

Beta, per allele, SD units of eBMD (95% CI)	Beta, per allele, g/cm ² units of eBMD (95% CI)	P-value	Genotype counts, RR RA AA genotypes	AAF
0.2 (0.13, 0.26)	0.024 (0.016, 0.032)	9.40 x 10 ⁻¹⁰	418982 754 1	9.00E-04

Figure 1

Genetic exposure	Beta, per allele, SD units of eBMD (95% CI)	Beta, per allele, g/cm ² units of eBMD (95% CI)	P-value	Genotype counts, RR RA AA genotypes	AAF
pLoF variants, AAF < 1%	0.24 (0.03, 0.44)	0.029 (0.004, 0.053)	0.024	419664 73 0	1.00E-04

Figure 2

Genetic exposure	Outcome	Per allele odds ratio (95% CI)	p-value	Genotype counts, RR RA AA genotypes in cases	Genotype counts, RR RA AA genotypes in controls
Burden of pLOF or predicted deleterious missense variants in WNT5B with AAF <1%	Any fracture	0.80[0.68,0.94]	0.006	115,047 176 0	485,800 918 1
	Major fracture	0.75[0.62,0.89]	0.001	91,605 128 0	485,729 918 1
Burden of pLOF variants in WNT5B with AAF <1%	Any fracture	0.83[0.53,1.32]	0.44	114,322 21 0	469,889 93 0
	Major fracture	0.76[0.46,1.27]	0.30	91,058 15 0	469,818 93 0

Figure 3

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1632816:T:G	c.239T>G; c.239T>G; c.239T>G; c.239T>G	p.Ile80Ser; p.Ile80Ser; p.Ile80Ser; p.Ile80Ser	FALSE	4.64E-06
12:1632803:G:T	c.226G>T; c.226G>T; c.226G>T; c.226G>T	p.Ala76Ser; p.Ala76Ser; p.Ala76Ser; p.Ala76Ser	FALSE	8.46E-06
12:1645824:A:G	c.652A>G; c.652A>G; c.652A>G	p.Lys218Glu; p.Lys218Glu; p.Lys218Glu	FALSE	1.16E-06
12:1639788:C:CAA	c.433_434insAA; c.433_434insAA; c.433_434insAA	p.Arg145fs; p.Arg145fs; p.Arg145fs	TRUE	4.64E-06
12:1632804:C:T	c.227C>T; c.227C>T; c.227C>T; c.227C>T	p.Ala76Val; p.Ala76Val; p.Ala76Val; p.Ala76Val	FALSE	3.48E-06
12:1632779:C:T	c.202C>T; c.202C>T; c.202C>T; c.202C>T	p.His68Tyr; p.His68Tyr; p.His68Tyr; p.His68Tyr	FALSE	1.16E-06
12:1645919:C:G	c.747C>G; c.747C>G; c.747C>G	p.Tyr249*; p.Tyr249*; p.Tyr249*	TRUE	1.16E-06
12:1646209:G:C	c.1037G>C; c.1037G>C; c.1037G>C	p.Cys346Ser; p.Cys346Ser; p.Cys346Ser	FALSE	6.48E-06
12:1646209:G:C	c.1037G>C; c.1037G>C; c.1037G>C	p.Cys346Ser; p.Cys346Ser; p.Cys346Ser	FALSE	1.69E-05
12:1646177:CT:C	c.1006delT; c.1006delT; c.1006delT	p.Cys336fs; p.Cys336fs; p.Cys336fs	TRUE	5.80E-06
12:1645978:G:T	c.806G>T; c.806G>T; c.806G>T	p.Arg269Leu; p.Arg269Leu; p.Arg269Leu	FALSE	6.48E-06
12:1646005:TG:T	c.835delG; c.835delG; c.835delG	p.Val279fs; p.Val279fs; p.Val279fs	TRUE	8.47E-06
12:1632770:T:C	c.193T>C; c.193T>C; c.193T>C	p.Tyr65His; p.Tyr65His; p.Tyr65His	FALSE	1.04E-05

Figure 4

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1639732:T:A	c.377T>A; c.377T>A; c.377T>A	p.Val126Asp; p.Val126Asp	FALSE	1.16E-06
12:1639722:G:C	c.367G>C; c.367G>C; c.367G>C	p.Ala123Pro; p.Ala123Pro	FALSE	1.16E-06
12:1645874:G:T	c.702G>T; c.702G>T; c.702G>T	p.Gln234His; p.Gln234His	FALSE	1.74E-05
12:1639836:T:C	c.481T>C; c.481T>C; c.481T>C	p.Cys161Arg; p.Cys161Arg	FALSE	1.16E-06
12:1639962:G:A	c.607G>A; c.607G>A; c.607G>A	p.Glu203Lys; p.Glu203Lys	FALSE	1.30E-05
12:1639962:G:A	c.607G>A; c.607G>A; c.607G>A	p.Glu203Lys; p.Glu203Lys	FALSE	1.69E-05
12:1639962:G:A	c.607G>A; c.607G>A; c.607G>A	p.Glu203Lys; p.Glu203Lys	FALSE	1.39E-05
12:1645885:T:C	c.713T>C; c.713T>C; c.713T>C	p.Phe238Ser; p.Phe238Ser	FALSE	1.16E-06
12:1645888:G:T	c.716G>T; c.716G>T; c.716G>T	p.Arg239Leu; p.Arg239Leu	FALSE	1.16E-06
12:1645888:G:T	c.716G>T; c.716G>T; c.716G>T	p.Arg239Leu; p.Arg239Leu	FALSE	6.48E-06
12:1645888:G:T	c.716G>T; c.716G>T; c.716G>T	p.Arg239Leu; p.Arg239Leu	FALSE	8.46E-06
12:1645888:G:T	c.716G>T; c.716G>T; c.716G>T	p.Arg239Leu; p.Arg239Leu	FALSE	5.15E-05
12:1646035:G:A	c.863G>A; c.863G>A; c.863G>A	p.Cys288Tyr; p.Cys288Tyr	FALSE	1.16E-06
12:1632735:G:A	c.158G>A; c.158G>A; c.158G>A	p.Gly53Glu; p.Gly53Glu	FALSE	1.16E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1639702:T:C	c.347T>C; c.347T>C; c.347T>C	p.Phe116Ser; p.Phe116Ser	FALSE	0.000185443
12:1639702:T:C	c.347T>C; c.347T>C; c.347T>C	p.Phe116Ser; p.Phe116Ser	FALSE	6.95E-06
12:1639702:T:C	c.347T>C; c.347T>C; c.347T>C	p.Phe116Ser; p.Phe116Ser	FALSE	6.48E-06
12:1632888:GGA:G	c.315_316delAG; c.315_316delAG; c.315_316delAG	p.Arg105fs; p.Arg105fs; p.Arg105fs	TRUE	1.16E-06
12:1645895:CG:C	c.727delG; c.727delG; c.727delG	p.Asp243fs; p.Asp243fs; p.Asp243fs	TRUE	8.47E-06
12:1646235:C:G	c.1063C>G; c.1063C>G; c.1063C>G	p.Gln355Glu; p.Gln355Glu	FALSE	1.16E-06
12:1645797:G:A	c.625G>A; c.625G>A; c.625G>A; c.332G>A	p.Val209Met; p.Val209Met; p.Val209Met; p.Cys111Tyr	FALSE	1.16E-06
12:1645993:C:T	c.821C>T; c.821C>T; c.821C>T	p.Thr274Ile; p.Thr274Ile; p.Thr274Ile	FALSE	1.16E-06
12:1645993:C:T	c.821C>T; c.821C>T; c.821C>T	p.Thr274Ile; p.Thr274Ile; p.Thr274Ile	FALSE	8.47E-06
12:1645947:C:T	c.775C>T; c.775C>T; c.775C>T	p.Arg259Cys; p.Arg259Cys	FALSE	8.47E-06
12:1645947:C:T	c.775C>T; c.775C>T; c.775C>T	p.Arg259Cys; p.Arg259Cys	FALSE	2.09E-05
12:1645947:C:T	c.775C>T; c.775C>T; c.775C>T	p.Arg259Cys; p.Arg259Cys	FALSE	0.000206157
12:1645947:C:T	c.775C>T; c.775C>T; c.775C>T	p.Arg259Cys; p.Arg259Cys	FALSE	1.30E-05
12:1645947:C:T	c.775C>T; c.775C>T; c.775C>T	p.Arg259Cys; p.Arg259Cys	FALSE	0.000113071

