

Supplementary material

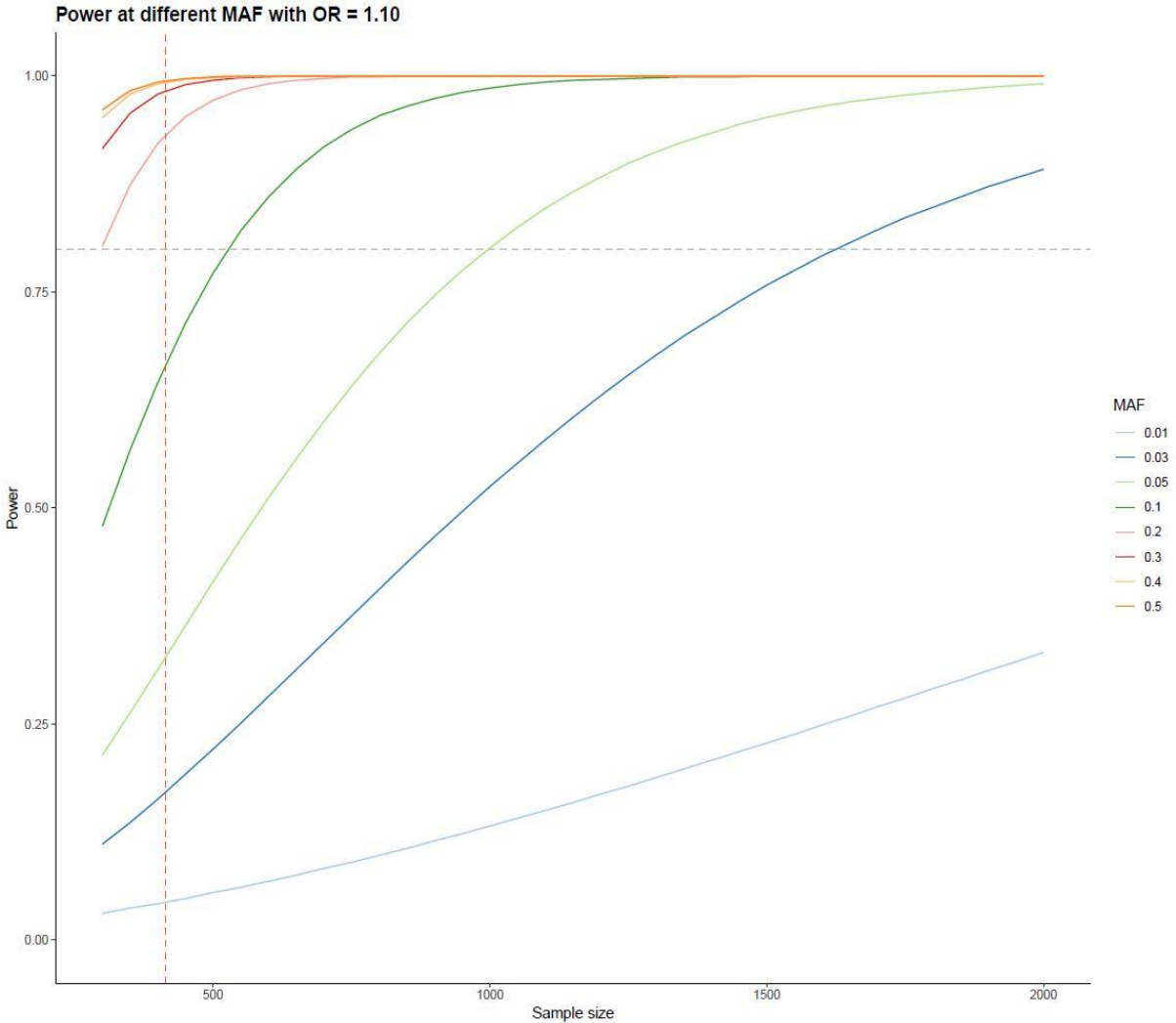
Manuscript title: Polygenic Susceptibility of Aortic Aneurysms Associates to the Diameter of the Aneurysm Sac: the Aneurysm-Express Biobank Cohort.

