

ONLINE SUPPLEMENT

Genetic drivers of von Willebrand Factor levels in an ischemic stroke population and association with risk for recurrent stroke.

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Supplemental Table I. Full list of SNPs associated with vWF in VISP.

CHR	SNP	BP	A1	A2	FRQ	IQ	BETA	SE	P
9	rs505922	136149229	C	T	0.636	0.9734	-0.3315	0.0285	2.32E-30
9	rs687289	136137106	A	G	0.6228	0.9788	-0.3284	0.0283	3.93E-30
9	rs554833	136147160	C	T	0.3777	0.9697	0.3291	0.0284	5.47E-30
9	rs687621	136137065	A	G	0.3783	0.9759	0.3275	0.0284	6.83E-30
9	rs529565	136149500	C	T	0.6352	0.9549	-0.3315	0.0288	1.09E-29
9	rs491626	136144873	C	T	0.3777	0.9575	0.3297	0.0287	1.59E-29
9	rs545971	136143372	C	T	0.3819	0.9743	0.3229	0.0284	5.92E-29
9	rs492488	136144960	A	G	0.6178	0.976	-0.3226	0.0284	5.93E-29
9	rs495203	136145240	C	T	0.3819	0.9767	0.3225	0.0284	5.93E-29
9	rs493246	136144994	A	G	0.6179	0.9764	-0.3225	0.0284	6.10E-29
9	rs582094	136145484	A	T	0.381	0.9781	0.3221	0.0284	6.70E-29
9	rs582118	136145471	A	G	0.3809	0.9786	0.322	0.0284	6.82E-29
9	rs674302	136146664	A	T	0.6185	0.9771	-0.322	0.0284	6.96E-29
9	rs612169	136143442	A	G	0.3802	0.9618	0.3247	0.0287	7.92E-29
9	rs8176663	136144427	C	T	0.6198	0.9699	-0.3232	0.0285	8.07E-29
9	rs514659	136142203	A	C	0.3813	0.9753	0.3219	0.0284	8.72E-29
9	rs576125	136144309	A	G	0.7133	0.673	-0.4207	0.0372	1.06E-28
9	rs543040	136143000	A	T	0.3781	0.9617	0.3238	0.0287	1.21E-28
9	rs676457	136146227	A	T	0.3769	0.9582	0.3244	0.0288	1.43E-28
9	rs2769071	136145974	A	G	0.3771	0.9578	0.3244	0.0288	1.47E-28
9	rs677355	136146046	A	G	0.6215	0.9498	-0.3253	0.0289	1.53E-28
9	rs527210	136146431	C	T	0.3745	0.9477	0.3259	0.029	1.68E-28
9	rs597988	136144284	A	T	0.6287	0.934	-0.3273	0.0292	3.25E-28
9	rs597974	136144297	A	G	0.3681	0.9225	0.3286	0.0295	5.37E-28
9	rs657152	136139265	A	C	0.6021	0.9857	-0.2993	0.028	7.22E-26
9	rs494242	136145118	C	T	0.4014	0.9796	0.3	0.0281	8.07E-26
9	rs544873	136143212	A	G	0.6003	0.9822	-0.2995	0.0281	9.02E-26
9	rs643434	136142355	A	G	0.5997	0.9854	-0.2988	0.0281	9.70E-26
9	rs644234	136142217	G	T	0.6012	0.9782	-0.2993	0.0282	1.35E-25
9	rs543968	136143121	C	T	0.6513	0.81	-0.3235	0.0321	2.76E-23
9	rs613534	136143120	A	G	0.3472	0.807	0.3159	0.0322	3.45E-22
9	rs532436	136149830	A	G	0.799	0.9768	-0.3347	0.0345	1.01E-21
9	rs2519093	136141870	C	T	0.2015	0.9662	0.3343	0.0346	1.53E-21
9	rs507666	136149399	A	G	0.7995	0.9787	-0.3316	0.0345	2.36E-21
9	rs635634	136155000	C	T	0.21	1.01	0.3127	0.0335	2.60E-20
9	rs550057	136146597	C	T	0.2609	0.9314	0.2765	0.0323	2.29E-17
9	rs579459	136154168	C	T	0.7782	1.0063	-0.2819	0.033	2.46E-17
9	rs651007	136153875	C	T	0.2213	1.0027	0.2825	0.0331	2.60E-17

