The COVID-19 pandemic and the increase in mortality of cancer patients in Brazil

Amanda Ramos da Cunha (amandaracunha@usp.br)
Universidade de São Paulo
José Leopoldo Ferreira Antunes
Universidade de São Paulo

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Abstract

Objectives

To analyze the impact of the COVID-19 pandemic on the mortality from all types and the five most common types of cancer in Brazil and investigate the relationship between the density of hospital beds and mortality from COVID-19 in cancer patients in Brazil's Intermediate Geographic Regions (RGIs).

Methods

The Brazilian Mortality Information System provided data on the deaths from trachea, bronchus, and lung, colorectal, stomach, female breast, and prostate cancer and all types of cancer, and from COVID-19 in individuals who had cancer as a contributing cause of death. Death rates from the pandemic years (2020–2022) were compared to pre-pandemic ones. An association analysis, through multivariate linear regression, was carried out between mortality from COVID-19 in cancer patients, the rate of hospital beds per 100,000 inhabitants, and the Human Development Index of the 133 RGIs of Brazil. *Results*: In 2022, mortality from all cancers was higher than in 2019 (3.0%), as well as the mortality from colorectal (8.5%), female breast (5.2%), and prostate cancer (2.2%). Mortality from COVID-19 in cancer patients, which reached its peak in 2021 (6.0/100,000), was negatively associated with the density of hospital beds in the public health system. *Conclusions*: This study suggests an increase in mortality from cancer, especially the treatable ones, in 2022 as an impact of the COVID-19 pandemic due to the burden that the new disease imposed on health services. Also, the findings suggest a protective role of the availability of hospital care concerning deaths due to COVID-19 in cancer patients.

INTRODUCTION

Since the first months of the COVID-19 pandemic, several publications worldwide have described the impact of this health crisis on cancer care. Decreases in diagnostic tests[1], in diagnosed cases[1, 2], interruption of screening programs[3–5], and reduction in surgeries, consultations, and hospital admissions for cancer patients[6] were identified in different countries as a consequence of adaptations and/or disruptions of the health services in this new scenario. Furthermore, the fear of contamination by the new disease kept patients away from health services, even when faced with symptoms that should be immediately investigated[7].

In Brazil, cancer-related hospital admissions for surgical purposes reduced by 28% from March to July 2020 compared to the same period of the previous year. This decline occurred in the entire country but was more significant in some regions, such as the South and Southeast[6]. There was a sustained decrease in hospitalizations due to oral and oropharyngeal cancer in Brazil that began in the first months of 2020 and continued until August 2021 – the last month documented[8]. In the first quarter of the pandemic, the number of surgeries for patients with lung cancer reduced by around 22% compared to the previous quarter, reaching a 51.5% reduction in the Northern region[9].

These and similar findings have concerned the medical and scientific community since the beginning of the pandemic, as delays in diagnosis and cancer treatment represent a risk for the progression of this disease and could lead to an increase in the number of avoidable deaths[10, 11]. Several statistical modeling studies worldwide projected that mortality from some types of cancer would increase as a result of the disorder in the screening, diagnosis, and treatment services caused by the COVID-19 pandemic[12–15]. When death registries and information systems began to release mortality data, still during the pandemic, some studies investigating the effects of the collapse on the actual number of deaths started to outline the scenario. Until now, most results have disagreed with predictions. In Sweden, there was a decrease in cancer deaths in 2020 compared to the average for the three years before the pandemic[16]. From 2019 to 2020, the number of cancer deaths in the United States of America, which had been increasing annually, has reducted[17]. In Mexico, the group of malignant neoplasms was one of the causes of death that showed the most significant decrease in the number of deaths in 2020 and 2021 compared to the expected number based on the pre-pandemic period: -5.3% (95% CI: -9.5 to -0.7)[18].

A study that analyzed the impact of the pandemic on mortality from neoplasms and cardiovascular diseases in Brazil in 2020 identified that, from March to December, the number of deaths with cancer as the underlying cause was 10% lower than expected[19]. Another study from the same country identified that deaths from neoplasms decreased in the age group over 40 years old in 2020 compared to the period between 2015 and 2019, while mortality from ill-defined causes increased[20]. However, these studies had just assessed the preliminary version of the data from 2020 of the Mortality Information System of Brazil (SIM), and the source's updates may have impacted the results.

Analyzing only the underlying cause of death is insufficient to understand the impact of the pandemic on the mortality of cancer patients as this population had a higher risk of death from COVID-19 than the general population[21–23]. A study carried out in the USA identified that, in 2020, mortality from cancer as the underlying cause of death was lower than in 2019. However, the deaths that had cancer as a contributing cause were higher in the pandemic year, reversing a decreasing trend that has been happening since 2015[24]. Another study from the USA analyzed deaths with any mention of cancer on death certificates and identified an increase in the cancer-related mortality burden during the first two years of the COVID-19 pandemic, also reversing the previous long-term declining trend[25]. These findings warn about the importance of monitoring the impact of the pandemic on people with cancer in a more comprehensive way, including investigating which factors may have influenced COVID-19 mortality in cancer patients.

