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Risk factors of breast cancer and knowledge about the disease: an integrative revision of Latin American studies

Fatores de risco do câncer de mama e o conhecimento sobre a doença: revisão integrativa de estudos Latino Americanos

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Abstract *The aim of this integrative review was to compare Latin American literature about risk and knowledge on breast cancer. Of 47 studies selected, 20 were about knowledge or awareness and 27 about risk of breast cancer. English was the dominant language in studies about risk, whereas studies about knowledge were mainly written in Spanish or Portuguese. Studies about knowledge were all cross- sectional, whereas case- control studies dominated authors' interest about risk of breast cancer. Studies about knowledge were mainly focused on early detection of the disease and the most common study objective was breast self- examination (N = 14). In contrast, few studies about risk of breast cancer focused on early detection (N = 5). Obesity and overweight (N = 14), family history (N = 13), decreased parity (N = 12), and short breastfeeding duration (N = 10) were among the most frequent identified risk factors. Socio- economic factors such as income and educational level had variable effects on breast cancer risk and affected also knowledge of women about risk factors and early detection. Present results indicated that studies about risk of breast cancer were more often based on a better sound analytical background, compared to studies about knowledge, which were mostly descriptive.*

Key words *Breast cancer, Early detection of cancer, Risk factors, Knowledge*

Resumo *Esta revisão teve por objetivo comparar a literatura Latino-Americana sobre o conhecimento da neoplasia mamária e seus fatores de risco. Foram selecionados 47 estudos, dos quais 27 eram sobre o risco de desenvolver câncer de mama e 20 sobre o conhecimento ou a consciência sobre a doença. Os estudos sobre fatores de risco eram principalmente do tipo caso-controle e sua maioria estava no idioma Inglês. Já as pesquisas sobre conhecimento eram, sobretudo, do tipo transversal e foram publicadas nos idiomas Português e Espanhol. As pesquisas sobre conhecimento destacaram o diagnóstico precoce da neoplasia mamária, e o autoexame da mama foi o método de detecção mais abordado (N = 14). Por outro lado, os estudos sobre fatores de risco avaliaram, principalmente, sobrepeso (N = 14), historia familiar (N = 13), baixa paridade (N = 12) e curto período de amamentação (N = 10). Fatores socioeconômicos, como a renda e o nível educacional tiveram efeitos variáveis e afetaram também o conhecimento das mulheres sobre fatores de risco e detecção precoce. Os resultados da pesquisa indicaram que os estudos sobre fatores de risco do câncer de mama apresentaram melhor delineamento metodológico e fundamentação teórica, comparado com os estudos sobre conhecimento que foram na maioria dos casos descritivos.*

Palavras-chave *Câncer de mama, Diagnóstico precoce, Fatores de risco, Conscientização*

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Introduction

The global burden of breast cancer (BC) is progressively shifting from developed to developing countries[1,2]. According to the Pan American Health Organization (PAHO), BC is the most common and also leading cause of death by cancer among women in Latin America and the Caribbean region, where each year 114.000 women are diagnosed and an estimated 37.000 patients die from this disease[3]. With exception of Guatemala, Honduras and El Salvador, BC ranks in all Latin American countries as one of the three most leading causes of death by cancer among women[4]. Aging combined with decreased fertility rates has caused a demographic shift of societies in these countries[3]. As aging is the most important risk factor of BC, the number of deaths is expected to double by 2013 each year to 74.000 if current trends are confirmed[3].

Changing lifestyle and reproductive patterns in Latin American countries may additionally increase the risk of BC[5,6]. In literature, delayed childbearing, low parity and short breastfeeding periods represent well-established reproductive risk factors for BC[7-9]. Additionally, early age at menarche and late age at menopause are reproductive factors that increase the risk of the disease[7]. Obesity and overweight are also risk factors for BC[6,10]. Other well-established lifestyle-related risk factors are physical inactivity and sedentarism, alcohol consumption, smoking and intake of several hormones like estrogens[11]. High intake of red meat was identified as a risk factor, whereas high intake of fruits and some dietary patterns such as the Mediterranean diet provided a protective effect[11,12].

If on the one hand, risk factors such as age or family history are not modifiable, on the other hand, lifestyle-related risk factors like smoking, alcohol consumption or overweight and also reproductive risk factors like breastfeeding are rather modifiable. Avoidance behaviour of modifiable risk factors depends on lifestyle and socioeconomic background and has been associated with the knowledge of women about BC[13,14].

Early detection (ED) of BC comprises mammography, clinical breast examination and breast self-examination (BSE)[1,14,15]. Similarly to the women's avoidance behaviour of risk factors, ED through participation on screening programs and BSE depends on knowledge about BC, awareness of its risk, which can be associated to the socio-economic status of women[1,15,16].

