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Ligia Maria Nascimento Arantes *, Andrey Oeiras Pedroso, Mayra Gonçalves Menegueti, Elucir Gir, Eliã Pinheiro Botelho, Ana Cristina de Oliveira e Silva, Renata Karina Reis

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*Article*

# Factors Associated with Late Diagnosis of HIV/AIDS in a University Hospital in Brazil: Challenges to Achieving the 2030 Target

**Ligia Maria Nascimento Arantes [1,*], Andrey Oeiras Pedroso [1], Mayra Gonçalves Menegueti [1], Elucir Gir [1], Eliã Pinheiro Botelho [2], Ana Cristina de Oliveira e Silva [3] and Renata Karina Reis [1]**

[1] Ribeirao Preto School of Nursing, University of Sao Paulo, Ribeirao Preto, SP, Brazil.
[2] Faculty of Nursing, Federal University of Pará, Belém, PA, Brazil.
[3] Federal University of Paraíba, João Pessoa, PB, Brazil.
* Correspondence: ligiausp@usp.br

**Abstract:** Introduction: This study aimed to identify factors associated with late diagnosis and clinically monitor newly diagnosed HIV/AIDS patients. Method: Retrospective longitudinal study, based on secondary data from a specialized unit at a tertiary hospital. Data collection included sociodemographic, behavioral, clinical, and laboratory data of newly diagnosed HIV patients between 2015-2019. Data analysis adopted inferential statistical tests using the SPSS program, considering $\alpha \leq 0.05$. Results: 314 individuals were newly diagnosed with HIV/AIDS. 70.3% (208) had a late diagnosis, and 57.1% (169) were diagnosed very late. There was an association of the very late diagnosis with the variables sex and education and with origin, entry, occurrence of opportunistic diseases, use of ARV therapy, and death, associated with late and very late diagnosis, respectively. The results of the regression model indicate that males had 2.28 [95% CI 1.11 - 4.46] higher chances of having a late diagnosis compared to females. **Conclusions:** This study evidenced a high prevalence of late and very late diagnoses in newly diagnosed male HIV patients who presented with opportunistic diseases, requiring hospitalization, and having a significant risk of progressing to death.

**Keywords:** HIV; Acquired Immunodeficiency Syndrome; late diagnosis; Nursing

## 1. Introduction

After four decades, human immunodeficiency virus (HIV) infection remains a global public health problem and continues to cause a high number of new infections. The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimates that in 2021, 1.5 million people were diagnosed with HIV[1]. The World Health Organization (WHO) has defined early diagnosis of HIV infection as one of the priorities for controlling new infections[2].

Currently, the combination of clinical and immunological aspects is used as a reference to define late diagnosis, aiming to identify the stage of HIV infection progression. For adults and adolescents, advanced HIV disease is defined as a CD4 cell count below 200 cells/mm3 or clinical stage 3 and/or 4[3]. Brazil adopts European parameters, where individuals with a CD4 count <350 cells/mm3 are considered to have a late diagnosis, and those with a count below 200 cells/mm3 are considered to have a very late diagnosis[4,5].

According to late diagnosis estimates by Collins et al. 2022, the European Union and South Africa have 51% and 55% of their diagnosed individuals with CD4 T-cell counts below 350 cells/mm3, respectively. When considering counts below 200 cells/mm3, this percentage drops to 31% in both regions[4].

Once early diagnosis is established, starting antiretroviral therapy (ART) and maintaining CD4+ cell counts above 500 cells/mm3 with undetectable viral load, life expectancy similar to that of individuals not living with the virus can be observed[6].

In Canada, a study reported that in order to achieve the priority goal of early diagnosis of HIV-infected individuals, it is essential not to miss opportunities in health services, increasing the

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availability of rapid tests to reach asymptomatic individuals with CD4+ cell counts above 500 cells/mm3 and without opportunistic diseases[6,7].

Chone et al. (2022), in Mozambique, observed that despite all the progress in combating the HIV epidemic in the region, some challenges remain, such as the high prevalence of late HIV diagnoses, even after the widespread availability and promotion of free diagnostic tests[8].

Late presentation continues to be a major challenge worldwide, despite all efforts made to prevent diseases and mortality associated with late initiation of antiretroviral therapy (ART) and ensure continuous HIV treatment adherence[9]. In this context, a study in China showed a 57.6% increase (95% CI: 54.5-60.7%) in late HIV diagnosis. Over four years, there was an increase in late presentation of HIV infection, with rates of 52.8% in 2017 and 61.2% in 2020[10].

Thus, the first CD4 T-cell count allows determining the stage of the disease. In Brazil, a high number of people living with HIV/AIDS (PLWHA) present themselves for the first time to the public health system (SUS) with a CD4 count below 200 cells/mm$^3$ [5]. Between 2012 and 2015, there was a decline in the trend of late presentation and advanced disease at healthcare facilities. However, in the historical series from 2015 to 2019, the rate of late diagnoses remained stable, with a 29% increase from September 2022[5]. Therefore, this study aimed to identify factors associated with late diagnosis and clinically monitor newly diagnosed HIV/AIDS patients.

## 2. Method

This is an observational, analytical study with a quantitative approach, retrospectively based on secondary data collected from the Electronic Patient Record (EPR).

The study was conducted at a specialized unit of a large tertiary hospital in the interior of São Paulo, the Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto da Universidade de São Paulo (HCFMRP-USP). The Specialized Unit for Infectious Diseases Therapy (UETDI) was inaugurated in 1996 with the aim of serving patients diagnosed with HIV/AIDS. It is considered a tertiary reference for the care of PLHIV in the Regional Health Department XIII (DRS XIII), which encompasses 26 municipalities. The healthcare is exclusively provided through the Unified Health System (SUS). The unit comprises three sectors: ward, day hospital, and outpatient clinic for patients requiring medium to high complexity care.

The study population consists of newly diagnosed cases of HIV/AIDS who sought initial care through outpatient appointments or hospitalization in the ward, whether referred from other services or not. Inclusion criteria were adopted as follows: To be aged 18 or older, of both sexes; have available electronic medical records; have been diagnosed with HIV/AIDS in the past 6 months; and be the first visit to UETDI, either through outpatient care or ward admission, between 2015 and 2019. Pregnant individuals were excluded.

Data collection for sociodemographic, behavioral, clinical, and laboratory variables was done using patient record entries through a questionnaire developed for this study (APPENDIX A). The chosen period was 2015 to 2019, as electronic medical records were implemented in 2015, replacing paper documents. A review of all patient records during the selected period who received care initially through the unit's outpatient clinic and later through the ward was conducted. Data for one year after the initial visit were also collected using the same instrument, aiming to gather information on clinical progress, latest viral load and CD4 T-cell count results, comorbidities during this period, number of recurrent hospitalizations, and deaths.

