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## MORTALITY IN ADULT PATIENTS WITH HIV: A RETROSPECTIVE STUDY IN THE COMPREHENSIVE CARE UNIT OF ROOSEVELT HOSPITAL (2003-2023)

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***Jessenia Sabrina Navas Castillo***

Dr. Carlos Rodolfo Mejía Villatoro  
Comprehensive HIV and Chronic Infections  
Care Unit, Roosevelt Hospital.  
Department of Molecular Biology, Faculty of  
Biology, Chemistry, and Pharmacy, Galileo  
University, Guatemala City, Guatemala.  
Latin American Researchers Network  
(Redilat)

***Diana Karina Baldizón Pernillo***

Dr. Carlos Rodolfo Mejía Villatoro  
Comprehensive HIV and Chronic Infections  
Care Unit, Roosevelt Hospital.

***Julio Alberto Paxtor Caté***

Dr. Carlos Rodolfo Mejía Villatoro  
Comprehensive HIV and Chronic Infections  
Care Unit, Roosevelt Hospital.

***Mircea Lisbeth Romero Trujillo***

Dr. Carlos Rodolfo Mejía Villatoro  
Comprehensive HIV and Chronic Infections  
Care Unit, Roosevelt Hospital.  
ORCID: [org/0009-0009-3217-9803](https://orcid.org/0009-0009-3217-9803)

***Corilia Sucely García Porres***

Dr. Carlos Rodolfo Mejía Villatoro  
Comprehensive HIV and Chronic Infections  
Care Unit, Roosevelt Hospital.



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**Ana Johanna Samayoa Bran**

Dr. Carlos Rodolfo Mejía Villatoro  
Comprehensive HIV and Chronic Infections  
Care Unit, Roosevelt Hospital.

**Rodolfo Pinzón Meza**

Dr. Carlos Rodolfo Mejía Villatoro  
Comprehensive HIV and Chronic Infections  
Care Unit, Roosevelt Hospital.

**Abstract: Introduction:** HIV/AIDS continues to be a significant public health problem. Despite improvements in access to antiretroviral treatment, challenges related to mortality persist, especially in contexts of late diagnosis and comorbidities. **Objective:** To describe the mortality trend, as well as the sociodemographic, clinical, immunological, virological characteristics, and cause of death of adult patients with HIV who died between 2003 and 2023 at Roosevelt Hospital, Guatemala. **Methodology:** Descriptive, longitudinal, retrospective study of 3,036 patients who died with HIV. Sociodemographic characteristics, causes of death, and laboratory tests were described. The Chi-square statistical test was used to compare immunological and virological variables and causes of death between two periods (2003-2017 vs. 2018-2023). **Results:** Mortality decreased by 75% between 2009 and 2023. The most affected age group was 25-49 years, although deaths increased in those over 50. Males predominated, and heterosexuals were the most common sexual orientation. A high proportion of patients with severe immunosuppression ( $CD4^+ \leq 100$  cells/ $\mu$ L) and high viral load ( $ly > 100,000$  cp/mL) were found. The main causes of death were mycobacteria, other bacterial, fungal, viral, and parasitic infections, as well as other non-infectious causes, with significant differences between periods. **Conclusion:** Although HIV mortality has declined in Guatemala, challenges remain, such as late diagnosis, advanced immunosuppression at death, and the emergence of comorbidities. Prevention, screening, and treatment adherence strategies need to be strengthened.

**Keywords:** HIV infections, Mortality, Antiretroviral therapy, Coinfection, Guatemala.

## INTRODUCTION

The human immunodeficiency virus (HIV) is the causative agent of acquired immunodeficiency syndrome (AIDS), which is the final or advanced stage. It is one of the leading causes of death worldwide (1). It mainly affects the immune system, making those affected vulnerable to attack by other infectious microorganisms (2). With the use of antiretroviral therapy (ART), the life expectancy and quality of life of people living with HIV (PLHIV) has improved (3).

According to the Pan American Health Organization (PAHO), in 2022, approximately 2.5 million people were living with HIV in Latin America and the Caribbean, approximately 130,000 people contracted the virus, and 33,000 died from AIDS. That same year, 46,600 cases of HIV were registered in Guatemala and fewer than 500 AIDS-related deaths were reported (4), a reduction of 9% compared to 2021 and 35% compared to 2010 (5). HIV/AIDS-related mortality, together with incidence, is an important indicator for assessing the evolution and impact of HIV as a public health problem (6).