According to most recent data published by PAHO in all Latin American countries, with the exception of Peru, clinical breast examination is available for women by the private and public health sector[4]. Mammography in contrast, is not available by the public but only by the private sector in Bolivia, the Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Panama and Paraguay, whereas in Peru, it is not available at all[4]. Information about prevailing risk factors, ED behaviour and women's knowledge about the disease may be important to improve public health politics. In Brazil for example, the Latin American country with the largest population, prevention strategy of BC are mainly focused on ED and so far, there is no public information campaign about risk factors[17]. A recent study identified breastfeeding as a protective factor in a population of North-eastern Brazil[18]. In this region, BC mortality rate increased 5.3% annually during the last decade[19].

To the best of our knowledge, there is no comparison of Latin American literature about knowledge and risk of BC. We hypothesized that literature about *knowledge* of risk and ED would be scarce compared to studies about prevailing risk factors and women's screening behaviour. Furthermore, we asked if Latin American studies about BC are more frequently focused on ED or identification of prevailing risk factors. In relation to Latin American studies on BC prevention, the present review addressed on following four basic questions: 1. Which Latin American studies on the risks of BC were performed in the last five years and which risk factors were identified in these studies? 2. How many studies on ED were performed focusing on women's screening behaviour and which forms of ED were analysed? 3. Studies about knowledge and awareness of BC aimed at which are the risk factors and forms of ED? 4. What have been the methods applied by the authors of these Latin American studies?

Method

An integrative review of the risk factors for BC and knowledge about them was conducted as previously described[20]. According to established criteria, the operational steps were conducted as followed: Definition of exclusion and inclusion criteria and database; selection of studies; extraction of information and categorization; Analysis and interpretation of data; Interpretation of results; Synthesis and resume of results. The search was conducted in the following databases: *National Library of Medicine (MEDLINE), PubMed;*

Scientific Electronic Library Online (SciELO) and in *Literatura Latino-Americana e do Caribe em Ciências da Saúde (Lilacs)*.

Terms such as "breast cancer", "risk factor", "risk", "knowledge" and "awareness" were identified in *Medical Subject Headings (MeSH; http://www.nlm.nih.gov/mesh/MBrowser.html),* of the U. S. National Library of Medicine. To identify a broader range of publications from Latin American countries, the term "risk" was applied instead of "risk factors". The term "breast cancer" was used in combination with "risk", "knowledge" or in combination with "awareness". All three combinations were used in English, Spanish ("Cáncer de mama" and "factor de riesgo", or "conocimiento" or "conciencia") and Portuguese ("Câncer de mama" and "fator de risco", or "conhecimento", or "consciência").

The search was conducted from 2 to 5 of March 2015. To establish an internal quality control, the literature selection procedure was performed twice independently by two of the authors. In the study, articles published during the last five years were included. By applying three combinations of search terms in *Medline,* 66.782 articles were identified. The application of filters "five years" and "free full text" led to the identification of 9.561studies in *Medline* (Figure 1). Combinations of search terms in all three languages led to the identification of 592 articles in the *SciELO* database that have been published within the last five years (Figure 1). Finally, in the *Lilacs* database, no article that met the criteria of search terms in any of the three languages was identified.

All together, 10.153 articles were used for further analysis (Figure 1). To select articles, title, abstract, authors' information and if necessary results were analysed. The following inclusion criteria were adopted: original research article or research communication, available for free and published over the last five years, in English, Spanish or Portuguese. Articles on BC that did not deal with risk factors or knowledge about them and review articles were excluded from the study. Articles on heritable genetic factors or viral infections that increase the risk of BC were also excluded from the study. Finally, 27 and 34 articles were selected from *Medline* and *SciELO* database, respectively (Figure 1). Articles repeated in different databases or with distinct selection terms, were also excluded (Figure 1). For further categorization, result, method and discussion sections were read and analysed. According to