9	rs600038	136151806	C	T	0.7781	1.005	-0.2817	0.033	2.68E-17
9	rs649129	136154304	C	T	0.2206	0.998	0.2831	0.0332	2.76E-17
9	rs495828	136154867	G	T	0.219	0.99	0.2849	0.0334	2.88E-17
9	rs630510	136149581	A	G	0.5423	0.9644	0.237	0.0279	4.32E-17
9	rs630014	136149722	A	G	0.5433	0.9695	0.2355	0.0279	5.64E-17
9	rs475419	136148231	C	T	0.5573	0.9855	0.2324	0.0279	1.67E-16
9	rs633862	136155444	C	T	0.5625	1.035	0.2215	0.0273	9.70E-16
9	rs581107	136147702	C	T	0.565	0.9708	0.2276	0.0282	1.15E-15
9	rs660340	136147553	A	G	0.5617	0.9829	0.2258	0.028	1.23E-15
9	rs659104	136147823	G	T	0.4377	0.9811	-0.2259	0.028	1.28E-15
9	rs476410	136148368	C	G	0.4379	0.9854	-0.2249	0.0279	1.45E-15
9	rs645982	136148409	A	G	0.5624	0.9866	0.2246	0.0279	1.54E-15
9	rs473533	136148035	C	T	0.4371	0.9885	-0.224	0.0279	1.73E-15
9	rs500498	136148647	C	T	0.4378	0.9864	-0.224	0.0279	1.87E-15
9	rs616154	136150466	C	T	0.5412	0.9385	0.2273	0.0284	2.01E-15
9	rs500499	136148648	C	G	0.4375	0.9874	-0.2236	0.0279	2.05E-15
9	rs559723	136150484	A	G	0.5108	0.9117	0.2318	0.029	2.12E-15
9	rs647800	136148000	A	G	0.577	0.9878	0.2165	0.0281	2.12E-14
9	rs9650778	136184798	C	T	0.0873	0.6039	0.4194	0.0631	3.80E-11
9	rs1633513	136140462	C	T	0.731	1.0018	0.2082	0.0313	3.91E-11
9	rs28446901	136308796	C	G	0.1882	0.9107	0.2471	0.0372	3.97E-11
9	rs514708	136133743	C	T	0.2655	1.0024	-0.2055	0.0313	7.06E-11
9	rs8176741	136131461	A	G	0.9026	1.0335	-0.3059	0.0467	7.14E-11
9	rs641959	136133699	A	C	0.2658	1.0044	-0.2047	0.0313	7.85E-11
9	rs641943	136133714	A	G	0.2647	0.9982	-0.2052	0.0314	8.47E-11
9	rs673578	136137857	G	T	0.7303	1.0061	0.2033	0.0312	9.13E-11
9	rs8176746	136131322	G	T	0.0972	1.0342	0.3044	0.0467	9.24E-11
9	rs8176749	136131188	C	T	0.0972	1.0342	0.3044	0.0467	9.24E-11
9	rs8176747	136131315	C	G	0.0972	1.0331	0.3043	0.0467	9.42E-11
9	rs8176759	136129647	A	G	0.9028	1.0332	-0.3042	0.0467	9.65E-11
9	rs1137827	136129715	C	T	0.0978	1.0256	0.304	0.0468	1.03E-10
9	rs10793962	136129115	A	T	0.0964	1.0192	0.304	0.0472	1.51E-10
9	rs8176743	136131415	C	T	0.0972	1.0342	0.2995	0.0467	1.84E-10
9	rs557317	136157037	A	C	0.2593	0.9977	-0.2031	0.0318	2.03E-10
9	rs12554336	136128663	A	G	0.1804	0.7103	-0.2731	0.0428	2.18E-10
9	rs8176736	136131785	C	T	0.795	0.8452	0.2376	0.0374	2.65E-10
9	rs8176737	136131783	C	T	0.2073	0.8553	-0.2349	0.037	2.79E-10
9	rs547495	136134995	C	T	0.7408	0.9589	0.2049	0.0324	3.15E-10
9	rs626035	136134994	G	T	0.7406	0.9579	0.2048	0.0324	3.28E-10
9	rs8176693	136137657	C	T	0.0916	0.9975	0.3057	0.0486	3.77E-10
9	rs8176728	136132561	C	G	0.7607	1.009	0.2036	0.0323	3.78E-10