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1645947:C:T	c.775C>T; c.775C>T; c.775C>T	p.Arg259Cys; p.Arg259Cys	FALSE	4.64E-05
12:1639774:C:T	c.419C>T; c.419C>T; c.419C>T	p.Thr140Ile; p.Thr140Ile; p.Thr140Ile	FALSE	1.94E-05
12:1639774:C:T	c.419C>T; c.419C>T; c.419C>T	p.Thr140Ile; p.Thr140Ile; p.Thr140Ile	FALSE	8.48E-06
12:1639896:C:T	c.541C>T; c.541C>T; c.541C>T	p.Arg181*; p.Arg181*; p.Arg181*	TRUE	6.48E-06
12:1639683:G:C	c.329-1G>C; c.329-1G>C; c.329-1G>C		TRUE	6.48E-06
12:1645968:GTC:G	c.797_798delTC; c.797_798delTC; c.797_798delTC	p.Val266fs; p.Val266fs; p.Val266fs	TRUE	1.16E-06
12:1639972:G:T	c.617G>T; c.617G>T; c.617G>T	p.Arg206Leu; p.Arg206Leu; p.Arg206Leu	FALSE	4.64E-05
12:1639972:G:T	c.617G>T; c.617G>T; c.617G>T	p.Arg206Leu; p.Arg206Leu; p.Arg206Leu	FALSE	1.16E-06
12:1639972:G:T	c.617G>T; c.617G>T; c.617G>T	p.Arg206Leu; p.Arg206Leu; p.Arg206Leu	FALSE	8.46E-06
12:1645861:C:G	c.689C>G; c.689C>G; c.689C>G	p.Thr230Ser; p.Thr230Ser; p.Thr230Ser	FALSE	1.16E-06
12:1645929:G:C	c.757G>C; c.757G>C; c.757G>C	p.Ala253Pro; p.Ala253Pro; p.Ala253Pro	FALSE	8.47E-06
12:1646101:G:T	c.929G>T; c.929G>T; c.929G>T	p.Gly310Val; p.Gly310Val; p.Gly310Val	FALSE	1.16E-06
12:1632825:G:T	c.248G>T; c.248G>T; c.248G>T	p.Cys83Phe; p.Cys83Phe; p.Cys83Phe	FALSE	8.46E-06
12:1639895:GC:G	c.541delC; c.541delC; c.541delC	p.Arg181fs; p.Arg181fs; p.Arg181fs	TRUE	1.16E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1632720:G:T	c.143G>T; c.143G>T; c.143G>T; c.143G>T	p.Cys48Phe; p.Cys48Phe; p.Cys48Phe; p.Cys48Phe	FALSE	1.16E-06
12:1645977:C:T	c.805C>T; c.805C>T; c.805C>T	p.Arg269Cys; p.Arg269Cys; p.Arg269Cys	FALSE	1.30E-05
12:1645977:C:T	c.805C>T; c.805C>T; c.805C>T	p.Arg269Cys; p.Arg269Cys; p.Arg269Cys	FALSE	2.32E-06
12:1645977:C:T	c.805C>T; c.805C>T; c.805C>T	p.Arg269Cys; p.Arg269Cys; p.Arg269Cys	FALSE	5.15E-05
12:1645868:G:T	c.696G>T; c.696G>T; c.696G>T	p.Trp232Cys; p.Trp232Cys; p.Trp232Cys	FALSE	8.46E-06
12:1639768:T:C	c.413T>C; c.413T>C; c.413T>C	p.Leu138Pro; p.Leu138Pro; p.Leu138Pro	FALSE	1.72E-05
12:1639844:C:A	c.489C>A; c.489C>A; c.489C>A	p.Asp163Glu; p.Asp163Glu; p.Asp163Glu	FALSE	6.49E-06
12:1639736:C:CGCCATCA	c.385_391dupATCAGCC; c.385_391dupATCAGCC; c.385_391dupATCAGCC	p.Arg131fs; p.Arg131fs; p.Arg131fs	TRUE	3.44E-05
12:1639861:A:G	c.506A>G; c.506A>G; c.506A>G	p.Tyr169Cys; p.Tyr169Cys; p.Tyr169Cys	FALSE	1.16E-06
12:1639887:G:T	c.532G>T; c.532G>T; c.532G>T	p.Alala178Ser; p.Alala178Ser; p.Alala178Ser	FALSE	6.95E-06
12:1639887:G:T	c.532G>T; c.532G>T; c.532G>T	p.Alala178Ser; p.Alala178Ser; p.Alala178Ser	FALSE	6.87E-05
12:1639887:G:T	c.532G>T; c.532G>T; c.532G>T	p.Alala178Ser; p.Alala178Ser; p.Alala178Ser	FALSE	1.30E-05
12:1639887:G:T	c.532G>T; c.532G>T; c.532G>T	p.Alala178Ser; p.Alala178Ser; p.Alala178Ser	FALSE	1.69E-05

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1632757:G:T	c.180G>T; c.180G>T; c.180G>T; c.180G>T	p.Lys60Asn; p.Lys60Asn; p.Lys60Asn	FALSE	1.16E-06
12:1639779:G:A	c.424G>A; c.424G>A; c.424G>A	p.Gly142Ser; p.Gly142Ser; p.Gly142Ser	FALSE	3.24E-05
12:1639779:G:A	c.424G>A; c.424G>A; c.424G>A	p.Gly142Ser; p.Gly142Ser; p.Gly142Ser	FALSE	1.16E-06
12:1639779:G:A	c.424G>A; c.424G>A; c.424G>A	p.Gly142Ser; p.Gly142Ser; p.Gly142Ser	FALSE	7.63E-05
12:1646229:G:A	c.1057G>A; c.1057G>A; c.1057G>A	p.Val353Met; p.Val353Met	FALSE	1.16E-06
12:1645938:C:T	c.766C>T; c.766C>T; c.766C>T	p.Arg256Cys; p.Arg256Cys	FALSE	3.48E-06
12:1646034:T:C	c.862T>C; c.862T>C; c.862T>C	p.Cys288Arg; p.Cys288Arg	FALSE	6.48E-06
12:1646034:T:C	c.862T>C; c.862T>C; c.862T>C	p.Cys288Arg; p.Cys288Arg	FALSE	3.48E-06
12:1639831:G:A	c.476G>A; c.476G>A; c.476G>A	p.Gly159Asp; p.Gly159Asp	FALSE	4.64E-06
12:1632768:T:C	c.191T>C; c.191T>C; c.191T>C; c.191T>C	p.Leu64Ser; p.Leu64Ser; p.Leu64Ser	FALSE	1.16E-06
12:1632849:G:A	c.272G>A; c.272G>A; c.272G>A; c.272G>A	p.Arg91Gln; p.Arg91Gln; p.Arg91Gln	FALSE	1.27E-05
12:1632849:G:A	c.272G>A; c.272G>A; c.272G>A; c.272G>A	p.Arg91Gln; p.Arg91Gln; p.Arg91Gln	FALSE	2.59E-05
12:1632849:G:A	c.272G>A; c.272G>A; c.272G>A; c.272G>A	p.Arg91Gln; p.Arg91Gln; p.Arg91Gln	FALSE	1.69E-05