The use of ART has led to a decrease in deaths associated with opportunistic infections, which are defining characteristics of HIV/AIDS; it has also improved life expectancy and quality of life (7). However, its long-term use has led to the emergence of chronic diseases such as high blood pressure, diabetes mellitus (DM), heart disease, neoplasms, and kidney disease, among others, which can lead to death (7,8).

It is important to consider that mortality from HIV/AIDS may be related to several factors, such as socioeconomic status, associated comorbidities, the presence of coinfections, and other risk factors, as well as the clinical, immunological, virological, and pharmacological context in which patients are treated (9). The objective of this study is to describe mor-

tality trends in HIV- d adult patients treated at the Dr. Carlos Rodolfo Mejía Villatoro Comprehensive HIV and Chronic Infections Care Unit at Roosevelt Hospital during the period 2003-2023, as well as to characterize these patients in terms of sociodemographic characteristics, immune status, virological parameters, and the causes associated with their death.

## METHODOLOGY

### TYPE OF STUDY

Descriptive, longitudinal, retrospective study.

### STUDY POPULATION

The study population consisted of a total of 3,036 adult patients with a confirmed diagnosis of HIV who were linked to comprehensive care at the Dr. Carlos Rodolfo Mejía Villatoro HIV and Chronic Infections Unit at Roosevelt Hospital and died during the period 2003-2023.

### INCLUSION CRITERIA

- Patients  $\geq 15$  years of age linked to the adult area of the Dr. Carlos Rodolfo Mejía Villatoro Comprehensive HIV and Chronic Infections Unit at Roosevelt Hospital, diagnosed with HIV and linked to comprehensive care during the period 2003–2023, and reported as deceased during the same period.

### EXCLUSION CRITERIA

- Patients who were being monitored in this unit but were transferred.

### DATA COLLECTION AND PROCESSING TOOL

Information was collected from the institutional electronic database Antiretroviral Management in Guatemala (Mangua) and an Excel 2019 database was designed, in which fields were added to enter the variables of interest. The data were transcribed in a prede-

terminated order in the following sections: a) Sociodemographic characteristics, including sex, age, residence, educational level, and marital status; b) Risk variables, such as sexual orientation; c) Clinical characteristics, including CD4+ T-cell count, viral load, and cause of death.

## DATA ANALYSIS

Data analysis was performed using Jamovi 2.3.28 software. Results related to HIV positivity, linkage, and deaths, as well as sociodemographic, epidemiological, immunological, and virological characteristics, are presented in contingency tables with frequencies and percentages.

To evaluate the evolution of positive cases in relation to screening, linkage in relation to positive cases, and mortality in relation to the linkage of patients with HIV, ratios expressed as percentages were calculated from 2003 to 2023. Variations in these ratios were analyzed over the years to identify trends and possible changes in care patterns and outcomes.

Comparisons were made between two periods: 2003–2017 and 2018–2023. Chi-square was applied, with a significance level of 0.05, to assess significant differences between CD4+ T-cell levels, HIV viral load, and cause of death between periods.

## POSSIBLE BIASES

- **Information bias:** Reliance on an institutional database (Mangua) to identify causes of death could lead to errors if the information was not completely accurate or if the causes of death were not correctly documented.
- **Selection bias:** Exclusion of patients who, despite having been followed up at the Unit, were subsequently transferred to another institution or classified as dropouts; since no information is available on their vital status, it is possible that some of these patients may have died

without being recorded in the analysis, which could affect the actual estimate of mortality in the study cohort.

## ETHICAL CONSIDERATIONS

Confidentiality was maintained throughout the research. The protocol was reviewed and approved by the authorities of the Department of Internal Medicine, the Comprehensive Care Unit for HIV and Chronic Infections, and the Teaching and Research Committee of Roosevelt Hospital, recorded in Minutes 745, Point 3, dated April 25, 2024.

## RESULTS

The number of screenings shows a significant increase between 2003 (4,602) and 2023 (28,462), with peaks in 2008 (29,295), 2009 (29,998), and 2019 (42,424), while positive cases show annual variations without a clear trend of increase or decrease. Most of the patients diagnosed were linked to the comprehensive care system, with percentages of those linked to positive cases of 84.6% in 2003, 95.8% in 2008, and 92.9% in 2023. With regard to mortality, deaths peaked in 2009 (258, 32.6% of those linked) and declined progressively to 62 in 2023 (13.8% of those linked), showing a reduction in the percentage of deaths relative to those linked over the years.

