

Oncological treatment in Brazil: a gender and region are associated to starting the therapeutics

Tratamento oncológico no Brasil: um risco associado ao início da terapêutica

Isabelle Maria dos Anjos Chaves¹, Vitória Alice Alves de Oliveira¹, Davi Neri Araujo^{2,3,4}, Fernanda Freitas Lemos Lopes^{1,3}, Artur Trancoso Lopo de Queiroz³, Maisa Almeida Silva⁵, Alexandre Souza Queiroz³, Lygia Accioli Tinoco⁶, Kiyoshi Ferreira Fukutani^{1,2,3,4}

ABSTRACT

Introduction: Malignant neoplasms are a major public health problem, being the second leading cause of death in the world. In 2012, the Ministry of Health (BR) instituted Law No. 12,732, which grants cancer patients the right to obtain, from the anatomopathological diagnosis, access to the first treatment in the Brazilian Healthcare System - *Sistema Único de Saúde (SUS)*, within up to sixty days. The change in the patient's prognosis is the aim of this program. **Objective:** To evaluate the panorama of the time to start cancer therapy in Brazil. **Methods:** This is a cross-sectional and analytical study on the time for the establishment of the beginning of cancer treatment in Brazil, in the period from 2013 to 2019. The data were extracted from the PANEL-Oncology of the informatics department of Unified Health System. Chi-square and Fisher's exact tests were used to analyze proportions and risk ratios, respectively. **Results:** The percentage of malignant neoplasms that had the longest delay in starting therapy (>60 days) in the country were prostate (59.6%) and cervix (50.9%). As for sex, the delay was present in 36.9% of men and 33.3% of women ($p < 0.05$). Differences in the rates of cancers with and without delay for the institution of treatment are also evident in the Brazilian macroregions ($p < 0.05$). Assessing the odds ratio for delayed cancer treatment, the male gender is shown to be a risk factor ($p < 0.05$) in all regions, except in the North of the country. The risk for delayed treatment differs depending on the type of cancer. **Conclusion:** Cancers that have a longer delay in starting therapy are those that have health policies aimed at their screening.

Keywords: Oncology; Therapeutics; Risk factors.

1. Centro Universitário FTC, Curso de Medicina, Salvador, Bahia, Brazil.
2. Universidade Federal da Bahia, Curso de Medicina, Salvador, Bahia, Brazil.
3. Fundação Oswaldo Cruz, Instituto Gonçalo Moniz, Salvador, Bahia, Brazil.
4. Multinational Organization Network Sponsoring Translational and Epidemiological Research, Department of Statistics, Salvador, Bahia, Brazil.
5. Faculdade Bahiana para o Desenvolvimento da Ciência, Curso de Fisioterapia, Salvador, Bahia, Brazil.
6. Hospital São Rafael, Departamento de Oncologia, Salvador, Bahia, Brazil.

Financial support: none to declare.

Conflicts of interest: The authors declare no conflict of interest relevant to this manuscript.

Correspondence author: Kiyoshi Ferreira Fukutani.

E-mail: ferreirafk@gmail.com

Received on: November 7, 2020 | Accepted on: November 23, 2020 | Published on: January 18, 2021

DOI: <https://doi.org/10.5935/2526-8732.20200045>

RESUMO

Introdução: As neoplasias malignas são a segunda causa de mortes no mundo, configurando importante problema de saúde pública. Em 2012, o Ministério da Saúde (BR) instituiu a Lei nº 12.732, que concede ao paciente oncológico o direito de obter, a partir do diagnóstico anatomopatológico, o acesso ao primeiro tratamento no Sistema Único de Saúde (SUS), em até sessenta dias. A mudança no prognóstico do paciente é o objetivo deste programa. **Objetivo:** Avaliar o panorama do tempo para início da terapêutica oncológica no Brasil. **Métodos:** Trata-se de um estudo transversal e analítico sobre o tempo de implantação para o início do tratamento oncológico no Brasil, no período de 2013 a 2019. Os dados foram extraídos do PAINEL-Oncologia do departamento de informática do Sistema Único de Saúde. Os testes de qui-quadrado e exato de Fisher foram usados para analisar proporções e razões de risco, respectivamente. **Resultados:** As neoplasias malignas com maiores percentuais para o retardo (>60 dias) na instituição da terapêutica foram: próstata (59,6%) e colo do útero (50,9%). Quanto ao sexo, o atraso esteve presente em 36,9% dos homens e 33,3% das mulheres ($p < 0,05$). Entre as macrorregiões brasileiras são evidenciadas diferenças relativas das taxas dos cânceres com e sem retardo no tempo para o início da terapêutica ($p < 0,05$). Avaliando o odds ratio para retardo no tratamento do câncer, o sexo masculino se mostra como um fator de risco ($p < 0,05$) em todas as regiões, exceto no norte do país. O risco de atraso no tratamento difere dependendo do tipo de câncer. **Conclusão:** Os cânceres que apresentam maior retardo no início da terapia são aqueles que possuem políticas de saúde voltadas ao seu rastreamento.

