

*Full Length Research Paper*

# **Cancer survival in Brazil: Estimate through the mortality to incidence ratio**

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**Information about cancer incidence, mortality and survival is one of the pillars for disease monitoring. In Brazil, only a few studies show population-based survival. The mortality to incidence ratio (M:I) is an indirect measure of cancer survival and can be used to estimate a population cancer survival. To calculate the mortality to incidence ratios (M:I), an official information for incidence and mortality rates in Brazil during 2002 to 2014 was used. A complement to the age-adjusted cancer mortality to incidence ratios [1-(M:I)] as a 5-year survival estimate for all cancers, excluding non-melanoma skin, breast, lung, prostate, cervical, colo-rectal and stomach cancers were calculated. The median survival estimate for all tumors was 52% for males and 56% for females. The lowest survival estimates, in both sexes, can be observed in North and Northeast regions for lung and stomach cancer. For colo-rectal cancer, the survival estimates were similar for both sexes, varying between 50 and 65%. Prostate and breast cancer had the highest survival estimates (79 and 74%, respectively). The survival estimate for cervical cancer in Brazil was 64%. Despite the limitation, the study showed that the methodology can be a simple predictor for calculating 5-year survival rates.**

**Key words:** Brazil, incidence, mortality, neoplasm, survival.

## **INTRODUCTION**

Cancer survival is the key piece of information that is useful in terms of controlling this disease. Even so, there are few studies in Brazil that evaluate the 5-year populational cancer survival. The available studies show survival data based on patients managed at some hospitals that are cancer reference units, though these studies are not population-based (Ayala, 2012;

Brito et al., 2009; Carneseca et al., 2013; Corrêa et al., 2016). This paper intends to present 5-year survival estimates by using the methodology of the mortality to incidence ratio (M:I) for the most recent years available on the official information systems, covering the first decade of the 21st Century. The study hopes to throw more light on this issue to expand knowledge about

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cancer and strategies for controlling it in our country.

Information about cancer incidence and mortality, and thus survival, is one of the pillars for monitoring the disease (Bray et al., 2012). Owing to changes in human behavioral patterns, lifestyles, industrialization and urbanization, all of which have contributed to populational aging, the rise of chronic diseases, including cancer, is an important part of Public Health concerns (Duchiade et al., 1999). The incidence of cancer in the world rose from 12.7 million new cases in 2008 to 14.1 million in 2012, with 8 million cancer deaths recorded in 2012. With the rise in the world's population and the aging thereof, if the same conditions are maintained, this upward trend should continue to rise by approximately 75%, which will lead to a figure somewhere near 25 million cancer cases in the next two decades (Ferlay et al., 2015). Cancer is already the principal cause of death in developed countries, and with the improvement in the social, economic and healthcare conditions and decline in cardiovascular diseases in developing countries, cancer will shortly be the leading cause of death among all the world's populations.

In populations where there is deficient information on the occurrence of cancer, being knowledgeable about mortality can aid in understanding the epidemiological pattern of the disease among the population. For tumors that are most lethal, such as lung and stomach cancers, the mortality rate allows us to approximate what the incidence would be. The magnitude of the mortality rates for lung cancer closely approximates the incidence rates (19.7 and 23.1 per 100,000 inhabitants, respectively), such that in the absence of information regarding incidence, mortality data can be used as a reference for actions and decision-making (Ferlay et al., 2015). Even so, having only such information available may not permit real knowledge about cancer, chiefly because there are important differences in terms of lethality and survival for each tumor. Nevertheless, for those tumors where prognosis is easier, for example prostate and breast cancer, using such inference is inappropriate. This is because there is a real difference in magnitude between the incidence and mortality rates (Parkin and Bray, 2009; Vostakolaei et al., 2011). According to the latest world estimate, the rate of incidence noted for breast cancer stands at around 43.3 for every 100,000 women, whereas, for mortality, there are 13 deaths for every 100,000 women (Ferlay et al., 2015). In this sense, knowledge about all these parameters is important for identification of populational risks. Moreover, such knowledge will further contribute to the formulation of strategies for allocating resources for prevention, early detection, assistance and control of cancer.

