A likelihood ratio approach for utilizing case-control data in the clinical classification of rare sequence variants: application to *BRCA1* and *BRCA2*

Supplementary Table S5. Case-control likelihood ratios and evidence for assignment to ACMG/AMP code strengths for the 92 *BRCA1* and *BRCA2* variants, using country-specific analyses with different penetrance models

							Case Carriers		Control Carriers		Country-stratified analysis (main analysis) [Dorling et al. 2021]		Country-stratified analysis using country-specific incidences [Dorling et al. 2021]		Country-stratified analysis [Kuchenbaecker et al. 2017]		Country-stratified analysis [Antoniou et al. 2003]		Country-stratified analysis [Li et al. 2021]		Country-unstratified analysis [Dorling et al. 2021]	
Gene	Variant_ID (GRCh37/hg19)	HGVS nucleotide	HGVS protein	ClinVar Class	Total cases	Total controls	N (Frequency)	†Age	N (Frequency)	†Age	LR	ACMG/AMP evidence strength PS4‡	LR	ACMG/AMP evidence strength PS4‡	LR	ACMG/AMP evidence strength PS4‡	LR	ACMG/AMP evidence strength PS4‡	LR	ACMG/AMP evidence strength PS4‡	LR	ACMG/AMP evidence strength PS4‡
BRCA1	chr17_41196683_C_T	c.*1012A>G	p.?	-	72564	50781	1 (1.38×10^{-5})	55	1 (1.97×10^{-5})	56	0.09	Benign Moderate	0.09	Benign Moderate	0.03	Benign Strong	0.01	Benign Strong	0.17	Benign Moderate	0.14	Benign Moderate
BRCA1	chr17_41197404_A_G	c.*291C>T	p.?	Uncertain	72523	50754	8 (1.10×10^{-4})	56.4±9.7 (38-69)	12 (2.36×10^{-4})	59.6±12 (27-74)	5.14×10^{-9}	Benign Very Strong	3.11×10^{-9}	Benign Very Strong	2.65×10^{-12}	Benign Very Strong	9.56×10^{-13}	Benign Very Strong	1.96×10^{-7}	Benign Very Strong	1.82×10^{-9}	Benign Very Strong
BRCA1	chr17_41267714_A_T	c.134+29T>A	p.?	-	72453	50706	2 (2.76×10^{-5})	38±1.4 (37-39)	1 (1.97×10^{-5})	42	2.69	No evidence§	2.70	No evidence§	1.93	No evidence	1.74	No evidence	1.74	No evidence	5.92	No evidence§
BRCA1	chr17_41245683_A_G	c.1865C>T	p.(Ala622Val)	Benign	72545	50769	14 (1.93×10^{-4})	58.1±11.2 (39-72)	11 (2.17×10^{-4})	53.6±12.7 (25-77)	7.28×10^{-10}	Benign Very Strong	2.21×10^{-10}	Benign Very Strong	5.41×10^{-13}	Benign Very Strong	5.38×10^{-15}	Benign Very Strong	2.96×10^{-7}	Benign Very Strong	5.72×10^{-9}	Benign Very Strong
BRCA1	chr17_41245577_C_T	c.1971A>G	p.(=)	Benign	72561	50778	4 (5.51×10^{-5})	47±6.9 (37-52)	1 (1.97×10^{-5})	56	3.05	No evidence§	3.63	No evidence§	1.42	No evidence	0.69	No evidence	4.11	No evidence§	1.44	No evidence
BRCA1	chr17_41245465_T_C	c.2083G>A	p.(Asp695Asn)	Conflicting	72564	50782	4 (5.51×10^{-5})	44.5±10.9 (32-58)	7 (1.38×10^{-4})	57.4±13.6 (38-75)	1.30×10^{-4}	Benign Very Strong	9.76×10^{-5}	Benign Very Strong	2.07×10^{-6}	Benign Very Strong	1.24×10^{-5}	Benign Very Strong	1.11×10^{-3}	Benign Very Strong	6.68×10^{-5}	Benign Very Strong
BRCA1	chr17_41244982_T_C	c.2566T>C	p.(Tyr856His)	Benign	72565	50780	2 (2.76×10^{-5})	59±0 (59-59)	1 (1.97×10^{-5})	55	0.11	Benign Moderate	0.11	Benign Moderate	0.04	Benign Strong	0.01	Benign Strong	0.23	Benign Moderate	0.11	Benign Moderate
BRCA1	chr17_41244886_A_G	c.2662C>T	p.(His888Tyr)	Conflicting	72557	50774	4 (5.51×10^{-5})	52.5±4.2 (47-57)	5 (9.85×10^{-5})	53.2±7.4 (46-65)	6.83×10^{-5}	Benign Very Strong	7.11×10^{-5}	Benign Very Strong	2.16×10^{-6}	Benign Very Strong	8.54×10^{-8}	Benign Very Strong	6.33×10^{-4}	Benign Very Strong	1.23×10^{-4}	Benign Very Strong
