

***BRCA1* and *BRCA2* Pathogenic Sequence Variants
in Women of African Origin or Ancestry**

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Abstract

BRCA1 and *BRCA2* (*BRCA1/2*) pathogenic sequence variants (PSV) confer elevated risks of multiple cancers. However, most *BRCA1/2* PSVs reports focus on European ancestry individuals. Knowledge of the PSV distribution in African descent individuals is poorly understood. We undertook a systematic review of the published literature and publicly available databases reporting *BRCA1/2* PSVs also accessed the Consortium of Investigators of Modifiers of *BRCA1/2* (CIMBA) database to identify African or African descent individuals. Using these data, we inferred which of the *BRCA* PSVs were likely to be of African continental origin. Of the 43,817 *BRCA1/2* PSV carriers in the CIMBA database, 469 (1%) were of African descent. Additional African descent individuals were identified in public databases (n=291) and the literature (n=601). We identified 164 unique *BRCA1* and 173 unique *BRCA2* PSVs in individuals of African ancestry. Of these, 83 *BRCA1* and 91 *BRCA2* PSVs are of likely or possible African origin. We observed numerous differences in the distribution of PSV type and function in African origin vs. non-African origin PSVs. Research in populations of African ancestry with *BRCA1/2* PSVs is needed to provide information needed for clinical management and decision-making in African descent individuals worldwide.

Introduction

Many women benefit from genetic testing information that can guide their knowledge of cancer risks and help them to make informed prevention and medical management decisions if they have inherited pathogenic sequence variants (PSV) in *BRCA1* (GenBank reference sequence: NG_005905.2) or *BRCA2* (GenBank reference sequence NG_012772.3) (*BRCA1/2*). Knowledge of genetic risk is valuable because it can lead to the use of risk-reducing salpingo-oophorectomy or bilateral mastectomy, which significantly decrease breast and/or ovarian cancer risk and mortality *BRCA1/2* PSV carriers[1-7]. However, the vast majority of information about cancer risk and risk reduction has to date been conducted in Caucasian and Ashkenazi Jewish women[8].

Because there has been limited capture of *BRCA1/2* PSVs in more diverse race/ethnicity groups, we anticipate that a large number of PSVs have yet to be reported. Similarly, there is very limited information about cancer risks and the effect of prevention strategies in non-White/non-Jewish women. Therefore, a better understanding of PSVs and cancer risks in underrepresented populations is a critical unmet need in the *BRCA1/2* field.

The *BRCA1/2* International Diversity by Geography and Ethnicity (BRIDGE) Study has been developed to provide information about *BRCA1/2* PSVs in populations who are currently underrepresented in research. We characterize PSVs in self-reported African ancestry (SRAA) individuals identifying commonly-reported PSVs that may have had their origins on the African continent and identify potential African founder PSVs and PSV hot spots.

Methods

The individuals included in this analysis were inferred to have African ancestry based on self-report or inference based on place of birth or residence. We included Africans from sub-Saharan Africa and black South Africans. We also included those reporting African origins from North America, South America, the Caribbean, Europe, or Asia. We excluded White (Afrikaners) and

Asian South Africans, mixed race (Coloured) South Africans, and individuals who self-reported to be of other race/ethnicity groups whose ancestral origins were from outside Africa (e.g., Asian and middle eastern) and North Africans (Morocco, Tunisia, Algeria, Libya, and Egypt). In addition, this report only includes females with PSVs. In some cases, the basis of the race/ethnicity determination was not stated in the original research, and the assumption was made that the source of race/ethnicity information was by self-report or determined by the research team. None of the information about race or ethnicity was based on ancestral genomic information.

To characterize the distribution of PSVs in SRAA individuals, we evaluated a series of data sources (**Figure 1**). First, we undertook a systematic literature review of published studies reporting a deleterious *BRCA1/2* PSV in an individual of SRAA, including sub-Saharan Africa, Caribbean, and African American. To identify reports of *BRCA1/2* PSVs in SRAA individuals, we used the following key words to search the medical literature: *BRCA1* or *BRCA2* and Africa or African (includes African American), or Caribbean. Each paper was reviewed to determine if it described an independent study done in SRAA individuals and reported the presence of a disease-associated PSV in *BRCA1/2*. PSVs reported in other genes were excluded. Reports of PSV testing for *BRCA1/2* that reported no disease-associated PSVs were not included in this report. Reports of variants of unknown significance were also excluded. All studies were included regardless of sampling design (e.g., family studies, population screening, genetic testing in clinical case series, etc.). In addition, a small number of papers or abstracts were identified from the citation list of the papers that were identified from the public literature search.

