

Supplementary Material:

“Sociodemographic, lifestyle and medical factors influencing testosterone and SHBG in men from the UK Biobank.”

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Supplementary Methods

Variables of interest

Values for moderate- or vigorous-level activity >1,080 minutes/day (n=13) or summed values of moderate- and vigorous-level activity >10,080 minutes/week (n=21) were treated as erroneous and not analysed.

Statistical Methods

Hexbin plots were plotted using the “hexMA.loess” function of the hexbin package.^{1,2} Smoothed centile plots were estimated using Generalised Additive Models for Location Scale and Shape (GAMLSS).^{3,4} Restricted cubic splines were used to model non-linear associations with continuous covariates, with 3 internal knots at the 27.5th, 50th, 72.5th percentiles and linear constraints outside of the outer knots at the 5th and 95th percentiles. A series of Linear Mixed Models (LMMs) with pre-specified terms were fitted, to investigate associations with sex hormones of sociodemographic and lifestyle factors, and prevalent medical conditions. Estimates of effect sizes and Intraclass Correlation Coefficients were estimated using Restricted Maximum Likelihood and the approximate statistical significance of independent associations of the fixed effects were determined using Likelihood Ratio tests of nested models.⁵ LMMs were used to predict hormone values for different combinations of sociodemographic and lifestyle factors, and prevalent medical conditions.⁶ Predicted values of the response variable (hormone concentration) are tabulated, which were made, marginal to the estimated random effects, using the fitted LMMs. Standard errors were obtained as the standard errors of 1000 parametric bootstrap replications of the predicted values using the bootMer function of the lme4 package in R.⁷ Joint modelling imputation, as suitable for individual participant data meta-analysis using linear mixed effects models, was performed with Monte Carlo Markov Chain burn-in of 500 and 5 post burn-in imputed datasets retained, with 100 imputations in-between each.^{8,9} To ensure the imputation model was consistent with the analysis model, we included in the datasets to be imputed the individual variables used to construct restricted cubic splines for age and BMI, with three internal knots at the 27.5th, 50th, 72.5th percentiles and linear constraints outside of the outer knots at the 5th and 95th percentiles of the marginal distribution of these covariates, and site as a clustering variable.¹⁰⁻¹² We used all variables included for constructing Model 2 terms, plus an additional auxiliary variable of waist circumference for multiple imputation analyses of Models 1 and 2. We included the additional variable of prevalent cardiovascular disease for multiple imputation analyses of Model 3. Multiple imputations were implemented using the jomo package in R version 3.6.0. Multiply-imputed estimates were pooled using Rubin’s rules.¹³ All data analyses were conducted in R version 3.6.0.¹⁴

Supplementary references

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Supplementary Table S1

Hospital diagnosis and cancer registry codes used to identify prevalent health conditions of interest.*

Prevalent health condition	ICD-9	ICD-10
CVD	410, 428, 430-437	I21, I22, I50, I60-I64, I69.0-I69.4
Cancer	140.x - 209.x	C00-C97
Diabetes	250.0 - 250.9	E10 - E14
Dementia	290.0, 290.1, 290.2, 290.3, 290.4, 290.8, 290.9, 294.1, 294.8, 331.0, 331.1, 331.2, 331.4, 331.82	F00, F01, F02.0, F02.2, F02.3, F02.8, F03, F05.1, G10, G30, G31.0, G31.1, G31.8, G31.9
Angina	413.0, 413.1, 413.9	I20.0, I20.1, I20.8, I20.9
Atrial Fibrillation	427.3	I48, and, where the 4th digit was provided**, I48.0, I48.1, I48.2, I48.9
Renal Impairment	582, 583, 585, 586	N03, N04, N05, N08.1-NO8.3, NO8.5, N11.1, N11.8, N11.9, N14, N18.2, N18.3, N18.4, N18.5, N18.6, N18.9, N19
Hypertension	401	I10
COPD	490, 491, 492, 494, 496	J43.1, J43.2, J43.8, J43.9, J44.0, J44.1, J44.8, J44.9

* = Additional data sources were also used for identifying these prevalent conditions (e.g., from self-report medical conditions, self-report medication usage, physical examination and blood chemistry measurements).

