

## Sociodemographic, lifestyle and therapeutic predictors of 2-year survival in HIV-infected persons receiving antiretroviral therapy in Benin

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### Abstract

The benefits of antiretroviral therapy (ART) for treating human immunodeficiency virus (HIV) infection have been well described. The objective of this study was to identify the predictors of two-year survival in persons living with HIV/AIDS (PLWHA) in Benin. This retrospective transversal study included all patients from 46 HIV/AIDS therapy sites across Benin who started ART between July 1<sup>st</sup>, 2011 and June 30<sup>th</sup>, 2012. The independent variables were patients' sociodemographic, clinical, biological and therapeutic characteristics and their ART regimen. The main dependent variable was the time of death. Data were collected from medical records, using documentary review. Cox proportional hazards regression models were used to investigate factors associated with survival. Among the 771 PLWHA participants of the study, 18 (2.3%) died within the two-year period. The estimated mortality of the 771 PLWHA was 3% at 24 months. Among the sociodemographic, lifestyle and therapeutic characteristics studied, the main predictor of two-year mortality was poor adherence [odds ratio = 4.15, 95% confidence interval (1.55-11.28)]. This study confirms that improving the survival of PLWHA receiving ART requires enhanced adherence.

### Introduction

The benefits of highly active antiretro-

viral therapy (ART) in the treatment of human immunodeficiency virus (HIV) infection have been well described. These benefits include viral suppression, CD4 lymphocyte repletion and durable reductions in acquired immunodeficiency syndrome (AIDS)-related opportunistic diseases and death.<sup>1</sup> In Benin, ART began in February 2002 at three sites. In scaling up from 3 to 5 initiatives, the National Programme for the Fight against AIDS (PNLS) opted for decentralized health centres for HIV/AIDS care.<sup>2</sup> Two studies of 1-year survival after starting ART were performed, and the rates varied from 88.5% (2006-2007) to 93.4% (2008-2009). To improve programme performance and the quality of services provided to people living with HIV/AIDS (PLWHA), two or more years of survival and its associated factors need to be assessed in PLWHA receiving ART.

In the literature, survival among patients receiving ART therapy is associated with good adherence,<sup>1,3,4</sup> a high CD4 cell count at baseline,<sup>5</sup> the interaction between the two latter factors,<sup>1</sup> youth,<sup>1,3,5,6</sup> and an early World Health Organization (WHO) stage.<sup>3,5</sup> However, coinfections or comorbidities, especially tuberculosis, being a single or unmarried or male,<sup>3,5</sup> ART therapeutic regimen, occupation and body mass index are predictors of death.<sup>6</sup> According to Kang'ethe and Nomngcoyiya,<sup>7</sup> poor adherence is also promoted by poverty and its ramifications, such as a lack of food, excessive alcohol intake, the capacity of antiretrovirals (ARVs) to deform body structure, the tandem use of both pharmaceuticals and traditional healing mixtures, and ARVs negatively influencing sexual libido. This study aimed to assess 2-year survival and predicting factors of death in PLWHA who started ART in Benin between July 1<sup>st</sup>, 2011 and June 30<sup>th</sup>, 2012.

### Materials and Methods

#### Study design and population

A cross-sectional, retrospective study was performed by the PNLS. The study population was HIV-infected patients receiving ART in centres of HIV/AIDS management in Benin. The study was performed in 2014.

#### Participant selection

The inclusion criteria were as follows: being HIV-positive, older than 15 years and having started ART between July 1<sup>st</sup>, 2011 and June 30<sup>th</sup>, 2012. The exclusion criteria included being a pregnant woman receiving

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Contributions: CSJ and MA: Study conception and design. GES, AIBC and MB: interpreted and analyzed the data of the study. CSJ and MA, reviewed literature and wrote the discussion. VA, MEO and LO: critically revised the article. All authors: proofread the manuscript for final approval.