Second, we obtained data from the CIMBA consortium[9] using the coded ethnicity variable for African American and countries in Sub-Saharan Africa, which included reports from Nigeria and South Africa only. White South Africans, Afrikaners, and mixed-race (Coloured) South Africans were excluded.

Third, we used publicly available data from the BIC (<https://research.nhgri.nih.gov/bic/>) database. A copy of the BIC database was downloaded on February 1, 2019 to identify reported *BRCA1/2* PSV carriers. The ethnicity and nationality variables were searched for any notation of African descent individuals, African, African American, or Caribbean.

Lastly, the NIH public database ClinVar (<https://www.ncbi.nlm.nih.gov/clinvar/>) was used as a check for PSV nomenclature and confirmation of the pathogenic status of each variant. CIMBA and BIC, among other sources, submitted their PSVs to ClinVar. The majority of sources did not contribute race/ethnicity information to ClinVar, so this database was determined not to be a useful data source for this report. Most PSVs reported here have been deposited into the ClinVar database.

PSVs were categorized according to type and function, including large deletion (DL), large duplication (DP), frameshift (FS), in-frame deletion (IFD), missense (MS), nonsense (NS), splice (SP), and individuals who carried multiple PSV types (including those listed above); No RNA, Premature Termination Codon (PTC), Nonsense-Mediated Decay (NMD), NMD with or without re-initiation; and mutation class (1, 2, or 3).

To establish the continental origin of *BRCA1/2* PSVs that were reported in SRAA individuals, we identified PSVs reported in regions in which non-African admixture was likely (i.e., North America, Caribbean, South America, South Africa) and where non-African admixture was less likely (i.e., Sub-Saharan Africa excluding South Africa). **Supplementary Table 1** presents PSVs reported only in Sub-Saharan Africa and PSVs reported only in the Americas. In addition, we evaluated whether any of these PSVs were reported in non-African ancestry groups (e.g., Europeans or European Americans). We judged a PSV to be likely African origin if the PSV has only been

reported in SRAA and never in a non-SRAA individual, and of possibly African origin if reported greater than 50% of the time in SRAA individuals. This inference was strengthened by the observation of a PSV reported in Africa. We judged the PSV to be likely non-African origin if it reported less than 50% of the time in SRAA individuals.

Collection of original data was undertaken under approved research and/or clinical human subjects protocols at each contributing center. Retrospective anonymized data analysis for the present research was undertaken under human subjects approvals at the Dana-Farber Cancer Institute.

Results

African Ancestry Individuals with BRCA1/2 PSVs

The results of our literature search are shown in **Figure 1**. When more than one paper from a research group was found, we included the largest or most recent in the series. Studies that searched for but did not find any *BRCA1/2* PSVs in SRAA women were excluded. Note that only eleven published studies were found that included male *BRCA1/2* PSV carriers, but no additional *BRCA1/2* PSVs were identified from these reports. 48 studies were included in the present report: 16 studies of Sub-Saharan Africans[10-25], 27 of African Americas[13, 26-54], and 3 of Afro-Caribbean populations[55-57] and one study reporting SRAA of unspecified geography [49]. From these papers, we identified 414 *BRCA1* and 187 *BRCA2* PSVs, and 108 unique *BRCA1* and 103 unique *BRCA2* PSVs.

The BIC database included 15,311 total submissions of *BRCA1* PSVs, of which 8,564 were reported to be pathogenic. Of these, 206 (2.4%) were identified as SRAA. The BIC database included 14,914 total submissions of *BRCA2* PSVs, of which 4,516 were deleterious. Of these, 85 (1.9%) identified as SRAA.

The CIMBA database consisted of 43,817 *BRCA1/2* female PSV carriers. Of these, 382 (0.9%) were identified as African Americans and 269 (0.6%) were ascertained in Africa. Thirty-two of these carriers were from Nigeria and 237 were from South Africa. After excluding White South Africans, Afrikaaners, or mixed-race (Coloured) South Africans, 11 black South Africans were included. In total, 435 (1%) women of African descent were found in the CIMBA database. Of these 273 were *BRCA1* and 162 were *BRCA2*. In addition, 34 African American carriers from the University of Illinois at Chicago, 14 *BRCA1* and 20 *BRCA2*, not previously reported to CIMBA, were also included in the CIMBA dataset after consultation with the University of Illinois center.

