Founder and Recurrent Mutations in BRCA1 and BRCA2 Genes in Latin American Countries: State of the Art and Literature Review

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Disclosures of potential conflicts of interest may be found at the end of this article.

Key Words. Breast cancer • BRCA1 • BRCA2 • Latin America • Hereditary cancer • Hispanics

Abstract

Background. Numerous epidemiological factors affect the probability of developing breast or ovarian cancer, but no predictor is as determinant as inheriting a mutation in BRCA1 or BRCA2. The concept of the founder effect explains the reduced genetic variability in some populations, according to the theory that new populations can be formed from a reduced number of individuals, so the new population would carry only a small fraction of the genetic variability of the original population. The main purpose of this review is to provide an update on the state of the art in founder mutations and some recurrent mutations that have recently been described in Latin America.

Methods. A literature search was performed in the electronic databases of PUBMED, EMBASE, LILACS, and BIREME using the terms BRCA1, BRCA2, founder mutation, Latin American population, and Hispanic. Sixty-two papers were identified, of which 38 were considered relevant for this review. Each result is shown per country.

Results. In Latin America, clear founder effects have been reported in Mexico (BRCA1 del exons 9–12), Brazil (BRCA1 5382insC and BRCA2 c.156–157insAlu), and Colombia (BRCA1 3450del4, A1708E, and BRCA2 3034del4) and in Latinas residing in Southern California (BRCA1 185delAG, IVS5 + 1G > A, S955x, and R1443x). Of these, mutation BRCA1 3450del4 has also been reported in Brazil and Chile, whereas mutation BRCA2 3034del4 has been reported in Argentina and Peru. These data support the idea that although most Hispanic populations are the result of a mixture between Europeans, Africans, and Amerindians, the relative proportion of each genetic component varies throughout the Hispanic populations, making it necessary to identify the mutations characteristic of each population to generate mutation profiles adjusted to each one of them.

Conclusion. In Latin American countries, and even among regions of the same country, there is great heterogeneity of ancestors. Therefore, Latinas should not be analyzed like other population groups without taking into account their genetic ancestry. The presence of founder mutations in specific population groups represents a cost-effective analysis. The importance of determining the founder mutations lies mainly in the decrease in costs. If we manage to decrease costs, screenings could be offered more widely and cover a larger number of women. The Oncologist 2016; 21:1–8

Implications for Practice: Hispanic and African-American populations are four to five times less likely than other populations worldwide to receive screening for BRCA mutations, a main reason being the high costs of these tools. The present study seeks to identify the prevalent mutations and the founder effect in the BRCA gene in the Hispanic population to address specific panels for this population group in the future and develop strategies for population screening.

Introduction

Although the genetic predisposition to cancer is considered mostly heterogeneous, founder mutations in genes with high penetrance have been identified in certain population groups through the observation of hundreds of different alterations in the genomic sequence that cause disease. As a consequence of their location in genomic regions with linkage disequilibrium, these mutations are segregated as a unit. Haplotype analysis gives the possibility to discriminate between a variant originating from a single mutation event (founder mutation) and a variant that results from an independent mutational event. A recurrent mutation is the first indication that we are facing a founder mutation, but not all carriers of recurrent pathogenic variants are expected to share a common ancestor, which means that not all recurrent mutations are founder
mutations. Thus, the analysis of haplotypes in families with the same mutation is recommended to determine whether the high frequency of a given number of alleles has migrated from one linked geographic area to another or whether the alleles originated independently [1]. The concept of founder effects was described by Ernst Mayr to explain the reduced genetic variability in some populations through the theory that new populations can be formed from a reduced group of individuals, so the new population would carry only a small fraction of the genetic variability of the original population. Founder alleles represent most mutations in that population, with very little probability of other nonfounder alleles explaining the same disease [2]. For this reason, these founder mutations are inherited and are frequently restricted to one or few populations or geographical regions that fulfill certain characteristics.

Almost 20 years have passed since the genes responsible for increased susceptibility to breast cancer and ovarian family cancer were characterized. This remains the most significant discovery for the genetics of hereditary cancer in humans, in part demonstrated by the fact that almost all ethical-legal debates regarding patents are focused on BRCA1 and BRCA2 genes, with few cases of debate about other genes for cancer susceptibility [3, 4]. A woman with a mutation in BRCA1/2 has a risk of up to 87% of developing breast cancer in her lifetime and up to 50% of developing ovarian cancer, but the risk can vary according to the mutation, country of residence, and family history [5, 6]. Additionally, mutations in the BRCA1/2 genes confer a higher risk for the development of a second primary cancer compared with non-mutation carriers, particularly among women who are diagnosed young (<45 years) [7]. Therefore, the classification of highly penetrant mutations in these genes has significant implications for both the affected women and their family members.