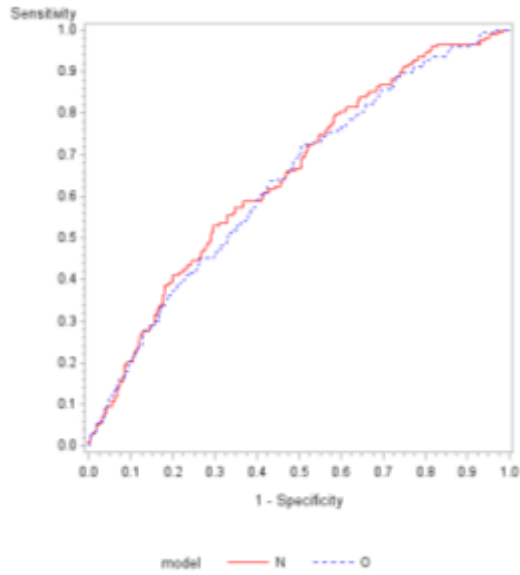
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9	rs62641783	136130653	C	G	0.895	0.3699	0.4669	0.0743	4.08E-10
9	rs62574567	136128421	C	G	0.2412	1.0101	-0.2013	0.0322	5.19E-10
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9	rs10901253	136128772	C	T	0.7596	1.021	0.2	0.0321	5.72E-10
9	rs4962114	136129611	A	G	0.7604	1.0162	0.2007	0.0322	5.72E-10
9	rs11244053	136129360	A	G	0.2379	1.0068	-0.2021	0.0324	5.73E-10
9	rs4962115	136129642	G	T	0.7628	1.0028	0.2027	0.0325	5.73E-10
9	rs4962116	136129716	A	G	0.7596	1.021	0.1999	0.0321	5.74E-10
9	rs8176644	136149150	C	T	0.0899	0.9712	0.3069	0.0496	7.39E-10
9	rs8176662	136144454	A	G	0.0899	0.9718	0.3069	0.0496	7.42E-10
9	rs8176671	136142313	A	C	0.0896	0.9722	0.3065	0.0496	8.02E-10
9	rs549331	136135195	C	G	0.2504	1.005	-0.1968	0.032	9.87E-10
9	rs663054	136146920	G	T	0.2623	0.9726	-0.1958	0.0319	9.98E-10
9	rs624601	136135365	A	G	0.75	1.0078	0.1963	0.032	1.06E-09
9	rs638756	136134472	A	C	0.2474	1.0213	-0.1953	0.0319	1.13E-09
9	rs672316	136138125	G	T	0.737	1.0015	0.1916	0.0314	1.32E-09
9	rs575259	136135752	A	G	0.2469	1.0123	-0.1948	0.0321	1.54E-09
9	rs2073825	136132707	A	T	0.2357	1.0276	-0.1909	0.0322	3.59E-09
9	rs8176732	136132303	A	G	0.236	1.0302	-0.19	0.0321	4.01E-09
9	rs8176740	136131472	A	T	0.2358	1.0251	-0.1902	0.0322	4.24E-09
9	rs12554339	136128737	A	C	0.2333	0.9898	-0.1942	0.0329	4.38E-09
9	rs11244052	136129125	A	C	0.7676	0.9855	0.1949	0.0331	4.40E-09
9	rs8176748	136131289	C	T	0.2351	1.0162	-0.1906	0.0324	4.78E-09
9	rs625593	136135096	A	G	0.7483	0.9801	0.1895	0.0323	5.37E-09
9	rs8176745	136131347	A	G	0.765	1.0272	0.1888	0.0322	5.55E-09
9	rs579622	136136242	A	G	0.7538	1.0099	0.1874	0.0321	6.21E-09
9	rs626792	136134864	A	C	0.244	1.0214	-0.1867	0.032	6.34E-09
9	rs547643	136135047	C	T	0.2438	1.0228	-0.1866	0.032	6.47E-09
9	rs579483	136136196	A	T	0.755	1.0156	0.1867	0.0321	6.67E-09
9	rs551322	136135444	A	G	0.2445	1.0195	-0.1855	0.032	8.14E-09
9	rs8176714	136133178	A	G	0.7593	0.998	0.188	0.0325	8.21E-09
9	rs574347	136135659	C	T	0.7562	1.0233	0.1849	0.032	8.83E-09
9	rs549446	136135238	C	T	0.2438	1.0233	-0.1849	0.032	8.83E-09
9	rs613423	136135478	A	G	0.7555	1.0193	0.185	0.032	8.84E-09
9	rs2073828	136137140	A	G	0.6201	1.0146	0.1661	0.0288	8.94E-09
9	rs8176690	136138317	A	G	0.3732	1.0261	-0.165	0.0287	1.02E-08
9	rs596141	136144689	G	T	0.2408	0.9823	-0.188	0.0327	1.04E-08
9	rs12554595	136128664	C	T	0.83	0.6654	0.2598	0.0452	1.06E-08
9	rs8176727	136132570	A	G	0.7677	1.0096	0.1876	0.0327	1.08E-08
9	rs1752339	136141135	C	T	0.7574	1.001	0.1858	0.0324	1.08E-08