BRCA1/2 PSVs in African Ancestry Individuals

Supplementary Table 1 presents the complete list of all SRAA PSVs identified in this study and relevant characteristics according to PSV designation, type, and function as well as where and in what populations they have been reported. From our 3 primary data sources, a *BRCA1* PSV in SRAA was reported 909 times: 404 (44.3%) in African Americans, 170 (18.6%) in Africans, 135 (14.8%) in the Caribbean, and 200 (21.9%) in SRAA of unknown or unreported geographic origin. From all data sources, we identified 164 unique *BRCA1* PSVs. For *BRCA2* a PSV in a woman of SRAA was reported 454 times, 262 (57.7%) in African Americans, 114 (25.1%) in Africans, 35 (7.7%) in the Caribbean and 43 (9.5%) in SRAA of unknown origin. Of these, we identified 173 unique *BRCA2* PSVs. We were not able to determine if an individual was included more than once in these data sources, so these figures do not represent the actual frequency of PSVs expected in SRAA.

The most commonly identified PSVs in *BRCA1* and *BRCA2* are presented in **Table 1**. Most of these PSVs have been reported in multiple geographical locations, and in particular most have been reported in both the new and old world. A small number of PSVs to date (n=39) have been reported only in Africans residing in Africa.

In order to identify PSVs that were most likely to be of African origin, we characterized PSVs according to the number of times they were reported in individuals of African and non-African descent (**Table 2**). We characterized those being reported only in SRAA populations and/or only in Africa as being of likely African origin (n=115), those reported $\geq 50-99\%$ as possibly African origin (n=59), those 25-50% as probably non-African (n=35), and those reported $<25\%$ of the time in SRAA individuals as likely non-African origin (n=128). For *BRCA1*, 50 (30.5%) PSVs are likely to be of African origin, 33 (20.1%) possibly of African origin, 19 (11.6%) probably non-African, and 62 (37.8%) likely of non-African origin. For *BRCA2*, 65 (37.6%) PSVs are likely to be of African origin, 26 (15.0%) possibly of African origin, 16 (9.2%) probably non-African, and 66 (38.2%) likely of non-African origin. The list of these PSVs and their corresponding designations is presented in **Supplementary Table 1**. Thus, about half of PSVs identified in SRAA can be inferred to be of likely or possibly African origin.

Figures 2 and 3 display the frequency and distribution of likely or possible African origin PSVs across the span of each gene. For *BRCA1*, two common PSVs (c.5324T>G and c.4357+1G>A) were observed in multiple populations of African descent. Among those identified as unlikely to be of African origin include the c.68_69del Jewish founder PSV, as well as PSVs that have been reported as common or founder PSVs in European populations (e.g., c.211A>G in Spain and c.5251C>T in Greece[58]) or in the CIMBA database (e.g., c.1504_1509del in Asians in Australia and c.5177_5180del in French Caucasians). Notably, the c.68_69del PSV was found in an African population in Burkina Faso[24] as well as many other populations in Europe, the Middle East, and North Africa. In *BRCA2*, c.5616_5620del was observed in multiple African descent populations. As with *BRCA1*, the most common PSVs that were inferred as unlikely to be of African origin have been reported as common or founder PSVs in European populations (e.g., c.2808_2811del in Spain and c.1310_1313del in Denmark, or in the CIMBA database (e.g., c.658_699del in

Germany and c.9382C>T globally, including Japan and in the CIMBA database in Europe) [58, 59].

Using the SRAA CIMBA PSV carriers we were also able to characterize the distribution of PSVs by type and effect (**Tables 3 and 4**). FS, PTC and NMD were less common in SRAA than in CIMBA overall for both *BRCA1* and *BRCA2*. IFD was more common in *BRCA1* SRAA (but this included very few PSVs), and PSV class was different between SRAA and non-SRAA in *BRCA2*. For *BRCA1*, large deletions and duplications were not significantly different in frequency in CIMBA SRAA versus the previously reported CIMBA distribution[8]. There was also no significant difference for splice variants, PSV class, or lack of nonsense mediated decay (NMD) with re-initiation, and marginally significant differences with missense PSVs, nonsense PSVs, no RNA, or re-initiation. Other PSV types or functions included frameshift, in-frame deletions, PSVs of multiple types, premature termination codon, and NMD. There were also significant differences in the number of PSVs with unknown PSV effect. There were approximately twice as many SRAA PSVs of unknown effect than in other groups.