Several epidemiologic factors affect the probability of developing breast cancer or ovarian cancer, but no predictor is as determinant as inheriting a mutation in BRCA1/2. Therefore, the analysis of these two genes in particular has gained great acceptance worldwide, not only because of the increased availability of prevention options in healthy women bearing a mutation, but also because of the development of new and personalized cancer therapies [8, 9]. However, genetic tests remain expensive and inaccessible for most women in developing countries. Analysis of the BRCA1/2 genes has been available in North America and Western Europe since 1996. In recent years, Eastern Europe and some Latin American countries have begun the introduction of genetic testing of BRCA1/2 mutations, in part because of the presence of founder mutations [1, 10]. The presence of founder mutations, which explains reduced genetic variability in a gene or group of genes in a specific population, allows the probability of focusing on the analysis of them because of the very low possibility that other nonfounder alleles explain the same disease.

In Hispanic populations, a limited number of studies have focused on analysis of the distribution and prevalence of mutations in BRCA1 and BRCA2 genes (Fig. 1). However, founder mutations in these genes have been described in this population group. The main purpose of this review is to provide an update on the state of founder mutations (variants originated from a single mutation event) and some recurrent mutations (variants that have not been proved to share a common ancestor) that have been recently described in Latin America.

Argentina

Only the three mutations characteristic of the Ashkenazi Jewish population have been reported as founder mutations in Argentina. Solano et al. [11] performed a sequencing analysis in 134 patients with breast and ovarian cancer, selected by diagnosis age or family history. The study included 40 Ashkenazi Jews who were analyzed only for the three founder mutations characteristic of this population (c.66_67delAG and c.5263insC in BRCA1 and c.5946delT in BRCA2), observing a high recurrence of these mutations, with a mutation frequency of 42.5% (17/40). The most recurrent founder mutation was BRCA2 6174delT (8/17), followed by BRCA1 185delAG (7/17). A less recurrent mutation was BRCA1 5382insC (2/17). In the second population group (non-Ashkenazi) 57/134, 24 deleterious mutations were identified; 16 in BRCA1 and 8 in BRCA2, but none of them were identified in more than 1 nonrelated patient. However, among the nonrecurrent mutations identified in BRCA2, the 3034del4 mutation had been previously reported as founder in a Colombian population by Torres et al. [12].

Brazil

Two founder mutations have been reported in Brazil: BRCA1 5382insC, which is characteristic of Ashkenazi Jews, and BRCA2 c.156_157insAlu. The BRCA1 5382insC mutation, the second most recurrent mutation in BRCA1 according to the Breast Cancer Information Core (BIC) (http://research.nhgri.nih.gov/bic/), with high prevalence in eastern and central Europe, was also reported in seven nonrelated Brazilian patients with hereditary breast cancer [13], in whom haplotype analysis revealed a founder effect [14]. The genomic rearrangement BRCA2 c.156_157insAlu (consisting of the insertion of an Alu sequence in exon 3 of gene BRCA2) was identified as a founder mutation by Machado et al. [15] in 17/210 (8%) Portuguese families with a high risk of developing breast or ovarian cancer. BRCA1/2 were fully screened for mutations (by polymerase chain reaction [PCR], reverse-transcriptase PCR, and direct sequencing) in 168 Brazilian women with breast cancer who reported having a strong history of familial cancer and having lived in Brazil for at least 3 generations. The BRCA2 c.156_157insAlu mutation was identified in three nonrelated subjects. Using genotyping, a common haplotype was observed for two of the markers used (D13S260 and D13S171), with sizes comparable to those described in Portuguese families. However, the size of the alleles for marker D13S1246 agreed in only two of the three families analyzed, suggesting that this haplotype could be present in only a subgroup of families as the result of two probable recombination events that occurred for this marker [15]. In fact, this mutation is highly prevalent in the center of Portugal and in Portuguese individuals established in the south of Brazil [16].

