Table S1A. Genotype frequency of FVIII SNPs included in the study (%)**(N = 10,434)**[1]

				EA Females (N = 4,282)			EA Males (N = 3,774)		AA Females (N = 1,505)			AA Males (N = 873)		
	SNP	**A**	**B**	**AA**	**AB**	**BB**	**A**	**B**	**AA**	**AB**	**BB**	**A**	**B**	**location**
1	RS1470586	C	T	59	35	5	76	24	58	37	5	78	22	Intron 1
2	RS5987077	A	T	55	38	7	74	26	10	42	48	31	69	Intron 3
3	RS7056252	A	G	100	0	0	100	0	87	12	0	93	7	Intron 6
4	RS5986899	A	G	100	0	0	100	0	93	7	0	96	4	Intron 9
5	RS5987073	A	G	99	1	0	99	1	92	8	1	95	5	Intron 9
6	**RS5945258**	**C**	**T**	**71**	**26**	**3**	**85**	**15**	**56**	**38**	**6**	**73**	**27**	**Intron 11**
7	**RS7061362**	**C**	**T**	**71**	**26**	**3**	**85**	**15**	**57**	**38**	**6**	**73**	**27**	**Intron 11**
8	RS5987061	C	T	100	0	0	100	0	93	7	0	96	4	Intron 13
9	RS5987068	G	A	100	0	0	100	0	93	7	0	96	4	Intron 13
10	**RS5945122**	**A**	**C**	**71**	**26**	**3**	**85**	**15**	**57**	**38**	**5**	**73**	**27**	**Intron 13**
11	RS6643622	T	G	48	42	10	69	30	3	27	70	17	83	Intron 13
12	**RS6643714**	**T**	**C**	**39**	**47**	**14**	**63**	**37**	**1**	**16**	**83**	**8**	**92**	**Intron 14**
13	**RS5987057**	**A**	**G**	**100**	**0**	**0**	**100**	**0**	**93**	**7**	**0**	**96**	**4**	**Intron 14**
14	RS12014480	G	A	100	0	0	100	0	56	39	5	75	25	Intron 14
15	RS5987056	C	T	100	0	0	100	0	94	6	0	96	4	Intron 14
16	RS4898352	A	T	54	38	7	74	26	3	29	68	17	83	Intron 18
17	RS1800297	T	C	100	0	0	100	0	58	37	5	76	24	Exon 26
18	RS7357998	C	T	100	0	0	100	0	91	8	0	96	4	Intron 26
19	RS12392769	G	T	100	0	0	100	0	92	8	1	96	4	Intron 26

Table S1B. Genotype frequencies of VWF SNPs included in the study (%) (N = 10,434)[1]

				EA Females (N = 4,282)			EA Males (N = 3,774)			AA Females (N = 1,505)			AA Males (N = 873)			
	SNP	A	B	AA	AB	BB	AA	AB	BB	AA	AB	BB	AA	AB	BB	Location*
1	RS933408	T	G	64	32	3	65	31	4	74	24	2	72	26	2	Intron 51
2	RS2270151	G	A	73	25	2	72	26	3	86	14	1	86	13	1	Intron 50
3	RS2270152	T	G	63	33	4	62	33	5	82	17	1	82	18	1	Intron 49
4	RS3759320	T	C	37	47	16	35	50	15	61	34	5	59	36	4	Intron 47
5	RS3759321	G	A	27	49	24	26	50	23	21	49	30	22	50	28	Intron 47
6	RS7958883	A	T	39	46	15	37	49	14	84	16	1	84	16	0	Intron 47
7	RS12317523	C	T	50	41	9	52	40	8	32	50	18	33	51	15	Intron 47
8	RS723190	T	C	89	11	0	89	11	0	77	22	1	76	22	2	Intron 47
9	RS11063953	A	G	52	40	8	54	38	8	53	39	8	54	40	6	Intron 47
10	RS12369177	G	T	38	47	15	38	48	15	57	38	5	58	37	5	Intron 47
11	RS4764478	T	A	60	34	6	61	34	5	61	33	6	62	32	6	Intron 46
12	RS7301070	A	G	43	46	11	42	46	12	54	38	8	49	42	9	Intron 44
13	RS216852	C	G	44	45	11	44	45	11	14	46	40	15	44	40	Intron 43
14	RS4764521	G	A	63	32	5	65	31	4	89	10	1	86	13	1	Intron 43
15	RS3819540	G	A	99	1	0	99	1	0	92	8	0	92	7	0	Intron 42
16	RS216855	G	A	54	39	7	55	38	7	26	50	24	25	50	25	Intron 42
17	RS216856	C	T	43	45	12	43	45	12	20	50	30	21	49	30	Intron 42
18	RS216865	C	T	43	45	12	43	45	12	21	50	29	22	50	28	Intron 42
19	RS6489686	C	T	72	26	2	72	25	2	64	32	4	63	34	3	Intron 42
20	RS11063975	C	A	84	15	1	85	15	1	93	7	0	97	3	0	Intron 38
21	RS216887	C	T	29	50	21	28	51	22	19	52	29	21	49	30	Intron 38