** = In many cases only "I48" was provided but in others the full 4 digit code was provided.

Supplementary Table S2

Analysis design and statistical hypotheses.

Model(s)	Mathematical Representation	Hypothesis(es)	Context
1	$T = f(\text{socio-demographic variables, site})$	Socio-demographic variable k has an independent association with the level of endogenous T .	That is, after controlling for other $K-1$ socio-demographic variables in the model, where $k = 1, \dots, K$.
2	$T = f(\text{Model 1 terms} + \text{lifestyle variables})$	Lifestyle variable l has an independent association with the level of endogenous T	That is, after controlling for other $L-1$ lifestyle and K socio-demographic variables in the model, where $l = 1, \dots, L$.
3	$T = f(\text{Model 2 terms} + \text{CVD})$	CVD has an independent association with the level of endogenous T	That is, after controlling for other L lifestyle and K socio-demographic variables in the model.
4-11	$T = f(\text{Model 2 terms} + \text{prevalent condition}_j)^*$	Health condition j has an independent association with the level of endogenous T	That is, after controlling for other L lifestyle and K socio-demographic variables in the model.

[§] Socio-demographic variables = Age, BMI, Ethnicity, Education/Qualifications, Partner.
Lifestyle variables = Alcohol consumption, Smoking status, Diet, Physical Activity.

* Where prevalent condition j is one from the set of interest: Cancer, Diabetes, Dementia, Angina, Atrial Fibrillation, Renal Impairment, Hypertension, COPD.

Supplementary Results

Supplementary Table S3

Summary statistics of variables by category of calculate free testosterone (cFT; pmol/L). To convert to ng/dL, multiply by 0.0288.

