Online Table 1. Sex hormone levels associated with CVD risk factors*,†,‡

	Total T (nmol/L)	Estradiol (nmol/L)	Total T / Estradiol	DHEA (nmol/L)	SHBG (nmol/L)
Hypertension	0.02 (-0.03, 0.07)	**0.16 (0.11, 0.22)**	**-0.14 (-0.22, -0.07)**	0.01 (-0.03, 0.05)	**-0.06 (-0.10, -0.02)**
Diabetes	0.03 (-0.05, 0.10)	**0.10 (0.02, 0.19)**	-0.08 (-0.18, 0.03)	-0.05 (-0.11, 0.01)	**-0.25 (-0.30, -0.19)**
Current smoking	**0.15 (0.07, 0.23)**	**-0.09 (-0.18, -0.00)**	**0.24 (0.12, 0.35)**	**0.12 (0.06, 0.19)**	0.02 (-0.04, 0.08)
BMI ≥30 kg/m²	**0.15 (0.09, 0.20)**	**0.24 (0.18, 0.29)**	**-0.09 (-0.17, -0.01)**	**0.05 (0.00, 0.09)**	**-0.29 (-0.34, -0.25)**
eGFR <60 mL/min/1.73 m²	-0.03 (-0.09, 0.04)	0.06 (-0.01, 0.13)	-0.09 (-0.18, 0.00)	-0.06 (-0.11, -0.01)	-0.02 (-0.07, 0.03)
Physical activity, met-min/wk	0.00 (-0.01, 0.02)	-0.02 (-0.04, 0.00)	0.02 (-0.00, 0.05)	-0.01 (-0.02, 0.01)	**0.02 (0.00, 0.03)**
Total cholesterol, per 10 mg/dl	-0.01 (-0.01, 0.00)	0.00 (-0.01, 0.01)	-0.01 (-0.02, 0.00)	**0.01 (0.01, 0.02)**	-0.00 (-0.01, 0.00)
CRP	**0.04 (0.02, 0.06)**	**0.13 (0.11, 0.15)**	**-0.09 (-0.12, -0.06)**	**0.04 (0.02, 0.06)**	**-0.08 (-0.10, -0.06)**
Fibrinogen	**0.24 (0.11, 0.37)**	0.13 (-0.01, 0.27)	0.11 (-0.08, 0.29)	**0.19 (0.08, 0.29)**	**-0.34 (-0.44, -0.24)**
D-dimer	0.03 (-0.00, 0.06)	-0.01 (-0.04, 0.03)	0.03 (-0.01, 0.07)	-0.02 (-0.04, 0.00)	0.01 (-0.01, 0.03)
IL-6	**0.11 (0.07, 0.15)**	**0.15 (0.11, 0.19)**	-0.04 (-0.10, 0.01)	0.01 (-0.02, 0.04)	**-0.14 (-0.17, -0.11)**

*Abbreviations: CVD, cardiovascular disease; T, testosterone; DHEA, dehydroepiandrosterone; SHBG, sex hormone binding globulin; BMI, body mass index; eGFR; estimated glomerular filtration rate; CRP, C-reactive protein; IL-6, interleukin-6.

†All sex-hormones are dependent variables and log-transformed. CRP, fibrinogen, D-dimer and IL-6 were log-transformed. Physical activity was modeled as log(score + 1).

‡Model was adjusted for age (year, continuous), race/ethnicity (white, black, Hispanic, and Chinese), study site (CA, MN, NY, IL, NC, and MD), education (<high school, high school, >high school), and hormone therapy (yes, no).

Online Table 2. Hazard Ratios (95% CI) for hard CVD, hard CHD, HFpEF, HFrEF and ischemic stroke associated with sex hormone levels.[*,†]