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1646076:C:T	c.904C>T; c.904C>T; c.904C>T	p.Arg302Cys; p.Arg302Cys	FALSE	4.64E-06
12:1646076:C:T	c.904C>T; c.904C>T; c.904C>T	p.Arg302Cys; p.Arg302Cys	FALSE	1.94E-05
12:1646076:C:T	c.904C>T; c.904C>T; c.904C>T	p.Arg302Cys; p.Arg302Cys	FALSE	1.72E-05
12:1646076:C:T	c.904C>T; c.904C>T; c.904C>T	p.Arg302Cys; p.Arg302Cys	FALSE	2.54E-05
12:1646076:C:T	c.904C>T; c.904C>T; c.904C>T	p.Arg302Cys; p.Arg302Cys	FALSE	4.64E-05
12:1639946:G:A	c.591G>A; c.591G>A; c.591G>A	p.Met197Ile; p.Met197Ile; p.Met197Ile	FALSE	0.000113071
12:1639744:G:A	c.389G>A; c.389G>A; c.389G>A	p.Ser130Asn; p.Ser130Asn	FALSE	1.16E-06
12:1646008:T:C	c.836T>C; c.836T>C; c.836T>C	p.Val279Ala; p.Val279Ala; p.Val279Ala	FALSE	6.95E-06
12:1639762:G:A	c.407G>A; c.407G>A; c.407G>A	p.Gly136Asp; p.Gly136Asp	FALSE	1.16E-06
12:1646095:C:G	c.923C>G; c.923C>G; c.923C>G	p.Ser308Trp; p.Ser308Trp; p.Ser308Trp	FALSE	1.16E-06
12:1646025:C:T	c.853C>T; c.853C>T; c.853C>T	p.Pro285Ser; p.Pro285Ser; p.Pro285Ser	FALSE	6.48E-06
12:1645860:A:G	c.688A>G; c.688A>G; c.688A>G	p.Thr230Ala; p.Thr230Ala; p.Thr230Ala	FALSE	3.48E-06
12:1631436:T:C	c.80+2T>C; c.80+2T>C; c.80+2T>C; c.80+2T>C		TRUE	1.16E-06
12:1632792:T:G	c.215T>G; c.215T>G; c.215T>G; c.215T>G	p.Ile72Arg; p.Ile72Arg; p.Ile72Arg	FALSE	1.16E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1639684:G:GCAGC	c.331_334dupAGCC; c.331_334dupAGCC	p.Arg112fs; p.Arg112fs; p.Arg112fs	TRUE	1.16E-06
12:1639747:G:A	c.392G>A; c.392G>A; c.392G>A	p.Arg131Gln; p.Arg131Gln; p.Arg131Gln	FALSE	1.94E-05
12:1639747:G:A	c.392G>A; c.392G>A; c.392G>A	p.Arg131Gln; p.Arg131Gln; p.Arg131Gln	FALSE	3.48E-06
12:1639747:G:A	c.392G>A; c.392G>A; c.392G>A	p.Arg131Gln; p.Arg131Gln; p.Arg131Gln	FALSE	0.000139095
12:1639747:G:A	c.392G>A; c.392G>A; c.392G>A	p.Arg131Gln; p.Arg131Gln; p.Arg131Gln	FALSE	1.72E-05
12:1639815:C:T	c.460C>T; c.460C>T; c.460C>T	p.Arg154Trp; p.Arg154Trp; p.Arg154Trp	FALSE	3.39E-05
12:1639815:C:T	c.460C>T; c.460C>T; c.460C>T	p.Arg154Trp; p.Arg154Trp; p.Arg154Trp	FALSE	4.64E-06
12:1639815:C:T	c.460C>T; c.460C>T; c.460C>T	p.Arg154Trp; p.Arg154Trp; p.Arg154Trp	FALSE	1.94E-05
12:1639782:T:C	c.427T>C; c.427T>C; c.427T>C	p.Cys143Arg; p.Cys143Arg; p.Cys143Arg	FALSE	2.32E-06
12:1639971:C:G	c.616C>G; c.616C>G; c.616C>G	p.Arg206Gly; p.Arg206Gly; p.Arg206Gly	FALSE	1.16E-06
12:1632858:G:T	c.281G>T; c.281G>T; c.281G>T	p.Cys94Phe; p.Cys94Phe; p.Cys94Phe	FALSE	2.32E-06
12:1646011:ATG:A	c.842_843delITG; c.842_843delITG	p.Val281fs; p.Val281fs; p.Val281fs	TRUE	8.47E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1646011:ATG:A	c.842_843delTG; c.842_843delTG	p.Val281fs; p.Val281fs; p.Val281fs	TRUE	3.48E-06
12:1646044:A:G	c.872A>G; c.872A>G; c.872A>G	p.Asn291Ser; p.Asn291Ser; p.Asn291Ser	FALSE	4.64E-06
12:1639755:C:A	c.400C>A; c.400C>A; c.400C>A	p.Arg134Ser; p.Arg134Ser; p.Arg134Ser	FALSE	5.10E-05
12:1639755:C:A	c.400C>A; c.400C>A; c.400C>A	p.Arg134Ser; p.Arg134Ser; p.Arg134Ser	FALSE	5.18E-05
12:1639755:C:A	c.400C>A; c.400C>A; c.400C>A	p.Arg134Ser; p.Arg134Ser; p.Arg134Ser	FALSE	9.27E-05
12:1639755:C:A	c.400C>A; c.400C>A; c.400C>A	p.Arg134Ser; p.Arg134Ser; p.Arg134Ser	FALSE	0.000163467
12:1639755:C:A	c.400C>A; c.400C>A; c.400C>A	p.Arg134Ser; p.Arg134Ser; p.Arg134Ser	FALSE	0.000113071
12:1646130:G:A	c.958G>A; c.958G>A; c.958G>A	p.Gly320Arg; p.Gly320Arg; p.Gly320Arg	FALSE	1.16E-06
12:1646130:G:A	c.958G>A; c.958G>A; c.958G>A	p.Gly320Arg; p.Gly320Arg; p.Gly320Arg	FALSE	0.00010305
12:1646061:C:G	c.889C>G; c.889C>G; c.889C>G	p.Leu297Val; p.Leu297Val; p.Leu297Val	FALSE	1.16E-06
12:1639821:TGGCTGTGGGGC:T	c.477_487delCGGCTGTGGGG; c.477_487delCGGCTGTGGGG; c.477_487delCGGCTGTGGGG	p.Gly160fs; p.Gly160fs; p.Gly160fs	TRUE	1.16E-05
12:1646143:A:G	c.971A>G; c.971A>G; c.971A>G	p.Asn324Ser; p.Asn324Ser; p.Asn324Ser	FALSE	2.32E-06
12:1631296:A:T	c.-57-2A>T; c.-57-2A>T; c.-57-2A>T		TRUE	9.27E-05

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1632905:G:C	c.328G>C; c.328G>C; c.328G>C; c.328G>C	p.Gly110Arg; p.Gly110Arg; p.Gly110Arg; p.Gly110Arg	FALSE	5.80E-06
12:1639767:C:T	c.412C>T; c.412C>T; c.412C>T	p.Leu138Phe; p.Leu138Phe; p.Leu138Phe	FALSE	8.48E-06
12:1639767:C:T	c.412C>T; c.412C>T; c.412C>T	p.Leu138Phe; p.Leu138Phe; p.Leu138Phe	FALSE	5.80E-06
12:1646110:G:A	c.938G>A; c.938G>A; c.938G>A	p.Gly313Asp; p.Gly313Asp; p.Gly313Asp	FALSE	1.30E-05
12:1632829:G:T	c.252G>T; c.252G>T; c.252G>T; c.252G>T	p.Gln84His; p.Gln84His; p.Gln84His; p.Gln84His	FALSE	3.44E-05
12:1632829:G:T	c.252G>T; c.252G>T; c.252G>T; c.252G>T	p.Gln84His; p.Gln84His; p.Gln84His; p.Gln84His	FALSE	6.48E-06
12:1632829:G:T	c.252G>T; c.252G>T; c.252G>T; c.252G>T	p.Gln84His; p.Gln84His; p.Gln84His; p.Gln84His	FALSE	1.27E-05
12:1632839:C:T	c.262C>T; c.262C>T; c.262C>T; c.262C>T	p.Arg88Trp; p.Arg88Trp; p.Arg88Trp; p.Arg88Trp	FALSE	3.24E-05
12:1632839:C:T	c.262C>T; c.262C>T; c.262C>T; c.262C>T	p.Arg88Trp; p.Arg88Trp; p.Arg88Trp; p.Arg88Trp	FALSE	0.000137438