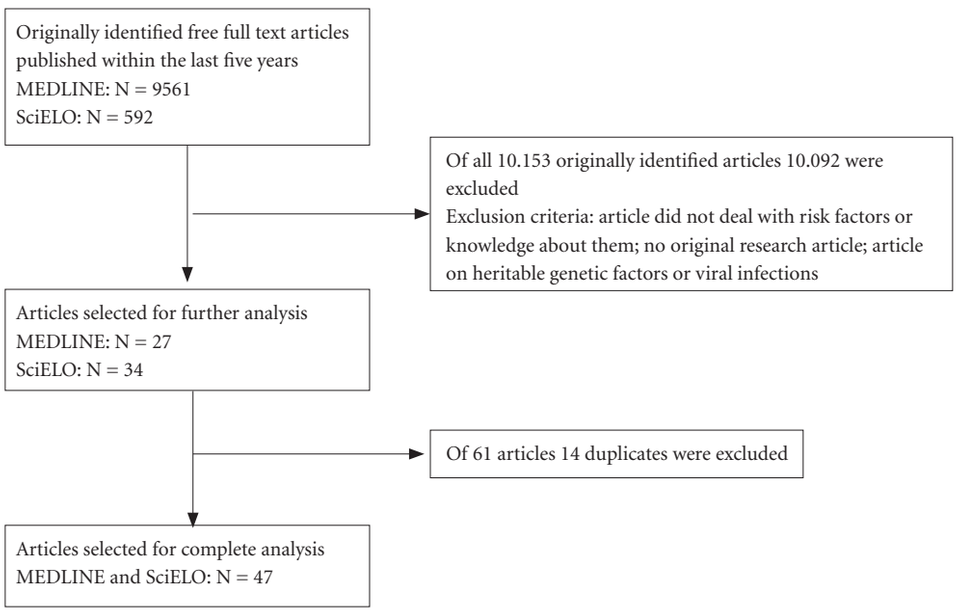

Figure 1. Flowchart of selection of articles.

previous studies, ED comprised mammography screening, breast examination and BSE[21].

All statistical analyses were performed on Prism™ software vers.6 (GraphPad, La Jolla, California, USA). The t-Test and Mann-Whitney (U) Test were applied to analyse continuous variables. The χ^{2} Test was performed to analyse categorical variables.

Results and discussion

Language variations among studies on risk factors and knowledge about BC

Combination of search terms "breast cancer" and "risk" led to the identification of 27 different articles that met the selection criteria (Table 1). Of these, 17 articles were written in English, eight in Spanish and two in Portuguese (Table 1). The search terms "breast cancer" and "knowledge" or "awareness" led to the identification of 20 different articles that met the selection criteria (Table 1). Of these, four were written in English, nine in Spanish and seven in Portuguese (Table 1).

Results indicated that the authors of studies on knowledge and awareness about BC preferentially published in Spanish or Portuguese, whereas studies on the risk of BC were mainly written in English ($p = 0.0094$; Chart 1). The authors of studies on knowledge and awareness about BC may have dedicated their work more often to a national or even local population and therefore preferred to publish in their native language. The authors of studies on the risk of BC in contrast, compared their results mainly with those obtained from other populations of different countries. In this case, it may have been more interesting to reach a broader population with studies written in English. This interpretation was supported by the fact that Latin American authors of 25 studies on the risk of BC mainly cited international literature published in English. There were only two exceptions of studies whose authors cited mainly previous publications of their own country written in Spanish and Portuguese[22,23]. In contrast, 16 studies on the knowledge and awareness about BC cited mainly previous publications of their own country written in Spanish or Portuguese ($p < 0.0001$). There were only four studies on the knowledge and awareness that mainly cited literature published in English[24-27].

The meaning of the term *risk* varied among studies

Articles on the risk of BC were from Cuba (N = 1), Colombia (N = 2), Venezuela (N = 2), Chile (N = 3), Uruguay (N = 5), Brazil (N = 6) and Mexico (N = 8; Chart 1). Of the 27 studies identified by terms "Risk" and "Breast cancer", 22 were exclusively focused on risk factors, whereas five studies focused on ED (Chart 1). The authors of two out of these five studies defined non-participation on ED and BSE as *risk* (Chart 1)[28,29]. Their

Table 1. Articles identified using all three search-term combinations from 9 of March 2015, found in PubMed and SciELO databases.

	PubMed	SciELO	Duplicates**	All selected
Search terms: "Breast cancer" and "risk"				
Without filter	55401	417	-	
With filter*	7596	-	-	
Selected	19	14	6	27
Search terms: "Breast cancer" and "knowledge"				
Without filter	9317	137	-	
With filter*	1566	-	-	
Selected	6	17	6	17
Search terms: "Breast cancer" and "awareness"				
Without filter	2064	38		
With filter*	399	-		
Selected	2	3	2	3
Total number of articles selected				**47**

* Full text articles published within the last five years. ** Found in more than one database or found two times by different search terms.

Chart 1. Studies identified by the combination of search terms "risk" and "breast cancer".

