# Time trend and causes of HIV/AIDS mortality in the state of Santa Catarina, 2010–2019

Tendência temporal e causas de mortalidade por HIV/AIDS no estado de Santa Catarina, 2010-2019

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## ABSTRACT

**Introduction:** Although the acquired immunodeficiency syndrome (AIDS) has no cure, antiretroviral treatment has considerably increased the survival of people living with the disease or with the human immunodeficiency virus (HIV), reducing the incidence of opportunistic infections in these patients. Thus, this treatment changed mortality rates and diversified the causes of death, including reasons related to increased longevity, such as chronic non-communicable diseases, common in the uninfected population. Therefore, the current epidemiological transition motivated us to study the death profile of people with HIV/AIDS in the state of Santa Catarina. **Objective:** To investigate case characteristics, as well as the time trend and distribution of deaths, among people with HIV/AIDS in Santa Catarina between 2010 and 2019. **Methods:** In this ecological, epidemiological study, we consulted all death records from the Santa Catarina Mortality Information System that had HIV/AIDS among the causes and occurred between 2010 and 2019. **Results:** A total of 5,174 death records were analyzed. In the period, the mean mortality rate among people with HIV/AIDS was 7.64 deaths per 100 thousand inhabitants (95% confidence interval — 95%CI 6.61–8.67) — 8.99 in 2010 and 6.06 in 2019 —, showing a downward trend of 0.38% per year. **Conclusion:** We identified a downward trend in mortality. Deaths were concentrated on the coast, in more populous cities. Furthermore, the finding of improper completion of the death certificate points to the need to invest in improving the training of professionals responsible for this document. **Keywords:** HIV. Acquired immunodeficiency syndrome. Mortality. Death certificate. Temporal distribution.

#### RESUMO

Introdução: Embora a síndrome da imunodeficiência adquirida (AIDS) não tenha cura, o tratamento antirretroviral aumentou consideravelmente a sobrevida das pessoas que vivem com a doença ou com o vírus da imunodeficiência humana (HIV), diminuindo a ocorrência de infecções oportunistas nesses pacientes. Assim, esse tratamento mudou as taxas de mortalidade e diversificou as causas de óbito, incluindo motivos relacionados ao aumento da longevidade, como doenças crônicas não transmissíveis comuns à população não infectada. Dessa forma, a atual transição epidemiológica motiva o estudo do perfil dos óbitos em pessoas com HIV/AIDS no estado de Santa Catarina. **Objetivo:** Investigar as características dos casos, a tendência temporal e a distribuição dos óbitos em pessoas com HIV/AIDS no estado de Santa Catarina entre os anos de 2010 e 2019. **Métodos:** Neste estudo epidemiológico com delineamento ecológico, foram consultados todos os registros de óbitos do Sistema de Informação sobre Mortalidade de Santa Catarina ocorridos entre os anos de 2010 e 2019 que apresentassem entre as causas o HIV/AIDS. **Resultados:** Foram analisados 5.174 registros de óbitos. A taxa de mortalidade média entre pessoas com HIV/AIDS do período foi de 7,64 óbitos a cada 100 mil habitantes (95% intervalo de confiança — IC95% 6,61–8,67), sendo de 8,99 em 2010 e 6,06 em 2019, mostrando tendência de queda de 0,38 pontos percentuais ao ano. **Conclusão:** Observou-se tendência de queda na mortalidade. A concentração dos óbitos foi na faixa litorânea, em cidades mais populosas. Ademais, a constatação do falho preenchimento da declaração de óbito aponta percentuais ao ano. **Canclusão:** HIV/AIDS na eriado de óbito aponta pera a necessidade de investir no aprimoramento do treinamento dos profissionais responsáveis por esse documento. **Palavras-chave:** HIV. Síndrome da Imunodeficiência Adquirida. Mortalidade. Atestado de Óbito. Distribuição Temporal.

## INTRODUCTION

AIDS, an acronym for acquired immunodeficiency syndrome, is a disease caused by the human immunodeficiency virus (HIV). The natural history of HIV infection has three progression stages: acute (with nonspecific symptomatology, similar to other viral infections); asymptomatic; and symptomatic clinical stage, when AIDS is manifested. AIDS is the most advanced stage of infection, given the progressive destruction of T-CD4+ lymphocytes in the immune system, leaving the body vulnerable to various opportunistic infections and neoplastic diseases. If not treated, these infections result in death. In the symptomatic stage, immunodeficiency progresses to fungal infections, tuberculosis, pneumonia, hepatitis, diarrhea, toxoplasmosis, and cytomegalovirus infection, among others. Neoplasms such as Kaposi sarcoma are also common<sup>(1-3)</sup>. We emphasize that, although AIDS has no cure, combined antiretroviral therapy (ART) was implemented in the 1990s, considerably increasing the survival of people living with HIV/AIDS and decreasing the occurrence of opportunistic infections typical of the symptomatic stage of the disease<sup>(4,5)</sup>. The advent of this therapy has strongly diversified deaths among individuals with HIV/AIDS. However, infectious and parasitic diseases are still the main cause of death in this group, especially in less developed countries<sup>(3-6)</sup>.