Characteristic**	Quintiles of cFT*					
	1 (n=38,411)	2 (n=38,411)	3 n=(38,410)	4 n=(38,411)	5 n=(38,411)	All n=(192,054)
Sociodemographic						
Age (years)	62.0 (56.0-66.0)	60.0 (54.0-65.0)	58.0 (51.0-63.0)	56.0 (48.0-62.0)	51.0 (45.0-59.0)	58.0 (50.0-63.0)
BMI (kg/m ²)	27.9 (25.2-31.2)	27.5 (25.1-30.3)	27.3 (25.0-30.0)	27.1 (24.9-29.6)	26.9 (24.8-29.3)	27.3 (25.0-30.1)
Waist circumference (cm)	98.0 (91.0-107.0)	97.0 (90.0-104.0)	96.0 (89.0-103.0)	95.0 (89.0-102.0)	94.0 (88.0-101.0)	96.0 (89.0-103.0)
Ethnicity: Asian	1.6 (619)	1.9 (733)	2.1 (818)	2.6 (983)	3.4 (1,280)	2.3 (4,433)
Black	1.1 (417)	1.1 (427)	1.3 (487)	1.7 (637)	2.3 (882)	1.5 (2,850)
Chinese	0.1 (37)	0.2 (65)	0.2 (70)	0.3 (117)	0.5 (193)	0.3 (482)
Mixed	0.4 (135)	0.4 (139)	0.5 (183)	0.5 (200)	0.7 (276)	0.5 (933)
Other	0.6 (212)	0.6 (222)	0.8 (308)	0.9 (359)	1.4 (533)	0.9 (1,634)
White	96.3 (36,753)	95.8 (36,622)	95.1 (36,349)	94.0 (35,911)	91.7 (35,024)	94.6 (180,659)
Partner: True	78.2 (29,917)	78.7 (30,129)	77.9 (29,792)	76.3 (29,181)	72.5 (27,694)	76.7 (146,713)
Quals: Below A levels	50.2 (19,042)	46.1 (17,517)	43.8 (16,649)	42.7 (16,222)	41.7 (15,833)	44.9 (85,263)
A levels (high school)	6.3 (2,378)	6.6 (2,491)	6.7 (2,528)	7.3 (2,771)	8.0 (3,053)	7.0 (13,221)
College/University	29.6 (11,206)	33.0 (12,519)	34.9 (13,269)	36.3 (13,784)	36.8 (13,982)	34.1 (64,760)
Professional/Other	13.9 (5,282)	14.4 (5,453)	14.6 (5,557)	13.7 (5,205)	13.4 (5,096)	14.0 (26,593)
Lifestyle						
Alcohol: Abstainers	31.3 (11,977)	28.0 (10,723)	27.4 (10,493)	27.1 (10,376)	26.4 (10,129)	28.0 (53,698)
Low	13.7 (5,234)	14.0 (5,370)	14.0 (5,373)	13.8 (5,275)	13.7 (5,258)	13.8 (26,510)
Moderate	14.3 (5,463)	14.9 (5,693)	15.0 (5,760)	14.6 (5,608)	13.9 (5,334)	14.5 (27,858)
Medium	13.6 (5,197)	14.3 (5,468)	14.4 (5,532)	14.7 (5,638)	14.8 (5,687)	14.4 (27,522)
High	27.2 (10,434)	28.9 (11,078)	29.2 (11,178)	29.8 (11,432)	31.1 (11,897)	29.2 (56,019)
Diet: High Red Meat eaters	17.2 (6,510)	16.2 (6,144)	16.0 (6,040)	16.3 (6,140)	16.7 (6,297)	16.5 (31,131)
Low Red Meat eaters	79.9 (30,171)	80.6 (30,476)	80.6 (30,475)	80.0 (30,216)	79.6 (30,017)	80.1 (151,355)
Poultry eaters	0.6 (245)	0.6 (226)	0.6 (237)	0.6 (222)	0.6 (219)	0.6 (1,149)
Fish eaters	1.2 (437)	1.3 (501)	1.4 (533)	1.6 (615)	1.6 (603)	1.4 (2,689)
Vegetarian	1.0 (375)	1.1 (434)	1.3 (480)	1.4 (547)	1.5 (556)	1.3 (2,392)
Vegan	0.1 (30)	0.1 (29)	0.1 (34)	0.1 (39)	0.1 (26)	0.1 (158)
PA: Insufficient	30.6 (9,090)	30.2 (9,354)	30.8 (9,626)	30.0 (9,387)	30.2 (9,527)	30.4 (46,984)
Sufficient	17.7 (5,269)	18.1 (5,603)	18.3 (5,719)	18.6 (5,834)	19.1 (6,009)	18.4 (28,434)

