

Factors associated with death among cancer patients hospitalized for COVID-19 in Mato Grosso, Brazil

Fatores associados ao óbito entre pacientes com câncer internados por COVID-19 em Mato Grosso, Brasil

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ABSTRACT: *Objective:* To analyze the prognostic factors for death from COVID-19 among cancer patients. *Methods:* This is a retrospective study based on data recorded in the reporting system for COVID-19 hospitalizations in Mato Grosso. We assessed cases of cancer patients reported between April 2020 and June 2021. We calculated absolute and relative frequencies of sociodemographic variables, hospital care variables, and comorbidities, as well as mean, median, and standard deviation of age and length of stay. Odds ratios and their respective 95% confidence intervals (95%CI) — crude and adjusted — were estimated using the logistic regression model. *Results:* We analyzed 948 cancer patients hospitalized for COVID-19 in Mato Grosso, with a mean age of 59.7 years. The proportion of deaths was 34.5%, the mortality rate was 3.73 deaths/day (95%CI 3.35–4.16), and the median time between admission and death was 18 days. The likelihood of death was greater among patients aged 60 years or older, with chronic lung disease, who were admitted directly to intensive care units, and required mechanical ventilation at the time of admission. Patients hospitalized from April to December 2020 and January to March 2021 had a greater chance of death than those hospitalized between April and June 2021. *Conclusion:* The likelihood of death from COVID-19 was greater in cancer patients hospitalized before their vaccination period in the state, as well as among older individuals and those admitted in worse clinical conditions.

Keywords: COVID-19. Cancer. Hospital mortality. Prognostic factors.

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Conflict of interests: nothing to declare – **Financial support:** none.

RESUMO: *Objetivo:* Analisar os fatores prognósticos para o óbito por COVID-19 em pacientes com câncer. *Métodos:* Estudo retrospectivo com base nos dados registrados no sistema de notificação de casos de internações por COVID-19 de Mato Grosso. Foram avaliados casos notificados entre abril de 2020 e junho de 2021 com câncer. Calcularam-se as frequências absolutas e relativas das variáveis sociodemográficas, de assistência hospitalar e comorbidades, assim como média, mediana e desvio padrão da idade e do tempo de internação. Estimaram-se o *odds ratio* e seu respectivo intervalo de confiança de 95%, bruto e ajustados, por meio do modelo de regressão logística. *Resultados:* Foram considerados 948 pacientes com câncer internados por COVID-19 em Mato Grosso, com média de idade de 59,7 anos. A proporção de óbitos foi de 34,5%, e a taxa de mortalidade, de 3,73 pessoas/dia (intervalo de confiança de 95% — IC95% 3,35–4,16), com mediana de tempo entre admissão e óbito de 18 dias. Foi maior a chance de óbito entre os pacientes com 60 anos ou mais de idade, com doença pulmonar crônica, que internaram em leitos de unidade de terapia intensiva e necessitaram de ventilação mecânica no momento da internação. Os pacientes internados no período de abril a dezembro de 2020 e janeiro a março de 2021 apresentaram maior chance de óbito quando comparados aos internados entre abril e junho de 2021. *Conclusão:* Foi maior a chance de óbitos por COVID-19 entre pacientes com câncer internados antes do período de vacinação desse grupo no estado e entre aqueles mais velhos e admitidos em piores condições clínicas.

Palavras-chave: COVID-19. Câncer. Mortalidade hospitalar. Fatores prognósticos.

INTRODUCTION

The infection caused by the novel coronavirus (SARS-CoV-2) had its first officially registered cases in China at the end of 2019 and arrived in Brazil in February 2020, when the first case of the disease was reported in the country. After more than a year of COVID-19 pandemic, Brazil stands out among the countries with the highest number of cases and deaths from the disease; among the country's regions, the Midwest Region is the second in incidence rate and the first in mortality per 100 thousand inhabitants. The state of Mato Grosso had its first case of COVID-19 confirmed on March 20, 2020, and the first death on April 3, 2020. Until August 11, 2021, the disease had been responsible for 497,463 cases and 14,277 deaths reported, placing the state in sixth place in incidence rate (14,277 cases per 100 thousand inhabitants) and first in mortality (368 deaths per 100 thousand inhabitants) among the 26 Brazilian states¹.

