

# Mortality after discharge from a public tertiary cardiovascular referral hospital

Carlos Lederman, BSc (CompSc), MBA (ProjectMan), PhD (Sciences)<sup>a,\*</sup> , João Fernando Monteiro Ferreira, MD<sup>a</sup>, Cicero Piva de Albuquerque, MD<sup>a</sup>, Antonio Carlos Pedroso de Lima, BSc, PhD<sup>b</sup>, Lucia Pereira Barroso, BSc, PhD<sup>b</sup>, João Cláudio Miranda de Souza, BSc<sup>b</sup>, Victor Hugo Vieira de Lima, BSc<sup>b</sup>, Guilherme Jordan de Castro, BSc<sup>b</sup>, Nicole Zukowski Luduvice, BSc<sup>b</sup>, Lilian Cristina Correia Morais, BSc (Math)<sup>c</sup>, Magaly De Losso Perdigao, BSc (CompSc)<sup>c</sup>, Rosa Maria Vieira De Freitas, BSocSc, MPH<sup>c</sup>, Monica LaPorte Teixeira, BSc (Math), PhD (Epidemiology)<sup>c</sup>, Bernadette Cunha Waldvogel, PhD (Public Health)<sup>c</sup>, Alfredo José Mansur, MD<sup>a</sup>

## Abstract

It is critically important for stakeholders with distinct foci of attention on healthcare to understand patient evolution in the presence of an established diagnosis or with a suspected diagnosis of various diseases, specially considering death as an outcome. To study the long-term mortality of patients at a cardiovascular referral hospital. Deterministic binding (selection of pairs of registers from the hospital electronic health records and the mortality records of São Paulo state) from 2002 to 2017 was performed. Studied variables were: age, sex, hospital treatment unit where the first visit occurred (Emergency Unit, Outpatient Unit, Hospital Admissions, Diagnostics Services), treatment type, elapsed time between the first visit and death, diagnosis at first and last visits and variables related to death. Statistical Methods: descriptive, survival (with Kaplan-Meier method), correspondence and competitive risks analyses; in case of nonoccurrence of death until the end of 2017, the patients were considered alive. Statistical significance was set at values of  $P < .05$ . Median age at the first visit to the Hospital was 51.9 years. Birth locations included 4496 cities, 17.33% in São Paulo, 0.41% in Rio de Janeiro, 0.40% in Osasco, 24.04% in other cities. Sex included females (46.7%), males (44.2%), not defined (6.3%), and other (2.8%). We observed an association between diseases in ICD-10 Chapter 16 (certain conditions originating in the perinatal period) and Chapter 17 (congenital malformations, deformations, and chromosomal abnormalities), both as diagnoses and underlying causes of death, as well as between neoplasms as diagnoses and as the underlying cause of death. In this sample, there was an association between admission diagnoses and underlying causes of death, such as neoplasms, cardiovascular diseases, and congenital heart malformations. Additionally, patients who underwent a cardiac intervention had a smaller less mortality rate than those who were not operated on. There were also differences in cardiovascular mortality between distinct treatment units of the hospital ((Emergency Unit, Outpatient Unit, Hospital Admissions, Diagnostic Services).

**Abbreviations:** CEA = Centro de Estatística Aplicada (Applied Statistics Center), Fundação SEADE = Fundação Sistema Estadual de Análise de Dados (São Paulo State Foundation for Data Analysis), ICD-10 = International Codes of Diseases, release 10, ID = patient's official identification number, IME-USP = Instituto de Matemática e Estatística da USP (Institute of Mathematics and Statistics of the University of São Paulo), InCor = Instituto do Coração (Heart Institute, São Paulo Medical School, Faculty of Medicine).

**Keywords:** deterministic binding, ICD-10, interaction, survival analysis correspondence analysis

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

Article related to the thesis, under development, "Long-term mortality of patients attended in an academic hospital from the SUS-Unified Health System, department of the Health Ministry network, with high volume of attended patients, specializing in cardiovascular diseases, using electronic health records" ("Mortalidade no longo prazo de pacientes que receberam atendimento de hospital acadêmico da rede SUS voltado para o atendimento médico cardiológico com o emprego de bases de dados assistenciais obtidas de prontuários eletrônicos") to be presented to Instituto do Coração (InCor)-Hospital das Clínicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo.

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<sup>a</sup> Instituto do Coração (InCor) – Hospital das Clínicas HCFMUSP, Faculdade Medicina, Universidade de São Paulo, São Paulo, Brazil, <sup>b</sup> Departamento de

Estatística, Instituto de Matemática e Estatística da Universidade de São Paulo, São Paulo, Brazil, <sup>c</sup> Fundação SEADE, São Paulo, Brazil.

**\*Correspondence:** Carlos Lederman, Faculdade de Medicina da Universidade de São Paulo, Ambulatório Geral, (InCor), Av. Dr. Eneas DE Carvalho Aguiar, 44, piso AB, São Paulo, SP 05403-904, Brazil (e-mails: carloslederman01@gmail.com).