BRCA1	chr17_41243840_A_C	c.3708T>G	p.(Asn1236Lys)	Benign	72562	50779	45 (6.20×10^{-4})	57.9±10.8 (34-74)	45 (8.86×10^{-4})	54.8±10.4 (30-78)	4.93×10^{-34}	Benign Very Strong	2.77×10^{-35}	Benign Very Strong	8.53×10^{-48}	Benign Very Strong	6.28×10^{-53}	Benign Very Strong	1.94×10^{-25}	Benign Very Strong	-	-
BRCA1	chr17_41243655_GAA_INDEL	c.3891_3893delTTC	p.(Ser1298del)	Uncertain	72563	50781	-	-	2 (3.94×10^{-5})	43±1.4 (42-44)	0.04	Benign Strong	0.04	Benign Strong	0.02	Benign Strong	6.61×10^{-3}	Benign Strong	0.05	Benign Moderate	0.02	Benign Strong
BRCA1	chr17_41243494_C_T	c.4054G>A	p.(Glu1352Lys)	Uncertain	72557	50777	1 (1.38×10^{-5})	65	-	-	0.64	No evidence	0.64	No evidence	0.59	No evidence	0.58	No evidence	0.83	No evidence	0.73	No evidence
BRCA1	chr17_41243449_C_T	c.4096+3A>G	p.?	Uncertain	72562	50778	4 (5.51×10^{-5})	63.5±10.8 (51-74)	1 (1.97×10^{-5})	69	0.20	Benign Moderate	0.19	Benign Moderate	0.09	Benign Moderate	0.02	Benign Strong	0.32	Benign Supporting	0.06	Benign Moderate
BRCA1	chr17_41243033_C_T	c.4113G>A	p.(=)	Likely benign	72563	50781	8 (1.10×10^{-4})	57.9±16.2 (33-80)	1 (1.97×10^{-5})	66	0.56	No evidence	0.39	Benign Supporting	0.23	Benign Moderate	0.05	Benign Strong	1.51	No evidence	0.74	No evidence
BRCA1	chr17_41234451_A_G	c.4327C>T	p.(Arg1443*)	Pathogenic	72558	50781	11 (1.52×10^{-4})	41±8.8 (26-54)	3 (5.91×10^{-5})	63±8.7 (57-73)	526.71	Pathogenic Very Strong	879.97	Pathogenic Very Strong	72.34	Pathogenic Strong	125.77	Pathogenic Strong	348.42	Pathogenic Strong	336.34	Pathogenic Strong
BRCA1	chr17_41251882_T_G	c.457A>C	p.(Ser153Arg)	Conflicting	72559	50779	7 (9.65×10^{-5})	49.9±12.5 (27-62)	3 (5.91×10^{-5})	57.7±11.4 (45-67)	0.36	Benign Supporting	0.24	Benign Supporting	0.14	Benign Moderate	9.38×10^{-3}	Benign Strong	0.64	No evidence	0.08	Benign Moderate
BRCA1	chr17_41226348_C_T	c.4675G>A	p.(Glu1559Lys)	Pathogenic	72546	50770	1 (1.38×10^{-5})	25	2 (3.94×10^{-5})	47.5±13.4 (38-57)	0.23	Benign Supporting	0.19	Benign Moderate	0.15	Benign Moderate	0.05	Benign Strong	0.38	Benign Supporting	0.29	Benign Supporting
BRCA1	chr17_41219642_C_T	c.5057A>G	p.(His1686Arg)	(Likely) pathogenic	72566	50779	1 (1.38×10^{-5})	31	-	-	5.92	No evidence§	5.92	No evidence§	6.40	No evidence§	7.54	No evidence§	4.06	No evidence§	6.74	No evidence§
BRCA1	chr17_41219619_C_G	c.5074+6C>G	p.?	Benign	72525	50754	22 (3.03×10^{-4})	55.7±12.1 (29-72)	5 (9.85×10^{-5})	56.6±10.7 (46-72)	1.05×10^{-3}	Benign Very Strong	3.18×10^{-4}	Benign Very Strong	1.81×10^{-5}	Benign Very Strong	8.68×10^{-6}	Benign Very Strong	0.05	Benign Moderate	2.32×10^{-3}	Benign Very Strong
BRCA1	chr17_41215947_T_G	c.5096G>T	p.(Arg1699Leu)	Uncertain	72560	50780	17 (2.34×10^{-4})	50.6±15.9 (24-76)	3 (5.91×10^{-5})	63.7±4.2 (59-67)	307.47	Pathogenic Strong	304.28	Pathogenic Strong	63.34	Pathogenic Strong	2.30	No evidence§	256.46	Pathogenic Strong	255.53	Pathogenic Strong
BRCA1	chr17_41209164_C_T	c.5194-12G>A	p.?	Pathogenic	72564	50782	1 (1.38×10^{-5})	65	-	-	0.52	No evidence	0.49	No evidence	0.47	Benign Supporting	0.49	No evidence	0.67	No evidence	0.73	No evidence
BRCA1	chr17_41203189_A_G	c.5278-55C>T	p.?	-	72559	50778	1 (1.38×10^{-5})	28	-	-	9.31	No evidence§	8.23	No evidence§	19.00	Pathogenic Strong	6.78	No evidence§	4.54	No evidence§	10.05	No evidence§