Hard CVD			
(N events / N total = 213 / 2,834; IR = 6.9 per 1000 person-years)			
	Model 1‡	Model 2§	Model 3‖
Total T (nmol/L)	**1.20 (1.05, 1.37)**	**1.18 (1.03, 1.35)**	**1.17 (1.02, 1.34)**
Bioavailable T (nmol/L)	**1.23 (1.06, 1.42)**	**1.16 (1.00, 1.34)**	1.13 (0.97, 1.32)
Free T (Percent)	1.17 (0.99, 1.39)	1.07 (0.89, 1.28)	1.00 (0.82, 1.21)
Estradiol (nmol/L)	0.97 (0.80, 1.16)	0.92 (0.76, 1.11)	0.88 (0.72, 1.06)
Total T / estradiol ratio	**1.21 (1.02, 1.44)**	**1.24 (1.04, 1.48)**	**1.29 (1.07, 1.56)**
DHEA (nmol/L)	1.01 (0.87, 1.16)	0.96 (0.84, 1.11)	0.94 (0.81, 1.08)
SHBG (nmol/L)	0.84 (0.71, 0.99)	0.92 (0.77, 1.09)	0.98 (0.81, 1.18)
Hard CHD			
(N events / N total= 119 / 2,834; IR = 3.8 per 1000 person-years)			
	Model 1‡	Model 2§	Model 3 ‖
Total T (nmol/L)	1.19 (0.99, 1.43)	1.17 (0.97, 1.40)	1.17 (0.98, 1.41)
Bioavailable T (nmol/L)	1.17 (0.96, 1.43)	1.09 (0.90, 1.34)	1.07 (0.87, 1.31)
Free T (Percent)	1.06 (0.85, 1.34)	0.93 (0.73, 1.19)	0.83 (0.64, 1.08)
Estradiol (nmol/L)	0.82 (0.64, 1.04)	**0.76 (0.59, 0.97)**	**0.69 (0.53, 0.88)**
Total T / estradiol ratio	1.36 (1.08, 1.72)	**1.42 (1.12, 1.81)**	**1.57 (1.22, 2.02)**
DHEA (nmol/L)	0.98 (0.81, 1.18)	0.93 (0.77, 1.13)	0.95 (0.78, 1.15)
SHBG (nmol/L)	0.92 (0.74, 1.16)	1.05 (0.83, 1.33)	1.18 (0.91, 1.52)
Ischemic stroke			
(N events / N total= 88 / 2,834; IR = 2.8 per 1000 person-years)			
	Model 1‡	Model 2§	Model 3 ‖
Total T (nmol/L)	1.22 (0.98, 1.51)	1.20 (0.96, 1.49)	1.17 (0.94, 1.46)
Bioavailable T (nmol/L)	**1.31 (1.04, 1.65)**	1.25 (0.99, 1.58)	1.21 (0.94, 1.54)
Free T (Percent)	**1.40 (1.05, 1.85)**	1.30 (0.97, 1.75)	1.24 (0.90, 1.72)
Estradiol (nmol/L)	1.17 (0.86, 1.60)	1.13 (0.83, 1.54)	1.11 (0.80, 1.55)
Total T / estradiol ratio	1.08 (0.82, 1.43)	1.10 (0.83, 1.46)	1.10 (0.81, 1.48)
DHEA (nmol/L)	1.02 (0.81, 1.29)	0.98 (0.78, 1.24)	0.91 (0.72, 1.15)
SHBG (nmol/L)	**0.72 (0.55, 0.94)**	0.77 (0.58, 1.02)	0.80 (0.58, 1.09)

*Abbreviations: CVD, cardiovascular disease; CHD, coronary heart disease; IR, incidence rates; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; T, testosterone; DHEA, dehydroepiandrosterone; SHBG, sex hormone binding globulin; HDL, high density lipoprotein; eGFR; estimated glomerular filtration rate; CRP, C-reactive protein; IL-6, interleukin-6.

†All sex-hormones are log-transformed and standardized. Hazard Ratios are associated with 1 SD increase in log sex hormones.

‡Model 1: adjusts for age (year, continuous), race/ethnicity (white, black, Hispanic, and Chinese), study site (CA, MN, NY, IL, NC, and MD), and use of hormone therapy (yes, no).

§Model 2: model 1 + education (<high school, high school, >high school), waist to hip ratio (continuous), physical activity, and smoking (never, former, current).

ǁModel 3: model 2 + systolic blood pressure (mmHg, continuous), use of antihypertensive medications (yes, no), total cholesterol (mg/dl, continuous), HDL-cholesterol (mg/dl, continuous), use of lipid lowering medications (yes, no), diabetes (yes, no), eGFR (mL/min/1.73 m2), CRP (mg/l, log-transformed continuous), IL-6 (pg/ml, log-transformed, continuous), fibrinogen (mg/dl, log-transformed continuous), D-dimer (ug/ml, log-transformed continuous).