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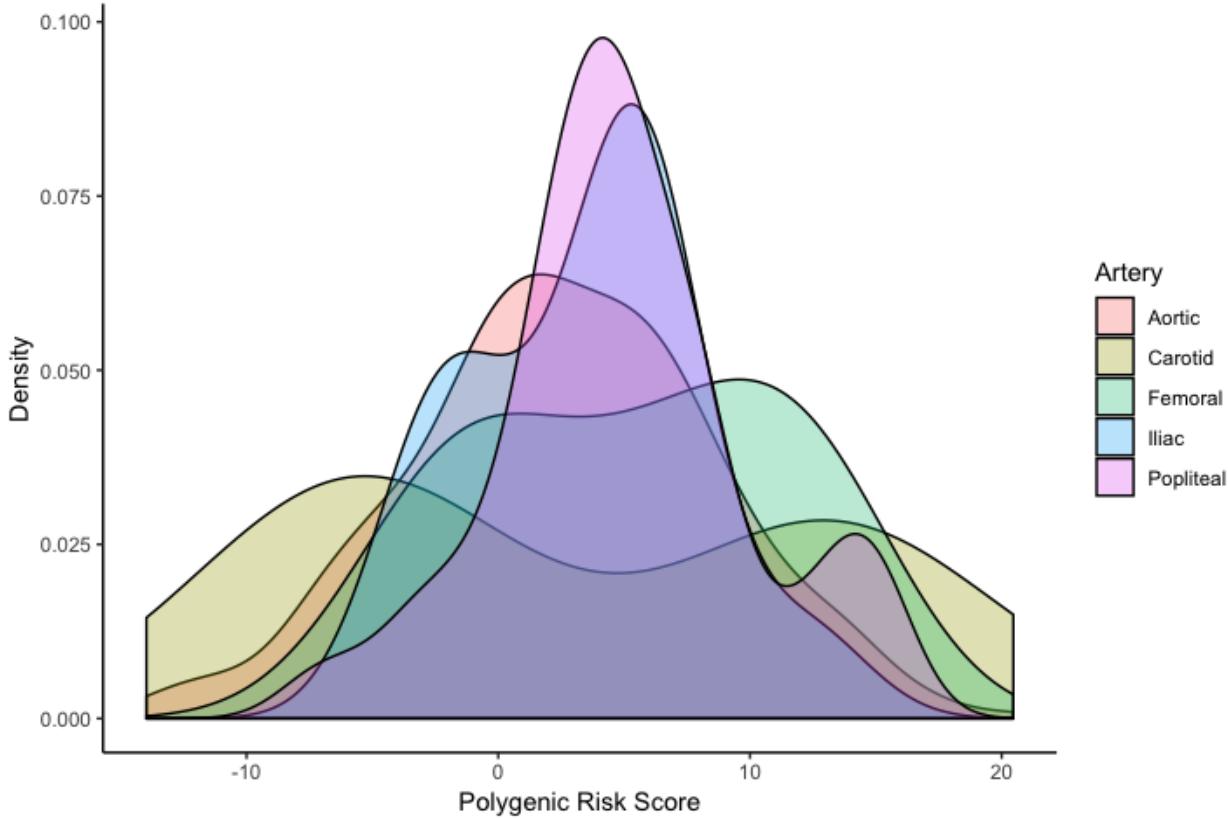
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Supplemental Figure 1



Supplemental Figure 1. Plot indicating study power estimates at different minor allele frequencies (MAF), with an average odds ratio (OR) of 1.10. Each solid colored line indicates a different MAF. Red dashed line indicates present study size of 415 samples, grey dashed line indicates a power estimate of $\pm 80\%$ for risk variants MAF < 0.2.

Supplemental Figure 2



Supplemental Figure 2. Overlay density plot of polygenic risk score (PRS) for diameter per artery type. Distribution of PRS is comparable per artery type (*Kruskal-Wallis test* p -value = 0.135).

Supplemental Table 1. Polygenic models.

A baseline model was constructed correcting for age, sex, ancestral background using four principal components, smoking status, and maximum diameter of the aneurysm sac or artery type if applicable. p_T : the GWAS p-value threshold of association.

Model	Includes
GWAS	Baseline + GWAS hits $p_T < 5 \times 10^{-8}$
$p < 5 \times 10^{-6}$	Baseline + all SNPs $p_T < 5 \times 10^{-6}$
$p < 5 \times 10^{-4}$	Baseline + all SNPs $p_T < 5 \times 10^{-4}$
$p < 0.001$	Baseline + all SNPs $p_T < 0.001$
$p < 0.01$	Baseline + all SNPs $p_T < 0.01$
$p < 0.05$	Baseline + all SNPs $p_T < 0.05$
$p < 0.1$	Baseline + all SNPs $p_T < 0.1$
$p < 0.2$	Baseline + all SNPs $p_T < 0.2$
$p < 0.5$	Baseline + all SNPs $p_T < 0.5$

Supplemental Table 2. Detailed polygenic risk score (PRS) models derived from AAA GWAS [12] for selected clinical phenotypes.