Reference	Country and Language*	Sample Size** and Type	Methodological approach		Objective (RF/ED)
			Type of Study	Analysis	
Amadou et al., 2013[21]	Mexico English	1000 BC cases 1074 controls	Case-control	Multivariate	RF
Amadou et al., 2014[30]	Mexico English	1000 BC cases 1074 controls	Case-control	Multivariate	RF
Balderas-Peña et al., 2013[31]	Mexico Spanish	43 healthy women	Cross-sectional	Univariate	RF
Bering et al., 2015[32]	Brazil English	78 BC cases	Cross-sectional	Univariate	RF
Matos et al., 2010[22]	Brazil Portuguese	439 healthy women	Cross sectional	Multivariate	RF
Matos et al., 2011[33]	Brazil Portuguese	439 healthy women	Cross-sectional	Multivariate	ED
Fejerman et al., 2010[34]	Mexico English	846 BC cases 1035 controls	Case- control	Multivariate	RF
Garmendia et al., 2013[35]	Chile Spanish	Database	Ecological	Univariate	RF
Girianelli et al., 2014[36]	Brazil English	Database	Ecological	Univariate	RF
Inumaru et al., 2012[37]	Brazil English	93 BC cases 186 controls	Case-control	Multivariate	RF
Iwasaki et al., 2011[38]	Brazil-Japan English	363 healthy women	Cross-sectional	Multivariate	RF
López-Carrillo et al., 2010[39]	Mexico English	233 BC cases 221 controls	Case-control	Multivariate	RF
López-Carrillo et al., 2014[28]	Mexico Spanish	1030 healthy women	Cross-Sectional	Multivariate	ED
Pereira et al., 2012[40]	Chile English	170 BC cases 170 controls	Case-control	Multivariate.	RF
Ronco et al., 2011[41]	Uruguay English	460 BC cases 638 controls	Case-control	Multivariate	RF
Ronco et al., 2012[42]	Uruguay English	367 BC cases 545 controls	Case-control	Multivariate	RF
Ronco et al., 2012[43]	Uruguay English	253 BC cases 497 controls	Case-control	Multivariate	RF
De Stefani et al., 2011[44]	Uruguay English	8875 BC cases 4326 controls	Case- Control	Multivariate	RF
De Stefani et al., 2012[45]	Uruguay English	3528 cases of different cancers 2532 controls	Case–control	Multivariate	RF
Cordero et al., 2012[46]	Mexico Spanish	115 BC cases 115 controls	Case-control	Multivariate	RF
Cabello et al., 2013[47]	Chile English	158 BC cases	Cross-sectional	Univariate	RF

it continues

Chart 1. continuation

Reference	Country and Language*	Sample Size** and Type	Methodological approach		Objective (RF/ED)
			Type of Study	Analysis	
Calderón- Garcidueñas et al., 2012[48]	Mexico English	300 healthy women	Cross-sectional	Multivariate	ED
Rodríguez et al., 2013[23]	Cuba Spanish	70 BC cases	Cross sectional	Descriptive	RF
Ferri et al., 2010[49]	Venezuela Spanish	100 BC cases 103 controls	Case-control	Univariate	RF
Font-Gonzalez et al., 2013[50]	Colombia English	Database 27.116 healthy women	Cross-sectional	Multivariate	ED
Hernández et al., 2010[51]	Venezuela Spanish	507 BC cases 505 controls	Case-control	Multivariate	RF
Ospina-Díaz et al., 2011[29]	Colombia Spanish	218 BC cases 225 controls	Case-control	Univariate.	ED

Abbreviations: BC = breast cancer; ED = Early detection; RF = Risk factors. Sampling numbers were not informed. *Studies were mainly written in English (χ^2- Test; p = 0.0094). **The average sample number was 363.0 cases (t- Test; p = 0.0552).

studies focused on determinants of women's behaviour regarding ED and the correct application of BSE: In a Colombian case- control study, Ospina-Díaz et al. analysed women's behaviour of BSE, and defined behavioural risk factors that were susceptible to educative intervention (Chart 2)[29]. Similarly, one Mexican study focused on socio-economic background of women and risk factors that affect ED (Chart 2)[28]. The authors of this study also analysed the correct application of BSE.

Alternatively, in the context of ED, authors determined different *risk groups* that were age-dependent (Chart 1)[33,50]: Carvalho de Matos et al.[33] interviewed 439 healthy women about ED behaviour (Chart 2). In a Colombian study that included data from 27.116 healthy women, ED behaviour was analysed and different risk groups were defined (Chart 2)[50].

Identified risk factors of BC

In studies on the risk of BC, obesity and overweight (N = 14), positive menopause status (N = 13), family history of BC (N = 13), early age at menarche (N = 12), nulliparity or decreased parity (N = 12), older age (N = 12) and short breastfeeding duration (N = 10) were the most often identified risk factors (Chart 2). Risk factors were subdivided into four main categories: Lifestyle-related, reproductive, socio economic and environmental risk factors, respectively, a category of history of BC (Chart 2). Several authors have analysed risk factors of all four categories[30,34,37,38,40-42]. Two studies performed in Uruguay for example, included a broad range of different risk factors[41,42]. The author's decision to analyse several distinct and unrelated risk factors may have been influenced by the high incidence of BC in Uruguay.