The impact of the COVID-19 pandemic on cancer mortality is not fully understood. The data projections that indicated an increase in cancer mortality, especially in cancers considered treatable, due to the overload on health services and the replacement of health priorities are not being confirmed by the first studies published with data from mortality records. However, cancer mortality is not an outcome that occurs immediately, and analyses with more extended follow-up periods, which are not yet available, are necessary. Furthermore, understanding which characteristics of the health system were associated with COVID-19 mortality in cancer patients can provide insights to mitigate the damage caused by this and

future health crises in this population. This study aims to investigate the impact of the COVID-19 pandemic on the mortality of cancer patients in Brazil by analyzing the variation in death rates from all types of cancer and the five most common types in the Brazilian regions before and after the pandemic and through the analysis of mortality from COVID-19 in cancer patients. Furthermore, it aims to analyze the relationship between the density of hospital beds and mortality from COVID-19 in cancer patients in Brazil's 133 Intermediate Geographic Regions (RGI).

METHODS

This ecological study analyzed the mortality from trachea, bronchus, and lung (TBL), colorectal, stomach, female breast, and prostate cancer and all types of cancer in the pre-pandemic (2017–2019) and pandemic (2020–2022) periods and the mortality from COVID-19 in individuals who had cancer as a contributing cause of death. The Brazilian Mortality Information System (SIM, for the acronym in Portuguese) was the data source on deaths. This study used the SIM databases from 2017 to 2021 in final versions and the 2022 database in a preliminary version, last updated in September 2023 and available on the “openDataSUS” platform of the Brazilian Ministry of Health.

For cancer mortality, the SIM provided the number of deaths for which the primary cause was cancer of the TBL (ICD-10 codes C33 and C34), colon and rectum (C18-C21), stomach (C16), female breast (C50, in women), prostate (C61) and cancer in general (all “C” codes), by sex, age group (every five years), month, and municipality of residence in Brazil. A few deaths without the information of sex, age, or sex plus age were redistributed according to the respective distribution in the 26 Brazilian states and the Federal District; deaths without information on the municipality of residence were distributed to the respective municipality of occurrence. The deaths, by sex and age group, were then summed for Brazil’s 133 RGI[26]. To correct cancer mortality considering the underreporting due to ill-defined underlying causes, which can mask the actual number of deaths due to specific causes[27], a statistical correction (i.e., redistribution) was performed. To this end, the SIM also provided the total number of deaths with known causes and the number of deaths that the underlying cause was a code from chapter XVIII of ICD-10 (“Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified”; the “R” codes), by sex, age group, month, and RGI.

The 2010 and 2022 demographic censuses and the intercensal projections of the Brazilian Institute of Geography and Statistics (IBGE) provided the Brazilian population by sex, age group, year, and RGI – the population for the years 2017 to 2022 was projected by a linear trend, based on the 2010 Census and intercensal projections from 2011 and 2012, by sex, age group, and RGI, and adjusted for the number of inhabitants from the 2022 Census by RGI, from which population distributions by sex and age group were not available until the conclusion of this article.

The rate calculation observed the following steps: (1) correction of the number of deaths for each type of cancer and for all cancers to consider deaths with an ill-defined underlying cause by sex, age group, month, and RGI, using the technique proposed by França et al.[27]. This technique recommends that the

amount of cancer deaths should receive a proportion of deaths with ill-defined causes, and this proportion should be ½ the percentage that cancer occupies in the total number of deaths with a known cause. This adjustment was made for each type of cancer by sex, age, and RGI and the corrected number of deaths was summed by the five Brazilian macro-regions – North (N), Northeast (NE), Southeast (SE), South (S), and Midwest (MW); and (2) calculation of the rate (corrected deaths divided by the respective population) for every 100 thousand inhabitants, as adjusted for sex and age group (5 years), by the direct method, using the WHO World Standard population distribution[28]. Final mortality rates for cancer and types of cancer were monthly obtained for each macro-region and the whole country. Prostate cancer and female breast cancer mortality exclusively refer to the sex-specific populations groups. Rates from the pandemic years – 2020, 2021, and 2022 – were then compared to rates from 2019 (pre-pandemic) by percentage of change.

For mortality from COVID-19 in individuals who had cancer as a contributing cause of death, the SIM provided the number of deaths for which the primary cause was COVID-19 (ICD-10 B34.2) and which had some cancer (any code “C”) as a contributing cause. The rates were calculated per 100 thousand inhabitants by RGI, by macro-region, and for Brazil, for all months from 2020 to 2022, and adjusted for sex and age group (five years), using the direct method, with the WHO World Standard population distribution as the reference[28].

Finally, an association analysis was carried out between mortality rates from COVID-19 in individuals who had cancer and the density of hospital beds in the 133 RGIs in Brazil, adjusted by the Human Development Index (HDI). The National Registry of Health Establishments (CNES) provided the total number of inpatient hospital beds and the number of inpatient hospital beds linked to the SUS from 2020 to 2022 in each RGI – the CNES provides this data in a monthly format; the number of beds in December of each year represented the respective year. The bed density was then calculated as a yearly rate for every 100 thousand inhabitants, for which the denominator was the annual population of each RGI. To calculate the HDI for each RGI, the Human Development Atlas in Brazil provided the HDI for each municipality in 2010. The municipal HDI was then aggregated by RGI using a weighted average, whose weight was the number of inhabitants of each municipality according to the 2022 Census. Linear regression analyses were used to evaluate the association, with models for Brazil and for each macro-region, by type of hospitalization bed (total or beds linked to the SUS). Results with $p \leq 0.05$ were considered statistically significant.