Estimates of survival are fundamental to monitor aggressiveness of the disease, effectiveness of treatment and access to the healthcare system. The best way of obtaining information about cancer survival is actively

following the cohorts of individuals diagnosed with the disease (Vostakolaei et al, 2011). Although understanding has improved in the oncologic area in Brazil over the years, there is still little information on populational survival from the disease in the country.

One indirect measure of cancer survival is the use of mortality to incidence ratio (M:I). This indicator compares the number of deaths due to a specific type of cancer during a given period with the number of new cases of such cancer registered in the same period. When the mortality data is considered sufficient in terms of quality, chiefly regarding preciseness as to cause of death, and incidence and survival are relatively stationary, that is, without major up- or down-swings, the M:I ratio is an approximate indicator of populational survival that can be reliably used (Parkin and Bray, 2009). Accordingly, 5-year survival is estimated as one less than the ratio between mortality and incidence [ $1-(M:I)$ ]. Furthermore, M:I is also an indicator used to evaluate the incompleteness of Population-Based Cancer Registries (PBCR) (Parkin and Bray, 2009).

For this, application of this methodology requires that the information, both regarding incidence and, above all, mortality, be at an acceptable quality level (Bray and Parkin, 2009; Jensen et al., 1991; Parkin and Bray, 2009). According to Parkin and Bray (2009), 5-year survival is possible if there are no significant alterations in the incidence trend, as well as if the death certificate information is accurate (Parkin and Bray, 2009).

In populations where studies of population survival are rare, such as in Brazil, using an alternative methodology is a valid strategy to estimate populational survival from cancer. The methodology applied allows us to arrive at approximate 5-years survival, since actively researched populational cancer survival is low in Brazil. Despite this, caution is required to analyze the information, as such methodology may not be valid for all types of cancer. According to Vostakolaei et al. (2011), survival estimates for some cancer may be biased by 10%. This bias may be random or systematic, according to the cancer, for over- or underestimating survival. Survival statistics regarding oral cavity and liver cancer appear to be overestimated, whereas the estimates for bone, breast, prostate and stomach cancers, as well as leukemia, are under-estimated (Vostakolaei et al., 2011).

## MATERIALS AND METHODS

Brazil is geopolitically divided into five regions (North, Northeast, Southeast, South, and Middle-West) and each one is composed of three or more states/provinces. This division considers geographic, social and economic factors. The data were grouped in these regions. Official incidence and mortality information was used, as available on the web-page of the Brazilian National Cancer Institute (*Instituto Nacional de Câncer José Alencar Gomes da Silva* – INCA - [www.inca.gov.br/vigilância](http://www.inca.gov.br/vigilância)).

Information on incidence was provided by 22 Population-Based Cancer Registries – PBCR: Aracaju/SE (2008-2012), Belém/PA (2006-2010), Belo Horizonte/MG (2005-2009), Cuiabá/MT (2003-2007), Curitiba/PR (2008-2012), Vitória/ES (2008-2012), Barretos/SP (2009-2013), Florianópolis/SC (2008-2012), Fortaleza/CE (2002-2006), Goiânia/GO (2007-2011), Jahu/SP (2010-2014), João Pessoa/PB (2006-2010), Manaus/AM (2002-2006), Natal/RN (2001-2005), Palmas/TO (2008-2012), Poços de Caldas/MG (2007-2011), Porto Alegre/RS (2002-2006), Recife/PE (2008-2012), Roraima (2006-2010), Salvador/BA (2001-2005), São Paulo/SP (2009-2013) and Teresina/PI (2002-2006). The incidence rates referred to the average values for the last 5-year period for each PBCR. The mortality rates were obtained for the same PBCR locations and for the same time periods.