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1632839:C:T	c.262C>T; c.262C>T; c.262C>T; c.262C>T	p.Arg88Trp; p.Arg88Trp; p.Arg88Trp; p.Arg88Trp	FALSE	0.000509968
12:1632839:C:T	c.262C>T; c.262C>T; c.262C>T; c.262C>T	p.Arg88Trp; p.Arg88Trp; p.Arg88Trp; p.Arg88Trp	FALSE	1.72E-05
12:1632839:C:T	c.262C>T; c.262C>T; c.262C>T; c.262C>T	p.Arg88Trp; p.Arg88Trp; p.Arg88Trp; p.Arg88Trp	FALSE	2.54E-05
12:1632839:C:T	c.262C>T; c.262C>T; c.262C>T; c.262C>T	p.Arg88Trp; p.Arg88Trp; p.Arg88Trp; p.Arg88Trp	FALSE	2.32E-05
12:1639711:C:T	c.356C>T; c.356C>T; c.356C>T; c.356C>T	p.Ala119Val; p.Ala119Val; p.Ala119Val; p.Ala119Val	FALSE	8.55E-06
12:1645920:G:A	c.748G>A; c.748G>A; c.748G>A; c.748G>A	p.Asp250Asn; p.Asp250Asn; p.Asp250Asn; p.Asp250Asn	FALSE	3.89E-05
12:1645920:G:A	c.748G>A; c.748G>A; c.748G>A; c.748G>A	p.Asp250Asn; p.Asp250Asn; p.Asp250Asn; p.Asp250Asn	FALSE	3.39E-05
12:1645920:G:A	c.748G>A; c.748G>A; c.748G>A; c.748G>A	p.Asp250Asn; p.Asp250Asn; p.Asp250Asn; p.Asp250Asn	FALSE	6.95E-06
12:1645920:G:A	c.748G>A; c.748G>A; c.748G>A; c.748G>A	p.Asp250Asn; p.Asp250Asn; p.Asp250Asn; p.Asp250Asn	FALSE	0.000137438
12:1645927:C:T	c.755C>T; c.755C>T; c.755C>T; c.755C>T	p.Ala252Val; p.Ala252Val; p.Ala252Val; p.Ala252Val	FALSE	6.48E-06
12:1645927:C:T	c.755C>T; c.755C>T; c.755C>T; c.755C>T	p.Ala252Val; p.Ala252Val; p.Ala252Val; p.Ala252Val	FALSE	4.64E-06
12:1639953:C:CA	c.602dupA; c.602dupA; c.602dupA; c.602dupA	p.Asn201fs; p.Asn201fs; p.Asn201fs; p.Asn201fs	TRUE	2.32E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1632833:CA:C	c.257delA; c.257delA; c.257delA; c.257delA	p.Gln86fs; p.Gln86fs; p.Gln86fs; p.Gln86fs	TRUE	1.16E-06
12:1645864:G:T	c.692G>T; c.692G>T; c.692G>T	p.Cys231Phe; p.Cys231Phe; p.Cys231Phe	FALSE	6.87E-05
12:1639944:A:T	c.589A>T; c.589A>T; c.589A>T	p.Met197Leu; p.Met197Leu; p.Met197Leu	FALSE	6.87E-05
12:1639944:A:T	c.589A>T; c.589A>T; c.589A>T	p.Met197Leu; p.Met197Leu; p.Met197Leu	FALSE	3.24E-05
12:1645887:C:T	c.715C>T; c.715C>T; c.715C>T	p.Arg239Cys; p.Arg239Cys; p.Arg239Cys	FALSE	1.27E-05
12:1645887:C:T	c.715C>T; c.715C>T; c.715C>T	p.Arg239Cys; p.Arg239Cys; p.Arg239Cys	FALSE	8.46E-06
12:1639873:AG:A	c.520delG; c.520delG; c.520delG	p.Glu174fs; p.Glu174fs; p.Glu174fs	TRUE	1.16E-06
12:1632840:G:A	c.263G>A; c.263G>A; c.263G>A; c.263G>A	p.Arg88Gln; p.Arg88Gln; p.Arg88Gln; p.Arg88Gln	FALSE	1.69E-05
12:1632840:G:A	c.263G>A; c.263G>A; c.263G>A; c.263G>A	p.Arg88Gln; p.Arg88Gln; p.Arg88Gln; p.Arg88Gln	FALSE	4.17E-05
12:1632852:G:A	c.275G>A; c.275G>A; c.275G>A; c.275G>A	p.Trp92*; p.Trp92*; p.Trp92*; p.Trp92*	TRUE	4.64E-06
12:1639723:C:T	c.368C>T; c.368C>T; c.368C>T	p.Ala123Val; p.Ala123Val; p.Ala123Val	FALSE	8.54E-06
12:1639723:C:T	c.368C>T; c.368C>T; c.368C>T	p.Ala123Val; p.Ala123Val; p.Ala123Val	FALSE	1.16E-06
12:1639767:C:G	c.412C>G; c.412C>G; c.412C>G	p.Leu138Val; p.Leu138Val; p.Leu138Val	FALSE	6.48E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1631434:GGTGA:G	c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA		TRUE	3.89E-05
12:1631434:GGTGA:G	c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA		TRUE	0.000206101
12:1631434:GGTGA:G	c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA		TRUE	4.64E-05
12:1631434:GGTGA:G	c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA		TRUE	1.04E-05
12:1631434:GGTGA:G	c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA; c.80+1_80+4delGTGA		TRUE	8.46E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1645878:G:A	c.706G>A; c.706G>A; c.706G>A	p.Ala236Thr; p.Ala236Thr; p.Ala236Thr	FALSE	3.44E-05
12:1645878:G:A	c.706G>A; c.706G>A; c.706G>A	p.Ala236Thr; p.Ala236Thr; p.Ala236Thr	FALSE	1.51E-05
12:1639781:CTGCAG:C	c.427_431delTGCAG; c.427_431delTGCAG; c.427_431delTGCAG	p.Cys143fs; p.Cys143fs; p.Cys143fs	TRUE	4.64E-06
12:1639962:G:T	c.607G>T; c.607G>T; c.607G>T	p.Glu203*; p.Glu203*; p.Glu203*	TRUE	1.30E-05
12:1646169:C:T	c.997C>T; c.997C>T; c.997C>T	p.Arg333Cys; p.Arg333Cys; p.Arg333Cys	FALSE	1.30E-05
12:1646169:C:T	c.997C>T; c.997C>T; c.997C>T	p.Arg333Cys; p.Arg333Cys; p.Arg333Cys	FALSE	8.46E-06
12:1646169:C:T	c.997C>T; c.997C>T; c.997C>T	p.Arg333Cys; p.Arg333Cys; p.Arg333Cys	FALSE	1.04E-05
12:1639793:G:GCAAGGAC	c.438_439insCAAGGAC; c.438_439insCAAGGAC; c.438_439insCAAGGAC	p.Ala147fs; p.Ala147fs; p.Ala147fs	TRUE	4.64E-06
12:1646003:C:A	c.831C>A; c.831C>A; c.831C>A	p.Asp277Glu; p.Asp277Glu; p.Asp277Glu	FALSE	1.16E-06
12:1646170:G:A	c.998G>A; c.998G>A; c.998G>A	p.Arg333His; p.Arg333His; p.Arg333His	FALSE	4.64E-05
12:1646170:G:A	c.998G>A; c.998G>A; c.998G>A	p.Arg333His; p.Arg333His; p.Arg333His	FALSE	0.000377851
12:1646170:G:A	c.998G>A; c.998G>A; c.998G>A	p.Arg333His; p.Arg333His; p.Arg333His	FALSE	1.16E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1646170:G:A	c.998G>A; c.998G>A; c.998G>A	p.Arg333His; p.Arg333His; p.Arg333His	FALSE	8.46E-06
12:1646170:G:A	c.998G>A; c.998G>A; c.998G>A	p.Arg333His; p.Arg333His; p.Arg333His	FALSE	6.87E-05
12:1639689:C:G	c.334C>G; c.334C>G; c.334C>G	p.Arg112Gly; p.Arg112Gly; p.Arg112Gly	FALSE	6.48E-06
12:1639689:C:G	c.334C>G; c.334C>G; c.334C>G	p.Arg112Gly; p.Arg112Gly; p.Arg112Gly	FALSE	3.48E-06
12:1646087:C:G	c.915C>G; c.915C>G; c.915C>G	p.Asn305Lys; p.Asn305Lys; p.Asn305Lys	FALSE	8.46E-06
12:1646157:G:A	c.985G>A; c.985G>A; c.985G>A	p.Val329Met; p.Val329Met; p.Val329Met	FALSE	4.64E-05
12:1646157:G:A	c.985G>A; c.985G>A; c.985G>A	p.Val329Met; p.Val329Met; p.Val329Met	FALSE	2.59E-05
12:1646157:G:A	c.985G>A; c.985G>A; c.985G>A	p.Val329Met; p.Val329Met; p.Val329Met	FALSE	9.27E-06
12:1632846:G:A	c.269G>A; c.269G>A; c.269G>A; c.269G>A	p.Arg90Gln; p.Arg90Gln; p.Arg90Gln; p.Arg90Gln	FALSE	3.48E-06
12:1645998:G:GA	c.827dupA; c.827dupA; c.827dupA	p.Asp277fs; p.Asp277fs; p.Asp277fs	TRUE	1.16E-06
12:1639716:A:G	c.361A>G; c.361A>G; c.361A>G	p.Ser121Gly; p.Ser121Gly; p.Ser121Gly	FALSE	2.32E-06
12:1646108:T:G	c.936T>G; c.936T>G; c.936T>G	p.Asp312Glu; p.Asp312Glu; p.Asp312Glu	FALSE	6.48E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1639864:G:A	c.509G>A; c.509G>A; c.509G>A	p.Arg170His; p.Arg170His; p.Arg170His	FALSE	8.46E-06
12:1645930:C:A	c.758C>A; c.758C>A; c.758C>A	p.Ala253Asp; p.Ala253Asp; p.Ala253Asp	FALSE	8.47E-06
12:1645926:G:A	c.754G>A; c.754G>A; c.754G>A	p.Ala252Thr; p.Ala252Thr; p.Ala252Thr	FALSE	1.16E-06
12:1639689:C:T	c.334C>T; c.334C>T; c.334C>T	p.Arg112*; p.Arg112*; p.Arg112*	TRUE	1.16E-06
12:1639847:C:G	c.492C>G; c.492C>G; c.492C>G	p.Asn164Lys; p.Asn164Lys; p.Asn164Lys	FALSE	1.16E-06
12:1632858:G:A	c.281G>A; c.281G>A; c.281G>A; c.281G>A	p.Cys94Tyr; p.Cys94Tyr; p.Cys94Tyr; p.Cys94Tyr	FALSE	6.48E-06
12:1639726:G:C	c.371G>C; c.371G>C; c.371G>C	p.Gly124Ala; p.Gly124Ala; p.Gly124Ala	FALSE	4.64E-05
12:1639726:G:C	c.371G>C; c.371G>C; c.371G>C	p.Gly124Ala; p.Gly124Ala; p.Gly124Ala	FALSE	1.16E-06
12:1639756:G:A	c.401G>A; c.401G>A; c.401G>A	p.Arg134His; p.Arg134His; p.Arg134His	FALSE	1.72E-05
12:1646134:G:A	c.962G>A; c.962G>A; c.962G>A	p.Arg321His; p.Arg321His; p.Arg321His	FALSE	3.48E-06
12:1646134:G:A	c.962G>A; c.962G>A; c.962G>A	p.Arg321His; p.Arg321His; p.Arg321His	FALSE	4.64E-05
12:1646134:G:A	c.962G>A; c.962G>A; c.962G>A	p.Arg321His; p.Arg321His; p.Arg321His	FALSE	5.08E-05