All analyses used Stata/IC 15.1 software. The delimitation of the “waves of the pandemic” (i.e., periods of recrudescence), which was used to represent some results graphically, was based on the number of weekly deaths from COVID-19 in the Brazilian population obtained from the World Health Organization observatory (https://www.who.int/data/gho).

RESULTS

Mortality from all cancers was 126.23 deaths per 100 thousand inhabitants in Brazil, 2019 – the pre-pandemic year. Among the types of cancer included in this study, prostate cancer had the highest mortality (20.56/100,000), followed by female breast (17.34/100,000), TBL (16.43/100,000), colon and rectum (11.10/100,000) and stomach cancer (8.45/100,000). The South region had the highest mortality from all cancers (147.65/100,000) and from TBL (16.15/100,000) and prostate cancer (22.11/100,000); the Southeast, for breast cancer (18.50/100,000) and colon and rectal cancer (13.33/100,000); and the North region, for stomach cancer (12.30/100,000) – Table 1.

Mortality from COVID-19 in cancer patients in Brazil in 2021 was the highest among the pandemic years analyzed: 5.98/100,000. This year, the Midwest and South regions had the highest rates – respectively, 7.44 and 7.21/100,000; however, in 2020, the Southeast had the most elevated rate, 5.69/100,000, being the only region with a rate above the national for the respective year (4.67/100,000). Figure 1 allows us to identify that mortality from COVID-19 among cancer patients was higher in the so-called waves of the pandemic, that is, in periods when this health crisis was most intense in the country, considering the number of deaths from COVID-19 in the general population. The highest monthly rates were, respectively, those of March and April 2021, which were part of the second wave of the pandemic in the country, the most extended and lethal one. A similar pattern was identified for the regions separately – results not shown.

In 2020, the first year of the pandemic, mortality from all cancers in Brazil reduced by 2.61% compared to 2019, and in 2021, it reduced by 0.24%. The variation changed direction in 2022: mortality increased by 2.96% compared to the reference year (Table 2), reaching 129.97/100,000 (Table 1). In the first year of the pandemic, the five types of cancer analyzed had a reduction in mortality in Brazil. The most significant reduction in 2020 was in stomach cancer rates, followed by TBL: -8.38% and − 2.65%, respectively, compared to 2019. This generalized reduction did not occur in 2021 and 2022 when only TBL and stomach cancers persisted to show a reduction. For Brazil, mortality from colon and rectal, prostate, and female breast cancer were higher in 2021 and 2022 than in 2019. In 2022, death rates from colon and rectal and female breast cancer were, respectively, 8.49% and 5.21% higher than in 2019, while for stomach cancer, mortality in 2022 reduced by 5.33% compared to 2019 (Table 2). The types of cancer that presented the highest mortality in 2020, 2021, and 2022 remained the same as in 2019 (in descending order, prostate, female breast, TBL, colon and rectum, and stomach) – Table 1.

The North region showed the most significant reduction in mortality from all cancers in the first year of the pandemic: -3.72%. Nonetheless, in 2022, this region had the second-highest increase percentage (5.01%), behind only the South, with 5.57%. Furthermore, mortality from female breast cancer in the North region in 2022 was 18.66% higher than in 2019, and mortality from colon and rectal cancer was 14.22% higher. For stomach cancer mortality, all regions showed a reduction in 2022, except for the North; the Southeast region had the highest decrease: -7.95% (Table 2).

Figure 2 shows that, for all regions of Brazil, the cancer mortality curve had an increasing trend from 2017 to 2019, and in 2020, the first year of the pandemic, this pattern was inverted. The increasing trend

was resumed in 2021; however, the North, Northeast, and Southeast regions remained with rates lower than those of 2019. In 2022, the increasing direction became more evident, and all regions of Brazil showed higher cancer mortality in 2022 than in 2019. From 2017 to 2022, the South region had the highest cancer death rates in Brazil, followed by the Southeast; the lowest rates were always in the North.

COVID-19 mortality in cancer patients was inversely associated with the rate of hospital beds maintained by the public health system, regardless of the HDI of the RGI. When these analyses were carried out for each region of Brazil, only the Northeast and South regions showed a statistically significant association, also with a negative direction. In the analysis between the outcome and the general availability of hospital beds – i.e., the rate of SUS plus private inpatient hospitalization beds per 100 thousand inhabitants – only the South showed a statistically significant association, which was negative (Table 3).

Table 1

Mortality (rate per 100,000 inhabitants) from tracheal, bronchus, and lung, colorectal, stomach, female breast, prostate, and all types of cancer, and from COVID-19 in individuals with cancer, between 2019 and 2022, for Brazil and Brazilian macro-regions