Between 2003 and 2017, most of the deaths were among men (60.7%-75.2%), with the most affected age group being 25-49 years (64.6%-79.4%). The proportion of deaths among people over 50 increased from 8.4% in 2003 to 29.8% in 2016. Heterosexuals predominated, ranging from 82.0% to 97.6%. The main causes of death were mycobacterial infections (5.2%-17.6%) and other infections, which increased to 27.2% in 2016. Cancer peaked at 10.2% in 2012, while lymphomas and malignant tumors remained low. Deaths classified as “unspecified” decreased from 55.2% in 2003 to 0% in 2017. Other causes remained low and variable.

Year	Screenings	Positive		Linked		Death	
		f	%	f	%	f	%
2003	4602	624	13.6	528	84.6	96	18.2
2004	4,661	814	17.5	603	74.1	102	16.9
2005	4379	825	18.8	650	78.8	107	16.5
2006	4,933	779	15.8	726	93.2	118	16.3
2007	24,024	906	3.8	845	93.3	151	17.9
2008	29,295	990	3.4	948	95.8	227	23.9
2009	29,998	825	2.8	792	96.0	258	32.6
2010	21,931	720	3.3	707	98.2	223	31.5
2011	20,649	584	2.8	575	98.5	185	32.2
2012	25068	523	2.1	514	98.3	206	40.1
2013	26,428	477	1.8	477	100.0	219	45.9
2014	28,526	532	1.9	531	99.8	193	36.3
2015	30063	577	1.9	550	95.3	181	32.9
2016	38,251	546	1.4	525	96.2	191	36.4
2017	34,088	540	1.6	521	96.5	129	24.8
2018	37,890	625	1.6	622	99.5	80	12.9
2019	42,424	612	1.4	583	95.3	78	13.4
2020	22,360	293	1.3	285	97.3	66	23.2
2021	24,116	404	1.7	399	98.8	83	20.8
2022	28360	443	1.6	443	100.0	81	18.3
2023	28462	482	1.7	448	92.9	62	13.8
Total	510,508	13121	2.6	12272	93.5	3036	24.7

Table 1. Trend in screening, treatment linkage, and mortality in adult patients with HIV at the Roosevelt Hospital Care Unit (2003–2023).

Characteristic	2003	2004	2005	2	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
<b>Gender</b>	(n=96)	(n=102)	(n=107)	(n=118)	(n=151)	(n=227)	(n=258)	(n=223)	(n=185)	(n=206)	(n=219)	(n=193)	(n=181)	(n=191)	(n=129)
Female	27.1	26.5	39.3	29.7	25.8	29.5	29.5	30.5	33.0	35.9	36.5	39.4	35.9	33.0	24.8
Male	72.9	73.5	60.7	70.3	74.2	70.5	70.5	69.5	67.0	64.1	63.5	60.7	64.1	67.0	75.2
<b>Age</b>	(n=95)	(n=102)	(n=107)	(n=118)	(n=151)	(n=227)	(n=258)	(n=223)	(n=185)	(n=206)	(n=219)	(n=193)	(n=181)	(n=191)	(n=129)
15–19	1.1	1.0	0.9	2.5	1.3	0.4	0.8	2.2	0.0	0.5	1.8	1.0	0.0	1.6	0.8
20–24	17.9	8.8	12.1	11.9	9.9	9.3	7.0	7.2	8.1	4.9	5.0	3.6	5.5	3.1	2.3
25–49	72.6	79.4	77.6	69.5	72.2	73.1	71.3	70.9	69.2	70.4	72.6	75.1	64.6	65.4	75.2
≥ 50	8.4	10.8	9.3	16.1	16.6	17.2	20.9	19.7	22.7	24.3	20.5	20.2	29.8	29.8%	21.7
<b>Orientation</b>	(n=68)	(n=85)	(n=80)	(n=80)	(n=114)	(n=182)	(n=225)	(n=188)	(n=170)	(n=195)	(n=210)	(n=125)	(n=114)	(n=167)	(n=123)
Bisexual	3.1	3.9	5.6	5.0	3.6	2.9	2.7	4.3	2.4	1.0	1.0	3.3	1.8	3.6	3.3
Heterosexual	92.2	93.4	91.7	92.5	89.2	90.9	93.3	93.0	96.4	97.4	97.6	90.2	92.0	91.0	82.0
HSH	4.7	2.6	2.8	2.5	7.2	6.3	4.0	2.7	1.2	1.5	1.4	6.5	6.2	5.4	14.8
<b>Cause of death</b>	(n=96)	(n=102)	(n=107)	(n=118)	(n=151)	(n=227)	(n=258)	(n=223)	(n=185)	(n=206)	(n=219)	(n=193)	(n=181)	(n=191)	(n=129)
Mycobacteria	5.2	9.8	15.0	13.6	9.9	9.7	14.0	12.1	14.6	15.5	13.2	17.6	16.6	14.7	16.3
Other infections	4.2	7.8	4.7	7.6	9.9	8.4	11.2	9.0	14.1	8.7	17.8	16.1	18.2	27.2	20.2
Cancer	1.0	4.9	3.7	3.4	4.6	3.5	3.5	2.7	4.3	10.2	4.1	7.8	6.6	5.2	6.2
Lymphoma	2.1	0.0	2.8	0.0	1.3	0.0	0.4	0.0	1.1	1.0	1.4	1.0	0.6	1.6	3.9
Solid tumors	0.0	0.0	0.0	0.0	0.7	0.4	1.2	0.4	1.1	0.0	1.8	1.6	1.1	0.0	0.0
Other causes	32.3	37.3	51.4	64.4	64.9	72.2	60.9	49.8	63.2	59.2	53.0	46.1	55.2	49.2	52.7
Not related to health	0.0	0.0	1.9	0.0	1.3	0.0	1.6	3.6	0.5	3.9	1.4	1.6	1.7	2.1	0.8
Not specified	55.2	40.2	20.6	11.0	7.3	5.7	7.4	22.4	1.1	1.5	7.3	8.3	0.0	0.0	0.0