Recurring mutations have also been reported in Brazil. Esteves et al. [17] analyzed 612 Brazilian patients from the five geographical regions of the country (central-western, northeast, north, southeast, and south) with medium and high risk of developing breast or ovarian cancer. In total, 21/612 (3.4%) deleterious mutations were identified by sequencing, 18 (2.9%) in BRCA1 and 3 (0.5%) in BRCA2. Of the mutations identified in BRCA1, four were recurrent (ins6Kb, 5382insC, 326+delGinsCC, and 185delAG). However, haplotype analyses
were not performed in the carriers of mutations ins6Kb or 2156delGinsCC; thus, the founder effect could not be confirmed in these patients. Gomes et al. [14] performed a screening of BRCA1/2 in 402 women diagnosed with breast cancer, who were not selected because of family background (ethnicity or family history of cancer). They used the protein truncation test (PTT), fluorescent multiplex denaturing gradient gel electrophoresis (DGGE), and denaturing high performance liquid chromatography (DHPLC), and all variants identified were confirmed by direct DNA sequencing. In total, nine deleterious mutations were identified, including three in the BRCA2 gene. Of these, two corresponded to mutation 6633del5 reported in two nonrelated women. Recently, Felix et al. [18] reported two new recurrent mutations in gene BRCA1 identified in 106 patients from the north of Brazil, mutation c.211A>G (p.R71G) followed by mutation 3450del4, which was previously reported as a founder in the Colombian population by Torres et al. [12]. In a second study in the Chilean population performed by Gallardo et al. [20], a group of 54 families with high risk of breast/ovarian cancer were evaluated (using SSCP, heteroduplex analysis, PTT, and sequencing analysis), identifying two mutations not previously reported: BRCA1 c.308_309insA and BRCA2 c.4970_4971insTG. However, none of them were found recurrently; thus, the founder effect could not be established.

**Colombia**

Torres et al. [12] performed an analysis of mutations in the BRCA1/2 genes (using a range of techniques, including DHPLC, SSCP, and PTT, followed by direct DNA sequencing). They included 53 patients with breast cancer selected by family history and reported the identification of 3 founder mutations: 2 in BRCA1 (A1708E and 3450del4) and 1 in BRCA2 (3034del4). Using haplotype analysis, it was concluded that each one of these mutations originated from a common ancestor. Recently,
Identifying the prevalence of mutations in BRCA1 and BRCA2 genes in patients with breast cancer had not been performed in Peru until 2014, when Abujattas et al. [28] reported the first study there. The study included 266 women, not selected by age or family history, in which the panel of 115 Hispanic's mutations (Hispanel) in BRCA1/2 genes was analyzed. In total, 13/114 (5%) deleterious mutations were identified: 11 in BRCA1 and 2 in BRCA2. Mutation BRCA1 185delAG was the most prevalent, observed in 7 (54%) of the 13 mutation carriers, and is the most common founder mutation in the Ashkenazi Jewish population. It has also been reported in other population groups living in Mexico, Chile, and the Bahamas [19, 29, 30]. The frequency observed in Peru (54%) is the highest yet reported in nonselected populations in Latin America. Additionally, three of the carriers of this mutation were self-identified as descendants of indigenous people from South America. BRCA1 2080delA and mutation BRCA2 3034del4 were two other recurrent mutations, and each one was identified in two nonrelated women. The latter mutation was reported in Colombia as a founder mutation [12] and is also one of the most frequent mutations in Spain.

Uruguay
In the study performed by Delgado et al. [31], 42 families with at least 3 cases of female breast cancer or 2 cases and subcriteria (paternal transmission, ovarian cancer, bilateral breast cancer, male breast cancer, Ashkenazi Jewish ancestry) in the same lineage, at least 1 diagnosed before age 50, were screened for BRCA1 germline mutations. In total, seven different truncating mutations in seven families were identified, two in BRCA1 (5583insT and 2687T>G) and five in BRCA2 (4359ins6d, 5579insA, 3829insTdel35, 4088delA, and 1617delAG), but none were recurrent.

Venezuela
No founder mutations have been described in Venezuela to date. Lara et al. [32] evaluated 58 high-risk families (using SSCP and sequencing) and found a positive rate of 17.2%, including 6 patients with mutations in BRCA1 (10.3%) and 4 in BRCA2 (6.9%), but none were recurrent.