The mortality to incidence ratios (M:I) were calculated based on data on incidence and mortality rates adjusted for the world population standard, as modified by Doll et al. (1966). The M:I reflects the disease's lethality and is considered an indirect measure of survival. Values of close to 1 indicate that the disease is highly lethal. Then we calculated a complement to the age-adjusted cancer mortality to incidence ratios  $[1-(M:I)]$  as a 5-year survival estimate for the following topographies:

1. All cancer, but non-melanoma skin cancer (C00-C97;D46/C44);
2. Breast cancer (C50);
3. Lung cancer (C33-34);
4. Prostate cancer (C61);
5. Cervical cancer (C53);
6. Colo-rectal cancer (C18-C21);
7. Stomach cancer (C16).

As Brazil does not have nation-wide incidence data, the median was used to measure central tendency in order to obtain an overall assessment of the distribution of the M:I ratios to the nation's survival estimate. The median M:I ratios were calculated for geographic regions and Brazil, by sex. The use of such methodology was only possible since the present information on incidence and mortality in Brazil has already reached a regular quality standard (<http://globocan.iarc.fr/old/method/method.asp?country=076>).

The results obtained are presented in table format with all the information regarding the study, allowing us to find the median 5-year survival estimate per type of cancer, geographic region and nation-wide total. The figures present the variability of the distribution of the values for each survival for cancer and geographic region, along with the distribution of the survival values.

## RESULTS

Table 1 shows the survival estimate by sex, geographical location and cancer. The median survival estimate for all tumors was 52% for males and 56% for females. Among men, the lowest survival estimate was observed in the North region of Brazil (Manaus and Roraima - 25%) while the highest survival estimate was in the Middle-West and South regions (Goiânia and Florianópolis - 63 and 67%, respectively). Among the women, the lowest survival estimates were in the North and Southeast regions (Roraima and Grande Vitória - 33 and 38%, respectively), while the highest was again in Florianópolis (76%). Concerning lung cancer, the lowest survival estimates, in both sexes, can be observed in such North region

locations as Manaus and Roraima, and in the Northeast (Recife, Salvador and Teresina). Once again, the highest were in the South (Porto Alegre). For colo-rectal cancer, the survival estimates were similar for both sexes, varying between 50 and 65%. Florianópolis showed survival estimates above those noted in the rest of Brazil, for both genders (76% in men and 73% in women). The lowest survival estimates for stomach cancer were in Manaus and Barretos, for both sexes and in Sao Paulo for men only. Prostate and breast cancer had the highest survival estimates (79 and 74%, respectively). For Brazil overall, the survival estimate for cervical cancer was 64%.

Figure 1 shows the variation of the survival estimates among the geographic regions and Brazil, for prostate cancer and for female breast cancer. The overall median survival estimate for prostate cancer was 79% with the North region having the lowest survival rate. For breast cancer, a huge variation is noted in the survival estimates between geographic regions. The Southeast region has the highest survival estimate, followed by the Middle-West region, while the North region has the lowest survival estimate.

Likewise, regional differences were observed for colo-rectal, lung, stomach and all cancers (Figure 2). Despite the regional differences, the survival estimate between the sexes in relation to colo-rectal cancer was similar. For lung cancer, the medians were 14% in men and 18% in women. The highest survival estimates for lung cancer were observed in the South, Southeast and Middle-West regions of the country. Stomach cancer had the lowest median survival estimates for both male and female (30 and 35%, respectively). The median survival estimates for all tumors, in males and females were greater in the Middle-West, Southeast and South regions than in entire country. On the other hand, the North and Northeast regions posted survival estimates below those noted for the country as a whole. We have not presented the graph of the survival estimate for cervical cancer, since in Brazil there are still problems in filling out death certificates in relation to this tumor.