BRCA1	chr17_41203002_A_G	c.5332+78C>T	p.?	Likely benign	72560	50780	8 (1.10×10^{-4})	58.8±12.7 (37-71)	4 (7.88×10^{-5})	67.5±6.8 (62-76)	5.50×10^{-3}	Benign Strong	2.19×10^{-3}	Benign Very Strong	4.22×10^{-4}	Benign Very Strong	1.52×10^{-3}	Benign Very Strong	0.02	Benign Strong	1.72×10^{-3}	Benign Very Strong
BRCA1	chr17_41201198_A_C	c.5346G>T	p.(Trp1782Cys)	Not Provided	72560	50778	-	-	1 (1.97×10^{-5})	55	0.25	Benign Supporting	0.25	Benign Supporting	0.14	Benign Moderate	0.07	Benign Moderate	0.36	Benign Supporting	0.16	Benign Moderate
BRCA1	chr17_41247921_C_G	c.612G>C	p.(Leu204Phe)	Conflicting	72320	50643	7 (9.68×10^{-5})	59.9±5.8 (49-67)	17 (3.36×10^{-4})	57.5±10.2 (45-74)	4.23×10^{-13}	Benign Very Strong	2.92×10^{-13}	Benign Very Strong	8.97×10^{-17}	Benign Very Strong	8.46×10^{-19}	Benign Very Strong	5.10×10^{-11}	Benign Very Strong	1.02×10^{-14}	Benign Very Strong
BRCA2	chr13_32972834_A_INDEL	c.10184del	p.(Glu3395Glyfs*32)	Conflicting	72549	50774	2 (2.76×10^{-5})	56±12.7 (47-65)	-	-	1.47	No evidence	1.41	No evidence	1.22	No evidence	1.38	No evidence	1.88	No evidence	1.76	No evidence
BRCA2	chr13_32906711_G_T	c.1096T>G	p.(Leu366Val)	Conflicting	72447	50706	1 (1.38×10^{-5})	52	3 (5.92×10^{-5})	54±22.9 (37-80)	0.04	Benign Strong	0.03	Benign Strong	0.01	Benign Strong	0.04	Benign Strong	0.05	Benign Strong	0.04	Benign Strong
BRCA2	chr13_32907078_G_T	c.1463T>G	p.(Ile488Arg)	Uncertain	72559	50777	1 (1.38×10^{-5})	74	4 (7.88×10^{-5})	55.8±13 (38-66)	6.44×10^{-3}	Benign Strong	6.22×10^{-3}	Benign Strong	2.88×10^{-4}	Benign Very Strong	2.17×10^{-4}	Benign Very Strong	8.52×10^{-3}	Benign Strong	4.57×10^{-3}	Benign Strong
BRCA2	chr13_32907359_A_C	c.1744A>C	p.(Thr582Pro)	Benign	72564	50781	1 (1.38×10^{-5})	55	1 (1.97×10^{-5})	65	0.35	Benign Supporting	0.32	Benign Supporting	0.11	Benign Moderate	0.09	Benign Moderate	0.31	Benign Supporting	0.32	Benign Supporting
BRCA2	chr13_32907403_C_T	c.1788T>C	p.(=)	Benign	72548	50772	34 (4.69×10^{-4})	58±13.5 (31-76)	18 (3.55×10^{-4})	54.6±16 (22-75)	3.02×10^{-5}	Benign Very Strong	1.10×10^{-5}	Benign Very Strong	6.94×10^{-12}	Benign Very Strong	1.01×10^{-7}	Benign Very Strong	1.51×10^{-4}	Benign Very Strong	1.54×10^{-7}	Benign Very Strong
BRCA2	chr13_32893377_T_G	c.231T>G	p.(=)	Benign	72559	50774	2 (2.76×10^{-5})	34.5±6.4 (30-39)	2 (3.94×10^{-5})	55±15.6 (44-66)	0.67	No evidence	0.58	No evidence	0.21	Benign Moderate	0.23	Benign Supporting	0.43	Benign Supporting	1.29	No evidence
BRCA2	chr13_32911030_A_C	c.2538A>C	p.(=)	Benign	72560	50780	18 (2.48×10^{-4})	57.3±10.7 (33-73)	8 (1.58×10^{-4})	56.8±15.6 (30-74)	4.40×10^{-3}	Benign Strong	3.62×10^{-3}	Benign Strong	1.55×10^{-6}	Benign Very Strong	1.23×10^{-4}	Benign Very Strong	5.03×10^{-3}	Benign Strong	1.06×10^{-3}	Benign Very Strong
BRCA2	chr13_32911172_A_G	c.2680G>A	p.(Val894Ile)	Benign	72557	50777	18 (2.48×10^{-4})	54.2±11.3 (35-74)	16 (3.15×10^{-4})	54.3±7.7 (43-69)	2.76×10^{-8}	Benign Very Strong	3.07×10^{-8}	Benign Very Strong	2.16×10^{-16}	Benign Very Strong	3.05×10^{-13}	Benign Very Strong	2.44×10^{-7}	Benign Very Strong	4.42×10^{-8}	Benign Very Strong
BRCA2	chr13_32911565_A_G	c.3073A>G	p.(Lys1025Glu)	Conflicting	72490	50734	15 (2.07×10^{-4})	60.3±11.9 (35-74)	7 (1.38×10^{-4})	52.4±17.3 (22-67)	2.40×10^{-4}	Benign Very Strong	1.71×10^{-4}	Benign Very Strong	1.54×10^{-7}	Benign Very Strong	3.21×10^{-7}	Benign Very Strong	8.15×10^{-4}	Benign Very Strong	4.17×10^{-4}	Benign Very Strong
