Title

Genetic model of MS severity predicts future accumulation of disability

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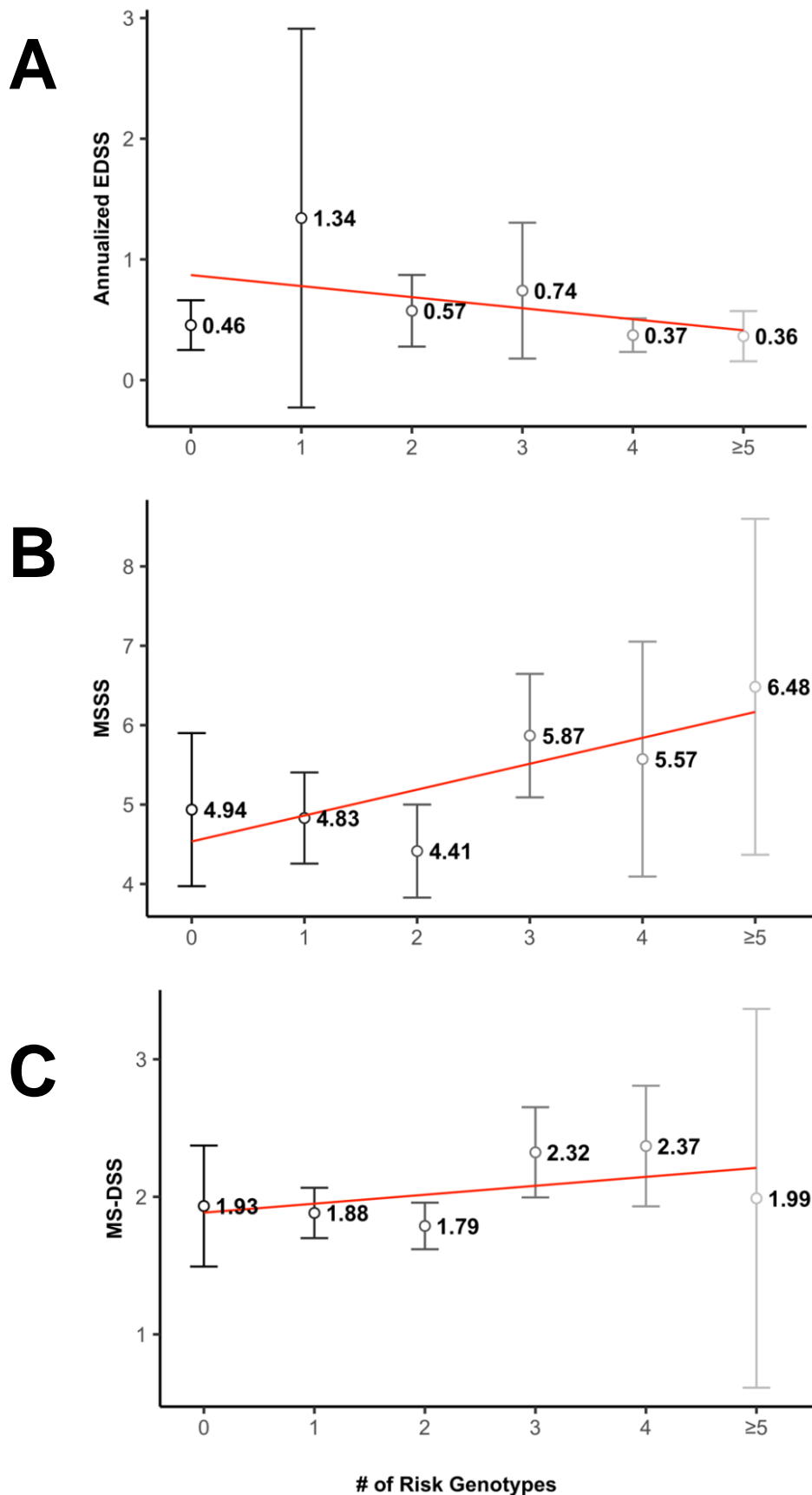
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Chr	Variant	Nearest Gene	Gene Name	Reference
12	rs4149584	TNFRSF1A	TNF Receptor Superfamily Member 1A	1
5	rs4704970	SGCD	Sarcoglycan Delta	2
4	rs10518025	RP11-584P21.2	N/A	2
11	rs180358	BUD13	BUD13 Homolog	2
8	rs2116078	RP11-351E7.1	N/A	2
7	rs17157903	RELN	Reelin	2
9	rs2842483	PCSK5	Proprotein Convertase Subtilisin/Kexin Type 5	2
19	rs299175	NLRP11	NLR Family Pyrin Domain Containing 11	2
2	rs1437898	NCKAP5	NCK Associated Protein 5	2
7	rs10243024	MET	MET Proto-Oncogene, Receptor Tyrosine Kinase	2
22	rs2283792	MAPK1	Mitogen-Activated Protein Kinase 1	3
5	rs2546890	IL12B	Interleukin 12B	3
16	rs7191888	C16orf47	Chromosome 16 Open Reading Frame 47	2
6	rs6941421	AL138720.1	N/A	2
18	rs1557351	LINC-ROR	Long Intergenic Non-Protein Coding RNA, Regulator Of Reprogramming	2
3	rs12638253	LEKR1	Leucine, Glutamate And Lysine Rich 1	2
11	rs1386330	AP005436.1	N/A	2
18	rs337718	RP11-736G13.1	N/A	2
4	rs1478091	RP11-401I19.1	N/A	2
7	rs10259085	C1GALT1	Core 1 Synthase, Glycoprotein-N-Acetylgalactosamine 3-Beta-Galactosyltransferase 1	2
4	rs6552511	TENM3	Teneurin Transmembrane Protein 3	23
17	rs7221818	WSCD1	WSC Domain Containing 1	23
16	rs12927173	XYLT1	Xylosyltransferase 1	23
16	rs2059283	XYLT1	Xylosyltransferase 1	23
10	rs1343522	HIF1AN	Hypoxia Inducible Factor 1 Subunit Alpha Inhibitor	23
2	rs4953911	MGAT5	Mannosyl (Alpha-1,6-)-Glycoprotein Beta-1,6-N-Acetyl-Glucosaminyltransferase	23
10	rs4573623	HIF1AN	Hypoxia Inducible Factor 1 Subunit Alpha Inhibitor	23
15	rs333548	MEGF11	Multiple EGF Like Domains 11	23
13	rs10508075	FGF14	Fibroblast Growth Factor 14	23
21	rs2839580	PDE9A	Phosphodiesterase 9A	23
10	rs2495725	HIF1AN	Hypoxia Inducible Factor 1 Subunit Alpha Inhibitor	23
2	rs3814022	MGAT5	Mannosyl (Alpha-1,6-)-Glycoprotein Beta-1,6-N-Acetyl-Glucosaminyltransferase	23
7	rs1078922	MTPN	Myotrophin	23
16	rs4315313	CDH13	Cadherin 13	23
7	rs7789940	YWHAG	Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Gamma	24
7	rs758944	YWHAG	Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Gamma	24
7	rs17149161	YWHAG	Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Gamma	24