Online Table 3. Hazard Ratios (95% CI) for all CVD, CHD and HF associated with sex hormone levels (all sex hormones included in the same model).*,†,‡

	CVD	CHD	HF
Total T (nmol/L)	**1.20 (1.06, 1.36)**	**1.29 (1.09, 1.51)**	1.19 (0.96, 1.47)
Estradiol (nmol/L)	0.93 (0.79, 1.11)	**0.74 (0.60, 0.91)**	0.79 (0.60, 1.03)
DHEA (nmol/L)	0.88 (0.77, 1.00)	0.91 (0.77, 1.09)	0.84 (0.68, 1.04)
SHBG (nmol/L)	1.06 (0.90, 1.25)	1.23 (0.99, 1.52)	1.08 (0.81, 1.42)

*Abbreviations: CVD, cardiovascular disease; CHD, coronary heart disease; IR, incident rates; HF, heart failure; T, testosterone; DHEA, dehydroepiandrosterone; SHBG, sex hormone binding globulin; HDL, high density lipoprotein; eGFR; estimated glomerular filtration rate; CRP, C-reactive protein; IL-6, interleukin-6.

†All sex-hormones are log-transformed and standardized. Hazard Ratios are associated with 1 SD increase in log sex hormones.

‡Model adjusts for age (year, continuous), race/ethnicity (white, black, Hispanic, and Chinese), study site (CA, MN, NY, IL, NC, and MD), use of hormone therapy (yes, no), education (<high school, high school, >high school), waist to hip ratio (continuous), physical activity, smoking (never, former, current), systolic blood pressure (mmHg, continuous), use of antihypertensive medications (yes, no), total cholesterol (mg/dl, continuous), HDL-cholesterol (mg/dl, continuous), use of lipid lowering medications (yes, no), diabetes (yes, no), eGFR (mL/min/1.73 m2), CRP (mg/l, log-transformed continuous), IL-6 (pg/ml, log-transformed, continuous), fibrinogen (mg/dl, log-transformed continuous), D-dimer (ug/ml, log-transformed continuous).

Online Table 4. Hazard Ratios (95% CI) for all CVD, CHD and HF associated with sex hormone levels excluding women taking hormone therapy (all sex hormones included in the same model).*,†,‡

	CVD	CHD	HF
Total T (nmol/L)	**1.16 (1.00, 1.35)**	**1.25 (1.03, 1.52)**	**1.28 (1.00, 1.63)**
Estradiol (nmol/L)	0.93 (0.75, 1.17)	**0.70 (0.54, 0.92)**	0.74 (0.53, 1.02)
DHEA (nmol/L)	0.95 (0.81, 1.12)	1.05 (0.85, 1.30)	0.88 (0.68, 1.13)
SHBG (nmol/L)	1.12 (0.91, 1.39)	**1.36 (1.03, 1.80)**	1.17 (0.83, 1.65)

*Abbreviations: CVD, cardiovascular disease; CHD, coronary heart disease; IR, incident rates; HF, heart failure; T, testosterone; DHEA, dehydroepiandrosterone; SHBG, sex hormone binding globulin; HDL, high density lipoprotein; eGFR; estimated glomerular filtration rate; CRP, C-reactive protein; IL-6, interleukin-6.

†All sex-hormones are log-transformed and standardized. Hazard Ratios are associated with 1 SD increase in log sex hormones.

‡Model adjusts for age (year, continuous), race/ethnicity (white, black, Hispanic, and Chinese), and study site (CA, MN, NY, IL, NC, and MD), education (<high school, high school, >high school), waist to hip ratio (continuous), physical activity, and smoking (never, former, current), systolic blood pressure (mmHg, continuous), use of antihypertensive medications (yes, no), total cholesterol (mg/dl, continuous), HDL-cholesterol (mg/dl, continuous), use of lipid lowering medications (yes, no), diabetes (yes, no), eGFR (mL/min/1.73 m2), CRP (mg/l, log-transformed continuous), IL6 (pg/ml, log-transformed, continuous), fibrinogen (mg/dl, log-transformed continuous), D-dimer (ug/ml, log-transformed continuous).