For *BRCA2*, there were significant differences between SRAA and the published CIMBA PSV distribution for large deletions, frameshift, in-frame deletions, missense, and multiple PSV types. There were also statistically significant differences for all PSV effects including premature termination codon PSVs, NMD, and PSV class. Again, the proportion of PSVs of unknown effect was significantly higher in SRAA than CIMBA as a whole.

Discussion

Despite the availability of substantial information regarding cancer risks in *BRCA1/2* PSV carriers, the amount of information available to women of African ancestry is extremely limited. The

worldwide CIMBA database containing over 30,000 families with *BRCA1/2* PSVs includes less than 1% individuals of African ancestry[60]. This very limited capture of PSVs in women of African ancestry presents a number of important limitations for the clinical implementation and decision-making for African ancestry women[44, 61].

We summarize all reported PSVs found in SRAA individuals and infer which of these PSVs may be of African origin. Approximately half of PSVs reported in SRAA are likely or possibly of African origin. A number of individuals who are SRAA have inherited PSVs of European origin. These PSVs were observed primarily in individuals in North America or the Caribbean and likely reflect recent European admixture. However, the c.68_69del PSV was also commonly observed in all SRAA populations. Haplotype analyses suggest that this PSV arose no more than 1500 years ago, suggesting that it was transmitted from the middle east to Africa, and did not arise there before the original migration of individuals out of Africa[62]. However, this PSV has been reported in native Africans[24] and has arisen in multiple populations independently, so it is not known whether this PSV is a new PSV at a locus that demonstrates high mutation rates, or if it is the common Jewish founder PSV, which has been observed in Middle Eastern or North African populations[24, 62, 63].

We also report that the distribution of PSV type or effect differs for some PSV groups between SRAA and the CIMBA population as a whole. It is well established that African women as well as African American women have an earlier average age of diagnosis and a higher proportion of hormone receptor negative and triple negative tumors than women of other ethnicities[64, 65]. It is not clear how much of this phenotypic pattern in African descent women could be explained by PSVs in *BRCA1/2*, but it is possible that, at least in Africa, a substantial proportion of breast cancer may be hereditary in nature. To the degree this is true, the observation in this report that

the distribution of PSV type or effect may be different in African descent populations compared with other populations could have clinical implications for assessing cancer risk in women of SRAA. It is also possible that the penetrance associated with mutations in SRAA is different than that of non-SRAA populations. However, the currently available data do not allow us to evaluate the relationship of PSVs in *BRCA1/2*, as well as specific types of PSVs, in cancer susceptibility. Reports in the literature do not provide consistent information about individual women and their cancer status that would be required to undertake association studies. Such associations could be undertaken in the CIMBA study, but the sample size of SRAA in the CIMBA data set remains underpowered for these analyses. In addition, the relatively larger proportion of PSVs that could not be characterized with respect to their effect compared with all PSV carriers suggests that additional research is required to understand the phenotypic consequences of *BRCA1/2* PSVs in SRAA.

We have also made initial *ad hoc* inferences about the likelihood that each PSV reported in SRAA is of African origin. We used a value of 50% of PSVs being observed in SRAA to suggest that the PSV was of African origin. However, given that the number of individuals tested for *BRCA1/2* is much higher in non-Africans, it is possible this number is too conservative. If a PSV exists in both African women and non-African women regardless of percentage, the PSV may have arisen prior to the initiation of migration out of Africa 200,000-300,000 years ago. Mutations found only in SRAA women may represent new mutations that arose in Africa (i.e., since the migration out of Africa) or arose in populations that did not migrate out of Africa. In the future, estimation of haplotype backgrounds and PSV age will be important to further characterize the origin of PSV with respect to African vs. non-African origin.

It is clear from our findings that there is a great need for increased participation among currently underserved populations in *BRCA1/2* research. Large-scale genomic studies of *BRCA1/2* in Africa have yet to be undertaken, although initiatives such as H3Africa

(<https://h3africa.org/initiative>) may provide relevant data in the future if *BRCA1/2* testing is undertaken by participating groups. Participation of these groups in *BRCA1/2* research will provide a more comprehensive evaluation of PSVs in non-European descent populations and improve risk assessment and an understanding of risk modifiers. It will be critical to evaluate in these groups the complete PSV spectrum, common/founder PSVs (that may aid in developing efficient genetic testing panels) and understand the origins of these PSVs through population/evolutionary genetics research. Additional research will be required to understand cancer risk and risk modifiers so that cancer prevention and treatment can be optimized in these populations.