Descritores: Oncologia; Terapêutica; Fatores de risco.

INTRODUCTION

Malignant neoplasm (MN) are cells with abnormal proliferation and it represents a worldwide public health problem.^[1,2] The MN is the second cause of death in the world and it has been related with several risk factors, especially, those associated to socioeconomic conditions and aging.^[3-5] Therefore, strategies to reduce cancer rates were made and, one of them, is a better understanding of the mechanisms that induce the formation of MN. In regard to that, the ability of the MN cells to: self-sufficiency, avoidance of cell death, development of an own angiogenesis system, invasion of local tissues, spreading to distant sites^[1,2,6] are determined by TNM staging system and it has been done to assist in determining therapy; predicts the patient's prognosis; helps to limit therapy time; and, standardizes the treatment protocol.^[2,6-8]

The Brazilian Ministry of Health (MH) through Ordinance No. 874 of May 2013,^[9] instituted the National policy for the prevention and control of cancer determines the elapsed time between the diagnosis and establishment of the cancer therapy leads to better prognosis and increase the proportions of cure.^[9,10] The establishment of the Law No. 12,732: "all patients with malignant neoplasm must be submitted to the first treatment, from the confirmation of the diagnosis, within up to 60 (sixty) days", recognizes that the early access to the treatment is effective against cancer and it guides the physicians decision.^[11,12]

Thus, we aim to analyze the time of the start of the oncological therapy in Brazil, through the data contained in the PANEL-Oncology (DATASUS). As well,

identify the most delayed MN in Brazil, between all the demographic regions and verify how the sex variable acts a risk factor for the delay in the establishment of the oncological treatment.

METHODS

This study is a cross-sectional and analytical study with secondary data, based on time to the establishment of the oncological treatment in Brazil, between the years 2013 to 2019. The data were extracted from the "time until the beginning of the oncological treatment - PANEL-Oncology of the informatics department of Unified Health System" (DATASUS). The time to start the treatment was stratified in two stages (up to 60 days and more than 60 days), following the Brazilian recommendations (Law No. 12,732/2012). The evaluated variables were sex, age and staging in different regions: North, Northeast, Midwest, Southeast, and South of Brazil. The study included the CID often MN that takes longer to be treated in Brazil based in DATASUS information. In the group of ten MN, CIDs were selected, common to all regions; resulting in eight MN to be analyzed.

From the data obtained in DATASUS, tables were built using *Microsoft Excel*, version 2019, and the proportions related to the delay for each variable under study were tested by Fisher's exact test, using the GraphPad Prism program, version 8.4.3, p -value less than 0.05 was considered significant and finally, the odds ratio (OR) was calculated and the forest plot was elaborated - with a 95% confidence interval, to ascertain the possibility of an association between the delay in the cancer treatment. This study uses

secondary data from Brazilian Government without patient identification and it was not necessary to apply informed consent term, but still in compliance with the resolution of the National Health Council (CNS/BR) No. 196, of October 10, 1996.

RESULTS

After obtaining the data, we evaluated the MN which takes more time to start the therapy; for that, the time to start the treatment was stratified in “up to 60 days” and “more than 60 days” (as recommended by Brazilian Law No. 12,732/12). The cancers that presented high percentages in “more 60 days” were: secondary from other locations/metastases (n=21,159; 64.0%), prostate (n=110,289; 59.6%), breast (n=120,456; 48.8%), rectum (n=20,426; 46.6%), stomach (n=16,962; 32.5%), colon (n=23,230; 30.6%), bronchi and lungs (n=17,388; 26.8%), and these proportion were significant ($p<0,01$). The sex rate of individuals who initiate cancer treatment after sixty days were 36.9% (n=286,311) and 33.3% (n=293,755) for males and females, respectively ($p<0,01$). However, regarding to age, younger patients were associated with early treatment, with a progressive decrease in the percentage of each age group as to the start of treatment within 60 days ($p<0,01$). In terms of staging, there are a predominance of

“not applicable” (n=307,170; 85,5%) and “ignored” (n=85,614; 18,1%) within up to 60 days; however, it is verified in stage 2 (about 121 thousand cases) with a high rate of delay when compared to the other groups in the segment ($p<0,05$) (Table 1).

Investigating the five demographic regions, the data depicted a different distribution of percentages between “up to 60 days” and “more 60 days” in age ($p<0,01$); the same difference are depicted in terms of staging ($p<0,01$). The Northern region was the only macro-region to present non-differences in sex between delayed treatment in comparison with another regions ($p=0,43$). In other hand, sex was homogeneous between all another regions (Table 2).

