

## Childhood cancer and pediatric oncologic care in Brazil: access and equity

O câncer infantil no Brasil: acesso e equidade

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### Abstract

*Cancer in children and adolescents is rare and highly curable if treatment is started early, yet it is still the main cause of death from disease in this age group. The aim of this study is to discuss access to health services for cancer patients under 19 years of age in Brazil, mapping deaths and treatment modalities in the Brazilian Unified National Health System (SUS). Data from 2000 to 2007 were analyzed according to health regions. Maps of cancer mortality rates and cancer care indicators – hospitalizations, chemotherapy, and radiotherapy financed by the national health system – revealed inequality in access, based on the small number of procedures for children in poorer regions of the country. Even with the usual concentration of specialized services in more heavily populated areas, access begins with clinical suspicion in primary care, followed by referral to more complex levels, where the diagnosis is made and treatment begins. Training pediatricians in clinical suspicion of childhood cancer and definition of more streamlined patient flows could improve the situation, thereby increasing the odds of cure.*

*Early Diagnosis; Neoplasms; Child; Health Services Accessibility; Equity*

### Introduction

Cancer in children and adolescents is a rare event, accounting for approximately 1% of all malignant neoplasms<sup>1</sup>. In the United States, the mean annual incidence rate for all cancers in individuals under 20 years of age is 14.9 cases per 100,000 person-years<sup>2</sup>. In Brazil, there were an estimated 9,386 new cases of cancer in children (up to 18 complete years of age) in 2010<sup>3</sup>, and the median childhood cancer incidence rate computed in 14 Population-Based Cancer Registries (PBCR) was 154.3 per million<sup>4</sup>. In the developed countries, cancer is the leading cause of death from disease in children and adolescents and ranks second in the total number of person-years saved by curative therapy<sup>5</sup>.

In the 1960s, the ability to diagnose and treat childhood cancer was rudimentary, and survival was less than 10%. Today, more than 70% of children diagnosed with cancer survive, and most are considered cured, thanks to strides in adequate diagnosis and treatment of the disease in the initial stages<sup>5,6,7,8</sup>. In fact, cancer is a highly curable disease when diagnosis and treatment are performed early. Early diagnosis is the main challenge, since various types of cancer in this age bracket present initial signs and symptoms that are similar to the more common childhood illnesses, and usually involve a short latency period and rapid growth<sup>1,7,8</sup>. They are rarely associated with carcinogenic agents like

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those involved in cancers in adulthood<sup>9</sup> and are aggressively invasive and sensitive to standard treatment, particularly chemotherapy<sup>5,6,9</sup>. Such conditions imply the need to quickly refer suspected cases to specialized centers. International studies indicate that the best results are obtained in centers staffed by professionals with experience in diagnosing and treating these patients and with adequate infrastructure for performing these procedures<sup>1,10,11</sup>. These guidelines orient the organization of cancer care in Brazil<sup>12</sup>.

The organization of health services according to level of care (primary, secondary, and tertiary) is based on the idea of a portal of entry, which should be easy to access. At the primary care level, physicians must be trained and have the adequate resources to identify suspected cases in the initial stages, thereby streamlining referral to specialized centers. According to Starfield<sup>13</sup>, greater ease in access to specialized services is directly associated with good quality primary care. Brazilian and international studies have demonstrated that cancer diagnosis in advanced stages is correlated with worse access to health services and lower survival rates<sup>14,15</sup>.

According to Travassos<sup>16</sup>, equity in use of health services can positively impact the health of populations, reducing incidence and mortality and increasing survival for given diseases. In addition, equity in the use of health services should be analyzed in at least two dimensions: geographic and social. The geographic dimension compares the variation between areas, while the social dimension compares variations between social groups within areas. At the national level, these two dimensions complement each other, and although the geographic dimension is necessary, it is not sufficient for equity to occur in the social dimension<sup>17</sup>.