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Table 1. Ten Most Common PSVs in *BRCA1* (GenBank reference sequence: NG_005905.2) or *BRCA2* (GenBank reference sequence NG_012772.3) in Self-Reported African Ancestry (SRAA) Individuals.

Gene	PSV	Total PSV in SRAA	All Reported PSVs	% SRAA PSVs of Total PSVs Reported	Countries in Which PSV Has Been Reported in SRAA individuals	Continent on Which PSV Has Been Reported in non-SRAA individuals
<i>BRCA1</i>	c.5324T>G	103	125	82%	Bahamas, Nigeria, Trinidad, USA	North America, Europe
	c.815_824dup	100	155	65%	Senegal, Bahamas, Ivory Coast, France, USA, Spain, France	North America, Europe, South America
	c.4357+1G>A	73	88	83%	Bahamas, USA	North America, Europe
	c.5177_5180del	54	142	38%	USA, Canada, Trinidad, Nigeria	North America, Europe
	c.4986+6T>C	35	45	78%	Bahamas, USA, Sudan	North America, Europe, South America
	c.68_69del	34	4834	1%	Bahamas	North America, Europe, South America, Australia, Asia
	c.303T>G	26	34	76%	Nigeria	North America, Europe
	c.190T>G	19	30	63%	USA	North America, Europe
	c.5467+1G>A	16	25	64%	USA	North America, Europe, Asia
	c.5251C>T	15	188	8%	USA	North America, Europe, South America, Australia, Asia

Gene	PSV	Total PSV in SRAA	All Reported PSVs	% SRAA PSVs of Total PSVs Reported	Countries in Which PSV Has Been Reported in SRAA individuals	Continent on Which PSV Has Been Reported in non-SRAA individuals
<i>BRCA2</i>	c.1310_1313del	26	192	14%	Bahamas, Nigeria, Trinidad, USA	North America, Europe, Australia, Asia
	c.9382C>T	23	205	11%	Trinidad, USA	North America, Europe, Caribbean, Australia, Asia
	c.2808_2811del	22	646	3%	Nigeria, Brazil, USA	North America, Europe, South America, Australia, Asia
	c.5616_5620del	18	23	78%	USA	North America, Europe
	c.658_659del	12	217	6%	USA	North America, Europe, Caribbean, Australia, Asia
	c.4552del	11	12	92%	USA	North America
	c.9253dup	10	69	14%	USA	North America, Europe, Asia
	c.5771_5774del	9	18	50%	South Africa	North America, Europe
	c.2402_2412del	7*	7	100%	Nigeria	
	c.2957_2958insG	7*	8	88%	USA, Nigeria	North America
	c.6405_6409del	7*	131	5%	USA, Brazil, Nigeria	North America, Europe, South America, Australia, Asia

Table 2. Determination of Continent of Origin for PSVs in *BRCA1* (GenBank reference sequence: NG_005905.2) or *BRCA2* (GenBank reference sequence NG_012772.3) Identified in Self-Reported African Ancestry Individuals, Including Likely African (100%), Possibly African (50-99%), Unlikely African (25-49%), and Likely Non-African (<25%).

Determination	<i>BRCA1</i>		<i>BRCA2</i>		Total
	N	%	N	%	
Likely African	50	30.5%	65	37.6%	115
Possibly African	33	20.1%	26	15.0%	59
Unlikely African	19	11.6%	16	9.2%	35
Likely Non-African	62	37.8%	66	38.7%	128
Total	164	100%	173	100%	337

Table 3: Characteristics of *BRCA1* (GenBank reference sequence: NG_005905.2) PSVs in the CIMBA Database[8], By Unique PSV, Compared to Likely or Possible PSVs of African Origin.

		N=1,650 CIMBA PSVs (All Ethnicities)		N=164 Likely or Possibly African PSVs		P-value*
		N	%	N	%	
PSV Type	Large Deletion (DL)	130	7.9	10	6.1	0.749
	Large Duplication (DP)	27	1.6	2	1.2	>0.999
	Frameshift (FS)	948	57.5	66	40.2	<0.0001
	In-Frame Deletion (IFD)	1	<0.1	4	2.4	<0.0001
	Missense (MS)	46	2.8	9	5.5	0.078
	Nonsense (NS)	313	19.0	40	24.4	0.081
	Splice (SP)	166	10.1	20	12.2	0.259
	Multiple Types (including those listed above)/Unknown	20	1.1	13	7.9	<0.0001
PSV Effect	No RNA	21	1.3	5	3.0	0.055
	Premature Termination Codon (PTC)	1,331	81.0	95	57.9	<0.0001
	Unknown/Other	298	18.0	64	39.0	<0.0001
	Nonsense-Mediated Decay (NMD)**	1,213	73.9	84	51.2	<0.0001
	No NMD	58	3.5	2	1.2	0.229
	Re-Initiation	4	0.2	2	1.2	0.080
	NMD/Re-initiation	60	3.7	8	4.9	0.492
	Unknown/Other	294	17.8	68	41.5	<0.0001