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1646134:G:A	c.962G>A; c.962G>A; c.962G>A	p.Arg321His; p.Arg321His; p.Arg321His	FALSE	2.59E-05
12:1646030:C:G	c.858C>G; c.858C>G; c.858C>G	p.Asp286Glu; p.Asp286Glu; p.Asp286Glu	FALSE	1.16E-06
12:1639890:C:T	c.535C>T; c.535C>T; c.535C>T	p.Arg179Trp; p.Arg179Trp; p.Arg179Trp	FALSE	6.95E-06
12:1639711:C:G	c.356C>G; c.356C>G; c.356C>G	p.Ala119Gly; p.Ala119Gly; p.Ala119Gly	FALSE	1.16E-06
12:1646001:G:A	c.829G>A; c.829G>A; c.829G>A	p.Asp277Asn; p.Asp277Asn; p.Asp277Asn	FALSE	1.72E-05
12:1646139:T:C	c.967T>C; c.967T>C; c.967T>C	p.Tyr323His; p.Tyr323His; p.Tyr323His	FALSE	4.64E-05
12:1632845:C:T	c.268C>T; c.268C>T; c.268C>T	p.Arg90Trp; p.Arg90Trp; p.Arg90Trp	FALSE	1.97E-05
12:1632845:C:T	c.268C>T; c.268C>T; c.268C>T	p.Arg90Trp; p.Arg90Trp; p.Arg90Trp	FALSE	6.48E-06
12:1632845:C:T	c.268C>T; c.268C>T; c.268C>T	p.Arg90Trp; p.Arg90Trp; p.Arg90Trp	FALSE	6.87E-05
12:1639788:C:T	c.433C>T; c.433C>T; c.433C>T	p.Arg145Trp; p.Arg145Trp; p.Arg145Trp	FALSE	2.54E-05
12:1639788:C:T	c.433C>T; c.433C>T; c.433C>T	p.Arg145Trp; p.Arg145Trp; p.Arg145Trp	FALSE	3.48E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1632838:C:G	c.261C>G; c.261C>G; c.261C>G; c.261C>G	p.Phe87Leu; p.Phe87Leu; p.Phe87Leu; p.Phe87Leu	FALSE	5.80E-06
12:1645833:G:A	c.661G>A; c.661G>A; c.661G>A	p.Gly221Ser; p.Gly221Ser; p.Gly221Ser	FALSE	1.16E-06
12:1646118:C:T	c.946C>T; c.946C>T; c.946C>T	p.Leu316Phe; p.Leu316Phe; p.Leu316Phe	FALSE	6.48E-06
12:1639799:GC:G	c.447delC; c.447delC; c.447delC	p.Lys150fs; p.Lys150fs; p.Lys150fs	TRUE	6.48E-06
12:1632881:G:A	c.304G>A; c.304G>A; c.304G>A; c.304G>A	p.Val102Ile; p.Val102Ile; p.Val102Ile; p.Val102Ile	FALSE	1.16E-06
12:1639779:G:T	c.424G>T; c.424G>T; c.424G>T	p.Gly142Cys; p.Gly142Cys; p.Gly142Cys	FALSE	8.47E-06
12:1646011:A:G	c.839A>G; c.839A>G; c.839A>G	p.Tyr280Cys; p.Tyr280Cys; p.Tyr280Cys	FALSE	1.94E-05
12:1646011:A:G	c.839A>G; c.839A>G; c.839A>G	p.Tyr280Cys; p.Tyr280Cys; p.Tyr280Cys	FALSE	1.69E-05
12:1646011:A:G	c.839A>G; c.839A>G; c.839A>G	p.Tyr280Cys; p.Tyr280Cys; p.Tyr280Cys	FALSE	1.16E-05
12:1646092:C:T	c.920C>T; c.920C>T; c.920C>T	p.Thr307Ile; p.Thr307Ile; p.Thr307Ile	FALSE	1.72E-05
12:1639704:A:C	c.349A>C; c.349A>C; c.349A>C	p.Thr117Pro; p.Thr117Pro; p.Thr117Pro	FALSE	1.16E-06
12:1646180:C:A	c.1008C>A; c.1008C>A; c.1008C>A	p.Cys336*; p.Cys336*; p.Cys336*	TRUE	6.48E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1632729:T:C	c.152T>C; c.152T>C; c.152T>C; c.152T>C	p.Leu51Pro; p.Leu51Pro; p.Leu51Pro; p.Leu51Pro	FALSE	1.72E-05
12:1632729:T:C	c.152T>C; c.152T>C; c.152T>C; c.152T>C	p.Leu51Pro; p.Leu51Pro; p.Leu51Pro; p.Leu51Pro	FALSE	8.46E-06
12:1639782:T:GCGCCGGAC	c.429_438dupCAGCCGGACG; c.429_438dupCAGCCGGACG; c.429_438dupCAGCCGGACG	p.Ala147fs; p.Ala147fs; p.Ala147fs	TRUE	1.16E-06
12:1645897:G:T	c.725G>T; c.725G>T; c.725G>T	p.Gly242Val; p.Gly242Val; p.Gly242Val	FALSE	6.87E-05
12:1646090:G:C	c.918G>C; c.918G>C; c.918G>C	p.Lys306Asn; p.Lys306Asn; p.Lys306Asn	FALSE	1.16E-06
12:1639818:G:A	c.463G>A; c.463G>A; c.463G>A	p.Asp155Asn; p.Asp155Asn; p.Asp155Asn	FALSE	6.87E-05
12:1639833:G:C	c.478G>C; c.478G>C; c.478G>C	p.Gly160Arg; p.Gly160Arg; p.Gly160Arg	FALSE	3.48E-06
12:1639789:G:T	c.434G>T; c.434G>T; c.434G>T	p.Arg145Leu; p.Arg145Leu; p.Arg145Leu	FALSE	3.48E-06
12:1639789:G:T	c.434G>T; c.434G>T; c.434G>T	p.Arg145Leu; p.Arg145Leu; p.Arg145Leu	FALSE	1.94E-05
12:1645854:C:G	c.682C>G; c.682C>G; c.682C>G	p.Leu228Val; p.Leu228Val; p.Leu228Val	FALSE	8.46E-06
12:1645854:C:G	c.682C>G; c.682C>G; c.682C>G	p.Leu228Val; p.Leu228Val; p.Leu228Val	FALSE	1.62E-05

