### DOI: 10.17058/reci.v13i1.17621

#### **ORIGINAL ARTICLE**

Accuracy of mortality indicators due sepsis-associated deaths in the Federal District Acurácia dos indicadores de mortalidade devido a sepse dos óbitos ocorridos no Distrito Federal

Precisión de los indicadores de mortalidad por sepsis de las defunciones ocurridas en el Distrito Federal

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> Submetido:10/05/2022 Aceito: 16/07/2022

#### ABSTRACT

**Background:** Sepsis currently represents a challenge for health systems, this fact may be related to the spread of bacterial resistance, the increase in the population of elderly, immunosuppressed individuals, and the improvement of emergency care, favoring the survival

of critically ill patients. This article aimed to evaluate the accuracy of mortality indicators due to sepsis in 2018. **Method:** Validation study of death certificates that occurred in the Federal District in 2018. Declarations whose basic causes of death identified were classified as garbage codes were identified, which were investigated by a multidisciplinary team, capable of reclassifying them with codes that allow for the improvement of health data. In order to assess accuracy, sensitivity, specificity, positive and negative predictive values, positive and negative likelihood ratios of death certificates from sepsis were calculated, with 95% confidence intervals. **Results:** A total of 6.244 statements were evaluated, of which 233 (3.74%) presented sepsis as the underlying cause before being investigated and only 35 (0.56%) maintained it after the investigation. The filling of statements with sepsis as the underlying cause by physicians showed a sensitivity of 0.9% (95%CI: 0.6 to 1.3) and a specificity of 92.0% (95%CI: 90.9 to 93.1). **Conclusion:** The low accuracy of the declarations demonstrates the non-reliability of the underlying cause of death from sepsis, especially the completion of death certificates that occurred in the Federal District in 2018.

Keywords: Sepsis. Data Accuracy. Cause of Death. Death Certificates.

## RESUMO

Justificativa: A sepse, atualmente, representa um desafio para os sistemas de saúde, tal fato pode estar relacionado com a disseminação da resistência bacteriana, o aumento da população de idosos, os indivíduos imunossuprimidos, e a melhoria do atendimento de emergência, favorecendo a sobrevivência de pacientes críticos. Este artigo teve por objetivo avaliar a acurácia dos indicadores de mortalidade devido à sepse em 2018. Método: Estudo de validação da causa básica dos óbitos ocorridos no Distrito Federal em 2018. Foram identificadas as declarações de óbito cujas causas básicas de morte apontadas foram classificadas como garbage code sepse, as quais foram investigadas por uma equipe multidisciplinar, capacitada para reclassificá-las com códigos que permitem o aprimoramento dos dados em saúde. A fim de avaliar a acurácia, foram calculados os valores de sensibilidade, especificidade, valores preditivos positivo e negativo, razões de verossimilhança positiva e negativa das declarações dos óbitos por sepse, com intervalos de confiança de 95%. Resultados: Um total de 6.244 declarações foram avaliadas, das quais 233 (3,74%) apresentavam a sepse como causa básica antes de serem investigadas e apenas 35 (0,56%) mantiveram-na após a investigação. O preenchimento das declarações com a sepse enquanto causa básica pelos médicos apresentou sensibilidade de 0,9% (IC95%: 0,6 a 1,3) e especificidade de 92,0% (IC95%: 90,9 a 93,1). Conclusão: A baixa acurácia das declarações demonstra a não fidedignidade da causa básica de óbito por sepse, sobretudo, do preenchimento das declarações dos óbitos ocorridos no Distrito Federal em 2018.

Descritores: Sepse. Confiabilidade dos Dados. Causas de Morte. Atestado de Óbito.

## RESUMEN

**Justificación:** Sepsis representa en la actualidad un desafío para los sistemas de salud, este hecho puede estar relacionado con propagación de resistencias bacterianas, aumento de la población de ancianos, inmunodeprimidos, y mejora de la atención de urgencias, favoreciendo la supervivencia de los pacientes críticos. Este artículo tuvo como objetivo evaluar la precisión de los indicadores de mortalidad por sepsis en 2018. **Método:** Estudio de validación de causa básica de muertes ocurridas en Distrito Federal en 2018. Se identificaron actas de defunción cuyas causas básicas de muerte fueron clasificadas como sepsis código basura y fueron investigadas por un equipo multidisciplinario capacitado para reclasificarlas con códigos que permitan la mejora de datos de salud. Para evaluar la precisión, se calcularon sensibilidad, especificidad, valores predictivos positivo y negativo y razones de verosimilitud positiva y negativa de certificados de defunción por sepsis, con intervalos de confianza del 95%.