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## 1. Introduction

The aim of this study was to analyze the long-term mortality of patients treated in all departments of a cardiovascular referral hospital, the underlying causes of death, and the elapsed times between the first and last visits to the hospital and the death. Patients admitted to tertiary hospitals often have multiple comorbidities with potentially complex resolution. After discharge, their follow-up is rarely recorded in the hospital's database except when the patient is under a research protocol. Moore et al,<sup>[1]</sup> with a 5-year follow-up and a relatively small sample of 86 patients after hospital discharge, reported 33.3% mortality and a 21.3% readmission rate, with an average time between discharge and readmission of 50 days.

Similarly, McCarthy et al,<sup>[2]</sup> also with a small sample size involving 359 patients admitted for myocardial infarction, found that 10% of them died in the hospital and 19.7% survived for 1 year. In addition, when assessing the total sample of patients, a 23.2% mortality from all causes and a 69.2% readmission rate from all causes were identified. "At 1-year, postdischarge all-cause mortality was 23.2%, all-cause readmission was 69.2%, and major adverse cardiovascular events (composite of all-cause mortality, recurrent myocardial infarction, or stroke) was 34.9%."

Published studies on death after hospital discharge are commonly specific to a small number of specialized clinics, including only 1 or 2 diseases, and with a short follow-up after hospital discharge, probably due to the natural difficulty to match hospital records with mortality data, since death can often occur outside the hospital to which the patients were initially admitted. The survival after hospital discharge is still incompletely understood for patients treated in a wide variety of specialized clinics, from tertiary public hospitals.

This study intends to understand the elapsed timeframe after hospital discharge, according to age and sex distribution, as well as the diagnoses associated with worse outcome and their relation to the cause of death of patients of a tertiary cardiovascular referral hospital.

## 2. Methods

### 2.1. Deterministic binding – experience of Fundação Seade and the hospital

This method has been used by the Hospital using data from the Outpatient Unit<sup>[3]</sup> and by Fundação Seade in studies of child mortality<sup>[4,5]</sup>; Silva et al<sup>[6-8]</sup>; in studies about AIDS<sup>[9-11]</sup>; and in accidents during work.<sup>[8,12-14]</sup>

### 2.2. Omitted data

Omitted data were considered highly important to understand their statistical contribution; for example, Figure S19, Supplemental Digital Content, <http://links.lww.com/MD/I875>, shows that the patients without diagnoses (diagnosis omitted) have a survival population higher than the patients with 1 or 2 diagnoses.

### 2.3. Data handling

The sharing of data between the Hospital and Fundação Sistema Estadual de Análise de Dados (São Paulo State Foundation for Data Analysis) (Fundação SEADE) was covered and regulated by one agreement signed by both parties on November 11, 2017. This agreement included clauses about data protection and privacy, and all researchers involved signed a corresponding Nondisclosure Agreement. Hospital records were transferred to Fundação SEADE in a secure manner under the Brazilian General Law for Data Protection, law number

13,709 from December 31, 2018. After the Fundação SEADE performed the binding process, the resulting data returned to the Hospital where they were anonymized prior to statistical analysis.

### 2.4. Population records

A total of 1,395,063 hospital records was selected, from 2002 to 2018, for binding with data originating from civil registries in the State of São Paulo, collected and treated by Fundação SEADE. (Due to the pandemic, Fundação SEADE was only able to bind records from 2002 to 2017). There was 1 record per patient ID; each record included the date of the first and last visits with this patient's ID. Occasionally, that same patient received another distinct ID number; there was a step to identify the records related to the same patient in order to consider all of that patient's diagnoses and surgeries; Figure S1, Supplemental Digital Content, <http://links.lww.com/MD/I857> and Figure S2, Supplemental Digital Content, <http://links.lww.com/MD/I858> show the age distribution at the first and last visit to the Hospital, and the "n" mentioned refers to the number of records with date of birth and date of visit (n = 963,388 for Figure S1, Supplemental Digital Content, <http://links.lww.com/MD/I857> and n = 967,503 for Figure S2, Supplemental Digital Content, <http://links.lww.com/MD/I858>). There were 3 situations related to the presence of the dates of the visits in the records: both dates (first and last visit); just the date of the first visit (n = 962,388 records); and just the date of the last visit (967,503 records). The number of patients with date of the first visit OR date of the last visit is presented in Figure S3, Supplemental Digital Content, <http://links.lww.com/MD/I859> and Figure S4, Supplemental Digital Content, <http://links.lww.com/MD/I860> (n = 971,392). A considerable number of records were observed related to patients who have come to the hospital just for exams, with no diagnoses included. To study the effect of the removal of these records (n = 463,541), we have generated Figure S5, Supplemental Digital Content, <http://links.lww.com/MD/I861> and Figure S6, Supplemental Digital Content, <http://links.lww.com/MD/I862>, that can be compared with Figure S3, Supplemental Digital Content, <http://links.lww.com/MD/I859> and Figure S4, Supplemental Digital Content, <http://links.lww.com/MD/I860> where such exclusion has not occurred. The binding method (deterministic binding<sup>[15]</sup>) uses matching standards of the following variables: patient name, sex, date of birth, wife/husband name, father and mother names, legal identification number, address). Only records with a perfect match were selected. Pairs of entries in registers that the binding process suspected to belong to the same person, were individually analyzed by pairs of the Hospital's researchers in a double-blinded process. For the patients with more than 1 hospital ID, the oldest first date was considered as the first date and the most recent last visit date was considered as the last visit date. Afterwards, 1 record per patient was generated in a total of 1351,070 patients, and 187,913 originated from the binded records and 1163,157 originated from the nonbinded records.