Verifying the panorama of treatment between Brazilian regions, we analyzed the risk to delay the treatment according to the sex. Therefore, the Northern region of the country was the only region with a non-significant p -value (p -value=0.43). This finding demonstrates the variable sex is not different between “up to 60 days” and “more 60 days” for initiating cancer treatment. Despite that, the differences in others regions presented the female sex as a protective factor against the delay in establishing cancer therapy, while males represents a risk, by calculating the odds ratio (OR). The

Table 1. Rate of time until the beginning of the treatment of malignant neoplasms in Brazil, considering the variables sex, age and staging (2013 to 2019); DATASUS: Oncological Panel.

	UP TO 60 DAYS	MORE THAN 60 DAYS	Does not report	Value p
TYPE OF CANCER, n (%)				<0.001
C50 – Malignant neoplasm of the breast	119.307 (48,3)	120.456 (48,8)	7.093 (2,9)	
C61 – Malignant prostate cancer	59.235 (32,0)	110.289 (59,6)	15.570 (8,4)	
C53 – Malignant neoplasm of the cervix	34.721 (44,3)	39.910 (50,9)	3.798 (4,8)	
C18 – Colon malignancy	44.747 (59,0)	23.230 (30,6)	7.843 (10,3)	
C79 – Secondary malignant neoplasm from other locations	9.915 (30,0)	21.159 (64,0)	1.963 (5,9)	
C20 – Malignant neoplasm of the rectum	20.355 (46,4)	20.426 (46,6)	3.058 (7,0)	
C34 – Malignant neoplasm of bronchi and lungs	43.132 (66,4)	17.388 (26,8)	4.403 (6,8)	
C16 – Malignant neoplasm of the stomach	26.670 (51,1)	16.962 (32,5)	8.513 (16,3)	
Other malignant neoplasms	394.414 (45,0)	210.246 (24,0)	276.693 (31,1)	
SEX, n (%)				<0,001
Male	347.411 (44,8)	286.311 (36,9)	141.183 (18,2)	
Female	405.085 (45,9)	293.755 (33,3)	183.751 (20,8)	
AGE, n (%)				<0.001
0 to 24 years	44.067 (61,5)	10.596 (14,8)	16.953 (23,7)	
25 to 35 years	37.451 (48,7)	18.769 (24,4)	20.607 (26,8)	
35 to 44 years	73.481 (46,5)	49.867 (31,6)	34.582 (21,9)	
45 to 54 years	134.733 (46,1)	104.358 (35,7)	53.354 (18,2)	
55 to 64 years	193.236 (45,1)	159.072 (37,1)	76.153 (17,8)	
65 to 74 years	169.309 (42,9)	152.308 (38,6)	73.247 (18,5)	
≥ 75 years	99.360 (41,8)	88.612 (37,3)	49.457 (20,8)	
STAGING, n (%)				<0.001
0	25.676 (49,0)	26.716 (51,0)	0 (0,0)	
1	35.686 (36,3)	62.675 (63,7)	0 (0,0)	
2	66.058 (35,4)	120.494 (64,6)	0 (0,0)	
3	105.931 (44,9)	130.192 (55,1)	0 (0,0)	
4	126.361 (50,4)	124.598 (49,6)	0 (0,0)	
Not applicable	307.170 (85,5)	52.072 (14,5)	0 (0,0)	
Unknown	85.614 (18,1)	63.319 (13,4)	324.934 (68,6)	

Table 2. Rate of time until the beginning of treatment of malignant neoplasms in the Brazilian demographic regions, considering the variables gender, age and staging (2013 to 2019); DATASUS: Oncological Panel.