In the late 1990s, the Brazilian Ministry of Health began to implement policies for organizing cancer care in Brazil, on grounds that “*access to cancer diagnosis and treatment is [currently] insufficient, because it is concentrated in the State capitals and in the more economically developed States*”<sup>18</sup> (p. 378). With the aim of integrating actions to establish a hierarchical and regular network of care for cancer patients at the local, State, and Federal levels<sup>12</sup>, the Ministry of Health created regulatory mechanisms like the Authorization for High Complexity Cancer Procedures (APAC/ONCO) and set minimum criteria for enrollment in High Complexity Cancer Centers (CACON)<sup>19,20</sup>. Considering only the CACONs that are equipped and staffed to treat children and adolescents, in 2001 there were 172 CACONs<sup>21</sup>, while by 2009<sup>22</sup> this figure had increased to 234, distributed across 132 municipalities (counties).

The well-known pattern of geographic inequality in Brazil has characteristic manifestations in the case of cancer. Considering that pediatric cancer cases are rarely associated with exposure to carcinogens, one could assume that spatial distribution of cases in the country would be approximately constant. It is thus reasonable to expect that differences in mortality rates between the country's various major geographic regions is directly related to health services' organization, involving better or worse conditions of access and quality of care. The current study aims to describe the geographic variations, mapping pediatric cancer deaths, hospitalizations, and treatment modalities under the Brazilian Unified National Health System (SUS) in order to orient potential planning measures.