In the COVID-19 pandemic, cancer patients have been considered a highly vulnerable group due to metabolic changes resulting from tumor growth and the suppression of their immune system during treatment². In a population-based cohort study — after adjustments for demographic characteristics, smoking, and comorbidities —, cancer diagnosis was independently associated with a higher chance of hospitalization and 30-day mortality from COVID-19³. A recent meta-analysis of risk factors for death from COVID-19 in cancer patients identified a higher mortality rate among men, individuals over 65 years of age, and those with comorbidities and symptoms such as dyspnea and cough⁴.

Among the factors that possibly aggravated the situation of many cancer patients during the pandemic period, delayed diagnosis, inadequate cancer care⁵, and suspension of cancer screening⁶ stand out. In Brazil, these effects may have been caused not only by the adoption of stricter social distancing measures and redirection of resources in periods when health services collapsed, but also by the individual perception of the risk of infection during treatment^{7,8}; yet, few studies have assessed factors associated with death among cancer patients hospitalized for COVID-19 in the country^{9,10}.

Thus, this study aimed to evaluate the prognostic factors for death among cancer patients hospitalized for COVID-19 in Mato Grosso.

METHODS

We conducted a retrospective study by analyzing the hospitalization of patients with confirmed COVID-19 in Mato Grosso between April 1, 2020, and June 10, 2021. Data were obtained by the Mato Grosso Health Department (*Secretaria do Estado de Saúde de Mato Grosso — SES-MT*) from the COVID-19 Panel, which, in turn, collected these data from the IndicaSUS System, established in Mato Grosso for the hospital reporting of inpatients with suspected or confirmed cases of severe acute respiratory syndrome (SARS) or COVID-19. Reporting is mandatory and made daily by all public and private health facilities that offer hospitalization in the state¹¹.

This study assessed reported cases of COVID-19 patients admitted to public and private hospitals in Mato Grosso, from March 2, 2020, to June 10, 2021, who had cancer among the registered comorbidities and whose outcome was discharge or death.

The dependent variable was death from COVID-19 during hospitalization among patients who declared having cancer. The demographic variables analyzed were gender (female and male), age group (<40 years, 40 to 49, 50 to 59, and 60 years or older), ethnicity/skin color (white, black/multiracial, Asian, indigenous, and ignored), and the patient's macroregion of residence (South, West, North, East, and Mid-North)¹². The main risk comorbidities (yes/no) for more severe cases of COVID-19 (hypertension, diabetes, cardiovascular disease, chronic lung disease, chronic kidney disease, and obesity) were included. Regarding admission aspects, we considered the type of unit at admission (ward and intensive care unit — ICU) and mechanical ventilation (yes and no) on the first day of hospitalization, in addition to the month the patient was admitted and a month grouping in five periods (in 2020: April–June, July–September, and October–December; in 2021: January–March and April–June).

We calculated absolute and relative frequencies of sociodemographic variables, hospital care variables, and comorbidities, as well as mean, median, and standard deviation (SD) of age (years) and length of stay (days). In-hospital mortality rates were calculated according to the total number of inpatients and the number of persons/day of follow-up, both multiplied by 100. Follow-up period was defined as the time elapsed between the date of admission and the date of death or discharge.

We estimated the odds ratios (OR) and their respective 95% confidence intervals (95%CI) — crude and adjusted —, using the logistic regression model since the variable defined as the study outcome is binary with the following categories: discharge and death from COVID-19. Variables with $p < 0.20$ in the bivariate analysis were included in the multivariate model, and variables with $p < 0.05$ were retained in the final model, except for gender, which was used for adjustment. The adequacy of the final model was verified by the Hosmer-Lemeshow test. All analyses were performed in the Stata software version 16.0 for Windows.

This study is part of the research project “Monitoring COVID-19 in Mato Grosso”, approved by the Research Ethics Committee of Universidade do Estado de Mato Grosso (opinion no. 4,602,628/2021).

RESULTS

From March 2, 2020, to June 10, 2021, 60,244 individuals were hospitalized for COVID-19 in Mato Grosso; 34,416 (57.1%) of them had comorbidities, and among those, 1,125 (3.3%) had cancer. We excluded cancer patients transferred to other hospitals (96% to hospitals in the same state) since it could lead to duplicate data analysis; those who had no information on the progress of the case; and those who died for a cause other than COVID-19 ($n=177$). The first hospitalization of a cancer patient whose outcome was discharge or death occurred on April 8, 2020. Thus, the results of this study refer to 948 cancer patients hospitalized for COVID-19 and 327 deaths.