### 2.5. Variables

Fundação SEADE receives mortality data from civil registries from all notaries in the State of São Paulo. All data are verified and corrected, when necessary. The underlying cause of death is obtained after this process as well as the causes of death. Three groups of variables were studied

-Demographic variables: Included age at the first and last visit to the Hospital, sex, and place and state of birth.

-Hospital variables: The number of registers in the database (from the same patient, identified using the ID generated by Fundação SEADE for the binded cases, or by an identifier generated using the name of the patient/birth date/mother's name

for the nonbinded cases), number of diagnoses per patient, Treatment Unit (Outpatient, Hospitalization, Emergency Unit, Diagnosis and Therapeutics Support Services), surgery (cardiac, not cardiac, not informed), diagnoses (International Codes of Diseases, release 10 [ICD-10 codes]), diagnoses of ICD-10 chapter 09 in the first and last visit to the Hospital.

**-Death variables:** Death date, the place of death (Hospital, other health establishment, street, other, not provided), underlying cause of death, elapsed time between the first and last visits to the hospital and the death. (See Table S1, Supplemental Digital Content, <http://links.lww.com/MD/I879>, that summarizes the baseline characteristics of the patients).

## 2.6. Place of the research

The study was executed at InCor, Instituto do Coração, Faculdade de Medicina da USP. Records were used from patients treated between January 1, 2002 and December 31, 2018, independent of age and sex. The Hospital receives a high volume of patients who require attention due to cardiac and respiratory diseases.

## 2.7. Patient population

The Hospital serves mostly (80%) patients from the SUS (Health Unique System), and a minority of patients from the private network. Included were 1,351,070 patients' records from the Hospital (information was not collected about whether the patients were private or not). The first unit that provided services was collected (Outpatient Unit, Emergency Unit, Hospitalization, Diagnosis and Therapeutics Support Services); the last unit that provided services was not collected. For multiple visits, the oldest date of visit was considered the date of the first visit, and the most recent date of visit as the date of the last visit. Collected surgeries were cardiac, not cardiac, and no surgery; the date of surgery was not collected. The binding process identified 187,913 patients (death was assessed) and 1,163,157 patients were considered alive until December 31, 2017.

## 2.8. Inclusion criteria

All Hospital patient records for between January 1, 2002 and December 31, 2018 were considered. Fundação SEADE had mortality data from 2002 to 2017. It was observed that 164 deaths were not included in the binding process; after investigation, it was concluded that these deaths occurred outside of the State of São Paulo and were communicated by the family, with no details of the underlying cause of death. No exclusion criteria were applied.

## 2.9. The binding process

The “Deterministic Binding” technique was used,<sup>[15]</sup> which was extensively used by researchers from Fundação SEADE (Waldvogel et al [2019] and Waldvogel [2020])<sup>[16]</sup> This method identifies pairs of individuals who were treated at the Hospital and died inside São Paulo State. In the binding process, the following variables were used: patient name, date of birth, sex, husband (wife) name, mother's name, father's name, patient's death date (when available in the Hospital record) and patient's ID card number. The binding process is based on 4 basic actions: variable standardization, variable derivation, finding, and clearing pairs with the possibility to being the same individual.

**2.9.1. Variable standardization, variable derivation, binding, clearing.** Variable standardization is a process that generates variables to be used in the comparison process; variable derivation is a process that allows comparisons when there are orthographic distinctions. The binding process identifies pairs of

records that belong to the same patient and generates variables that allow the comparison of data from the Hospital records with data from Fundação SEADE. The binding process selects pairs with a perfect match and pairs that have at least 80% similarity; each pair of records from this second set is verified one by one, by two researchers in a double-blinded process, in order to accept or reject the pair. In our process, from the second set, 46,780 pairs were accepted and 18,150 were rejected. By the end of the process, 202,707 pairs were binded and 1192,355 were not binded. Afterwards, 1 record per patient was generated, obtaining 187,913 binded records and 1163,157 not binded records.

**2.9.2. Anonymization.** For anonymization purposes, the Hospital officials responsible for patient data protection and privacy, required the removal of all personal data (names and addresses), public IDs, zip codes, and patient IDs from the database. The last zip code was preserved with the removal of the control digits. After data anonymization, the files were transferred to IME/CEA through one Hospital infrastructure created just for this transference, with login and password of the user who retrieved the files. This infrastructure was disassembled after data transfer. Requests for data access: refer to item 2.13.