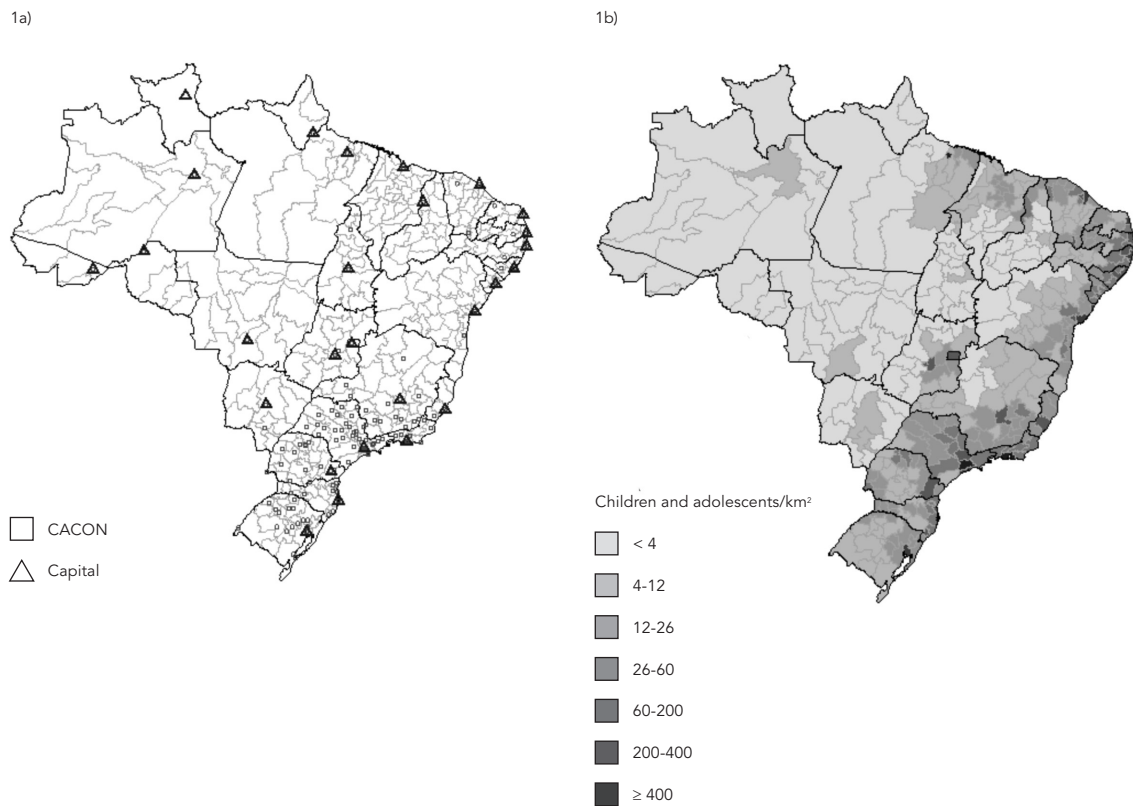
## Methods

This was an ecological study that used as the units of analysis the 352 health regions in Brazil in 2008 (Health Statistics and Information Technology Division of the SUS. <http://www.datasus.gov.br>, accessed on 22/May/2009), defined by each of the State Health Secretariats, based on the country's *Operational Healthcare Guidelines* (NOAS-SUS 01/2001)<sup>23</sup>. To map the cases, we used the grid of municipalities from the Brazilian Institute of Geography and Statistics (IBGE) for the year 2005, aggregated by health region. Brazil's health regions are highly heterogeneous, especially in terms of scale, varying from 2 to 54 municipalities (besides the special case of the Federal District, which represents a single health region), and from 8,191 to 6,813,024 inhabitants under 19 years of age. However, since the health regions reflect a planning logic integrated in linked networks, they provide the most adequate analytical unit for this study. The concentration of services and children and adolescents per square kilometer can be seen in the maps showing the location of the CACONs (Figure 1a) and density (Figure 1b).

The study population consisted of children and adolescents of both sexes younger than 19 years with malignant neoplasms from 2000 to 2007, throughout Brazil. We chose to analyze the aggregate data for the 8-year period, since childhood cancer is a rare disease. The data came from the Health Information Systems (SIS), and more specifically the Mortality Information System (SIM), from the Hospital Information System and Outpatient Information System of the Unified National Health System (SIH/SUS and SIA/SUS), APAC/ONCO module, and are available on the DATASUS website (<http://www.datasus>).

Figure 1

State capitals, High Complexity Cancer Centers (CACONs) equipped to treat children and adolescents (1a), and concentration of children and adolescents by health region (1b).



gov.br). The population estimate was that of the study period's midpoint, namely the mean of the populations for 2003 and 2004.

Case selection and database organization were based on the codes from the International Classification of Diseases, 10<sup>th</sup> Revision (ICD-10) for malignant neoplasms (C00 to C97)<sup>20,24</sup>. This filter was used to select deaths and hospitalizations, with details on surgical procedures in the case of hospitalizations. The APAC/ONCO system was used to select the set of chemotherapy and radiotherapy procedures performed in the under-19 bracket<sup>20</sup>. Service use indicators were constructed based on the total number of recorded procedures for the period by health region (for patient's place of residence), using the mean mid-period population for each health region as the denominator. The mortality rate was constructed with the total number of under-19 cancer deaths for each health region as the nominator and the

study population for each health region multiplied by 1 million as the denominator.

A boxplot was used for the data description, with the median marked by the center line in bold and the narrowest part representing the 95% confidence intervals (95%CI) around the median. When the 95%CI do not overlap, there is strong evidence that the medians differ from each other<sup>25</sup>.

The maps of indicators present classes defined according to their distribution in quintiles, so as to allow comparison and visual analysis of the various spatial patterns.

The proportion of deaths from ill-defined causes (ICD-10, R00-R99) was used to assess the quality of data on mortality from underlying causes. Fewer than 4%-6% deaths from ill-defined causes are considered a low and thus acceptable rate<sup>26</sup>.

Tabulations were performed on TabWin, version 3.6 (DATASUS; <http://www.datasus.gov.br>), and the statistical analysis and mapping used the *spdep* library<sup>27</sup> from the public domain software R (The R Foundation for Statistical Computing, Vienna, Austria; <http://www.r-project.org>).

## Results

There were a total of 383,568 hospitalizations in the study population during the eight-year period in Brazil as a whole, based on Authorizations for Hospital Admissions (AIH), including clinical and surgical procedures. Of this total, 15,343 admissions (4%) were for surgeries in cancer patients. Most hospitalizations were for clinical reasons and were classified as *chemotherapy with continuous administration or for patients in acute phase leukemia* (24%) and *intercurrent illnesses in cancer patients* (22%). The latter may be performed in hospitals that may or may not be equipped for high complexity procedures<sup>28</sup>. Appendectomy was the most frequent surgical procedure (5.5%), and nearly 100% of these procedures presented ICD-10 codes for malignant neoplasm of the colon or appendix (C18 or C18-1).

For the same population and period, there were a total of 29,151 radiotherapy procedures and 465,289 chemotherapy procedures, with acute lymphoblastic leukemia (ALL) accounting for 47.8% of the latter.