**Resultados:** se evaluaron 6.244 declaraciones, de las cuales 233 (3,74%) tenían como causa básica la sepsis antes de ser investigadas y solo 35 (0,56%) mantuvieron después de investigación. Realización de declaraciones con sepsis como causa subyacente por parte de los médicos mostró sensibilidad del 0,9% (95%IC: 0,6 a 1,3) y especificidad del 92,0% (95%IC: 90,9 a 93,1). **Conclusión:** Baja precisión de las declaraciones demuestra la poca confiabilidad de la causa subyacente de muerte por sepsis, especialmente la finalización de los certificados de defunción ocurridos en Distrito Federal en 2018.

Palabras clave: Sepsis. Exactitud de los Datos. Causas de Muerte. Certificado de Defunción.

### **INTRODUCTION**

Sepsis consists of potentially fatal organic dysfunction triggered by the dysregulation of the host's immune response to infections. Sepsis is diagnosed from the association between multiple organ failure and suspected or confirmed infectious processes.<sup>1–3</sup> Classically, the characteristic organic dysfunction of sepsis is diagnosed by scores of two or more points on the Sequential Organ Failure Assessment (SOFA) scale, which assesses the functioning of the central, cardiovascular, respiratory and renal nervous systems, in addition to liver and platelet function.<sup>1</sup> Sepsis and septic shock are associated with significant morbidity and mortality in individuals admitted to the intensive care unit (ICU) because they acquire hospital infections more frequently.<sup>1,4</sup>

Risk factors for sepsis are extremes of age, a sedentary lifestyle, immunosuppression, alcohol consumption, cancer, diabetes, and prolonged use of catheters or other conditions that compromise skin integrity. However, among patients with established infections, other risk factors for sepsis have been reported, such as comorbidities and genetic factors of the host and infectious agent.<sup>1</sup> ICU admission, previous hospitalizations, bacteremia, obesity and community-acquired pneumonia have also been described as potential risk factors for sepsis.<sup>4</sup>

Today, sepsis represents a growing challenge for health systems in countries around the world. With the advancement of health technologies, the longevity of the populations most vulnerable to sepsis, such as elderly and immunocompromised patients have increased, thus leading to a subsequent increased incidence of sepsis. It is estimated that 17 million cases of sepsis occur worldwide each year, but estimates are likely to underestimate the actual number of cases.<sup>5</sup>

It is believed that 600,000 of the annual cases of sepsis occur in Brazil, where the lethality rates of sepsis and septic shock exceeded 30% and 60%, respectively, in 2003.<sup>5</sup> In 2015 alone, 110,049 hospitalizations for sepsis were recorded in the country, of which only 925 occurred in the Federal District. However, the federative unit had the highest average length of

hospital stay, at 20.11 days, and ranked eighth in the sepsis mortality rate, which corresponded to 50.38%.<sup>6</sup>

In addition to triggering significant morbidity and mortality, sepsis negatively impacts health systems in relation to bed occupancy and hospital costs. Estimates indicate that approximately 30% of Brazilian ICU vacancies are occupied by individuals with sepsis or septic shock. In addition, for each hospitalized patient, the average hospitalization cost is \$10,595.00.<sup>5</sup>

Although sepsis has higher lethality rates in underdeveloped or developing countries5, the vast majority of scientific publications on the subject come from developed countries. Perceived disproportionality skews the available evidence regarding sepsis, which may compromise understanding of the subject in contexts of countries with limited resources.<sup>1</sup> Therefore, it is likely that the underestimation of the incidence of sepsis in underdeveloped countries compromises the direction of resources for the study and treatment of sepsis regionally.

