

Online Supplementary Materials**Serum free testosterone and asthma, asthma hospitalizations, and lung function in British adults**

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Supplemental Table E1. Multivariable analysis of serum free testosterone and asthma

	Model 1	Model 2*	Model 3†
Serum levels of sex hormones	Odds ratio (95% confidence interval)		
Women	n=123,921	n=121,147	n=105,754
Quartiles (Q) of free testosterone, pmol/L			
Q1 (< 6.4)	1.0	1.0	1.0
Q2 (6.4- < 10.2)	0.84 (0.80, 0.88) [§]	0.84 (0.80, 0.88) [§]	0.85 (0.80, 0.89) [§]
Q3 (10.2- < 15.3)	0.76 (0.73, 0.80) [§]	0.76 (0.73, 0.80) [§]	0.76 (0.72, 0.80) [§]
Q4 (≥ 15.3)	0.67 (0.64, 0.71) [§]	0.67 (0.64, 0.71) [§]	0.67 (0.64, 0.71) [§]
Estradiol, pmol/L			
< 123.7	1.0	1.0	1.0
≥ 123.7	1.08 (1.02, 1.13) [‡]	1.08 (1.02, 1.13) [‡]	1.09 (1.03, 1.16) [‡]
Men	n=132,498		
Quartiles (Q) of free testosterone, pmol/L			
Q1 (< 123.4)	1.0	-	-
Q2 (123.4- < 160.3)	0.91 (0.87, 0.96) [§]	-	-
Q3 (160.3- < 200.4)	0.89 (0.84, 0.93) [§]	-	-
Q4 (≥ 200.4)	0.87 (0.82, 0.91) [§]	-	-
Estradiol, pmol/L			
< 123.7	1.0	-	-
≥ 123.7	0.98 (0.93, 1.05)	-	-

All models adjusted for age, race/ethnicity, annual household income, body mass index, smoking status, pack-years of cigarette smoking, current use of birth control pills or hormone replacement therapy (in women), menopause status (in women), and the season and the time of the day when the examination was performed.

*Model 2 additionally adjusted for number of livebirths and menstruating on the day of examination.

†Model 3 excluded the 15% of participating women who answered “not sure” to the menopause question

‡P<0.05, §P<0.01

Supplemental Table E2. Multivariable analysis of serum free testosterone and asthma, by smoking status

	Current smokers	Never smokers and former smokers with < 10 pack-years of cigarette smoking
Serum levels of sex hormones	Odds ratio (95% confidence interval)	
Women	n=11,289	n=94,983
Quartiles (Q) of free testosterone, pmol/L		
Q1 (< 6.4)	1.0	1.0
Q2 (6.4- < 10.3)	0.82 (0.69, 0.97)*	0.85 (0.80, 0.89) [†]
Q3 (10.3- < 15.3)	0.71 (0.60, 0.84) [†]	0.77 (0.73, 0.82) [†]
Q4 (≥ 15.3)	0.62 (0.52, 0.73) ^{†‡}	0.69 (0.65, 0.73) ^{†‡}
Estradiol, pmol/L		
< 123.7	1.0	1.0
≥ 123.7	0.94 (0.80, 1.09)	1.09 (1.03, 1.16) [†]
Men	n=14,782	n=87,472
Quartiles (Q) of free testosterone, pmol/L		
Q1 (< 123.2)	1.0	1.0
Q2 (123.2- < 160.0)	0.93 (0.78, 1.09)	0.91 (0.86, 0.97) [†]
Q3 (160.0- < 200.1)	0.83 (0.70, 0.98)*	0.91 (0.85, 0.96) [†]
Q4 (≥ 200.1)	0.79 (0.67, 0.93) ^{†‡}	0.88 (0.82, 0.93) ^{†‡}
Estradiol, pmol/L		
< 123.7	1.0	1.0
≥ 123.7	0.94 (0.77, 1.14)	1.04 (0.97, 1.12)

All models included both serum levels of free testosterone and serum estradiol, and were adjusted for age, ethnicity, annual household income, body mass index, pack-years of cigarette smoking (in current smokers), current use of birth control pills or hormone replacement therapy and menopause status (in women), and the season and the time of the day when the examination was performed.

*P<0.05, [†]P<0.01, [‡]P for trend < 0.05

Supplemental Table E3 – Multivariable analysis of serum free testosterone and lung function measures, as z-scores

	Women (n = 87,137)	Men (n = 94,491)
Lung function measures	β (95% Confidence Interval)	
Serum free testosterone (pmol/L), per quartile increment		
FEV ₁ z-score	-0.007 (-0.014, -0.002)*	0.036 (0.029, 0.042)†
FVC z-score	-0.009 (-0.015, -0.003)†	0.043 (0.037, 0.049)†
FEV ₁ /FVC z-score	0.003 (-0.002, 0.007)	-0.007 (-0.012, 0.001)
Detectable serum estradiol		
FEV ₁ z-score	-0.016 (-0.036, 0.005)	-0.101 (-0.125, -0.077)†
FVC z-score	0.0004 (-0.019, 0.020)	-0.095 (-0.117, -0.072)†
FEV ₁ /FVC z-score	-0.021 (-0.035, -0.007)†	-0.020 (-0.040, 0.001)

All models included both serum levels of free testosterone and serum estradiol, and were adjusted for annual household income, body mass index, smoking status, pack-years of cigarette smoking, current use of birth control pills or hormone replacement therapy and menopause status (in women), the season and the time of the day when the examination was performed.