Figure 2 shows that the distribution of all the indicators is asymmetrical, with a shift to the left and with extreme values in the upper classes. There were no health regions with zero cases, except for surgery in cancer patients and radiotherapy. The health regions are distributed by major geographic region and appear in Figure 2 in the following order, from top to bottom: Central-West (CO), South (S), Southeast (SE), Northeast (NE), and North (N). In Figure 2a, the first hatched vertical line represents what is considered the acceptable value for the proportion of deaths from ill-defined causes<sup>26</sup>. The dotted vertical line in squares *a* through *f* indicates the median for Brazil as a whole for each indicator. Except for the South, all the other major geographic regions show high median values for the proportion of deaths from ill-defined causes, with the highest values in the North and Northeast.

In squares *b* through *f*, the pattern is similar, with the North and Northeast showing the lowest values for use of services and cancer mortality rate for residents of those regions, in contrast to the other major geographic regions, especially the South. The Central-West and Southeast showed similar figures for cancer mortality

rates, chemotherapy, and radiotherapy, while the Central-West, Southeast, and South were similar for surgery in cancer patients and the North and Northeast showed similar hospitalization profiles (the medians were not statistically different). The Brazilian reference median (dotted vertical line) clearly separates the North and Northeast from the other geographic regions, showing that the former are at a disadvantage in terms of access to medical care and quality of mortality data.

Figure 3 shows that the cancer mortality rate pattern is almost opposite that for the proportion of deaths from ill-defined causes. The majority of the health regions located in the North and Northeast geographic regions experience both low cancer mortality rates and high proportions of deaths from ill-defined causes. In most of the health regions in the Southeast, South, and Central-West geographic regions, the high cancer mortality rates and low proportions of deaths from ill-defined causes indicate better data recording and better access to health services. The health regions in the State capitals in the South of Brazil showed fewer than 6% of deaths from ill-defined causes. In the other major geographic regions, the quality of mortality data varied, even in the State capitals: in the Northeast, the proportion of deaths from ill-defined causes varied from as low as 3.66% in Recife to 15.09% in Maceió.

The spatial pattern of chemotherapy and radiotherapy procedures financed by the SUS was similar (Figures 4a and 4b), with a greater dispersion of radiotherapy and greater concentration of chemotherapy in the country. Residents of the health regions in the North and the more peripheral health regions in the Northeast (Maranhão, southern Piauí, western Bahia) had less access to chemotherapy and radiotherapy when compared to the Southeast, South, and Central-West.