Online Table 5. Hazard Ratios (95% CI) for all CVD, CHD and HF associated with sex hormone levels in competing risk analysis: MESA 2000-2013[*,†]

All CVD
(N events / N total= 283 / 2,834; IR = 9.3 per 1000 person-years)

	Model 1‡	Model 2§	Model 3∥
Total T (nmol/L)	**1.23 (1.09, 1.39)**	**1.21 (1.07, 1.37)**	**1.21 (1.07, 1.37)**
Bioavailable T (nmol/L)	**1.28 (1.12, 1.46)**	**1.21 (1.05, 1.39)**	**1.19 (1.03, 1.38)**
Free T (Percent)	1.21 (1.02, 1.42)	1.10 (0.93, 1.30)	1.03 (0.85, 1.24)
Estradiol (nmol/L)	1.06 (0.88, 1.27)	1.01 (0.84, 1.22)	0.97 (0.80, 1.18)
DHEA (nmol/L)	1.00 (0.87, 1.13)	0.96 (0.85, 1.09)	0.95 (0.83, 1.08)
SHBG (nmol/L)	**0.83 (0.70, 0.97)**	0.90 (0.76, 1.07)	0.97 (0.81, 1.16)

All CHD
(N events / N total= 171 / 2,834; IR = 5.5 per 1000 person-years)

	Model 1‡	Model 2§	Model 3∥
Total T (nmol/L)	**1.31 (1.10, 1.56)**	**1.30 (1.09, 1.54)**	**1.31 (1.10, 1.56)**
Bioavailable T (nmol/L)	**1.31 (1.09, 1.57)**	**1.23 (1.02, 1.48)**	**1.22 (1.01, 1.47)**
Free T (Percent)	1.13 (0.92, 1.40)	1.00 (0.81, 1.24)	0.92 (0.73, 1.15)
Estradiol (nmol/L)	0.92 (0.74, 1.16)	0.87 (0.69, 1.10)	0.80 (0.64, 1.01)
DHEA (nmol/L)	0.98 (0.82, 1.16)	0.94 (0.80, 1.11)	0.95 (0.81, 1.12)
SHBG (nmol/L)	0.88 (0.72, 1.08)	1.00 (0.81, 1.24)	1.10 (0.88, 1.38)

All HF
(N events / N total= 103 / 2,834; IR = 3.3 per 1000 person-years)

	Model 1‡	Model 2§	Model 3∥
Total T (nmol/L)	**1.26 (1.00, 1.59)**	1.23 (0.98, 1.56)	1.25 (0.98, 1.60)
Bioavailable T (nmol/L)	**1.36 (1.09, 1.69)**	**1.32 (1.05, 1.65)**	**1.31 (1.04, 1.67)**
Free T (Percent)	1.23 (0.91, 1.66)	1.18 (0.87, 1.61)	1.12 (0.79, 1.58)
estradiol (nmol/L)	0.94 (0.65, 1.34)	0.92 (0.64, 1.32)	0.84 (0.60, 1.18)
DHEA (nmol/L)	0.83 (0.67, 1.03)	0.81 (0.65, 1.00)	0.84 (0.68, 1.05)
SHBG (nmol/L)	0.81 (0.60, 1.08)	0.84 (0.62, 1.14)	0.89 (0.63, 1.25)

* Abbreviations: CVD, cardiovascular disease; CHD, coronary heart disease; HF, heart failure; IR, Incidence Rates; T, Testosterone; DHEA, Dehydroepiandrosterone; SHBG, Sex Hormone Binding Globulin;

† Mortality due to non-CVD causes as competing risks. All sex-hormones are log-transformed and standardized. Hazard Ratios are associated with 1 SD increase in log sex hormones. Bolded results are statistically significant.

‡ Model 1: adjusts for age (year, continuous), race/ethnicity (white, black, Hispanic, and Chinese), study site (CA, MN, NY, IL, NC, and MD), and use of hormone therapy (yes, no).

§ Model 2: model 1 + education (<high school, high school, >high school), waist to hip ratio (continuous), physical activity, and smoking (never, former, current).

∥ Model 3: model 2 + systolic blood pressure (mmHg, continuous), use of antihypertensive medications (yes, no), total cholesterol (mg/dl, continuous), HDL-cholesterol (mg/dl, continuous), use of lipid lowering medications (yes, no), diabetes (yes, no), eGFR (mL/min/1.73 m2), CRP (mg/l, log-transformed continuous), IL6 (pg/ml, log-transformed, continuous), fibrinogen (mg/dl, log-transformed continuous), D-dimer (ug/ml, log-transformed continuous).