BRCA2	chr13_32911644_C_T	c.3152T>C	p.(Leu1051Ser)	Uncertain	72557	50778	4 (5.51×10^{-5})	67±7.7 (60-77)	-	-	0.54	No evidence	0.43	Benign Supporting	0.29	Benign Supporting	0.42	Benign Supporting	0.92	No evidence	0.50	No evidence
BRCA2	chr13_32893467_A_G	c.316+5G>A	p.?	Pathogenic	72564	50776	1 (1.38×10^{-5})	40	-	-	2.54	No evidence§	2.63	No evidence§	2.84	No evidence§	2.85	No evidence§	2.68	No evidence§	2.19	No evidence§
BRCA2	chr13_32911756_C_T	c.3264T>C	p.(=)	Benign	72564	50780	11 (1.52×10^{-4})	55.7±9.6 (39-68)	6 (1.18×10^{-4})	61.5±9.8 (46-72)	4.50×10^{-3}	Benign Strong	3.10×10^{-3}	Benign Strong	1.91×10^{-6}	Benign Very Strong	6.75×10^{-5}	Benign Very Strong	8.65×10^{-3}	Benign Strong	3.42×10^{-3}	Benign Strong
BRCA2	chr13_32912174_A_G	c.3682A>G	p.(Asn1228Asp)	Benign	72533	50756	21 (2.90×10^{-4})	57.7±9.9 (35-73)	11 (2.17×10^{-4})	48.5±11.4 (29-71)	2.90×10^{-6}	Benign Very Strong	2.05×10^{-6}	Benign Very Strong	5.31×10^{-12}	Benign Very Strong	4.43×10^{-8}	Benign Very Strong	1.96×10^{-5}	Benign Very Strong	5.81×10^{-6}	Benign Very Strong
BRCA2	chr13_32890548_C_T	c.-39-11C>T	p.?	Uncertain	72565	50782	-	-	1 (1.97×10^{-5})	45	0.37	Benign Supporting	0.37	Benign Supporting	0.21	Benign Moderate	0.36	Benign Supporting	0.37	Benign Supporting	0.26	Benign Supporting
BRCA2	chr13_32890547_INDEL_TCT	c.-39-12_-39-10del	p.?	Conflicting	72563	50781	3 (4.13×10^{-5})	58.3±9.5 (51-69)	6 (1.18×10^{-4})	54.7±9.5 (44-68)	2.57×10^{-4}	Benign Very Strong	2.61×10^{-4}	Benign Very Strong	8.22×10^{-7}	Benign Very Strong	4.61×10^{-6}	Benign Very Strong	3.36×10^{-4}	Benign Very Strong	3.17×10^{-4}	Benign Very Strong
BRCA2	chr13_32890555_G_T	c.-39-4G>T	p.?	Benign	72564	50779	1 (1.38×10^{-5})	65	2 (3.94×10^{-5})	57±5.7 (53-61)	0.04	Benign Strong	0.04	Benign Strong	5.33×10^{-3}	Benign Strong	5.20×10^{-3}	Benign Strong	0.06	Benign Moderate	0.05	Benign Moderate
BRCA2	chr13_32899354_A_G	c.425+33A>G	p.?	(Likely) benign	72417	50701	46 (6.35×10^{-4})	58.7±9.6 (39-74)	40 (7.89×10^{-4})	54.6±11.9 (21-78)	8.39×10^{-20}	Benign Very Strong	2.43×10^{-20}	Benign Very Strong	4.77×10^{-37}	Benign Very Strong	4.02×10^{-30}	Benign Very Strong	1.01×10^{-17}	Benign Very Strong	-	-
BRCA2	chr13_32912868_A_G	c.4376A>G	p.(Asn1459Ser)	Conflicting	72472	50739	1 (1.38×10^{-5})	67	-	-	0.80	No evidence	0.80	No evidence	0.70	No evidence	0.71	No evidence	0.95	No evidence	0.85	No evidence
BRCA2	chr13_32913148_C_T	c.4656T>C	p.(=)	Likely benign	72558	50780	9 (1.24×10^{-4})	54.3±11.4 (33-67)	13 (2.56×10^{-4})	52.2±8.1 (41-67)	2.23×10^{-7}	Benign Very Strong	2.21×10^{-7}	Benign Very Strong	1.03×10^{-12}	Benign Very Strong	1.46×10^{-10}	Benign Very Strong	1.34×10^{-6}	Benign Very Strong	1.42×10^{-7}	Benign Very Strong
BRCA2	chr13_32913173_C_A	c.4681C>A	p.(His1561Asn)	Conflicting	72560	50782	3 (4.13×10^{-5})	63.3±4.7 (58-67)	1 (1.97×10^{-5})	70	0.38	Benign Supporting	0.37	Benign Supporting	0.12	Benign Moderate	0.40	Benign Supporting	0.42	Benign Supporting	0.21	Benign Moderate
BRCA2	chr13_32900313_C_T	c.475+26T>C	p.?	Likely benign	72469	50740	7 (9.66×10^{-5})	48.1±11.4 (33-61)	2 (3.94×10^{-5})	53.5±16.3 (42-65)	4.87	No evidence§	5.18	No evidence§	0.69	No evidence	1.64	No evidence	3.72	No evidence§	5.98	No evidence§
