# Early Detection Actions of Breast Cancer in Brazil: Analysis of Data from the Breast Cancer Control Information System (Sismama), 2009-2015

doi: https://doi.org/10.32635/2176-9745.RBC.2022v68n3.2189

Ações de Detecção Precoce do Câncer de Mama no Brasil: Análise dos Dados do Sistema de Informação do Controle do Câncer de Mama (Sismama), 2009-2015

Detección Temprana Acciones de Cáncer de Mama en Brasil: Análisis de Datos del Sistema de Información para el Control del Cáncer de Mama (Sismama), 2009-2015

#### Maurício Cavalcanti de Andrade<sup>1</sup>; Adalgisa Peixoto Ribeiro<sup>2</sup>; Katharina Lanza<sup>3</sup>; Lucas Martins de Lima<sup>4</sup>; Graziella Lage Oliveira<sup>5</sup>

#### ABSTRACT

**Introduction:** Breast cancer is the type of neoplasm with the highest incidence and mortality in the female population worldwide. Early detection of breast cancer is associated with incidence increase and mortality reduction. **Objective:** To analyze indicators of breast cancer screening from the records of mammograms performed in Brazilian women from June 2009 to July 2015. **Method:** Cross-sectional study with secondary data of the Breast Cancer Control Information System (Sismama) extracted from the records of mammography performed by the National Health System (SUS) in the female population between June 2009 and July 2015. The proportions of each variable were calculated to determine the selected indicators annually. **Results:** A total of 14,926,700 records of mammograms were analyzed, 96.8% of which were screening (MMGr) and 3.2%, diagnostic (MMGd). A little more than half of the MMGr (52.5%) were performed in the age group from 50 to 69 years, followed by the age group from 40 to 49 years (35.9%). There was a rising trend in the proportion of MMGr in the recommended range (50-69 years) in the period studied, in addition to a higher proportion of delivery of the test result in less than 30 days (both for MMGd and MMGr), with differences between the regions. **Conclusion:** Compliance with the Ministry of Health recommendations for early diagnosis of breast cancer is not uniform across the country. The necessity to develop health strategies addressing the existing inequalities among the country regions emerges.

Key words: breast neoplasms; early detection of cancer; mass screening; mammography; women's health.

#### RESUMO

Introdução: O câncer de mama é o tipo de neoplasia com maior incidência e mortalidade na população feminina no mundo. Observa-se aumento da incidência do câncer de mama e redução da mortalidade associados à detecção precoce. Objetivo: Analisar indicadores de rastreamento de câncer de mama a partir dos registros de mamografias realizadas em mulheres brasileiras, no período de junho de 2009 a julho de 2015. Método: Estudo transversal, utilizando dados secundários do Sistema de Informação do Controle do Câncer de Mama (Sismama), referentes aos registros dos exames de mamografia realizados pelo Sistema Único de Saúde (SUS) na população feminina entre junho de 2009 e julho de 2015. Foram calculadas as proporções de cada variável para compor os indicadores selecionados por ano. Resultados: Foram analisados 14.926.700 registros de mamografias, sendo 96,8% de rastreamento (MMGr) e 3,2% diagnósticas (MMGd). Pouco mais da metade das MMGr (52,5%) foram realizadas na faixa etária de 50 a 69 anos, seguida pela faixa etária de 40 a 49 anos (35,9%). Observou-se uma tendência de aumento na proporção de MMGr na faixa preconizada (50-69 anos) no período estudado, além de maior proporção de entrega do resultado do exame inferior a 30 dias (tanto para MMGd como MMGr), com diferencas entre as Regiões. Conclusão: O cumprimento das medidas propostas pelo Ministério da Saúde para diagnóstico precoce do câncer de mama não ocorre de maneira uniforme no território nacional. Emerge a necessidade de desenvolver estratégias em saúde que contemplem as inequidades existentes entre as Regiões do país.