## 2.10. Statistical analysis

To study long-term mortality, the Survival Analysis method was used.<sup>[17]</sup> The time between some events of interest was studied, such as the follow-up time (time between the first and last visit to the Hospital and the death, or the time until the end of the study, December 31, 2017). Figure S3, Supplemental Digital Content, <http://links.lww.com/MD/I859> shows a high number of patients with follow-up time under 1 year, for all the hospital types of Treatment Units (Figure S4, Supplemental Digital Content, <http://links.lww.com/MD/I860>). A significant number of one date visits was observed. Figure S5, Supplemental Digital Content, <http://links.lww.com/MD/I861> and Figure S6, Supplemental Digital Content, <http://links.lww.com/MD/I862> show the effect of the inclusion and removal of these records (with the same date as the first and last visits to the Hospital). The proportion of patients with follow-up time under 1 year is reduced from 67% (Figure S3, Supplemental Digital Content, <http://links.lww.com/MD/I859>) to less than 40% (Figure S5, Supplemental Digital Content, <http://links.lww.com/MD/I861>). For all patients who had data, the time between the first and last visits to the hospital and the death were evaluated, as well as the time between the first and last visits to the Hospital (see Table S2, Supplemental Digital Content, <http://links.lww.com/MD/I880>, which shows descriptive statistics for these variables including the maximum time between the visit to the Hospital and the death, which was close to 2 decades). The 3 times have a strong asymmetric behavior, with a considerable concentration of values between 0 and 1 year (Figure S3, Supplemental Digital Content, <http://links.lww.com/MD/I859>, Figure S7, Supplemental Digital Content, <http://links.lww.com/MD/I863>, and Figure S8, Supplemental Digital Content, <http://links.lww.com/MD/I864>). The values vary from 0 to approximately 20 years. For the average and the median, the times between the last visit to the hospital and death are shorter than the times between the first and the last visit to the Hospital (means 2.5 and 4.7; medians 0.8 and 3.6 years, respectively). A descriptive analysis and an exploratory analysis were performed, followed by a survival analysis, using the Kaplan–Meier<sup>[18]</sup> method. The records with the same date for the first and last visit were considered in the analysis but did not contribute to it. Data after 2017 were censored and the patients were considered alive. The mortality rate was calculated during the time with hazard estimates by using the Cox proportional-hazards model.<sup>[19]</sup> To evaluate the relation between the patient diagnosis during life and their underlying cause of death, correspondence analysis was

performed using biplot graphics analysis, showing the categories of each variable, and the distance between the dots shows the relation between the categories.<sup>[20]</sup> Two Cox models were adjusted to the data, one for the time (in years) between the first visit to the Hospital and patient death, and a second for the time (in years) between the last visit to the Hospital and patient death. The Cox model is a semi-parametric model of proportional rates, i.e., this model assumes that the rate of the mortality for 2 distinct individuals is constant over time. To test this hypothesis, descriptive techniques and statistical tests can be used. The visual verification of the survival functions estimated by the Kaplan–Meier method was used because the sample is very large, and this would make the statistical tests reject the proportionality, even in settings where this hypothesis would be adequate.

### 2.11. Software used

R version 4.1.3 (2022-03-10) – “One Push-Up” Copyright (C); 2022 The R Foundation for Statistical Computing; Platform: x86\_64-w64-mingw32/x64 (64-bit).

### 2.12. Ethical aspects

The project was approved by the Ethics Committee for Research on Human Beings of the Hospital das Clínicas da USP (CAAE n. 02071418.1.0000.0068).

### 2.13. Data access statement

All institutions in Brazil must obey a law that regulates access to personal data (“LGPD 13.709/2018 – Lei Geral de Proteção de Dados”); in addition, our institution (Hospital das Clínicas da USP) has signed one nondisclosure agreement with Fundação Seade (that maintains the mortality data), which establishes that both institutions cannot give access to the data to third parties. It is important to express that the data were analyzed in computers without any internet access and closed to external access, with 3 distinct consecutive passwords, and that the interchange of encrypted data between the institutions was executed in one infrastructure specifically created for a very limited time with access only through a temporary login and password.

But we are willing to be checked for specific additional questions regarding our data from the editor or referees. We are open to a local visit by a professional to inspect our databases.

## 3. Results

### 3.1. General characteristics of the studied records

All results are related, except when noted, to provided data. The results per Treatment Unit refer to the date of the first visit. Demographic details and clinical diagnoses are shown in Table S1, Supplemental Digital Content, <http://links.lww.com/MD/I879>. In 5% of the registers, patients were under 5 years of age and 3% of the registers had newborn patients. Figure S1, Supplemental Digital Content, <http://links.lww.com/MD/I857> and Figure S2, Supplemental Digital Content, <http://links.lww.com/MD/I858> show a symmetric distribution of ages in the first and last visits to the Hospital.