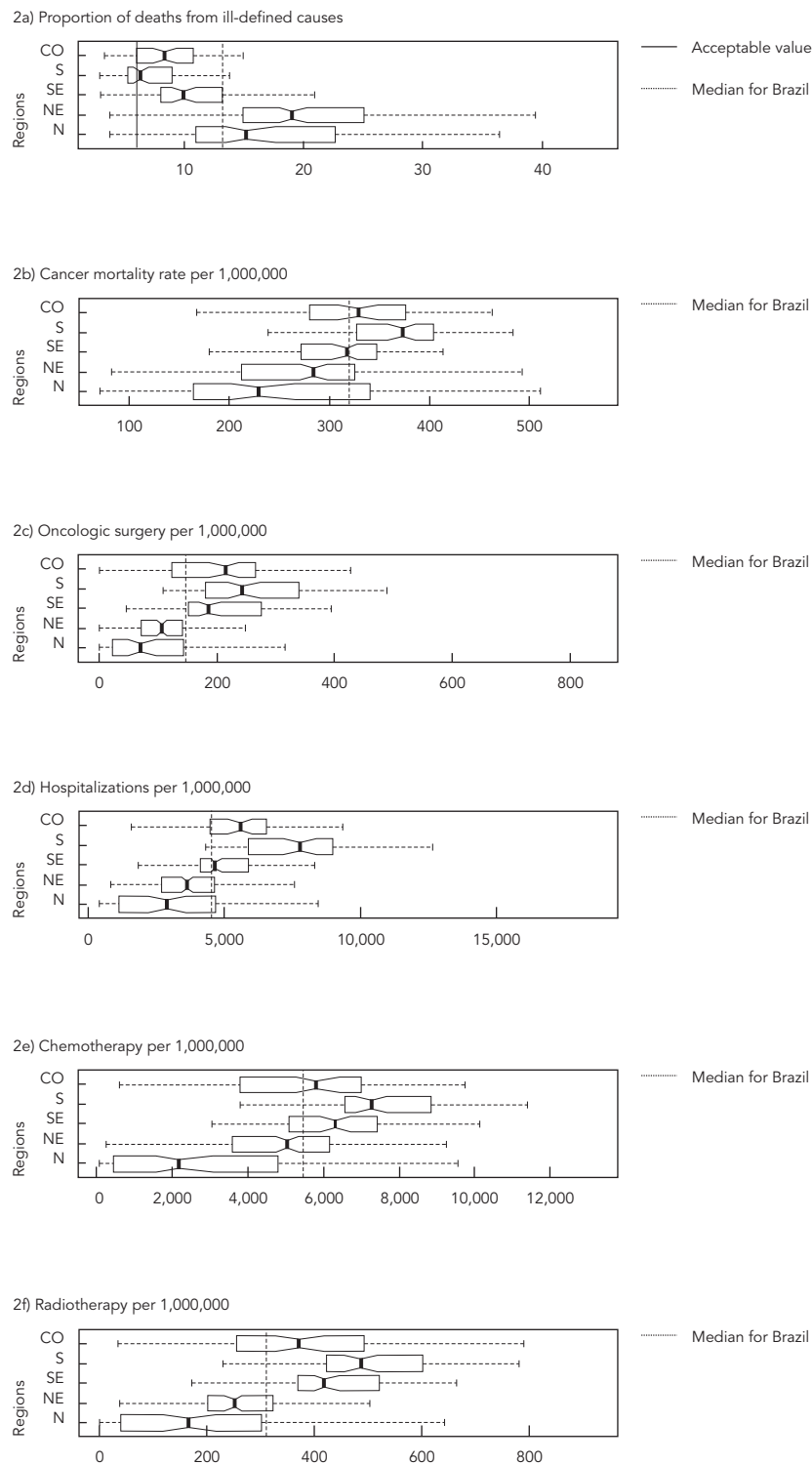
Oncologic surgeries and hospitalizations due to cancer in children and adolescents also showed similar spatial patterns (Figures 4c and 4d), with surgeries more concentrated than hospitalizations. Residents in the majority of the health regions in the North and Northeast had less access to hospitalization and oncologic surgery. Interestingly, the State of Bahia stood out from the health regions in the Northeast as a whole, showing a similar pattern to the States of Amazonas and Pará.

## Discussion

Mapping indicators for use of services in pediatric cancer care – hospitalizations, chemotherapy, and radiotherapy financed by the SUS – showed evidence of inequality in access, due

Figure 2

Boxplot by major geographic region of Brazil for proportion of deaths from ill-defined causes (2a), cancer mortality rate (2b), oncologic surgery (2c), hospitalizations (2d), chemotherapy (2e), and radiotherapy (2f) by health region for place of residence in individuals younger than 19 years, 2000-2007.

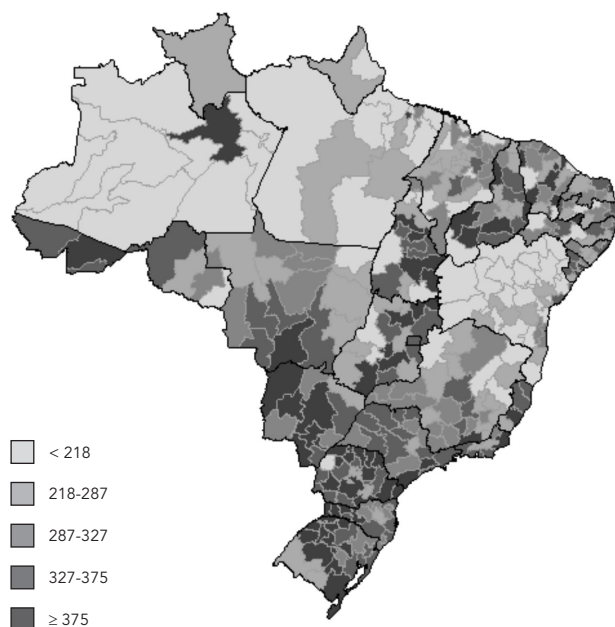


CO: Central-West; N: North; NE: Northeast; S: South; SE: Southeast.