Palavras-chave: neoplasias da mama; detecção precoce de câncer; programas de rastreamento; mamografia; saúde da mulher. RESUMEN

Introducción: El cáncer de mama es el tipo de cáncer con mayor incidencia y mortalidad en la población femenina a nivel mundial. Hay un aumento en la incidencia de cáncer de mama y una reducción en la mortalidad asociada con la detección temprana. Objetivo: Analizar indicadores de cribado de cáncer de mama a partir de los registros de mamografías realizadas en mujeres brasileñas, de junio de 2009 a julio de 2015. Método: Estudio transversal, con datos del Sistema de Información para el Control del Cáncer de Mama (Sismama), referido a los registros de mamografías realizadas por el Sistema Único de Salud (SUS) en la población femenina entre junio de 2009 y julio de 2015. Se calcularon las proporciones de cada variable para componer los indicadores seleccionados, según el año. Resultados: Se analizaron un total de 14.926.700 registros de mamografías, de los cuales el 96,8% eran de seguimiento (MMGr) y el 3,2% eran diagnósticos (MMGd). Un poco más de la mitad de las MMGr (52,5%) se realizaron en el grupo de edad de 50 a 69 años, seguido del grupo de 40 a 49 años (35,9%). Hubo una tendencia hacia un aumento en la proporción de MMGr en el rango recomendado (50-69 años) en el período estudiado, además de una mayor proporción de entrega del resultado de la prueba en menos de 30 días (tanto para MMGd como para MMGr), con diferencias entre Regiones. Conclusión: El cumplimiento de las medidas de diagnóstico del cáncer de mama no se da de manera uniforme en todo el país. Surge la necesidad de desarrollar estrategias de salud que aborden las desigualdades existentes entre las regiones del país.

Palabras clave: neoplasias de la mama; detección precoz del cáncer; tamizaje masivo; mamografía; salud de la mujer.

<sup>&</sup>lt;sup>4</sup>UFMG, Faculdade de Filosofia e Ciências Humanas. Belo Horizonte (MG), Brazil. E-mail: lucasmlima@ufmg.br. Orcid iD: https://orcid.org/0000-0001-8581-7690 **Corresponding author:** Graziella Lage Oliveira. Avenida Professor Alfredo Balena, 190, Sala 823 – Santa Efigênia. Belo Horizonte (MG), Brazil. CEP 30130-100. E-mail: graziellage@ufmg.br



<sup>&</sup>lt;sup>1</sup>Secretaria Municipal de Saúde de Belo Horizonte. Belo Horizonte (MG), Brazil. E-mail: mauriciodeandrade@gmail.com. Orcid iD: https://orcid.org/0000-0002-4217-010x <sup>235</sup>Universidade Federal de Minas Gerais (UFMG), Faculdade de Medicina. Belo Horizonte (MG), Brazil. E-mails: adalpeixoto@yahoo.com.br; lanzakatharina@gmail.com; graziellage@ufmg.br. Orcid iD: https://orcid.org/0000-0001-9415-8068; Orcid iD: https://orcid.org/0000-0001-7488-6906; Orcid iD: https://orcid.org/0000-0002-3387-3583

# INTRODUCTION

Breast cancer is the most incident and high mortality type of neoplasm for the female population in Brazil and worldwide<sup>1,2</sup>. In Brazil, it is estimated 66,280 new cases of breast cancer for each year of the triennium 2020-2022, equivalent to a risk of 61.61 new cases for each 100 thousand women<sup>3</sup>. Except non-melanoma skin cancer, this type of cancer is the most frequent in Brazilian women with risk of 81.06/100 thousand in the Southeast region; 71,16/100 thousand in the South region, 45.24/100 thousand in the Midwest region, 44.29/100 thousand in the Northeast region and 21.34/100 thousand women in the North region<sup>3</sup>.

For high-income countries as the United States of America, United Kingdom and Norway, the registers point out to a rising incidence of breast cancer followed by reduction of mortality, possibly associated with early detection and offer of timely treatment. In Brazil as in other low-and-middle-income countries, the increase of the incidence and mortality may be attributed to poor access to screening initiatives, late diagnosis and loss of therapeutic opportunity<sup>4-6</sup>. When detected earlier, breast cancer has better prognosis and low treatment-related morbidity<sup>4</sup>.