The most frequent surgery was cardiac surgery (see Table S3, Supplemental Digital Content, <http://links.lww.com/MD/I881>, which illustrates the percentages of Surgeries: Cardiac, Other, No surgeries). The number of visits to the Outpatient Unit and Diagnosis and Therapeutics Support Services were similar (see Table S4, Supplemental Digital Content, <http://links.lww.com/MD/I882>, which illustrates the percentages of visits per Treatment Unit). Among the registers with informed diagnostics, the most frequent number of diagnoses per patient was

one; 62.3% of the sample had no information about diagnoses (see Table S5, Supplemental Digital Content, <http://links.lww.com/MD/I883>, which illustrates the frequency of the number of patients with 0 to 5 or more diagnoses).

The remaining diagnoses per ICD-10 chapter are shown schematically in Figure S9, Supplemental Digital Content, <http://links.lww.com/MD/I865>. Figure S10, Supplemental Digital Content, <http://links.lww.com/MD/I866> shows schematically the remaining diagnoses. The most frequent diseases diagnosed on the first and last visit to the Hospital (see Table S6, Supplemental Digital Content, <http://links.lww.com/MD/I884>, which illustrates the importance of ICD-10 E78 disease) were disorders of lipoprotein metabolism and other dyslipidemias were the second most diagnosed disease. The frequency distribution of the ICD-10 chapter 09 diseases most frequently diagnosed, for all the patients in the sample, considering the first and the last visits to the Hospital, revealed the diagnosis I10, Essential (primary) hypertension, as predominant; (see Table S7, Supplemental Digital Content, <http://links.lww.com/MD/I885>, which illustrates that ICD-10 diseases I10, Essential [primary] hypertension, I50, Heart failure, and I25, Chronic ischemic heart disease, represent nearly 50% of all diagnosed diseases); additional details can be found in item 4.2.2, Number of Registers, below.

### 3.2. Mortality results

During the study timeframe (2002–2017), 201,707 deaths were identified, including those in all binded records. Of these records, 187,913 were related to specific patients whose death was assessed. The distribution of the frequencies of the diseases as Underlying Cause of Death revealed that the ICD-10 chapter 09 (diseases of the circulatory system) and chapter 02 (Neoplasms) were related to 60% of the Underlying Causes of Death (see Table S8, Supplemental Digital Content, <http://links.lww.com/MD/I886>, which illustrates how the ICD-10 chapter 10, Diseases of the respiratory system, as underlying cause of death, comes in third place, with 12.2%, immediately after Neoplasms and distant from Endocrine diseases, and nutritional and metabolic diseases come in fourth place, with 4.6%).

### 3.3. Estimated survival rates

**3.3.1. Kaplan–Meier – estimate of the probability of the survival time.** For the total number of registers, the estimate of the survival probability using the Kaplan–Meier method was 73% of the sample after 20 years (Figure S11, Supplemental Digital Content, <http://links.lww.com/MD/I867>, and Figure S12, Supplemental Digital Content, <http://links.lww.com/MD/I868>). This estimate was distinctly related to sex at both visits to the Hospital, on the first visit (Figure S13, Supplemental Digital Content, <http://links.lww.com/MD/I869>) and on the last visit (Figure S14, Supplemental Digital Content, <http://links.lww.com/MD/I870>).

The estimate of the probability of survival related to the variable Unit of Treatment was statistically significant when comparing the first and last visit to the Hospital (Figure S15, Supplemental Digital Content, <http://links.lww.com/MD/I871> and Figure S16, Supplemental Digital Content, <http://links.lww.com/MD/I872>).

The estimate of the probability of survival related to the variable Diagnoses, when comparing the ICD-10 chapter 09 diagnoses with diagnoses of other ICD-10 chapters, in the first and in the last visits to the Hospital (Figure S17, Supplemental Digital Content, <http://links.lww.com/MD/I873> and Figure S18, Supplemental Digital Content, <http://links.lww.com/MD/I874>) were significantly distinct.

The estimate of the probability of survival related to the variable Surgery (cardiac, not cardiac, not informed) was significantly distinct when these 3 options were compared (Figure S19, Supplemental Digital Content, <http://links.lww.com/MD/I875>).

The estimate of the probability of survival related to the number of diagnoses in the last visit to the Hospital was statistically significant (Figure S20, Supplemental Digital Content, <http://links.lww.com/MD/I876>).

**3.3.2. Estimate of the death risks. First visit to the Hospital** – the estimate of relative mortality rates revealed that men had a mortality rate 37% higher than the mortality rate of women (see Table S9, Supplemental Digital Content, <http://links.lww.com/MD/I887>, which illustrates, additionally, that the estimates of the relative mortality rates revealed that the patients who were treated in the Emergency Unit had a mortality rate 19% higher than patients treated in the Outpatient Unit and that patients treated by the Diagnosis and Therapeutics Support Services had a mortality rate 28% higher than that of patients treated in the Outpatient Unit).

*Last visit to the Hospital* – the estimate of the relative mortality rates revealed that the patients with a diagnosis of ICD-10 chapter 09 (circulatory system diseases) have had a mortality rate 24% higher than that of patients who did not have this diagnosis (see Table S10, Supplemental Digital Content, <http://links.lww.com/MD/I888>, which illustrates, additionally, that the men had a mortality rate 32% higher than that of the female patients). For the patients treated in the Emergency Unit, similar values were observed in the estimates of the mortality rates for the patients with cardiac surgery and the patients with other surgeries (see Table S11, Supplemental Digital Content, <http://links.lww.com/MD/I889>, which illustrates, additionally, that the hospitalized patients had similar values in the estimates of the mortality rates of the patients with cardiac surgery and the patients with other surgeries).