MSM: men who have sex with men.  
 Other infections: opportunistic infections of fungal, viral, bacterial, or parasitic etiology.  
 Other causes: non-infectious causes, such as metabolic, cardiovascular, hepatic, respiratory, neurological, and gastrointestinal diseases.  
 Cancer: lung, colon, liver, and cervix.  
 Lymphomas: non-Hodgkins in multiple variants.  
 Solid tumors: Kaposi's sarcoma, neoplasms of the nervous system, digestive tract, and genitourinary tract.

Table 2. Sociodemographic and epidemiological characteristics of HIV patients who died between 2003 and 2017



Characteristic	2	2	2	2	2022	2023
Gender	(n=80)	(n=78)	(n=66)	(n=83)	(n=81)	(n=62)
Female	26.3	25.6	30.3	34.9	35.8	25.8
Male	73.8	74.4	69.7	65.1	64.2	74.2
Age	(n=80)	(n=78)	(n=66)	(n=83)	(n=81)	(n=62)
15–19	0.0	1.3	0.0	2.4	3.7	0.0
20 – 24	6.3	2.6	1.5	3.6	1.2	4.8
25 – 49	63.7	69.2	68.2	59.0	56.8	56.5
≥ 50	30.0	26.9	30.3	34.9	38.3	38.7
Orientation	(n=76)	(n=78)	(n=64)	(n=83)	(n=81)	(n=62)
Bisexual	5.3	6.4	6.3	3.6	6.2	4.9
Heterosexual	85.5	84.6	84.4	84.3	84.0	75.4
HSH	9.2	9.0	9.4	12.0	9.9	19.7
Cause of death	(n=80)	(n=78)	(n=66)	(n=83)	(n=81)	(n=62)
Mycobacteria	20.0	26.9	13.6	4.8	7.4	12.9
Other infections	23.8	21.8	25.8	18.1	14.8	6.5
Cancer	6.3	3.8	3.0	1.2	6.2	1.6
Lymphoma	0.0	1.3	1.5	3.6	0.0	3.2
Solid tumors	0.0	5.1	4.5	2.4	2.5	1.6
Other causes	50.0	39.7	51.5	69.9	67.9	71.0
Not related to health	0.0	1.3	0.0	0.0	1.2	3.2

MSM: men who have sex with men.

Other infections: opportunistic infections of fungal, viral, bacterial, or parasitic etiology; COVID-19.

Other causes: non-infectious causes, such as metabolic, cardiovascular, hepatic, respiratory, neurological, and gastrointestinal diseases.

Cancer: lung, colon, liver, and cervix.

Lymphomas: non-Hodgkin's in multiple variants.