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ART for preventing mother-to-child HIV infection and having incomplete medical record data. Patients meeting the inclusion criteria with complete medical records were enrolled from all 46 centres of HIV/AIDS management, which are in all parts of Benin.

#### Study variables

The independent variables studied were sociodemographic (sex, age, marital status, education, occupation, family network, social network), lifestyle (smoking and alcohol consumption) and therapeutic characteristics (adherence to ART). The main

dependent variable was the time of death. Data were collected from patients' medical records and from the periodic reports of centres of HIV/AIDS management.

### Data collection

Data collectors were divided in teams of two; each team was responsible for one or more centres of HIV/AIDS management according to the number of patients receiving ART in the centres and the distance between sites.

Data were collected through a documentary review of the medical records of patients and the periodic reports from the centres of HIV/AIDS management. At each centre, data collectors extracted information regarding the variables from these documents.

Data collectors and data managers were enrolled for two days of training on the study procedure and the data collection technique (documentary review) and tools (report sheets). Deaths were verified by professional or site mediator information, if possible, and were otherwise verified by a death certificate in the patient file, by a death record in the death register, or by a phone call using the phone number in the patient file. National supervision of the data collection was set up by the principal investigator and PNLs's monitoring evaluation representatives.

### Statistical analysis

Data were analysed using SPSS version 20.0 (SPSS, Inc., Chicago, IL, USA). Proportions were used to describe patients' baseline characteristics. Cox proportional hazards regression models were used to investigate factors associated with survival.<sup>8</sup> Hazard ratios (HRs) and 95% confidence intervals (95% CIs) were also calculated.

### Ethics

The study was approved by the Benin National Health Research Ethics Committee before the operational stage began. An interviewer explained the purpose of the study and procedures to each participant and gained written informed consent before commencing the interview. Each participant was also informed that their participation was voluntary and that they could withdraw from the interview/discussion at any time without consequences. The participants were assured that their responses would remain confidential, and they were assured anonymity through the use of strict coding measures.

## Results

### Participants' characteristics

The records of patient enrolled between July 1<sup>st</sup>, 2011 and June 30<sup>th</sup>, 2012 were reviewed, and 771 patients had the complete sociodemographic, therapeutic and lifestyle data required for the estimation of survival predictors. Table 1 shows that most patients were female (71.6%). The mean age at the time of ART initiation was 36.4±10.6 years. Most patients (65.8%) were married, and 49% had received no education. Among the 771 participants, 89.1% were not members of any social associations (*e.g.*, working groups, self-help groups), and 41.8% were living with a partner

and infants. Only 2.3% and 10.8% of participants smoked and consumed alcohol, respectively, according to medical records reviewed. ART initiation was based on the 2006 WHO recommendations ( $CD4 < 350$  cells/mm<sup>3</sup>), and 97% of the PLWHA were receiving first-line ART.

### Survival in HIV-infected persons receiving ART

The mortality rate was estimated to be 2% and 3% at 12 and 24 months, respectively, among the 771 PLWHA included in the study (Figure 1). Table 2 shows that during the study period, 16 (2.1%) and 18 patients (2.3%) of the 771 participants died at 12 and 24 months, respectively.

