3 - 2.4]	18 (60)	4 (13)
S13	35 (4)	4.6 (5.5)	1.9 [1.1 - 6.5]	9 (26)	10 (29)
S14	80 (9)	4.5 (5.2)	2.6 [1.2 - 5.8]	11 (14)	18 (22)
S15	21 (2)	3.4 (5.3)	1.1 [0.4 - 2.8]	10 (48)	5 (24)
HSP4	180 (21)	3.4 (5.7)	1.0 [0.2 - 3.5]	93 (52)	31 (17)
S16	5 (1)	4.5 (4.7)	1.9 [1.0 - 8.1]	1 (20)	2 (40)
S17	47 (6)	3.9 (6.1)	1.4 [0.2 - 3.4]	22 (47)	10 (21)
S18	77 (9)	3.1 (5.4)	0.5 [0.2 - 3.3]	48 (62)	13 (17)
S19	51 (6)	3.5 (5.9)	1.4 [0.2 - 3.7]	22 (43)	6 (12)
Total	847 (100)	4.0 (5.8)	1.6 [0.5-4.3]	298 (35)	168 (20)

Abbreviations: PLWHIV: People living with HIV; ART: Antiretroviral treatment; SD: Standard Deviation; IQR: Interquartile range; HSP: HIV service profile

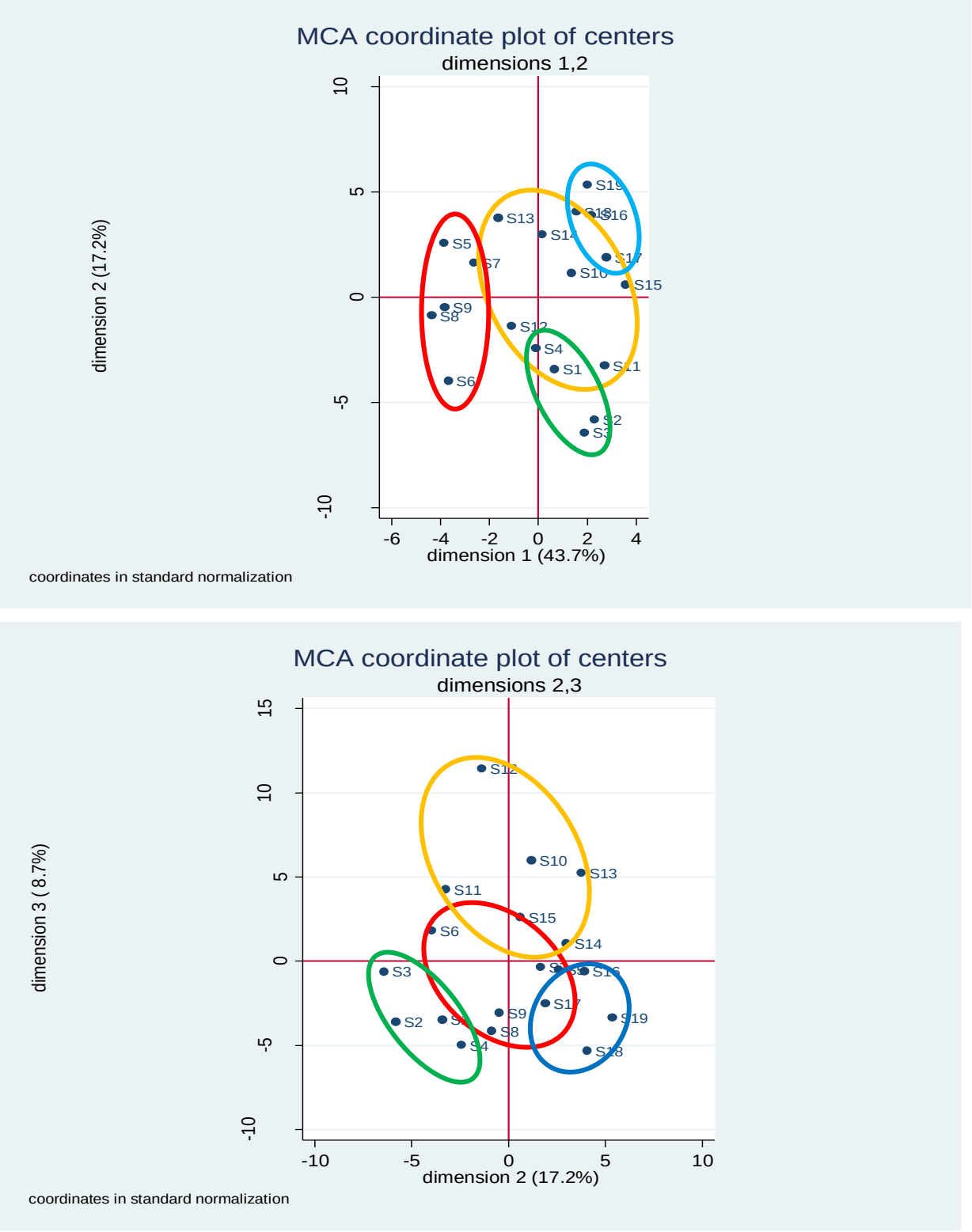
Figure 1: Main characteristics of the HIV services profiles (EVOLCam survey, ANRS 12288, n=19)