Currently, the offer of ART enables virologic suppression with immunological reconstitution, consequently reducing the deleterious effects of the infection and the number of deaths from opportunistic diseases, as well as increasing life expectancy for the infected individual, with the possibility of years of life proportional to the general population<sup>(7)</sup>. On the other hand, the increased longevity among people living with HIV puts them at the mercy of chronic non-communicable diseases, common in the uninfected population, such as cancer, obesity, and cardiovascular diseases<sup>(8)</sup>.

Deaths attributable to HIV/AIDS decreased from 34% between 1999 and 2000 to 22% between 2009 and 2011. In contrast, the proportion of all deaths caused by non-AIDS-related cancers increased

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(from 9 to 23%) among people living with HIV, becoming the leading non-AIDS-related cause of death<sup>(8)</sup>. In addition, the mortality among people living with HIV/AIDS and cancer can be 30 times higher compared to the uninfected population<sup>(9)</sup>. In addition, the number of fatalities involving cardiovascular diseases in HIV-infected individuals is substantial. Cardiovascular diseases have become a clear problem for these individuals, considering the deaths caused by the pathophysiological process of the natural history of the disease, the adverse effects of ART — related to oxidative stress, inflammatory processes, and chronic metabolic disorders —, or even their increased life expectancy<sup>(10)</sup>.

Brazil pioneered and revolutionized the approach to combating the HIV/AIDS pandemic in 1996, becoming the world's first middle-income country to offer free ART to all people with AIDS. In 2013, it was the third country to provide ART to all people living with HIV, regardless of T-CD4+ lymphocyte counts<sup>(11)</sup>. These public health care measures enabled a significant change in mortality and diversified the causes of death, including more non-AIDS-related causes<sup>(11,12)</sup>. We can also note a decreased incidence of hospitalizations and length of stay, as well as a change in causality and, consequently, a relative improvement in the quality of life and survival of people living with HIV/AIDS<sup>(13)</sup>. However, disease management remains a challenge because poor treatment adherence and late diagnosis are still problems in Brazil and worldwide<sup>(11,12)</sup>.

Studies to understand the progression of deaths from HIV/AIDS, as well as the socioeconomic profile of the population affected, are crucial both to promote health programs and to governmental decision-making when tackling and providing care for these cases<sup>(14)</sup>.

# **OBJECTIVE**

Based on the arguments above, this study contributes to identifying and analyzing causes of death of people living with HIV/AIDS in the state of Santa Catarina, aiming at investigating case characteristics, as well as the time trend and the distribution of deaths, among these individuals between 2010 and 2019.

# **METHODS**

This is an ecological, epidemiological study on case characteristics and the time trend of deaths among people with HIV/AIDS in Santa Catarina between 2010 and 2019. Santa Catarina is located in the Southern Region of Brazil, and its estimated population was 7,252,502 inhabitants in 2020<sup>(15)</sup>. This study obtained and analyzed the death records of Santa Catarina's residents — retrieved from the Mortality Information System (*Sistema de Informações sobre Mortalidade* — SIM) — that had HIV/AIDS (International Statistical Classification of Diseases and Related Health Problems — ICD B20–B24) among its causes, between 2010 and 2019.

Data were collected from SIM by a technician from the Santa Catarina State Epidemiological Surveillance Board. To ensure data confidentiality, this professional excluded duplicates. The filtered digital database was then exported as a .dfb file and analyzed in the SPSS IBM Statistics software, version 21, ensuring the anonymity of personal information such as name, address, and mother's name, among other data that could identify the individual investigated.