**Table 1. Sociodemographic characteristics of HIV infected persons receiving ART (n=771), Benin 2014.**

| Characteristics                     | Absolute frequency | Relative frequency, % |
|-------------------------------------|--------------------|-----------------------|
| Sex                                 |                    |                       |
| Male                                | 219                | 28.4                  |
| Female                              | 552                | 71.6                  |
| Age (years)                         |                    |                       |
| 15-29                               | 213                | 27.6                  |
| 30-49                               | 459                | 59.5                  |
| ≥50                                 | 99                 | 12.8                  |
| Marital status                      |                    |                       |
| Unmarried                           | 105                | 13.6                  |
| Married                             | 507                | 65.8                  |
| Widowed                             | 99                 | 12.8                  |
| Other                               | 60                 | 7.8                   |
| Education                           |                    |                       |
| No schooling                        | 378                | 49.0                  |
| Primary school                      | 206                | 26.7                  |
| Secondary school                    | 170                | 22.0                  |
| University                          | 17                 | 2.2                   |
| Occupation                          |                    |                       |
| Housewife or farmers                | 286                | 37.1                  |
| Student and jobless                 | 30                 | 3.9                   |
| Craftsmen, artists and traders      | 223                | 28.9                  |
| Employee (private or public sector) | 103                | 13.4                  |
| Others                              | 129                | 16.7                  |
| Family network                      |                    |                       |
| Living alone                        | 88                 | 11.4                  |
| Living with a partner               | 187                | 24.3                  |
| Living with infants                 | 123                | 16.0                  |
| Living with partner and infants     | 322                | 41.8                  |
| Living with friends                 | 5                  | 0.6                   |
| Living in extended family           | 42                 | 5.4                   |
| Others                              | 4                  | 0.5                   |
| Social network                      |                    |                       |
| Not a member an association         | 687                | 89.1                  |
| Active member of an association     | 59                 | 7.7                   |
| Passive member of an association    | 25                 | 3.2                   |
| Smoking                             |                    |                       |
| No                                  | 753                | 97.7                  |
| Yes                                 | 18                 | 2.3                   |
| Alcohol consumption                 |                    |                       |
| No                                  | 691                | 89.6                  |
| Yes                                 | 80                 | 10.4                  |

## Sociodemographic, lifestyle and therapeutic predictors of 2-year survival

Table 3 shows the unadjusted Cox regression analyses for sociodemographic, lifestyle and therapeutic factors. A significantly higher trend for poor survival was found in men (HR=3.20; 95%CI: 1.00-10.23) and in patients with poor ART adherence (HR=4.18; 95%CI: 1.55-11.28). Marital status, social network, occupation, education, family network and alcohol consumption did not significantly influence survival in the study participants.

## Discussion

This study of 2-year survival in PLWHA receiving ART revealed an estimated survival rate of 97% at 24 months. Using unadjusted Cox regression HRs, we

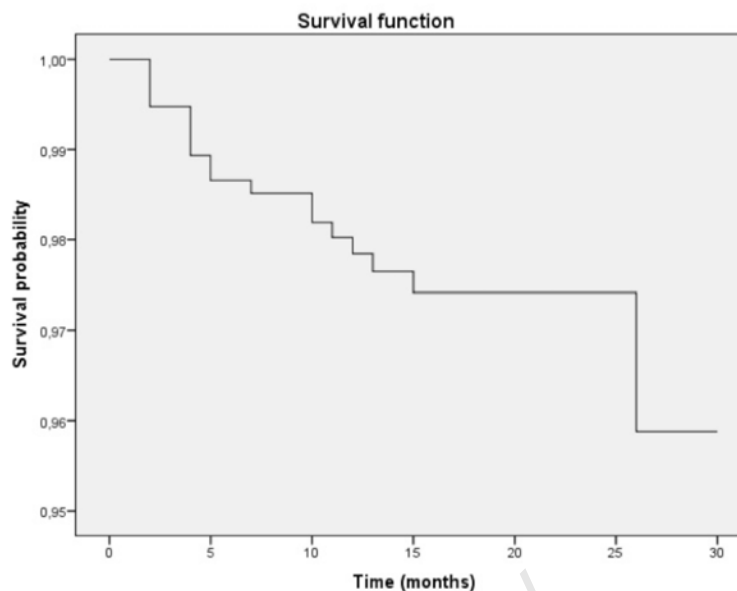


Figure 1. Two-year survival function in HIV infected persons (n=771), Benin 2014.