The following variables were selected: a) sociodemographic: sex (female/male), sexual orientation, date of birth, age, place of birth and origin, marital status, and education level; b) behavioral: smoking, alcohol consumption, illicit drug use, types of illicit drugs, and duration of illicit drug use; c) clinical-epidemiological: date of first visit, patient's origin, duration of HIV infection diagnosis, use of antiretroviral therapy (ART), duration of ART use, CD4 T-cell count, individual viral load quantification, associated comorbidities, number of recurrent hospitalizations, and treatment abandonment; d) death criteria (death report mentioning AIDS or HIV and cause of death associated with immunodeficiency - without classification by another criteria after investigation; date

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of death; reason and location), described according to the B20-B24 codes of the International Classification of Diseases (ICD-10) and recorded in the electronic medical records.

The data were entered into an Excel spreadsheet for Windows, with double entry and data validation to identify possible typing errors. Subsequently, the spreadsheet was imported into the Statistical Package for the Social Sciences (SPSS), version 25.0 for Windows, for data analysis. Descriptive statistics, such as mean, median, standard deviation, minimum, and maximum, were used for continuous variables, while relative and absolute frequencies were used for categorical variables. Inferential statistics, such as Fisher's exact test, paired t-test, and Logistic regression to find the odds ratio was performed, adopting a value of $\alpha \geq 0.05$.

The present research project was submitted and approved by the Research Ethics Committee of the Ribeirão Preto School of Nursing, University of São Paulo, under protocol number 4,143,945.

## 3. Results

A total of 1,120 HIV/AIDS patients were treated at the tertiary hospital during the study period, of whom 314 (28%) were newly diagnosed with HIV infection. Among the total, 70.3% (208) had a late diagnosis, and 57.1% (169) had a very late diagnosis.

Table 1 presents the sociodemographic and behavioral variables associated with receiving a late and very late diagnosis of HIV infection. An association was identified with the variables of gender (p-value = 0.01 and 0.04, respectively) and education level for the very late diagnosis (p-value = 0.03).

**Table 1.** Sociodemographic and behavioral factors of patients with late and very late diagnosis of HIV infection. Ribeirão Preto, SP, Brazil, 2022.

| Variables | Late Diagnosis (CD4 < 350) | | | Very Late Diagnosis (CD4 < 200) | | |
|---|---|---|---|---|---|---|
| | No n(%) | Yes n(%) | *p | No n(%) | Yes n(%) | *p |
| **Gender** | | | | | | |
| Female | 32 (36.36) | 46 (22.12) | 0.01 | 41 (32.28) | 37 (21.89) | 0.04 |
| Male | 56 (63.64) | 162 (77.88) | | 86 (67.72) | 132 (78.11) | |
| **Nationality** | | | | | | |
| Ribeirão Preto | 15 (17.05) | 43 (20.67) | 0.37 | 26 (20.47) | 32 (18.93) | 0.17 |
| Ribeirão Preto Region | 17 (19.32) | 30 (14.42) | | 24 (18.90) | 23 (13.61) | |
| State of São Paulo | 37 (42.05) | 75 (36.06) | | 51 (40.16) | 61 (36.09) | |
| Outside the state of São Paulo | 19 (21.59) | 60 (28.85) | | 26 (20.47) | 53 (31.36) | |
| **Origin** | | | | | | |
| Ribeirão Preto | 31 (35.23) | 74 (36.63) | 0.37 | 41 (32.80) | 64 (38.79) | 0.11 |
| Ribeirão Preto Region | 18 (20.45) | 49 (24.26) | | 29 (23.20) | 38 (23.03) | |
| State of São Paulo | 39 (44.32) | 74 (36.63) | | 55 (44.00) | 58 (35.15) | |
| Outside the State of São Paulo | 0 (0) | 5 (2.48) | | 0 (0) | 5 (3.03) | |
| **Marital State** | | | | | | |
| Single | 48 (54.55) | 114 (55.07) | 0.90 | 72 (56.69) | 90 (53.57) | 0.72 |
| Married/Common-law/Living as married | 28 (31.82) | 61 (29.47) | | 38 (29.92) | 51 (30.36) | |
| Widower | 4 (4.55) | 8 (3.86) | | 6 (4.72) | 6 (3.57) | |
| Separated/Divorced | 8 (9.09) | 24 (11.59) | | 11 (8.66) | 21 (12.50) | |
| **Education Level** | | | | | | |
| Elementary School | 39 (44.83) | 108 (52.68) | 0.52 | 53 (42.40) | 94 (56.29) | 0.03 |
| High School | 33 (37.93) | 72 (35.12) | | 48 (38.47) | 57 (34.13) | |
| University | 12 (13.79) | 20 (9.76) | | 20 (16.00) | 12 (7.19) | |
| Illiterate | 3 (3.45) | 5 (2.44) | | 4 (3.20) | 4 (2.40) | |
| **Sexual Orientation** | | | | | | |
| Straight | 50 (60.98) | 129 (67.89) | 0.89 | 73 (61.34) | 106 (69.28) | 0.34 |

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| | | | | | | |
|---|---|---|---|---|---|---|
| Bisexual | 8 (9.76) | 12 (6.32) | | 10 (8.40) | 10 (6.54) | |
| Homosexual | 16 (19.51) | 27 (14.21) | | 24 (20.17) | 19 (12.42) | |
| MSM | 8 (9.76) | 21 (11.05) | | 12 (10.08) | 17 (11.11) | |
| Others | 0 (0) | 1 (0.53) | | 0 (0) | 1 (0.65) | |
| **Smoker** | | | | | | |
| Yes | 55 (63.22) | 128 (61.84) | 0.89 | 101 (80.16) | 127 (76.05) | 0.47 |
| No | 32 (36.78) | 79 (38.16) | | 25 (19.84) | 40 (23.95) | |
| **Drug Use** | | | | | | |
| Yes | 33 (37.50) | 76 (37.07) | 1.00 | 46 (36.22) | 63 (37.95) | 0.80 |
| No | 55 (62.50) | 129 (62.50) | | 81 (63.78) | 103 (62.05) | |

Source: Study Data, Ribeirão Preto/SP, 2022.

Regarding the clinical variables, an association was identified between the variables of origin, admission, and the occurrence of opportunistic diseases [p < 0.001] with late and very late diagnosis. There was also an association between the use of antiretroviral therapy (p-value = 0.04 and 0.01) and death (p-value = 0.01 and <0.001) with late and very late diagnosis, respectively (Table 2).