9	rs551100	136146740	C	T	0.2414	1.005	-0.1855	0.0323	1.11E-08
9	rs62574565	136128259	A	G	0.769	0.9668	0.1916	0.0334	1.16E-08
9	rs8176718	136132957	C	T	0.2404	1.0259	-0.1837	0.032	1.16E-08
9	rs8176717	136133034	G	T	0.2399	1.0282	-0.1833	0.032	1.23E-08
9	rs488775	136144534	A	G	0.2399	1.0151	-0.184	0.0323	1.34E-08
9	rs517414	136134034	A	G	0.7588	1.0236	0.1828	0.0321	1.36E-08
9	rs675201	136146466	A	G	0.7601	1.0142	0.1839	0.0323	1.39E-08
9	rs474279	136139617	C	T	0.2399	1.0168	-0.1837	0.0322	1.39E-08
9	rs2073826	136136963	G	T	0.3745	1.0416	-0.1621	0.0285	1.50E-08
9	rs2073827	136137133	C	G	0.6282	1.0305	0.1631	0.0287	1.53E-08
9	rs574311	136144110	A	G	0.2395	1.0114	-0.1834	0.0323	1.62E-08
9	rs8176681	136139754	C	T	0.6247	1.011	0.1635	0.0289	1.77E-08
9	rs7853989	136131592	C	G	0.8879	1.0005	-0.2472	0.0444	2.90E-08
9	rs502361	136155589	C	G	0.7585	1.0108	0.1789	0.0322	3.13E-08
9	rs1633514	136140513	C	T	0.2368	1.0127	-0.18	0.0324	3.20E-08
9	rs549443	136135237	A	G	0.7619	1.0073	0.1801	0.0324	3.21E-08
9	rs500428	136155343	A	G	0.7603	1.0217	0.1779	0.0321	3.45E-08
9	rs9411395	136184782	A	G	0.2555	0.5634	0.2362	0.0427	3.52E-08
9	rs3124766	136316942	A	G	0.8176	0.9771	-0.2019	0.0365	3.67E-08
9	rs493211	136136516	A	G	0.7611	0.9979	0.1799	0.0326	3.73E-08
9	rs3124761	136339755	C	T	0.1897	0.885	0.2092	0.0379	3.77E-08
9	rs537895	136150403	A	G	0.7652	0.9653	0.1838	0.0333	3.82E-08
9	rs663367	136153451	A	G	0.7606	1.0224	0.1771	0.0321	3.97E-08
9	rs3094379	136334910	C	T	0.1887	0.9003	0.2074	0.0376	3.99E-08
9	rs3124764	136329954	C	T	0.1833	0.9249	0.2067	0.0375	4.03E-08
9	rs552148	136153481	C	T	0.2396	1.0232	-0.1765	0.0321	4.31E-08