Table 2. Two-year survival changes in HIV infected patients receiving ART (n=771), Benin 2014.

| Time (months) | Participants alive at time T | N. of participants censored | Number of deaths | Survival function |
|---------------|------------------------------|-----------------------------|------------------|-------------------|
| 0             | 771                          | 0                           | 0                | 1.00              |
| 1             | 771                          | 19                          | 4                | 0.99              |
| 2             | 748                          | 9                           | 0                | 0.99              |
| 3             | 739                          | 10                          | 4                | 0.99              |
| 4             | 725                          | 9                           | 2                | 0.99              |
| 5             | 714                          | 19                          | 0                | 0.99              |
| 6             | 695                          | 22                          | 1                | 0.99              |
| 7             | 672                          | 24                          | 0                | 0.99              |
| 8             | 648                          | 23                          | 0                | 0.99              |
| 9             | 625                          | 26                          | 2                | 0.98              |
| 10            | 597                          | 30                          | 1                | 0.98              |
| 11            | 566                          | 36                          | 1                | 0.98              |
| 12            | 529                          | 54                          | 1                | 0.98              |
| 13            | 474                          | 45                          | 0                | 0.98              |
| 14            | 429                          | 27                          | 1                | 0.97              |
| 15            | 401                          | 33                          | 0                | 0.97              |
| 16            | 368                          | 30                          | 0                | 0.97              |
| 17            | 338                          | 32                          | 0                | 0.97              |
| 18            | 306                          | 28                          | 0                | 0.97              |
| 19            | 278                          | 31                          | 0                | 0.97              |
| 20            | 247                          | 25                          | 0                | 0.97              |
| 21            | 222                          | 37                          | 0                | 0.97              |
| 22            | 185                          | 26                          | 0                | 0.97              |
| 23            | 159                          | 35                          | 0                | 0.97              |
| 24            | 124                          | 47                          | 0                | 0.97              |
| 25            | 77                           | 27                          | 1                | 0.96              |
| 26            | 49                           | 25                          | 0                | 0.96              |
| 27            | 24                           | 15                          | 0                | 0.96              |
| 28            | 9                            | 7                           | 0                | 0.96              |
| 29            | 2                            | 2                           | 0                | 0.96              |

found that ART adherence was associated with 2-year survival in these patients.

The findings of this study are in accordance with others performed worldwide, which have reported that the introduction of ART has significantly reduced morbidity and mortality in HIV-infected patients in various developed and developing countries.<sup>9,10</sup> Indeed, the goal of universal access to ART adopted at the June 2006 General Assembly High-Level Meeting on HIV/AIDS has had a positive impact on survival in HIV-infected persons.<sup>11</sup> In a study on estimating the impact of ART in adults, Mahy *et al.*<sup>12</sup> reported that 14.4 million life-years were gained among adults globally between 1995 and 2009 as a result of ART. In recent years, the growth in life-years has occurred more rapidly in sub-Saharan Africa and Asia. Indeed, the benefits of highly active ART in the treatment of HIV infection have been well described. These benefits include viral suppression, CD4 lymphocyte repletion, and durable reductions in AIDS-related opportunistic diseases and death.<sup>13,14</sup>

As indicated by an unadjusted Cox regression HR, the male sex was associated with a high likelihood of death within the first two years after ART initiation. This result is similar to that reported by Gezahegn in Ethiopia<sup>3</sup> and by Meda in Burkina Faso.<sup>5</sup> Another influence of sex was reported in Dar es Salam in Tanzania, where researchers determined that one-year after ART initiation, women have a better immunological response, with a high rate of undetectable virus load.<sup>15</sup>

A high adherence to ART was associated with a decreased death rate, which has also been described elsewhere; however, 12 months of inpatient care increases the death rate.<sup>1,5</sup> The benefits of highly active ART in the treatment of HIV infection have been well described and include viral suppression, CD4 lymphocyte repletion, and durable reductions in HIV infection-related opportunistic diseases and death.<sup>1</sup> These findings underline the need to take action by networking PLWHA, organizing adherence training for patients, families and communities. In the present study, a survey of the managers of HIV infection care centres showed that nearly one-third (28.6%) of the managers have not taken any action toward networking PLWHA. Studies have reported that good adherence was itself associated with gender and belonging to an HIV support group.<sup>16</sup>