**Table 2.** Clinical factors associated with late and very late diagnosis among people diagnosed with HIV/AIDS infection. Ribeirão Preto, SP, Brazil, 2022.

| Variable | Late Diagnosis (CD4 < 350) | | | Very Late Diagnosis (CD4 < 200) | | |
|---|---|---|---|---|---|---|
| | No n(%) | Yes n(%) | *p | No n(%) | Yes n(%) | *p |
| **Time of Diagnosis (month)** | | | | | | |
| **< 1** | 34 (38.64) | 103 (49.52) | | 54 (42.52) | 83 (49.11) | |
| **1 a 3** | 44 (50.00) | 79 (37.98) | 0.15 | 56 (44.09) | 67 (39.64) | 0.53 |
| **3 a 6** | 10 (11.36) | 26 (12.50) | | 17 (13.39) | 19 (11.24) | |
| **Origin** | | | | | | |
| Home | 73 (84.88) | 98 (48.28) | | 103 (82.40) | 68 (41.46) | |
| UBDS | 2 (2.33) | 27 (13.30) | | 4 (3.20) | 25 (15.24) | |
| Emergency Unit | 2 (2.33) | 21 (10.34) | <0.001 | 5 (4.00) | 18 (10.98) | <0.001 |
| Transfer within the HC | 1 (1.16) | 13 (6.40) | | 3 (2.40) | 11 (6.71) | |
| Transfer from another city | 6 (6.98) | 39 (19.21) | | 7 (5.60) | 38 (23.17) | |
| Transfer from an institution in RP | 2 (2.33) | 5 (2.46) | | 3 (2.40) | 4 (2.44) | |
| **Admission** | | | | | | |
| Hospital Ward – Inpatient | 13 (14.77) | 115 (55.29) | | 22 (17.32) | 106 (62.72) | |
| Emergency Care | 60 (68.18) | 67 (32.21) | <0.001 | 86 (67.72) | 41 (24.36) | <0.001 |
| Outpatient Clinic | 15 (17.05) | 26 (12.50) | | 19 (14.96) | 22 (13.02) | |
| **Opportunistic Disease** | | | | | | |
| Yes | 33 (37.50) | 181 (87.02) | <0.001 | 54 (42.52) | 160 (94.67) | <0.001 |
| No | 55 (62.50) | 27 (12.98) | | 73 (57.48) | 9 (5.33) | |
| **ART** | | | | | | |
| Yes | 10 (11.36) | 44 (21.15) | 0.04 | 15 (11.81) | 39 (23.08) | 0.01 |
| No | 78 (88.64) | 164 (78.85) | | 112 (88.19) | 130 (76.92) | |
| **Time of ART (month)** | | | | | | |
| **< 1** | 3 (33.33) | 16 (37.21) | | 4 (30.77) | 15 (38.46) | |
| 1 a 3 | 5 (55.56) | 19 (44.19) | 1.00 | 6 (46.15) | 18 (46.15) | 0.83 |
| 3 a 6 | 1 (11.11) | 8 (18.60) | | 3 (23.08) | 6 (15.38) | |
| **Death** | | | | | | |
| Yes | 5 (5.68) | 32 (15.38) | | 9 (7.09) | 28 (16.57) | |
| No | 59 (67.05) | 120 (57.69) | 0.01 | 89 (70.08) | 90 (53.25) | <0.001 |
| Transfer | 13 (14.77) | 44 (21.15) | | 17 (13.39) | 40 (23.67) | |
| Loss of Segment | 11 (12.50) | 12 (5.77) | | 12 (9.45) | 11 (6.51) | |

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Source: Study Data, Ribeirão Preto/SP, 2022.

The results of the regression model indicate that male individuals had 2.28 [1.11 - 4.46] times higher odds of having a late diagnosis compared to females. Having a higher education level (college degree) was a protective factor compared to having only a primary education for late diagnosis. Additionally, not having an opportunistic disease was a protective factor for not having a late diagnosis compared to individuals with an opportunistic disease [OR=0.12, 95% CI 0.06 - 0.24], as shown in Table 3.

Furthermore, individuals who entered through the emergency department had a lower chance [0.11, 95% CI 0.01 - 0.66] of having a very late diagnosis compared to those diagnosed in the ward/inpatient unit. Not having an opportunistic disease [0.6, 95% CI 0.02 - 0.14] and having a higher education level [0.09, 95% CI 0.09 - 0.90] were protective factors for not having a very late diagnosis of HIV infection, as shown in Table 4.

**Table 3.** Factor associated with late diagnosis of HIV infection according to the logistic regression model. Ribeirão Preto, SP, Brazil, 2022.

| **CD4 < 350 *** | **Odds Ratio Bruto** | **CI95%** | ***p valor*** | **Odds Ratio Ajustado** | **CI95%** | ***p valor*** |
|---|---|---|---|---|---|---|
| **Age** | 1.022 | 1.001 – 1.044 | 0.04 | 1.013 | 0.987 – 1.039 | 0.32 |
| **Gender** | | | | | | |
| Female | | *Comparison Category* | | | *Comparison Category* | |
| Male | 2.01 | 1.16 – 3.46 | 0.01 | 2.28 | 1.11 – 4.46 | 0.02 |
| **Origin** | | | | | | |
| Home | | *Comparison Category* | | | *Comparison Category* | |
| UBDS | 6.4 | 1.47 – 27.73 | 0.01 | 1.32 | 0.117 -15.046 | 0.82 |
| Emergency unit | 4.8 | 1.111 – 21.146 | 0.04 | 0.79 | 0.071 – 8.878 | 0.85 |
| Transfer within the HC | 5.8 | 0.749 – 45.175 | 0.09 | 1.85 | 0.115 – 30.028 | 0.66 |
| Transfer from another city | 3.1 | 1.289 – 7.799 | 0.01 | 0.52 | 0.073 – 3.749 | 0.52 |
| Transfer from another unit in Ribeirão Preto | 1.0 | 0.202 – 5.576 | 0.94 | 0.21 | 0.019 – 2.292 | 0.20 |
| **Admission** | | | | | | |
| Hospital Ward - Inpatient | | *Comparison Category* | | | *Comparison Category* | |
| Emergency Care | 0.222 | 0.129 – 0.378 | <0.0001 | 0.238 | 0.035 – 1.618 | 0.14 |
| Outpatient Clinic | 0.695 | 0.348 – 1.388 | 0.30 | 0.292 | 0.038 – 2.242 | 0.24 |
| **Opportunistic Disease** | | | | | | |
| Yes | | *Comparison Category* | | | *Comparison Category* | |
| No | 0.08 | 0.04–0.16 | <0.0001 | 0.12 | 0.06 – 0.24 | <0.0001 |
| **Viral Load (VL)_1** | 1 | 0.99–1.00 | 0.10 | 1 | 0.999 – 1,0 | 0.49 |
| **ART** | | | | | | |
| Yes | | *Comparison Category* | | | *Comparison Category* | |
| No | 0.478 | 0.228–0.999 | 0.05 | 0.781 | 0.310–1.964 | 0.60 |
| **Death** | | | | | | |
| Yes | | *Comparison Category* | | | *Comparison Category* | |
| No | 0.670 | 0.397–1.130 | 0.13 | 1.029 | 0.295 – 3.585 | 0.96 |
| Transfer | 1.548 | 0.787–3.044 | 0.21 | 0.706 | 0.173 – 2.886 | 0.63 |

