

Assessing the causal relationship between obesity and venous thromboembolism through a Mendelian Randomization study

Sara Lindström¹, Marine Germain^{2,3}, Marta Crous-Bou^{4,5}, Erin N. Smith^{6,7}, Pierre-Emmanuel Morange⁸, Astrid van Hylckama Vlieg⁹, Hugoline G. de Haan⁹, Daniel Chasman^{10,11}, Paul Ridker^{10,11}, Jennifer Brody¹², Mariza de Andrade¹³, John A Heit¹⁴, Weihong Tang¹⁵, Immaculata DeVivo^{4,5}, Francine Grodstein⁴, Nicholas L. Smith^{1,16,17}, David Tregouet^{2,3} and Christopher Kabrhel^{11,18} for the INVENT Consortium.

¹Department of Epidemiology, University of Washington, Seattle WA, USA; ²Sorbonne Universités, UPMC Univ. Paris 06, INSERM, UMR_S 1166, Team Genomics & Pathophysiology of Cardiovascular Diseases, Paris, France; ³ICAN Institute for Cardiometabolism and Nutrition, Paris, France; ⁴Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA; ⁵Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA, USA; ⁶Department of Pediatrics, Rady Children's Hospital, University of California, San Diego, La Jolla, CA, USA; ⁷K.G. Jebsen Thrombosis Research and Expertise Centre (TREC), Department of Clinical Medicine, UiT The Arctic University of Norway, Tromsø, Norway; ⁸INSERM, UMR_S1062, Nutrition Obesity and Risk of Thrombosis, Aix-Marseille University, Marseille, France; ⁹Department of Clinical Epidemiology, Leiden University Medical Center, Leiden, The Netherlands; ¹⁰Division of Preventive Medicine, Brigham and Women's Hospital, Boston MA USA; ¹¹Harvard Medical School, Boston MA, USA; ¹²Department of Medicine, University of Washington, Seattle WA, USA; ¹³Biomedical Statistics and Informatics, Mayo Clinic and College of Medicine, Rochester, MN, USA; ¹⁴Division of Cardiovascular Diseases, Mayo Clinic and College of Medicine, Rochester, MN, USA; ¹⁵Division of Epidemiology & Community Health, School of Public Health, University of Minnesota, Minneapolis, MN, USA; ¹⁶Group Health Research Institute, Group Health Cooperative, Seattle WA USA; ¹⁷Seattle Epidemiologic Research and Information Center, Department of Veterans Affairs Office of Research and Development, Seattle WA USA; ¹⁸Department of Emergency Medicine, Massachusetts General Hospital, Boston MA, USA

* Corresponding Author:

Sara Lindström
Department of Epidemiology
University of Washington, Seattle, WA.
Email: saralind@uw.edu.
Phone: +1-206-221-3148
ORCID: 0000-0002-7137-7281

Supplementary Table 2: Association between BMI SNPs and VTE sorted by VTE association p-value

SNP	Chromosome	Pos (hg18)	Closest gene	Effect allele	Beta* BMI	SE* BMI	Beta VTE	SE VTE	P VTE	Comment
rs1558902	16	52361075	<i>FTO</i>	A	0.082	0.003	0.066	0.024	0.005	
rs2287019	19	50894012	<i>QPCTL</i>	C	0.036	0.004	0.078	0.030	0.010	
rs16951275	15	65864222	<i>MAP2K5</i>	T	0.031	0.004	0.062	0.027	0.023	
rs2080454	16	47620091	<i>CBLN1</i>	C	0.017	0.003	0.052	0.024	0.033	
rs977747	1	47457264	<i>TAL1</i>	T	0.017	0.003	0.047	0.024	0.047	
rs12885454	14	28806589	<i>PRKD1</i>	C	0.021	0.003	-0.048	0.025	0.052	
rs205262	6	34671142	<i>C6orf106</i>	G	0.022	0.004	0.048	0.025	0.056	
rs13107325	4	103407732	<i>SLC39A8</i>	T	0.048	0.007	0.082	0.044	0.065	
rs4740619	9	15624326	<i>C9orf93</i>	T	0.018	0.003	0.042	0.023	0.074	
rs3736485	15	49535902	<i>DMXL2</i>	A	0.018	0.003	0.041	0.024	0.085	
rs11727676	4	145878514	<i>HHIP</i>	T	0.036	0.006	0.086	0.053	0.104	
rs17724992	19	18315825	<i>PGPEP1</i>	A	0.019	0.004	0.044	0.027	0.107	
rs10733682	9	128500735	<i>LMX1B</i>	A	0.017	0.003	-0.037	0.023	0.112	
rs17024393	1	109956211	<i>GNAT2</i>	C	0.066	0.009	0.109	0.069	0.115	
rs2121279	2	142759755	<i>LRP1B</i>	T	0.025	0.004	0.053	0.035	0.126	
rs6567160	18	55980115	<i>MC4R</i>	C	0.056	0.004	0.041	0.027	0.133	
rs3888190	16	28796987	<i>ATP2A1</i>	A	0.031	0.003	0.034	0.024	0.152	
rs6477694	9	110972163	<i>EPB41LAB</i>	C	0.017	0.003	0.034	0.024	0.153	
rs657452	1	49362434	<i>AGBL4</i>	A	0.023	0.003	-0.031	0.024	0.189	
rs3817334	11	47607569	<i>MTCH2</i>	T	0.026	0.003	-0.030	0.024	0.201	
rs9641123	7	93035668	<i>CALCR</i>	C	0.019	0.004	0.030	0.024	0.206	
rs9400239	6	109084356	<i>FOXO3</i>	C	0.019	0.003	0.032	0.025	0.206	
rs9540493	13	65103705	<i>MIR548X2</i>	A	0.017	0.003	-0.031	0.024	0.207	
rs11126666	2	26782315	<i>KCNK3</i>	A	0.021	0.003	0.032	0.026	0.216	
rs7715256	5	153518086	<i>GALNT10</i>	G	0.016	0.003	0.029	0.023	0.218	