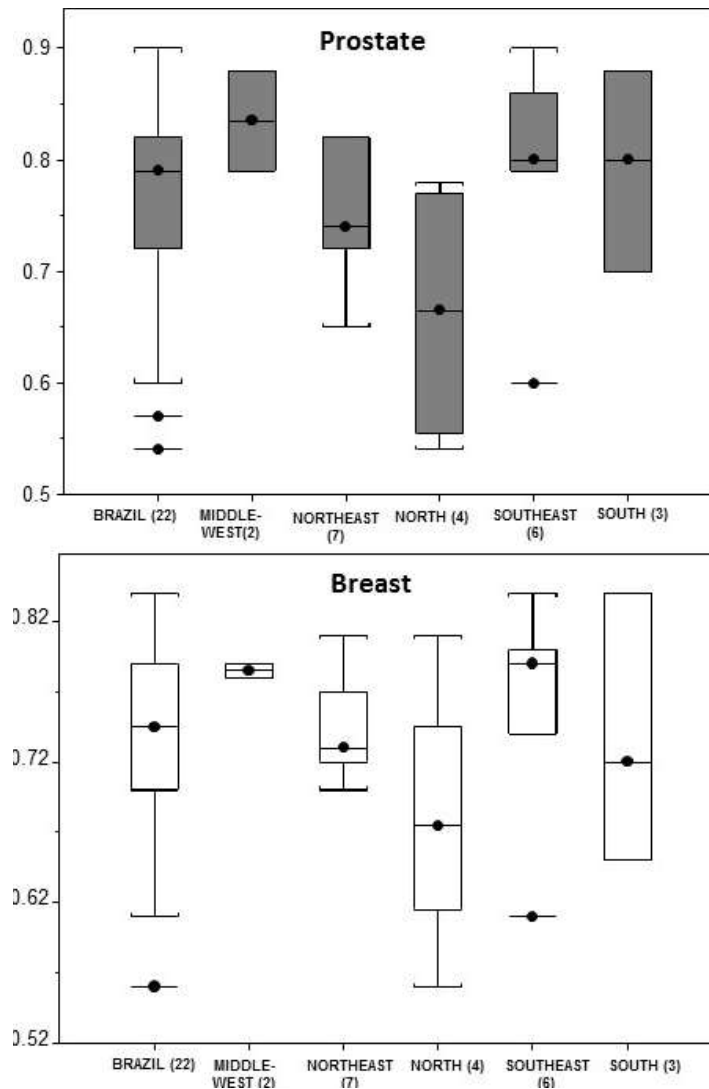
## DISCUSSION

With the rise in the population's life expectancy, one of the consequences anticipated is an increase in the occurrence of cancer. Such a situation creates challenges for healthcare system, from diagnosis to treatment and management, but chiefly in terms of maintenance of the patient's quality of life index (QLI). This is because cancer, considered a chronic disease, can lead to major side-effects in an individual. Such challenges are greater, however, in low- and middle-income countries such as Brazil (Duchiade, 1999). Knowledge of population survival is highly important, not just from an individual standpoint,

**Table 1.** Estimated survival, all cancer\*, lung, colo-rectal, stomach, prostate, breast and cervical, by gender, region and period.