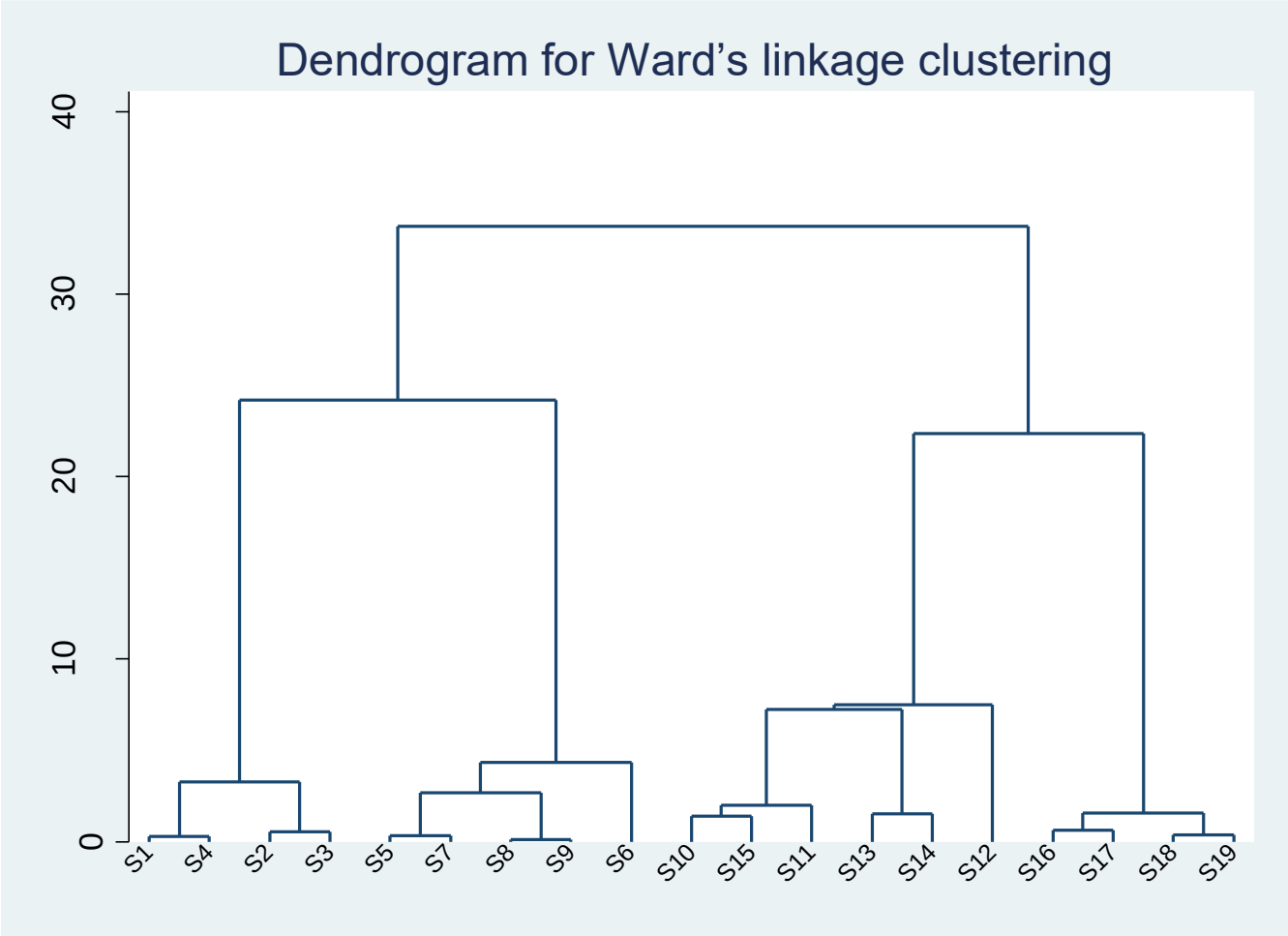
Supplementary material



Supplementary Figure 1. Multiple correspondence analysis (MCA) coordinate plots of categories of active variables (characteristics of centers) (EVOLCam survey, ANRS 12288).