The current focus should be on how to maximize the positive effects of ART, especially in resource-poor settings, such as Benin. According to Oguntibeju,<sup>14</sup> there is a need to provide more support to HIV/AIDS

patients and to organize awareness programmes that can address the issues of stigma and discrimination, since such awareness programmes could contribute to improved ART adherence. Clinically assessing adverse reactions during the course of ART and carefully monitoring patients after any ART switch could contribute to improved quality of life and survival in HIV-infected patients receiving ART.<sup>14</sup> Some limitations of this study should be mentioned, the main one being the exclusion of some potential participants due to incomplete medical records. This limitation could have induced selection bias leading to less representativeness of the participant's sampling. In addition, the statistical conclusions may not be generalized to encompass all HIV-infected persons receiving ART. However, these findings do confirm other results that have been reported in the scientific literature.

## Conclusions

Our study shows that the probability of two-year survival in patients initiating ART was 97%. Among the sociodemographic, lifestyle and therapeutic factors considered, adherence to ART was the main determinant of 2-year survival. Focusing on how to maximize ART adherence by monitoring any ART switch is needed for continuously improving the survival of HIV-infected persons receiving ART in Benin.

**Table 3. Cox regression 2-year survival of HIV infected persons on socio-demographic, lifestyle and therapeutic factors, Benin 2014, n=771.**

| Variables                           | Hazard ratio | 95%CI      | P     |
|-------------------------------------|--------------|------------|-------|
| Sex                                 |              |            |       |
| Women                               | 1            | -          | -     |
| Men                                 | 3.20         | 1.00-10.23 | 0.050 |
| Age                                 |              |            |       |
| 15-29                               | 1            | -          | 0.39  |
| 30-49                               | 1.02         | 0.25-4.06  | 0.98  |
| ≥50                                 | 2.28         | 0.45-11.51 | 0.32  |
| Marital status                      |              |            |       |
| Unmarried                           | 1            | -          | -     |
| Married                             | 0.76         | 0.11-5.43  | 0.78  |
| Widowed                             | 1.06         | 0.11-10.05 | 0.96  |
| Other                               | 4.89         | 0.60-40.03 | 0.14  |
| Adherence to antiretroviral therapy |              |            |       |
| Good adherence                      | 1            | -          | -     |
| Poor adherence                      | 4.18         | 1.55-11.28 | 0.01  |
| Social network                      |              |            |       |
| Member of no association            | 1            | -          | -     |
| Active member of an association     | 0.81         | 0.10-6.79  | 0.85  |
| Passive member of an association    | nd           | nd         | nd    |
| Occupation                          |              |            |       |
| Housewife or farmers                | 1            | -          | 0.55  |
| Student and jobless                 | nd           | nd         | nd    |
| Craftsmen, artists and traders      | 0.34         | 0.08-1.43  | 0.14  |
| Employee (private or public sector) | 0.33         | 0.05-2.05  | 0.23  |
| Others                              | 0.59         | 0.15-2.33  | 0.45  |
| Education                           |              |            |       |
| No schooling                        | -            | -          | 0.96  |
| Primary school                      | 1.25         | 0.34-4.55  | 0.73  |
| Secondary school or university      | 1.34         | 0.34-5.29  | 0.68  |
| Family network                      |              |            |       |
| Living alone                        | 1            | -          | 0.39  |
| Living with a partner               | 0.69         | 0.10-4.72  | 0.71  |
| Living with infants                 | 0.12         | 0.01-1.35  | 0.08  |
| Living with partner and infants     | 0.84         | 0.14-5.18  | 0.85  |
| Living with friends                 | 3.48         | 0.27-45.52 | 0.34  |
| Living in extended family           | 1.11         | 0.15-8.46  | 0.92  |
| Alcohol consumption                 |              |            |       |
| No                                  | 1            | -          | -     |
| Yes                                 | 0.44         | 0.05-3.69  | 0.45  |

Nd: non determined due to small number.

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