Region[a]	All Cancer	TBL[b]	Stomach	Colon	Prostate	Breast	COVID-19 with Cancer
Mortality 2019							
N	112.59	13.86	12.30	6.67	20.12	13.34	-
NE	110.68	12.80	8.04	6.74	21.20	15.72	-
SE	130.05	16.26	8.30	13.33	19.62	18.50	-
S	147.65	23.99	8.79	13.31	22.11	18.10	-
MW	123.28	16.15	7.19	11.33	21.86	17.08	-
BR	**126.23**	**16.43**	**8.45**	**11.10**	**20.56**	**17.34**	-
Mortality 2020							
N	108.40	12.85	11.62	7.20	19.91	13.71	4.08
NE	108.41	12.18	7.37	6.85	21.60	15.56	3.72
SE	125.46	16.02	7.47	12.72	19.00	18.11	5.69
S	145.93	23.36	8.22	13.54	22.35	17.86	3.69
MW	122.49	16.06	6.91	11.35	22.12	17.03	4.32
BR	**122.93**	**16.00**	**7.74**	**10.92**	**20.43**	**17.10**	**4.67**
Mortality 2021							
N	110.80	12.79	11.57	6.91	20.53	14.09	4.21
NE	110.04	12.25	7.41	7.23	21.08	16.11	3.94
SE	128.85	16.06	7.74	13.41	19.90	18.23	6.74
S	150.96	23.77	8.67	14.49	23.85	18.34	7.21
MW	124.12	16.68	6.70	11.50	22.48	16.79	7.44
BR	**125.93**	**16.14**	**7.94**	**11.48**	**20.99**	**17.37**	**5.98**
Mortality 2022							
N	118.23	14.36	12.45	7.62	19.71	15.83	1.65

[a]N – North, NE – Northeast, SE – Southeast, S – South, MW – Midwest, BR – Brazil

[b]TBL – tracheal, bronchus, and lung cancer

Region[a]	All Cancer	TBL[b]	Stomach	Colon	Prostate	Breast	COVID-19 with Cancer
NE	113.45	12.73	7.73	7.43	21.18	16.17	1.30
SE	132.43	15.82	7.64	14.20	20.03	19.21	2.54
S	155.87	24.54	8.31	14.74	23.68	19.45	2.54
MW	128.81	17.66	7.13	12.46	22.70	18.60	2.54
BR	**129.97**	**16.43**	**8.00**	**12.04**	**21.01**	**18.24**	**2.16**

[a]N – North, NE – Northeast, SE – Southeast, S – South, MW – Midwest, BR – Brazil

[b]TBL – tracheal, bronchus, and lung cancer

Table 2
Percentage of change in mortality from tracheal, bronchus, and lung, colorectal, stomach, female breast, prostate, and all types of cancer in 2020, 2021, and 2022 compared with 2019, for Brazil and Brazilian macro-regions

Region[a]	All Cancer	TBL[b]	Stomach	Colon	Prostate	Breast
	% Change in Mortality – 2020/2019					
N	-3.72	-7.28	-5.55	7.94	-1.03	2.71
NE	-2.05	-4.83	-8.27	1.58	1.87	-1.06
SE	-3.53	-1.49	-10.10	-4.60	-3.18	-2.11
S	-1.16	-2.64	-6.46	1.74	1.09	-1.35
MW	-0.64	-0.56	-3.89	0.11	1.20	-0.34
BR	**-2.61**	**-2.65**	**-8.38**	**-1.66**	**-0.64**	**-1.35**
	% Change in Mortality – 2021/2019					
N	-1.58	-7.72	-5.94	3.53	2.05	5.58
NE	-0.57	-4.27	-7.82	7.17	-0.55	2.43
SE	-0.93	-1.25	-6.80	0.60	1.40	-1.43
S	2.24	-0.94	-1.41	8.81	7.91	1.32
MW	0.68	3.25	-6.82	1.43	2.85	-1.74
BR	**-0.24**	**-1.81**	**-6.03**	**3.44**	**2.07**	**0.17**
	% Change in Mortality – 2022/2019					
N	5.01	3.56	1.23	14.22	-2.01	18.66
NE	2.50	-0.52	-3.84	10.14	-0.10	2.86
SE	1.83	-2.72	-7.95	6.55	2.09	3.87
S	5.57	2.29	-5.41	10.75	7.11	7.47
MW	4.48	9.35	-0.74	9.90	3.82	8.85
BR	**2.96**	**-0.04**	**-5.33**	**8.49**	**2.18**	**5.21**

[a]N – North, NE – Northeast, SE – Southeast, S – South, MW – Midwest, BR – Brazil

[b]TBL – tracheal, bronchus, and lung cancer

Table 3
Rate of hospital beds and SUS hospital beds (beds per 100,000 inhabitants) in the Intermediate Geographic Regions of Brazil, by macro-region and for Brazil, between 2020 and 2022, and its association with mortality from COVID-19 in individuals with cancer

Region[a]	2020	2021	2022	Coeff[b]	p-value
	Hospital Beds [median (IQR)]				
N (n. 22)	171.1 (152.7-207.9)	168.5 (152.4-203.3)	175.7 (156.7-210.5)	0.005	0.694
NE (n. 42)	208.5 (176.5-238.5)	208.7 (181.2-241.6)	210.0 (184.1-233.9)	-0.007	0.067
SE (n. 33)	202.7 (182.0-265.9)	200.6 (187.0-266.2)	202.7 (188.7-259.5)	-0.001	0.696
S (n. 21)	232.6 (207.5-296.9)	235.2 (204.4-283.8)	239.2 (197.7-284.8)	-0.013	*0.026*
MW (n. 16)	208.4 (178.0-263.7)	222.2 (178.5-265.9)	230.1 (179.6-265.1)	0.004	0.590
BR (n. 133)	207.8 (174.3-242.8)	207.1 (178.5-243.6)	208.7 (179.4-245.1)	-0.002	0.333
	SUS Hospital Beds [median (IQR)]				
N (n. 22)	146.2 (128.6-183.2)	144.9 (128.8–175.0)	152.1 (132.9–188.0)	-0.004	0.799
NE (n. 42)	173.9 (154.0-206.6)	176.2 (154.6-208.7)	173.6 (156.5-208.1)	-0.009	*0.024*
SE (n. 33)	140.0 (118.6-181.3)	138.2 (112.5-175.5)	139.7 (110.7-170.3)	-0.004	0.462
S (n. 21)	167.7 (144.3-212.8)	163.5 (136.8-203.1)	161.9 (130.8-211.3)	-0.019	*0.018*
MW (n. 16)	155.2 (135.1-184.6)	159.1 (136.0-190.7)	153.2 (138.1-190.5)	0.000	0.990
BR (n. 133)	157.1 (135.1-190.4)	160.0 (136.0-191.6)	159.8 (134.9-195.1)	-0.006	*0.047*