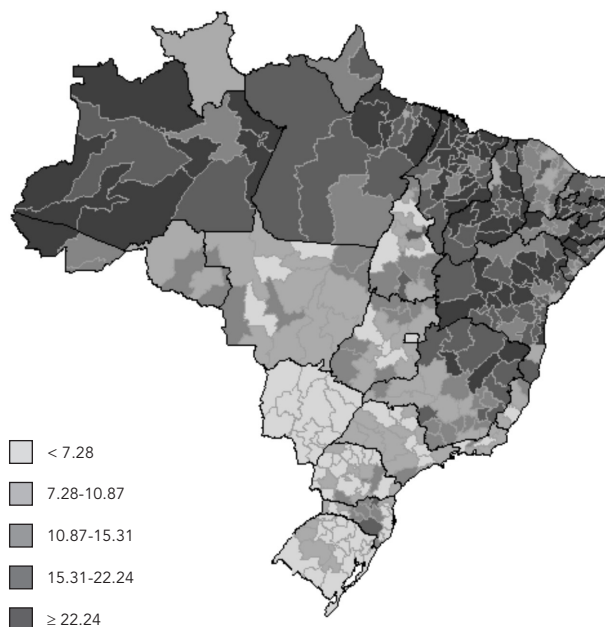
Figure 3

Cancer mortality rate (3a) and deaths from ill-defined causes (3b) by health region for place of residence in individuals younger than 19 years, 2000-2007.

3a) Cancer mortality rate (per 1,000,000)



3b) Proportion of deaths from ill-defined causes



to the small number of treatments for children in Brazil's poorer regions. The high proportion of deaths from ill-defined causes is traditionally used to assess the quality of mortality data: the higher the proportion, the worse the data recording, suggesting insufficient access and deficient diagnostic and therapeutic services<sup>26</sup>. The lower cancer mortality rate combined with the high proportion of deaths from ill-defined causes in children in the majority of the health regions in the North and Northeast reinforces the hypothesis of inequality in geographic access.

Another possible explanation for the low cancer mortality rate in children would be the under-reporting of deaths, which is still high, especially in the North and Northeast, especially in infants under one year of age<sup>29</sup>, and reaches rates as high as 47.5% in the country<sup>30</sup>. However, cancer deaths in children less than one year of age represented only 4.7% of the study population, and did not exceed 3.8% in the States of the South, where coverage is practically complete<sup>30</sup>.

There are also problems with the quality of information on the AIH. For example, the frequency of appendectomies, which is related to diagnosis

of cancer of the colon/appendix, should be verified, since this cancer is rare in this age bracket. However, since ICD-10 classification is mainly by location of the primary tumor rather than by histological type, they may have been cases of Burkitt lymphoma, the usual location of which is in the abdomen (especially the ileocecal region), with symptoms that are frequently confused with those of acute appendicitis. In these cases, exploratory laparotomy is indicated for diagnostic purposes and can lead to complete resection of the tumor, including appendectomy<sup>31</sup>. In order to avoid such problems, reducing doubts, it would be interesting to adopt the International Classification of Childhood Cancers, which is based on morphology (histology), rather than on location of the primary tumor as in adults<sup>32</sup>.

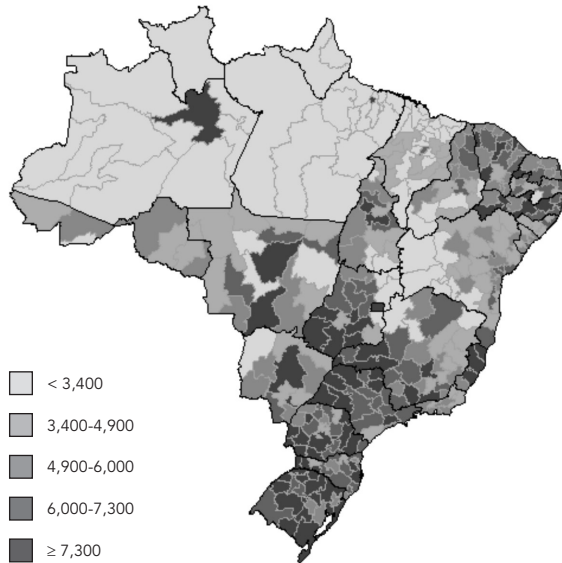
Correct information on the patient's address also correlates with quality of records. Some problems, such as the family moving due to the disease itself or furnishing erroneous information to facilitate treatment access lead to an increase in differences between places with and without access. Mapping in quintiles is an attempt to resolve this potential bias, because regardless of