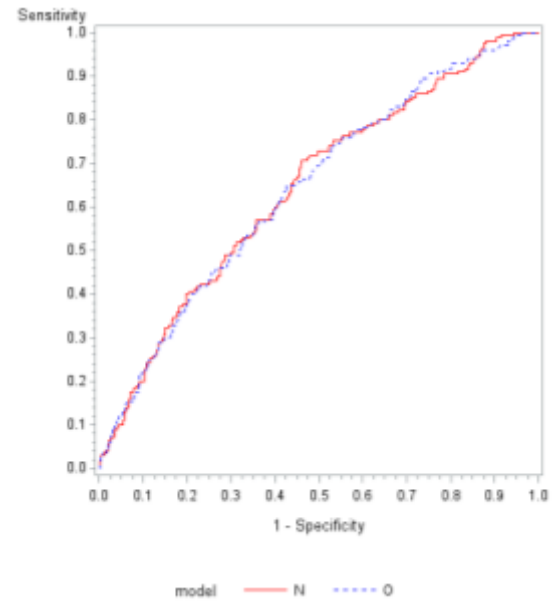
Supplemental Table II. Prediction performance of the conventional clinical variables, vWF, and *ABO* SNP rs505922 for the risk of recurrent stroke

Model	Variables	AUC	Comparison	NRI (SE) p-value	IDI (SE) p-value
Original	Conventional clinical variables: age, diabetes status, hypertension, smoking, prior stroke, and treatment groups	0.635			
New 1	Model 1 + vWF	0.648	New 1 vs. Original	0.106 (0.035) 0.0028	0.004 (0.002) 0.0388
New 2	Model 1 + rs505922	0.643	New 2 vs. Original	0.008 (0.029) 0.7772	0.001 (0.001) 0.4685
New 3	Model 1 + vWF + rs505922	0.654	New 3 vs. Original	0.110 (0.042) 0.0091	0.006 (0.002) 0.0137

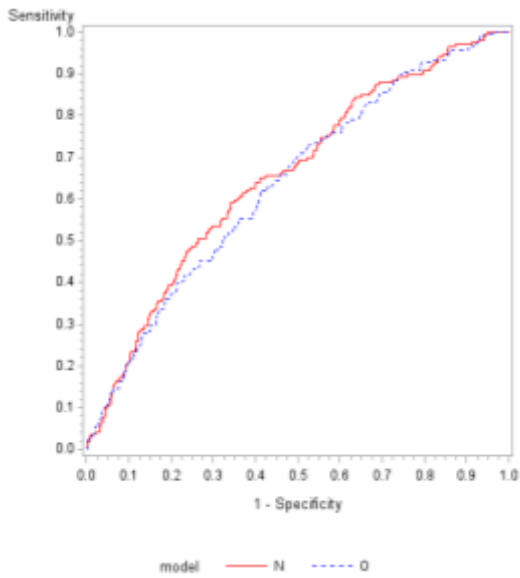
A



B



C



Supplemental Figure I. ROC curves. Original model [O] including adjustments for age, diabetes status, hypertension, smoking, prior stroke, and treatment groups vs. the New model [N] including addition of (A) vWF, (B) rs505922, and (C) vWF and rs505922.