Solid tumors: Kaposi's sarcoma, neoplasms of the nervous system, digestive tract, and genitourinary tract.

Table 3. Sociodemographic and epidemiological characteristics of HIV patients who died between 2018 and 2023

During the period 2018-2023, 64.2%-74.4% of deaths were men, while women accounted for between 26.3% and 35.8%, with a decrease to 25.8% in 2023. Most of the deceased were between 25 and 49 years old (56.5%-69.2%), representing the age group most affected by HIV, while those over 50 increased from 30.0% to 38.7%. Heterosexual patients accounted for 75.4%–85.5%, with a gradual decrease, while men who have sex with men (MSM) increased from 9.2% to 19.7%. The most frequent cause of death was “other” (50.0%–71.0%). Deaths from mycobacteria decreased from 20.0% in 2018 to 4.8% in 2021, with a rebound to 12.9% in 2023, and deaths from other infections also decreased

from 23.8% to 6.5%. Cancer and malignant tumors and lymphomas showed low and fluctuating percentages.

Comparing the periods 2003–2017 and 2018–2023, there was a decrease in the proportion of male deaths, from 68.7% to 60.5%, while female deaths increased from 31.3% to 39.5%. In addition, the median age increased significantly, from 37 years in 2003-2017 to 45 years in 2018-2023, reflecting an aging of the population affected by HIV. The MSM proportion grew from 16.3% to 23.7%. Statistically significant differences in causes of death were identified between the periods 2003–2017 and 2018–2023, according to the Chi-square analysis ( $p < 0.001$ ).

				95% CI	
		<i>f</i>	%	Lower	Upper
CD4+ T lymphocytes (cells/μL)	≤ 10	1252	58.9	56.8	61
	101	407	19.2	17.5	20.9
	201 - 350	270	12.7	11.3	14.2
	351 - 500	127	6.0	5.0	7.1
2003-2017 (n= ,2125)	> 500	69	3.2	2.5	4.1
	≤ 4	86	5.1	4.1	6.2
HIV CV (cp/mL)	41 - 1000	98	5.8	4.7	7
	1001 - 50,000	384	22.6	20.6	24.6
	50,001 - 100,000	23	13	12	15.3
	> 100,000	902	53.0	50.6	55.4

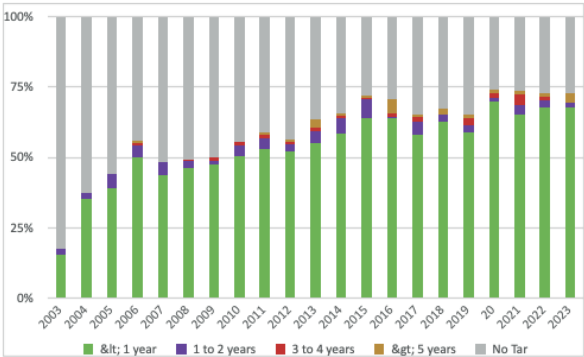
Table 4. Immunological and virological characteristics of patients before death, 2003–2017

A total of 2,125 patients were analyzed from 2003 to 2017, of whom 58.9% had a CD4+ T-lymphocyte count ≤100 cells/μL. Of 1,701 patients who underwent HIV viral load testing, 53.0% had> 100,000 cells/mL.

				95% CI	
		<i>f</i>	%	Lower	Upper
CD4+ T lymphocytes (cells/μL)	≤ 100	14	72.	65.7	78.3
	101 - 200	37	18	13	23.9
	201 - 350	12	5.8	3.0	10
	351 - 500	6	2.9	1.1	6.2
2018-2023 (n= 206)	> 500	2	1.0	0.1	3.5
	≤ 40	9	4.	2.2	8.9
HIV CV (cp/mL)	41	6	3.2	1.2	6.8
	1001 - 50,000	29	15.3	10.5	21.3
	50,001 - 100,000	18	9.5	5.7	14.6
2018-2023 (n= 189)	> 100,000	127	67.2	60.0	73.8

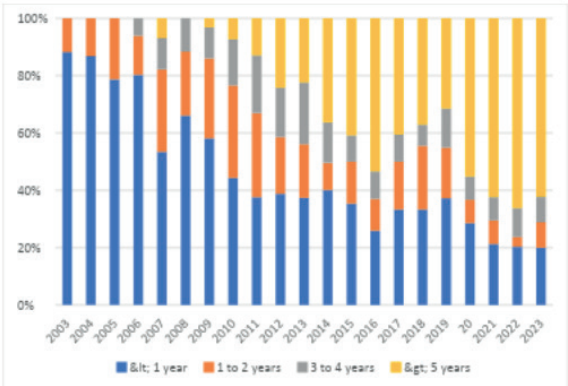
Table 5. Immunological and virological characteristics of patients before death. 2018–2023