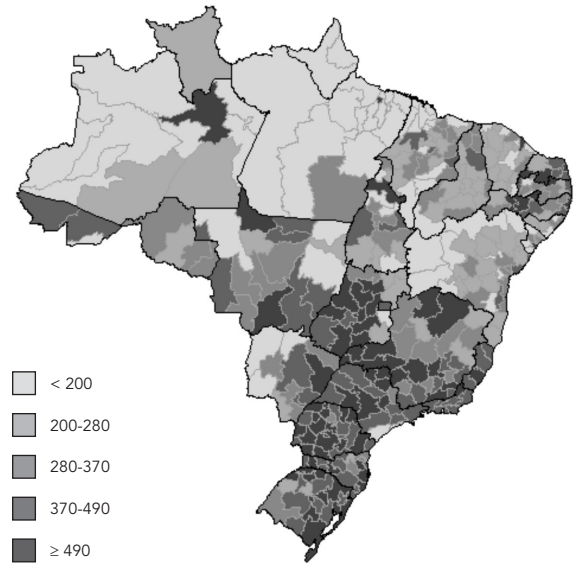
Figure 4

Chemotherapy (4a), radiotherapy (4b), and oncologic surgery procedures (4c) and hospitalizations (4d) by health region for place of residence in individuals younger than 19 years in Brazil, 2000-2007.

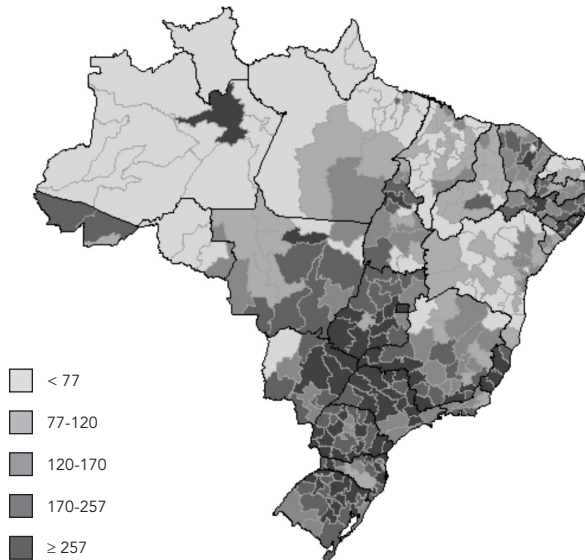
a) Chemotherapy (1,000,000)



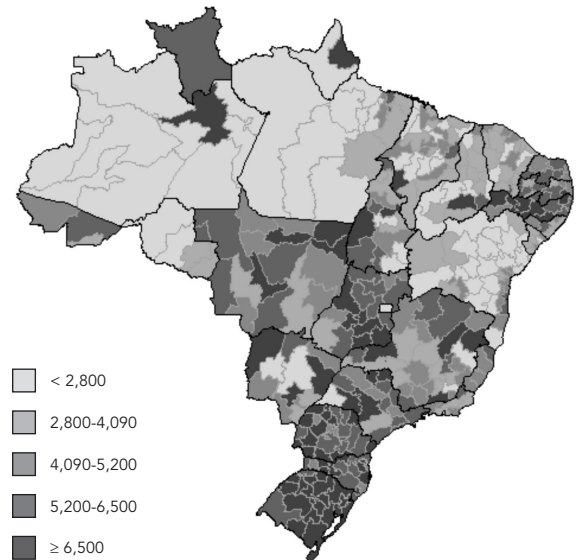
b) Radiotherapy (1,000,000)



c) Oncologic surgery procedures (1,000,000)



d) Hospitalizations (1,000,000)



the size of the real values, each class represents 20% of the cases – which allows comparison of the geographic distribution patterns for the various indicators. Mapping the medical care indi-

cators suggests that residents in the majority of the health regions in the North and in the more peripheral regions in the Northeast (Maranhão, southern Piauí, and western Bahia) receive fewer

procedures in chemotherapy, radiotherapy, and oncologic surgery and hospitalizations when compared to residents in the South and Southeast, thus demonstrating inequality in access. Importantly, being in the upper quintile for use of services merely indicates greater access to diagnosis and treatment, and does not necessarily mean better quality of care or the necessary early diagnosis.