The following variables were assessed: age, gender, ethnicity/ skin color, schooling, marital status, city of residence, health district, cause of death, place of death, and date of death. Regarding causes of death, we analyzed separately all ICDs in the fields, which include, in Part I, the immediate cause (A) and the contributing or intermediate causes, that is, comorbidities that the patient presented at the time of death (B, C, and D), and, in Part II, pre-existing conditions. The underlying cause was also evaluated. ICDs were grouped by body systems or similar causes and organized according to ICD-10 chapters. These groupings consisted of: Certain infectious and parasitic diseases (A00-B99), Neoplasms (C00-D48), Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism (D50-D89), Endocrine, nutritional and metabolic diseases (E00-E90), Mental and behavioral disorders and Diseases of the nervous system (F00-G99), Diseases of the circulatory system (I00-I99), Diseases of the respiratory system (J00-J99), Diseases of the digestive system (K00-K93), Diseases of the skin and subcutaneous tissue (L00-L99), Diseases of the musculoskeletal system and connective tissue (M00-M99), Diseases of the genitourinary system (N00-N99), and Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified and External causes of morbidity and mortality (P00-Z00). In addition, ICDs belonging to the certain infectious and parasitic diseases group (A00-B99) were divided into the subgroups: sepsis, unspecified infection, infection-induced encephalopathy, lung infection, infection-induced cancer, intestinal infection, and eye infection, according to the sites affected.

Quantitative variables were expressed as measures of central tendency and dispersion. Qualitative variables were described as absolute numbers and proportions. The mortality rate was calculated based on the estimated population living in Santa Catarina, information obtained from the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística* — IBGE) <sup>(15)</sup>. We used the linear regression model to evaluate the trend in AIDS case fatality and mortality in the period, considering the year as the independent variable. The confidence level adopted was 5%.

## Geoprocessing

To map the analyzed phenomenon, we used the software Quantum GIS – QGIS and Microsoft Excel (2016), as well as tabulated SIM data with entries identified by patient, month, year, and municipality, among other information. Tables totaling cases per year per municipality were created in Microsoft Excel (2016).

The cartographic data used were maps in shapefile format, in the official Brazilian mapping system, of municipalities and health districts based on official data provided by IBGE. We also used annual population data from the same institute, published in the Brazilian Official Gazette (*Diário Oficial da União* — DOU).

Using QGIS, we correlated the tables of total cases and annual population per municipality, based on municipal codes; lastly, we calculated the incidence of cases per 100 thousand inhabitants in the same Geographic Information System (GIS) environment. This variable was thematically mapped, using the Jenks natural breaks classification method in the map with the widest distribution, and maintained in the remaining maps to allow comparisons and trend analyses of the phenomenon, producing several maps. Jenks natural breaks classification method generates a defined set of thematic classes, based on natural arrangements, according to types of data with similar values, maximizing the variance between classes. Thus, the features are divided into classes, with relatively large differences in data values, minimizing the variance sum within each class. This method is appropriate for mapping unevenly distributed values, as in the phenomenon investigated in this study.

The study was approved by the Human Research Ethics Committee of Universidade do Sul de Santa Catarina, number 4,538,034, CAAE 40159420.2.0000.5369, on February 12, 2021, and by the Research Ethics Committee of the Santa Catarina Health Department, opinion number 4,640,669, CAAE 40159420.2.3001.0115, on April 9, 2021.

## RESULTS

We analyzed 5,174 death records — retrieved from SIM — of Santa Catarina's residents with HIV/AIDS (ICD B20–B24) listed among the causes of death between 2010 and 2019. All records in the study met the inclusion criteria and had no elements of the exclusion criteria.

Most participants were male (n=3,325; 64.26%), and the mean age was 44.43 years (standard deviation — SD $\pm$ 12.33), ranging from 1 to 92 years. **Table 1** shows the sociodemographic profile of the study population.