Supplementary Figure 2. Multiple correspondence analysis (MCA) coordinate plots of centers (as supplementary variable) and clustering: HSP 1 (S1, S2, S3, S4), HSP 2 (S5, S6, S7, S8, S9), HSP 3 (S10, S11, S12, S13, S14, S15), HSP 4 (S16, S17, S18, S19) (EVOLCam survey, ANRS 12288).



Supplementary Figure 3. Dendrogram for center clustering (EVOLCam survey, ANRS 12288).

Supplementary Table 1. Multiple correspondence analysis (MCA) of the center characteristics (EVOLCam survey, ANRS 12288).

Variable categories	Label	% of overall inertia	Contribution dimension 1	Contribution dimension 2	Contribution dimension 3
Facility general features					
Location (region)					
Centre	Centre	0.018	0.000	0.064	0.009
Littoral	Littoral	0.024	0.000	0.089	0.012
Date of opening					
≤2001	≤2001	0.050	0.091	0.004	0.000
>2001	>2001	0.029	0.053	0.003	0.000
Legal status					
Public	Public	0.008	0.001	0.016	0.000
Private	Private	0.017	0.002	0.035	0.000
Type of HIV service					
HMU	HMU	0.037	0.066	0.002	0.013
ATC	ATC	0.050	0.091	0.003	0.018
Number of beds					
≤100	Beds≤10	0.034	0.061	0.000	0.010
>100	Beds>100	0.058	0.105	0.000	0.016
Number of healthcare providers					
Number of physicians					
≤4	Doc≤4	0.021	0.039	0.003	0.007
>4	Doc>4	0.035	0.067	0.004	0.012
Number of nurses					
≤2	Nurses≤2	0.019	0.005	0.040	0.019
>2	Nurses>2	0.026	0.007	0.055	0.027
Number of nursing assistants					
0	Assist=0	0.012	0.000	0.000	0.089
≥1	Assist≥1	0.017	0.000	0.000	0.122
Number of psychologists					
0	Psy=0	0.008	0.007	0.001	0.015
≥1	Psy≥1	0.014	0.012	0.002	0.026
Number of social workers					
≤1	SW≤1	0.024	0.021	0.042	0.007
>1	SW>1	0.021	0.019	0.037	0.007
Services available					
Number of ART-treated patients					
≤1803	Pts≤1803	0.033	0.031	0.048	0.038
>1803	Pts>1803	0.036	0.034	0.054	0.042
Subsidized biological check-up					
No	SubBio0	0.009	0.000	0.005	0.016
Yes	SubBio1	0.020	0.000	0.010	0.035
Educational support					
No	EduSupp0	0.008	0.003	0.000	0.034
Yes	EduSupp1	0.010	0.004	0.000	0.047
Nutritional support					
No	NutrSupp0	0.037	0.028	0.085	0.020
Yes	NutrSupp1	0.017	0.013	0.039	0.009
Financial support					
No	FinSupp0	0.007	0.004	0.001	0.017
Yes	FinSupp1	0.016	0.009	0.002	0.038
Organisation					
Task-shifting for consultation and medical follow-up					
No	TSCons0	0.022	0.004	0.021	0.095
Yes	TSCons1	0.013	0.003	0.012	0.055
Task-shifting for prescription					

No	TSPres0	0.025	0.000	0.091	0.022
Yes	TSPres1	0.018	0.000	0.066	0.016
HIV community-based organisation involvement					
No	Comm0	0.032	0.037	0.053	0.010
Yes	Comm1	0.029	0.033	0.048	0.009
Specific ART management					
No	ARTManag0	0.019	0.014	0.010	0.006
Yes	ARTManag1	0.007	0.005	0.003	0.002
Technical capacities					
Medical imaging equipment					
No	Imag0	0.019	0.033	0.002	0.002
Yes	Imag1	0.053	0.094	0.004	0.007
Availability of CD4 count machine					
No	CD4Count0	0.013	0.001	0.008	0.017
Yes	CD4Count1	0.015	0.001	0.009	0.019
ARV stock-out					
No	ARVStOut0	0.010	0.001	0.013	0.018
Yes	ARVStOut1	0.009	0.001	0.012	0.017

Abbreviations: HMU: Management Units; ATC: Accredited Treatment Centres; ARV: Antiretroviral drugs; ART: Antiretroviral treatment.