BRCA2	chr13_32900405_A_C	c.502C>A	p.(Pro168Thr)	Benign	72558	50779	12 (1.65×10^{-4})	57±11.4 (33-71)	4 (7.88×10^{-5})	56.8±12.7 (41-68)	9.31×10^{-3}	Benign Strong	8.30×10^{-3}	Benign Strong	3.26×10^{-5}	Benign Very Strong	1.19×10^{-4}	Benign Very Strong	0.03	Benign Strong	0.05	Benign Strong
BRCA2	chr13_32913910_A_G	c.5418A>G	p.(=)	Benign	72543	50766	9 (1.24×10^{-4})	55±9.5 (39-68)	7 (1.38×10^{-4})	59±11.1 (44-72)	8.24×10^{-4}	Benign Very Strong	5.87×10^{-4}	Benign Very Strong	2.47×10^{-7}	Benign Very Strong	1.19×10^{-5}	Benign Very Strong	1.61×10^{-3}	Benign Very Strong	8.88×10^{-4}	Benign Very Strong
BRCA2	chr13_32914127_A_G	c.5635G>A	p.(Glu1879Lys)	Conflicting	72565	50780	14 (1.93×10^{-4})	55.2±9.6 (38-66)	10 (1.97×10^{-4})	57.6±5.5 (48-67)	4.11×10^{-4}	Benign Very Strong	3.57×10^{-4}	Benign Very Strong	3.40×10^{-9}	Benign Very Strong	7.85×10^{-8}	Benign Very Strong	1.91×10^{-3}	Benign Very Strong	1.86×10^{-5}	Benign Very Strong
BRCA2	chr13_32900691_A_G	c.572A>G	p.(Asp191Gly)	Not Provided	72563	50780	2 (2.76×10^{-5})	54.5±31.8 (32-77)	-	-	3.53	No evidence§	3.72	No evidence§	3.52	No evidence§	3.72	No evidence§	3.05	No evidence§	3.25	No evidence§
BRCA2	chr13_32900694_C_T	c.575T>C	p.(Met192Thr)	Conflicting	72555	50773	6 (8.27×10^{-5})	59.3±6.4 (50-67)	-	-	0.44	Benign Supporting	0.44	Benign Supporting	0.05	Benign Moderate	0.22	Benign Moderate	0.65	No evidence	0.97	No evidence
BRCA2	chr13_32900706_A_G	c.587G>A	p.(Ser196Asn)	Uncertain	72565	50779	1 (1.38×10^{-5})	67	1 (1.97×10^{-5})	38	0.26	Benign Supporting	0.26	Benign Supporting	0.17	Benign Moderate	0.22	Benign Moderate	0.33	Benign Supporting	0.29	Benign Supporting
BRCA2	chr13_32914467_C_T	c.5975C>T	p.(Ser1992Leu)	Conflicting	72560	50780	2 (2.76×10^{-5})	60±9.9 (53-67)	1 (1.97×10^{-5})	45	0.32	Benign Supporting	0.36	Benign Supporting	0.12	Benign Moderate	0.25	Benign Supporting	0.35	Benign Supporting	0.26	Benign Supporting
BRCA2	chr13_32914470_C_T	c.5978T>C	p.(Leu1993Ser)	-	72547	50766	3 (4.14×10^{-5})	62±17.3 (43-77)	1 (1.97×10^{-5})	55	0.30	Benign Supporting	0.27	Benign Supporting	0.07	Benign Moderate	0.10	Benign Moderate	0.56	No evidence	0.30	Benign Supporting
BRCA2	chr13_32915240_A_G	c.6748A>G	p.(Thr2250Ala)	Benign	72566	50779	17 (2.34×10^{-4})	54.1±10.5 (31-71)	8 (1.58×10^{-4})	61.4±7.9 (48-70)	0.14	Benign Moderate	0.12	Benign Moderate	3.24×10^{-5}	Benign Very Strong	3.15×10^{-4}	Benign Very Strong	0.10	Benign Moderate	1.89×10^{-3}	Benign Very Strong
BRCA2	chr13_32903812_A_T	c.681+183T>A	p.?	-	72485	50738	2 (2.76×10^{-5})	59.5±10.6 (52-67)	-	-	0.58	No evidence	0.60	No evidence	0.32	Benign Supporting	0.43	Benign Supporting	0.66	No evidence	1.00	No evidence
BRCA2	chr13_32918701_A_C	c.6848C>A	p.(Pro2283His)	Uncertain	72547	50769	3 (4.14×10^{-5})	60±20 (40-80)	1 (1.97×10^{-5})	68	1.20	No evidence	1.12	No evidence	0.93	No evidence	0.17	Benign Moderate	1.72	No evidence	0.64	No evidence
BRCA2	chr13_32918769_C_G	c.6916G>C	p.(Ala2306Pro)	Uncertain	72312	50628	3 (4.15×10^{-5})	54.3±16.5 (38-71)	2 (3.95×10^{-5})	66±5.7 (62-70)	0.23	Benign Supporting	0.17	Benign Moderate	0.03	Benign Strong	0.08	Benign Moderate	0.16	Benign Moderate	0.29	Benign Supporting
BRCA2	chr13_32918788_A_T	c.6935A>T	p.(Asp2312Val)	Benign	72417	50682	6 (8.29×10^{-5})	55.5±16.3 (32-72)	2 (3.95×10^{-5})	59.5±3.5 (57-62)	0.24	Benign Supporting	0.22	Benign Moderate	0.02	Benign Strong	0.02	Benign Strong	0.37	Benign Supporting	0.36	Benign Supporting