**Interaction** – (The interaction between 2 independent variables occurs when the effect of the levels of one variable is dependent on the levels of another variable). The interaction was studied between the variables Sex, ICD-10 chapter 09 disease in the first and last visits to the Hospital, Unit of Treatment, Age at the last visit to the Hospital, and Surgery type (cardiac, not cardiac, not informed).

Based on the Martingale residuals in the Cox model, it can be presumed that the interaction does not exist between the variables Sex and ICD-10 chapter 09 disease in the first visit to the Hospital and Unit of Treatment (see Table S12, Supplemental Digital Content, <http://links.lww.com/MD/I890>, which illustrates, additionally, that by adding 1 year to patient age, the estimated coefficient increases the patient mortality rate by 5%); (see Table S13, Supplemental Digital Content, <http://links.lww.com/MD/I891>, which illustrates, additionally, that patients with a circulatory system disease at the first visit to the Hospital have an estimated mortality rate of 22% compared with mortality of the patients with no circulatory system disease at the first visit to the Hospital). The study of the same Martingale residuals in the Cox model has shown, in addition, that for the time between the last visit to the Hospital and the death, it can be presumed that there is an interaction between the variables Treatment Unit and Surgery type at the last visit to the Hospital and between Treatment Unit and Surgery type (see Table S14, Supplemental Digital Content, <http://links.lww.com/MD/I892>, which illustrates, additionally, that all *P* values, except one, Treatment Unit Hospital (HO), are under .001).

### 3.4. Correspondence analysis

By comparing diagnoses at the Hospital with Underlying Cause of Death, it is clear that ICD-10 chapter 09 diseases are predominant as the Underlying Cause of Death, related to the diagnosis

at the first visit to the Hospital (see Table S15, Supplemental Digital Content, <http://links.lww.com/MD/I893>, that illustrates, additionally, that the ICD-10 chapters less diagnosed in the first visit, for the underlying cause of death as a disease of chapter 9, are chapter 16, Certain conditions originating in the perinatal period and chapter 15, Pregnancy, Childbirth, and the Puerperium) as well as in the last visit to the Hospital (Table S16, Supplemental Digital Content, <http://links.lww.com/MD/I894>, shows the same result of ICD-10 chapters 15 and 16 as less diagnosed in the last visit to the Hospital). The graphical analysis of these Correspondences shows 2 associations between the diagnoses and the underlying causes of death, the first one between the ICD-10 chapter 16, diseases (Certain conditions originating in the perinatal period) and chapter 17 diseases (Congenital malformations, deformations, and chromosomal abnormalities) and the second one between Neoplasms as diagnosis and as underlying cause of death, both for the diagnosis made on the first visit (Figure S21, Supplemental Digital Content, <http://links.lww.com/MD/I877>) and on the last visit to the Hospital (Figure S22, Supplemental Digital Content, <http://links.lww.com/MD/I878>). The high values for diseases of ICD-10 chapters 16 and 17 in the first coordinate allow the supposition that these cases are related to deaths of children up to 5 years of age.

## 4. Discussion

### 4.1. Results interpretation

**4.1.1. Age and sex.** The predominant age group was around the 5th decade of life and the 3rd Quartile was around the 6th decade of life. In the State of São Paulo, for 2022, the predominant age group includes 12.3% of the population and the 3rd quartile includes 9.2% of the population.<sup>[21]</sup>

We discussed the use of the concept of “Gender” instead of “Sex,” but we decided to keep the term “Sex.”

**4.1.2. Number of registers.** The majority of patients in the sample had 1 register. After researching the Hospital system, we concluded that the entries were related to visits to the Diagnosis and Therapeutics Support Services, 97.1% of the patients (*n* = 1,311,841) had one record, demonstrating that these patients have not returned after the last visit or these patients have died. Of these cases (*n* = 352,496), 26.9% were related to visits to the Diagnosis and Therapeutics Support Services; the visits to the Emergency Unit represent a significant part of the Hospital services. In the research sample, the first visit to the Emergency Unit occurred for 15.7% of the patients.

**4.1.3. Number of diagnoses.** The number of registers without diagnoses was predominant. This may have occurred due to the collection method. From the records with diagnoses reported, 20% of the sample had one diagnosis per record, almost 3 times the frequency of 2 diagnoses per record (6.8% of the sample). Over 5 diagnoses per record were reported for 4.7% of the sample (*n* = 64,056 records), one important indication of comorbidities; 62.3% of the records did not report diagnoses, which can indicate that patients visited the Hospital just for exams. The most frequent comorbidities, for the underlying cause of death from ICD-10 chapter 09 disease were, in this order: diseases of the respiratory system, endocrine, nutritional and metabolic diseases, diseases of the genitourinary system, certain infectious and parasitic diseases, and diseases of the musculoskeletal system and connective tissue (Table S17, Supplemental Digital Content, <http://links.lww.com/MD/I895> and Table S18, Supplemental Digital Content, <http://links.lww.com/MD/I896>).