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| | | | | | | |
|---|---|---|---|---|---|---|
| Loss of Segment | 0.429 | 0.181–1.012 | 0.05 | 0.313 | 0.068 – 1.454 | 0.14 |

**Table 4.** Factor associated with very late diagnosis of HIV infection according to the logistic regression model. Ribeirão Preto, SP, Brazil, 2022.

| CD4 < 200 ** | Odds Ratio Bruto | CI95% | p valor | Odds Ratio Adjusted | CI95% | p valor |
|---|---|---|---|---|---|---|
| **Age** | 1.019 | 0.999 - 1.038 | 0.06 | 0.997 | 0.968 – 1.027 | 0.84 |
| **Gender** | | | | | | |
| Female | | *Comparison Category* | | | *Comparison Category* | |
| Male | 1.70 | 1.01 – 2.86 | 0.04 | 1.92 | 0.91 – 4.05 | 0.08 |
| **Origin** | | | | | | |
| Home | | *Comparison Category* | | | *Comparison Category* | |
| UBDS | 5.441 | 1.842 -16.073 | 0.002 | 0.902 | 0.1005 – 8.098 | 0.93 |
| Emergency Unit | 2.959 | 1.067 – 8.204 | 0.04 | 0.381 | 0.050 – 2.907 | 0.35 |
| Transfer within the HC | 2.924 | 0.798 – 10.713 | 0.10 | 1.044 | 0.119 – 9.185 | 0.97 |
| Transfer from another city | 5.084 | 2.185 – 11.827 | <0.0001 | 0.522 | 0.083 – 3.284 | 0.49 |
| Transfer from another unit in Ribeirão Preto | 1.017 | 0.223 – 4.627 | 0.98 | 0.261 | 0.024 – 2.881 | 0.27 |
| **Admission** | | | | | | |
| Hospital Ward - Inpatient | | *Comparison Category* | | | *Comparison Category* | |
| Emergency Care | 0.153 | 0.092 – 0.255 | <0.0001 | 0.11 | 0.01 – 0.66 | 0.01 |
| Outpatient Clinic | 0.851 | 0.439 – 1.649 | 0.63 | 0.24 | 0.03- 1.608 | 0.14 |
| **Opportunistic Disease** | | | | | | |
| Yes | | *Comparison Category* | | | *Comparison Category* | |
| No | 0.042 | 0.019 – 0.089 | <0.0001 | 0.06 | 0.02 – 0.14 | <0.0001 |
| **Viral Load (VL)_1** | 1.0 | 1.0 – 1.0001 | 0.03 | 1.0 | 0.999 – 1.00 | 0.13 |
| **ART** | | | | | | |
| Yes | | *Comparison Category* | | | *Comparison Category* | |
| No | 0.446 | 0.234 – 0.853 | 0.01 | 0.629 | 0.259 – 1.528 | 0.31 |
| **Education Level** | | | | | | |
| Elementary School | | *Comparison Category* | | | *Comparison Category* | |
| High School | 0.849 | 0.521 – 1.385 | 0.51 | 0.257 | 0.034 – 1.957 | 0.19 |
| University | 0.432 | 0.201 – 0.927 | 0.03 | 0.09 | 0.09 – 0.90 | 0.04 |
| Technical Education | 0.744 | 0.148 – 3.749 | 0.72 | 0.129 | 0.008 – 2.087 | 0.15 |
| **Death** | | | | | | |
| Yes | | *Comparison Category* | | | *Comparison Category* | |
| No | 0.486 | 0.299 – 0.790 | 0.004 | 1.429 | 0.492 – 4.153 | 0.51 |
| Transfer | 2.006 | 1.077 – 3.737 | 0.03 | 1.159 | 0.342 – 3.935 | 0.81 |
| Loss of Segment | 0.667 | 0.284 – 1.565 | 0.35 | 0.713 | 0.162 – 3.129 | 0.65 |

*CI = 95% Confidence Interval; Valor-p Source: Study Data, Ribeirão Preto/SP, 2022.

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## 4. Discussion

This study revealed that although patients seen in the initial care arrive as newly diagnosed cases of HIV, the majority can be considered as having a late diagnosis. Of the patients, 66.2% had a CD4+ T-cell count below 350 cells/mm³ (late diagnosis), and 53.8% had a CD4+ T-cell count below 200 cells/mm³ (very late diagnosis). This high rate is similar to a study conducted in a state in Northeast Brazil, which reported 59.1% in 2017[6], and to other countries such as China, where a percentage greater than 60% was observed from 2015 to 2016[11], and Ethiopia, with 68.8% in 2014[12]. These data are alarming and higher when compared to national figures, which identified percentages of 42% in 2015[13] and 48% in 2022[5] of individuals diagnosed with a CD4+ T-cell count below 350 cells/mm³.

Certain sociodemographic factors, such as educational level and knowledge, may be directly linked to access to healthcare, impacting the prevalence of late or very late diagnosis[14]. In this study, it was found that 56.29% (n=94) of patients detected with a CD4+ T-cell count below 200 cells/mm³ had only a primary education, similar to findings from a European cohort study conducted from 1996 to 2013, which identified that lower educational attainment was associated with a higher chance of individuals having lower CD4+ T-cell counts and a lower chance of viral suppression[15]. Another study conducted in Minas Gerais, Brazil, between 2012 and 2018, also found evidence of an association between lower education and a lower chance of achieving viral suppression[16].

Regarding gender, this study found that being male was a factor associated with late diagnosis, which is consistent with previous research. In Nigeria, a high percentage of men were also identified as receiving a late HIV diagnosis (90.1% vs. 83.3% for women; $P < 0.001$) or having advanced disease (70.4% vs. 59.2% for women; $P < 0.001$)[17]. Another study conducted in Salvador, Brazil, found that being male increased the chances of delayed diagnosis, with an adjusted odds ratio of 3.02; 95% CI, 2.0-4.6[18]. According to data from the Brazilian Ministry of Health, when stratified by gender, men stand out compared to women. Regarding late diagnosis (CD4+ T-cell count < 350 cells/mm³), as of September 2022, the proportion between sexes was 49% male and 46% female. When it comes to very late diagnosis (CD4+ T-cell count < 200 cells/mm³), this proportion was 29% among men and 27% among women[5].

