

Supporting Information

This appendix has been provided by the authors to give readers additional information about their work. Supplement to: Eric Jorgenson, Navneet Matharu, Melody R. Palmer, Jie Yin, Jun Shan, Thomas J. Hoffmann, Khanh K. Thai, Xujia Zhou, James M. Hotaling, Gail Jarvik, Nadav Ahituv, Hunter Wessells, and Stephen K. Van Den Eeden. Genetic Variation in the SIM1 locus is associated with erectile dysfunction.

Contents

Tables

Supplementary Table 1: 95% Credible Set of SNPs in the Chromosome 6 Erectile Dysfunction Risk Region	3
Supplementary Table 2: U.K. Biobank Subject Characteristics	4
Supplementary Table 3: GERA and UKB Meta-Analysis Results for the 95% Credible Set SNPs	5
Supplementary Table 4. Characteristics of GERA Men by Response to the Health Survey	6
Supplementary Table 5: Primer Sequences for Enhancer Assays	7
Supplementary Table 6: Imputation r^2 of SNPs in the Chromosome 6 Erectile Dysfunction Risk Region	8

Figure

Supplementary Figure 1. Forest plot of the subgroup and sensitivity analyses in GERA	9-10
---	-------------

Supplementary Table 1: 95% Credible Set of SNPs in the Chromosome 6 Erectile Dysfunction Risk Region

Chromosome	Position	SNP	Posterior Inclusion Probability	Cumulative Inclusion Probability
6	100,610,044	rs78677597	0.298	0.298
6	100,600,097	rs17789218	0.296	0.595
6	100,620,931	rs17185536	0.151	0.745
6	100,602,753	rs9496567	0.137	0.882
6	100,613,551	rs9496614	0.112	0.995

Supplementary Table 2: U.K. Biobank Subject Characteristics

Case/Control Status	Race/Ethnicity	no. (%)	Age — yrs	Body Mass Index
Cases (n = 2,959)				
	European/White	2,783 (94.1)	61.2 ± 6.3	29.1 ± 4.6
	South Asian	70 (2.4)	59.3 ± 7.3	28.5 ± 5.0
	Mixed/other	36 (1.6)	58.2 ± 7.8	28.6 ± 4.4
	African British	68 (1.6)	58.8 ± 7.5	28.9 ± 3.9
	East Asian	2 (0.3)	61.0 ± 1.4	27.0 ± 5.1
Controls (n = 220,079)				
	European/White	206,975 (94.0)	57.4 ± 8.1	27.8 ± 4.2
	South Asian	5,234 (2.4)	53.8 ± 8.7	27.0 ± 3.9
	Mixed/other	3,626 (1.2)	54.3 ± 8.6	27.9 ± 4.3
	African British	3,566 (2.3)	52.0 ± 8.2	28.3 ± 4.3
	East Asian	678 (0.1)	52.3 ± 8.1	25.5 ± 3.2

Age and Body Mass Index are presented as means ± standard deviation.

Supplementary Table 3: GERA and UKB Meta-Analysis Results for the 95% Credible Set SNPs

Chromosome	Position	SNP	Risk Allele	GERA		UKB		Combined	
				OR	p	OR	p	OR	p
6	100,600,097	rs17789218	C	1.26	1.40*10 ⁻²⁵	1.15	5.64*10 ⁻¹³	1.25	7.02*10 ⁻³⁷
6	100,602,753	rs9496567	A	1.26	1.60*10 ⁻²⁵	1.14	1.73*10 ⁻¹³	1.25	2.31*10 ⁻³⁷
6	100,610,044	rs78677597	C	1.27	1.23*10 ⁻²⁵	1.16	4.21*10 ⁻¹³	1.25	4.61*10 ⁻³⁷
6	100,613,551	rs9496614	C	1.26	1.81*10 ⁻²⁵	1.14	3.83*10 ⁻¹³	1.25	6.00*10 ⁻³⁷
6	100,620,931	rs17185536	T	1.26	3.36*10 ⁻²⁵	1.20	6.78*10 ⁻¹⁴	1.25	1.84*10 ⁻³⁷

Supplementary Table 4. Characteristics of GERA Men by Response to the Health Survey