>Of the patients who died between 2018 and 2023, 72.3% of 206 had a CD4+ T lymphocyte count of≤ 100 cells/μL. Of the 189 patients who underwent viral load testing, 67.2% had a viral load of 100,000 copies/mL. CD4+ T lymphocyte levels and HIV viral load showed significant differences between the periods 2003-2017 and 2018-2023 (chi-square test, p < 0.05).



Graph 1. Distribution of deceased HIV patients according to the time elapsed between diagnosis and initiation of antiretroviral therapy (ART)

Graph 1 shows that in 2003, 82% of patients did not receive treatment, and this figure declined steadily, reaching 27% in 2023. Among patients who received treatment, ART initiation within one year of diagnosis gradually increased from 16% in 2003 to 68% in 2023.



Graph 2. Distribution of HIV patients according to time elapsed between initiation of antiretroviral therapy (ART) and death



Between 2003 and 2006, most patients died within one year of starting ART, with a percentage close to 80%. Over time, this proportion decreased, stabilizing between 20% and 40% in 2020-2023. In contrast, deaths after more than 5 years of ART increased significantly since 2007, exceeding 30% in 2014 and reaching up to 62% in 2021 and 2023. Deaths between 1-2 years and 3-4 years of treatment remained relatively low, ranging from 8% to 32%.

## DISCUSSION

Between 2003 and 2023, screenings increased significantly, from 4,602 to 28,462, representing an increase of more than 500% (Table 1). This growth reflects improvements in access to diagnostic tests, the implementation of screening for all women who seek emergency maternity care, 24 hours a day, 365 days a year since 2006, the implementation of testing in adult emergency departments since 2012, and greater voluntary acceptance of testing. This phenomenon has also been observed in Colombia, where increased testing has led to earlier detection of HIV (10). However, the percentage of positive diagnoses decreased from 13.6% in 2003 to 1.7% in 2023, which could indicate a lower prevalence of HIV in the general population, while also reflecting the need for a screening approach targeted at risk groups (4).

As for the linkage of patients diagnosed with HIV to the care system, the increase from 84.6% in 2003 to 92.9% in 2023 is attributed to stricter follow-up strategies implemented in the Unit, as well as the implementation of assisted linkage. This consists of accompanying patients who have tested positive for HIV at another center to the Comprehensive HIV Care Unit for confirmation of the diagnosis.

After confirmation, the patient is accompanied by Unit staff during the first few months to ensure that they attend their follow-up

appointments. This process is strengthened by the active participation of healthcare personnel and the willingness of the patient, which are key elements in ensuring adherence to and continuity of the comprehensive approach, which is in line with the integration of health services at the national level (4).

Mortality in HIV patients decreased significantly, with 62 deaths in 2023, representing a 75% reduction from the peak of 258 in 2009. This decline is associated with improved access to antiretroviral treatment (ART), supporting what has been documented in previous studies (7,11).

Although the COVID-19 pandemic had a particularly severe impact in 2020 and 2021, leading to the temporary suspension of outpatient consultations, the HIV Unit and the emergency service continued to provide screening and comprehensive care without interruption, recognizing that HIV is a life-threatening infection that requires ongoing monitoring.

In terms of gender, men accounted for the majority of deaths between 2003 and 2017, with percentages ranging from 60.7% to 75.2% (Table 2). However, between 2018 and 2023, there was an increase in the proportion of female deaths, from 26.2% to 35.8% (Table 3). Comparing both periods, there was an increase in deaths among women from 31.3% to 39.5%, which could be related to late diagnoses, barriers to access to health services, and difficulties in adhering to treatment.

Furthermore, this phenomenon highlights greater biological vulnerability in women, as well as profound gender inequalities, including violence, less bargaining power in sexual relationships, and economic constraints, which increase their exposure to risk (12). Although men continue to account for the majority of deaths, these structural conditions may have contributed significantly to the proportional increase in deaths among women.

These findings are consistent with those observed by Genero (2020) in Argentina, where, although men were the most affected group, female mortality has increased in recent years (6).