Characteristic**	Quintiles of cFT*					
	1 (n=38,411)	2 (n=38,411)	3 (n=38,410)	4 (n=38,411)	5 (n=38,411)	All (n=192,054)
Additional	51.7 (15,390)	51.7 (15,987)	50.9 (15,932)	51.4 (16,074)	50.7 (15,989)	51.3 (79,372)
Smoking: Current	12.2 (4,666)	11.8 (4,496)	11.9 (4,566)	12.3 (4,701)	14.2 (5,417)	12.5 (23,846)
Never	42.5 (16,224)	47.3 (18,075)	49.8 (19,037)	51.7 (19,750)	54.1 (20,693)	49.1 (93,779)
Previous	45.3 (17,268)	40.9 (15,638)	38.3 (14,631)	36.0 (13,767)	31.7 (12,124)	38.4 (73,428)
Prevalent medical conditions						
CVD: True	9.0 (3,438)	6.6 (2,554)	5.8 (2,234)	4.8 (1,859)	3.5 (1,351)	6.0 (11,436)
Cancer: True	10.0 (3,827)	7.8 (3,013)	7.2 (2,752)	6.2 (2,387)	4.6 (1,785)	7.2 (13,764)
Diabetes: True	12.7 (4,876)	9.0 (3,471)	7.4 (2,857)	6.4 (2,451)	4.8 (1,860)	8.1 (15,515)
Dementia: True	0.1 (54)	0.1 (34)	0.1 (20)	0.1 (21)	0.0 (9)	0.1 (138)
Angina: True	8.6 (3,298)	6.6 (2,538)	5.7 (2,175)	4.4 (1,698)	3.1 (1,188)	5.7 (10,897)
Atrial Fibrillation: True	3.5 (1,336)	2.6 (987)	2.1 (806)	1.8 (679)	1.4 (548)	2.3 (4,356)
Renal impairment: True	1.1 (441)	0.8 (320)	0.7 (286)	0.7 (254)	0.6 (223)	0.8 (1,524)
Hypertension: True	71.2 (27,335)	67.1 (25,770)	63.6 (24,444)	60.5 (23,220)	54.1 (20,782)	63.3 (121,551)
COPD: True	1.8 (706)	1.1 (404)	0.8 (319)	0.7 (269)	0.4 (170)	1.0 (1,868)
Hormone variables						
Testosterone (nmol/L)	8.4 (6.9-10.3)	10.4 (8.9-12.2)	11.5 (9.9-13.5)	12.7 (11.0-14.7)	14.8 (12.9-17.2)	11.6 (9.4-14.1)
Testosterone (ng/dL)	242 (199-297)	300 (256-352)	331 (285-389)	366 (317-424)	427 (372-496)	334 (271-406)
SHBG (nmol/L)	40.8 (30.4-54.5)	39.3 (29.6-51.1)	37.6 (28.6-48.5)	35.7 (27.3-45.7)	32.6 (24.9-41.6)	36.9 (27.9-48.1)
cFT (pmol/L)	149 (131-160)	185 (178-193)	213 (206-221)	245 (236-255)	300 (281-330)	213 (178-255)

* = Quintile boundaries Q1/2 169 pmol/L, Q2/3 199 pmol/L, Q3/4 228 pmol/L and Q4/5 266 pmol/L. 2.5th percentile = 116 pmol/L, 97.5th = 361 pmol/L.

** = Continuous variables (BMI, age, waist circumference, testosterone, SHBG, cFT) represented as median (interquartile range); other variables as percentages (numbers) per category.

§ = BMI, body mass index (kg/m²); PA, level of physical activity categories (min/week; see Methods); Qualls, qualifications (highest level of education / training attained); Partner, living with partner?; Alcohol, level of alcohol consumption (standard units of alcohol consumed/week); Smoking, smoking status; CVD, Cardiovascular Disease.

Supplementary Table S4

Intra-class correlation (ICC) coefficients for linear mixed models, examining effects of site.

Model	ICC Analysis:		
	Testosterone	SHBG	cFT
1	0.0018	0.0010	0.0016
2	0.0018	0.0009	0.0016
3	0.0018	0.0009	0.0016
4	0.0017	0.0009	0.0016
5	0.0018	0.0009	0.0016
6	0.0018	0.0009	0.0016
7	0.0018	0.0009	0.0016
8	0.0018	0.0009	0.0016
9	0.0018	0.0009	0.0016
10	0.0018	0.0009	0.0016
11	0.0018	0.0009	0.0016

Supplementary Table S5

Effect sizes and tests for fixed effects on SHBG.