Most studies focused on a specific topic or a complex of thematically related risk factors: Amadou et al. for example, analysed in their study the effect of hormone replacement therapy and contraceptive use on the risk of BC (Chart 2)[21]. Iwasaki et al. compared blood concentrations of several sex hormones among Japanese and Brazilian women of Japanese ancestry[38]. This exceptional comparative study revealed that Brazilian women of Japanese ancestry had increased blood concentrations of several sex hormones like estradiol and testosterone[38]. Populations differed regarding several risk factors and increased hormone concentrations were positively associated with body mass index (BMI; Chart 2)[38]. The study of Ronco et al. was the only one that identified diabetes as a risk factor for BC (Chart 2)[42]. The authors determined the risk of diabetes in combination with overweight, high fat-to-muscle ratio and hypertension (Chart 2)[42]. In a similar study, Bering et al. described a high prevalence of increased body mass index (BMI), high levels

Chart 2. Summary of risk factors identified by 27 studies on the risk of BC.

Risk Factor	Reference
Early detection	
No mammography	22, 28, 33, 50
No clinical breast examination	22, 28, 33, 50
No BSE	22, 28, 29, 33, 50
Reproductive	
Early age at menarche	21, 22, 23, 32, 34, 38, 39, 41, 42, 43, 46, 48
Positive status of menopause	22, 23, 31, 32, 34, 38, 40, 41, 42, 43, 46, 48, 51
Nulliparity or decreased parity	21, 22, 30, 34, 38, 39, 40, 41, 42, 43, 46, 51
Short total breastfeeding time	21, 22, 23, 30, 34, 39, 42, 43, 46, 51
Old age at first gestation	21, 30, 38, 39, 42, 46
Lifestyle- related	
Smoking	22, 23, 38, 40, 46, 48
High alcohol consumption	21, 22, 30, 34, 38, 40, 41, 42, 46, 48
No physical exercise and sedentarism	21, 23, 29, 30, 37, 38, 40, 42, 43, 46
Overweight and obesity	21, 22, 23, 31, 32, 34, 35, 38, 40, 42, 43, 46, 48, 49
Diet rich in fried foods and/or meat	21, 40, 41, 42, 43, 44, 45, 50
Diet poor in vegetables and fruits	43
Increased caloric intake	30, 34
Decreased BMI	30, 34
Increased BMI	32, 38, 46
Round body shape (Endomorphy)	30, 32, 41
Diabetes	42
Hypertension	31, 40, 42, 43
Hormone replacement therapy	21, 22, 30, 32, 34, 40, 48
Use of contraceptives	21, 30, 40, 42, 43
Harmful hormone concentrations	32, 38
Ethical, socioeconomic and environment factors	
Increased educational level	34, 36, 40
Decreased educational level	22, 29, 37, 50
Increased HDI	36
Lower income	22, 29, 37, 50
Higher income	22, 30, 34
No Caucasian or Caucasian ancestry	34, 50
Rural living place	37, 41, 50
Chemical contaminants	39, 47
Age and history of breast cancer	
Family history of breast cancer	21, 22, 23, 30, 34, 37, 40, 41, 42, 43, 47, 48, 51
Personal history of breast cancer	22, 34, 51
Older age	28, 30, 32, 33, 34, 37, 39, 40, 41, 42, 47, 50

Abbreviations: BMI = Body mass index; HDI = Human development index.

of cholesterol, round body shape, overweight and obesity among 78 BC patients in Brazil (Chart 2)[32]. In this study, a set of body shape associated nutritional status parameters were analysed. Association between body shape and risk of BC was also the objective of a Mexican study performed

by Amadou et al.[30]. High prevalence of overweight and obesity in Latin American countries may explain the author's interest in these risk factors, body shape and BMI.

Two studies identified *increased* BMI as risk factor (Chart 2)[32,46]. In contrast, two other studies identified *decreased* BMI as risk factor, in pre and post- menopause women, respectively (Chart 2)[30,34]. As all these three studies were from Mexico, it was difficult to attribute population-based biological differences. Furthermore, logistic regression modelling showed in each study that BMI represented an independent variable. It was also pointed out that findings about BMI as risk factor are contradictory[32]. Therefore, the context in which BMI acts as a risk factor remained unresolved.

Education and income were context-dependent risk factors of BC [

In studies on the risk of BC, four authors identified *decreased* educational level as risk factor (Chart 2) [22,29,37,50]. In contrast, three authors identified *increased* educational level as risk factor (Chart 2)[34,36,40]. Decreased educational level may explain increased *risk* of non-participation on screening programs and BSE in three out of four studies (Chart 2)[22,29,50]. This argument cannot explain the results of Inamuru et al., who compared in a case- control study several reproductive risk factors among women from rural regions and urbanized centres of Mid-western Brazil (Chart 2)[37]: Additionally, the authors of this study also identified lower income and *decreased* educational level as risk factors for women living in rural areas (Chart 2)[37]. In contrast, two studies from Mexico and Chile that identified *higher* educational level as risk factor were based on data obtained from hospitals of urban centres (Chart 2)[34,40]. The third study that identified higher educational level as risk factor was based on a large data set of BC mortality rates and selected socioeconomic and health care indicators in Brazil[36]. The latter study included data from urbanized centres and rural regions.