[a]N – North, NE – Northeast, SE – Southeast, S – South, MW – Midwest, BR – Brazil

[b]coefficient adjusted by the Intermediate Geographic Regions' Human Development Index from 2010

DISCUSSION

This study found that mortality from all types of cancer and the five most common types in Brazil decreased in 2020, the first year of the COVID-19 pandemic, compared to the previous year. However, in

2022, mortality from all cancers was higher than in the reference year, as well as the mortality from colorectal, female breast, and prostate cancer. During the pandemic, mortality from COVID-19 in cancer patients (i.e., cancer as a contributing cause), a direct impact of the pandemic on this population, was higher, respectively, in 2021 and 2020, and the highest rates followed the waves of the pandemic in the country. The findings showed that this mortality was negatively associated with the number of hospital beds in the public health system (SUS) per inhabitant, considering the 133 RGI in Brazil, suggesting a protective role of the availability of hospital care concerning deaths due to COVID-19 in cancer patients.

For 2020, the present study's findings seem to align with the competing cause hypothesis, as the reduction in the death rate from all cancers in 2020 appears to have been partly compensated by the death rate from COVID-19 in cancer patients from that same year. This explanation supports that many individuals with cancer, at a higher risk of death from this disease, may have died from COVID-19, as this population had a higher risk of death from COVID-19 than the general population[21–23]. However, this rationale needs additional reflection: the contributing cause of death is likely underreported in the mortality information system, especially considering the first pandemic year, in which the unprepared health services – responsible for completing the causes of death – were under massive pressure and overload in the fight against COVID-19.

A study in Brazil identified that mortality from ill-defined causes increased in 2020 compared to the period between 2015 and 2019[20]. In the present study, death rates from cancer as the underlying cause were adjusted for ill-defined causes, according to redistribution techniques established in the literature[27], but there are no statistical procedures to correct the underreporting of deaths due to COVID-19 that had cancer as a contributing cause. Thus, the present study suggests that mortality from COVID-19 in cancer patients (1) is probably much higher than recorded, and (2) was not just a competing cause but an additional cause of death in this population since the first year of the pandemic. In other words, mortality from COVID-19 not only took the lives of patients who would die from cancer but added preventable deaths to the mortality burden of this population, especially at the peaks of the pandemic. The results from 2021 contribute to these rationales, as both mortality from cancer as the underlying cause of death and mortality from COVID-19 in cancer patients increased in 2021 compared to 2020.

Compared to 2019, mortality from all types of cancer increased nearly 3.0% in 2022 countrywide, reaching 5.6% in the South region. A study that monitored 40 years of cancer mortality in Brazil reported an increasing trend for all cancers between 2003 and 2017, however, with an average annual percentage variation for the period of 0.2%[29], a much lower increase than observed in 2022. Unlike 2020 and 2021, the 2022 findings align with the hypothesis raised at the beginning of the pandemic – mainly from statistical modeling studies – that cancer mortality would increase due to disruptions in the provision of cancer care[12–15]. As cancer mortality is not an outcome that occurs immediately, analyses with longer follow-ups are necessary. However, the findings from 2022 justify the fear that this worrying movement has already begun.

Results by type of cancer reveal that the mortality from colorectal, female breast, and prostate cancer, despite having reduced in the first year of the pandemic, began to increase from 2021 onwards, with even more significant percentages of increase in 2022. The growth reached 8.5% for colorectal cancer. According to Maruthappu et al.[30], who use the survival analysis of Quaresma, Coleman, and Rachet[31] as a basis for the classification, these are cancers considered treatable, as their five-year survival rate is greater than 50%. Still considering the hypothesis that cancer mortality would increase as a result of delays in diagnosis and treatment of cases, it is reasonable to expect that this impact would be more evident in treatable cancers, i.e., those that would benefit more from timely diagnosis and treatment.