Predictor		Model [§]	Effect (nmol/L SHBG)* [¶]	p-value (term) [†]
Sociodemographic				
Age [¶]		Model 1	+5.06 (0.13)	<0.001
BMI [¶]		Model 1	-3.81 (0.12)	<0.001
Ethnicity:	Asian (ref)	Model 1	0	<0.001
	Black		+6.49 (0.43)	
	Chinese		-1.35 (0.83)	
	Mixed		+4.49 (0.62)	
	Other		+4.26 (0.52)	
	White		+6.28 (0.29)	
Partner:	True	Model 1	-1.26 (0.09)	<0.001
Qualifications:	Below A levels (ref)	Model 1	0	<0.001
	A levels (High school)		-0.98 (0.16)	
	College/University		-1.18 (0.09)	
	Professional		-0.94 (0.12)	
Lifestyle				
Alcohol:	Abstainers (ref)	Model 2	0	0.019
	Low		-1.12 (0.13)	
	Moderate		-1.32 (0.12)	
	Medium		-1.55 (0.13)	
	High		-2.25 (0.11)	
Diet:	High Red Meat eaters (ref)	Model 2	0	<0.001
	Low Red Meat eaters		+0.28 (0.11)	
	Poultry eaters		+3.12 (0.50)	
	Fish eaters		+2.12 (0.32)	
	Vegetarian		+0.16 (0.35)	
	Vegan		+3.48 (1.29)	
Physical Activity:	Insufficient (ref)	Model 2	0	<0.001
	Sufficient		+0.82 (0.11)	
	Additional		+2.18 (0.09)	
Smoking:	Current (ref)	Model 2	0	<0.001
	Never		-3.34 (0.13)	
	Previous		-3.51 (0.13)	
Prevalent medical conditions				
CVD:	True	Model 3	-0.38 (0.17)	0.031
Cancer:	True	Model 4	-0.05 (0.15)	0.753
Diabetes:	True	Model 5	-2.95 (0.16)	<0.001
Dementia:	True	Model 6	+0.91 (1.55)	0.556
Angina:	True	Model 7	-1.41 (0.18)	<0.001
Atrial Fibrillation:	True	Model 8	+2.75 (0.26)	<0.001
Renal impairment:	True	Model 9	-1.18 (0.47)	0.013
Hypertension:	True	Model 10	-1.52 (0.08)	<0.001
COPD:	True	Model 11	+0.50 (0.45)	0.272

§ = See Table S2 (Supplementary statistical methods) for specifications of statistical models and hypothesis tests.

* = Values in parentheses are standard errors of the estimates.

¶ = For Age, BMI: difference between that estimated for the mean + 1 standard deviation and that estimated for the mean; all other predictors: mean difference to that estimated for the reference level (reference level=False, not shown for: Prevalent health conditions, Partner).

† = Likelihood Ratio tests of nested models with and without the term, as listed in Table S2.

Supplementary Table S6

Effect sizes and tests for fixed effects on calculated free testosterone (cFT). To convert to ng/dL, multiply by 0.0288.

Predictor		Model [§]	Effect (pmol/L cFT)* [¶]	p-value (term) [†]
Sociodemographic				
Age [¶]		Model 1	-21.23 (0.51)	<0.001
BMI [¶]		Model 1	-8.10 (0.46)	<0.001
Ethnicity:	Asian (ref)	Model 1	0	<0.001
	Black		1.08 (1.75)	
	Chinese		14.43 (3.36)	
	Mixed		-1.38 (2.50)	
	Other		1.30 (2.09)	
	White		-6.87 (1.15)	
Partner:	True	Model 1	-7.35 (0.38)	<0.001
Qualifications:	Below A levels (ref)	Model 1	0	<0.001
	A levels		1.96 (0.63)	
	College/University		1.08 (0.36)	
	Professional		1.95 (0.47)	
Lifestyle				
Alcohol:	Abstainers (ref)	Model 2	0	<0.001
	Low		4.09 (0.52)	
	Moderate		4.14 (0.51)	
	Medium		6.69 (0.51)	
	High		7.72 (0.43)	
Diet:	High Red Meat eaters (ref)	Model 2	0	0.030
	Low Red Meat eaters		-0.21 (0.43)	
	Poultry eaters		-3.47 (2.01)	
	Fish eaters		-2.35 (1.31)	
	Vegetarian		-3.46 (1.43)	
	Vegan		-6.21 (5.29)	
Physical Activity:	Insufficient (ref)	Model 2	0	<0.001
	Sufficient		0.57 (0.46)	
	Additional		-1.06 (0.36)	
Smoking:	Current (ref)	Model 2	0	<0.001
	Never		4.04 (0.52)	
	Previous		0.94 (0.53)	
Prevalent medical conditions				
CVD:	True	Model 3	-3.73 (0.71)	<0.001
Cancer:	True	Model 4	-3.46 (0.61)	<0.001
Diabetes:	True	Model 5	-7.39 (0.63)	<0.001
Dementia:	True	Model 6	-20.60 (6.32)	0.001
Angina:	True	Model 7	-3.37 (0.72)	<0.001
Atrial Fibrillation:	True	Model 8	-2.06 (1.07)	0.055
Renal impairment:	True	Model 9	-4.94 (1.93)	0.010
Hypertension:	True	Model 10	-0.87 (0.34)	0.011
COPD:	True	Model 11	-10.84 (1.85)	<0.001