Type of Cancer, N (%)	MIDWEST			NORTHEAST			NORTH			SOUTHWEST			SOUTH		
	Up to 60 Days	More Than 60 Days	p-Value	Up to 60 Days	More Than 60 Days	p-Value	Up to 60 Days	More Than 60 Days	p-Value	Up to 60 Days	More Than 60 Days	p-Value	Up to 60 Days	More Than 60 Days	p-Value
C16 - Malignant neoplasm of the stomach	1.519 (63,9)	859 (36,1)	<0,0001	6.670 (61,8)	4.118 (38,2)	<0,0001	1.125 (49,1)	1.167 (50,9)	<0,0001	10.842	8.057 (42,6)	<0,0001	6.514 (70,2)	2.761 (29,8)	<0,0001
C18 - Colon malignancy	3.031 (71,4)	1.213 (28,6)		6.955 (64,7)	3.787 (35,3)		746 (53,1)	660 (46,9)		21.487	12.892 (37,5)		12.528	4.678 (27,2)	
C20 - Malignant neoplasm of the rectum	1.265 (50,9)	1.218 (49,1)		3.436 (51,2)	3.281 (48,8)		477 (38,0)	779 (62,0)		9.673 (46,2)	11.260 (53,8)		5.504 (58,6)	3.888 (41,4)	
C34 - Malignant neoplasm of bronchi and lungs	2.592 (72,5)	983 (27,5)		8.246 (73,0)	3.049 (27,0)		1.128 (63,6)	646 (36,4)		17.371	8.419 (32,6)		13.795	4.291 (23,7)	
C50 - Malignant neoplasm of the breast	7.344 (53,7)	6.323 (46,3)		28.023	25.905 (48,0)		3.876 (44,9)	4.760 (55,1)		51.770	62.138 (54,6)		28.294	21.330 (43,0)	
C53 - Malignant neoplasm of the cervix	2.717 (51,9)	2.520 (48,1)		10.772	11.973 (52,6)		2.190 (30,9)	4.907 (69,1)		11.458	14.818 (56,4)		7.584 (57,1)	5.692 (42,9)	
C61 - Malignant prostate cancer	3.189 (34,0)	6.188 (66,0)		13.595	25.372 (65,1)		1.666 (29,2)	4.034 (70,8)		29.208	56.132 (65,8)		11.577	18.563 (61,6)	
C79 - Secondary malignant neoplasm from other locations	242 (20,8)	919 (79,2)		1.917 (28,6)	4.780 (71,4)		260 (19,7)	1.057 (80,3)		4.418 (32,5)	9.176 (67,5)		3.078 (37,1)	5.227 (62,9)	
Other neoplasms	24.463 (66,7)	12.213 (33,3)		86.331 (68,4)	46.141 (36,6)		11.476 (55,1)	9.337 (44,9)		162.860 (64,7)	100.031 (38,1)		109.284 (75,9)	42.504 (29,5)	
SEX, n (%)	<0,0001			<0,0001			0.4367			<0,0001			<0,0001		
Male	20.861 (56,1)	16.332 (43,9)		71.003 (54,0)	60.490 (46,0)		9.896 (45,8)	11.700 (54,2)		151.899 (51,7)	141.858 (48,3)		93.752 (62,6)	55.931 (37,4)	
Female	25.501 (61,3)	16.104 (38,7)		94.942 (58,3)	67.916 (41,7)		13.048 (45,5)	15.647 (54,5)		167.188 (54,2)	141.085 (45,8)		104.406 (66,3)	53.003 (33,7)	
AGE, n (%)	<0,0001			<0,0001			<0,0001			<0,0001			<0,0001		
0 to 24 years	3.341 (83,2)	673 (16,8)		12.227 (82,0)	2.676 (18,0)		2.013 (65,7)	1.053 (34,3)		17.379 (79,5)	4.475 (20,5)		9.139 (84,6)	1.659 (15,4)	
25 to 35 years	2.650 (69,5)	1.163 (30,5)		9.676 (66,7)	4.833 (33,3)		1.617 (50,9)	1.557 (49,1)		14.193 (64,3)	7.892 (35,7)		9.378 (74,6)	3.199 (25,4)	
35 to 44 years	5.275 (62,5)	3.163 (37,5)		19.003 (60,0)	12.672 (40,0)		3.174 (46,4)	3.672 (53,6)		28.168 (56,4)	21.740 (43,6)		18.029 (68,3)	8.386 (31,7)	

Continue...

Continuation...