**Table 1** – Sociodemographic characteristics of HIV/AIDS deaths in Santa Catarina, Brazil, 2010 to 2019.

Age in years0–19591.1420–294660.0930–391,32625.6340–491,66232.1250–591,09021.07≥6056911.00Ignored20.04Ethnicity/skin color $V$ White4,22381.62Black4568.81Asian30.06Multiracial4047.81Indigenous180.35Ignored701.35Married98319.00Widower4017.75Legally separated/divorced55510.73Domestic partnership3907.54Ignored3226.22Schooling1893.65None1893.651 to 3 years96718.694 to 7 years1,68232.518 to 11 years1,48428.68	Epidemiological profile	n	%
20-29       466       0.09         30-39       1,326       25.63         40-49       1,662       32.12         50-59       1,090       21.07         ≥60       569       11.00         Ignored       2       0.04         Ethnicity/skin color       V       V         White       4,223       81.62         Black       456       8.81         Asian       3       0.06         Multiracial       404       7.81         Indigenous       18       0.35         Ignored       2,523       48.76         Marital status       V       Vidower         Single       2,523       48.76         Married       983       19.00         Vidower       401       7.75         Legally separated/divorced       555       10.73         Domestic partnership       390       7.54         Ignored       322       6.22         Schooling       V       189       3.65         None       189       3.65       1 to 3 years       967       18.69         4 to 7 years       1,682       32.51       8 to 11 years       <	Age in years		
30-39       1,326       25.63         40-49       1,662       32.12         50-59       1,090       21.07         ≥60       569       11.00         Ignored       2       0.04         Ethnicity/skin color           White       4,223       81.62         Black       456       8.81         Asian       3       0.06         Multiracial       404       7.81         Indigenous       18       0.35         Ignored       2       55         Marital status           Single       2,523       48.76         Married       983       19.00         Widower       401       7.75         Legally separated/divorced       555       10.73         Domestic partnership       390       7.54         Ignored       322       6.22         Schooling           None       189       3.65         1 to 3 years       967       18.69         4 to 7 years       1,682       32.51         8 to 11 years       1,484       28.68	0–19	59	1.14
40–49         1,662         32.12           50–59         1,090         21.07           ≥60         569         11.00           Ignored         2         0.04           Ethnicity/skin color	20–29	466	0.09
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≥60         569         11.00           Ignored         2         0.04           Ethnicity/skin color	40–49	1,662	32.12
Ignored         2         0.04           Ethnicity/skin color	50–59	1,090	21.07
Ethnicity/skin color           White         4,223         81.62           Black         456         8.81           Asian         3         0.06           Multiracial         404         7.81           Indigenous         18         0.35           Ignored         70         1.35           Marital status             Single         2,523         48.76           Married         983         19.00           Widower         401         7.75           Legally separated/divorced         555         10.73           Domestic partnership         390         7.54           Ignored         322         6.22           Schooling             None         189         3.65           1 to 3 years         967         18.69           4 to 7 years         1,682         32.51           8 to 11 years         1,484         28.68	≥60	569	11.00
White         4,223         81.62           Black         456         8.81           Asian         3         0.06           Multiracial         404         7.81           Indigenous         18         0.35           Ignored         70         1.35           Marital status             Single         2,523         48.76           Married         983         19.00           Widower         401         7.75           Legally separated/divorced         555         10.73           Domestic partnership         390         7.54           Ignored         322         6.22           Schooling             None         189         3.65           1 to 3 years         967         18.69           4 to 7 years         1,682         32.51           8 to 11 years         1,484         28.68	Ignored	2	0.04
Black         456         8.81           Asian         3         0.06           Multiracial         404         7.81           Indigenous         18         0.35           Ignored         70         1.35           Marital status             Single         2,523         48.76           Married         983         19.00           Widower         401         7.75           Legally separated/divorced         555         10.73           Domestic partnership         390         7.54           Ignored         322         6.22           Schooling             None         189         3.65           1 to 3 years         967         18.69           4 to 7 years         1,682         32.51           8 to 11 years         1,484         28.68	Ethnicity/skin color		
Asian         3         0.06           Multiracial         404         7.81           Indigenous         18         0.35           Ignored         70         1.35           Marital status	White	4,223	81.62
Multiracial       404       7.81         Indigenous       18       0.35         Ignored       70       1.35         Marital status	Black	456	8.81
Indigenous         18         0.35           Ignored         70         1.35           Marital status	Asian	3	0.06
Ignored         70         1.35           Marital status	Multiracial	404	7.81
Marital status         Single       2,523       48.76         Married       983       19.00         Widower       401       7.75         Legally separated/divorced       555       10.73         Domestic partnership       390       7.54         Ignored       322       6.22         Schooling	Indigenous	18	0.35
Single         2,523         48.76           Married         983         19.00           Widower         401         7.75           Legally separated/divorced         555         10.73           Domestic partnership         390         7.54           Ignored         322         6.22           Schooling             None         189         3.65           1 to 3 years         967         18.69           4 to 7 years         1,682         32.51           8 to 11 years         1,484         28.68	Ignored	70	1.35
Married         983         19.00           Widower         401         7.75           Legally separated/divorced         555         10.73           Domestic partnership         390         7.54           Ignored         322         6.22           Schooling             None         189         3.65           1 to 3 years         967         18.69           4 to 7 years         1,682         32.51           8 to 11 years         1,484         28.68	Marital status		
Widower         401         7.75           Legally separated/divorced         555         10.73           Domestic partnership         390         7.54           Ignored         322         6.22           Schooling	Single	2,523	48.76
Legally separated/divorced         555         10.73           Domestic partnership         390         7.54           Ignored         322         6.22           Schooling	Married	983	19.00
Domestic partnership         390         7.54           Ignored         322         6.22           Schooling         189         3.65           None         189         3.65           1 to 3 years         967         18.69           4 to 7 years         1,682         32.51           8 to 11 years         1,484         28.68	Widower	401	7.75
Ignored3226.22Schooling1893.65None1893.651 to 3 years96718.694 to 7 years1,68232.518 to 11 years1,48428.68	Legally separated/divorced	555	10.73
Schooling         189         3.65           None         189         3.65           1 to 3 years         967         18.69           4 to 7 years         1,682         32.51           8 to 11 years         1,484         28.68	Domestic partnership	390	7.54
None1893.651 to 3 years96718.694 to 7 years1,68232.518 to 11 years1,48428.68	Ignored	322	6.22
1 to 3 years         967         18.69           4 to 7 years         1,682         32.51           8 to 11 years         1,484         28.68	Schooling		
4 to 7 years         1,682         32.51           8 to 11 years         1,484         28.68	None	189	3.65
8 to 11 years 1,484 28.68	1 to 3 years	967	18.69
-	4 to 7 years	1,682	32.51
40 040 0.07	8 to 11 years	1,484	28.68
12 or more years 313 6.05	12 or more years	313	6.05
Ignored 539 10.42	Ignored	539	10.42