§ = See Table S2 (Supplementary statistical methods) for specifications of statistical models and hypothesis tests.

* = Values in parentheses are standard errors of the estimates.

¶ = For Age, BMI: difference between that estimated for the mean + 1 standard deviation and that estimated for the mean; all other predictors: mean difference to that estimated for the reference level (reference level=False, not shown for: Prevalent health conditions, Partner). Note that the effect of BMI on cFT is not well represented by a single estimate; for instance, a +1 standard deviation increase in BMI, from 21.37 kg/m² to 25.41 kg/m² had an estimated +14.30 (0.74) pmol/L effect on cFT, whereas a +1 standard deviation increase from 25.41 kg/m² to 29.45 kg/m² had an estimated -5.54 (0.33) pmol/L effect on cFT.

† = Likelihood Ratio tests of nested models with and without the term, as listed in Table S2.

Supplementary Table S7 All effect sizes for fixed effects on testosterone.

Predictor	<i>Effect (nmol/L Testosterone)*†</i>			
	Model 1	Model 2	Model 3	Model 5
<i>Sociodemographic</i>				
Age †	-0.23 (0.03)	-0.20 (0.03)	-0.19 (0.03)	-0.18 (0.03)
BMI †	-1.04 (0.03)	-1.01 (0.03)	-1.01 (0.03)	-0.96 (0.03)
Ethnicity:				
Asian (ref)	0	0	0	0
Black	+1.20 (0.10)	+1.18 (0.10)	+1.17 (0.10)	+1.11 (0.10)
Chinese	+0.48 (0.18)	+0.53 (0.18)	+0.52 (0.18)	+0.43 (0.18)
Other	+0.87 (0.14)	+0.85 (0.14)	+0.84 (0.14)	+0.74 (0.14)
White	+0.75 (0.12)	+0.75 (0.12)	+0.74 (0.12)	+0.68 (0.12)
Partner:				
True	-0.55 (0.02)	-0.51 (0.02)	-0.52 (0.02)	-0.53 (0.02)
Qualifications:				
Below A levels (ref)	0	0	0	0
A levels (high school)	-0.08 (0.04)	-0.04 (0.04)	-0.04 (0.04)	-0.05 (0.04)
College/University	-0.14 (0.02)	-0.10 (0.02)	-0.10 (0.02)	-0.11 (0.02)
Professional	-0.07 (0.03)	-0.04 (0.03)	-0.05 (0.03)	-0.05 (0.03)
<i>Lifestyle</i>				
Alcohol:				
Abstainers (ref)		0	0	0
Low		+0.03 (0.03)	+0.03 (0.03)	+0.01 (0.03)
Moderate		+0.01 (0.03)	+0.00 (0.03)	-0.02 (0.03)
Medium		+0.08 (0.03)	+0.08 (0.03)	+0.06 (0.03)
High		+0.00 (0.02)	+0.00 (0.02)	-0.03 (0.02)
Diet:				
High red meat eaters (ref)		0	0	0
Low red meat eaters		+0.06 (0.02)	+0.06 (0.02)	+0.06 (0.02)
Poultry eaters		+0.27 (0.11)	+0.27 (0.11)	+0.26 (0.11)
Fish eaters		+0.29 (0.07)	+0.29 (0.07)	+0.28 (0.07)
Vegetarian		-0.08 (0.08)	-0.09 (0.08)	-0.09 (0.08)
Vegan		+0.36 (0.29)	+0.35 (0.29)	+0.34 (0.29)
Physical Activity:				
Insufficient (ref)		0	0	0
Sufficient		+0.17 (0.03)	+0.17 (0.03)	+0.17 (0.03)
Additional		+0.34 (0.02)	+0.34 (0.02)	+0.32 (0.02)
Smoking:				
Current (ref)		0	0	0
Never		-0.38 (0.03)	-0.38 (0.03)	-0.39 (0.03)
Previous		-0.55 (0.03)	-0.55 (0.03)	-0.54 (0.03)
<i>Prevalent health conditions</i>				
CVD:			-0.26 (0.04)	
Diabetes:				-0.84 (0.03)