Diameter of the aneurysm sac					
p_T	R^2	β	SE	p -value	Number of SNPs
5×10^{-8}	0.001	-1.932	2.143	0.368	1
5×10^{-6}	0.000	0.075	1.419	0.958	3
5×10^{-4}	0.001	0.371	0.431	0.390	24
0.001	0.004	0.493	0.299	0.100	40
0.01	0.018	0.394	0.116	0.001*	267
0.01015	0.019	0.398	0.115	0.001*	272
0.05	0.004	0.095	0.061	0.120	1,008
0.1	0.004	0.075	0.046	0.105	1,634
0.2	0.004	0.054	0.036	0.133	2,494
0.5	0.004	0.045	0.029	0.125	4,086
Artery type					
p_T	R^2	β	SE	p -value	Number of SNPs
5×10^{-8}	0.005	-0.886	0.681	0.193	1
5×10^{-6}	0.003	-0.382	0.411	0.353	3
5×10^{-4}	0.000	0.055	0.138	0.688	24
0.001	0.004	0.110	0.096	0.252	39
0.0022	0.007	0.099	0.063	0.114	88
0.01	0.007	0.056	0.038	0.140	267
0.05	0.030	0.020	0.020	0.321	1,008
0.1	0.001	0.006	0.014	0.652	1,632
0.2	0.000	0.000	0.012	0.989	2,493
0.5	0.000	-0.001	0.009	0.950	4,086
Symptom status					
p_T	R^2	β	SE	p -value	Number of SNPs
5×10^{-8}	0.000	0.032	0.342	0.925	1
5×10^{-6}	0.000	0.023	0.226	0.921	3
5×10^{-4}	0.003	0.064	0.069	0.350	24
0.001	0.001	0.025	0.049	0.604	39
0.01	0.002	0.013	0.019	0.491	270
0.05	0.002	0.007	0.010	0.483	1,009
0.0637	0.007	0.012	0.009	0.173	1,213
0.1	0.000	0.002	0.007	0.768	1,632
0.2	0.001	0.002	0.006	0.692	2,494
0.5	0.000	0.001	0.005	0.818	4,086

Bold indicates best fitted model, * indicates $p < 0.05$.

Abbreviations: p_T = p -value threshold. β = beta coefficient. SE = standard error, SNPs = single nucleotide polymorphisms.

Supplemental Table 3. Detailed polygenic risk score (PRS) models derived from attention deficit hyperactivity disorder GWAS [39] for selected clinical phenotypes.

Diameter of the aneurysm sac					
p_T	R^2	β	SE	p -value	Number of SNPs
5×10^{-8}	0.003	-0.973	0.714	0.174	10
5×10^{-6}	0.004	-1.105	0.703	0.117	77
5×10^{-4}	0.000	-0.256	0.710	0.719	1,179
0.001	0.000	0.306	0.716	0.670	1,858
0.01	0.002	-0.702	0.727	0.335	8,155
0.05	0.002	-0.907	0.745	0.224	20,395
0.1	0.001	-0.494	0.745	0.507	28,657
0.2	0.000	-0.298	0.741	0.688	39,167
0.5	0.000	-0.409	0.741	0.581	55,850
Artery type					
p_T	R^2	β	SE	p -value	Number of SNPs
5×10^{-8}	0.000	0.086	0.230	0.707	10
5×10^{-6}	0.010	-0.424	0.234	0.070	77
5×10^{-4}	0.001	-0.168	0.240	0.486	1,179
0.001	0.000	-0.045	0.239	0.851	1,858
0.01	0.001	-0.115	0.235	0.625	8,155
0.05	0.003	-0.254	0.239	0.289	20,395
0.1	0.000	-0.006	0.226	0.979	28,657
0.2	0.000	-0.008	0.232	0.972	39,167
0.5	0.000	-0.026	0.234	0.913	55,850
Symptom status					
p_T	R^2	β	SE	p -value	Number of SNPs
5×10^{-8}	0.000	0.028	0.115	0.809	10
5×10^{-6}	0.010	-0.184	0.114	0.106	77
5×10^{-4}	0.001	-0.070	0.113	0.533	1,179
0.001	0.002	-0.081	0.114	0.481	1,858
0.01	0.000	-0.038	0.116	0.740	8,155
0.05	0.000	-0.032	0.119	0.791	20,395
0.1	0.001	-0.071	0.120	0.553	28,657
0.2	0.001	-0.074	0.119	0.531	39,167
0.5	0.000	-0.005	0.118	0.969	55,850

Bold indicates best fitted model, * indicates $p < 0.05$.

Abbreviations: p_T = p -value threshold. β = beta coefficient. SE = standard error, SNPs = single nucleotide polymorphisms.