Characteristic	Always (n = 13,753)	Usually (n = 8,681)	Sometimes (n = 7,136)	Never (n = 7,079)	Total (n = 36,649)	
Race/Ethnicity — no. (%)	Non-Hispanic white	11,090 (80.6)	6,905 (79.5)	5,704 (79.9)	6,160 (87.0)	29,859 (81.5)
	Hispanic/Latino	1,214 (8.8)	740 (8.5)	579 (8.1)	437 (6.2)	2,970 (8.1)
	East Asian	1,061 (7.7)	738 (8.5)	579 (8.1)	359 (5.1)	2,737 (7.5)
	African American	388 (2.8)	298 (3.4)	274 (3.8)	123 (1.7)	1,083 (3.0)
Age — yrs	54.1 ± 11.4	59.3 ± 10.7	64.9 ± 10.2	72.9 ± 9.8	61.1 ± 12.8	
Body Mass Index	26.7 ± 4.2	27.2 ± 4.5	27.6 ± 4.7	27.7 ± 4.8	27.2 ± 4.5	
Diabetes — no. (%)	Yes	1,669 (12.1)	1,596 (18.4)	1,835 (25.7)	2,405 (34.0)	7,505 (20.5)
	No	12,084 (87.9)	7,085 (81.6)	5,301 (74.3)	4,674 (66.0)	29,144 (79.5)
Smoking History — no. (%)	Never	8,245 (61.1)	4,341 (51.1)	3,009 (43.6)	2,536 (37.7)	18,131 (50.9)
	Former	4,543 (33.7)	3,638 (42.8)	3,382 (49.1)	3,853 (57.3)	15,416 (43.3)
	Current	704 (5.2)	516 (6.1)	503 (7.3)	338 (5.0)	2,061 (5.8)
EHR Diagnosis — no. (%)	Yes	2,325 (16.9)	2,912 (33.5)	3,059 (42.9)	2,532 (35.8)	10,828 (29.5)
	No	11,428 (83.1)	5,769 (66.5)	4,077 (57.1)	4,547 (64.2)	25,821 (70.5)
PDE5i Prescription — no. (%)	Yes	2,595 (18.9)	3,918 (45.1)	4,654 (65.2)	3,768 (53.2)	14,935 (40.8)
	No	11,158 (81.1)	4,763 (54.9)	2,482 (34.8)	3,311 (46.8)	21,714 (59.2)

Age and Body Mass Index are presented as means ± standard deviation; Abbreviations: EHR, electronic health record; PDE5i, phosphodiesterase type 5 inhibitor. Some participants did not have smoking history (n = 1,041).

Supplementary Table 5: Primer Sequences for Enhancer Assays

SNP	Forward Primer Sequence	Reverse Primer Sequence	Coordinates (hg19)	Length (bp)
rs17789218 T>C	GGACAGGAGGAAAACCTG	ATAGCCATATTCATGAAGGTCC	chr6:100598913+100600880	1968bp
rs9496567 G>A	GTGCAAAACCTCTCCCATAGG	GGAGTGTGTCCAAAGGCTATC	chr6:100601759+100602947	1189bp
rs78677597 A>C	GGAAGCAAGCAAAGATGTCAAC	GGCATATAGCAAATCATGCAGC	chr6:100608132+100610164	2033bp
rs9496614 G>A	CTCCTGCTCTCTGAGTACAATCC	TCACGACAGCCATGATCAC	chr6:100613365+100615275	1911bp
rs17185536 C>T	GGGAAATGTTGAGCTAACTGG	TTCAAAGCATAATGTGAAGGG	chr6:100619173+100621103	1931bp
rs57989773 T>C	ATGTTCCAGCACCCACAGCTT	TGAAGTCCTACAACCAGAAGGAC	chr6:100628727+100630559	1833bp