Observational studies have reported changes in the diagnosis and treatment of these cancers during the pandemic in Brazil. The number of mammograms performed by the SUS in 2020 decreased by more than 40%, reaching a 67% reduction in Rondônia, a state in the North of the country[32]. We highlight that this region, which in 2019 already had the worst mammography coverage by the SUS in Brazil[33], showed the most significant increase in mortality from female breast cancer in 2022. Also, the situation remained unfavorable in 2021: 15% fewer exams than in 2019 in Brazil[34]. Analysis that compared new cases of colorectal and anal cancer in the outpatient clinics of a reference center for cancer treatment in São Paulo, reported a decrease in newly diagnosed patients referred and an increase in locally advanced disease from March to July 2020 compared to the same period in 2019. The authors argue that the difficulty of having colonoscopies and the patient's fear of going to hospital during the pandemic may explain the decrease[35]. Concerning prostate cancer, a study that analyzed the number of therapeutic procedures for this type of cancer (radical prostatectomy plus radiotherapy) in Brazil, carried out by the SUS during the pandemic, indicated that there was a 22% reduction between August 2020 and March 2021, compared to the same period in previous years[36]. The present study suggests that the increase in mortality from colorectal, female breast, and prostate cancer (i.e., treatable cancers) identified in 2022 may be due to the disruptive effect of the pandemic on the cancer care network – and warns that this consequence may last for a few years.

TBL neoplasms were those with the lowest variation in mortality in 2022 compared to the pre-pandemic year. The literature considers this type of cancer non-treatable, as its five-year survival rate is less than 10%[30]. Given that the pandemic impacted the provision of care for TBL cancer, with a relevant reduction in the number of surgeries in the SUS[9], one explanation could be that the disruption of health services less impacts mortality due to neoplasms that are more lethal – and less responsive to the acting of health services. However, the 9.35% increase in mortality from this type of cancer in the Midwest region in 2022 draws attention. A study that analyzed mortality from TBL neoplasms in the Midwest states from 2000 to 2015 found an increasing trend in only two of its four states for the female population, which presented an average annual percentage change (APC) of approximately 1.6%, and in only one state for the male population, with an APC of 0.6%[37]. Therefore, the result of the present study is atypical and deserves more careful investigation. The reductions found in deaths from stomach cancer seem compatible with recent trends for this type of cancer in Brazil[29], with the reduction peaking in 2020 and 2021, following the logic of a competitive cause. It is noteworthy that this type of cancer is not

considered a non-treatable neoplasm, but its low five-year survival rate (18.8%[31]) also indicates a non-favorable prognosis.

The North and Northeast had the lowest mortality from COVID-19 in cancer patients in the three pandemic years. There is a substantial chance of underreporting in these regions, as these regions (1) were severely affected by the pandemic, in which the first spikes in mortality due to COVID-19 occurred in the country[38, 39]; and (2) have the most room for improvements concerning the quality of records in SIM[40]. For Brazil and each region separately (results not shown), these rates were higher in the periods corresponding to the peaks of deaths from COVID-19 in the country. These are expected results, as these deaths are a direct consequence of the pandemic and followed its dynamics of resurgence and slowdown. Studies with the American population have identified similar results[24, 25]. The rate of COVID-19 in cancer patients, which is not irrelevant, makes it clear that relying only on the underlying cause of death may lead to underestimating the impact of the pandemic on patients with cancer.

The density of SUS hospital beds was negatively associated with mortality from COVID-19 in cancer patients in the Northeast, South, and the whole country, in an analysis adjusted for the HDI of the analysis units – the 133 RGI in Brazil. These regions correspond to an intermediate geographical stratification between states and cities, which always includes large urban centers. The RGI likely covers the entire path through the health system that a resident of these goes through, with larger cities acting as a reference for smaller nearby cities, which do not have hospitals or health services of greater technological complexity[41]. If a cancer patient with COVID-19 lives in a small town without a hospital and needs hospital attention, they are likely to be referred for hospital treatment in a more structured city close to their local residence. This characteristic makes RGI an opportune territorial division to study the determinants of mortality from COVID-19 in cancer patients, identifying which factors are associated with more favorable regional outcomes. The availability of beds may be crucial in protecting this vulnerable population from preventable deaths, as cancer patients were more likely to develop severe cases of COVID-19[21–23] and, consequently, to depend more on the hospital network. The present results align with this rationale; however, additional investigations that analyze the flow of bed occupancy and/or ICU beds in different regions can contribute to this understanding and support decisions on allocating health resources in possible future crises. Also, the significant results for SUS beds, even with adjustment for HDI, point to the crucial role of the public health system for the cancer population during this outbreak.

The decrease in death rates from cancer as the underlying cause that the present study found in the first year of the pandemic is compatible with the findings of other studies in Brazil[19] and other countries[16–18]. However, this study observed lower decreases than those reported for Brazil[19]. Differences in the definition of the reference rate for comparison and, mainly, the characteristics of the present study could explain these discrepancies. As far as we know, this study is the first to analyze cancer mortality using the final version of the SIM from 2020 and 2021, as well as extending the analysis to the year 2022, and to use data from the 2022 Census of Brazil to calculate the mortality rates. The final versions of the annual mortality databases contain more recorded deaths than preliminary versions, and

the 2022 Census reported a smaller population than estimates based on previous censuses. These differences could justify the discrepancies in the results.

The main limitation of this study concerns the registration of deaths. As already mentioned, the quality of recording the underlying cause of death decreased during the pandemic, with an increase in the percentage of deaths with an ill-defined underlying cause compared to previous years[20], which may be an expected consequence of a collapsing health system. To minimize this limitation, the methodology of this study included the redistribution of ill-defined deaths, considering variations by sex, age group, month, and RGI for the analysis of the underlying cause of death; however, no statistical correction replaces qualified registration.