rs11688816	2	62906552	<i>EHBPI</i>	G	0.017	0.003	-0.028	0.023	0.221	
rs2650492	16	28240912	<i>SBKI</i>	A	0.021	0.004	0.028	0.026	0.290	
rs9925964	16	31037396	<i>KAT8</i>	A	0.019	0.003	0.024	0.024	0.325	
rs9914578	17	1951886	<i>SMG6</i>	G	0.02	0.004	0.028	0.029	0.326	
rs1808579	18	19358886	<i>Cl8orf8</i>	C	0.017	0.003	0.022	0.023	0.335	
rs11583200	1	50332407	<i>ELAVL4</i>	C	0.018	0.003	0.022	0.024	0.353	
rs11847697	14	29584863	<i>PRKD1</i>	T	0.049	0.008	0.052	0.057	0.361	
rs4256980	11	8630515	<i>TRIM66</i>	G	0.021	0.003	-0.021	0.024	0.383	
rs12940622	17	76230166	<i>RPTOR</i>	G	0.018	0.003	-0.020	0.023	0.396	
rs12446632	16	19842890	<i>GPRC5B</i>	G	0.04	0.005	0.027	0.033	0.411	
rs7599312	2	213121476	<i>ERBB4</i>	G	0.022	0.003	0.021	0.026	0.413	
rs17203016	2	207963763	<i>CREB1</i>	G	0.021	0.004	-0.024	0.030	0.421	
rs2820292	1	200050910	<i>NAVI</i>	C	0.02	0.003	0.018	0.023	0.441	
rs13021737	2	622348	<i>TMEM18</i>	G	0.06	0.004	0.023	0.030	0.442	
rs6465468	7	95007450	<i>ASB4</i>	T	0.017	0.004	-0.020	0.026	0.443	
rs1016287	2	59159129	<i>LINC01122</i>	T	0.023	0.003	0.019	0.025	0.446	
rs16907751	8	81538012	<i>ZBTB10</i>	C	0.035	0.007	-0.029	0.038	0.446	
rs1528435	2	181259207	<i>UBE2E3</i>	T	0.018	0.003	-0.018	0.024	0.453	
rs2836754	21	39213610	<i>ETS2</i>	C	0.016	0.003	0.018	0.024	0.454	
rs1000940	17	5223976	<i>RABEP1</i>	G	0.019	0.003	0.018	0.025	0.461	
rs7138803	12	48533735	<i>BCDIN3D</i>	A	0.032	0.003	0.017	0.024	0.462	
rs1460676	2	164275935	<i>FIGN</i>	C	0.02	0.004	0.022	0.031	0.482	
rs2033529	6	40456631	<i>TDRG1</i>	G	0.019	0.003	0.018	0.026	0.484	
rs17094222	10	102385430	<i>HIF1AN</i>	C	0.025	0.004	0.020	0.029	0.484	
rs1167827	7	75001105	<i>HIP1</i>	G	0.02	0.003	0.016	0.023	0.488	
rs1441264	13	78478920	<i>MIR548A2</i>	A	0.018	0.003	0.016	0.023	0.488	
rs12016871	13	26915782	<i>MTIF3</i>	T	0.03	0.005	0.020	0.029	0.497	
rs7903146	10	114748339	<i>TCF7L2</i>	C	0.023	0.003	0.017	0.025	0.502	