June to August 2020 and March and May 2021 were the months with the highest numbers of recorded hospitalizations for COVID-19 among cancer patients, with June 2020 and March 2021 as the months with the greatest numbers of reported deaths among cancer patients (Figure 1).

The mortality rate was 3.73 deaths/day (95%CI 3.35–4.16) among cancer patients hospitalized for COVID-19. The median time between admission and death was 18 days and ranged from one to 147 days. The mean age was 59.7 years (SD=19.7), ranging from 0 to 99 years, and was higher among those who died (65.5 years and SD=16.0) compared to those who were discharged (56.6 years and SD=20.7). When stratified by gender (Figure 2), the median age was greater among those who died for both genders (female: 64 years for death and 56 years for discharge; male: 69 years for death and 65 years for discharge).

The proportion of deaths was higher among male patients, those in older age groups (Table 1), with hypertension, diabetes, chronic lung disease, who were admitted directly to the ICU, required mechanical ventilation at admission, and in the first months of the pandemic (Table 2).

In the multivariate model, patients aged 60 years or older (OR=2.39; 95%CI 1.46–3.92), with chronic lung disease (OR=1.64; 95%CI 1.05–2.55), who were admitted directly to the ICU (OR=2.26; 95%CI 1.63–3.12), required mechanical ventilation at admission (OR=5.61;

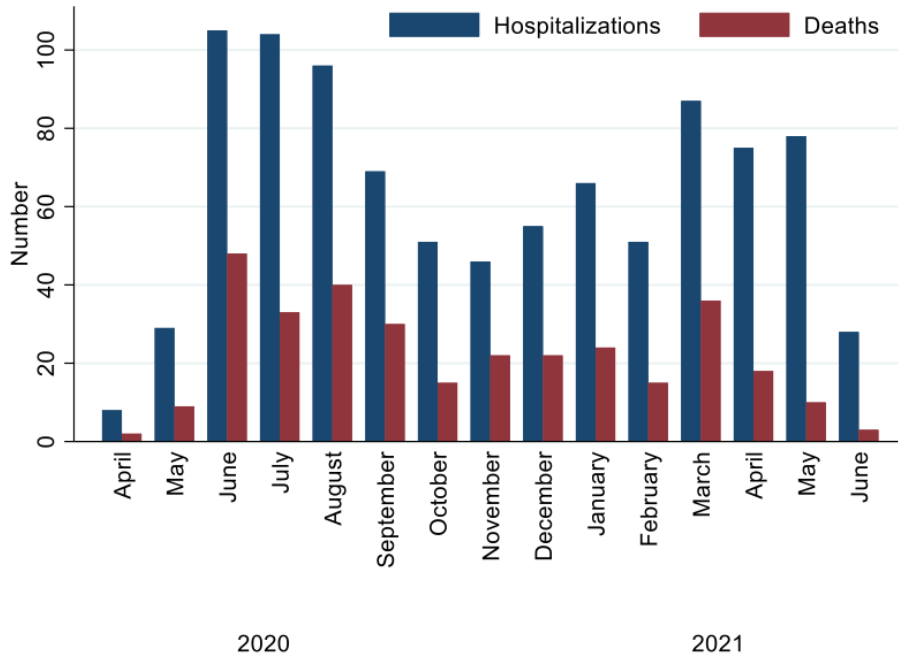


Figure 1. Number of hospitalizations and in-hospital deaths among cancer patients hospitalized for COVID-19 according to month. Mato Grosso, 2020-2021.