The higher prevalence observed in males may be related to advances and achievements in HIV response policies for women[19] and pregnant women, such as individual or group counseling, family planning, regular gynecological care, prenatal care, HIV testing centers, and maternity wards[20]. Therefore, access to screening for infections like HIV serves as a facilitator for preventive measures and timely diagnosis. A study conducted in Ghana in 2018 confirmed that the prevalence of HIV among pregnant women was lower compared to the general population[21]. On the other hand, the testing policy during prenatal care has certain effects on the male population, as women discover the presence of HIV infection during pregnancy or through illness, leading to the diagnosis being discovered by their male partners[22].

It is worth noting that the majority of HIV infections occur in men who identify as heterosexual, accounting for 59.6% (n=187) of cases. The literature suggests that this population perceives themselves to be at low risk and does not consider themselves part of the at-risk population[22]. A systematic review conducted in Africa found that factors such as the role of being the head of the family, fear of sexual behavior after a positive result, stigma, and the societal construction of men as strong and self-sufficient contribute to the higher likelihood of late HIV diagnosis among heterosexual men[23].

Nationally, despite the increasing prevalence of HIV/AIDS cases among men who have sex with men (MSM) in recent years, the proportion of cases related to heterosexual exposure remains significant. In the southern region of Brazil, for example, heterosexual exposure accounted for 45.2% of AIDS cases in 2021[24].

A study conducted in the southern region of Brazil in 2019 showed that low risk perception is extremely relevant. Over 90% of individuals interviewed identified themselves as having low or no risk of HIV infection, and over 30% had never been tested for HIV because they did not consider themselves at risk or saw no reason to get tested[25].

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Regarding the mode of entry, entering the healthcare facility through the ward was associated with late diagnosis compared to patients who came for outpatient consultations. This finding is similar to a study conducted in Malawi in 2020, which found that 53.3% of hospitalized patients newly diagnosed with HIV had a CD4+ T-cell count below 200 cells/mm$^3$, and 32% already had counts below 100 cells/mm$^3$ [26]. Another study conducted in South Africa between 2014 and 2015 showed that patients entering the healthcare system through inpatient settings were more likely to have late HIV diagnosis compared to those entering through outpatient settings. Hospitalized patients had very low CD4+ T-cell counts, with a median of 37 cells/mm$^3$, which was higher than the counts observed in outpatient patients[27].

Hospitalized patients had very low CD4+ T-cell counts, with a median of 37 cells/mm$^3$, which was higher than the counts observed in outpatient patients. In this study, the use of antiretroviral therapy (ART) was a protective factor against late diagnosis, with a p-value of 0.050 and a 95% confidence interval of 0.228-0.999. The literature highlights the positive impact of immediate initiation of ART after HIV diagnosis[28]. Viral suppression through ART has both individual and collective health effects, as the treatment serves as prevention of new infections[29]. In the United Kingdom, a significant number of people living with HIV achieved viral suppression, reaching 97%, further emphasizing the effectiveness of ART treatment[30].

A retrospective cohort study conducted in China between 2006 and 2020 demonstrated that the early initiation of ART in people living with HIV significantly reduced the mortality rate in this population, directly impacting overall mortality rates. However, the same study found that factors such as being male, having a very late HIV diagnosis, initiating ART after 12 months of diagnosis, and virologic failure (detectable viral load after 6 months of treatment initiation or modification) influenced a higher mortality rate[31,32].

Despite advances in treatment and care for people living with HIV, mortality rates remain high in cases of late diagnosis[24]. A study conducted in Colombia between 2009 and 2014 with people living with HIV found that 80% of ICU admissions were associated with opportunistic infections, with 57% attributed to respiratory failure as the leading cause of death in this population[33]. Similarly, another study conducted in French hospitals between 1997 and 2020 showed that although the proportion of admissions for HIV-diagnosed patients and the rate of opportunistic infections significantly decreased, the reasons for admission remained consistent over time, with respiratory failure being the main cause[34].

A similar study in Korea between 2004 and 2018 demonstrated that the development of opportunistic diseases within 6 months after HIV diagnosis was more common in men. Additionally, individuals overall had higher mortality rates when they had AIDS-defining illnesses and AIDS-associated cancers[35]. It is important to highlight the significance of treatment adherence, as higher mortality rates are observed in people living with HIV who are not adequately treated[36].

It is known that initiating ART as early as possible leads to health benefits for the individual, reducing the occurrence of severe events, preventing progression to AIDS, and reducing the risk of HIV transmission[37]. However, it is worth noting that even after immune recovery in individuals who initiated ART with a CD4+ T-cell count below 200 cells/mm$^3$, they may still be at high risk of AIDS-related complications and death, as shown in a study in Greece in 2019[38]. In South Africa, laboratory data from 2010 to 2014 were used to analyze the immune recovery in individuals on ART and it was found that those who initiated ART with a very late diagnosis and a CD4+ T-cell count below 50 cells/mm$^3$ continued to have an average CD4+ T-cell count below 200 cells/mm$^3$ after 12 months of treatment[39].

Late HIV diagnosis has consequences for both individual and public health[40], as well as economic implications[12]. Therefore, strategies are needed to improve timely diagnosis, such as targeted campaigns for prevention and diagnosis, promotion of early testing, and care[41]. Overcoming barriers such as difficulties in accessing tests, lack of awareness of HIV-related risks and diseases, stigma, and prejudice can significantly reduce cases of late diagnosis[42].

The implementation of effective strategies that enable early detection of HIV diagnosis is clearly necessary, leading to a reduction in disease transmissibility and consequently decreasing the

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likelihood of late diagnoses[43]. In Spain, in 2019, it was found that 16% of patients diagnosed with HIV had missed opportunities for diagnosis in the previous 5 years, as they sought medical attention for other associated illnesses but did not undergo testing for HIV[43]. Similarly, a study in Canada from 2001 to 2014 showed that 7 to 14% of individuals had one or more missed opportunities for HIV diagnosis, even in a setting with unrestricted healthcare[7].

AIDS-related mortality is strongly associated with late presentation, particularly in the first year following HIV diagnosis. It is clear that one of the causes is the missed opportunities for serological testing when individuals seek healthcare services prior to diagnosis[44].