For that matter, strategies of early detection with immediate impact on the identification of signs and symptoms and fast and easy access to health services<sup>5</sup> have been recommended by the World Health Organization (WHO). Among them, early diagnosis or agile and timely approach to individuals with signs and symptoms of cancer and screening with regular mammograms for apparently healthy persons on the age-range of higher risk with the objective of identification in pre-clinical phase and reduce mortality<sup>7</sup>.

Effective early diagnosis of breast cancer is a public health strategy involving multiple actions developed around education in health for the population for cancer suspicious signs and symptoms and preparation of the health services for timely diagnostic confirmation. It is important to have quality diagnosis, assurance of integrality and continuous care through all the course of the process<sup>4</sup>.

Breast cancer screening, diagnosis and treatment in Brazil started to be incorporated into health public policies since mid-1980's<sup>8</sup>. An important historical milestone was the publication of a Consensus in 2004<sup>2</sup> containing the recommendations for prevention, early detection, diagnosis, treatment, follow-up and palliative care. Among them, the implementation of mammogram screening for women in the age-range of 50-69 years old every two-years with ensured diagnosis, timely treatment and follow-up and the creation and implementation of information system at the mammograms services. These recommendations were updated by the Breast Cancer Early Detection Guidelines in Brazil in 2015<sup>4</sup>.

The National Policy of Oncologic Attention was launched in 2005<sup>9</sup> which included breast cancer control as an important part of the Municipal and State Health Plans. In 2009 the Breast Cancer Control Information System (Sismama) was implemented nationally with the objective of monitoring the actions of breast cancer early detection. Sismama registered information about mammograms, cytopathology and histopathology exams conducted at Brazil's National Health System (SUS) from 2009 to 2015<sup>10</sup>. Breast cancer control was incorporated into the Strategic Actions Plan to cope with noncommunicable diseases (DCNT) from 2011 to 2022<sup>11</sup>.

The access to breast cancer screening exams in Brazil appears to have been influenced by social inequities. At the North, Northeast, and Midwest regions where these inequities are more evident, poor access is a noticeable feature<sup>6</sup>.

The objective of the present study is to analyze markers of breast cancer screening extracted from registers of mammograms performed on Brazilian women from June 2009 to July 2015. These markers will be shown for the entire period of Sismama.

## METHOD

Descriptive, cross-sectional study which investigated the registers of mammograms performed at SUS in Brazilian women from June 2009 to July 2015 collected from Sismama<sup>12</sup>.

Sismama monitors the screening, diagnosis, treatment and quality of the exams performed at SUS<sup>13,14</sup> network. It is a subsystem of SUS Outpatient Information System (SIA/SUS) which allows the analysis of the indicators directly impacting the management and planning of required interventions to adjust the offer and qualifications of the services and training of the team involved and improvement of the work process<sup>14</sup>. Since 2013, Sismama was gradually replaced by Cancer Information System (Siscan) which gathered the Cervix Cancer Information System (Siscolo) and Sismama at a web platform<sup>15</sup>.

The registers of all the mammograms of the Brazilian female population at Sismama were included in the analysis and those done in men and classified as inconsistent were excluded. The variables of the mammograms registers were: 1) clinical indication (screening, when women were asymptomatic and diagnosis in patients with signs/or symptoms of breast cancer); 2) screening for the age-range of 50-69 years old; 3) elevated risk of breast cancer (group

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of 35-49 years women with history of breast cancer); and 4) presence of palpable node > 20 mm identified in screening mammograms (MMGr).