* = Values in parentheses are standard errors of the estimates. To convert testosterone from nmol/L to ng/dL, divide by 0.0347.

¶ = For Age, BMI: difference between that estimated for the mean + 1 standard deviation and that estimated for the mean; all other predictors: mean difference to that estimated for the reference level (reference level=False, not shown for: Prevalent health conditions, Partner).

Supplementary Table S8

Comparison of effect estimates from complete-case analysis for effects on testosterone, versus pooled estimates from analysis of five multiply-imputed datasets.

Predictor		Model [§]	Effect (nmol/L Testosterone)* [¶]	
			Complete-case (N=162,887)	Multiply- imputed (N=208,677)
Sociodemographic				
Age [¶]		Model 1	-0.23 (0.03)	-0.24 (0.03)
BMI [¶]		Model 1	-1.04 (0.03)	-1.08 (0.02)
Ethnicity:	Asian (ref)	Model 1	0	0
	Black		+1.20 (0.10)	+1.19 (0.08)
	Chinese		+0.48 (0.18)	+0.60 (0.16)
	Mixed		+0.87 (0.14)	+0.90 (0.12)
	Other		+0.75 (0.12)	+0.84 (0.10)
	White		+0.81 (0.06)	+0.87 (0.05)
Partner:	True	Model 1	-0.55 (0.02)	-0.52 (0.02)
Qualifications:	Below A levels (ref)	Model 1	0	0
	A levels (high school)		-0.08 (0.04)	-0.09 (0.03)
	College/University		-0.14 (0.02)	-0.14 (0.02)
	Professional		-0.07 (0.03)	-0.06 (0.02)
Lifestyle				
Alcohol:	Abstainers (ref)	Model 2	0	0
	Low		+0.03 (0.03)	+0.06 (0.03)
	Moderate		+0.01 (0.03)	+0.03 (0.02)
	Medium		+0.08 (0.03)	+0.11 (0.03)
	High		+0.00 (0.02)	+0.05 (0.02)
Diet:	High Red Meat eaters (ref)	Model 2	0	0
	Low Red Meat eaters		+0.06 (0.02)	+0.06 (0.02)
	Poultry eaters		+0.27 (0.11)	+0.29 (0.10)
	Fish eaters		+0.29 (0.07)	+0.31 (0.07)
	Vegetarian		-0.08 (0.08)	-0.06 (0.07)
	Vegan		+0.36 (0.29)	+0.30 (0.26)
Physical Activity:	Insufficient (ref)	Model 2	0	0
	Sufficient		+0.17 (0.03)	+0.16 (0.02)
	Additional		+0.34 (0.02)	+0.32 (0.02)
Smoking:	Current (ref)	Model 2	0	0
	Never		-0.38 (0.03)	-0.40 (0.02)
	Previous		-0.55 (0.03)	-0.58 (0.03)
Prevalent medical conditions				
CVD:	True	Model 3	-0.26 (0.04)	-0.27 (0.03)

§ = See Table S2 (Supplementary statistical methods) for specifications of statistical models and hypothesis tests.

* = Values in parentheses are standard errors of the estimates. To convert testosterone from nmol/L to ng/dL, divide by 0.0347.