As a retrospective cohort study, this study is subject to limitations that include obtaining secondary data from electronic medical records, which means that some information could not be further explored, such as monitoring and clinical outcomes of patients who were transferred to other HIV and AIDS reference centers within and outside Ribeirão Preto, as well as inadequate completion of the available electronic data collection instruments during the initial assessment, resulting in a lack of important social and behavioral information. Another limitation was the emergence of the COVID-19 pandemic, which may have influenced some current significant results in the care and treatment of patients diagnosed with HIV, as the data collection period extended until 2019.

## 5. Discussion

This study demonstrated a high prevalence of late and very late diagnosis in patients newly diagnosed with HIV within the past 6 months, who predominantly presented with opportunistic diseases, particularly when requiring hospitalization in a tertiary hospital, with a significant risk of progression to death, posing a challenge to public health authorities in the prevention, control, and transmissibility of the disease.

Therefore, attention should be directed towards factors related to late presentation, both behavioral and clinical, such as being male adults with lower education levels, presence of opportunistic diseases, and use of ART, as evidenced in this study. It is known that late presentation is directly correlated with higher mortality rates, as also highlighted by this study. Clinical outcomes are of utmost importance when evaluating diagnosis and treatment adherence, as they reflect the barriers to prevention and the quality of care provided to this population.

The implementation of new protective measures and campaigns is essential in reducing cases of late presentation, not only among high-risk populations but also among those who perceive themselves as low or no risk. However, further research needs to be conducted to fill the gaps identified in this study, including the impact of the COVID-19 pandemic on the diagnosis and treatment of these individuals and professional training, which can be considered a barrier to timely diagnosis and treatment adherence.

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Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 19 July 2023 doi:10.20944/preprints202307.1335.v1



## References


1. UNAIDS Brasil - Website institucional do Programa Conjunto das Nações Unidas sobre HIV/AIDS (UNAIDS) no Brasil. [Internet]. [quoted 27 jun 2023]. Available in: https://unaids.org.br/wp-content/uploads/2022/07/2022_07_27_Factsheet_PT.pdf
2. UNAIDS Brasil - Website institucional do Programa Conjunto das Nações Unidas sobre HIV/AIDS (UNAIDS) no Brasil. [Internet]. [quoted 27 jun 2023]. Available in: http://apps.who.int/iris/bitstream/handle/10665/179870/9789241508926_eng.pdf?sequence=1
3. World Health Organization (WHO) [Internet]. HIV and AIDS; [quoted 27 jun 2023]. Available in: http://www.who.int/mediacentre/factsheets/fs360/en/.
4. Collins S, Namiba A, Sparrowhawk A, Strachan S, Thompson M, Nakamura H. Late diagnosis of HIV in 2022: Why so little change? HIV Med [Internet]. 17 nov 2022 [quoted 27 jun 2023]. Available in: https://doi.org/10.1111/hiv.13444
5. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Relatório de Monitoramento Clínico do HIV [Internet]. [Brasília]: Ministério da Saúde (BR); 2022 [updated 05 dec 2022] [quoted 03 jul 2023]. Available in: https://www.gov.br/aids/pt-br/centrais-de-conteudo/publicacoes/2022/relatorio-de-monitoramento-clinico-do-hiv-setembro-2022.pdf/view
6. Ribeiro LC, Freitas MI, Tupinambás U, Lana FC. Late diagnosis of Human Immunodeficiency Virus infection and associated factors. Rev Lat Am Enferm [Internet]. 2020 [quoted 27 jun 2023];28. Available in: https://doi.org/10.1590/1518-8345.4072.3342
7. Nanditha NG, St-Jean M, Tafessu H, Guillemi SA, Hull MW, Lu M, Henry B, Barrios R, Montaner JS, Lima VD. Missed opportunities for earlier diagnosis of HIV in British Columbia, Canada: A retrospective cohort study. PLOS ONE [Internet]. 21 mar 2019 [quoted 27 jun 2023];14(3):e0214012. Available in: https://doi.org/10.1371/journal.pone.0214012
8. Chone JS, Abecasis AB, Varandas L. Determinants of Late HIV Presentation at Ndlavela Health Center in Mozambique. Int J Environ Res Public Health [Internet]. 11 apr 2022 [quoted 27 jun 2023];19(8):4568. Available in: https://doi.org/10.3390/ijerph19084568
9. Sogbanmu OO, Goon DT, Obi LC, Iweriebor BC, Nwodo UN, Ajayi AI, Okoh AI. Socio-demographic and clinical determinants of late presentation among patients newly diagnosed with HIV in the Eastern Cape, South Africa. Medicine [Internet]. Feb 2019 [quoted 27 jun 2023];98(8):e14664. Available in: https://doi.org/10.1097/md.0000000000014664
10. Xu Z, Shen Q, Wang D, Dong Z, Han W, Tian R, Zhou K, Ya X, Hu H. Real-world data in late presentation of HIV infection in Suzhou, China: Results from four consecutive cross-sectional surveys, 2017–2020. Front Public Health [Internet]. 21 feb 2023 [quoted 27 jun 2023];11. Available in: https://doi.org/10.3389/fpubh.2023.1084840
11. Xie J, Hsieh E, Sun MQ, Wang HL, Lv W, Fan HW, Li TS. Delays in HIV diagnosis and associated factors among patients presenting with advanced disease at a tertiary care hospital in Beijing, China. PLOS ONE [Internet]. 9 aug 2017 [quoted 27 jun 2023];12(8):e0182335. Available in: https://doi.org/10.1371/journal.pone.0182335
12. Assen A, Molla F, Wondimu A, Abrha S, Melkam W, Tadesse E, Yilma Z, Eticha T, Abrha H, Workneh BD. Late presentation for diagnosis of HIV infection among HIV positive patients in South Tigray Zone, Ethiopia. BMC Public Health [Internet]. 12 jul 2016 [quoted 27 jun 2023];16(1). Available in: https://doi.org/10.1186/s12889-016-3263-y
13. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde - Departamento de DST, Aids e Hepatites Virais. Boletim Epidemiológico HIV/Aids. [Internet]. [Brasília]: Ministério da Saúde (BR); 2015 [updated 04 may 2017] [quoted 03 jul 2023]. Available in: http://antigo.aids.gov.br/pt-br/pub/2015/boletim-epidemiologico-hivaids-2015
14. Cota VL, Cruz MM. Barreiras de acesso para Homens que fazem Sexo com Homens à testagem e tratamento do HIV no município de Curitiba (PR). Saude Debate. 2021;45(129):393-405.
15. Del Amo J. Inequalities by educational level in response to combination antiretroviral treatment and survival in HIV-positive men and women in Europe. AIDS [Internet]. Jan 2017 [quoted 28 jun 2023];31(2):253-62. Available in: https://doi.org/10.1097/qad.0000000000001270
16. Raposo MA, Miranda JC, Guimarães NS, Tupinambás U. Efetividade do tratamento antirretroviral após 12 e 66 meses em centro de referência para pessoas vivendo com HIV, Belo Horizonte, Minas Gerais - 2012 a