Local	All cancer		Lung		Colo-rectal		Stomach		Prostate	Breast	Cervical
	Male	Female	Male	Female	Male	Female	Male	Female			
<b>North Region</b>	<b>0.36</b>	<b>0.42</b>	<b>0.09</b>	<b>0.09</b>	<b>0.45</b>	<b>0.49</b>	<b>0.21</b>	<b>0.18</b>	<b>0.66</b>	<b>0.68</b>	<b>0.61</b>
Belém <sup>1</sup> (2006-2010)	0.47	0.44	0.16	0.11	0.56	0.47	0.33	0.29	0.76	0.68	0.63
Manaus (2002-2006)	0.25	0.41	0.02	-0.03	0.34	0.33	0.11	0.09	0.54	0.67	0.58
Palmas (2008-2012)	0.56	0.57	0.24	0.31	0.66	0.69	0.32	0.26	0.78	0.81	0.71
Roraima (2006-2010)	0.25	0.33	0.03	0.07	0.30	0.51	-0.02	-0.06	0.57	0.56	0.60
<b>Northeast Region</b>	<b>0.47</b>	<b>0.54</b>	<b>0.09</b>	<b>0.16</b>	<b>0.57</b>	<b>0.58</b>	<b>0.24</b>	<b>0.38</b>	<b>0.74</b>	<b>0.73</b>	<b>0.68</b>
Aracaju (2008-2012)	0.59	0.62	0.14	0.19	0.60	0.70	0.44	0.49	0.82	0.72	0.58
Fortaleza (2002-2006)	0.47	0.55	0.22	0.24	0.57	0.56	0.24	0.39	0.74	0.75	0.74
Joao Pessoa (2006-2010)	0.42	0.54	-0.14	-0.02	0.58	0.60	-0.02	0.32	0.72	0.73	0.76
Natal (2001-2005)	0.54	0.61	0.17	0.21	0.63	0.66	0.36	0.42	0.82	0.81	0.68
Recife (2008-2012)	0.44	0.53	0.09	0.11	0.49	0.53	0.24	0.34	0.73	0.72	0.73
Salvador (2001-2005)	0.53	0.54	0.07	0.16	0.57	0.54	0.28	0.38	0.80	0.77	0.59
Teresina (2002-2006)	0.40	0.48	0.09	0.08	0.53	0.58	0.19	0.16	0.65	0.70	0.59
<b>Middle-West Region</b>	<b>0.59</b>	<b>0.60</b>	<b>0.16</b>	<b>0.26</b>	<b>0.62</b>	<b>0.64</b>	<b>0.42</b>	<b>0.39</b>	<b>0.83</b>	<b>0.78</b>	<b>0.69</b>
Cuiabá <sup>2</sup> (2003-2007)	0.56	0.59	0.13	0.24	0.64	0.66	0.41	0.35	0.79	0.78	0.70
Goiânia (2007-2011)	0.63	0.61	0.19	0.28	0.61	0.61	0.43	0.44	0.88	0.79	0.67
<b>Southeast Region</b>	<b>0.55</b>	<b>0.61</b>	<b>0.15</b>	<b>0.21</b>	<b>0.59</b>	<b>0.57</b>	<b>0.26</b>	<b>0.36</b>	<b>0.80</b>	<b>0.79</b>	<b>0.53</b>
Barretos (2009-2013)	0.43	0.50	0.00	-0.28	0.56	0.52	0.09	0.17	0.79	0.79	0.66
Belo Horizonte (2005-2009)	0.61	0.64	0.20	0.25	0.62	0.64	0.40	0.47	0.86	0.79	0.70
Grande Vitória <sup>3</sup> (2008-2012)	0.29	0.38	0.18	0.16	0.49	0.46	0.16	0.23	0.60	0.61	0.55
Jahu (2010-2014)	0.53	0.64	0.20	0.26	0.63	0.59	0.36	0.76	0.80	0.80	0.51
Poços De Caldas (2007-2011)	0.61	0.64	0.13	0.37	0.61	0.73	0.35	0.50	0.90	0.84	0.44
São Paulo (2009-2013)	0.56	0.58	-0.32	-0.06	0.51	0.55	0.05	0.25	0.80	0.74	0.52
<b>South Region</b>	<b>0.52</b>	<b>0.59</b>	<b>0.21</b>	<b>0.27</b>	<b>0.50</b>	<b>0.56</b>	<b>0.33</b>	<b>0.35</b>	<b>0.80</b>	<b>0.72</b>	<b>0.65</b>
Curitiba (2008-2012)	0.40	0.51	-0.04	0.00	0.44	0.50	0.21	0.27	0.70	0.72	0.61
Florianopolis (2008-2012)	0.67	0.76	0.21	0.27	0.76	0.73	0.51	0.60	0.88	0.84	0.79
Porto Alegre (2002-2006)	0.52	0.59	0.31	0.40	0.50	0.56	0.33	0.35	0.80	0.65	0.65
<b>Median</b>	<b>0.52</b>	<b>0.56</b>	<b>0.14</b>	<b>0.18</b>	<b>0.57</b>	<b>0.57</b>	<b>0.30</b>	<b>0.35</b>	<b>0.79</b>	<b>0.74</b>	<b>0.64</b>