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1645924:G:T	c.752G>T; c.752G>T; c.752G>T	p.Ser251Ile; p.Ser251Ile; p.Ser251Ile	FALSE	8.47E-06
12:1639690:G:A	c.335G>A; c.335G>A; c.335G>A	p.Arg112Gln; p.Arg112Gln; p.Arg112Gln	FALSE	3.48E-06
12:1639690:G:A	c.335G>A; c.335G>A; c.335G>A	p.Arg112Gln; p.Arg112Gln; p.Arg112Gln	FALSE	1.72E-05
12:1639856:CGGCT:C	c.502_505delGGCT; c.502_505delGGCT; c.502_505delGGCT	p.Gly168fs; p.Gly168fs; p.Gly168fs	TRUE	1.16E-06
12:1645857:A:C	c.685A>C; c.685A>C; c.685A>C	p.Lys229Gln; p.Lys229Gln; p.Lys229Gln	FALSE	1.16E-06
12:1639789:G:A	c.434G>A; c.434G>A; c.434G>A	p.Arg145Gln; p.Arg145Gln; p.Arg145Gln	FALSE	1.69E-05
12:1639789:G:A	c.434G>A; c.434G>A; c.434G>A	p.Arg145Gln; p.Arg145Gln; p.Arg145Gln	FALSE	5.80E-06
12:1646133:C:T	c.961C>T; c.961C>T; c.961C>T	p.Arg321Cys; p.Arg321Cys; p.Arg321Cys	FALSE	3.39E-05
12:1646133:C:T	c.961C>T; c.961C>T; c.961C>T	p.Arg321Cys; p.Arg321Cys; p.Arg321Cys	FALSE	1.94E-05
12:1646133:C:T	c.961C>T; c.961C>T; c.961C>T	p.Arg321Cys; p.Arg321Cys; p.Arg321Cys	FALSE	6.87E-05
12:1646133:C:T	c.961C>T; c.961C>T; c.961C>T	p.Arg321Cys; p.Arg321Cys; p.Arg321Cys	FALSE	2.32E-06
12:1632833:C:T	c.256C>T; c.256C>T; c.256C>T	p.Gln86*; p.Gln86*; p.Gln86*	TRUE	6.48E-06
12:1632833:C:T	c.256C>T; c.256C>T; c.256C>T	p.Gln86*; p.Gln86*; p.Gln86*	TRUE	8.46E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1639747:G:C	c.392G>C; c.392G>C; c.392G>C	p.Arg131Pro; p.Arg131Pro	FALSE	4.64E-05
12:1639747:G:C	c.392G>C; c.392G>C; c.392G>C	p.Arg131Pro; p.Arg131Pro; p.Arg131Pro	FALSE	4.64E-06
12:1639749:GC:G	c.396delC; c.396delC; c.396delC	p.Cys133fs; p.Cys133fs; p.Cys133fs	TRUE	8.51E-06
12:1645843:G:T	c.671G>T; c.671G>T; c.671G>T	p.Gly224Val; p.Gly224Val; p.Gly224Val	FALSE	8.46E-06
12:1646068:C:T	c.896C>T; c.896C>T; c.896C>T	p.Thr299Met; p.Thr299Met; p.Thr299Met	FALSE	6.48E-06
12:1646068:C:T	c.896C>T; c.896C>T; c.896C>T	p.Thr299Met; p.Thr299Met; p.Thr299Met	FALSE	2.54E-05
12:1646068:C:T	c.896C>T; c.896C>T; c.896C>T	p.Thr299Met; p.Thr299Met; p.Thr299Met	FALSE	2.32E-06
12:1646068:C:T	c.896C>T; c.896C>T; c.896C>T	p.Thr299Met; p.Thr299Met; p.Thr299Met	FALSE	1.72E-05
12:1645888:G:A	c.716G>A; c.716G>A; c.716G>A	p.Arg239His; p.Arg239His; p.Arg239His	FALSE	1.16E-06
12:1645936:T:C	c.764T>C; c.764T>C; c.764T>C	p.Met255Thr; p.Met255Thr; p.Met255Thr	FALSE	1.16E-06
12:1646053:C:CG	c.884dupG; c.884dupG; c.884dupG	p.Ser296fs; p.Ser296fs; p.Ser296fs	TRUE	2.32E-06
12:1646235:C:A	c.1063C>A; c.1063C>A; c.1063C>A	p.Gln355Lys; p.Gln355Lys; p.Gln355Lys	FALSE	8.46E-06
12:1632804:C:G	c.227C>G; c.227C>G; c.227C>G; c.227C>G	p.Ala76Gly; p.Ala76Gly; p.Ala76Gly; p.Ala76Gly	FALSE	1.16E-06
12:1632852:G:T	c.275G>T; c.275G>T; c.275G>T; c.275G>T	p.Trp92Leu; p.Trp92Leu; p.Trp92Leu; p.Trp92Leu	FALSE	8.46E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1646023:G:T	c.851G>T; c.851G>T; c.851G>T	p.Ser284Ile; p.Ser284Ile; p.Ser284Ile	FALSE	8.47E-06
12:1639790:G:GACGGCGCGGCCCA	c.437_449dupCGGCGCGGCCCAA; c.437_449dupCGGCGCGGCCCAA; c.437_449dupCGGCGCGGCCCAA	p.Lys150fs; p.Lys150fs; p.Lys150fs	TRUE	1.30E-05
12:1639790:G:GACGGCGCGGCCCA	c.437_449dupCGGCGCGGCCCAA; c.437_449dupCGGCGCGGCCCAA; c.437_449dupCGGCGCGGCCCAA	p.Lys150fs; p.Lys150fs; p.Lys150fs	TRUE	1.69E-05
12:1639790:G:GACGGCGCGGCCCA	c.437_449dupCGGCGCGGCCCAA; c.437_449dupCGGCGCGGCCCAA; c.437_449dupCGGCGCGGCCCAA	p.Lys150fs; p.Lys150fs; p.Lys150fs	TRUE	9.27E-06
12:1639935:C:T	c.580C>T; c.580C>T; c.580C>T	p.Arg194Trp; p.Arg194Trp; p.Arg194Trp	FALSE	0.000113071
12:1639935:C:T	c.580C>T; c.580C>T; c.580C>T	p.Arg194Trp; p.Arg194Trp; p.Arg194Trp	FALSE	2.90E-05
12:1639953:C:T	c.598C>T; c.598C>T; c.598C>T	p.Gln200*; p.Gln200*; p.Gln200*	TRUE	1.16E-06
12:1639840:G:T	c.485G>T; c.485G>T; c.485G>T	p.Gly162Val; p.Gly162Val; p.Gly162Val	FALSE	8.46E-06
12:1639761:G:GGCGA	c.409_412dupGAGC; c.409_412dupGAGC; c.409_412dupGAGC	p.Leu138fs; p.Leu138fs; p.Leu138fs	TRUE	2.32E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1646053:C:T	c.881C>T; c.881C>T; c.881C>T	p.Thr294Met; p.Thr294Met; p.Thr294Met	FALSE	6.87E-05
12:1646053:C:T	c.881C>T; c.881C>T; c.881C>T	p.Thr294Met; p.Thr294Met; p.Thr294Met	FALSE	1.69E-05
12:1646053:C:T	c.881C>T; c.881C>T; c.881C>T	p.Thr294Met; p.Thr294Met; p.Thr294Met	FALSE	2.59E-05
12:1646053:C:T	c.881C>T; c.881C>T; c.881C>T	p.Thr294Met; p.Thr294Met; p.Thr294Met	FALSE	3.25E-05
12:1646053:C:T	c.881C>T; c.881C>T; c.881C>T	p.Thr294Met; p.Thr294Met; p.Thr294Met	FALSE	0.000113071
12:1639867:T:A	c.512T>A; c.512T>A; c.512T>A	p.Phe171Tyr; p.Phe171Tyr; p.Phe171Tyr	FALSE	1.30E-05
12:1639867:T:A	c.512T>A; c.512T>A; c.512T>A	p.Phe171Tyr; p.Phe171Tyr; p.Phe171Tyr	FALSE	8.11E-06
12:1639867:T:A	c.512T>A; c.512T>A; c.512T>A	p.Phe171Tyr; p.Phe171Tyr; p.Phe171Tyr	FALSE	1.69E-05
12:1639692:G:A	c.337G>A; c.337G>A; c.337G>A	p.Glu113Lys; p.Glu113Lys; p.Glu113Lys	FALSE	1.16E-06
12:1639966:C:T	c.611C>T; c.611C>T; c.611C>T	p.Ala204Val; p.Ala204Val; p.Ala204Val	FALSE	1.16E-06
12:1646083:G:T	c.911G>T; c.911G>T; c.911G>T	p.Cys304Phe; p.Cys304Phe; p.Cys304Phe	FALSE	1.16E-06
12:1646250:T:C	c.1078T>C; c.1078T>C; c.1078T>C	p.Ter360Glnext*?; p.Ter360Glnext*?; p.Ter360Glnext*?	TRUE	1.16E-06
12:1632720:G:A	c.143G>A; c.143G>A; c.143G>A; c.143G>A	p.Cys48Tyr; p.Cys48Tyr; p.Cys48Tyr; p.Cys48Tyr	FALSE	3.48E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1639856:C:G	c.501C>G; c.501C>G; c.501C>G	p.Tyr167*; p.Tyr167*; p.Tyr167*	TRUE	1.16E-06
12:1646017:A:G	c.845A>G; c.845A>G; c.845A>G	p.Asp282Gly; p.Asp282Gly; p.Asp282Gly	FALSE	1.16E-06
12:1645980:T:G	c.808T>G; c.808T>G; c.808T>G	p.Phe270Val; p.Phe270Val; p.Phe270Val	FALSE	8.47E-06
12:1639747:G:T	c.392G>T; c.392G>T; c.392G>T	p.Arg131Leu; p.Arg131Leu; p.Arg131Leu	FALSE	1.30E-05
12:1639747:G:T	c.392G>T; c.392G>T; c.392G>T	p.Arg131Leu; p.Arg131Leu; p.Arg131Leu	FALSE	5.11E-05
12:1646151:A:T	c.979A>T; c.979A>T; c.979A>T	p.Lys327*; p.Lys327*; p.Lys327*	TRUE	8.46E-06
12:1645849:G:C	c.677G>C; c.677G>C; c.677G>C	p.Cys226Ser; p.Cys226Ser; p.Cys226Ser	FALSE	2.32E-06
12:1639718:C:G	c.363C>G; c.363C>G; c.363C>G	p.Ser121Arg; p.Ser121Arg; p.Ser121Arg	FALSE	1.16E-06
12:1645875:C:A	c.703C>A; c.703C>A; c.703C>A	p.Leu235Met; p.Leu235Met; p.Leu235Met	FALSE	8.46E-06
12:1639759:A:AG	c.407dupG; c.407dupG; c.407dupG	p.Glu137fs; p.Glu137fs; p.Glu137fs	TRUE	1.16E-06
12:1639823:G:A	c.468G>A; c.468G>A; c.468G>A	p.Trp156*; p.Trp156*; p.Trp156*	TRUE	1.16E-06
12:1646114:T:G	c.942T>G; c.942T>G; c.942T>G	p.Cys314Trp; p.Cys314Trp; p.Cys314Trp	FALSE	6.87E-05