7	rs7779014	YWHAG	Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Gamma	24
6	rs11962089	POPDC3	Popeye Domain Containing 3	24
4	rs12644284	TRIM2	Tripartite Motif Containing 2	24
2	rs4848821	ANAPC1	Anaphase Promoting Complex Subunit 1	24
9	rs10977017	PTPRD	Protein Tyrosine Phosphatase, Receptor Type D	24
10	rs1832745	RBM20	RNA Binding Motif Protein 20	24
9	rs1820314	IFNA16	Interferon Alpha 16	24
9	rs10811505	IFNA10	Interferon Alpha 10	24
16	rs1448239	GRIN2A	Glutamate Ionotropic Receptor NMDA Type Subunit 2A	24
8	rs7015570	PSD3	Pleckstrin And Sec7 Domain Containing 3	24
9	rs8729	KLHL9	Kelch Like Family Member 9	24
7	rs17170015	NPSR1	Neuropeptide S Receptor 1	24
2	rs10178552	ASXL2	ASXL Transcriptional Regulator 2	24
6	rs17080959	AKAP12	A-Kinase Anchoring Protein 12	2
4	rs987694	CAMK2D	Calcium/Calmodulin Dependent Protein Kinase II Delta	2
20	rs6089621	CDH4	Cadherin 4	2
8	rs9644362	CSMD1	CUB And Sushi Multiple Domains 1	2
16	rs205420	GSG1L	GSG1 Like	2
9	rs2792226	KDM4C	Lysine Demethylase 4C	2

20	rs10485772	MACROD2	MACRO Domain Containing 2	2
7	rs246462	MAGI2	Membrane Associated Guanylate Kinase, WW And PDZ Domain Containing 2	2
6	rs7349940	MTHFD1L	Methylenetetrahydrofolate Dehydrogenase (NADP+ Dependent) 1 Like	2
1	rs12127450	AGBL4	ATP/GTP Binding Protein Like 4	24
1	rs17505688	NTNG1	Netrin G1	24
1	rs17541777	PTGER3	Prostaglandin E Receptor 3	24
2	rs13019537	STON1-GTF2A1L	Stonin 1-General Transcription Factor IIA Subunit 1 Like Readthrough	24
2	rs13387792	MYT1L	Myelin Transcription Factor 1 Like	24
4	rs8192678	PPARGC1A	PPARG Coactivator 1 Alpha	24
5	rs11750073	CTNND2	Catenin Delta 2	24
6	rs7744583	ARID1B	AT-Rich Interaction Domain 1B	24
7	rs2530548	NPSR1	Neuropeptide S Receptor 1	24
7	rs626065	RELN	Reelin	24
7	rs11765693	YWHAG	Tyrosine 3-Monooxygenase/Tryptophan 5-Monooxygenase Activation Protein Gamma	24
8	rs7812549	INTS10	Integrator Complex Subunit 10	24
8	rs10505082	ZFPM2	Zinc Finger Protein, FOG Family Member 2	24
9	rs10985528	TBC1D2	TBC1 Domain Family Member 2	24
10	rs2399849	CAMK1D	Calcium/Calmodulin Dependent Protein Kinase I Delta	24
10	rs2766051	DOCK1	Dedicator Of Cytokinesis 1	24
11	rs1476203	OR6T1	Olfactory Receptor Family 6 Subfamily T Member 1	24
12	rs7134248	KDM2B	Lysine Demethylase 2B	24
15	rs7167473	FAM189A1	Family With Sequence Similarity 189 Member A1	24