Brazil is a very large and highly diverse country, and the location of health services must consider the conditions of the population's accessibility to the places where such services are installed. The distribution of CACONs (Figure 1a), which increased from 172 in 2001<sup>21</sup> to 234 in 2009<sup>22</sup>, mirrors the concentration of children and adolescents per square kilometer, which in turn shows the same distribution as the overall population. Inequality in geographic distribution of services should not be confused with inequity in access to services financed by the SUS. However, one should consider that the presence of medical services does not guarantee access to them by residents in the same location. Obviously, since childhood cancer is a rare event and population density varies greatly from one region to the next, it would not be appropriate to install a CACON in each location, since it would result in under-utilization. In addition, size and throughput in healthcare facilities are known to be an indirect measure of professional performance and quality of patient care, especially for children with cancer<sup>10,11</sup>, as reported by various authors<sup>11,33</sup> in the management of children with brain tumors by neurosurgeons experienced in these diseases, as well as in other rare or complex diseases, as demonstrated by Carvalho et al.<sup>34</sup> for

survival analysis of patients with chronic renal failure in dialysis.

One of the current study's limitations relates to the study population, restricted to patients under the public SUS and not including patients covered by private health plans. Interestingly, there is evidence that this sector tends to limit the insured population's access to medium and high complexity procedures in their own services<sup>35</sup>, suggesting that limiting the study population to patients treated under the SUS would not mean a major distortion in the overall pattern, even in areas where there is a larger share of care provided by private health insurance.

Another limitation is that the study did not investigate quality of care, but only its distribution. In order to deal with this issue, studies that explore the time transpired between diagnosis and treatment, between relapses, and until death are more adequate.

Early diagnosis of childhood cancer is the main challenge, because if adequate treatment is begun immediately, when the burden of disease is still minimal, the odds of cure are maximal, as proposed in the model by Goldie & Coldman<sup>36</sup>. However, some steps are needed for this to happen. First, primary care health professionals need to be trained to suspect the disease. Second, the guidelines of the SUS and the health regions need to be followed, the logic of which includes integrated planning, forming networks that provide access to all levels of complexity, including high complexity, as is the case with cancer care. With intercommunication within and between these networks, access by patients even from most remote corners of Brazil could happen quickly, and thus with better chances for cure.



## Resumo

*O câncer em crianças e adolescentes é raro e altamente curável se o tratamento for iniciado precocemente, no entanto representa a principal causa de óbito por doença nesse grupo. O objetivo deste estudo é discutir o acesso aos serviços de saúde de menores de 18 anos de idade com câncer no Brasil, a partir do mapeamento de óbitos e modalidades de tratamento no Sistema Único de Saúde (SUS). Os dados do período de 2000-2007 foram analisados por regional de saúde. Os mapas das taxas de mortalidade por câncer e indicadores de assistência – internações, quimioterapias e radio-terapias – mostraram desigualdade no acesso pelo pequeno volume de tratamentos para residentes nas regiões mais carentes do país. Mesmo com a usual concentração de serviços especializados onde é maior a população, o acesso começa com a suspeita clínica na assistência básica seguido pelo encaminhamento para níveis mais complexos onde se estabelece o diagnóstico e se inicia o tratamento. Treinamento de pediatras para a suspeita clínica e definição de fluxos rápidos podem mudar esse quadro, aumentando a chance de cura.*

*Diagnóstico Precoce; Neoplasias; Criança; Acesso aos Serviços de Saúde; Equidade*

## Contributors

M. F. Grabojs participated in the definition of the research theme, study design, data analysis, and elaboration of the article. E. X. G. Oliveira participated in the data analysis and elaboration of the article. M. S. Carvalho participated in the definition of the research theme, study design, data analysis, and elaboration of the article.

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