These variables are the indicators of the process defined in the Technical File of Indicators of Breast Cancer Control Actions<sup>16</sup> and presented in other articles on the theme: 1) percentage of MMGr on the recommended age-range (number of MMGr for the female population between 50 and 69 years/total of MMGr\*100); 2) percentage of MMGr in the age range from 35 to 49 years with high risk cancer reported on the request for exam (number of MMGr between 35 and 49 years old with high risk reported in the request for exam /total of MMGr\*100); 3) percentage of MMGr with palpable nodes >20 mm – number of MMGr with palpable nodes/ total of MMGr\*100 - and the percentage of diagnostic mammograms (MMGd) and MMGr according to the time from the request and delivery of the results (number of MMGd delivered between 0-30 days; 31-60 days and more than 60 days/total of MMGd\*100; number of MMGr delivered between = 0-30 days; 31-60 days and more than 60 days /total of MMGr\*100). A calculation was made for each time range. All the indicators were calculated for Brazil and geographic macroregions.

The data were analyzed with Microsoft Excel<sup>®</sup>. Descriptive analyzes were performed and the proportions of each variable were calculated to form the indicators selected per year of the period investigated.

## RESULTS

SUS-funded 15,104,577 mammograms were identified from June 2009 to July 2015, 14,926,700 in Brazilian women and 8,658 in men. 177,877 were excluded, of which 169,219 with inconsistent information and in men (1.18% exclusion).

Most of them were screening mammograms for all Brazilian regions. The MMGd accounted for 3.6% in average, with low percentage in the South regions (2.4%) and high in the North (4.6%) region as shown in Graph 1.

MMGr for the age-range of 50-69 years were the most frequent registered at Sismama (52.5%). For all regions, this percentage was above 50%, except in the North region (47.8%). For other age-ranges, 40-49 years was the second highest with 35.9% in the whole country (unlisted in the table).

A rising trend of percentage of MMGr in the recommended age-range 50-69 was detected until 2014, year when it reached 56.6% of all MMGr performed in Brazil registered at Sismama. The Northeast region stood out in the same year with the higher percentage than the Brazilian mean (65.82%). Until July 2015,





**Graph 1**. Distribution of mammograms done at SUS according to clinical indication. Brazil and Regions, June 2009 to July 2015 **Source** Sismama<sup>12</sup>.

records diminished to 54.9% of the total of the country's mammograms. Percentages well below the national mean for the whole period investigated were found at the North region (Graph 2).



**Graph 2**. Annual percentage of MMGr in the age-range recommended (50 to 69 years). Brazil, June 2009 to July 2015 Source: Sismama<sup>12</sup>

The percentage of MMGr in the age-range from 35 to 49 years with information of high risk of breast cancer when requested (condition justifying the exam for this population according to Consensus of 2004<sup>2</sup>, in force during the whole period analyzed) was 9.7% of the total of MMGr for Brazil in this age-range. Among the regions, the highest percentage (10.6%) was in the South, and the lowest (8.7%) in the North. The annual analysis showed that the Brazilian mean was around 11% from 2009 to 2013, increasing in the last two years, reaching 12.5% in 2014. The Midwest Region, with a percentage well below the national mean until 2012, presented an expressive rise in the following years with 19.4% in 2015 (Graph 3).

Of the screening exams done in the period, 11.2% were MMGr with the presence of nodes > 20 mm



**Graph 3**. Screening mammograms with information of high risk of cancer between 35 and 49 years of age. Brazil and Regions, June 2009 to July 2015



**Graph 4**. Percentage of Screening Mammograms with palpable nodes >20 mm. Brazil and Regions, June 2009 to July 2015

Source: Sismama<sup>12</sup>.

diagnosable at the clinical exam of the breasts (CEB) for all MMGr registered at Sismama. This percentage ranged from 10.2% in the South to 15.1% in the North regions. The annual analysis revealed that the percentage of the country was kept stable, but the South region had a variation from 10.1% in 2009 to 0% in 2015 and the North Region from 19% in 2009 to 11.2% in 2015 (Graph 4).

The time since a woman requested the mammogram and the results, ideally less than 30 days, was similar for both indications (screening and diagnostic) according to Sismama for all regions, except the North and South regions, which delivered more results of MMGr against MMGd (difference of 10.6% for the North and 4.9% for the South) as indicated in Table 1. The highest percentage of delivery of results in less than 30 days with 77.5% for MMGd and 73.3% for MMGr was found in the Northeast region, quite similar to the Southeast region, 52.7% for MMGr and 52.6% for MMGd respectively, but with the highest percentage of delivery for both in over 60 days (24.0% for MMGr and 27.2% for MMGd), when compared to the other regions.