16	rs8056098	CLEC16A	C-Type Lectin Domain Containing 16A	24
17	rs9892479	ASIC2	Acid Sensing Ion Channel Subunit 2	24
20	rs4814783	DTD1	D-Tyrosyl-TRNA Deacylase 1	24
22	rs9616098	CERK	Ceramide Kinase	24
2	rs7588193	LOC100506047	Uncharacterized LOC100506047	3
2	rs842639	LINC01185	Long Intergenic Non-Protein Coding RNA 1185	3
1	rs35967351	SLAMF7	SLAM Family Member 7	3
14	rs3825568	ZFP36L1	ZFP36 Ring Finger Protein Like 1	3
17	rs8070345	VMP1	Vacuole Membrane Protein 1	3
6	rs4959786	PSMG4	Proteasome Assembly Chaperone 4	25
19	rs471979	NLRP5	NLR Family Pyrin Domain Containing 5	25
2	rs6721763	ITGA4	Integrin Subunit Alpha 4	26
4	rs6532040	SPP1	Secreted Phosphoprotein 1	26
2	rs1250249	FN1	Fibronectin 1	26
1	rs699	AGT	Angiotensinogen	27
1	rs5051	AGT	Angiotensinogen	27
19	rs394221	PVRL2	Nectin Cell Adhesion Molecule 2	28
19	rs419010	PVRL2	Nectin Cell Adhesion Molecule 2	28
19	rs4803766	PVRL2	Nectin Cell Adhesion Molecule 2	28
19	rs2972566	PVRL2	Nectin Cell Adhesion Molecule 2	28
2	rs1143634	IL1B	Interleukin 1 Beta	29
22	rs755622	MIF	Macrophage Migration Inhibitory Factor	30
18	rs12959006	MBP	Myelin Basic Protein	36
2	rs3116496	CD28	CD28 Molecule	31
3	rs6641	TIMMDC1	Translocase Of Inner Mitochondrial Membrane Domain Containing 1	31
3	rs17281995	CD86	CD86 Molecule	31
1	rs1801133	MTHFR	Methylenetetrahydrofolate Reductase	32
5	rs6189	NR3C1	Nuclear Receptor Subfamily 3 Group C Member 1	33
5	rs10052957	NR3C1	Nuclear Receptor Subfamily 3 Group C Member 1	33
5	rs6190	NR3C1	Nuclear Receptor Subfamily 3 Group C Member 1	33
5	rs6198	NR3C1	Nuclear Receptor Subfamily 3 Group C Member 1	33
3	rs1801282	PPARG	Peroxisome Proliferator Activated Receptor Gamma	34
19	rs7412	APOE	Apolipoprotein E	35
19	rs429358	APOE	Apolipoprotein E	35

Supplemental Figure 1 The cumulative genetic risk score (CGRS; (Pan et al., 2016)) aggregates 116 validated MS susceptibility variants in early-MS patients followed over a 5-year period. In contrast to the original publication, we fail to detect a dose-response relationship between the CGRS when predicting (A) annualized Expanded Disability Status Scales (EDSS), or the EDSS-based (B) MS severity score. Similarly, the CGRS did not show a dose-response relationship with the more sensitive severity scale, (C) MS disease severity scale.