This study suggests an increase in mortality from cancer, especially treatable cancers – colorectal, breast, and prostate –, in 2022 as an impact of the COVID-19 pandemic in Brazil due to the burden that the new disease imposed on health services, especially at the hospital level, and the replacement of health priorities during the health crisis. With cancer diagnoses and treatments delayed due to the overload of hospital care, the patients likely arrived in cancer care services with more advanced diseases and lower chance of survival. As it is a chronic disease whose cure may require years of treatment, which causes sequelae and has the potential for recurrence – factors in part related to access to timely diagnosis and treatment – the deleterious impact of COVID-19 on cancer care may continue to have an impact on mortality from this disease years after the pandemic's control. The literature reports that cancer care disruptions during the COVID-19 pandemic could lead to significant life loss but also argues that this damage could be mitigated by increasing diagnostic and treatment capacity in the short term to address the service backlog[14]. The results of the present study highlight the need to understand what consequences the pandemic may have brought on health services, which can be worked on to prevent the increase in mortality in the coming years. Surveillance in health in the coming years is critical, as well as monitoring the production of cancer diagnosis and treatment services and the delay in the onset of treatment.

Also, concerning the cancer patients, COVID-19 not only took the lives of patients who would die of cancer – it was not one cause of death that replaced another; it likely added preventable deaths to the mortality burden of this population. The availability of SUS hospital beds may have acted as a protective factor against this additional mortality source for the cancer population in Brazil. This evidence can join the accumulated knowledge about the COVID-19 pandemic to assist in equitable strategies to mitigate the COVID-19 impact on the cancer patients and to contribute to decision-making in health crisis.

Declarations

Ethics approval and consent to participate:

This study did not require consent for participation as it used only public, anonymous, and aggregated data. The School of Public Health of the University of São Paulo Research Ethics Committee approved the project in December 2021 under opinion number 5.183.030.

Consent of publication:

Not applicable

Availability of data and materials:

This study used publicly available databases. The datasets generated, developed, and analyzed during this study are available from the corresponding author upon reasonable request.

Competing interests:

The authors declare that they have no competing interests.

Funding declaration:

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Author contributions:

ARC and JLFA contributed to the study's conception and design. ARC performed material preparation, data collection, and analysis. ARC wrote the first draft of the manuscript. JLFA revised and commented on previous versions of the manuscript. ARC and JLFA read and approved the final manuscript.