Source: Epidemiological Surveillance Board of the State Health Department (*Diretoria de Vigilância Epidemiológica da Secretaria de Estado da Saúde* — DIVE-SES). 
 Table 2 presents clinical and death characteristics of the individuals investigated, listing the diseases in the death certificate grouped

Among the immediate causes of death (A), infectious and parasitic diseases stand out, corresponding to the main cause in all fields analyzed and comprising 41.34% of all immediate causes of death. As for underlying causes (D) (disease or situation that originally led the patient to die), ignored causes (75.72%) stand out, followed by infectious and parasitic diseases (19.85%).

by similar causes, based on ICD-10.

**Table 3** details the main causes of mortality found in field (A) related to the infectious and parasitic diseases group combined into common causes. Individually, the most prevalent diseases in field (A) were, in order: pneumocystosis, with 102 cases (4.77%); tuberculosis, with 100 cases (4.68%); cryptococcosis, with 97 cases (4.53%); and toxoplasmosis, with 94 cases (4.39%).

Seventeen deaths were reported to SIM as maternal deaths, five of them during pregnancy, three up to 42 days after delivery, and nine from 43 days up to one year after delivery.

**Figure 1** shows the HIV/AIDS mortality between 2010 and 2019, as well as the total values for the entire period, with an expressive prevalence of cases on the coast, especially the metropolitan area of Florianópolis and Foz do Rio Itajaí.

Figure 2 illustrates the time trend of HIV/AIDS deaths in Santa Catarina between 2010 and 2019. In the period, the mean mortality rate was 7.64 deaths per 100 thousand inhabitants (95% confidence interval — 95%CI 6.61–8.67) — 8.99 in 2010 and 6.06 in 2019 —, showing a downward trend of 0.38% per year. We can note a decreasing number of cases in the analyzed period, with a value  $R^2$ =0.64.

# DISCUSSION

The analysis of 5,174 death records revealed that the study sample consisted mainly of middle-aged adults, males, white individuals, and single people, similar to data from other investigations<sup>(13,16,17)</sup>.

The low schooling identified may be related to insufficient knowledge regarding the prevention of HIV infection and the low demand for health care and drug treatment, which might have resulted in fatal and early outcome in these individuals<sup>(13,16)</sup>. HIV infection seems to be related to the low schooling and socioeconomic conditions of the population, and the disease is highly prevalent in developing countries<sup>(18)</sup>. Furthermore, populations with a lower level of education tend to be economically disadvantaged and have less access to health care, making early diagnosis and proper treatment difficult in this group. This scenario reinforces the need to monitor vulnerable populations for changes in the characteristics of infection patterns<sup>(19)</sup>.

The lower number of female deaths in the analyzed period may reveal women's greater interest in seeking medical care and health promotion. In 2019, the proportion of women who visited a physician in Brazil was 82.30%, in contrast to 69.40% of men, according to IBGE<sup>(20)</sup>. Historically, the proportion of HIV/AIDS cases is higher among men, given the high number of injecting drug users, their greater vulnerability to risky sexual practices, and their greater propensity to have contact with sex workers<sup>(21,22,23)</sup>.

After analyzing the small number of deaths in people under 20 years of age, we can infer that vertical HIV prevention has advanced, with better prenatal care and prophylaxis during delivery. Recent data revealed a 77.00% drop — from 4.80% in 2010 to 2.40% in

Table 2 – Clinical characteristics of HIV/AIDS deaths in Santa Catarina, Brazil, 2010 to 2019.