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 19 July 2023 doi:10.20944/preprints202307.1335.v1



2018. Rev Medica Minas Gerais [Internet]. 2021 [quoted 28 jun 2023];31. Disponível em: https://doi.org/10.5935/2238-3182.20210001

17. Agaba P, Meloni S, Sule H, Agbaji O, Ekeh P, Job G, Nyango N, Ugoagwu P, Imade G, Idoko J, Kanki P. Patients who present late to HIV care and associated risk factors in Nigeria. HIV Med [Internet]. 20 jan 2014 [quoted 28 jun 2023];15(7):396-405. Available in: https://doi.org/10.1111/hiv.12125
18. MacCarthy S, Hoffmann M, Nunn A, Silva LA, Dourado I. Barriers to HIV testing, linkage to care, and treatment adherence: a cross-sectional study from a large urban center of Brazil. Rev Panam Salud Publica. 2016;40(6):418-26.
19. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Boletim Epidemiológico Especial HIV/Aids. [Internet]. [Brasília]: Ministério da Saúde (BR); 2019 [updated 05 aug 2022] [quoted 03 jul 2023]. Available in: https://www.gov.br/saude/pt-br/centrais-de-conteudo/publicacoes/boletins/epidemiologicos/especiais/2019/boletim-epidemiologico-especial-hiv-aids-2019/view.
20. Ministério da Saúde (BR). Secretaria Executiva. Coordenação Nacional de DST e Aids. Políticas e diretrizes de prevenção das DST/aids entre mulheres. [Internet]. [Brasília]: Ministério da Saúde (BR); 2003 [quoted 03 jul 2023]. Available in: https://bvsms.saude.gov.br/bvs/publicacoes/cd04_19.pdf
21. Abuku VG, Allotey EA, Akonde M. Clinical and laboratory presentation of first-time antenatal care visits of pregnant women in Ghana, a hospital-based study. PLOS ONE [Internet]. 4 jan 2023 [quoted 28 jun 2023];18(1):e0280031. Available in: https://doi.org/10.1371/journal.pone.0280031
22. Knauth DR, Hentges B, Macedo JL, Pilecco FB, Teixeira LB, Leal AF. O diagnóstico do HIV/aids em homens heterossexuais: a surpresa permanece mesmo após mais de 30 anos de epidemia. Cad Saude Publica [Internet]. 2020 [quoted 28 jun 2023];36(6). Available in: https://doi.org/10.1590/0102-311x00170118
23. Sileo KM, Fielding-Miller R, Dworkin SL, Fleming PJ. What Role Do Masculine Norms Play in Men's HIV Testing in Sub-Saharan Africa?: A Scoping Review. AIDS Behav [Internet]. 18 may 2018 [quoted 28 jun 2023];22(8):2468-79. Available in: https://doi.org/10.1007/s10461-018-2160-z
24. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Departamento de Doenças de Condições Crônicas e Infecções Sexualmente Transmissíveis. Boletim Epidemiológico HIV/Aids. [Internet]. [Brasília]: Ministério da Saúde (BR); 2022 [updated 31 jan 2023] [quoted 03 jul 2023]. Available in: https://www.gov.br/aids/pt-br/centrais-de-conteudo/boletins-epidemiologicos/2022/hiv-aids/boletim_hiv_aids_-2022_internet_31-01-23.pdf/view
25. Damacena GN, Cruz MM, Cota VL, Souza Júnior PR, Szwarcwald CL. Conhecimento e práticas de risco à infecção pelo HIV na população geral, homens jovens e HSH em três municípios brasileiros em 2019. Cad Saude Publica [Internet]. 2022 [quoted 28 jun 2023];38(4). Available in: https://doi.org/10.1590/0102-311xpt155821
26. Heller T, Damba D, Kumwenda T, Huwa J, Kamamia C, Nhlema A, Wallrauch C, Chawinga C, Kanyama C, Gondwe-Chunda L, Ngoma J, Matanje B, Tweya H. Implementing Advanced HIV Disease Care for Inpatients in a Referral Hospital in Malawi – Demand, Results and Cost Implications. Ann Glob Health [Internet]. 2022 [quoted 28 jun 2023];88(1). Available in: https://doi.org/10.5334/aogh.3532
27. Coetzee LM, Cassim N, Sriruttan C, Mhlanga M, Govender NP, Glencross DK. Cryptococcal antigen positivity combined with the percentage of HIV-seropositive samples with CD4 counts <100 cells/μl identifies districts in South Africa with advanced burden of disease. PLOS ONE [Internet]. 12 jun 2018 [quoted 28 jun 2023];13(6):e0198993. Available in: https://doi.org/10.1371/journal.pone.0198993
28. Tymejczyk O, Brazier E, Yiannoutsos CT, Vinikoor M, van Lettow M, Nalugoda F, Urassa M, Sinayobye JD, Rebeiro PF, Wools-Kaloustian K, Davies MA, Zaniewski E, Anderegg N, Liu G, Ford N, Nash D. Changes in rapid HIV treatment initiation after national "treat all" policy adoption in 6 sub-Saharan African countries: Regression discontinuity analysis. PLOS Med [Internet]. 10 jun 2019 [quoted 28 jun 2023];16(6):e1002822. Available in: https://doi.org/10.1371/journal.pmed.1002822
29. Kay ES, Batey DS, Mugavero MJ. The HIV treatment cascade and care continuum: updates, goals, and recommendations for the future. AIDS Res Ther [Internet]. 8 nov 2016 [quoted 28 jun 2023];13(1). Available in: https://doi.org/10.1186/s12981-016-0120-0
30. Shah A, Sun S, Brown A, Nash S, Harris R, Kirwan P, Birrell P, Angelis DD, Presanis A, Chau C, Khawam J, Aghaizu A, Lister AN, Kall M, Shonaike J, Mohammed H, Ratna N, Murphy G, Hughes G, Sullivan AK,

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 19 July 2023 doi:10.20944/preprints202307.1335.v1



Connor N, Delpech V. Trends in HIV testing, new diagnoses and people receiving HIV-related care in the United Kingdom: data to the end of December 2019. Health Prot Rep. 2020;14(20).