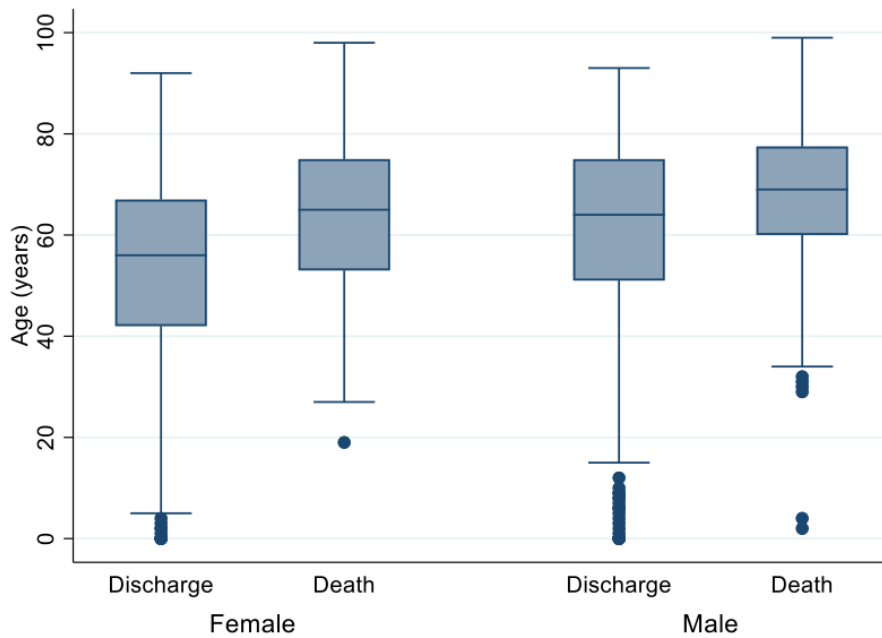


Figure 2. Boxplot of the age of cancer patients hospitalized for COVID-19 according to gender and hospital outcome. Mato Grosso, 2020-2021.

95%CI 3.66–8.58), and were admitted from April to December 2020 and January to March 2021 were more likely to die (Table 3).

DISCUSSION

The proportion of deaths was high among cancer patients hospitalized for COVID-19 in Mato Grosso; older adult patients, those with chronic lung disease, and admitted in apparently worse clinical conditions had a higher chance of death, which was approximately twice as high for those admitted directly to the ICU and more than five times greater for those who required invasive mechanical ventilation at admission. In addition, we emphasize the greater likelihood of death in the months prior to the start of vaccination for this group in Mato Grosso.

Table 1. Characterization of hospitalizations for COVID-19 and proportion of in-hospital deaths among cancer patients according to sociodemographic variables. Mato Grosso, 2020-2021.

Variables	Total		Death		p-value
	n	%	n	%	
Gender					
Female	423	44.6	131	31	0.040
Male	525	55.4	196	37.3	
Age group (years)					
<40	140	14.8	28	20.0	<0.001
40 to 49	96	10.1	21	21.9	
50 to 59	155	16.3	45	29.0	
60 or older	557	58.8	233	41.8	
Ethnicity/skin color					
White	223	23.5	77	34.5	0.654
Black	26	2.7	6	23.1	
Multiracial	520	54.8	183	35.2	
Asian/indigenous/ignored*	179	18.8	61	34.1	
Macroregion of residence					
South	123	13	46	37.4	0.596
West	50	5.3	18	36	
North	152	16	60	39.5	
East	41	4.3	15	36.6	
Mid-North	574	60.6	186	32.4	
Other states [†]	8	0.8	2	25	

*Ignored (n=170; 17.9%), Asian (n=7; 0.74%), and indigenous (n=2; 0.21%); [†]Espírito Santo (n=1), Minas Gerais (n=1), Pernambuco (n=1), Rondônia (n=3), São Paulo (n=1), Tocantins (n=1).

Cancer patients are susceptible to severe complications from SARS-CoV-2 infection due to the immunosuppression caused by the disease or its treatment. Therefore, they are considered individuals at high risk of hospitalization and death in the COVID-19 pandemic.

Table 2. Characterization of hospitalizations for COVID-19 and proportion of in-hospital deaths among cancer patients according to comorbidities and hospitalization-related aspects. Mato Grosso, 2020-2021.

Variables	Total		Death		p-value
	n	%	n	%	
Hypertension					
No	637	67.2	201	31.6	0.006*
Yes	311	32.8	126	40.5	
Diabetes					
No	773	81.5	251	32.5	0.006
Yes	175	18.5	76	43.4	
Cardiovascular diseases					
No	824	86.9	284	34.5	0.963
Yes	124	13.1	43	34.7	
Chronic lung disease					
No	830	87.6	271	32.7	0.002
Yes	118	12.4	56	47.5	
Kidney disease					
No	878	92.6	296	33.7	0.073
Yes	70	7.4	31	44.3	
Obesity					
No	891	94	308	34.6	0.849
Yes	57	6.0	19	33.3	
Type of hospitalization unit at admission					
Ward	644	67.9	160	24.8	<0.001
ICU	304	32.1	167	54.9	
Mechanical ventilation at admission					
No	797	84.1	216	27.1	<0.001
Yes	151	15.9	111	73.5	
Month of hospitalization					
April–June 2020	142	15	59	41.5	<0.001
July–September 2020	269	28.4	103	38.3	
October–December 2020	152	16	59	38.8	
January–March 2021	204	21.5	75	36.8	
April–June 2021	181	19.1	31	17.1	

*Bold text indicates statistical significance at a 5% level; ICU: intensive care unit.