## DISCUSSION

Source: Sismama<sup>12</sup>

The present study analyzed the cohesiveness of the recommendations for breast cancer screening and what was actually implemented and registered at Sismama<sup>12</sup>. The inclusion of age-ranges lower than 50 years is justifiable because of the current recommendation for breast cancer screening in the age-range from 35 to 49 years with information of elevated breast cancer risk in the request for mammograms<sup>2</sup>. The current measures for breast cancer control updated by the Guidelines of Breast Cancer Early Detection in Brazil<sup>4</sup>, elaborated from the systematization of scientific literature-based evidences consistent with the National Policy of Management of Health Technologies<sup>17</sup>, do not recommend anymore MMGr for this age-range nor auto-exam or CEB as screening strategies because there are no evidences enough to support these procedures<sup>4</sup>.

The analysis of the markers related to mammograms at Sismama performed on women from June 2009 and July 2015 in Brazil allowed to detect inconsistency of the actions in comparison with the recommendations of

	Total		0-30 days				31-60 days				>60 days			
Region	MMGr	MMGd	MMGr		MMGd		MMGr		MMGd		MMGr		MMGd	
	n	n	n	%	n	%	n	%	n	%	n	%	n	%
Brazil	14,442,883	483,817	8,770,898	60.7	290,481	60.0	2,882,997	20.0	87,804	18.1	2,788,988	19.3	105,532	21.8
North	461,380	22,124	327,437	71.0	13,373	60.4	65,610	14.2	4,077	18.4	68,333	14.8	4,674	21.1
Northeast	2,740,133	84,282	2,007,986	73.3	65,351	77.5	406,257	14.8	11,622	13.8	325,890	11.9	7,309	8.7
Southeast	8,288,442	290,443	4,370,503	52.7	152,898	52.6	1,930,969	23.3	58,567	20.2	1,986,970	24.0	78,978	27.2
South	2,290,097	56,316	1,620,510	70.8	37,116	65.9	375,687	16.4	10,608	18.8	293,900	12.8	8,592	15.3
Midwest	662,831	30,652	444,462	67.1	21,743	70.9	104,474	15.8	2,930	9.6	113,895	17.2	5,979	19.5

 Table 1. Distribution of mammograms according to the time between the request of mammogram and delivery of the result. Brazil and Regions,

 June 2009 to July 2015

Source: Sismama<sup>12</sup>.

Captions: MMGr = Screening Mammogram; MMGd = Diagnostic mammogram.

the National Program of Breast Cancer Control of the Ministry of Health<sup>18</sup> for breast cancer early detection.

Brazil has been following WHO's recommendations for early detection by mammogram screening and early diagnosis of breast cancer. However, even with the increase of the absolute number of exams from 1,869,285 mammograms performed in 2002 to 4,713,530 in 2014<sup>8</sup>, no actual advance of the percentage of MMGr in the recommended age-range (50 to 69 years) was found as the current study concluded, although these percentages improved from 2009 (49.8%) to 2015 (54.89%).

Little more than half of MMGr registered at Sismama (52.5%) for the whole country were for the targetpopulation, similar for nearly all the regions, except the North where most of MMGr were off the recommended age-range. The percentage of MMGr for women in the age-range of 50 to 69 years old is one of the markers of the process utilized to evaluate the adequacy of breast cancer screening<sup>16</sup>. Although there is no parameter, it was found a percentage of 53% of MMGr in Brazil for the recommended age-range in 2013<sup>16</sup>. Until 2012, the percentages were lower than this result, reaching 53.13% in 2013 and 56.6% in 2014 with difference among regions.