An opportunity for the future would be the application of the Elixhauser method and/or de Charlson Comorbidity Index

to identify the comorbidity profile of the patients who visit the Hospital.

**4.1.4. Diagnostics.** Because the main speciality of the Hospital is to treat diseases of the circulatory system, it is not a surprise that 49.8% (n = 157,590) of the patients received this ICD-10 chapter 09 diagnosis in their first visit and that 60.6% (n = 308,240) of the patients had this ICD-10 chapter 09 diagnosis on the last visit to the Hospital (Figure S9, Supplemental Digital Content, <http://links.lww.com/MD/I865>, and Figure S10, Supplemental Digital Content, <http://links.lww.com/MD/I866>). The next 3 diagnoses by frequency order are symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified, mental, behavioral and neuro-developmental disorders, and factors influencing health status and contact with health services that demand better qualification for analysis. The next two, Endocrine, nutritional and metabolic diseases and Diseases of the respiratory system, are part of the assistant scope. Consequently, for groups of less specific diagnoses, there are opportunities for evolution in their identification. Table S17, Supplemental Digital Content, <http://links.lww.com/MD/I895> and Table S18, Supplemental Digital Content, <http://links.lww.com/MD/I896> show that for the crossing between diagnoses and underlying causes of death (both for ICD-10 chapters), only 3 ICD-10 chapters show one distinct behavior, indicating that ICD-10 chapter 09 was not the main underlying cause of death. Neoplasms; congenital malformations, deformations and chromosomal abnormalities; and certain conditions originating in the perinatal period were the most frequent underlying causes of death. Analyzing the underlying cause of death due to ICD-10 chapter 09, the most frequent diagnoses were ICD-10 chapter 09, followed by symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified (underlying causes of death not adequately defined), and in third place, Endocrine, nutritional, and metabolic diseases. Comorbidities before and after the visits to the Hospital can influence mortality rates, such as Neoplasms,<sup>[22]</sup> which can affect the survival of patients with heart diseases who underwent myocardial revascularization.<sup>[23]</sup>

**4.1.5. ICD-10 I.10 essential (primary) hypertension.** The most frequent disease that emerged from the study was the ICD-10 I.10 disease, Essential (primary) hypertension. In June 2022, in the State of São Paulo, 582 patients who were treated at the public health system (SUS) were hospitalized with this disease.<sup>[24]</sup> One possibility for this disease being the most frequently diagnosed is because of the lack of precision when the SUS is used.

**4.1.6. Surgery type.** It was observed that 59,062 patients (4.4%) underwent cardiac surgery;  $n = 17,060$  patients (1.2%) underwent other surgeries, and  $n = 1274,928$  patients (94.4%) did not undergo any surgery between the first and last visits to the Hospital. InCor (the Hospital of this study), for 24 years, from 1984 to 2007, has conducted an average of 2971 cardiac surgeries per year.<sup>[25,26]</sup> In our study, 59,062 cardiac surgeries were performed from 2002 to 2018, with an average of 3474 cardiac surgeries per year, showing one increase of 16.9% in comparison with the average in a published report.<sup>[25]</sup>

**4.1.7. Hospital's treatment unit.** The Treatment Unit most visited was Outpatient (27.6%), followed by the Diagnosis and Therapeutics Support Services (26.1%). In comparison, the study “The relationship between nurse staffing levels and nursing-sensitive outcomes in hospitals: Assessing heterogeneity among unit and outcomes types.” shows that, in the United States, the Treatment Unit most visited is Internal Medicine (38%); this percentage was obtained by the division of all the visits to the Internal Medicine unit, 8,033,099, by the total number of visits to all units 21,020,219.<sup>[27]</sup>

**4.1.8. Mortality data.** Looking for the patients who died during this study time frame (2002 to 2017), the diseases most frequently diagnosed were, in descending order, by ICD-10 chapter: Circulatory System Diseases (n = 18,536 in the first visit and n = 38,551 in the last visit) (Table S17, Supplemental Digital Content, <http://links.lww.com/MD/I895> and Table S18, Supplemental Digital Content, <http://links.lww.com/MD/I896>); Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified, (n = 4217 patients in the first visit and n = 16,053 patients in the last visit). “Brazil is the 4th country in the world with a higher number of patients with diabetes”<sup>[28]</sup>; in our study, the mortality rate for Endocrine, nutritional and metabolic diseases was 4.44% and the Brazilian guidelines on prevention of cardiovascular disease in patients with diabetes<sup>[29]</sup> states that for the Brazilian southeast region the mortality rate was 27.3%; this fact suggests that the patient profile for this Hospital deserves a more extensive analysis.