Compared to patients without cancer, cancer patients have an eight times greater chance of death and three to five times greater chance of requiring mechanical ventilation and ICU hospitalization^{9,13,14}. A multicenter cohort study evaluating 2,215 adults in 65 hospitals in the United States for one month revealed that active cancer was associated with increased mortality¹⁵. In contrast, Jarahzadeh et al.¹⁶ analyzed 12 cohort studies exclusively of SARS-CoV-2-infected cancer patients and found that these individuals had a lower risk of requiring mechanical ventilation or dying than those who did not have cancer.

Cancer encompasses several diseases, classified by subtypes and stages, which can lead to very different prognoses and outcomes. However, these particularities aside, during the

Table 3. Crude and adjusted odds ratios of socioeconomic characteristics, comorbidities, and hospitalization conditions associated with death from COVID-19. Mato Grosso, 2020-2021.

Variables	Crude	Adjusted*
	OR (95%CI)	OR (95%CI)
Gender		
Female	1.00	1.00
Male	1.33 (1.01–1.74)**	1.13 (0.82–1.54)
Age group (years)		
<40	1.00	1.00
40 to 49	1.12 (0.59–2.12)	1.05 (0.52–2.09)
50 to 59	1.64 (0.95–2.81)	1.56 (0.86–2.83)
60 or older	2.88 (1.84–4.5)	2.39 (1.46–3.92)
Chronic lung disease		
No	1.00	1.00
Yes	1.86 (1.26–2.75)	1.64 (1.05–2.55)
Type of hospitalization unit at admission		
Ward	1.00	1.00
ICU	3.69 (2.76–4.92)	2.26 (1.63–3.12)
Mechanical ventilation at admission		
No	1.00	1.00
Yes	7.46 (5.03–11.07)	5.61 (3.66–8.58)
Month of hospitalization		
April–June 2020	3.44 (2.06–5.73)	2.79 (1.58–4.92)
July–September 2020	3.00 (1.90–4.75)	2.46 (1.49–4.07)
October–December 2020	3.07 (1.85–5.09)	2.50 (1.43–4.38)
January–March 2021	2.81 (1.74–4.55)	2.53 (1.49–4.28)
April–June 2021	1.00	1.00

OR: odds ratio; 95%CI: 95% confidence interval; *Hosmer-Lemeshow test — $p=0.383$; **bold text indicates statistical significance at a 5% level.

COVID-19 pandemic, drastic changes occurred in the care of cancer patients, resulting in a decrease in or postponement of radiotherapy sessions, a switch from intravenous to oral chemotherapy regimens, and changes in the use of immunotherapy¹⁷. Studies point to the effects of the pandemic on the care of cancer patients, leading to increased mortality from the disease^{5,18}.

Concerning sociodemographic characteristics, the present study found a higher chance of in-hospital death among older patients (aged 60 years or older), similar to findings reported for the general population of Rio de Janeiro and Espírito Santo^{19,20} and for cancer patients of both genders hospitalized in the United Kingdom²¹. Nonetheless, a study of women with cancer in Pernambuco did not find this association¹⁰. As for gender, although the proportion of deaths was higher among men, this association did not remain significant in the adjusted model, unlike some studies, such as those by Gupta et al.¹⁵ and Lee et al.²¹, who found, after adjustments, a higher likelihood of death from COVID-19 in the male population and among male cancer patients, respectively.

The months of hospitalization prior to vaccination against SARS-CoV-2 were associated with a higher chance of death among hospitalized cancer patients, which can be explained not only by the higher susceptibility of this risk group, still without the vaccine, but also by the inadequate care in health services during periods of high demand from COVID-19 cases. Like many Brazilian states, Mato Grosso has gone through periods of collapse of health services, with patients having to wait for ICU beds. From June to July 2020 and February to May 2021, the occupancy rate of COVID-19-dedicated beds remained above 90%, as indicated in several publications by the COVID-19 Observatory, from Fundação Oswaldo Cruz²², and the COVID-19 Panel, from SES-MT²³. The same pattern was observed in the analysis of the first 250 thousand hospitalizations for COVID-19 in Brazil, with greater in-hospital mortality during weeks with high admission rates, especially in the North, Midwest, and South regions²⁴.