\* Exclude non-melanoma skin cancer (C44); 1. Belém e Ananindeua; 2. Cuiabá e Várzea Grande; 3. Cariacica. Fundão. Guarapari. Viana. Vila Velha. Vitória e Serra. Sources: Brazilian Population-based Cancer Registries; MS/SVS/DASIS/CGIAE/Sistema de Informação sobre Mortalidade – SIM; MP/Fundação Instituto Brasileiro de Geografia e Estatística - IBGE; MS/INCA/Divisão de Vigilância e Análise de Situação.



**Figure 1.** Survival estimates for prostate and breast (female) cancer by geographic region.

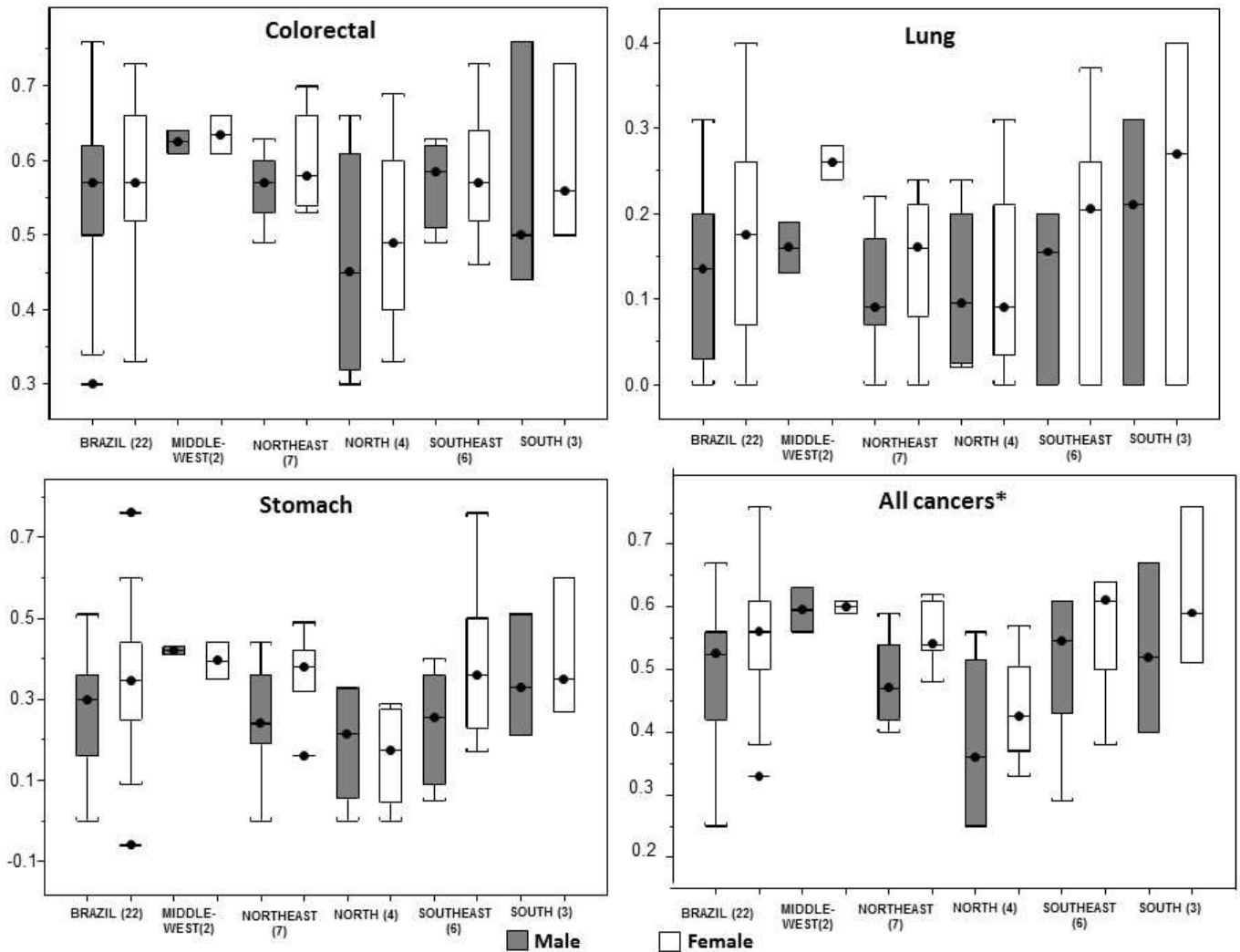
but also in relation to public health. The survival estimate based on the complement of the mortality and incidence ratios is an alternative given the absence of comprehensive population survival studies (Vostakolaei et al., 2011). Nonetheless, it is no substitute for actively researched survival studies, as it only allows us to find out the order of magnitude of survival, in the absence of such studies.