		N=1,650 CIMBA PSVs (All Ethnicities)		N=164 Likely or Possibly African PSVs		
		N	%	N	%	P-value*
PSV Class	1	1,298	78.6	99	60.6	0.756
	2	112	6.8	10	6.1	
	3	240	14.6	19	11.6	
	Unknown			36	22.0	

*P-values from Fisher's Exact Test reflect the comparison of All Ethnicities vs Likely or Possible African PSVs, for the specific mutation group vs. all other mutations.

**References [66-70]

Table 4: Characteristics of *BRCA2* (GenBank reference sequence NG_012772.3) PSVs in the CIMBA Database[8], By Unique PSV, Compared to Likely and Possible PSVs of African Origin.

		N=1,731 CIMBA PSVs (All Ethnicities)		N=173 Likely or Possibly African PSVs		P-Value*
		N	%	N	%	
PSV Type	Large Deletion (DL)	34	1.9	1	0.01	0.003
	Large Duplication (DP)	11	0.6	0	0.0	NE
	Frameshift (FS)	1,141	65.9	106	61.3	<0.0001
	In-Frame Deletion (IFD)	2	0.1	0	0.0	NE
	Missense (MS)	13	0.8	1	0.01	NE
	Nonsense (NS)	380	22.0	47	27.2	0.617
	Splice (SP)	131	7.6	8	4.6	0.062
	Multiple Types (including those listed above)	19	1.1	10	5.8	<0.0001
PSV Effect	No RNA	6	0.3	0	0.0	NE
	Premature Termination Codon (PTC)	1,542	89.0	132	76.3	<0.0001
	Unknown/Other	183	10.6	41	23.7	<0.0001
Nonsense-Mediated Decay (NMD)**	Nonsense-Mediated Decay (NMD)**	1,523	88.0	132	76.3	<0.0001
	No NMD	16	0.9	0	0	NE
	Re-Initiation	0	0.0	0	0	NE
	NMD/Re-initiation	0	0.0	0	0	NE
	Unknown/Other	187	10.7	41	23.7	<0.0001

		N=1,731 CIMBA PSVs (All Ethnicities)		N=173 Likely or Possibly African PSVs		
		N	%	N	%	P-Value*
PSV Class	1	1,529	88.3	131	75.7	<0.0001
	2	36	2.1	0	0	
	3	167	9.6	6	3.5	
	Unknown			36	20.8	

*P-values from Fisher's Exact Test reflect the comparison of All Ethnicities vs Likely or Possible African PSVs, for the specific mutation group vs. all other mutations.

**References [66-70]

NE: not estimable.

Figure 1: Summary of Literature Review Used in This Report for *BRCA1* (GenBank reference sequence: NG_005905.2) or *BRCA2* (GenBank reference sequence NG_012772.3)