Therefore, especially in countries with limited resources, such as Brazil, the expansion of epidemiological data on sepsis, along with the implementation of public policies aimed at the prevention and proper management of sepsis nationally, and determining the underlying cause of death would all help to improve healthcare for septic patients. Thus, this study, conducted in the Federal District, aimed to evaluate the accuracy of mortality indicators due to sepsis in 2018.

### **METHODS**

## Study design and context

A validation study was conducted in the Federal District, which has the smallest territory and one of the smallest populations among the federative units in Brazil. The estimated population of the Federal District in 2021 corresponded to 3,094,325 individuals.<sup>7</sup> At the same time, the federative unit has the highest population density and the highest income in the country<sup>7</sup>, in addition to the second highest rate of life expectancy at birth, which was estimated to be 77.6 years in 2014.<sup>8</sup>

#### Data source, investigation steps and data collection procedures

Data collection for this research was carried out at the State Department of Health of the Federal District (SES-DF). This department manages mortality information systems, as well as diseases, injuries and compulsory notification events in the Federal District.<sup>9</sup> In Brazil,

mortality data are regulated through the Mortality Information System (SIM), whose standard document corresponds to death certificates.<sup>10</sup>

The information was collected through a standardized form (elaborated by the authors) based on the screening and investigation of potentially eligible death certificates. During screening, the garbage codes used *in field* 40 of the document, referring to the causes of death related to sepsis, were identified. Medical records, examinations and reports issued by health institutions linked to death certificates were accessed by the exclusive SES-DF system and analyzed. The information collected is presented and described in the variables section.

## Population and eligibility criteria

In this study, the population was composed of people who died in the Federal District in 2018, whose underlying causes of death indicated sepsis, represented in the International Classification of Diseases version 10 (ICD 10) by codes A40, A40.0, A40.1, A40.2, A40.3, A40.9, A41.0, A41.1, A41.2, A41.3, A41.4, A41.5 and A41.9; all death certificates of children under one year of age were excluded. Sepsis is considered a *garbage code*<sup>11</sup>. *Garbage codes* are basic causes of death that do not provide fundamental information about the triggering circumstance of death, so a valid underlying cause of death is not understood.

#### Variables

The main variable of this study is sepsis, as the underlying cause of death, which is recorded on the death certificate. In addition, other variables were used to characterize the population, which included age ranges (1 to 11 years, 12 to 18 years, 19 to 39 years, 40 to 59 years, and 60 years or more), sex (male and female), race or skin color (Asian, white, indigenous, African American and black), years of study (none, 1 to 3 years, 4 to 7 years, 8 to 12 years, 12 years or more), marital status (divorced/single/widowed and married/stable union), and place of death (hospital, other health facilities and other places).

### Data analysis

After data collection, the underlying causes of death from sepsis were compared, recorded in the original statements and the causes defined after the investigation by the multidisciplinary team, which was considered the gold standard. Subsequently, the death certificates were divided into four groups: true-positive, false-positive, true-negative and false-negative.

In the true-positive group, the death certificates that remained with the same underlying cause after the investigation, were grouped. The false-positive group included death certificates that initially had the underlying cause of death from sepsis but were reclassified to others after being investigated. In the true-negative group, all declarations that did not present the cause of sepsis and remained with the original underlying cause of death after the investigation were grouped. In the false-negative group, all statements that had another underlying cause and were reclassified for sepsis after investigation were included.

Finally, sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio were estimated, with 95% confidence intervals. Data analysis was performed using the data analysis and *statistical software* (STATA) statistical package, version 16.

The research was conducted respecting the ethical standards required in Resolutions 466/2012, 510/2016 and 580/2018 of the Ministry of Health and was approved by the Research Ethics Committee (CEP) of the School of Health Sciences (ESCS), CAAE:15457719.0.0000.5553, under opinion number 4,482,501. The researchers involved claim no conflicts of interest related to the development of the study.

### RESULTS

At the end of the data analysis, 6,244 death certificates were evaluated. The population analyzed had a mean age of 62.78 years (standard deviation  $\pm$  22.35) and a median of 67 years, whose amplitude was 1 to 112 years. Most deaths occurred among patients aged 60 years or older, male, white skin color, divorced, single or widowed, and with 1 to 3 years of study. In most deaths, the place of occurrence was the hospital. Before being investigated, 233 declarations presented sepsis as the underlying cause, which corresponds to 3.74% of the population. After the investigation, only 35 statements had sepsis maintained as the underlying cause, which represents 0.56% of the results, as shown in Table 1. Therefore, the investigation of death certificates rectifies the underlying cause of 84.97% of the declarations.