These discrepancies might be associated with regional differences of access to breast cancer screening. Between 2008 and 2015 the access<sup>6</sup> was lower in the North, Northeast and Midwest regions and strongly influenced by socioeconomic indicators where as great the inequality is, poorer is the access to screening and as high is the Human Development Index (HDI), bigger is the number of mammograms.

The high percentage of MMGr off the target-population in the country regions exposes the challenges of meeting the guidelines of breast cancer screening as incognizance about the screening program or non-adherence to these recommendations by the requesting professionals and the complexity of the Brazilian health system in regard to the political, financial and administrative autonomy of the Brazilian States on health initiatives, a barrier to the homogeneity of the actions. The Ministry of Health should not only establish the guidelines but also support technically and financially the state and municipal entities for improved materialization of the policy<sup>19</sup>.

It was found at Sismama's registers that MMGr in the age-range from 35 to 49 years old between 2009 and 2015 was 11% approximately, reaching 12.5% in 2014, and 19.4% in the Midwest in 2015. For this age-range, mammograms were justified only when there was information of high risk of cancer in the request for the exam. In the field "Anamnesis" of the request form, the question number 2 "Is there elevated risk for breast cancer?" the response options are yes, no and does not know. This field is mandatory to allow the billing at SIA/SUS according to Article  $4^{th}$  of Ordinance SAS number  $779/08^{20}$ .

For the period investigated, of the total of MMGr of the country in the age-range of 35 to 49 years, only 9.7% were reported as elevated risk of cancer and not for all the requests. However, more than 90% of the exams did not have this information and yet, MMGr was requested and performed in contrast with the guidelines for early detection of breast cancer<sup>4</sup>. The outcome is that this group of women may have been exposed to unnecessary risks for not meeting the required conditions for MMGr, or the registers were flawed in regard to the indication of high risk of cancer.

Although the prevalence of Brazilian women with elevated risk of breast cancer is barely known<sup>21</sup>, a systematic review of the literature by Pinho *e* Coutinho<sup>22</sup> identified three studies with large sample of this population showing prevalence from 2.7% to 3.7% of family history of breast cancer in first degree relatives. However, when all the factors to determine the elevated risk are considered, the prevalence dropped to 1%<sup>21</sup>. The form to request MMGr in the age-range from 35 to 49 years may have been filled up erroneously by the health professional or even left blank. More recent data from INCA<sup>23</sup> reinforce elevated volume of mammograms of the recommended age-range close to 40%.

Higher number of mammograms off the recommended age-range do not represent whatsoever the actual number of women with elevated risk. Notwithstanding representing a reduced portion of the female population, this group should be followed-up individually with indication for annual screening<sup>24</sup>, which requires closer monitoring by the health services within the concept of full care mainly in primary attention with more agile referral and counter-referral flows.

Mammogram is the only exam utilized to screen asymptomatic women given the capacity of detecting very small unpalpable lesions still in pre-clinical phase<sup>22</sup>. It is the first imaging method to evaluate most of the mammary clinical alterations<sup>25</sup>. MMGr is the most sensitive method to detect initial breast cancers with possible cure of 95%<sup>26</sup>. Another aspect is the presence and size of palpable nodes<sup>4</sup>, an important warning sign for breast cancer<sup>27</sup>, in addition to the asymmetry of the breast, skin retraction, recent retraction of the nipple, bloody nipple discharge and eczematous changes of the areola<sup>27</sup>. The appearance of mammary node corresponds to 90% of the initial form of confirmed asymptomatic cancer<sup>24</sup>.

CEB is the breast cancer detection method at the gynecological routine and it is not only a moment for

professional evaluation but also to promote health education through orientations offered to the women about the breast structure and warning signs of cancer<sup>24</sup>. Studies strengthen the importance of CEB since approximately 40% of the cases of breast cancer can be detected with palpation<sup>28</sup>, which places professionals of PHA in a key position to help early breast cancer diagnosis. Although quite useful, CEB can identify only nodes > 20 mm<sup>8</sup>.