*P<0.05; [†]P<0.01

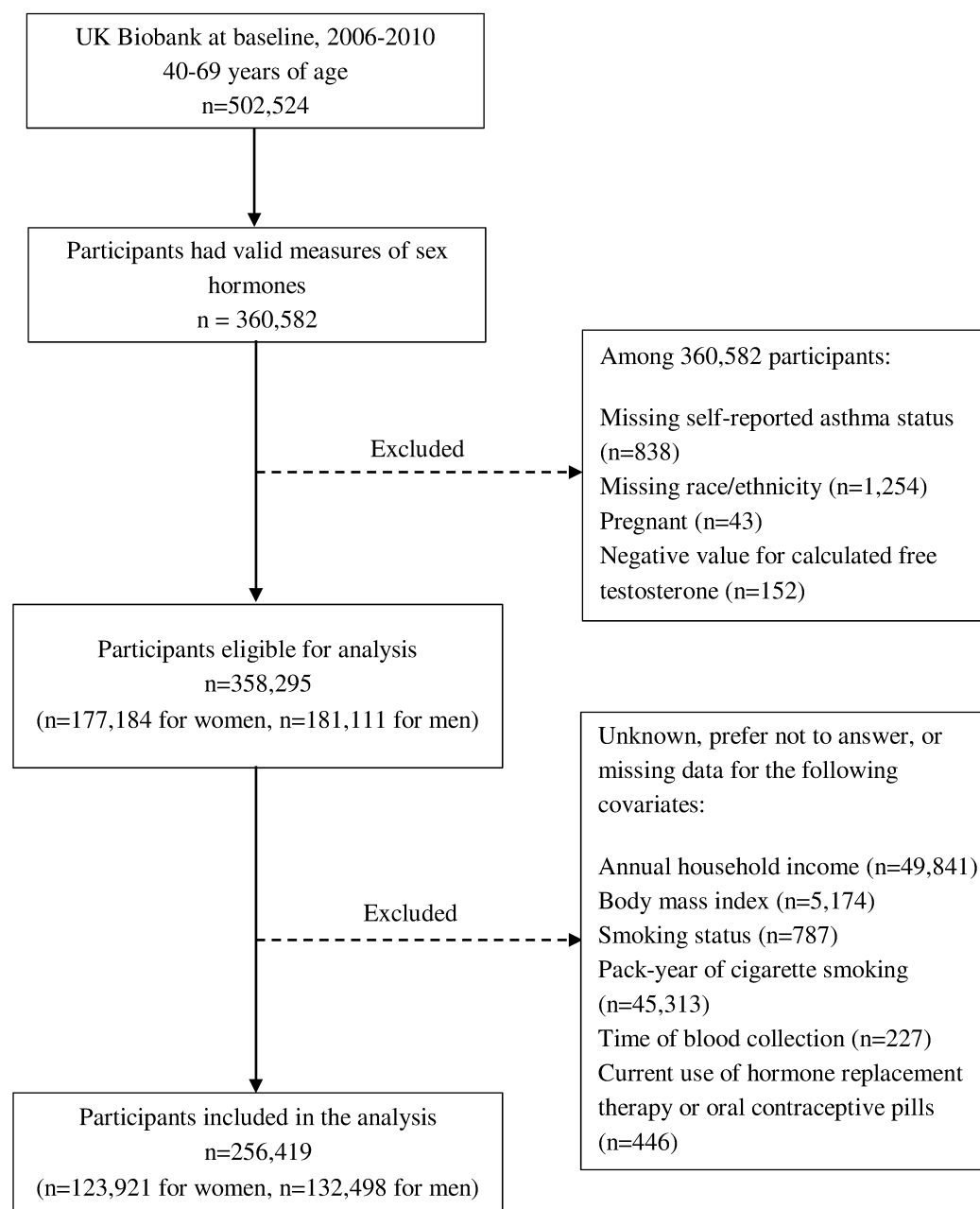
Supplemental Table E4. Sensitivity analysis (using multiple imputation for missing covariates) of serum free testosterone and asthma in all eligible participants

Serum levels of sex hormones	Odds ratio (95% confidence interval)
Women (n=177,184)	
Quartiles (Q) of free testosterone, pmol/L	
Q1 (< 6.3)	1.0
Q2 (6.3- < 10.2)	0.85 (0.81, 0.88) [†]
Q3 (10.2- < 15.2)	0.77 (0.74, 0.80) [†]
Q4 (≥ 15.2)	0.68 (0.66, 0.71) [†]
Estradiol, pmol/L	
< 123.7	1.0
≥ 123.7	1.07 (1.02, 1.12) [*]
Men (n=181,111)	
Quartiles (Q) of free testosterone, pmol/L	
Q1 (< 122.4)	1.0
Q2 (122.4- < 159.3)	0.91 (0.87, 0.95) [†]
Q3 (159.3- < 199.3)	0.88 (0.84, 0.92) [†]
Q4 (≥ 199.3)	0.85 (0.82, 0.89) [†]
Estradiol, pmol/L	
< 123.7	1.0
≥ 123.7	0.99 (0.94, 1.04)