45 to 54 years	8.900 (59,3)	6.108 (40,7)	30.515 (56,7)	23.283 (43,3)	4.504 (45,6)	5.372 (54,4)	55.602 (53,0)	49.229 (47,0)	35.448 (64,2)	19.785 (35,8)
55 to 64 years	11.390 (57,1)	8.556 (42,9)	38.295 (54,7)	31.726 (45,3)	5.244 (43,6)	6.776 (56,4)	86.096 (51,7)	80.570 (48,3)	52.434 (63,3)	30.402 (36,7)
65 to 74 years	9.530 (54,4)	7.999 (45,6)	34.194 (51,3)	32.412 (48,7)	4.179 (41,9)	5.788 (58,1)	74.593 (49,6)	75.819 (50,4)	46.950 (61,6)	29.296 (38,4)
≥ 75 years	5.276 (52,5)	4.772 (47,5)	22.035 (51,4)	20.800 (48,6)	2.213 (41,4)	3.129 (58,6)	43.056 (49,9)	43.197 (50,1)	26.780 (62,3)	16.205 (37,7)
STAGING, n(%)	<0,0001	<0,0001	<0,0001	<0,0001	<0,0001	<0,0001	<0,0001	<0,0001	<0,0001	<0,0001
0	1.523 (58,0)	1.105 (42,0)	3.257 (55,0)	2.668 (45,0)	312 (57,6)	230 (42,4)	14.521 (45,1)	17.648 (54,9)	6.063 (54,5)	5.065 (45,5)
1	1.373 (28,4)	3.469 (71,6)	7.407 (36,9)	12.668 (63,1)	766 (27,6)	2.008 (72,4)	12.893 (30,2)	29.770 (69,8)	13.247 (47,3)	14.760 (52,7)
2	3.446 (36,9)	5.888 (63,1)	18.226 (38,3)	29.381 (61,7)	2.502 (26,3)	7.005 (73,7)	26.811 (31,8)	57.466 (68,2)	15.073 (42,1)	20.754 (57,9)
3	6.653 (47,3)	7.405 (52,7)	28.944 (44,6)	35.929 (55,4)	3.750 (35,9)	6.710 (64,1)	40.597 (41,1)	58.285 (58,9)	25.987 (54,3)	21.863 (45,7)
4	8.583 (53,1)	7.586 (49,6)	26.581 (50,6)	25.953 (49,4)	3.472 (39,7)	5.270 (60,3)	53.060 (46,5)	60.966 (53,5)	34.665 (58,3)	24.823 (41,7)
Not applicable	19.285 (85,7)	3.212 (14,3)	61.614 (88,7)	7.848 (11,3)	8.857 (75,5)	2.871 (24,5)	134.008 (81,7)	29.986 (18,3)	83.406 (91,1)	8.155 (8,9)
Ignored	5.499 (59,3)	3.771 (40,7)	19.916 (58,8)	13.959 (41,2)	3.285 (50,2)	3.253 (49,8)	37.197 (56,3)	28.822 (43,7)	19.717 (56,3)	13.514 (40,7)

most tumors occurs in advanced stages. This fact is linked to the precariousness of the provision of diagnostic services in the oncological sphere.^[12,14,19,20] The scarce investment in the elaboration and/or to implement actions in primary healthcare, is linked to the prevention in the most prevalent types of cancers in the Brazil.^[3,18] The delay to start the cancer treatment for MN of the breast and cervix are probably related to the screening policies recommended by the MH, which generate a large number of diagnoses for these cancers.^[22-25] Rodrigues et al. (2015),^[26] evaluate the breast cancer, using the campaign for active screening of this cancer and found an elevation in the identification. The prostate cancer is the second most common cancer in men in the country and there is a preventive campaign called "Blue November" that campaign was elaborated nationwide, which increases the number of diagnosed for that cancer in Brazil,^[3,5,27,28] it is noted that the screening policies, despite contributing to the diagnosis of MN in early stages.^[9-11,25] Wherever, the early diagnoses are not correlated with treatment within sixty days.

The malignant tumors of the cervix is potentially preventable and it is the third most common type of cancer in the female population.^[23,25] The MH is acting improving the vaccination campaigns against human papilloma virus (HPV),^[23,25,29-33] but it does not seems to be enough to reduce the high mortality generated by this cancer.^[30] This situation is related with the social and economic differences between regions, which results in an uneven distribution of care centers for cancer patients and a delay in establishing the therapy for this type of malignant tumor.^[12-14,16,17,20]

The colorectal cancer presents several risk factors, like: male gender, black ethnicity, inflammatory bowel diseases, age over 50 years, smoking, and eating habits.^[34,35] Brazilian demographic regions have similar socioeconomic patterns to developed countries, such as the southern region of Brazil express a higher incidence of this cancer.^[34] Poor Brazilian regions such the Northeast region of the country, also express a higher prevalence of this type of neoplasm and due to a poor healthcare system, culminating in the delay to start the cancer therapy.

In the North, unlike the other regions, there was no risk relationship between sex and the delay in starting the establishment of cancer treatment. On the other hand, being male in the other regions (Midwest, Northeast, South and Southeast) is a risk factor for delay the cancer treatment. According to Rodrigues et al. (2015),^[26] the North region, especially the state of Amazonas, has higher incidence and mortality rates due to cancer, it is explained by socioeconomic inequalities and low accessibility to services for the prevention.^[12,14,16,18,26]

The physiopathology mechanisms of MN include intrinsic (genetic predisposition) and extrinsic factors, which are directly linked to the individual's time of exposure to a

certain type of agent (biological, physical or chemical).^[2,4] When analyzing this finding, it is concluded that the sex of the subject and a distinct ways to treat the different type of cancers are risk factors for the delay the cancer treatment.^[2]

This study has limitations for using secondary data from the PANEL-Oncology/DATASUS. DATASUS is an administrative-based reimbursement system and sub notifications are not archived in this study, although it, this study still innovative measuring the delay to treatment and the risk associated with this delay, giving evidence in which cancer the MH needs a more informative approach.