Guatemala, El Salvador, Honduras, Nicaragua, Panama, Bolivia, Ecuador, and Paraguay
There are no reports of population studies on mutations in BRCA1 or BRCA2 genes in these countries.

Materials and Methods
A literature search was performed in the electronic databases of PUBMED, EMBASE, LILACS (Latin American and Caribbean
Health Sciences Literature), and BIREME using the terms BRCA1, BRCA2, founder mutation, Latin American population, and Hispanic. These words were crossed with each of the Latin American countries (e.g., Colombia, Mexico). The search was performed in Spanish, English, and Portuguese. In some cases, the research groups related with the subject were contacted by e-mail in search of preliminary data or more information.

A total of 62 papers were identified, 38 of which were selected because they were considered relevant for this review. Each result is shown per country.

**DISCUSSION**

The term “Hispanic/Latino” refers to a diverse ethnic group inhabiting Latin America native from other parts of the world, originating from groups of people who migrated to that region of the continent. Hispanics/Latinos now have a complex population structure with significant genetic contributions from indigenous Americans and European populations [33] (mainly immigrants from the Iberian Peninsula and southern Europe), along with West African populations that came to the Americas in the transatlantic slave route [34, 35].

It has been observed that the risk of breast cancer in Latin women is associated with a larger proportion of European ancestry. This association was demonstrated in a study performed by Fejerman et al. [36], in which a greater proportion of European ancestry in Mexican women residing in Mexico was associated with an increased risk of breast cancer. When the percentages of European ancestry were compared, it was observed that the risk considerably increased in those with higher percentages. Women who were 51%–75% and 76%–100% European had odds ratios of 1.35 (95% confidence interval [CI], 0.96–1.91) and 2.44 (95% CI, 0.94–6.35), respectively. For every increase of 25 percentage points of European ancestry, an increase of 20% was observed in the risk of breast cancer (95% CI, 1.03–1.41; \( p = 0.019 \)).

Precarious socioeconomic conditions, such as low income, lack of health system coverage, and limited access to counseling and genetic testing, and certain ethnic/racial groups are associated in general with a significant increase in cancer incidence. Breast cancer is the most commonly diagnosed cancer in Hispanic women and the main cause of death by cancer. Although the incidence of breast cancer is lower in Hispanic women than in non-Hispanic white women, prevalence studies of mutations in the BRCA1 and BRCA2 genes suggest that these mutations can explain a greater proportion of breast cancer than in other populations [37].

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The large sizes of the BRCA1/2 genes, together with the great variety of described mutations along them, means that analysis—at least in Latin America and other regions of the world—remains expensive and complex and therefore inaccessible to a high proportion of the women at risk. The presence of founder mutations (reduced genetic variability explaining a disease) in a population provides the opportunity to design economically feasible tests with the probability of increasing the detection rate in the population group with which they are identified [38].

The best example of the founder effect is the one observed in the Ashkenazi Jewish population, in which the genetic predisposition for ovarian or breast cancer is much higher than in the general population because of the presence of three founder mutations. Mutation BRCA1 185delAG has been found with a 1% frequency and contributes to 16%–20% of the cases of breast cancer diagnosed before age 50. Mutations BRCA1 5382insC and BRCA2 6174delT have been identified at frequencies of 0.13% and 1.5%, respectively, in this population. The overall rate of these three founder mutations is 2.6% (1/40) compared with the rate of 0.2% (1/500) of mutation carriers in BRCA1/2 in the general population [1]. Interestingly, these three founder mutations represent 79% of all BRCA1/2 mutations found in the Jewish Ashkenazi population [39].

Founder mutations are not always specific to a certain population. Mutation BRCA1 5382insC, for example, is the second most recurrent mutation reported in the BRCA1 gene according to the BIC and has been identified in several countries, such as Russia, Poland, the Czech Republic, Lithuania, Hungary, Greece, Germany, France, Italy, Canada, and Spain, suggesting that this mutation could have existed before the Jewish diaspora [2]. In Latin America, the same mutation has been identified as a founder in Argentina and Brazil, so it is believed that this mutation likely originated in the Baltic zone at least 38 generations ago, with a gradual descent from East to West, according to haplotype analyses indicating a single founder effect for this mutation that occurred for both Europe and North America [40]. Mutation BRCA1 185delAG has been reported as a founder in Argentinian people, whereas it has also been reported as recurrent in Brazil, Chile, and Peru and Mexico. Mutation BRCA2 6174delT is also a founder in Irish people [41] and has been reported as a founder in Argentinian people.