Results indicated that the effect of education on the risk of BC was different in urbanized centres compared to rural regions. Education can have a direct effect on ED behaviour, but it is not a direct risk factor of BC. Therefore, increased and decreased educational level may be associated in distinct ways with reproductive and lifestyle-related risk factors in rural regions and urbanized centres. This argument was supported by the fact that regression modelling revealed several independent reproductive and lifestyle-related risk factors, whereas increased educational level was not identified as an independent variable[34,40].

Similarly, two Mexican studies based on data obtained from hospitals of urban centres identified *high* income as risk factor, in contrast to a Brazilian study, which identified *low* income and living in rural areas as risk factors (Chart 2)[30,34,37]. Low income was also identified as a risk factor for ED behaviour in studies from Brazil and Colombia (Chart 2)[29,37,50]. Carvalho de Matos et al. showed that mammography screening behaviour was positively associated with high income, whereas clinical breast examination was less common among women with high socioeconomic status (Chart 2)[22].

Methodological approaches differed considerably among studies on the risk and knowledge about BC

Of the 27 studies on the risk of BC, 24 were based on interviews. In a Chilean study on the relationship between BC and malathion aerial spraying, Cabello et al. extracted additional data on BC patients from medical records[47]. Three studies used databases instead of interviews (Chart 1)[35,36,50]. Most studies were case-control (N = 15) or cross- sectional (N = 10) (Chart 1). Sampling numbers varied from 93 to 8.875 cases for case-control studies and from 43 to 27.116 cases or healthy women for cross-sectional studies (Chart 1).

Several studies on the risk of BC (N = 7) exclusively applied univariate methods to analyse data (Chart 1). In this case, methods included descriptive statistics like t-Test, χ^{2}- Test, correlation analysis and also univariate logistic regression. Balderas-Peña et al., for example, analysed correlations between expression of hormone receptors, obesity and hypertension, respectively[31]. To express odds ratios, the authors applied univariate logistic regression. Most studies on the risk of BC applied multivariate logistic regression to analyse data (N = 19; Chart 1). These studies were typically composed of two analytical steps: Hernández et al. for example, compared different risk factors between patients with benign and invasive BC and healthy women[46]. Firstly, the authors applied univariate statistical analysis to detect significant differences among the three groups. To reveal which of these variables, increase risk of BC independently, multivariate logistic regression was applied. In this study, fam-

ily history was the unique independent variable.

In contrast to most studies on the risk of BC, the authors of studies on the knowledge and awareness about BC did not perform case- control studies ($p < 0.0001$; Chart 3). All 20 studies on the knowledge and awareness about BC were cross- sectional and data sampling was based on interviews. Sample numbers varied from 18 to 1899 cases of BC or healthy women (Chart 3). The average sample number of studies on the knowledge and awareness about BC was 117.5, compared to 363.0 studies on the risk of BC ($p = 0.0552$; Chart 1). Furthermore, in contrast to studies on the risk of BC, most studies on the knowledge and awareness about BC (N = 16) did not use any statistical method to analyze data, but were purely descriptive ($p < 0.0001$; Chart 3). Six studies on the knowledge and awareness about BC were intervention studies performed in Cuba and Brazil[52-57]. Grego et al. for example, applied a questionnaire before and after a workshop and did not perform any statistical analysis[52]. Hechvarría et al. in contrast, analyzed concordance between data obtained before and after a workshop[54]. Only two out of 20 studies on the knowledge and awareness about BC performed multivariate regression analysis: Banegas et al., and Oliveira-Brito et al. applied multivariate logistic regression to analyze factors that affect women's perceived risk of BC and socio-economic factors associated with BSE, respectively[24,58].

Present results indicated that Latin American studies on the knowledge and awareness about BC used more often, descriptive methodological approach and smaller sample size. Interestingly, no case- control study on the knowledge and awareness about BC was identified. The lack of case-control approach may be due to the idea that women's knowledge about risk factors of BC and ED might improve during the course of the disease, leading to a bias of sampled data. Furthermore, knowledge about modifiable risk factors does not necessarily affect women's prevention behavior.