Characteristics	n	%
Immediate cause (A)	0.405	
Infectious and parasitic diseases	2,139	41.34
Neoplasms	110	2.13
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	21	0.41
Endocrine, nutritional and metabolic diseases	40	0.77
Mental and behavioral disorders and Diseases of the nervous system	149	2.88
Diseases of the circulatory system	107	2.07
Diseases of the respiratory system	1,338	25.86
Diseases of the digestive system	87	1.68
Diseases of the skin and subcutaneous tissue	2	0.04
Diseases of the musculoskeletal system and connective tissue	1	0.02
Diseases of the genitourinary system	69	1.33
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified and External causes of morbidity and mortality	1,027	19.85
Ignored	84	1.62
Cause (B)		
Infectious and parasitic diseases	2,559	49.46
Neoplasms	151	2.92
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	63	1.22
Endocrine, nutritional and metabolic diseases	46	0.89
Mental and behavioral disorders and Diseases of the nervous system	124	2.40
Diseases of the circulatory system	85	1.64
Diseases of the respiratory system	1,096	21.18
Diseases of the digestive system	150	2.90
Diseases of the skin and subcutaneous tissue	9	0.17
Diseases of the musculoskeletal system and connective tissue	10	0.19
Diseases of the genitourinary system	154	2.98
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified and External causes of morbidity and mortality	176	3.40
Ignored	551	10.65
Jnderlying cause (C)		
Infectious and parasitic diseases	1,246	24.08
Neoplasms	65	1.26
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	34	0.66
Endocrine, nutritional and metabolic diseases	89	1.72
Mental and behavioral disorders and Diseases of the nervous system	172	3.32
Diseases of the circulatory system	118	2.28
Diseases of the respiratory system	72	1.39
Diseases of the digestive system	66	1.28
Diseases of the skin and subcutaneous tissue	5	0.10
Diseases of the musculoskeletal system and connective tissue	6	0.10
Diseases of the genitourinary system	114	2.20
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified and External causes of		
morbidity and mortality	53	1.02
Ignored	3,134	60.57
Cause (D)		
Infectious and parasitic diseases	1,027	19.85
Neoplasms	26	0.50
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	9	0.17
Endocrine, nutritional and metabolic diseases	20	0.39
Mental and behavioral disorders and Diseases of the nervous system	27	0.52
Diseases of the circulatory system	20	0.39
Diseases of the respiratory system	61	1.18
Diseases of the digestive system	9	0.17
Diseases of the skin and subcutaneous tissue	1	0.02
Diseases of the musculoskeletal system and connective tissue	1	0.02
Diseases of the genitourinary system	17	0.33
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified and External causes of morbidity and mortality	38	0.74
Ignored	3,918	75.72
<u>v</u>	-,	Continue

Table 2 – Continuation.

Characteristics	n	%
Cause (II)		
Infectious and parasitic diseases	2,282	44.10
Neoplasms	111	2.15
Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	43	0.83
Endocrine, nutritional and metabolic diseases	39	0.75
Mental and behavioral disorders and Diseases of the nervous system	65	1.26
Diseases of the circulatory system	54	1.04
Diseases of the respiratory system	328	6.34
Diseases of the digestive system	66	1.28
Diseases of the skin and subcutaneous tissue	6	0.12
Diseases of the musculoskeletal system and connective tissue	0	0.00
Diseases of the genitourinary system	67	1.29
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified and External causes of morbidity and mortality	70	1.35
Ignored	2,043	39.49
Necropsy		
Performed	146	2.82
Not performed	4,296	83.03
Ignored	732	14.15
Place of death		
Hospital	4,769	92.17
Other health facilities	62	1.20
Home	286	5.53
Street/Road	15	0.29
Other	40	0.77
Ignored	2	0.04

Source: Epidemiological Surveillance Board of the State Health Department (Diretoria de Vigilância Epidemiológica da Secretaria de Estado da Saúde — DIVE-SES).

**Table 3** – Clinical characteristics of the immediate cause of death due to infectious and parasitic diseases among HIV/AIDS patients in Santa Catarina, Brazil, 2010 to 2019.

Infectious and parasitic diseases	n	%
Sepsis	1,222	57.13
Unspecified infection	538	25.15
Infection-induced encephalopathy	205	9.56
Lung infection	139	6.50
Infection-induced cancer	19	0.89
Intestinal infection	14	0.65
Eye infection	2	0.09

Source: Epidemiological Surveillance Board of the State Health Department (*Diretoria de Vigilância Epidemiológica da Secretaria de Estado da Saúde* — DIVE-SES).