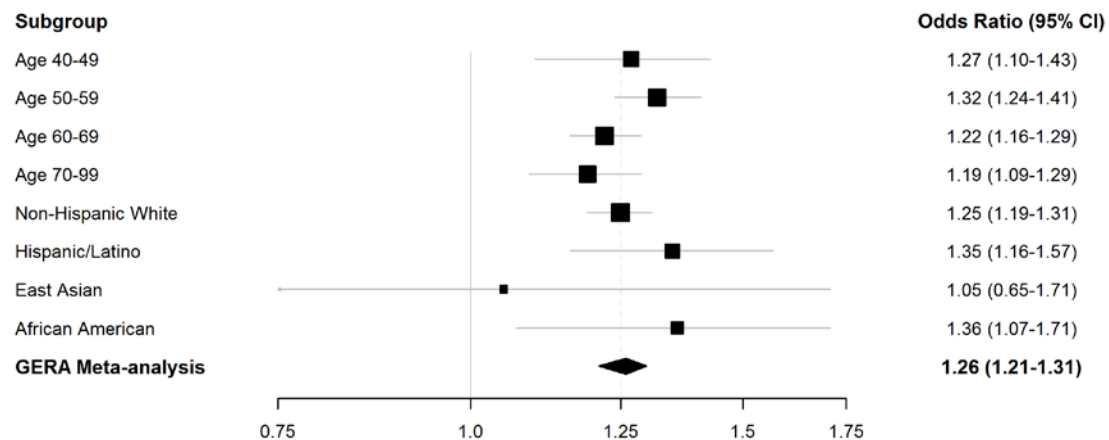
Supplementary Table 6: Imputation r^2 of SNPs in the Chromosome 6 Erectile Dysfunction Risk Region

Chromosome	Position	SNP	GERA				UKB			
			Non-Hispanic white	East Asian	African American	Hispanic /Latino	White	South Asian	Mixed	African British
6	100,600,097	rs17789218	1.00	1.00	0.87	0.93	1.00	1.00	1.00	1.00
6	100,602,753	rs9496567	0.99	0.97	1.00	1.00	0.99	0.99	0.99	0.99
6	100,610,044	rs78677597	0.99	0.99	0.88	0.94	1.00	1.00	1.00	1.00
6	100,613,551	rs9496614	0.99	0.98	0.99	0.99	0.99	0.99	0.99	0.99
6	100,620,931	rs17185536	0.97	0.91	0.94	0.97	0.99	0.99	0.99	0.99

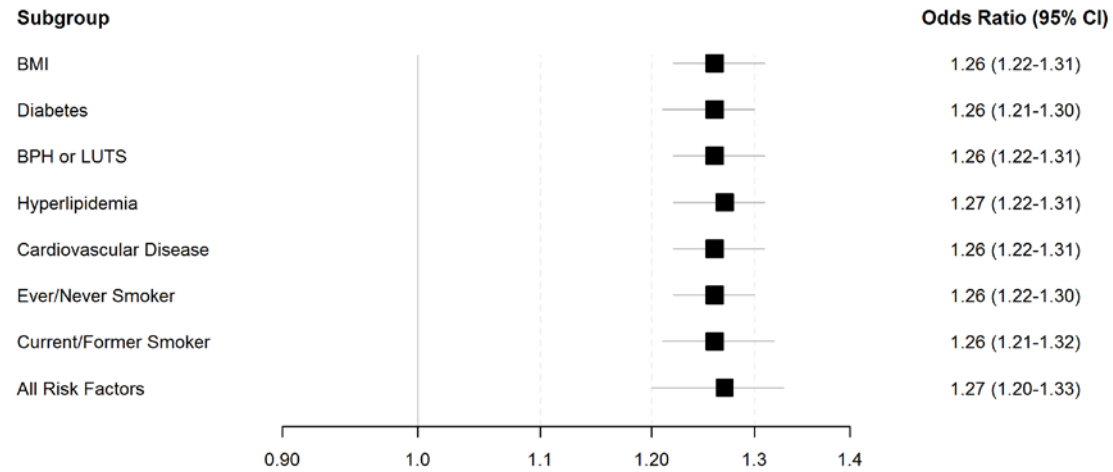
Supplementary Figure 1. Forest plot of the subgroup and sensitivity analyses in GERA

Odds ratios (OR) and 95% confidence interval lower (LCL) and upper (UCL) bounds for association analyses between the SNP rs17185536 and the risk of erectile dysfunction. A. Results stratified by decade of age and by GERA cohort race/ethnicity group. B. Results adjusting for known erectile dysfunction risk factors. C. Results by health survey response level, clinical definition, treatment definition, and combined survey, clinical, and treatment definition.

A. Results by Decade of Age and GERA Race/Ethnicity Group



B. Sensitivity Analyses by Erectile Dysfunction Risk Factor



C. Sensitivity Analyses by Diagnostic Subgroup