**4.1.9. Diagnostics of other ICD-10 chapters.** Of the 1635 patients diagnosed with Neoplasms, 106 died due to a Circulatory System Disease (as the underlying cause of death), according to the first visit to the Hospital (6.48% of the patients with Neoplasms). “Patients with cancer that have died due to a circulatory system disease, previously diagnosed with a circulatory system disease, have had a shorter survival in comparison with the patients not previously diagnosed with a circulatory system disease, and the proportion of patients with cancer that remained alive after 5 years of follow-up was 10% higher than the ones that were not diagnosed with a circulatory system disease.”<sup>[30]</sup>

**4.1.10. Circulatory system diseases.** As mentioned in the Fundação SEADE report from January 2020, circulatory system diseases are the major cause of death in the State of São Paulo, representing 29% of deaths. Our study shows that 42.3% of the patients had a circulatory system disease as the underlying cause of death (Table S8, Supplemental Digital Content, <http://links.lww.com/MD/1886>). These rates can be explained by the fact that the Hospital attracts more patients with diseases of the circulatory system, because that is its specialty, which indicates the relevance of diseases of the circulatory system.

**4.1.11. Kaplan-Meier – estimate of the survival time.** The estimate of the probability of survival was distinct for the variable Sex on both visits to the Hospital (Figure S13, Supplemental Digital Content, <http://links.lww.com/MD/I869> and Figure S14, Supplemental Digital Content, <http://links.lww.com/MD/I870>) and for the Treatment Unit.

Comparing the study results with results in the article “O que mostram os registros de óbito de 2018? Tendências e padrões demográficos no Estado de São Paulo” da Fundação SEADE (*What are the mortality records from 2018 showing? Tendencies and demographic standards in the State of São Paulo*), it can be observed that one high concentration of men survived until 75 years of age; however, the higher concentration of women survived until 90 years of age, and in 40 years these concentrations for both sexes almost doubled.<sup>[31]</sup>

**4.1.12. Limitations.** The following data were not collected: the Treatment Unit in the last visit to the Hospital, the surgery date, deaths communicated by the family that did not occur inside the State of São Paulo, and whether the patient was a member of the public or private system.

## 5. Conclusions

Diseases of the circulatory system are critical risk factors; patients diagnosed with circulatory system diseases have mortality rates 22% higher than rates in patients without this disease. For patients who underwent cardiac surgeries, the mortality rate was higher than that for those who did not undergo

such surgery, and these rates varied depending on the Treatment Unit. Patients with 2 or more diagnoses had a mortality rate higher than that in patients with one diagnosis, depending on the Treatment Unit. The study has shown one association between the diseases of ICD-10 chapters 16 (Certain conditions originating in the perinatal period) and 17 (Congenital malformations, deformations, and chromosomal abnormalities) diseases, both as diagnosis and basic cause of death as well as one association between ICD-10 chapter 2 (Neoplasms) (as diagnosis and underlying cause of death). The study of the association of underlying causes of death with previous diseases is highly important for planning policies for the Health arena, and the database that we are delivering as a result can be used for new epidemiological studies.

## Author contributions

**Conceptualization:** Carlos Lederman.

**Data curation:** Carlos Lederman, Lilian Cristina Correia Moraes, Magaly De Losso Perdigao, Rosa Maria Vieira De Freitas.

**Formal analysis:** Carlos Lederman, Antonio Carlos Pedroso de Lima, Lucia Barroso Pereira Barroso, Alfredo José Mansur.

**Investigation:** Carlos Lederman, João Cláudio Miranda de Souza, Victor Hugo Vieira de Lima, Lilian Cristina Correia Moraes, Magaly De Losso Perdigao, Rosa Maria Vieira De Freitas.

**Methodology:** Antonio Carlos Pedroso de Lima, Lucia Barroso Pereira Barroso, Monica LaPorte Teixeira, Alfredo José Mansur.

**Project administration:** Carlos Lederman, Monica LaPorte Teixeira, Bernadette Cunha Waldvogel, Alfredo José Mansur.

**Resources:** João Cláudio Miranda de Souza, Victor Hugo Vieira de Lima, Lilian Cristina Correia Moraes, Magaly De Losso Perdigao, Rosa Maria Vieira De Freitas, Alfredo José Mansur.

**Software:** Carlos Lederman, João Cláudio Miranda de Souza, Victor Hugo Vieira de Lima, Guilherme Jordan de Castro, Nicole Zukowski Luduvice, Lilian Cristina Correia Moraes, Magaly De Losso Perdigao, Rosa Maria Vieira De Freitas.

**Supervision:** Antonio Carlos Pedroso de Lima, Lucia Barroso Pereira Barroso, Bernadette Cunha Waldvogel, Alfredo José Mansur.

**Validation:** Carlos Lederman, João Fernando Monteiro Ferreira, Cicero Piva de Albuquerque, Lilian Cristina Correia Moraes, Magaly De Losso Perdigao, Rosa Maria Vieira De Freitas.

**Visualization:** Carlos Lederman.

**Writing – original draft:** Carlos Lederman.

**Writing – review & editing:** Carlos Lederman, Cicero Piva de Albuquerque, Alfredo José Mansur.

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