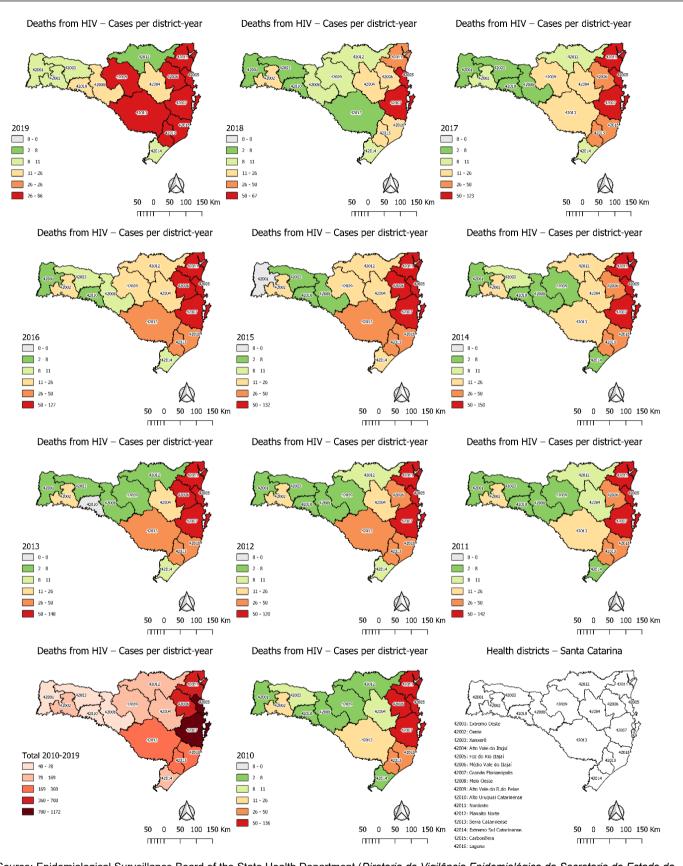
2017 — in the number of children up to 18 months infected by HIV on follow-up in the Brazilian public service<sup>(16,24)</sup>. In addition, disease control has increased due to the ART currently available, extending the life of infected individuals, and to the growing demand for preand post-exposure prophylaxis (PrEP and PEP)<sup>(12,13,16)</sup>.

Concerning causes of death, the record review demonstrated the difficulty of identifying the disease or situation that initially led the patient to the fatal condition. When filling out the death certificate, the physician must provide the underlying cause of the sequence of events that resulted in the fatal outcome. This cause corresponds to field D when fields C, B, and A are filled, with A being the immediate cause of death. If the sequence of events does not have that many elements, the

underlying cause that led to death can be reported in the other fields (C and B, respectively). Since fields D, C, and B are usually incomplete, we cannot correlate underlying causes with the immediate cause of death.

The analysis of immediate causes of death allowed us to identify a high prevalence of situations related to infectious and parasitic diseases, especially respiratory diseases and other unspecified causes. These data are in line with other studies, revealing opportunistic diseases as the main cause of mortality among people living with HIV/AIDS<sup>(3,4,5,6)</sup>. HIV-induced immunosuppression explains the development of opportunistic infections, which could be avoided by early diagnosis and start of ART, as recommended by clinical protocols for people living with HIV/AIDS. In addition, the implementation of preventive, pharmacological, and behavioral practices, the vaccination against infectious agents, and multidisciplinary care for this population can change this scenario<sup>(3,5)</sup>.

In the infectious and parasitic diseases group, sepsis was the most prevalent cause, corresponding to more than half of the cases, followed by unspecified infections and infection-induced encephalopathy. Sepsis is one of the main causes of death in patients with an immune deficit since this group is vulnerable to a greater range of pathogenic agents, in addition to presenting a higher number of inflammatory markers associated with mediating the response to sepsis, leading to a 28% higher risk of disease progression compared to the general population<sup>(25,26)</sup>. When the most incident diseases with a well-defined causative agent were analyzed, pneumocystosis, tuberculosis, cryptococcosis, and toxoplasmosis stood out among the immediate causes of death. Tuberculosis is a major cause of case fatality in HIV/AIDS patients, especially in countries with a high prevalence of this infection, such as those in Latin



Source: Epidemiological Surveillance Board of the State Health Department (*Diretoria de Vigilância Epidemiológica da Secretaria de Estado da Saúde* — DIVE-SES).

Figure 1 - HIV/AIDS mortality in Santa Catarina, Brazil, between 2010 and 2019.