rs16851483	3	142758126	<i>RASA2</i>	T	0.048	0.008	0.031	0.046	0.504	
rs6804842	3	25081441	<i>RARB</i>	G	0.019	0.003	-0.016	0.024	0.507	
rs12566985	1	74774781	<i>FPGT-TNNI3K</i>	G	0.024	0.003	0.016	0.024	0.509	
rs12286929	11	114527614	<i>CADM1</i>	G	0.022	0.003	-0.015	0.023	0.523	
rs17405819	8	76969139	<i>HNF4G</i>	T	0.022	0.003	0.016	0.025	0.530	
rs17001654	4	77348592	<i>SCARB2</i>	G	0.031	0.005	0.020	0.033	0.548	
rs13191362	6	162953340	<i>PARK2</i>	A	0.028	0.005	0.020	0.035	0.579	
rs2033732	8	85242264	<i>RALYL</i>	C	0.019	0.004	-0.014	0.027	0.605	
rs2176598	11	43820854	<i>HSD17B12</i>	T	0.02	0.004	0.014	0.027	0.613	
rs11165643	1	96696685	<i>PTBP2</i>	T	0.022	0.003	-0.012	0.024	0.617	
rs13201877	6	137717234	<i>IFNGR1</i>	G	0.023	0.005	0.016	0.034	0.647	
rs1516725	3	187306698	<i>ETV5</i>	C	0.045	0.005	-0.016	0.035	0.651	
rs12401738	1	78219349	<i>FUBP1</i>	A	0.021	0.003	0.010	0.025	0.673	
rs9374842	6	120227364	<i>LOC285762</i>	T	0.019	0.004	-0.011	0.027	0.673	
rs2176040	2	226801046	<i>LOC646736</i>	A	0.014	0.003	0.010	0.024	0.682	
rs12429545	13	53000207	<i>OLFM4</i>	A	0.033	0.005	-0.013	0.035	0.699	
rs543874	1	176156103	<i>SEC16B</i>	G	0.048	0.004	0.011	0.030	0.725	
rs3101336	1	72523773	<i>NEGR1</i>	C	0.033	0.003	-0.008	0.024	0.725	
rs7243357	18	55034299	<i>GRP</i>	T	0.022	0.004	0.011	0.031	0.731	
rs10938397	4	44877284	<i>GNPDA2</i>	G	0.04	0.003	0.008	0.024	0.737	
rs13078960	3	85890280	<i>CADM2</i>	G	0.03	0.004	-0.009	0.029	0.746	
rs7141420	14	78969207	<i>NRXN3</i>	T	0.024	0.003	-0.007	0.023	0.761	
rs11191560	10	104859028	<i>NT5C2</i>	C	0.031	0.005	-0.012	0.041	0.770	
rs10132280	14	24998019	<i>STXBP6</i>	C	0.023	0.003	-0.007	0.026	0.792	
rs2112347	5	75050998	<i>POC5</i>	T	0.026	0.003	0.006	0.025	0.820	
rs4569374	18	38402879	<i>LOC284260</i>	T	0.016	0.003	0.005	0.024	0.823	proxy for rs7239883
rs7899106	10	87400884	<i>GRID1</i>	G	0.04	0.007	0.012	0.054	0.827	
rs2075650	19	50087459	<i>TOMM40</i>	A	0.026	0.005	0.007	0.034	0.838	

rs2365389	3	61211502	<i>FHIT</i>	C	0.02	0.003	0.005	0.024	0.842	
rs3849570	3	81874802	<i>GBE1</i>	A	0.019	0.003	0.005	0.025	0.845	
rs1928295	9	119418304	<i>TLR4</i>	T	0.019	0.003	0.004	0.023	0.848	
rs4787491	16	29922838	<i>INO80E</i>	G	0.016	0.003	0.004	0.023	0.853	
rs2207139	6	50953449	<i>TFAP2B</i>	G	0.045	0.004	-0.005	0.031	0.864	
rs3810291	19	52260843	<i>ZC3H4</i>	A	0.028	0.004	-0.005	0.028	0.868	
rs11030104	11	27641093	<i>BDNF</i>	A	0.041	0.004	-0.004	0.028	0.883	
rs10182181	2	25003800	<i>ADCY3</i>	G	0.031	0.003	-0.003	0.023	0.892	
rs7164727	15	70881044	<i>LOC100287559</i>	T	0.018	0.003	0.003	0.025	0.910	
rs10968576	9	28404339	<i>LINGO2</i>	G	0.025	0.003	-0.001	0.025	0.955	
rs758747	16	3567359	<i>NLRC3</i>	T	0.023	0.004	0.001	0.026	0.972	
rs492400	2	219057996	<i>USP37</i>	C	0.016	0.003	-0.001	0.025	0.981	
rs29941	19	39001372	<i>KCTD15</i>	G	0.018	0.003	0.000	0.025	0.984	
rs6091540	20	50521269	<i>ZFP64</i>	C	0.019	0.004	0.000	0.026	0.996	

* Beta and standard error estimates for BMI is extracted from the European ancestry analysis in Locke et al, Nature 2015 (ref 10)