BRCA2	chr13_32919384_G_T	c.6937+594T>G	p.?	Benign	72531	50758	42 (5.79×10^{-4})	55.2±12.4 (30-79)	16 (3.15×10^{-4})	51.9±11.1 (37-71)	3.35×10^{-4}	Benign Very Strong	2.88×10^{-4}	Benign Very Strong	2.25×10^{-11}	Benign Very Strong	1.03×10^{-7}	Benign Very Strong	3.82×10^{-3}	Benign Strong	-	-
BRCA2	chr13_32921033_A_G	c.7007G>A	p.(Arg2336His)	Pathogenic	72565	50781	4 (5.51×10^{-5})	46±20.1 (28-74)	3 (5.91×10^{-5})	56±11.5 (47-69)	1.13	No evidence	0.97	No evidence	0.54	No evidence	0.28	Benign Supporting	0.87	No evidence	0.51	No evidence
BRCA2	chr13_32929309_A_G	c.7319A>G	p.(His2440Arg)	Benign	72565	50781	8 (1.10×10^{-4})	55.2±9.8 (39-68)	6 (1.18×10^{-4})	61.5±9.8 (46-72)	3.69×10^{-3}	Benign Strong	3.10×10^{-3}	Benign Strong	3.66×10^{-6}	Benign Very Strong	5.62×10^{-5}	Benign Very Strong	5.61×10^{-3}	Benign Strong	3.44×10^{-3}	Benign Strong
BRCA2	chr13_32930598_T_C	c.7469T>C	p.(Ile2490Thr)	Benign	72560	50777	35 (4.82×10^{-4})	50.2±10.6 (31-69)	19 (3.74×10^{-4})	55.3±12.7 (31-73)	3.93×10^{-3}	Benign Strong	4.79×10^{-3}	Benign Strong	5.24×10^{-11}	Benign Very Strong	2.33×10^{-5}	Benign Very Strong	1.86×10^{-3}	Benign Very Strong	1.17×10^{-4}	Benign Very Strong
BRCA2	chr13_32931973_A_C	c.7712A>C	p.(Glu2571Ala)	-	72559	50779	2 (2.76×10^{-5})	59.5±7.8 (54-65)	3 (5.91×10^{-5})	49±3.6 (46-53)	0.01	Benign Strong	0.01	Benign Strong	6.34×10^{-4}	Benign Very Strong	3.50×10^{-3}	Benign Strong	0.02	Benign Strong	0.01	Benign Strong
BRCA2	chr13_32936671_A_G	c.7817A>G	p.(Asp2606Gly)	-	72554	50777	4 (5.51×10^{-5})	64.5±13.7 (44-73)	-	-	0.99	No evidence	0.90	No evidence	0.55	No evidence	0.57	No evidence	1.55	No evidence	1.07	No evidence
BRCA2	chr13_32936680_A_G	c.7826G>A	p.(Gly2609Asp)	Likely pathogenic	72563	50781	2 (2.76×10^{-5})	51.5±0.7 (51-52)	1 (1.97×10^{-5})	56	0.20	Benign Moderate	0.23	Benign Supporting	0.03	Benign Strong	0.06	Benign Moderate	0.24	Benign Supporting	0.29	Benign Supporting
BRCA2	chr13_32936722_A_G	c.7868A>G	p.(His2623Arg)	(Likely) pathogenic	72545	50765	5 (6.89×10^{-5})	47.8±10.6 (35-64)	2 (3.94×10^{-5})	56.5±16.3 (45-68)	0.88	No evidence	0.95	No evidence	0.10	Benign Moderate	0.27	Benign Supporting	0.85	No evidence	1.38	No evidence
BRCA2	chr13_32936724_C_T	c.7870T>C	p.(Tyr2624His)	-	72561	50779	3 (4.13×10^{-5})	57.3±14.2 (41-67)	-	-	2.56	No evidence§	2.47	No evidence§	3.06	No evidence§	2.76	No evidence§	3.59	No evidence§	1.60	No evidence
BRCA2	chr13_32936725_A_G	c.7871A>G	p.(Tyr2624Cys)	Uncertain	72533	50769	3 (4.14×10^{-5})	45.7±6.1 (39-51)	2 (3.94×10^{-5})	62.5±0.7 (62-63)	1.10	No evidence	1.13	No evidence	0.28	Benign Supporting	0.16	Benign Moderate	0.69	No evidence	0.82	No evidence
BRCA2	chr13_32936742_A_C	c.7888A>C	p.(Lys2630Gln)	Likely pathogenic	72544	50775	-	-	3 (5.91×10^{-5})	55.7±10.2 (44-63)	0.01	Benign Strong	0.01	Benign Strong	3.40×10^{-4}	Benign Very Strong	1.00×10^{-3}	Benign Very Strong	0.01	Benign Strong	0.02	Benign Strong
BRCA2	chr13_32936782_C_G	c.7928C>G	p.(Ala2643Gly)	Conflicting	72409	50694	3 (4.14×10^{-5})	53.3±7 (46-60)	3 (5.92×10^{-5})	58.7±6.7 (51-63)	0.04	Benign Strong	0.05	Benign Strong	2.26×10^{-3}	Benign Very Strong	2.30×10^{-3}	Benign Very Strong	0.05	Benign Moderate	0.04	Benign Strong
BRCA2	chr13_32937333_A_G	c.7994A>G	p.(Asp2665Gly)	Benign	72555	50775	33 (4.55×10^{-4})	59±11.6 (29-79)	27 (5.32×10^{-4})	50.8±14.4 (23-80)	3.51×10^{-13}	Benign Very Strong	1.37×10^{-13}	Benign Very Strong	2.04×10^{-23}	Benign Very Strong	4.36×10^{-20}	Benign Very Strong	8.95×10^{-12}	Benign Very Strong	-	-