The information on the M:I ratio for cancers published by INCA in 2012 is quite similar to what is reported in this paper for all types of cancer analyzed, except for lung cancer in men. In the INCA study, the survival estimate for lung cancer was 5%, whereas, in this study, the survival estimate was 14%. Such a difference can be partly explained by the updating of the period analyzed,

as well as the improvement in the quality of the lung cancer mortality rates (Health Ministry of Brazil, 2012).

The study conducted by Justo et al. (2013) analyzed healthcare related to breast cancer in Latin America using the M:I ratio. In their study, the authors used the incidence and mortality information taken from Globocan 2002 (Parkin et al., 2005) and Globocan (2008) (Ferlay et al., 2010) to appraise the potential change in the behavior of the lethality of breast cancer. For Brazil, the results obtained in calculation of these M:I ratio showed that the country had the least progress in caring for breast cancer (Justo et al., 2013).

Allemani et al. (2015) published data on survival of different populations around the world, including Brazil (CONCORD-2 study). The results presented for the 5-



**Figure 2.** Survival estimates for colo-rectal cancer, lung cancer, stomach cancer and all cancer by gender and geographic region. \*C00-C97;D46/C44

year survival rate for the last period analyzed (2005-2009) in Brazil were for lung (18%), colon (58%), rectum (56%), stomach (25%) and cervical (61%) cancers, and were quite similar to those found in this study. However, for breast (87%) and prostate (96%) cancers, the survival rates showed in CONCORD-2 were higher than those shown in this study (Allemani et al., 2015). This fact is corroborated based on certain studies showing the limitation of using such parameter as a survival rate predictor. The study conducted by Janssen-Heijnen et al. (2007) emphasized the importance of fulfilling the requisites for which such measure is best applied and thus reaching the closest possible actual survival. Such requisites consider significant changes in the time tendency of the tumor, mortality or incidence, upwards or downwards, over time; rise in the mortality risk rate after

5 years of survival; and the level of preciseness and completeness of the disease registries (incidence and mortality) (Janssen-Heijnen et al., 2007). Bore et al. (2005) shows that for some types of tumors, such as prostate and breast cancers, for instance, such conditions may not be valid, meaning that the alternative measure [1-(M:I)] underestimates the survival rate. In the case of prostate cancer, for example, most men diagnosed with the disease do not die of it, even though their official cause of death may be considered as prostate cancer, such that there is a classification error. This can overestimate the mortality rates and of course underestimate the survival rate (Bore et al., 2005).