For the period investigated, 11.2% of the screening mammograms had indication of nodes > 20 mm, possibly suggesting that there has been no early detection for this group of women or errors in filling up the exam request. The identification of palpable lesions after CEB can reveal possible late diagnosis of the disease which worsens the prognosis. These findings may suggest difficulty of access to PHA for timely CEB with mammary node identified only when mammogram is made; wrong indication for MMGr and frequency; poorly prepared health professionals, mainly nurses and doctors of PHA<sup>4</sup> who need to be trained for CEB, creating obstacles to identify clinical alterations of breast cancer and inadequate dissemination of the recommendations of the Breast Cancer Control National Program<sup>18</sup>.

Another important marker investigated was the monitoring of the time the woman took to get the results. The time starts when she has the request of the exam and ends when she is given the results and it should be reviewed according to the clinical indication, screening or diagnostic. It is anticipated high percentage of MMGd and results in less than 30 days<sup>16</sup> for timely detection of more advanced cases of the disease<sup>8</sup>. In addition, it is possible to evaluate whether the visits scheduling prioritizes MMGd of the symptomatic cases because the agility to deliver the results of the mammogram<sup>29</sup> favors the treatment as quickly as possible.

The results found for this marker show that MMGd is not a priority on some country regions, only in the Northeast and Midwest with reports delivered in less than 30 days when compared to time of delivery of the results of MMGr, which can delay the sequence of investigation of women with signs and symptoms. It is quite surprising that in the Southeast and North regions, more than 20% of the MMGd take more than 60 days to have the results delivered. This delay may lead to the aggravation of the disease and less odds of cure or better prognosis.

CONCLUSION

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Overall, although in some regions the markers presented a trend of improvement, the findings of the present study showed there are difficulties of fully meeting the current recommendations of the Ministry of Health for breast cancer control. This reality can contribute for the continuous high rates of mortality by this neoplasm compared to other which affect women.

The utilization of secondary data as the Sismama's can lead to the occurrence of some limitations as: 1) outdate of the database that may have occurred when Sismama was replaced by Siscan since 2013 and difficulties of the States in feeding the system as homogeneously as possible; 2) Sismama registers exams and not individuals, which hampers the correlation of the exams done in different periods; 3) important aspects related to filling out the request form may cause errors since it is an open field completed manually and it is possible that the health professional is unable to detect these aspects; 4) utilizes simpler criteria to request MMGr, possibly inducing the requesting professional to choose this option.

Despite these limitations, Sismama allowed the opportunity to verify what was being offered and how many mammograms were performed in the country, in addition to fragile aspects which can be corrected. These information can help managers and health professionals not only to materialize the policy of breast cancer screening but also in reducing the mortality with early diagnosis and timely treatment.

It is anticipated that this article helps to deepen the discussion about the actions of early detection considering the country's regional differences. It is necessary to: 1) strengthen the PHA with training and qualification of health professionals because it is the preferred access to SUS and main ally in preventing and detecting breast cancer; 2) continuous improvement of information systems; 3) improvement of the quality of diagnostic investigation and treatment.

### CONTRIBUTIONS

Maurício Cavalcanti de Andrade and Graziella Lage Oliveira contributed to the study design, acquilistion, analysis and interpretation of the data, wording and critical review. Adalgisa Peixoto Ribeiro, Katharina Lanza and Lucas Martins de Lima participated of the wording and critical review. All the authors approved the final version to be published.

# **DECLARATION OF CONFLICT OF INTERESTS**

There is no conflict of interests to declare.

### **FUNDING SOURCES**

None.

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Associate-Editor: Jeane Tomazelli. Orcid iD: https://orcid.org/0000-0002-2472-3444 Scientific-Editor: Anke Bergmann. Orcid iD: https://orcid.org/0000-0002-1972-8777 São Leopoldo, RS: Universidade do Vale do Rio dos Sinos; 2017 [acesso 2020 nov 20]. Disponível em: http://www.repositorio.jesuita.org.br/bitstream/handle/ UNISINOS/6282/Brunize%20Altamiranda%20 Finger\_.pdf?sequence=1&isAllowed=y

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Recebido em 28/6/2021 Aprovado em 29/11/2021