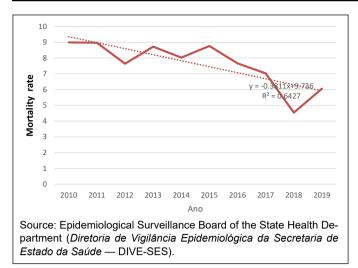


Figure 2 – Time trend of HIV/AIDS deaths in Santa Catarina, Brazil, between 2010 and 2019.

America, as other studies<sup>(3-6,27)</sup> have demonstrated. Although its prevalence was significant in the immediate cause of death (field A), tuberculosis was not the main individual cause in the present study. We found a large number of diseases caused by fungi, such as pneumocystosis and cryptococcosis, similar to tuberculosis fatalities in AIDS patients worldwide. This high mortality is due to the easy contagion in immunocompromised patients when inhaling pathogenic hyphae, to the lack of rapid and effective tests to detect fungal diseases and start early treatment, and to its insidious development, as these diseases become more symptomatic only in more advanced stages of infection<sup>(1,6,28)</sup>.

As to other causes of death, the proportion of total mortality attributable to cancer and cardiovascular diseases has increased among HIV-infected individuals since the introduction of ART. Nonetheless, this finding does not necessarily reflect an upward trend in mortality rates from these causes; the rise in these rates results from the overall increase in survival among the study population. The present research found rates of 2.92% for cancer and 2.07% for cardiovascular diseases. These values are below those identified in an analysis made in the British Columbia region, Canada, which presented rates of 8.50% for neoplasms and 7.00% for cardiovascular diseases<sup>(7)</sup>.

The district analysis revealed that most deaths occurred on the state's coast, which has a higher population concentration, similar to national data from the HIV clinical monitoring report and epidemiological data <sup>(16,29)</sup>. The most affected locations were Vale do Itajaí and the metropolitan area of Florianópolis, a pattern also observed in another study carried out in Santa Catarina<sup>(17)</sup>.

From 2010 to 2019, AIDS mortality showed a downward trend in Santa Catarina. This information is in line with the national epidemiological bulletin, which points to a 15.7% decrease in mortality from the disease between 2012 and 2017, which can be attributed to public health policies<sup>(16)</sup>. Moreover, another study also conducted in the country's Southern Region identified values similar to those found herein, indicating a downward trend in AIDS mortality<sup>(30)</sup>.

The number of necropsies performed during the ten years assessed suggests a possible system failure in identifying the real cause of death because, from the total number of deaths studied, only 2.82% were submitted to a confirmatory examination of the cause. In contrast, 19.85% of deaths in field (A) were grouped into symptoms,

signs and abnormal clinical and laboratory findings, not elsewhere classified and external causes of morbidity and mortality, cases that could benefit from a more detailed *post-mortem* investigation.

#### Strengths

The current study had a robust database, collected over a 10-year interval, allowing the time analysis of deaths in people infected by HIV/AIDS in Santa Catarina and of the profile of these cases. Also, the geoprocessing analysis made it possible for us to determine the spatial distribution of deaths, contributing to decision-making about early diagnosis and proper treatment to prevent a fatal outcome.

## Limitations

Among the limitations of the present study, we underline the restrictions regarding the quality of the records analyzed, which can be noted by the lack of some data and the inadequate filling of documents. The underreporting of HIV/AIDS deaths and the use of generic ICDs are also possible, limiting the analysis of the real cause of death.

# CONCLUSION

Based on the data analyzed, the mean HIV/AIDS mortality rate in Santa Catarina was 7.64 deaths per 100 thousand inhabitants between 2010 and 2019, with a downward trend of 0.38% per year. Deaths were concentrated on the coast, in cities with a higher population density. Most of the sample consisted of middle-aged, single, white men with low schooling. The main causes of death were infectious and opportunistic diseases. The still improper completion of the death certificate indicates the need to invest in improving medical training so that this document can, more reliably, serve as an instrument for understanding the population's mortality pattern.

## Approval by the Human Research Ethics Committee

This study was approved by the Research Ethics Committee of Universidade do Sul de Santa Catarina, opinion number 4,538,034, and by the Research Ethics Committee of the Santa Catarina Health Department, opinion number 4,640,669.

## Participation of each author

BSE, IVAC: Conceptualization, Data curation, Writing – original draft. GOCP: Formal Analysis and Writing – review & editing. BPMI: Writing – review & editing; FS-T: Conceptualization, Project administration, Supervision and Writing – review & editing. All authors have approved the final version of the manuscript and are responsible for all aspects of the work, ensuring its accuracy and integrity.

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## **Conflict of interest**

The authors declare no conflicts of interest.

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