BRCA2	chr13_32906415_A_G	c.800G>A	p.(Gly267Glu)	Conflicting	72553	50778	7 (9.65×10^{-5})	50±7.7 (39-63)	2 (3.94×10^{-5})	51±12.7 (42-60)	3.09	No evidence§	3.37	No evidence§	0.18	Benign Moderate	1.17	No evidence	2.74	No evidence§	3.20	No evidence§
BRCA2	chr13_32937396_C_T	c.8057T>C	p.(Leu2686Pro)	(Likely) pathogenic	72547	50767	2 (2.76×10^{-5})	58.5±7.8 (53-64)	1 (1.97×10^{-5})	68	0.17	Benign Moderate	0.17	Benign Moderate	0.04	Benign Strong	0.04	Benign Strong	0.19	Benign Moderate	0.28	Benign Supporting
BRCA2	chr13_32937506_C_G	c.8167G>C	p.(Asp2723His)	Pathogenic	72392	50680	18 (2.49×10^{-4})	48.5±10.9 (27-74)	1 (1.97×10^{-5})	64	8193.33	Pathogenic Very Strong	9472.75	Pathogenic Very Strong	1784.63	Pathogenic Very Strong	3934.35	Pathogenic Very Strong	9412.08	Pathogenic Very Strong	17698.20	Pathogenic Very Strong
BRCA2	chr13_32937582_A_G	c.8243G>A	p.(Gly2748Asp)	Pathogenic	72565	50780	2 (2.76×10^{-5})	45.5±2.1 (44-47)	-	-	3.60	No evidence§	3.28	No evidence§	3.20	No evidence§	3.82	No evidence§	4.31	No evidence§	4.30	No evidence§
BRCA2	chr13_32906446_T_G	c.831T>G	p.(Asn277Lys)	Conflicting	72558	50776	20 (2.76×10^{-4})	58±14.1 (33-78)	12 (2.36×10^{-4})	55.5±14.5 (22-71)	6.16×10^{-6}	Benign Very Strong	3.75×10^{-6}	Benign Very Strong	9.75×10^{-12}	Benign Very Strong	1.08×10^{-9}	Benign Very Strong	1.15×10^{-5}	Benign Very Strong	1.94×10^{-5}	Benign Very Strong
BRCA2	chr13_32944549_A_T	c.8342A>T	p.(Asn2781Ile)	Conflicting	72384	50656	4 (5.53×10^{-5})	61.5±9.4 (50-73)	3 (5.92×10^{-5})	60±10.8 (51-72)	7.12×10^{-3}	Benign Strong	7.28×10^{-3}	Benign Strong	1.12×10^{-4}	Benign Very Strong	1.13×10^{-3}	Benign Very Strong	0.02	Benign Strong	8.76×10^{-3}	Benign Strong
BRCA2	chr13_32944563_A_G	c.8356G>A	p.(Ala2786Thr)	Conflicting	72565	50781	3 (4.13×10^{-5})	49±18.3 (29-65)	1 (1.97×10^{-5})	52	1.19	No evidence	1.28	No evidence	1.31	No evidence	0.73	No evidence	1.22	No evidence	1.06	No evidence
BRCA2	chr13_32944713_A_G	c.8487+19A>G	p.?	Benign	72545	50773	13 (1.79×10^{-4})	57.4±10.8 (33-71)	12 (2.36×10^{-4})	63.6±9.2 (43-75)	1.59×10^{-6}	Benign Very Strong	6.48×10^{-7}	Benign Very Strong	3.32×10^{-12}	Benign Very Strong	2.95×10^{-10}	Benign Very Strong	1.89×10^{-6}	Benign Very Strong	4.60×10^{-7}	Benign Very Strong
BRCA2	chr13_32953453_A_G	c.8755-1G>A	p.?	Pathogenic	72562	50776	3 (4.13×10^{-5})	31.7±1.2 (31-33)	-	-	41.18	Pathogenic Strong	39.64	Pathogenic Strong	65.19	Pathogenic Strong	71.35	Pathogenic Strong	20.71	Pathogenic Strong	75.29	Pathogenic Strong
BRCA2	chr13_32953473_A_G	c.8774A>G	p.(Gln2925Arg)	Uncertain	72561	50781	2 (2.76×10^{-5})	51.5±2.1 (50-53)	-	-	1.53	No evidence	1.61	No evidence	0.62	No evidence	1.25	No evidence	1.38	No evidence	1.41	No evidence
BRCA2	chr13_32953529_A_T	c.8830A>T	p.(Ile2944Phe)	Benign	72510	50745	9 (1.24×10^{-4})	50.4±8.8 (39-66)	9 (1.77×10^{-4})	52.6±7 (38-59)	3.89×10^{-4}	Benign Very Strong	8.80×10^{-4}	Benign Very Strong	2.39×10^{-8}	Benign Very Strong	1.11×10^{-6}	Benign Very Strong	3.57×10^{-3}	Benign Strong	1.22×10^{-4}	Benign Very Strong
BRCA2	chr13_32954180_C_T	c.9154C>T	p.(Arg3052Trp)	Pathogenic	72563	50779	10 (1.38×10^{-4})	49.1±15.6 (30-78)	1 (1.97×10^{-5})	56	86.82	Pathogenic Strong	104.46	Pathogenic Strong	20.23	Pathogenic Strong	42.62	Pathogenic Strong	84.20	Pathogenic Strong	117.18	Pathogenic Strong