¶ = For Age, BMI: difference between that estimated for the mean + 1 standard deviation and that estimated for the mean; all other predictors: mean difference to that estimated for the reference level (reference level=False, not shown for: Prevalent health conditions, Partner)

Supplementary Table S9

Predicted hormone values for different combinations of sociodemographic and lifestyle factors, and prevalent medical conditions, in men from the UK Biobank.

Factors								
Age (years)	50	50	50	50	70	70	70	70
BMI (kg/m ²)	25	40	25	40	25	40	25	40
Ethnicity	White	White	Asian	Asian	White	White	Asian	Asian
Partner	No	No	Yes	Yes	No	No	Yes	Yes
Qualifications	Below A levels	Below A levels	College/ university	College/ university	Below A levels	Below A levels	College/ university	College/ university
Alcohol	Low	Low	Medium	Medium	Low	Low	Medium	Medium
Diet	Fish eater	Fish eater	Low red meat	Low red meat	Fish eater	Fish eater	Low red meat	Low red meat
Phys. activity	Sufficient	Sufficient	Insufficient	Insufficient	Sufficient	Sufficient	Insufficient	Insufficient
Smoking	Never	Never	Previous	Previous	Never	Never	Previous	Previous
<i>Predicted testosterone (nmol/L) §</i>								
CVD: No	13.7 (0.1)*	10.3 (0.1)	11.8 (0.1)	8.4 (0.1)	13.2 (0.1)	9.8 (0.1)	11.3 (0.1)	7.9 (0.1)
CVD: Yes	13.4 (0.1)	10.0 (0.1)	11.5 (0.1)	8.1 (0.1)	12.9 (0.1)	9.6 (0.1)	11.0 (0.1)	7.6 (0.1)
Diabetes: No	13.7 (0.1)	10.5 (0.1)	11.9 (0.1)	8.7 (0.1)	13.3 (0.1)	10.0 (0.1)	11.5 (0.1)	8.2 (0.1)
Diabetes: Yes	12.9 (0.1)	9.6 (0.1)	11.1 (0.1)	7.8 (0.1)	12.4 (0.1)	9.2 (0.1)	10.6 (0.1)	7.4 (0.1)
<i>Predicted SHBG (nmol/L) §</i>								
CVD: No	40.6 (0.4)*	31.3 (0.4)	28.8 (0.4)	19.5 (0.4)	53.0 (0.4)	43.7 (0.4)	41.2 (0.4)	31.9 (0.4)
CVD: Yes	40.2 (0.4)	30.9 (0.5)	28.4 (0.4)	19.1 (0.4)	52.7 (0.4)	43.3 (0.5)	40.8 (0.4)	31.5 (0.5)
Diabetes: No	40.7 (0.4)	32.0 (0.4)	29.3 (0.4)	20.6 (0.4)	53.3 (0.4)	44.6 (0.5)	41.9 (0.4)	33.2 (0.4)
Diabetes: Yes	37.7 (0.4)	29.0 (0.4)	26.3 (0.4)	17.6 (0.4)	50.3 (0.4)	41.6 (0.5)	38.9 (0.4)	30.2 (0.4)
<i>Predicted calculated free testosterone (pmol/L) §</i>								
CVD: No	251 (2)*	212 (2)	254 (1)	215 (2)	199 (2)	161 (2)	202 (2)	164 (2)
CVD: Yes	247 (2)	209 (2)	250 (2)	212 (2)	196 (2)	157 (2)	198 (2)	160 (2)
Diabetes: No	251 (2)	214 (2)	255 (1)	218 (2)	199 (2)	162 (2)	203 (1)	166 (2)
Diabetes: Yes	243 (2)	206 (2)	247 (2)	210 (2)	192 (2)	155 (2)	196 (2)	159 (2)

§ = Linear mixed models were used (see Supplementary statistical methods).

* = numbers in parentheses are standard errors of the model-predicted values. For testosterone, these ranged from 0.08 to 0.10 nmol/L and are shown rounded to one decimal place. To convert testosterone from nmol/L to ng/dL, divide by 0.0347.

Supplementary Figure S1

Study cohort.