During the period 2003–2017, there was a higher percentage of deaths in the 25–49 age group, representing between 64.6% and 79.4% of annual cases (Table 2), which highlights the importance of early detection and rapid initiation of ART in this population. At the same time, the percentage of deaths in people over 50 increased from 8.4% in 2003 to 29.8% in 2016, possibly due to the effectiveness of ART, which has resulted in an aging population with HIV (13).

Between 2018 and 2023, the proportion of deaths among people aged 50 and older continued to rise, reaching 38.7% in 2023 (Table 3). Although the 25–49 age group continued to be the most affected, the aging of HIV patients poses new challenges related to age-associated comorbidities, as described in the literature (6,13), highlighting the need for a comprehensive approach in this context (14).

With regard to sexual orientation, men who have sex with men (MSM) represented a smaller group, although their proportion increased to 14.8% in 2017. Between 2018 and 2023, the proportion of MSM increased to 19.7% in the last year. This increase reflects a change in epidemiological dynamics, with greater recognition and diagnosis of MSM as a risk group in terms of HIV, which was carried out in 2017 in the central region of the country and resumed in 2023, coinciding with trends observed in the literature indicating that this group remains vulnerable due to their sexual practices and exposure to HIV (15).

Previous studies have highlighted tuberculosis as one of the leading causes of mortality in HIV patients (16,17), which is consistent with the findings of this study, where mycobacterial infections accounted for between

5.2% and 17.6% of deaths between 2003 and 2017 (Table 2). In 2021, a decrease to 4.8% was observed, followed by rebound to 12.9% in 2023 (Table 3). These results underscore the importance of continuous monitoring and reinforce the need for early intervention to prevent serious complications associated with mycobacterial infections in HIV patients.

Although deaths associated with cancer, lymphomas, and solid tumors accounted for a relatively low percentage in this study, reaching a peak of 10.2% in 2012, they remain an important cause of mortality in patients with HIV (17, 18, 19). This highlights the need for a comprehensive approach to HIV management, which not only includes the treatment of infections but also the early detection of neoplasms and the management of chronic complications. Collaboration with other disciplines, such as oncology, surgery, and palliative care, is essential to facilitate a multidisciplinary and timely approach.

The category “other causes” had a high percentage, ranging from 32.3% to 72.2% between 2003 and 2017 (Table 2), with a notable increase starting in 2018, reaching 71.0% in 2023 (Table 3). This behavior could be due to phenomena that are not yet fully understood, as well as underreporting of unidentified diseases. This situation highlights the importance of strengthening death cause coding and classification systems, as well as improving documentation and clinical analysis processes, to achieve a more accurate characterization of outcomes in this population.

Similarly, the “unspecified” category showed a notable decrease, falling from 55.2% in 2003 to 0% in 2017 (Table 2). In the early years, this imprecise recording may have been due to diagnostic or clinical limitations that made it difficult to clearly identify the primary cause of death. Over time, these deficiencies were overcome, reflecting a progressive improvement in the quality of the registry. Ini-

tially, information was recorded only in physical files, but with the gradual incorporation of digital platforms, awareness of the importance of accurate documentation was strengthened. However, migration between platforms and changes in information systems have been a challenge, as they can lead to data loss due to transcription errors or failures in the migration process.

The statistical significance observed in the causes of mortality between the two periods suggests a change in the profile of deaths. While between 2018 and 2020 there was a predominance of deaths from mycobacteria and other infections, possibly related to outbreaks, antimicrobial resistance, or late diagnosis, from 2021 onwards there was a sustained increase in deaths classified as “other causes” ( $\geq 67\%$ ), pointing to a transition toward non-infectious causes or comorbidities not directly associated with HIV. This change in the cause-effect distribution reflects a significant shift in mortality patterns.

The analysis reveals a growing trend toward severe immunosuppression among deceased HIV patients. Between 2003 and 2017, 58.9% had a CD4+ T-cell count  $\leq 100$  cells/ $\mu\text{L}$  (Table 4), which increased to 72.3% in the period 2018–2023 (Table 5), suggesting an increased risk of opportunistic infections (2). The statistically significant difference confirms a shift in the distribution of cases toward more critical immunosuppression in recent years and elevated HIV VC values, despite expanded diagnostic access and the implementation of rapid initiation of antiretroviral treatment. This finding contrasts with expectations, as a reduction in the proportion of deaths associated with low CD4+ T-cell counts and an increase in those attributable to comorbidities not directly related to severe immunosuppression were anticipated.