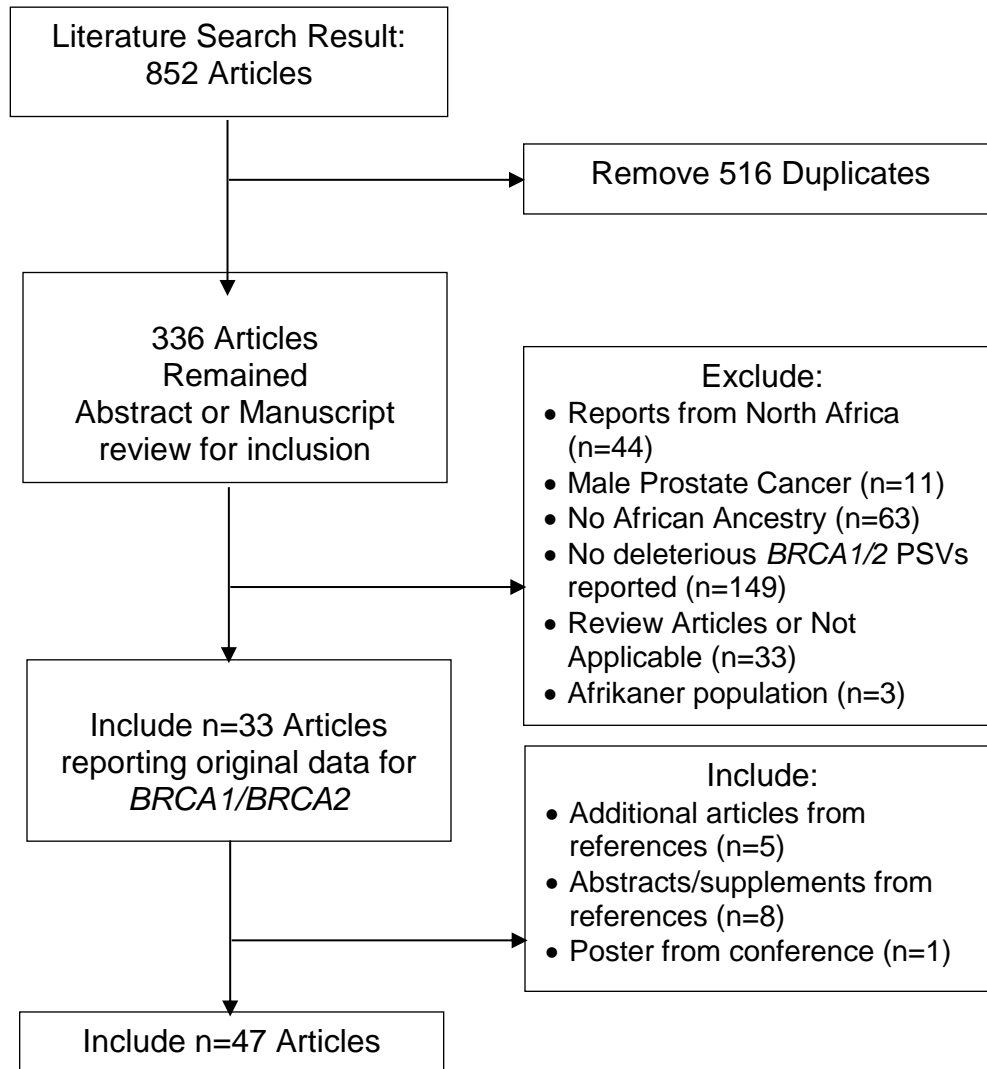


Figure 2: *BRCA1* (GenBank reference sequence: NG_005905.2) PSVs by Determination of African Origin and Self-Identification. a. Likely or Possible African Origin, b. Unlikely African Origin.