				EA Females (N = 4,282)			EA Males (N = 3,774)			AA Females (N = 1,505)			AA Males (N = 873)			
	SNP	A	B	AA	AB	BB	AA	AB	BB	AA	AB	BB	AA	AB	BB	Location*
22	RS7968035	G	A	100	0	0	100	0	0	90	10	0	90	9	0	Intron 38
23	RS216888	G	A	29	50	21	28	51	22	19	52	29	21	50	29	Intron 38
24	RS10849375	G	C	85	14	1	84	15	1	94	5	0	97	3	0	Intron 38
25	RS216896	T	C	28	50	21	27	51	22	18	50	32	20	49	31	Intron 38
26	RS12579603	A	G	42	46	12	40	47	12	86	14	0	87	13	0	Intron 37
27	RS216903	C	T	29	50	21	28	51	22	32	50	18	32	51	17	Intron 34
28	RS216904	T	C	38	48	15	38	47	14	50	41	9	48	42	10	Intron 34
29	RS216905	C	T	58	36	6	59	36	5	74	24	2	71	26	3	Intron 34
30	RS216801	G	A	37	48	15	38	47	15	50	42	9	47	43	10	Intron 34
31	RS542993	T	C	27	50	23	27	50	23	51	41	8	51	41	8	Intron 34
32	RS216308	C	T	35	47	17	35	47	18	77	20	2	78	19	3	Intron 31
33	RS1800385	C	A	83	16	1	83	16	1	95	5	0	96	4	0	Exon 28
34	RS216312	C	T	30	50	20	29	52	19	57	39	4	55	39	6	Intron 27
35	RS216313	A	G	88	12	1	88	12	0	97	3	0	98	2	0	Intron 27
36	RS2854871	T	C	85	15	1	85	15	1	77	22	1	80	19	1	Intron 24
37	RS11609815	C	G	56	38	7	55	38	7	36	49	16	32	50	18	Intron 24
38	RS11063995	T	C	56	38	6	55	38	7	36	49	16	32	51	17	Intron 22
39	RS216315	G	A	83	16	1	84	15	1	94	6	0	93	7	0	Intron 22
40	RS11612401	G	C	56	38	6	55	38	7	74	24	2	69	29	3	Intron 22
41	RS11610629	A	C	56	38	6	55	39	6	54	40	6	50	43	7	Intron 22
42	RS1800380	C	T	56	38	6	55	38	7	50	42	8	46	44	10	Exon 22
43	RS216318	C	A	83	16	1	84	15	1	92	8	0	92	8	0	Intron 21
44	RS11609728	C	A	56	38	6	56	38	7	81	19	1	77	22	1	Intron 21