Chronic lung disease was positively associated with death from COVID-19 in the present study. The predisposition of cancer patients to a higher incidence of cardiovascular and lung diseases can affect the severity of the coronavirus infection¹⁸. Among patients hospitalized in Rio de Janeiro¹⁹ and Espírito Santo²⁰, comorbidity was positively associated with in-hospital mortality from COVID-19, with cardiovascular diseases and diabetes as the most prevalent. In Pernambuco, a study evaluated the case fatality rate of COVID-19 among women with cancer and showed that approximately 40% presented other comorbidities, especially cardiovascular diseases (27.9%) and diabetes (13.2%)¹⁰.

Patients admitted directly to the ICU or who required invasive mechanical ventilation at admission had a higher chance of death. International studies report high mortality rates, relating them to ICU hospitalization and the use of mechanical ventilation^{25,26}, a fact that demonstrates the clinical progression toward severe forms of the disease, with respiratory failure. In Brazil, admission directly to the ICU was higher in the North and Southeast regions compared to the Midwest Region, with an overall mortality rate of 59% in patients admitted to the ICU and 80% in those who required mechanical ventilation²⁵.

Although the cancer patients' macroregions of residence did not remain associated with the likelihood of death, we highlight the heterogeneity of the health care system for severe

cases of COVID-19 in Mato Grosso, which can be a significant barrier to equitable access to health care for patients in general. All state macroregions had ICU beds dedicated to the care of severe cases of COVID-19; however, more than half of these beds were located in the metropolitan area; in mid-2020, only nine out of the 141 municipalities had this type of dedicated bed²⁷, a number that increased to 19 in June 2021, according to state bulletins²³. In the Midwest Region, 52% of ICU beds are located in capitals²⁴.

Even though we used an official source of SES-MT secondary data — very useful for the epidemiological description of cases, hospitalizations, and deaths from COVID-19 in Mato Grosso —, some study limitations stand out, including the lack of socioeconomic variables, such as schooling and income, and those related to clinical aspects, such as length of stay in each type of hospitalization unit and the use of mechanical ventilation.

Also, despite the relevance of identifying the main comorbidities among patients hospitalized for COVID-19 in Mato Grosso, the data provided did not include details about cancer, such as incident or recurrent cancer, its typology, staging, and treatment. For instance, a Chinese study with national representation by Liang et al.²⁸ identified cancer and other comorbidities among Chinese patients hospitalized for COVID-19 and revealed that although lung cancer was the most frequent type, it did not present a higher probability of severe events than other types of cancer, with advanced age being the only associated risk factor.

Despite concerns about complications related to cancer treatment, Vos et al.²⁹ revealed that imaging findings or hospitalizations of patients with cancer and COVID-19 are predominantly associated with SARS-CoV-2 infection rather than their cancer history or the status of cancer treatment. We also underline the quality of data from the IndicaSUS System for inpatients. As proposed by Romero and Cunha³⁰, the variables used were classified for health information systems and presented excellent quality, with less than 5% incompleteness, except for the variable ethnicity/skin color, which presented 17.9%, a value considered regular. Although health information systems have improved, the completeness of the variable ethnicity/skin color still has low quality³¹.

This study identified demographic and clinical factors associated with death from COVID-19 in cancer patients, which, albeit little explored in the literature, can contribute to improving care for this type of patient during the pandemic, which persists. Additional assessments are required to determine the clinical consequences, if any, of treatment interruptions, changes, or delayed cancer diagnoses for cancer patients due to the social distancing imposed by the COVID-19 pandemic. To mitigate the expected impact of the COVID-19 pandemic on these patients, we will need different strategies to manage the backlog in diagnostic and treatment services for people with cancer in the state.

ACKNOWLEDGMENTS

We would like to thank SES-MT for providing anonymous data of inpatients registered in IndicaSUS.

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Received on: 08/13/2021

Reviewed on: 12/21/2021

Accepted on: 01/10/2022

Preprint: 04/18/2022

<https://preprints.scielo.org/index.php/scielo/preprint/view/3965>

Author's contributions: Muraro, A.P.: writing – original draft, writing – review & editing, methodology. Oliveira, L.R.: writing – original draft, writing – review & editing, methodology. Andrade, A.C.S.: formal analysis, writing – original draft, writing – review & editing, methodology. Terças-Trettel, A.C.P.: writing – original draft, writing – review & editing. Guimarães, L.V.: writing – original draft, writing – review & editing. Souza, B.S.N.: writing – original draft, writing – review & editing.

