

**Supplemental Table 5: Sensitivity analysis for enrichment of HSP variants in 48 PPMS patients**

Variant selection criteria					Variants within 58 HSP genes				
MAF < 1% in public cohorts	Functionally deleterious (missense or splice site)	CADD score > 10	PhyloP Conservation <i>p-value</i> < 0.01	Damaging in SIFT or PolyPhen2 (missense only)	# unique variants	Mean in 48 PPMS	Mean in 100 controls	Relative Risk	Logistic regression <i>p-value</i>
+	+	-	-	-	368	0.69	0.30	2.29	0.0019
+	+	+	-	-	303	0.52	0.19	2.74	8.6 x 10 <sup>-4</sup>
+	+	-	+	-	171	0.29	0.12	2.43	0.036
+	+	-	-	+	157	0.25	0.11	2.27	0.043
+	+	+	+	-	<b>167</b>	<b>0.29</b>	<b>0.11</b>	<b>2.65</b>	<b>0.028</b>
+	+	+	+	+	111	0.15	0.05	2.92	0.056