Supplemental Table 4

Supplemental Table 4.

Clinical characteristics of the upper 20th percentile and lower 80th percentile of PRS.

	Lower 80 th of PRS n = 332	Upper 20 th of PRS n = 83	p
Male gender	285 (81%)	68 (19%)	.371 ^a
Age at surgery, median (range)	69.5 (46-89)	71.0 (28-87)	.460 ^b
In-hospital days, median (range)	9 (1-81)	10 (1-65)	.216 ^b
Any in-hospital reintervention post-operatively	37 (13%)	9 (12%)	.747 ^a
In-hospital death	16 (6%)	3 (4%)	.576 ^a
Aneurysm			
Aortic	281 (81%)	69 (19%)	.311 ^a
Iliac	8 (62%)	5 (39%)	
Femoral	7 (87%)	1 (13%)	
Popliteal	28 (80%)	7 (20%)	
Carotid	8 (89%)	1 (11%)	
IL-6* , mean±sd	4.0 ± 1.8	3.7 ± 2.3	.321 ^c
IL-8*	4.6 ± 1.5	4.1 ± 1.6	.051 ^c
MCP-1*	1.9 ± 2.1	1.8 ± 2.0	.782 ^c
OPG*	8.3 ± 1.0	8.3 ± 1.0	.964 ^c

Abbreviations: PRS = polygenic risk score, IL = interleukin, sd = standard deviation, MCP = monocyte chemotactic protein, OPG = osteoprotegerin. * natural log transformed, all inflammatory markers are extracted from the tissue sample, analyzed by Luminex and corrected for inter assay variability with pooled and blank sample.

^a Chi-squared test, ^b Mann-Whitney U test, ^c Student's T-test.

Supplemental Table 5

Supplemental Table 5.

AAA associated SNPs reported by GWAS and the association results for artery type and symptom status.

Reported by literature								This study							
SNP	Chr	BP	Near(est) gene(s)	Alleles	EAF	β^a	p	Artery type				Symptom status			
								EAF	β	SE	p	EAF	β	SE	p
rs602633	1	109821511	<i>PSRC1- CELSR2- SORT1</i>	T* - G	0.199	-0.129	6.58×10^{-9}	0.208	0.034	0.306	0.911	0.208	-0.694	0.192	0.132
rs4129267	1	154426264	<i>IL6R</i>	T* - C	0.370	-0.132	4.76×10^{-13}	0.355	0.173	0.270	0.522	0.361	0.564	0.171	0.133
rs1795061	1	214409280	<i>SMYD2</i>	T* - C	0.337	0.123	8.80×10^{-11}	0.307	0.149	0.276	0.591	0.315	-0.550	0.165	0.125
rs10757274	9	22096055	<i>CDKN2BAS 1/ANRIL</i>	A* - G	0.462	-0.216	1.54×10^{-33}	0.504	-0.015	0.263	0.955	0.506	-0.377	0.160	0.276
rs10985349	9	124425243	<i>DAB2IP</i>	T* - C	0.195	0.158	2.40×10^{-11}	0.200	-0.015	0.339	0.964	0.204	0.149	0.200	0.711
rs1466535	12	57534470	<i>LRP1</i>	G* - A	0.679	0.199 ^b	9.99×10^{-7}	0.655	0.039	0.267	0.885	0.655	-0.255	0.166	0.124
rs9316871	13	22861921	<i>LINC00540</i>	A* - G	0.201	-0.136	4.75×10^{-10}	0.796	0.176	0.348	0.613	0.794	0.037	0.197	0.930
rs6511720	19	11202306	<i>LDLR</i>	T* - G	0.096	-0.218	7.90×10^{-14}	0.094	0.306	0.469	0.514	0.098	0.069	0.273	0.902
rs3827066	20	44586023	<i>PCIF1- ZNF335- MMP9</i>	T* - C	0.179	0.201	2.13×10^{-17}	0.167	0.190	0.345	0.583	0.176	-0.879	0.207	0.048
rs2836411	21	39819830	<i>ERG</i>	T* - C	0.369	0.107	5.80×10^{-9}	0.361	0.433	0.311	0.164	0.364	-0.500	0.194	0.224

Abbreviations: AAA = abdominal aortic aneurysm, SNP = single nucleotide polymorphism, Chr = chromosome, BP = base pair, EAF = effect allele frequency, β = beta-coefficient, SE = standard error.

* Effect allele, ^a β converted from combined odds ratio's (discovery and validation phase) of summary statistics of *Jones et al.(2017)* [12].

^b β converted from discovery phase of summary statistics of *Bown et al. (2011)* [7].