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1646114:T:G	c.942T>G; c.942T>G; c.942T>G	p.Cys314Trp; p.Cys314Trp; p.Cys314Trp	FALSE	0.000113071
12:1646114:T:G	c.942T>G; c.942T>G; c.942T>G	p.Cys314Trp; p.Cys314Trp; p.Cys314Trp	FALSE	3.89E-05
12:1646114:T:G	c.942T>G; c.942T>G; c.942T>G	p.Cys314Trp; p.Cys314Trp; p.Cys314Trp	FALSE	6.14E-05
12:1646114:T:G	c.942T>G; c.942T>G; c.942T>G	p.Cys314Trp; p.Cys314Trp; p.Cys314Trp	FALSE	4.64E-05
12:1646114:T:G	c.942T>G; c.942T>G; c.942T>G	p.Cys314Trp; p.Cys314Trp; p.Cys314Trp	FALSE	0.000137438
12:1639694:G:C	c.339G>C; c.339G>C; c.339G>C	p.Glu113Asp; p.Glu113Asp; p.Glu113Asp	FALSE	1.16E-06
12:1645896:G:A	c.724G>A; c.724G>A; c.724G>A	p.Gly242Arg; p.Gly242Arg; p.Gly242Arg	FALSE	2.32E-06
12:1645896:G:A	c.724G>A; c.724G>A; c.724G>A	p.Gly242Arg; p.Gly242Arg; p.Gly242Arg	FALSE	1.72E-05
12:1645896:G:A	c.724G>A; c.724G>A; c.724G>A	p.Gly242Arg; p.Gly242Arg; p.Gly242Arg	FALSE	6.48E-06
12:1632887:G:T	c.310G>T; c.310G>T; c.310G>T; c.310G>T	p.Gly104Trp; p.Gly104Trp; p.Gly104Trp	FALSE	8.46E-06
12:1639806:G:T	c.451G>T; c.451G>T; c.451G>T	p.Asp151Tyr; p.Asp151Tyr; p.Asp151Tyr	FALSE	2.32E-06
12:1646202:G:A	c.1030G>A; c.1030G>A; c.1030G>A	p.Val344Ile; p.Val344Ile; p.Val344Ile	FALSE	5.80E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1639710:G:A	c.355G>A; c.355G>A; c.355G>A	p.Ala119Thr; p.Ala119Thr; p.Ala119Thr	FALSE	8.56E-06
12:1639965:G:A	c.610G>A; c.610G>A; c.610G>A	p.Ala204Thr; p.Ala204Thr; p.Ala204Thr	FALSE	1.16E-06
12:1646026:C:G	c.854C>G; c.854C>G; c.854C>G	p.Pro285Arg; p.Pro285Arg; p.Pro285Arg	FALSE	1.16E-06
12:1631356:T:C	c.2T>C; c.2T>C; c.2T>C; c.2T>C	p.Met1?; p.Met1?; p.Met1?; p.Met1?	TRUE	2.32E-06
12:1639752:T:A	c.397T>A; c.397T>A; c.397T>A	p.Cys133Ser; p.Cys133Ser; p.Cys133Ser	FALSE	1.16E-06
12:1639765:AGCTCTCCACCT:A	c.413_423delITCTCCACCTGC; c.413_423delITCTCCACCTGC; c.413_423delITCTCCACCTGC	p.Leu138fs; p.Leu138fs; p.Leu138fs	TRUE	1.72E-05
12:1646083:G:A	c.911G>A; c.911G>A; c.911G>A	p.Cys304Tyr; p.Cys304Tyr; p.Cys304Tyr	FALSE	1.16E-06
12:1639948:A:G	c.593A>G; c.593A>G; c.593A>G	p.Asn198Ser; p.Asn198Ser; p.Asn198Ser	FALSE	1.16E-06
12:1639971:C:T	c.616C>T; c.616C>T; c.616C>T	p.Arg206Cys; p.Arg206Cys; p.Arg206Cys	FALSE	1.16E-06
12:1646196:T:C	c.1024T>C; c.1024T>C; c.1024T>C	p.Cys342Arg; p.Cys342Arg; p.Cys342Arg	FALSE	1.16E-06
12:1639897:G:A	c.542G>A; c.542G>A; c.542G>A	p.Arg181Gln; p.Arg181Gln; p.Arg181Gln	FALSE	1.72E-05
12:1632826:C:A	c.249C>A; c.249C>A; c.249C>A; c.249C>A	p.Cys83*; p.Cys83*; p.Cys83*; p.Cys83*	TRUE	2.32E-06

Figure 4 (cont.)

Genomic coordinates and alleles for genetic variant	Coding DNA change	Protein change	Variant classified as pLOF	AAF, fraction of 1
12:1646031:T:A	c.859T>A; c.859T>A; c.859T>A	p.Tyr287Asn; p.Tyr287Asn; p.Tyr287Asn	FALSE	2.32E-06
12:1639778:C:G	c.423C>G; c.423C>G; c.423C>G	p.Cys141Trp; p.Cys141Trp; p.Cys141Trp	FALSE	1.16E-06
12:1645836:G:A	c.664G>A; c.664G>A; c.664G>A	p.Val222Ile; p.Val222Ile; p.Val222Ile	FALSE	5.80E-06
12:1639798:G:C	c.443G>C; c.443G>C; c.443G>C	p.Arg148Pro; p.Arg148Pro; p.Arg148Pro	FALSE	1.16E-06
12:1639879:T:C	c.524T>C; c.524T>C; c.524T>C	p.Phe175Ser; p.Phe175Ser; p.Phe175Ser	FALSE	1.16E-06
12:1645873:A:T	c.701A>T; c.701A>T; c.701A>T	p.Gln234Leu; p.Gln234Leu; p.Gln234Leu	FALSE	1.16E-06
12:1639926:G:A	c.571G>A; c.571G>A; c.571G>A	p.Glu191Lys; p.Glu191Lys; p.Glu191Lys	FALSE	2.67E-05
12:1646095:C:T	c.923C>T; c.923C>T; c.923C>T	p.Ser308Leu; p.Ser308Leu; p.Ser308Leu	FALSE	8.46E-06
12:1646095:C:T	c.923C>T; c.923C>T; c.923C>T	p.Ser308Leu; p.Ser308Leu; p.Ser308Leu	FALSE	2.32E-06
12:1631402:G:A	c.48G>A; c.48G>A; c.48G>A; c.48G>A	p.Trp16*; p.Trp16*; p.Trp16*; p.Trp16*	TRUE	1.72E-05
12:1632734:G:A	c.157G>A; c.157G>A; c.157G>A; c.157G>A	p.Gly53Arg; p.Gly53Arg; p.Gly53Arg; p.Gly53Arg	FALSE	2.32E-06
12:1639869:G:C	c.514G>C; c.514G>C; c.514G>C	p.Ala172Pro; p.Ala172Pro; p.Ala172Pro	FALSE	1.16E-06
12:1646127:T:C	c.955T>C; c.955T>C; c.955T>C	p.Cys319Arg; p.Cys319Arg; p.Cys319Arg	FALSE	4.64E-05
12:1639861:AC:A	c.508delC; c.508delC; c.508delC	p.Arg170fs; p.Arg170fs; p.Arg170fs	TRUE	6.95E-06

Figure 4 (cont.)