			EA Females (N = 4,282)			EA Males (N = 3,774)			AA Females (N = 1,505)			AA Males (N = 873)			
	SNP	A B	AA	AB	BB	AA	AB	BB	AA	AB	BB	AA	AB	BB	Location*
45	RS216327	C T	43	44	12	43	45	12	64	33	3	60	34	6	Intron 18
46	RS216329	C T	43	44	12	43	45	12	64	33	3	60	34	6	Intron 18
47	RS1063857	A G	41	46	13	40	47	13	16	50	33	15	48	37	Exon 18
48	RS216295	C T	82	17	1	83	16	1	66	31	3	69	27	3	Intron 17
49	RS16932374	C T	100	0	0	100	0	0	68	29	3	68	29	3	Exon17
50	RS216298	T C	82	17	1	83	16	1	71	27	3	73	24	3	Intron 16
51	RS216299	G A	82	17	1	83	16	1	71	27	3	73	24	3	Intron 16
52	RS2239161	A G	79	20	2	79	20	1	89	11	0	88	12	0	Intron 15
53	RS2239160	G A	79	19	2	79	19	1	75	23	2	73	25	2	Intron 15
54	RS7954351	A T	52	41	7	52	40	8	20	49	32	18	50	31	Intron 15
55	RS12304995	C T	40	48	13	39	48	13	19	52	30	17	49	34	Intron 15
56	RS10744696	C A	36	48	16	35	48	16	54	39	7	50	44	7	Intron 13
57	RS7139057	T G	67	30	4	67	30	4	76	23	2	72	27	1	Intron 13
58	RS12319392	G T	84	15	1	84	15	1	44	45	10	44	45	11	Intron 13
59	RS2109122	T C	85	14	1	86	14	1	45	45	10	45	45	10	Intron 13
60	RS3213721	C T	100	0	0	100	0	0	100	0	0	100	0	0	Intron 8
61	RS1800387	A T	95	5	0	94	6	0	35	48	17	32	50	18	Exon 8
62	RS7135976	T C	26	50	25	25	50	25	6	36	58	6	36	58	Intron 6
63	RS763580	G C	51	41	8	53	40	8	86	14	1	85	15	0	Intron 6
64	RS2238103	A T	41	46	13	42	45	13	56	38	6	55	38	7	Intron 6
65	RS1610056	C G	75	24	2	74	24	2	64	33	4	63	34	3	Intron 6
66	RS2239147	T C	75	24	2	74	24	2	64	33	3	63	34	3	Intron 6
67	RS2239145	C T	75	24	2	74	24	2	64	33	4	63	34	3	Intron 6

				EA Females (N = 4,282)			EA Males (N = 3,774)			AA Females (N = 1,505)			AA Males (N = 873)			
	SNP	A	B	AA	AB	BB	AA	AB	BB	AA	AB	BB	AA	AB	BB	Location*
68	RS2239144	C	A	74	24	2	74	24	2	63	33	4	63	34	3	Intron 6
69	RS2239143	A	G	100	0	0	99	1	0	99	1	0	99	1	0	Intron 6
70	RS11064019	A	G	75	24	2	74	24	2	65	31	4	63	33	4	Intron 6
71	RS11064020	T	C	75	24	2	74	24	2	65	32	3	64	33	3	Intron 6
72	RS11064021	A	G	75	24	2	74	24	2	64	33	4	63	34	3	Intron 5
73	RS41388848	T	C	93	7	0	93	7	0	58	36	6	58	37	5	Intron 5
74	RS12307072	A	T	42	45	13	40	47	13	45	44	11	47	43	10	Intron 3
75	RS10849385	A	G	40	46	14	38	49	14	9	42	50	10	40	50	Intron 3

[1]The major alleles were labeled with ‘A’ and the minor alleles with ‘B’ defined based on frequencies in EA subjects. A “0” was entered for an allele frequency of 0 - < 0.5%.

* An intron was numbered as that of exon immediately before the intron.