Supplemental Table III. Expanded Association of SNPs identified in current study.

Chr	BP	RS	PMID	Author	Trait	Gene	Published p-value	Current Study p-value
9	133279294	rs495828	20066004	Chung CM ¹	Angiotensin-converting enzyme activity	ABO	3.x10-8	2.88x10-17
			24816252	Shin SY ²	Blood metabolite ratios	ABO	6x10-34	
			20139978	Kamatani Y ³	Hematological and biochemical traits	ABO	4x10-59	
			20139978	Kamatani Y ³	Red blood cell count	ABO	3x10-12	
			22672568	Heit JA ⁴	Venous thromboembolism	ABO	3x10-16	
			24262325	Dichgans M ^b	Coronary artery disease	ABO	2x10-7	
			24262325	Dichgans M ^b	Coronary artery disease or ischemic stroke	ABO	2x10-9	
			24262325	Dichgans M ⁵	Coronary artery disease or large artery stroke	ABO	3x10-8	
			21378990	Schunkert H ⁶	Coronary heart disease	ABO	4x10-14	
			22001757	Chambers JC ⁷	Liver enzyme levels (alkaline phosphatase)	ABO	3x10-123	
			23222517	van der Harst P ⁸	Red blood cell traits	ABO	9x10-18	
			19729612	Paterson AD ⁹	Soluble E-selectin levels	ABO	1x10-29	
			20167578	Barbalic M ¹⁰	Soluble levels of adhesion molecules	ABO	2x10-41	
			24586186	Rueedi R ¹¹	Urinary metabolites (H-NMR features)	ABO	2x10-32	
9	133279871	rs633862	25134534	Chen K ¹²	Epithelial ovarian cancer	SURF6, ABO	9x10-7	9.7x10-16
9	133279427	rs635634	20686565	Teslovich TM ¹³	Cholesterol, total	ABO	9x10-21	2.6x10-20
			20686565	Teslovich TM ¹³	LDL cholesterol	ABO	8x10-22	
9	133278860	rs649129	24816252	Shin SY ²	Blood metabolite ratios	ABO	9x10-37	2.76x10-17
			20167578	Barbalic M ¹⁰	Soluble levels of adhesion molecules	ABO	1x10-15	
9	133278431	rs651007	23381943	Williams FM ¹⁴	End-stage coagulation	ABO	2x10-25	2.6x10-17
			20147318	Qi L ¹⁵	E-selectin levels	ABO	2x10-82	
			25352340	Benyamin B ¹⁶	Iron status biomarkers (ferritin levels)	ABO	1x10-8	
			21909109	Kim YJ ¹⁷	Metabolite levels	ABO	6x10-9	
			24094242	Li J ¹⁸	Serum alkaline phosphatase levels	SURF6, ABO	1x10-56	
9	133262254	rs8176693	25552591	Lieb W ¹⁹	Endothelial growth factor levels	ABO	2x10-33	3.77x10-10
			25028398	Weiss FU ²⁰	High serum lipase activity	ABO	1x10-22	
			25028398	Weiss FU ²⁰	Serum lipase activity	ABO	1x10-30	

9	133256074	rs8176741	24941225	Liang Y ²¹	Elevated serum carcinoembryonic antigen levels	ABO	2x10 ⁻²⁴	7.14x10 ⁻¹¹
9	133256028	rs8176743	25173106	Hysi PG ²²	Intraocular pressure	ABO	3x10 ⁻¹¹	1.84x10 ⁻¹⁰
9	133255935	rs8176746	20139978	Kamatani Y ³	Mean corpuscular hemoglobin concentration	ABO	4x10 ⁻⁸	9.24x10 ⁻¹¹
9	133255801	rs8176749	23300138	He M ²³	Tumor biomarkers	ABO	7x10 ⁻¹⁰⁵	9.24x10 ⁻¹¹

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