Studies on the knowledge and awareness about the risk of BC were mainly focused on ED

Articles on the knowledge or awareness about BC were from Chile (N = 1), Venezuela (N = 1), Mexico (N = 2), Cuba (N = 5) and Brazil (N = 11; Chart 3). Few studies on the risk factors were focused on ED (Chart 1). In contrast, 12 out of 20 studies on knowledge and awareness were exclusively focused on ED, two on risk factors and six on both, ED and risk factors ($p < 0.0001$; Chart 3). This result indicated that authors interested in women's knowledge on BC prevention were mainly focused on ED. There might be different reasons for this preference: Curiel et al. argued in their Mexican study that many women in Latin American countries, mainly from rural areas, have no knowledge about ED at all[59]. The authors pointed to socio economic and geographic barriers, limiting possibilities of ED. Similarly, the authors of studies carried out in Brazil exclusively focused on women's knowledge about ED emphasized the existence of social and geographical barriers that limit possibilities of mammography and clinical breast examination[26,60]. Silva et al., pointed out in their study that ED techniques have been largely studied in developed countries and little is known about their efficiency in developing countries[25]. In one case, the authors also argued that possibilities to avoid risk of BC are limited, as causal relationships between these risk factors and disease have not been well established[60].

Interestingly, none of the 16 studies on ED included questions about knowledge regarding possible disadvantages of clinical BC screening, like false- positive diagnosis, or unnecessary operative and chemotherapeutic interventions. Both represent well-known harms of mammography and clinical breast examination[61,62]. Furthermore, in their interviews, the authors of these 16 studies did not ask women if screening techniques may serve to *prevent* or alternatively to *early detect* the breast tumour.

Most studies on the knowledge of ED were based on BSE

The most often cited objectives of BC studies on the knowledge and awareness were BSE (N = 14), mammography (N = 7) clinical breast examination (N = 6), followed by short total breastfeeding time, smoking and family history of BC (N = 4; Chart 4). The fact that BSE dominated literature of knowledge about ED was surprising because, as pointed out by Oliveira- Brito et al., there is no direct evidence of reduction of mortality by BSE[58]. The authors of this Brazilian study emphasized that, especially for women from developing countries, easy performance and low costs of BSE may be helpful to detect early breast alterations[58]. Less than half of women performed BSE[58]. The authors of other studies argued that despite the ongoing debate, BSE may significantly contribute to the ED of breast tumours[60,63].

Chart 3. Studies identified by the search term combinations "breast cancer" and "knowledge" or "awareness".

Reference	Country and Language	Sample Size and type	Methodological approach*	Objective (RF/ED)**
Banegas et al., 2012[24]	Chile English	500 healthy women	Multivariate	RF
Silva, Riul, 2011[64]	Brazil Portuguese	18 BC cases	Descriptive	ED
Silva et al., 2013[25]	Brazil English	248 BC cases	Univariate	ED
Schneider et al., 2013[26]	Brazil English	1899 healthy women	Univariate	ED
Grego et al., 2011[52]	Brazil English	474 adolescent women	Descriptive	RF and ED
Kim et al., 2010[53]	Brazil Portuguese	72 healthy women	Descriptive	ED
Hechavarría et al., 2011[54]	Cuba Spanish	94 healthy women	Univariate	ED
Sáez et al., 2011[55]	Cuba Spanish	54 BC cases	Descriptive	RF and ED
Jacobo-Galindo et al., 2014[63]	Mexico Spanish	105 healthy women	Descriptive	ED
Muñoz et al., 2012[65]	Cuba Spanish	80 healthy women	Descriptive	ED
Guerrero et al., 2011[56]	Cuba Spanish	119 healthy women	Descriptive	RF and ED
Gomes et al., 2012[66]	Brazil Portuguese	202 healthy women	Descriptive	ED
Brito et al., 2010[58]	Brazil Portuguese	552 healthy women	Multivariate	ED
Montañez et al., 2011[57]	Cuba Spanish	30 healthy women	Univariate	RF and ED
Freitas et al., 2011[67]	Brazil Portuguese	50 healthy women	Descriptive	RF
Silva et al., 2013[60]	Brazil Spanish	116 healthy women	Univariate	ED
González et al., 2012[68]	Venezuela Spanish	1525 healthy women	Descriptive	RF and ED
Santos, Chubaci, 2011[69]	Brazil Portuguese	98 healthy women	Univariate	ED
Batiston et al., 2011[27]	Brazil Portuguese	393 healthy women	Univariate	RF and ED
Curiel et al., 2014[59]	Mexico Spanish	135 healthy women	Descriptive	ED

Abbreviations: BC = breast cancer; ED = Early detection; RF = Risk factors. Authors cited mainly previous publications written in Spanish or Portuguese (χ^{2} Test; $p < 0.0001$). *Authors did not perform case- control studies (χ^{2} Test; $p < 0.0001$) and most studies were purely descriptive (χ^{2} Test; $p < 0.0001$). **Most studies focused exclusively on early detection (χ^{2} Test; $p < 0.0001$).