BRCA2	chr13_32954340_A_T	c.9256+58A>T	p.?	Likely benign	72345	50651	24 (3.32×10^{-4})	53.9±12.2 (27-75)	14 (2.76×10^{-4})	52.6±10.5 (31-66)	8.70×10^{-7}	Benign Very Strong	1.03×10^{-6}	Benign Very Strong	5.01×10^{-13}	Benign Very Strong	2.52×10^{-11}	Benign Very Strong	4.90×10^{-6}	Benign Very Strong	8.17×10^{-6}	Benign Very Strong
BRCA2	chr13_32968940_A_T	c.9371A>T	p.(Asn3124Ile)	Pathogenic	72548	50755	16 (2.21×10^{-4})	50.3±10.5 (38-74)	-	-	3530.99	Pathogenic Very Strong	4197.75	Pathogenic Very Strong	1337.24	Pathogenic Very Strong	4557.92	Pathogenic Very Strong	5079.21	Pathogenic Very Strong	4957.08	Pathogenic Very Strong
BRCA2	chr13_32969073_A_T	c.9501+3A>T	p.?	Benign	72442	50723	25 (3.45×10^{-4})	53.6±11.1 (32-76)	22 (4.34×10^{-4})	57.6±10.8 (32-73)	6.12×10^{-9}	Benign Very Strong	5.06×10^{-9}	Benign Very Strong	2.30×10^{-18}	Benign Very Strong	8.76×10^{-15}	Benign Very Strong	4.12×10^{-8}	Benign Very Strong	6.08×10^{-10}	Benign Very Strong
BRCA2	chr13_32969079_A_C	c.9501+9A>C	p.?	Benign	72550	50761	25 (3.45×10^{-4})	58.4±10.5 (38-76)	13 (2.56×10^{-4})	49.1±14.1 (25-74)	4.01×10^{-7}	Benign Very Strong	1.70×10^{-7}	Benign Very Strong	1.98×10^{-13}	Benign Very Strong	1.99×10^{-9}	Benign Very Strong	1.09×10^{-5}	Benign Very Strong	1.17×10^{-6}	Benign Very Strong
BRCA2	chr13_32971023_C_T	c.9502-12T>C	p.?	(Likely) benign	72494	50742	30 (4.14×10^{-4})	56.2±11.9 (26-78)	30 (5.91×10^{-4})	52±8.5 (29-74)	3.54×10^{-16}	Benign Very Strong	5.06×10^{-16}	Benign Very Strong	1.89×10^{-30}	Benign Very Strong	4.18×10^{-24}	Benign Very Strong	2.49×10^{-14}	Benign Very Strong	-	-
BRCA2	chr13_32971042_A_G	c.9509A>G	p.(Asp3170Gly)	Benign	72523	50748	6 (8.27×10^{-5})	48.7±14 (32-65)	3 (5.91×10^{-5})	52±21.7 (29-72)	0.78	No evidence	0.71	No evidence	0.06	Benign Moderate	0.55	No evidence	0.87	No evidence	0.71	No evidence
BRCA2	chr13_32971125_C_T	c.9592T>C	p.(Cys3198Arg)	Benign	72506	50747	12 (1.66×10^{-4})	53.8±12 (37-78)	6 (1.18×10^{-4})	54.5±10.8 (38-68)	0.05	Benign Moderate	0.05	Benign Strong	5.98×10^{-5}	Benign Very Strong	5.61×10^{-4}	Benign Very Strong	0.06	Benign Moderate	0.03	Benign Strong
BRCA2	chr13_32972279_C_T	c.9649-20C>T	p.?	Benign	72559	50780	13 (1.79×10^{-4})	55.3±13.2 (34-75)	9 (1.77×10^{-4})	55.4±6.7 (47-65)	2.43×10^{-4}	Benign Very Strong	1.61×10^{-4}	Benign Very Strong	3.85×10^{-8}	Benign Very Strong	3.43×10^{-7}	Benign Very Strong	1.21×10^{-3}	Benign Very Strong	2.20×10^{-4}	Benign Very Strong
BRCA2	chr13_32906579_A_C	c.964A>C	p.(Lys322Gln)	Conflicting	72483	50722	2 (2.76×10^{-5})	56.5±13.4 (47-66)	1 (1.97×10^{-5})	67	0.50	No evidence	0.46	Benign Supporting	0.19	Benign Moderate	0.15	Benign Moderate	0.58	No evidence	0.49	No evidence

† Age: mean±sd (range), ‡Aligned ACMG/AMP evidence strengths are modified following cut-offs resulted from the analysis of simulated datasets; Moderate and Supporting evidence strengths in favor of pathogenicity are noted as "No evidence§"

LR, Likelihood ratio; ACMG/AMP, American College of Medical Genetics and Genomics (ACMG) and Association for Molecular Pathology (AMP); NA, LR value not available due to overflowaing. Variant nomenclature according to: *BRCA1* (NM_007294.4, NP_009225.1), *BRCA2* (NM_000059.3, NP_000050.2).