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Figures

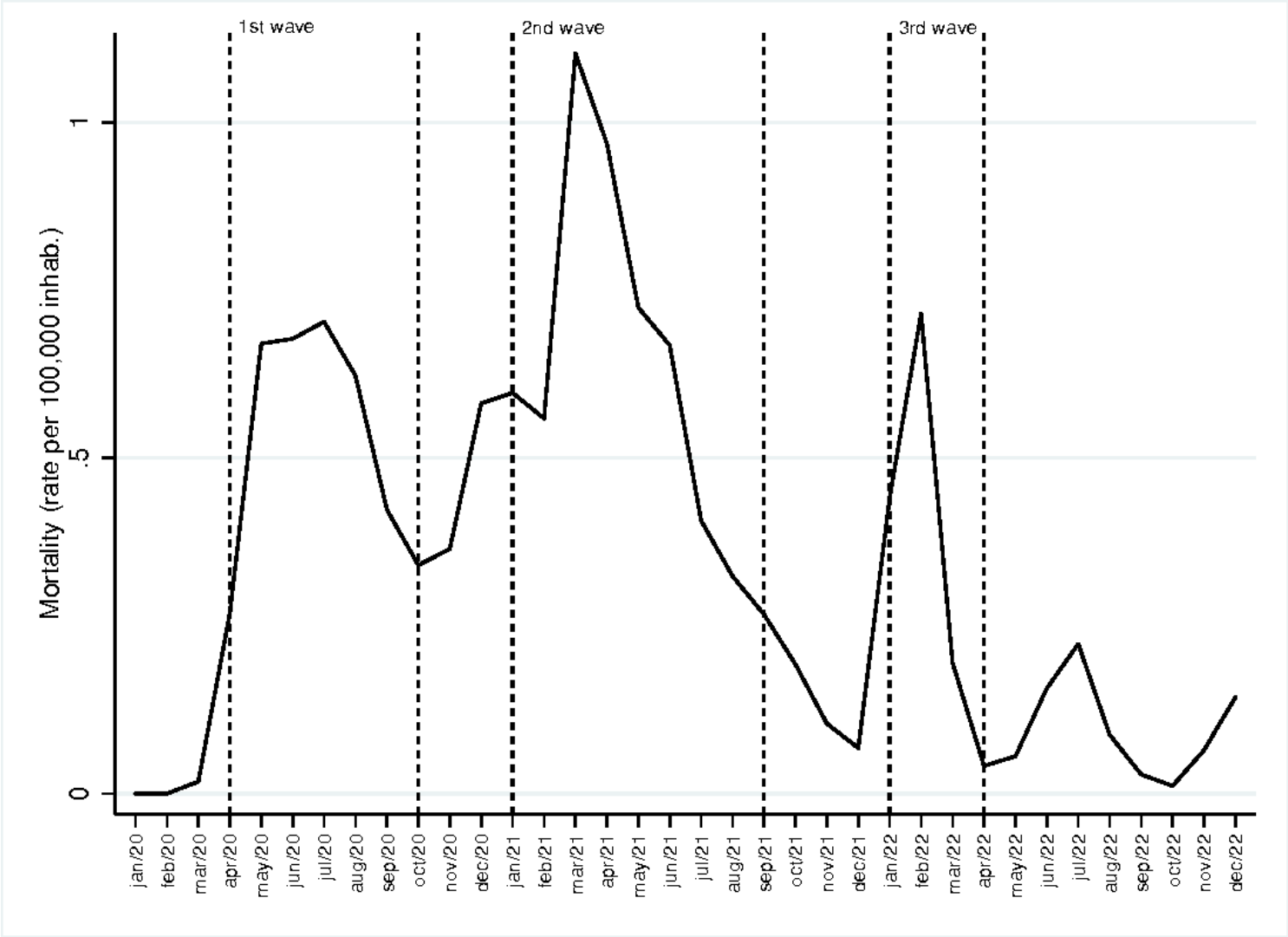

Figure 1

Mortality (rate per 100,000 inhabitants) from COVID-19 in individuals with cancer per month, between 2020 and 2022, in Brazil

Note: 1st, 2nd and 3rd waves refer to periods of worsening of the COVID-19 pandemic in Brazil, considering the number of deaths from this disease.

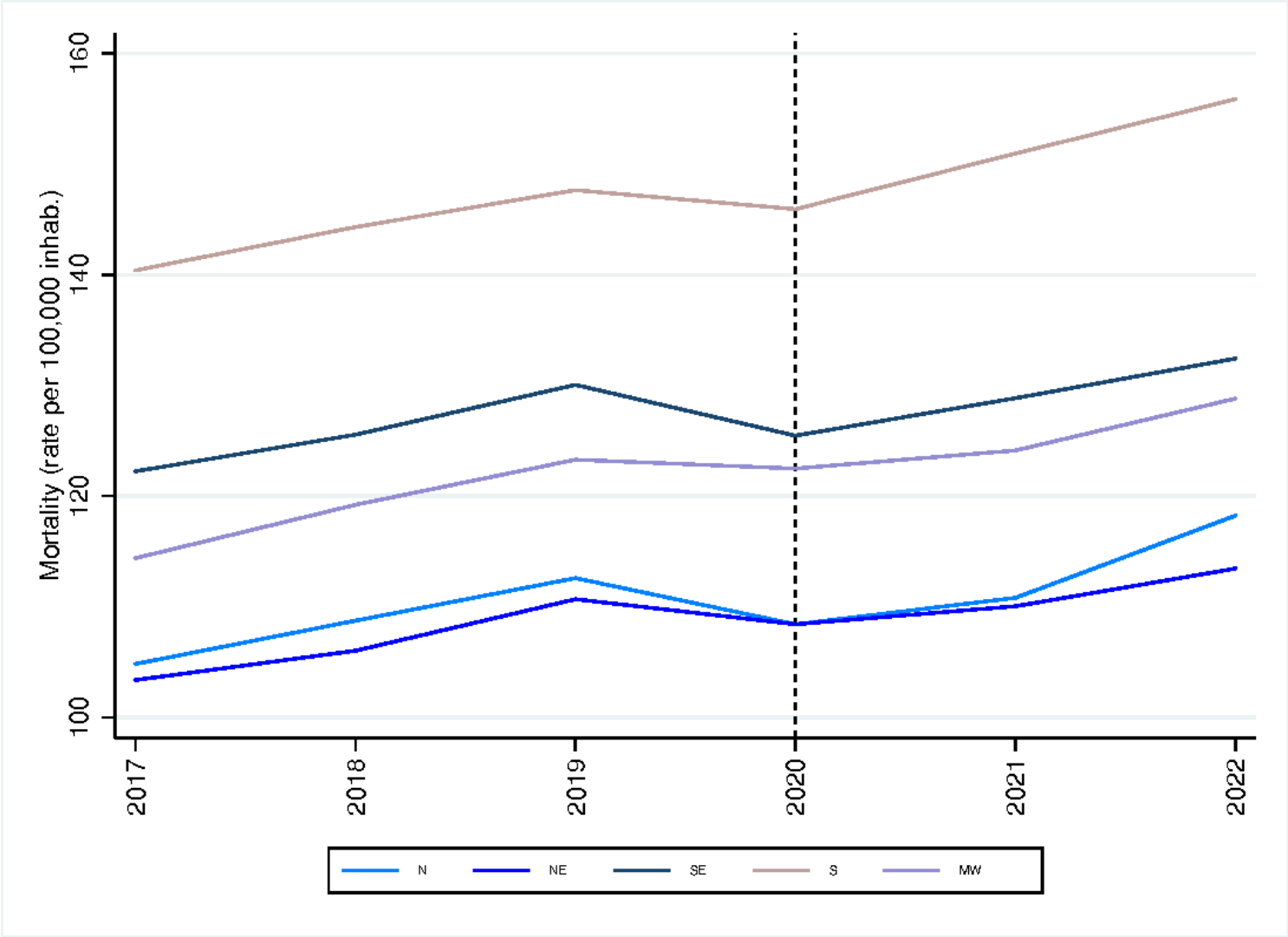

Figure 2

Mortality (rate per 100,000 inhabitants) from all types of cancer between 2017 and 2022 for Brazilian macro-regions

Note: N – North, NE – Northeast, SE – Southeast, S – South, MW – Midwest