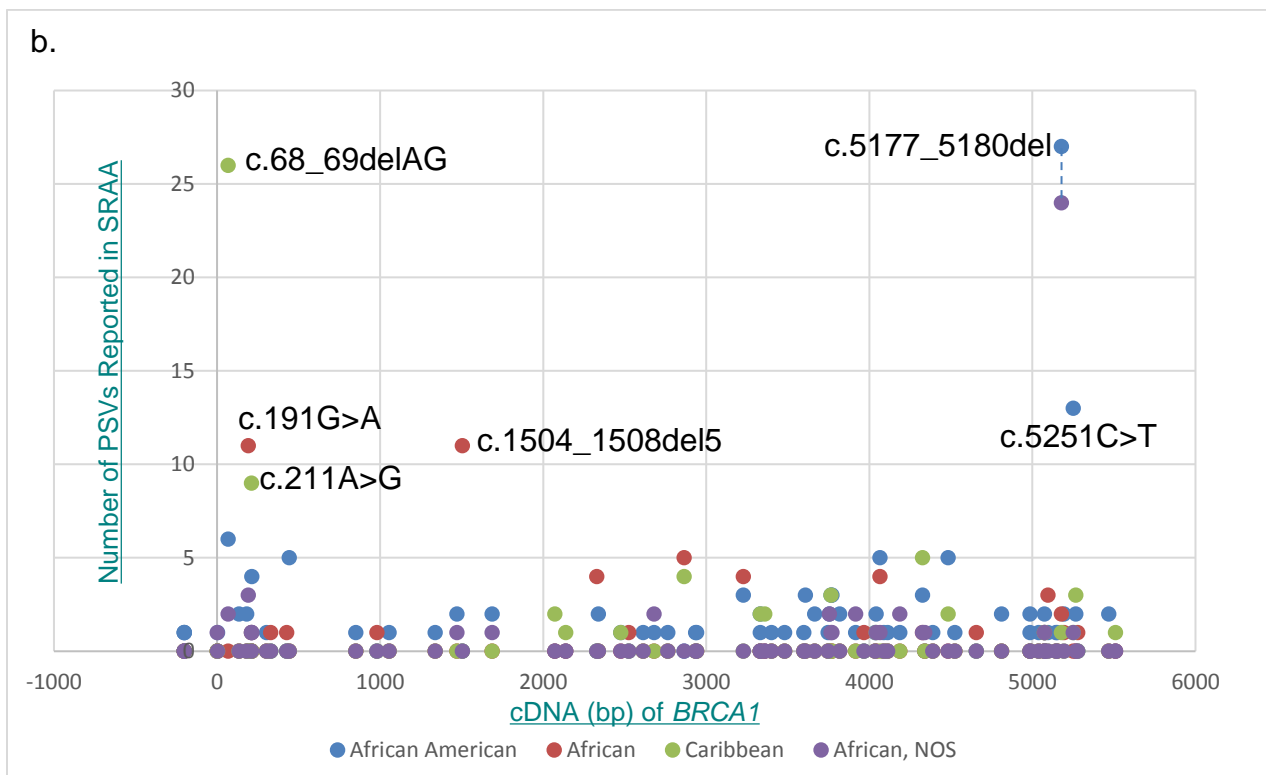
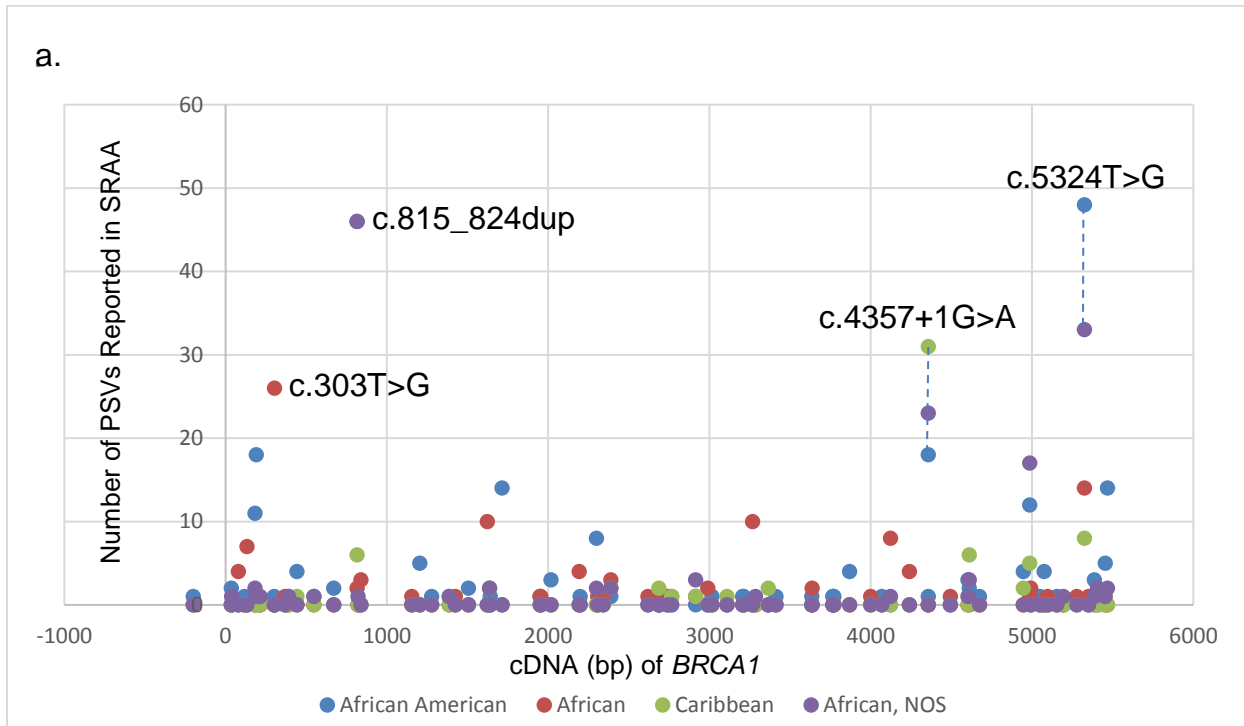


Figure 3: *BRCA2* (GenBank reference sequence NG_012772.3) PSVs by Determination of African Origin and Self-Identification. a. Likely or Possible African Origin, b. Unlikely African Origin.