Founder mutations in BRCA1/2 have been identified in countries such as Norway [42], Finland [43], Sweden [44], France [45], Holland [46], Italy [47], Canada [48], Pakistan [49], Japan [50], China [51], Malaysia [52], and the Philippines [53]. This has led to a more cost-effective approach in these populations, where the initial analysis of these genes focuses on the most recurrent mutations [54]. The complete evaluation of BRCA1 and BRCA2 is necessary only in cases where there is strong family history and none of the corresponding founder mutations is identified. This approach requires previous knowledge of the prevalence of the mutations in the population of interest.

Clear founder effects have been reported (Table 1) in Mexico (BRCA1 del exons 9–12), Brazil (BRCA1 5382insC and BRCA2 c.156_157insAlu), and Colombia (BRCA1 3450del4, BRCA1 A1708E, and BRCA2 3034del4) and in Latinas residing in Southern California (BRCA1 185delAG, IVS5 +1G>A, S955X, and R1443x) [53]. Of these, mutation BRCA1 3450del4 has also been reported in Brazil and Chile, whereas mutation BRCA2 3034del4 has been reported in Argentina and Peru. These data imply that although Hispanic populations share common
In some Latin American countries, a wide spectrum of mutations in both genes has been identified, along with some founder or recurrent mutations. In these cases, it is necessary to analyze whether it is really more cost beneficial to first study the recurrent/founder mutations and then perform a complete study of both genes in the negative cases.

Germinal mutations in the BRCA1/2 genes significantly contribute to the development of breast and/or ovarian cancer, but the penetrance (mutation-specific risk) can vary among mutations. In Latin America, there are no systematic studies of the penetrance of the BRCA mutations identified. It would be very interesting to determine the genotype/phenotype relationships of the founder/recurrent mutations described up to this date.

Some of the studies mentioned report very low mutation rates in the BRCA1/2 genes, owing in part to the limited number of mutations analyzed in these genes. Additionally, the use of indirect mutation detection methods (SSCP, conformation-sensitive gel electrophoresis [CSGE], PTT, and DHPLC) [55] could restrict the search of mutations and detect only a fraction of the variants present in the sample screened. The sensitivity of SSCP ranges from 50% to 96%, whereas CSGE and PTT are estimated to detect only 75% and 76% of the BRCA1 and BRCA2 variants, respectively [55]. To establish the real prevalence of all mutations in the BRCA1 and BRCA2 genes in a population, ideally a complete BRCA analysis (i.e., complete sequencing and study of large rearrangements) should be performed. The prevalence of rearrangement variants varies significantly in different populations [56]. Large genomic rearrangements may account for up 21.4% of the variants in high risk patients from Latin America and the Caribbean [57]. The development of clinically useful BRCA mutation panels will require a deep knowledge of the mutation spectrum and prevalence in each Latin American country.