Table S2. Demographics and covariates for study subjects by race and sex (N = 10,434)

Characteristic		EA Female (N = 4,282)	EA Male (N = 3,774)	AA Female (N = 1,505)	AA Male (N =873)	P value
Age at visit 1 (years)[1]	Mean (s.d)	53.88 (5.67)	54.59 (5.70)	53.34 (5.73)	53.36 (5.92)	$<1 \times 10^{-8}$
BMI (kg/m^2)[1]	Mean (s.d)	26.58 (5.39)	27.38 (3.94)	30.69 (6.51)	27.88 (4.79)	$<1 \times 10^{-8}$
Cigarette smoking[2, *]		2134 (50%)	2708 (72%)	637 (42%)	620 (71%)	$<1 \times 10^{-8}$
Diabetes[2]		304 (7%)	367 (10%)	291 (19%)	141 (16%)	$<1 \times 10^{-8}$
Hypertension[2]		1,110 (26%)	1,031 (27%)	834 (55%)	459 (53%)	$<1 \times 10^{-8}$

[1] Analysis of Variance
[2] Chi-square tes;
* Cigarette smoking included current smokers and those who ever smoked.

Table S3A. Quartile of VWF antigen by quartile of FVIII activity for EA females (N = 4,282)

		VWF				
	Quartile	**1st**	**2nd**	**3rd**	**4th**	**Total**
FVIII	**1st**	753 (63%)	257 (22%)	74 (7%)	19 (2%)	1,103 (26%)
	2nd	348 (29%)	451 (39%)	247 (24%)	67 (8%)	1,113 (26%)
	3rd	81 (7%)	345 (30%)	415 (40%)	251 (29%)	1,092 (26%)
	4th	20 (2%)	105 (9%)	312 (30%)	537 (61%)	974 (23%)

Table S3B. Quartile of VWF antigen by quartile of FVIII activity for EA males (N = 3,774)

		VWF				
	Quartile	**1st**	**2nd**	**3rd**	**4th**	**Total**
FVIII	**1st**	729 (75%)	305 (31%)	85 (9%)	27 (3%)	1,146 (30%)
	2nd	187 (19%)	410 (42%)	321 (33%)	108 (13%)	1,026 (27%)
	3rd	47 (5%)	214 (22%)	369 (38%)	292 (34%)	922 (24%)
	4th	13 (1%)	48 (5%)	184 (19%)	435 (50%)	680 (18%)

Table S3C. Quartile of VWF antigen by quartile of FVIII activity for AA females (N = 1,505)

		VWF				
	Quartile	**1st**	**2nd**	**3rd**	**4th**	**Total**
FVIII	**1st**	151 (51%)	44 (15%)	26 (7%)	7 (1%)	228 (15%)
	2nd	92 (31%)	117 (39%)	69 (20%)	25 (4%)	303 (20%)
	3rd	43 (15%)	94 (31%)	138 (39%)	98 (18%)	373 (25%)
	4th	8 (3%)	45 (15%)	120 (34%)	428 (77%)	601 (40%)

Table S3D. Quartile of VWF antigen by quartile of FVIII activity for AA males (N = 873)

		VWF				
	Quartile	**1st**	**2nd**	**3rd**	**4th**	**Total**
FVIII	**1st**	120 (65%)	36 (18%)	9 (4%)	3 (1%)	168 (19%)
	2nd	51 (28%)	93 (47%)	55 (25%)	14 (5%)	213 (24%)
	3rd	12 (7%)	52 (26%)	79 (36%)	63 (23%)	206 (24%)
	4th	1 (1%)	19 (10%)	76 (35%)	190 (70%)	286 (33%)

Table S4. P-value and partial R squares from a multiple linear regression model for FVIII activity

	P-value	Partial R^2	Percentage of Variation Explained
Gender	$<1 \times 10^{-8}$	0.00680	0.68
Age	$<1 \times 10^{-8}$	0.02239	2.2
Race	$<1 \times 10^{-8}$	0.04041	4.0
BMI	$<1 \times 10^{-8}$	0.00962	1.0
Hypertension	8.7×10^{-5}	0.00149	0.15
Diabetes	$<1 \times 10^{-8}$	0.03536	3.5
Ever Smoker	9.8×10^{-3}	0.00065	0.06
ABO Genotype	$<1 \times 10^{-8}$	0.10708	10.7
Residual		0.776	77.6

* Residual Partial $R^2 = 1 - R^2$