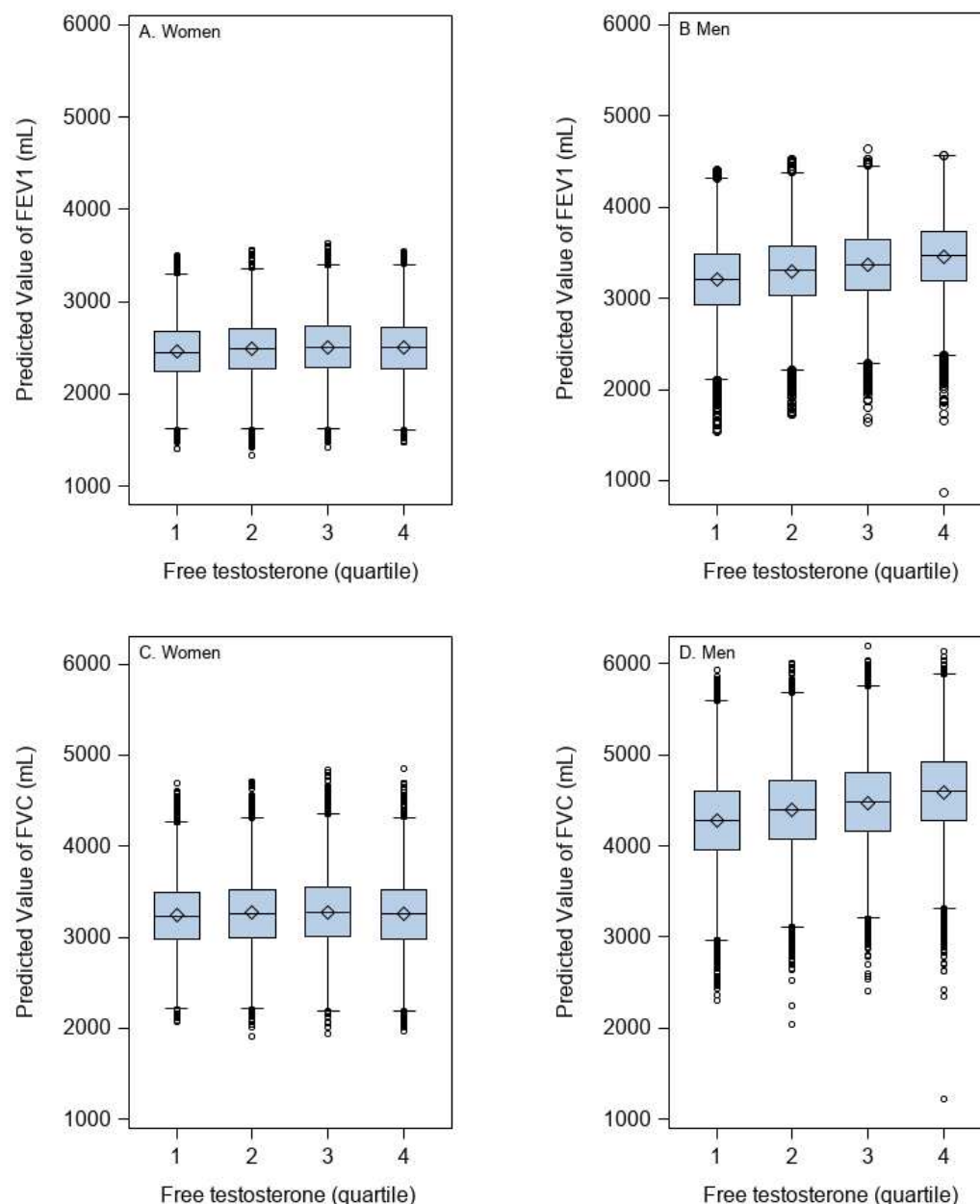
All models included both serum levels of free testosterone and serum estradiol, and were adjusted for age, race/ethnicity, annual household income, body mass index, smoking status, pack-years of cigarette smoking, current use of birth control pills or hormone replacement therapy (in women), menopause status (in women), the season and the time of the day when the examination was performed.

*P<0.05, [†]P<0.01

Supplemental Figure E1- Flowchart for selection of participants from the UK biobank included in the current analysis



Supplemental Figure E2- Predicted values of FEV₁ (upper panels A and B) and FVC (lower panels C and D) by serum level of free testosterone quartiles, in women and men



All models included both serum free testosterone and serum estradiol, and were adjusted for age, race/ethnicity, annual household income, body mass index, asthma status, smoking status, pack-years of cigarette smoking, current use of birth control pills or hormone replacement therapy and menopause status (in women), height, height squared, and the season and the time of the day when the examination was performed.