One possible explanation for this contradiction is that, although strategies have im-

proved, the health system continues to have significant weaknesses in the timely detection of new cases. Early initiation of antiretroviral therapy is more effective if HIV is diagnosed at an early stage, as it preserves immune function and avoids the need for prophylactic treatment for opportunistic infections (OIs), given that the immune system is not yet compromised (20).

However, current screening strategies focus mainly on risk groups (21), without adequately extending to the general population, which limits their coverage and impact. Added to this are the restricted hours of health services, which are predominantly administrative, making it difficult to access testing outside of these hours and reducing opportunities for early detection.

Furthermore, strengthening adherence to ART plays a key role in the favorable evolution of HIV patients (22), and, conversely, discontinuation of treatment or abandonment of medical follow-up can lead to rapid disease progression and severe relapses. In these cases, when patients return to the health system, they often do so with very low CD4+ cell counts and advanced complications, which could also be influencing the observed increase in severe immunosuppression at the time of death.

In 2003, the percentage of patients without access to ART was clearly high, reaching 82% (Figure 1). However, starting in 2008, the proportion gradually decreased to 27% in 2023. This trend may be related to significant changes in treatment initiation guidelines that were progressively implemented in the region, as well as the availability and evolution of ART regimens (23,24).

In the past, clinical decisions to initiate ART in people with HIV were based on CD4+ cell counts, following guidelines that recommended initiation in patients with counts  $\leq 350$  cells/ $\mu\text{L}$ , regardless of the presence

of symptoms (25,26). The threshold was subsequently lowered to counts  $\leq 500$  cells/ $\mu\text{L}$ , with priority given to people with advanced or symptomatic disease (23). Currently, rapid initiation of ART is recommended in all people diagnosed with HIV, regardless of CD4+ cell count (24,26), recognizing the clinical, individual, and population benefits of starting treatment as soon as possible after diagnosis.

Furthermore, in the early years, treatment was limited to a small number of antiretroviral combinations, some with significant toxicities, complex dosing requirements, or poor tolerability, which hindered both large-scale implementation and patient adherence (25,27,28). However, over time, more effective, safer, and simplified regimens were introduced, including single-tablet daily combinations (24,29), which facilitated both early initiation and continuity of treatment. This pharmacological evolution, combined with expanded public health coverage, played a crucial role in the progressive reduction of the percentage of people without access to ART.

In terms of early mortality, between 2003 and 2006, approximately 80% of patients died within one year of starting ART (Figure 2). This high percentage can be attributed to the fact that, during that period, ART was administered based on current guidelines that conditioned initiation on immune status (23,25). Although early mortality declined significantly after 2007, the persistence of deaths between 20% and 40% in subsequent years suggests that challenges remain, such as late diagnosis and initiation of treatment in advanced stages of the disease, when HIV-associated comorbidities or complications already exist that limit the effectiveness of ART, despite its availability.

Despite these challenges, the steady decline in mortality suggests that improvements in early detection, expanded diagnostic coverage, and timely initiation of treatment (24) have

had a positive impact on survival. The introduction of ART has increased life expectancy in adults, demonstrating its effectiveness at the public health level, associated in part with the cost-benefit of simplified treatments (30). However, there is still a gap to be addressed in terms of equitable access, early diagnosis, and treatment adherence, especially in populations and regions with lower service coverage.

The main contribution of the findings from this study is the evidence of improvements in the care of HIV patients, reflected in increased screening, greater adherence to treatment, and a reduction in HIV-related mortality. The implementation of screening in maternity and adult emergency departments allowed more cases to be detected and patients to be linked to ART. In addition, there was an increase in the number of patients who died before  $\geq$  , which implies new challenges related to the development of comorbidities that are classified as other causes of death. Finally, improvements in treatment adherence and access reflect advances in institutional management, while mycobacterial infections and neoplasms highlight the need for comprehensive approaches to the management of complications.

## CONCLUSION

Analysis of mortality data and sociodemographic characteristics of HIV patients who died at Roosevelt Hospital from 2003 to 2023 reveals a picture in which efforts to improve early detection, access to antiretroviral treatment, and linkage to the health system have had a positive impact on reducing mortality and improving patients' quality of life. However, challenges remain, especially in the care of older patients and in improving infection control. It is essential to continue strengthening prevention, early detection, and comorbidity management strategies to further reduce HIV-related mortality.

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## CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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