Table 1. Number (N) and percentage (%) of the variables of characterization of de	aths o	ccurred
in the Federal District in 2018 (N=6,244)		

Ν	%
2.507	40,33
3.709	59,67
74	1.19
	N 2.507 3.709 74

12 to 18	127	2.05
19 to 39	929	14.97
40 to 59	1.363	21.96
60 or more	3.713	59.83
Etnia/Raça/cor <sup>*79</sup>		
Asian	28	0.45
White	2.703	43.84
Indigenous	7	0.11
African American	2.895	46.96
Black	532	8.64
Marital status <sup>*285</sup>		
Divorced, single or widowed	3.972	66.67
Married or in stable union	1.987	33.33
Years of study <sup>*694</sup>		
None	896	16.14
1 to 3	1.463	26.36
4 to 7	1.290	23.24
8 to 11	1.266	22.82
12 or more	635	11.44
Place of death <sup>*28</sup>		
Hospital	5.116	82.30
Other health services	309	4.97
Other	791	12.73
Underlying cause of death prior to investigation		
Sepsis	233	3.74
Other underlying causes of death	6.011	96.26
Underlying cause of death after investigation		
Sepsis	35	0.56
Other underlying causes of death	6.209	99.44

\*Number of information unavailable for each variable; N: sample; %: percentage.

Table 2 shows that the sensitivity of the evaluated statements about sepsis was approximately 0.93% (95% CI: 0.64 to 1.29). On the other hand, there was a high probability of an individual who did not develop sepsis obtaining a statement that did not present sepsis as the underlying cause, since the specificity found was 92.00% (95% CI: 90.90 to 93.10). The chance of a death certificate whose underlying cause was sepsis belonging to a septicemic individual was 15.00% (95% CI: 10.70 to 20.30), which consists of the positive predictive value of the evaluated statements. The probability of a declaration that the individual who did not develop sepsis as the underlying cause was 38.00% (95% CI: 36.80 to 39.30), which represents the negative predictive value.

Additionally, according to Table 2, it was found that the chance of a death certificate indicating sepsis as the underlying cause is 0.12 times higher (95% CI: 0.08 to 0.16) for a septicemic person than for an individual with another underlying cause of death, which consists

of the positive likelihood ratio of the evaluated statements. At the same time, the probability of a declaration not indicating sepsis as the underlying cause is 1.08 times higher for septicemic people than for individuals who have not developed sepsis, which corresponds to the negative likelihood ratio found.

**Table 2**. Validation measures and predictive characteristics of the death certificate for sepsis disease in 2018, Federal District (N = 6,244)

Parameter	Value IC <sub>95%</sub> *
Sensitivity (%)	0.93  0.64 - 1.29
Specificity (%)	92.00 90.90 - 93.10
Positive predictive value (%)	$15.00\ 10.70 - 20.30$
Negative predictive value (%)	38.00 36.80 - 39.30
Positive likelihood ratio	0.11  0.08 - 0.16
Negative likelihood ratio	1.08 1.06 - 1.09
C = C = C = C = C = C = C = C = C = C =	- filmer internal

\*Confidence interval at 95%; N: sample; CI: confidence interval.

### DISCUSSION

A total of 233 deaths that occurred in the Federal District in 2018 presented sepsis as the underlying cause in the death certificate before being investigated. Generally, the profile of the population studied consisted of males; White; divorced, single or widowed; 60 years or older; and low educational level. After the investigation, there were 35 statements left in which sepsis was the underlying cause of death. Thus, the investigation rectifies the underlying cause of 198 statements, which corresponded to 84.97% of the original 233. The death certificates evaluated showed low sensitivity and high specificity.