CONCLUSION

Several cancers are associated with the delay to start the treatment and it is influenced by Brazilian regions. The male gender is considered a risk factor for delayed initiation of treatment in all demographic regions, except in the North. Several cancers are a risk to start the treatment and it is different between Brazilian regions. Our study was tried to associate the risk of some cancer to start the treatment urging for the implementation of individualized and standardized public policies able to handle the differences in geographic areas.

REFERENCES

1. Kumar V, Abbas AK, Aster JC. Robbins & Cotran pathologic basis of disease. 9th ed. Rio de Janeiro: Elsevier; 2015.
2. Ministério da Saúde (BR). Secretaria de Atenção Especializada à Saúde. SAI/SUS - Sistema de Informações Ambulatoriais. Oncologia. Manual de Bases Técnicas [Internet]. Brasília (DF): Ministério da Saúde; 2016 Nov; [access in 2020 Sep 28]. Available from: <https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/manual-oncologia-26a-edicao.pdf>
3. Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Estimate/2020: cancer incidence in Brazil [Internet]. Rio de Janeiro (RJ): INCA; 2019; [access in 2020 Sep 28]. Available from: <https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/estimativa-2020-incidencia-de-cancer-no-brasil.pdf>
4. Ministério da Saúde (BR). Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). A situação do câncer no Brasil [Internet]. Rio de Janeiro (RJ): Rio de Janeiro: Ministério da Saúde/ INCA; 2006; [access in 2020 Sep 28]. Available from: https://bvsms.saude.gov.br/bvs/publicacoes/situacao_cancer_brasil.pdf
5. Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Duas décadas de dia mundial do câncer e "estimativa 2020" marcam o 4 de fevereiro no INCA [Internet]. Rio de Janeiro (RJ): INCA; 2020 Jan; [access in 2020 Sep 28]. Available from: <https://www.inca.gov.br/noticias/duas-decadas-de-dia-mundial-do-cancer-e-estimativa-2020-marcam-o-4-de-fevereiro-no-inca#:~:text=Portug%C3%AAs->