### Table 1. Recurrent and founder mutations in BRCA1 and BRCA2 genes described in Latin America

<table>
<thead>
<tr>
<th>Country</th>
<th>BRCA1 Mutations</th>
<th>BRCA2 Mutations</th>
<th>BRCA1 Mutations</th>
<th>BRCA2 Mutations</th>
<th>Mutation detection method</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>3034del4</td>
<td>185delAG, 5382insC</td>
<td>6174delT</td>
<td>Direct DNA sequencing</td>
<td>Solano et al., 2012 [11]</td>
<td></td>
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<tr>
<td>Brazil</td>
<td>185delAG, ins6kb, 3450del4, 2156delGinsCC, and c.211A&gt;G</td>
<td>6633del5</td>
<td>5382insC</td>
<td>c.156_157insAlu</td>
<td>PCR, reverse-transcriptase PCR, PTT, DGGE, and DHPLC; all variants identified were confirmed by direct DNA sequencing</td>
<td>Da Costa et al., 2008 [13]; Gomes et al., 2007 [14]; Machado et al., 2007 [15]; Esteves et al., 2009 [17]; Felix et al., 2014 [18]</td>
</tr>
<tr>
<td>Chile</td>
<td>185delAG, 2605delTT, and 3450del4</td>
<td>4969insTG, 5374del4, and 6593delTT</td>
<td>3034del4</td>
<td>SSCP; all variants identified were confirmed by direct DNA sequencing</td>
<td>Jara et al., 2006 [19]</td>
<td></td>
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<tr>
<td>Colombia</td>
<td>6076del4 and 6593delTT</td>
<td>A1708E, 3450del4</td>
<td>DHPLC, SSCP, and PTT, followed by DNA sequencing analysis</td>
<td>Torres et al., 2007 [12]</td>
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<tr>
<td>Costa Rica</td>
<td>5531delITT</td>
<td>Only exon 10 of BRCA1 and exons 10 and 11 of BRCA2 were screened by PTT; all mutations were confirmed by direct sequencing</td>
<td>Gutiérrez Espeleta et al., 2012 [23]</td>
<td></td>
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<tr>
<td>Cuba</td>
<td>c.3394C&gt;T</td>
<td>DGGE and PTT followed by DNA sequencing analysis</td>
<td>Rodriguez et al., 2008 [24]</td>
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<tr>
<td>Mexico</td>
<td>del exon 9–12</td>
<td>Hispanic screening of 115 recurrent BRCA1/2 Hispanic mutations; all mutations were confirmed by direct sequencing</td>
<td>Villarreal-Garza et al., 2015 [25]</td>
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<tr>
<td>Peru</td>
<td>2080delA, 3034del4, 185delAG</td>
<td>Hispanic screening and direct DNA sequencing</td>
<td>Abugattas et al. 2015 [28]</td>
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Abbreviations: DGGE, denaturing gradient gel electrophoresis; DHPLC, denaturing high-performance liquid chromatography; PCR, polymerase chain reaction; PTT, protein truncation test; SSCP, single-strand conformation polymorphism gel electrophoresis.
Some of the difficulties found in this review include the different techniques used for the processing of samples, the type of mutations analyzed, and the lack of haplotype analyses in most of them. These difficulties did not allow us to differentiate the presence or absence of a founder effect in the recurrent mutations (without haplotype analysis it is not possible to distinguish whether a variant has migrated from a geographic area or is the result of an independent mutational event) and limited the final conclusions of the study.

**CONCLUSION**

The risks associated with mutations in the BRCA1 and BRCA2 genes are different in geographically and historically defined groups, highlighting the importance of evaluating the risk for each patient regarding their own genetic and environmental context. It is important to highlight that among Latin American countries and even among regions of the same country, there is great heterogeneity in ancestors. Therefore, Latinas should not be analyzed as one population group without taking into account their genetic ancestry.

The presence of founder mutations in specific populations can lead to a cost-effective alternative of panel testing, given that a rapid and inexpensive test can increase the detection of mutations in these population groups. However, it is necessary to first determine the prevalence of such mutations in the population under study.

The range of possibilities now available for the treating physician, the patient, and the health care system in making appropriate and timely decisions in hereditary breast and ovarian cancer has caused a daily increase in the demand of mutation analyses for the BRCA1/2 genes. Therefore, it is necessary to genetically characterize the affected populations to establish mutation screening guidelines and more adequate and appropriate treatments for each population. The importance of identifying founder mutations lies mainly in the decrease in costs. If we are able to achieve this by focusing first on founder mutations, screening could be offered more widely and could cover a larger number of women, by establishing criteria for testing patients from a population with founder mutations to be less strict than for populations that do not have them.

Even though BRCA1/2-founder mutations associated with increased risk of breast and other cancers have been identified in some Latin American countries, several other founder mutations may exist that have not yet been identified because of the limited number of investigations performed to date. Further studies need to be done in Latin America considering the economic advantages that bring the analysis of founder mutations in contrast to full gene sequencing testing, especially for countries with limited economic resources.

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**AUTHOR CONTRIBUTIONS**

Conception/Design: Carlos Andrés Ossa, Diana Torres

 Provision of study material or patients: Carlos Andrés Ossa, Diana Torres

Collection and/or assembly of data: Carlos Andrés Ossa, Diana Torres

Data analysis and interpretation: Carlos Andrés Ossa, Diana Torres

Manuscript writing: Carlos Andrés Ossa, Diana Torres

Final approval of manuscript: Carlos Andrés Ossa, Diana Torres

**DISCLOSURES**

The authors indicated no financial relationships.

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Prevalence of BRCA1 and BRCA2 mutations in breast cancer patients in Latin America: A systematic review and meta-analysis.


