

**Table S7: Results of the MVMR analysis of the effect of SHBG and testosterone on FVC, FEV1, and FEV1/FVC decline separately in males and females.**  
 Outlier SNPs and “weak” SNPs (F-statistic  $\leq 10$ ) excluded

	FVC (mL-yr <sup>-1</sup> )					FEV <sub>1</sub> /FVC (%-yr <sup>-1</sup> )					FEV <sub>1</sub> (mL-yr <sup>-1</sup> )													
	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	4.17	16.94	-29.02	37.37	0.805	0.340			0.000	0.002	-0.004	0.004	0.923	0.440			21.94	15.70	-8.83	52.72	0.162	0.876		
MR R-IVW	4.17	17.32	-29.76	38.11	0.810	0.340			0.000	0.002	-0.004	0.004	0.923	0.440			21.94	15.70	-8.83	52.72	0.162	0.876		
MR median	10.43	23.82	-36.25	57.10	0.662				0.001	0.003	-0.004	0.007	0.658				23.91	21.51	-18.26	66.07	0.266			
MR robust	6.08	15.70	-24.70	36.86	0.699				0.000	0.002	-0.003	0.004	0.873				24.87	15.28	-5.09	54.82	0.104			
MR-Egger	5.22	17.42	-28.93	39.36	0.765		0.328		0.000	0.002	-0.004	0.004	0.936		0.450		23.55	15.80	-7.43	54.52	0.136		0.375	
MR-2SLS	6.15	14.22	-21.71	34.02	0.665		0.973		-0.002	0.001	-0.005	0.000	0.095		0.856		-1.03	13.31	-27.11	25.06	0.938			0.924
<b>Females</b>																								
MR F-IVW	7.26	6.21	-4.92	19.43	0.243	0.562			0.001	0.001	-0.001	0.002	0.246	0.136			0.79	4.69	-8.40	9.98	0.866	0.568		
MR R-IVW	7.26	6.21	-4.92	19.43	0.243	0.562			0.001	0.001	-0.001	0.002	0.275	0.136			0.79	4.69	-8.40	9.98	0.866	0.568		
MR median	1.83	9.52	-16.82	20.49	0.847				0.001	0.001	-0.002	0.003	0.574				4.87	6.91	-8.68	18.41	0.481			
MR robust	6.23	6.27	-6.07	18.52	0.321				0.001	0.001	-0.001	0.002	0.303				1.17	4.03	-6.74	9.08	0.772			
MR-Egger	6.81	6.23	-5.41	19.02	0.275		0.558		0.001	0.001	-0.001	0.002	0.286		0.958		1.14	4.70	-8.07	10.35	0.808		0.225	
MR-2SLS	1.92	4.64	-7.17	11.02	0.679		0.784		0.000	0.001	-0.001	0.001	0.605		0.235		3.51	3.78	-3.89	10.92	0.352			0.662
<b>SHBG</b>																								
<b>Males</b>																								
MR F-IVW	-4.46	9.05	-22.19	13.27	0.622	0.340			0.000	0.001	-0.002	0.002	0.900	0.440			-11.55	8.21	-27.65	4.55	0.160	0.876		
MR R-IVW	-4.46	9.25	-22.59	13.66	0.629	0.340			0.000	0.001	-0.002	0.002	0.901	0.440			-11.55	8.21	-27.65	4.55	0.160	0.876		
MR median	-11.49	12.70	-36.38	13.40	0.366				-0.001	0.002	-0.004	0.002	0.533				-13.61	11.29	-35.74	8.52	0.228			
MR robust	-6.51	8.52	-23.21	10.18	0.444				0.000	0.001	-0.002	0.002	0.661				-13.77	7.86	-29.17	1.64	0.080			
MR-Egger	-7.07	10.06	-26.78	12.64	0.482		0.328		0.000	0.001	-0.002	0.002	0.890		0.450		-14.51	8.86	-31.89	2.86	0.102		0.375	
MR-2SLS	1.42	7.69	-13.65	16.48	0.854		0.973		0.001	0.001	-0.001	0.002	0.296		0.856		-1.36	7.10	-15.28	12.56	0.848			0.924
<b>Females</b>																								
MR F-IVW	-5.63	3.26	-12.02	0.77	0.085	0.562			0.000	0.000	-0.001	0.001	0.884	0.136			-1.38	2.55	-6.38	3.61	0.587	0.568		
MR R-IVW	-5.63	3.26	-12.02	0.77	0.085	0.562			0.000	0.000	-0.001	0.001	0.891	0.136			-1.38	2.55	-6.38	3.61	0.587	0.568		
MR median	-10.71	5.43	-21.34	-0.07	<b>0.048</b>				0.000	0.001	-0.001	0.001	0.909				-0.76	3.96	-8.53	7.01	0.848			
MR robust	-6.55	4.37	-15.11	2.01	0.134				0.000	0.000	-0.001	0.001	0.962				-1.68	2.39	-6.37	3.01	0.483			
MR-Egger	-3.24	4.18	-11.44	4.96	0.439		0.558		0.000	0.001	-0.001	0.001	0.942		0.958		-4.03	3.36	-10.61	2.55	0.230		0.225	
MR-2SLS	-4.90	3.02	-10.82	1.01	0.104		0.784		0.000	0.000	0.000	0.001	0.206		0.235		-2.24	2.43	-7.01	2.53	0.358			0.662

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: FVC = 141, FEV1/FVC = 125, FEV1 = 111; Females: FVC = 135, FEV1/FVC = 140, FEV1 = 128.

N in 2SLS = Males = 6,812; Females = 7,470.

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