

**Table S3: Results of the MVMR analysis of the effect of SHBG and testosterone on FVC, FEV1, and FEV1/FVC separately in males and females.**

	FVC (mL)								FEV <sub>1</sub> /FVC (%)								FEV <sub>1</sub> (mL)								
	b	SE	LCI	UCI	p-value	Q test p-value	P-value intercept	Sargan P-value	b	SE	LCI	UCI	p-value	Q test p-value	P-value intercept	Sargan P-value	b	SE	LCI	UCI	p-value	Q test p-value	P-value intercept	Sargan P-value	
<b>Testosterone (TT)</b>																									
<b>Males</b>																									
MR F-IVW	0.16	41.52	-81.22	81.53	0.997	1.82E-49			0.52	0.40	-0.26	1.31	0.189	8.15E-24			26.75	35.48	-42.79	96.28	0.451	1.76E-45			
MR R-IVW	0.16	77.39	-151.53	151.84	0.998	1.82E-49			0.52	0.63	-0.70	1.75	0.403	8.15E-24			26.75	64.72	-100.10	153.59	0.679	1.76E-45			
MR median	132.08	77.62	-20.05	284.20	0.089				0.88	0.69	-0.47	2.23	0.200				202.66	70.64	64.20	341.11	<b>4.12E-03</b>				
MR robust	172.03	134.22	-91.04	435.09	0.200				0.54	0.57	-0.57	1.65	0.338				193.18	80.60	35.21	351.15	<b>1.65E-02</b>				
MR-Egger	-0.01	77.58	-152.07	152.05	1.000				0.52	0.63	-0.71	1.76	0.405		0.918		26.62	64.88	-100.54	153.77	0.682		0.709		
MR -2SLS	-3.94	48.11	-98.23	90.36	0.935		4.12E-38		0.35	0.47	-0.58	1.28	0.460			2.29E-10	16.10	41.31	-64.87	97.07	0.697				4.47E-31
<b>Females</b>																									
MR F-IVW	41.61	12.18	17.75	65.48	<b>6.32E-04</b>	3.08E-37			0.21	0.15	-0.08	0.50	0.147	1.12E-22			37.47	10.22	17.44	57.50	<b>2.46E-04</b>	5.01E-32			
MR R-IVW	41.61	21.25	-0.05	83.27	0.050	3.08E-37			0.21	0.23	-0.24	0.67	0.353	1.12E-22			37.47	17.21	3.74	71.21	<b>0.029</b>	5.01E-32			
MR median	28.31	23.85	-18.44	75.06	0.235				0.39	0.24	-0.08	0.87	0.105				47.96	19.97	8.81	87.11	<b>0.016</b>				
MR robust	40.78	29.48	-16.99	98.56	0.166				0.24	0.17	-0.09	0.56	0.159				38.23	24.21	-9.22	85.69	0.114				
MR-Egger	44.85	21.31	3.08	86.62	<b>0.035</b>				0.23	0.23	-0.23	0.68	0.333		0.656		40.20	17.25	6.39	74.01	<b>0.020</b>		0.138		
MR -2SLS	49.67	15.49	19.32	80.03	<b>1.34E-03</b>		1.24E-17		0.05	0.18	-0.31	0.40	0.795			1.78E-12	39.41	12.88	14.18	64.65	<b>2.21E-03</b>				2.00E-15
<b>SHBG</b>																									
<b>Males</b>																									
MR F-IVW	11.01	23.18	-34.43	56.45	0.635	1.82E-49			-0.71	0.22	-1.14	-0.27	<b>1.52E-03</b>	8.15E-24			-24.28	19.81	-63.11	14.55	0.220	1.76E-45			
MR R-IVW	11.01	43.22	-73.69	95.71	0.799	1.82E-49			-0.71	0.35	-1.39	-0.02	<b>0.043</b>	8.15E-24			-24.28	36.14	-95.11	46.55	0.502	1.76E-45			
MR median	-72.11	41.38	-153.20	8.99	0.081				-0.99	0.38	-1.74	-0.24	<b>0.010</b>				-112.34	37.53	-185.90	-38.78	<b>2.76E-03</b>				
MR robust	-78.34	67.84	-211.30	54.63	0.248				-0.76	0.34	-1.43	-0.09	<b>0.026</b>				-107.06	41.08	-187.58	-26.53	<b>9.16E-03</b>				
MR-Egger	3.68	47.31	-89.05	96.40	0.938				-0.72	0.38	-1.48	0.03	0.059		0.918		-30.21	39.56	-107.75	47.33	0.445		0.709		
MR -2SLS	25.82	26.90	-26.90	78.55	0.337		4.12E-38		-0.60	0.26	-1.12	-0.08	<b>0.023</b>			2.29E-10	-8.47	23.08	-53.70	36.76	0.714				4.47E-31
<b>Females</b>																									
MR F-IVW	-11.49	7.12	-25.43	2.46	0.106	3.08E-37			-0.16	0.09	-0.33	0.01	0.063	1.12E-22			-12.46	5.97	-24.16	-0.75	<b>0.037</b>	5.01E-32			
MR R-IVW	-11.49	12.42	-35.83	12.86	0.355	3.08E-37			-0.16	0.13	-0.42	0.10	0.233	1.12E-22			-12.46	10.06	-32.17	7.26	0.216	5.01E-32			
MR median	-7.68	13.72	-34.58	19.22	0.576				-0.17	0.15	-0.47	0.12	0.244				-23.99	11.51	-46.55	-1.43	<b>0.037</b>				
MR robust	-15.14	16.74	-47.95	17.66	0.366				-0.13	0.12	-0.37	0.10	0.268				-13.48	13.95	-40.82	13.86	0.334				
MR-Egger	-27.01	16.48	-59.32	5.29	0.101				-0.21	0.18	-0.57	0.14	0.235		0.656		-25.51	13.34	-51.67	0.64	0.056		0.138		
MR -2SLS	-7.27	9.00	-24.91	10.36	0.419		1.24E-17		-0.17	0.11	-0.38	0.04	0.110			1.78E-12	-9.55	7.52	-24.28	5.19	0.204				2.00E-15

SHBG = Sex Hormone Binding Globulin; TT = Total Testosterone.

MR = Mendelian Randomisation; F-IVW = Fixed effect Inverse variance weighted meta-analysis; R-IVW = Random effect Inverse variance weighted meta-analysis; 2SLS = Two-Stage least squares regression.

b = beta (regression estimate for a 1 unit increase in log TT or SHBG). SE = Standard Error of the mean, LCI/UCI = lower/upper confidence interval (95%)

N SNPs included -> Males: Total = 178, TT = 67, SHBG = 138; Females: Total = 174, TT = 55, SHBG = 120.

N in 2SLS = Males = 139,433; Females = 133,662.

The effect estimate for a 10% increase in TT or SHBG can be calculated by multiplying the beta (b) by ln(1.1)