- , Duas % 20 d % C 3 % A 9 c a d a s % 20 d e % 20 Dia % 20 Mundial % 20 do % 20 C % C 3 % A 2 n c e r % 20 e % 20 E 2 % 8 0 % 9 C e s t i m a t i v a % 20 2 0 2 0 , 4 % 2 0 d e % 2 0 F e v e r e i r o % 2 0 n o % 2 0 I N C A & t e x t = E m % 2 0 2 0 2 0 % 2 C % 2 0 o % 2 0 D i a % 2 0 M u n d i a l , C e n t r o % 2 0 d o % 2 0 R i o % 2 0 d e % 2 0 J a n e i r o
6. DeNittis A, Goldwein JW, Dilling TJ. The biology of cancer. OncoLink Penn Medicine [Internet]. 2002 May; [access in 2020 Sep 28]. Available from: <https://www.oncolink.org/healthcare-professionals/oncolink-university/general-oncology-courses/an-introduction-to-the-nature-of-cancer/the-biology-of-cancer>
 7. OncoLink Penn Medicine. An introduction to the nature of cancer – Cancer treatment. OncoLink [Internet]. 2002 May; [access in 2020 Sep 28]. Available from: <https://www.oncolink.org/cancer-treatment>
 8. Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Basic approaches to the cancer control [Internet]. 4th ed. Rio de Janeiro (RJ): INCA; 2012; [access in 2020 Oct 4]. Available from: <https://www.inca.gov.br/sites/ufu.sti.inca.local/files/media/document/livro-abc-4-edicao.pdf>
 9. Ordinance No. 874, 2013 May 16 (BR). Institutes the national policy for the prevention and control of cancer in the health care network of people with chronic diseases within the scope of the Sistema Único de Saúde (SUS) [Internet]. Brasília (DF): Ministry of Health; [access in 2020 Sep 28]. Available from: http://bvsms.saude.gov.br/bvs/saudelegis/gm/2013/prt0874_16_05_2013.html
 10. Ordinance No. 876, 2013 May 16 (BR). Requirements on the application of Law No. 12,732, of November 22 2012, which deals with the first treatment of patients with proven malignancy, within the scope of the Sistema Único de Saúde (SUS) [Internet]. Brasília (DF): Ministry of Health; 2016; [access in 2020 Sep 28]. Available from: http://bvsms.saude.gov.br/bvs/saudelegis/gm/2013/prt0876_16_05_2013.html
 11. Law No. 12,732, 2012 November 22 (BR). Provides for the first treatment of a patient with proven malignancy and establishes a deadline for its beginning. Official Gazette, 23 Nov 2012; [access in 2020 Sep 28]. Available from: http://www.planalto.gov.br/ccivil_03/_ato2011-2014/2012/lei/l12732.htm
 12. IQVIA™. Cancer in Brazil: the patient's journey in the health system and its social and financial impacts [Internet]. Danbury: IQVIA; 2016 [cited 2020 Sep 29]. Available from: <https://www.interfarma.org.br/public/files/biblioteca/cancer-no-brasil-n-a-jornada-do-paciente-no-sistema-de-saude-e-seus-impactos-sociais-e-financeiros-interfarma.pdf>
 13. Xavier DC, Oliveira RAD, Matos VP, Viacava F, Carvalho CC. Mammograms coverage, allocation and use of equipment in the Health Regions. Saúde Debate [Internet]. 2016 Sep; [cited 2020 Sep 30]; 40(110):20-35. Available from: <https://www.scielo.br/pdf/sdeb/v40n110/0103-1104-sdeb-40-110-0020.pdf> DOI <https://doi.org/10.1590/0103-1104201611002>
 14. Kaliks RA, Matos TF, Silva VA, Barros LHC. Differences in systemic cancer treatment in Brazil: my Public Health System is different from your Public Health System. Braz J Oncol [Internet]. 2017 Jun; [cited 2020 Sep 29]; 13(44):1-12. Available from: <https://cdn.publisher.gn1.link/brazilianjournalofoncology.com.br/pdf/v13n44a05.pdf>
 15. Felippu AWD, Freire EC, Silva RA, Guimarães AV, Dedivitis RA. Impact of delay in the diagnosis and treatment of head and neck cancer. Braz J Otorhinolaryngol. 2016 Feb;82(3):140-143.
 16. Silva ICM, Restrepo-Mendez MC, Costa JC, Ewerling F, Hellwig F, Ferreira LZ, et al. Measurement of social inequalities in health: concept and methodological approaches in the Brazilian context. Epidemiol Serv Saúde. 2018 Mar;27(1):e000100017. DOI: <https://doi.org/10.5123/s1679-49742018000100017>
 17. Barata RB. How and why social inequalities harm health [Internet]. Rio de Janeiro (RJ): Ed. FIOCRUZ; 2009; [access in 2020 Sep 29]. Available from: <https://static.scielo.org/scielobooks/48z26/pdf/barata-9788575413913.pdf>
 18. Pitombeira DF, Oliveira LC. Poverty and social inequality: tensions between rights and austerity and its implications for primary healthcare. Ciênc Saúde Coletiva. 2020 May;25(5):1699-708. DOI: <http://dx.doi.org/10.1590/1413-81232020255.33972019>
 19. Kaliks RA, Matos TF, Silva VA, Barros LHC. Differences in systemic cancer treatment in Brazil: my Public Health System is different from your Public Health System. Braz J Oncol [Internet]. 2017 Jun; [cited 2020 Sep 30]; 13(44):1-12. Available from: <https://cdn.publisher.gn1.link/brazilianjournalofoncology.com.br/pdf/v13n44a05.pdf> - ref. é igual a n. 14.
 20. Teixeira LA, Porto M, Habib BABB. Public policies for cancer control in Brazil: elements of a trajectory. Cad Saúde Coletiva [Internet]. 2012; [cited 2020 Sep 29]; 20(3):375-80. Available from: <https://www.arca.fiocruz.br/handle/icict/23906>
 21. Gadelha MIP. 30 years of cancer care in the Brazilian National Health System. Rev Bras Cancerol [Internet]. 2018 Jun;64(2):237-45. DOI: <https://doi.org/10.32635/2176-9745.RBC.2018v64n2.83>
 22. Silva MJS, Lima FLT, O'Dwyer G, Osorio-de-Castro CGS. Cancer care policy in Brazil after creation of Unified Health System. Rev Bras Cancerol [Internet]. 2017 Jan; [cited 2020 Sep 29]; 63(3):177-8. Available from: <https://rbc.inca.gov.br/revista/index.php/revista/article/view/133/71> DOI <https://doi.org/10.32635/2176-9745.RBC.2017v63n3.133>
 23. Ministério da Saúde (BR). Secretaria de Atenção à Saúde. Departamento de Atenção Básica. Caderno de Atenção Primária – Rastreamento. In: Ministério da Saúde, ed. Detecção precoce de câncer [Internet].