31. Niu D, Xiao T, Chen Y, Tang H, Chen F, Cai C, Qin Q, Zhao D, Jin Y, Wang S, Hou Y, Lu Z, Yang L, Liu H, Xie D, Zou H, Lyu F. Excess mortality and associated factors among people living with HIV initiating highly active antiretroviral therapy in Luzhou, China 2006–2020. BMC Infect Dis [Internet]. 29 mar 2023 [quoted 28 jun 2023];23(1). Available in: https://doi.org/10.1186/s12879-023-08165-4
32. Ministério da Saúde (BR). Secretaria de Vigilância em Saúde. Departamento de Vigilância, Prevenção e Controle das Infecções Sexualmente Transmissíveis, do HIV/Aids e das Hepatites Virais. Protocolo Clínico e Diretrizes Terapêuticas para Manejo da Infecção pelo HIV em Adultos. [Internet]. [Brasília]: Ministério da Saúde (BR); 2018 [updated 29 jul 2022] [citado 03 jul 2023]. Available in: https://www.gov.br/aids/pt-br/centrais-de-conteudo/pcdts/2013/hiv-aids/pcdt_manejo_adulto_12_2018_web.pdf/view
33. Penagos Gaviria S, Zapata N, Villa P, Agudelo CA, Molina FJ, González MA, Durango LV, Zapata S, Galeano C, Cardona J, Rivera S, Hidron AI. HIV/AIDS infection in critical care: epidemiological profile and risk factors for mortality in a Colombian cohort. J Infect Dev Ctries [Internet]. 31 jan 2023 [quoted 28 jun 2023];17(01):102-10. Available in: https://doi.org/10.3855/jidc.15859
34. Gaillet A, Azoulay E, de Montmollin E, Garrouste-Orgeas M, Cohen Y, Dupuis C, Schwebel C, Reignier J, Siami S, Argaud L, Adrie C, Mourvillier B, Ruckly S, Forel JM, Timsit JF. Outcomes in critically Ill HIV-infected patients between 1997 and 2020: analysis of the OUTCOMEREA multicenter cohort. Crit Care [Internet]. 13 mar 2023 [quoted 28 jun 2023];27(1). Available in: https://doi.org/10.1186/s13054-023-04325-9
35. Park B, Choi Y, Kim JH, Seong H, Kim YJ, Lee M, Seong J, Kim SW, Song JY, Choi HJ, Park DW, Kim HY, Choi JY, Kim SI, Choi BY. Mortality and Causes of Death among Individuals Diagnosed with Human Immunodeficiency Virus in Korea, 2004–2018: An Analysis of a Nationwide Population-Based Claims Database. Int J Environ Res Public Health [Internet]. 18 set 2022 [quoted 28 jun 2023];19(18):11788. Available in: https://doi.org/10.3390/ijerph191811788
36. de Coninck Z, Hussain-Alkhateeb L, Bratt G, Ekström AM, Gisslén M, Petzold M, Svedhem V. Non-AIDS Mortality Is Higher Among Successfully Treated People Living with HIV Compared with Matched HIV-Negative Control Persons: A 15-Year Follow-Up Cohort Study in Sweden. AIDS Patient Care STDs [Internet]. Aug 2018 [quoted 28 jun 2023];32(8):297-305. Available in: https://doi.org/10.1089/apc.2018.0015
37. Initiation of Antiretroviral Therapy in Early Asymptomatic HIV Infection. New Engl J Med [Internet]. 27 aug 2015 [quoted 30 jun 2023];373(9):795-807. Available in: https://doi.org/10.1056/nejmoa1506816
38. Pantazis N, Paparizos V, Papastamopoulos V, Metallidis S, Antoniadou A, Adamis G, Psichgiou M, Chini M, Sambatakou H, Chrysos G, Sipsas NV, Gogos C, Barbunakis E, Panagopoulos P, Katsarou O, Touloumi G. Low pre-ART CD4 count is associated with increased risk of clinical progression or death even after reaching 500 CD4 cells/μL on ART. PLOS ONE [Internet]. 30 mar 2023 [quoted 30 jun 2023];18(3):e0283648. Available in: https://doi.org/10.1371/journal.pone.0283648
39. Kufa T, Shubber Z, MacLeod W, Takuva S, Carmona S, Bor J, Gorgens M, Pillay Y, Puren A, Eaton JW, Fraser-Hurt N. CD4 count recovery and associated factors among individuals enrolled in the South African antiretroviral therapy programme: An analysis of national laboratory based data. PLOS ONE [Internet]. 31 may 2019 [quoted 30 jun 2023];14(5):e0217742. Available in: https://doi.org/10.1371/journal.pone.0217742
40. Darling K, Hachfeld A, Cavassini M, Kirk O, Furrer H, Wandeler G. Late presentation to HIV care despite good access to health services: current epidemiological trends and how to do better. Swiss Med Wkly [Internet]. 21 aug 2016 [quoted 30 jun 2023]. Available in: https://doi.org/10.4414/smw.2016.14348
41. Guaraldi G, Zona S, Menozzi M, Brothers TD, Carli F, Stentarelli C, Dolci G, Santoro A, Da Silva AR, Rossi E, Falutz J, Mussini C. Late presentation increases risk and costs of non-infectious comorbidities in people with HIV: an Italian cost impact study. AIDS Res Ther [Internet]. 16 feb 2017 [quoted 30 jun 2023];14(1). Available in: https://doi.org/10.1186/s12981-016-0129-4
42. Kirwan PD, Croxford S, Aghaizu A, Murphy G, Tosswill J, Brown AE, Delpech VC. Re-assessing the late HIV diagnosis surveillance definition in the era of increased and frequent testing. HIV Med [Internet]. 7 set 2022 [quoted 30 jun 2023]. Available in: https://doi.org/10.1111/hiv.13394
43. Salmerón-Béliz OJ, Pérez-Fernández E, Miró O, Salido-Mota M, Diez-Diez V, Gil-Mosquera M, Robert-Boter N, Arranz-Betegón M, Navarro-Bustos C, Guardiola-Tey JM, González-del-Castillo J. Evaluation of emergency department visits prior to an HIV diagnosis: Missed opportunities. Enfermedades Infecc Microbiol Clin (English Ed ) [Internet]. Jun 2022 [quoted 30 jun 2023]. Available in: https://doi.org/10.1016/j.eimce.2021.12.010

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 19 July 2023 doi:10.20944/preprints202307.1335.v1



44. Chadwick DR, Freedman A. Treating late HIV diagnosis as a patient safety issue in the UK. Lancet HIV [Internet]. Jun 2019 [quoted 30 jun 2023];6(6):e346-e348. Available in: https://doi.org/10.1016/s2352-3018(19)30044-x

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