Dongiu Kim et al. argued in their interventional study that ED success could be limited due to insufficient knowledge about it[53]. The author's interest on women's knowledge about mammography screening was mainly encouraged by increased efficiency of this technique compared to BSE in the early detection of breast tumours (Chart 4)[25,26,64,69]. Schneider et al. performed a study about ED that exclusively focused on mammography and pointed out that this screening method reduces mortality by ED of breast tumours of women aged 50-69 years (Chart 4)[26].

Studies on the knowledge and awareness about BC focused on few modifiable risk factors

The authors of studies from Cuba emphasized the importance of women's knowledge about BC (Chart 4)[56,68]. Pires-Batiston et al. analysed the knowledge on several lifestyles related and reproductive risk factors, emphasizing in the introduction of their Brazilian study, that changing lifestyle may contribute to increased risk of BC (Chart 3)[27]. However, in studies on the knowledge and awareness about BC, the number of references per risk factor was low: If ED was excluded in the analysis, the mean number of references in studies on the risk of BC was 5.84 (s = 4.19) compared to 2.44 (s = 1.04) of studies on the knowledge of BC ($p = 0.0015$). On one hand, the decreased number of references of risk factors in studies on the knowledge of BC may be partially explainable by the fact that many of these risk factors are not modifiable and therefore the authors did not focus on women's knowledge about them. On the other hand, many risk factors, especially those related to lifestyle and protective factors like breastfeeding, are modifiable. The knowledge and awareness about these risk factors could change women's behaviour towards avoiding risk of BC.

Socio-economic factors affect women's knowledge

Studies also aimed at assessing socio- economic factors that influence knowledge about ED. Schneider et al., showed in their study that women with low income, no private health insurance and low educational level participate less frequently in mammography screening programs[26]. Older women had in general better knowledge about ED than younger ones[26,58,64,65,66]. In a study from Venezuela, the authors reported that low income and educational level not only affected knowledge about BSE negatively, but also knowledge about reproductive and life-

Chart 4. Summary of knowledge on BC analysed by 20 studies about knowledge and awareness of BC.

Knowledge	Reference
Early Detection	
Mammography	25, 26, 27, 53, 63, 64, 69
Clinical breast examination	25, 27, 53, 63, 64, 69
BSE	25, 52, 53, 54, 55, 56, 58, 60, 63, 64, 65, 66, 68, 69
Reproductive risk factors	
Nulliparity or decreased parity	55, 68
Early age at menarche	68
Old age at first gestation	55, 68
Positive status of menopause	55, 67, 68
Short total breastfeeding time	27, 55, 67, 68
Lifestyle-related risk factors	
Smoking	27, 52, 56, 68
Alcohol consumption	27, 52, 68
Use of contraceptives	56, 67
No physical exercise and sedentarism	52, 67
Diet poor in vegetables and fruits	27, 52, 67
Overweight and obesity	55, 67, 68
Hormone replacement therapy	27, 67, 68
Insufficient auto-care	27
Stress	27
Risk perception	24
Age and history of breast cancer as risk factors	
Family history of breast cancer	27, 55, 56, 68
Personal history of breast cancer	27, 55, 68
Older age	55, 68

style-related risk factors (Chart 4)[68]. Similarly, a Brazilian study revealed that the knowledge about risk factors was negatively associated with low educational level and family history of BC[27].

Final considerations

Knowledge does not necessarily affect women's behaviour and it is not clear if knowledge about modifiable risk factors alone could lead to a decreased incidence of breast cancer. Case- control studies could help to elucidate the effect of women's knowledge on prevention behaviour of modifiable risk factors. In contrast to modifiable risk factors, knowledge about ED can directly affect women's screening behaviour. On the one hand, this may have led authors to focus their studies on the knowledge mainly on ED and a reduced number of known risk factors for BC. On the other hand, the prevention of identified modifiable risk factors can be easily propagated in media, as it is relatively inexpensive and may be effective in the long-term. Breastfeeding for example, was identified as a protective factor for BC in a population of North-eastern Brazil and is often propagated as a factor that improves child health, but rarely in the context of BC prevention[17,18]. Furthermore, knowledge about risk factors that women cannot change in a given phase of their life such as age, age at first gestation or menopause status, could encourage their participation on BC screening programs. Therefore both, identification of prevailing risk factors and women's knowledge about risk of BC and ED are important for public health institutions to develop BC prevention strategies. Information on both types of studies can be used to improve campaigns of ED and prevention of risk factors.

Collaboration

All the three authors contributed to acquisition of data. AFA Jerônimo contributed to creation of tables. AFA Jerônimo and AGQ Freitas contributed to manuscript draft and critical review. Study design, manuscript draft and data analysis were mainly performed by M Weller.

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