The profile of the participants in this study is similar to that described in the literature. In 2015, 53 patients were admitted to the ICU due to sepsis or septic shock at the University Hospital of Brasília (HUB). Most of the hospitalized patients were also male and older than 60 years, in addition to living in the Federal District or Goiás. Additionally, 90.60% of them had pathological antecedents, including systemic arterial hypertension (SAH), diabetes mellitus (DM), maternal diseases and previous episodes of sepsis.<sup>12</sup>

Another investigation corroborated the findings of the survey, conducted in 2017, where 37,082 death certificates were investigated, which occurred in 17 municipalities in northern Brazil. During the screening of the documents, some of the underlying causes of death considered garbage codes were classified as priority, which included sepsis. After the investigation, 79.1% of the statements coded with garbage codes had the underlying cause rectified, and the number of deaths whose underlying cause was sepsis decreased by 24.9%.<sup>13</sup>

However, inadequate completion of the underlying cause in death certificates is not restricted to the aforementioned sites. Between 2007 and 2016, more than 4 million of the deaths in Brazil were reported with garbage codes as the underlying cause, which represented 34.0% of the total number of deaths. Thus, the investigation of these statements is essential for the improvement of health data.<sup>13</sup> According to DATASUS, in 2015 only, sepsis was responsible for 110,049 hospitalizations in the country, which incarcerated costs of R\$400,387,078.76.6 In the event that health actions and public policies promote the effective improvement of the population's health conditions, in the tangent of sepsis to other diseases and diseases with high prevalence in Brazil, the quality of available health information is crucial.<sup>13-15</sup>

Moreover, this study presented limitations. Among them, the main one consists of inadequate completion of the death certificates analyzed, which was verified both in the face of unfilled fields and incorrect information. Of the 6,244 statements, 694 did not present the field referring to the years of study of the deceased completed, corresponding to 11.11% of the sample. It is likely that the misconceptions observed in the statements are due to medical ignorance about the importance of proper filling of all fields of the document, as well as the malpractice of the medical class in informing the chain of pathological events questioned in the field of cause of death.<sup>13,16</sup>

In addition, the second limitation of this study is the existence of outdated, incomplete or even blank medical records, referring to individuals who died, which was also reported in the study conducted at the hub in 2015.<sup>6</sup> Inadequate medical records may be related to the negligence of the responsible health professionals and the existence of multiple disintegrated electronic medical records systems, since care provided in certain health institutions may not be recorded in the medical records to which the researchers had access.

However, all death certificates whose underlying cause was a garbage code were investigated individually by a multidisciplinary and previously qualified team. Thus, in addition to rectifying the underlying epidemiological cause in the Mortality Information System by investigating the medical records and medical examination reports of individuals who died, the other fields filled out incorrectly or neglected were also corrected during the typing of the document whenever possible. The death review committees (CROs) of health institutions where the deaths occurred were also triggered in the face of outdated, incomplete or blank medical records to obtain the information necessary for the correct investigation of deaths. Moreover, this is the first study in the Federal District to evaluate the accuracy of death certificates that indicate sepsis as the underlying cause. Death certificates that occurred in the Federal District in 2018 that indicated sepsis as the underlying cause of death, present low sensitivity and positive predictive value, which indicate the low reliability and low usefulness of mortality indicators due to sepsis for planning health actions and public policies. Nevertheless, the low accuracy of the statements demonstrates the lack of reliability of the diagnostic investigation of sepsis and, above all, of the completion of the declarations. The need for health institutions to implement programs aimed at improving the proper completion of death certificates and care for septicemic individuals is evident. Moreover, it is crucial that undergraduate medical courses and medical residency programs include the task of correctly completing death certificates as an educational objective.

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# Authors' contributions:

Fernanda Alves Ramires, Elivan Silva Souza, Amanda Oliveira Lyrio, Sarah dos Santos Conceição, Ana Claudia Morais Godoy Figueiredo and Josicélia Estrela Tuy Batista contributed to the conception, article design, analysis and writing of the article;

Cauê Sousa Cruz e Silva, Luísa Caroline Costa Abreu, Ana Laura de Queiróz Pereira, Elaine Ramos de Moraes Rego and Delmason Soares Barbosa de Carvalho contributed to the planning and design of the article, review and final approval of the article;

All authors have approved the final version to be published and are responsible for all aspects of the work, including ensuring its accuracy and integrity.