Outcome	Case definition	Controls definition
Any fracture	ICD10: M80, M840, S22, S32, S42, S62, S72, S82, S92, T02, T142, T912, X5909, Z094, Z470, Z544, Z8731, Z8781, M841, M842, M843, M844, M484, M485, S12, S220, S221, S320, S321, S322, S327, S328, S329, T08, T911, S222, S223, S224, S225, S420, S421, S427, S428, S429, M8001, M8051, M8081, M8091, M8401, M8411, M8421, M8431, M8441, S422, S423, S424, M8002, M8052, M8082, M8092, M8402, M8412, M8422, M8432, M8442, S52, S620, S621, T922, M8003, M8053, M8083, M8093, M8403, M8413, M8423, M8433, M8443, S323, S324, S325, S326, M8005, M8055, M8085, M8095, M8405, M8415, M8425, M8435, M8445, S720, S721, S722, S820, S821, S822, S823, S824, S825, S826, S827, S828, S829, M8006, M8056, M8086, M8096, M8406, M8416, M8426, M8436, M8446, M8007, M8057, M8087, M8097, M8407, M8417, M8427, M8437, M8447, S920, S921, S922, S927, S929, S924, S925, S02, T902, S622, S623, S624, S628, M8004, M8054, M8084, M8094, M8404, M8414, M8424, M8434, M8444, S625, S626, S627, S723, S724, S727, S728, S729, T931, T10, T921, T12, T932; ICD10CM: M80, S22, S32, S42, S62, S72, S82, S92, Z8731, Z8781, M84, M484, M485, S12, S220, S221, S320, S321, S322, S327, S329, M8008, M8088, S222, S223, S224, S225, S420, S421, S427, S428, S429, M8001, M8051, M8081, M8091, M8401, M8411, M8421, M8431, M8441, S422, S423, S424, M8002, M8052, M8082, M8092, M8402, M8412, M8422, M8432, M8442, S52, S620, S621, M8003, M8053, M8083, M8093, M8403, M8413, M8423, M8433, M8443, S323, S324, S325, S326, S328, M8415, M8425, M8435, M8445, S720, S721, S722, M8005, M8055, M8085, M8095, M8405, S820, S821, S822, S823, S824, S825, S826, S827, S828, S829, M8006, M8056, M8086, M8096, M8406, M8416, M8426, M8436, M8446, M8007, M8057, M8087, M8097, M8407, M8417, M8427, M8437, M8447, S920, S921, S922, S927, S929, S924, S925, S02, S622, S623, S624, S629, M8004, M8054, M8084, M8094, M8404, M8414, M8424, M8434, M8444, S625, S626, S627, S723, S724, S727, S728, S729, T10, T921, T12, T932; ICD9CM: 7331, 7338, 73395, 809, 829, 9055, E887, V664, V674, V1351, V1352, V1551, V5419, V5429, 805, 806, 73313, V5417, V5427, 9051, 807, 810, 811, 812, 73311, V5411, V5421, 813, 814, 73312, V5412, V5422, 808, 73398, 820, 73314, 73396, V5413, V5423, 9053, 822, 823, 824, 73316, 73393, V5416, V5426, 825, 73394, 826, 800, 801, 802, 803, 804, 9050, 815, 817, 816, 821, 73315, 73397, V5415, V5425, 818, 819, V5410, V5420, 9052, 827, 828, V5414, V5424, 9054;	Participants were excluded from the control group if they were a case for "Any fracture".

Figure 5

Outcome	Case definition	Controls definition
Any fracture	OPCS4: O17, W19, W20, W21, W22, W23, W24, W25, W26, W332, W651, W653, W654, W655, W661, W663, W664, W671, W673, W675, W677, V44, V45, V46, O171, U502, W191, W241, W205, C082, C083, C085, V053, V054, V08, V09, V15; f.20002: 1630, 1646, 1644, 1645, 1631, 1632, 1633, 1634, 1635, 1636, 1637, 1647, 1648, 1650, 1651, 1652, 1653, 1654, 1655, 1656, 1627, 1628, 1629, 1638, 1639, 1640, 1649; f.20004: 1439; UKB_Otherfields: 2463; NOMESCO: NHJ, NAI, NCJ, NEJ, NGJ, NHJ02, NHJ03, NHJ10, NHJ11, NHJ12, NHJ23, NHJ41, NHJ42, NHJ60, NHJ62, NHJ63, NHJ71, NHJ73, NHJ80, NHJ81, NHJ07, NHJ44, NHJ47, NHJ85, NHJ18, AAD40, DHD10, DHD20, DHD30, DJD30, DJD40, EDC32, EDC34, EDC36, EDC38, EEC20, EEC25, EEC30, EEC35, EFB20, EFB30, NDJ, NFJ, NBJ; NOMESCO_Op6: 8120, 8121, 8203, 8204, 8205, 8206, 8207, 8210, 8211, 8212, 8213, 8217, 8214, 8215, 8216, 8221, 8391, 0301, 0200, 2150; Subjects in MDCS reporting having ever sustained a fracture were also included as cases.	Participants were excluded from the control group if they were a case for "Any fracture".
Major fracture	ICD10: S22, S32, S42, S62, S72, S82, T912, M484, M485, S12, S220, S221, S320, S321, S322, S327, S328, S329, T08, T911, S222, S223, S224, S225, S420, S421, S427, S428, S429, M8001, M8051, M8081, M8091, M8401, M8411, M8421, M8431, M8441, S422, S423, S424, M8002, M8052, M8082, M8092, M8402, M8412, M8422, M8432, M8442, S52, S620, S621, T922, M8003, M8053, M8083, M8093, M8403, M8413, M8423, M8433, M8443, S323, S324, S325, S326, M8005, M8055, M8085, M8095, M8405, M8415, M8425, M8435, M8445, S720, S721, S722, S820, S821, S822, S823, S824, S825, S826, S827, S828, S829, M8006, M8056, M8086, M8096, M8406, M8416, M8426, M8436, M8446, M8007, M8057, M8087, M8097, M8407, M8417, M8427, M8437, M8447, S723, S724, S727, S728, S729, T931, T10, T921, T12, T932; ICD10CM: S22, S32, S42, S62, S72, S82, M484, M485, S12, S220, S221, S320, S321, S322, S327, S329, M8008, M8088, S222, S223, S224, S225, S420, S421, S427, S428, S429, M8001, M8051, M8081, M8091, M8401, M8411, M8421, M8431, M8441, S422, S423, S424, M8002, M8052, M8082, M8092, M8402, M8412, M8422, M8432, M8442, S52, S620, S621, M8003, M8053, M8083, M8093, M8403, M8413, M8423, M8433, M8443, S323, S324, S325, S326, S328, M8415, M8425, M8435, M8445, S720, S721, S722, M8005, M8055, M8085, M8095, M8405,	Participants were excluded from the control group if they were a case for "Any fracture".

Figure 5 (cont.)

Outcome	Case definition	Controls definition
Major fracture	S820, S821, S822, S823, S824, S825, S826, S827, S828, S829, M8006, M8056, M8086, M8096, M8406, M8416, M8426, M8436, M8446, M8007, M8057, M8087, M8097, M8407, M8417, M8427, M8437, M8447, S723, S724, S727, S728, S729, T10, T921, T12, T932; ICD9CM: 805, 806, 73313, V5417, V5427, 9051, 807, 810, 811, 812, 73311, V5411, V5421, 813, 814, 73312, V5412, V5422, 808, 73398, 820, 73314, 73396, V5413, V5423, 9053, 822, 823, 824, 73316, 73393, V5416, V5426, 821, 73315, 73397, V5415, V5425, 818, 819, V5410, V5420, 9052, 827, 828, V5414, V5424, 9054; OPCS4: V44, V45, V46, O171, U502, W191, W241, W205; f.20002: 1630, 1646, 1644, 1645, 1631, 1632, 1633, 1634, 1635, 1636, 1637, 1647, 1648, 1650, 1651, 1652, 1653, 1649; UKB_Otherfields: 2463; NOMESCO: NAJ, NCJ, NEJ, NGJ, NHJ02, NHJ03, NHJ10, NHJ11, NHJ12, NHJ23, NHJ41, NHJ42, NHJ60, NHJ62, NHJ63, NHJ71, NHJ73, NHJ80, NHJ81, NFI, NBI; NOMESCO (Op6): 0301	Participants were excluded from the control group if they were a case for "Any fracture".

Figure 5 (cont.)