Another important issue that should be taken into consideration is registration of the disease. For some cancer, a relapse or even a metastasis may be

misconstrued as a new diagnosis, as in the case of oral cavity and liver cancers. Such inconsistencies in registration may lead to false information, both regarding incidence and mortality, thus making it difficult to use the alternative method to calculate survival (Vostakolaei et al., 2011). Some considerations can be speculated about possible explanations for the negative values noted for stomach cancer and, above all, for lung cancer. Since lung cancer has a great potential for metastases, registration on the death certificate of this type of tumor tends to get overestimated.

In colo-rectal cancer, a similar pattern was noted between the sexes, which corroborate what is described in the literature on the subject. This tumor does not feature differences between the sexes in terms of its etiology. According to data in the study conducted by Jemal et al. (2017), the survival rate for colo-rectal cancer on US registers (SEER) was 66.2% in the 2006 to 2012 period.

The major difficulty of the methodology encountered for this study was related to cervical cancer. It is known that the North and Northeast regions of Brazil feature the greatest levels of inequality in relation to socio-economic conditions and therefore health statistics. The differences among Brazil's regions in the health-care area have been the target of study in the medical literature (Martins Júnior et al., 2011). Survival estimates for cervical cancer have been hampered owing to the under-estimation of mortality due to this cancer. According to Girianelli et al. (2014), the mortality rates for cervical cancer are in fact higher than those disclosed in the nation's Mortality Information System (SIM), if they are corrected by the death certificates that give ill-defined causes and, moreover, cases classified as deaths due to malignant neoplasm of the uterus, which are unspecified. According to Gamarra's study, after correction for ill-defined causes and the unspecified portion of the uterus, cervical cancer mortality rates have actually risen by no less than 103.4% for Brazil overall. The North and Northeast regions were those requiring the highest corrections. The adjusted mortality rates noted in these two regions in the 1996 to 2005 period were 8.1/100,000 and 4.8/100,000, respectively. With the correction, the mortality rates rose to 15.6/100,000 in the North and 14.8/100,000 in the Northeast. Such variations represent an overall increase of 93.1% in the mortality rate in the North and an enormous 209.3% in the Northeast (Gamarra et al., 2010). It is believed that such correction is a possible explanation for the results obtained in this study, where a false better survival estimate was noted for the North and Northeast regions of the country.

An important limitation of this study has been the fact that analysis has been based on second-hand information. It should be borne in mind that there still are considerable differences in relation to the information on mortality between locations and the respective periods

analyzed.

It is important to highlight, nonetheless, that in Brazil the SIM is nation-wide in scope and has been in effect since 1979, with information gathered, stored and analyzed in an ongoing and systematic manner. Since 2005, the Ministry of Health has been pro-actively trying to upgrade the quality of death certificate completeness, and since 2010 Brazil has less than 10% of its deaths attributed to poorly defined causes (Health Ministry of Brazil, 2017; França et al., 2014). According to França et al. (2014), in the year 2010, no less than roughly 20% of the poorly defined death certificates were cancer-related re-classified. Cancer-related deaths rose by 17% due to the correction of the certificates showing death due to poorly defined causes. Besides the work on improving the SIM information, the Federal Health Ministry has also been striving over the last two decades to enhance the quality of the Brazil's Population-based cancer registries [PBCR]. Such improvements can be noted in recent publications regarding world cancer incidence [Cancer in Five Continents – International Association of Cancer Registries (IARC)] (Curado et al., 2007; Forman et al., 2013; Parkin et al., 2002). With this, it is believed that in the forthcoming updates of the databases, both SIM's and those of the RCBP's, this methodology can be used more frequently to obtain the magnitude of cancer survival statistics, in the absence of active research studies.

## Conclusion

Even so, despite the limitations and certain differences encountered between the survival rates informed through active research studies and the results in this study, it is concluded that the [1-(M:I)] can be a simple predictor for calculating 5-year survival rates. It should be emphasized, however, that such alternative measure may not be so valid for tumors involving low lethality, or for those tumors that pose difficulty in terms of codification, regarding mortality, and for those considered rare among the general population.

## CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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