- 29th ed. Brasília (DF): Ministério da Saúde; 2010; [access in 2020 Sep 29]; p. 67-79. Available from: http://bvsms.saude.gov.br/bvs/publicacoes/caderno_atencao_primaria_29_rastreamento.pdf
24. Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Guidelines for the early detection of breast cancer in Brazil [Internet]. Rio de Janeiro (RJ): INCA; 2015; [access in 2020 Sep 29]. Available from: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document//diretrizes_deteccao_precoce_cancer_mama_brasil.pdf
25. Instituto Nacional de Câncer José Alencar Gomes da Silva (INCA). Brazilian cervical cancer screening guidelines [Internet]. 2nd ed. Rio de Janeiro (RJ): INCA; 2016; [access in 2020 Sep 29]. Available from: https://www.inca.gov.br/sites/ufu.sti.inca.local/files//media/document/diretrizesparaorastreamentodocancerdo colodoutero_2016_corrigido.pdf
26. Rodrigues JD, Cruz MS, Paixão AN. An analysis of breast cancer prevention in Brazil. *Ciênc Saúde Coletiva* [Internet]. 2015 Jul; [cited 2020 Sep 29]; 20(10):3163-76. Available from: <https://www.scielo.br/pdf/csc/v20n10/1413-8123-csc-20-10-3163.pdf>
27. Sociedade Brasileira de Patologia Clínica/Medicina Laboral (SBPC/ML). Sociedade Brasileira de Urologia (SBU). Posicionamento da SBPC/ML e SBU sobre rastreio de câncer de próstata. Rio de Janeiro (RJ): SBPC/SBU; 2018 Nov; [access in 2020 Sep 30]. Available from: <http://www.sbpc.org.br/noticias-e-comunicacao/posicionamento-da-sbpcml-e-sbu-sobre-rastreio-de-cancer-de-prostata/>
28. Steffen RE, Trajman A, Santos M, Caetano R. Population screening for cancer prostate cancer: more risks than benefits. *Physis*. 2018 Mar.; 28(2):e280209. DOI: <http://dx.doi.org/10.1590/S0103-73312018280209>
29. Alves CM, Bastos RR, Guerra MR. Mortality due to cancer of the uterine cervix in the state of Minas Gerais, Brazil, 1980- 2005: period and cohort analysis. *Cad Saúde Pública* [Internet]. 2010 Jul; [cited 2020 Oct 04]; 26(7):1446-56. Available from: https://www.scielo.br/scielo.php?script=sci_arttext&pid=S0102-311X2010000700024/DOI:http://dx.doi.org/10.1590/S0102-311X2010000700024
30. Santana PM. Retardo do tratamento de mulheres com câncer do colo do útero [dissertation]. Salvador (BA): FIOCRUZ; 2016; [access in 2020 Oct 04]. Available from: <https://www.arca.fiocruz.br/bitstream/icict/18010/2/Perla%20Machado%20Santana.%20Retardo%20do%20tratamento...2016.pdf>
31. Löwy I. Cancer, women, and public health: the history of screening for cervical cancer. *Hist Ciênc Saúde-Manguinhos* [Internet]. 2010 Jul; [cited 2020 Oct 04]; 17(Suppl 1):53-67. Available from: <https://www.scielo.br/pdf/hcsm/v17s1/04.pdf>
32. Barbosa IR, Souza DLB, Bernal MM, Costa ICC. Regional inequalities in cervical cancer mortality in Brazil: trends and projections through to 2030. *Ciênc Saúde Coletiva* [Internet]. 2016 Jan; [cited 2020 Oct 04]; 21(1):253-62. Available from: https://www.scielo.br/scielo.php?script=sci_arttext&pid=S1413-81232016000100253 DOI: <http://dx.doi.org/10.1590/1413-81232015211.03662015>
33. Souto R. The human papillomavirus: a factor related with the formation of neoplasias. *Rev Bras Cancerol* [Internet]. 2005 May; [cited 2020 Oct 04]; 51(2):155-60. Available from: https://rbc.inca.gov.br/site/arquivos/n_51/v02/pdf/revisao2.pdf
34. Mutschall L, França PC, Ferreira LE, Fronza JR H, Blasios R, Pinho M. Analysis of Relationship Between VEGF Protein Expression and Colorectal Câncer Staging. *Rev bras Coloproct* [Internet]. 2009 [cited 2020 Oct 2]; 29(1): 15-22. Available from: http://sbcp.org.br/revista/nbr291/p15_22.htm
35. Assis RVBF. Tracking and surveillance of colorectal: guidelines world. *GED Gastroenterol Endosc Dig* [Internet]. 2011 Jan; [cited 2020 Oct 04]; 30(2):62-74. Available from: <http://files.bvs.br/upload/S/0101-7772/2011/v30n2/a2916.pdf>
36. Araujo LH, Baldotto C, Castro Junior G, Katz A, Ferreira CG, Mathias C, et al. Câncer de pulmão no Brasil. *J Bras Pneumol* [Internet]. 2018 Jan; [cited 2020 Oct 22]; 44(1):55-64. Available from: https://www.scielo.br/pdf/jbpneu/v44n1/pt_1806-3713-jbpneu-44-01-00055.pdf DOI: <https://doi.org/10.1590/s1806-37562017000000135>