

**Supplementary Table 1.** Distributions of Examined Variables Among Controls by Study.

Variable	PLCO (n=101)	ATBC (n=124)	CPSII (n=34)	P-value*
Mean age at baseline, y (SD)	63.0 (4.6)	58.0 (5.0)	71.0 (5.5)	<0.001
Caucasian race, n (%)	98 (97.0)	124 (100.0)	34 (100.0)	0.09
Mean body mass index (kg/m <sup>2</sup> ), n (%)				
18.5–<25	22 (21.8)	63 (50.8)	10 (29.4)	
25–<30	54 (53.5)	51 (41.1)	18 (52.9)	
≥30	23 (22.8)	10 (8.1)	4 (11.8)	
Missing	2 (2.0)	0	2 (5.9)	<0.001
Smoking Status, n (%)				
Never	44 (43.6)	0	10 (29.4)	
Current	8 (7.9)	124 (100.0)	2 (5.9)	
Former	49 (48.5)	0	22 (64.7)	<0.0001
Cigarettes/day, n (SD)	25.0 (12.8)	20.0 (9.0)	15.0 (7.1)	0.54
History of diabetes, n (%)	5 (5.0)	7 (5.6)	8 (23.5)	<0.001
Education, n (%)				
Less than high school	8 (7.9)	36 (29.0)	1 (2.9)	
High school or GED	17 (16.8)	0	3 (8.8)	
Some college/technical	36 (35.6)	82 (66.1)	10 (29.4)	
College graduate	40 (39.6)	6 (4.8)	19 (55.9)	
Missing	0	0	1 (2.9)	<0.001
Hormone Concentrations, age-adjusted mean (95% CI) <sup>†</sup>				
DHEA (nmol/L)	5.49 (3.87–7.79)	11.05 (7.59–16.11)	2.44 (1.60–3.70)	<0.001
Androstenedione (nmol/L)	2.73 (2.46–3.03)	4.70 (4.20–5.25)	1.93 (1.71–2.18)	<0.001
Testosterone (nmol/L)	14.49 (14.18–14.81)	20.32 (19.85–20.80)	10.69 (10.41–10.97)	<0.001
DHT (pmol/L)	1070.43 (972.87–1177.76)	1502.83 (1355.76–1665.86)	799.54 (712.94–896.65)	<0.001
Estrone (pmol/L)	124.15 (114.12–135.05)	137.34 (125.43–150.39)	80.83 (73.07–89.42)	<0.001
Estradiol (pmol/L)	89.15 (84.41–94.15)	81.22 (76.58–86.14)	62.81 (58.83–67.06)	<0.001
SHBG (nmol/L)	46.96 (39.93–55.24)	66.94 (56.20–79.74)	47.29 (38.92–57.46)	<0.001
Parent estrogens (pmol/L)	216.18 (202.08–231.27)	220.65 (205.18–237.29)	147.41 (135.95–159.83)	<0.001
Testosterone: Parent estrogens ratio	66.87 (62.64–71.38)	92.08 (85.82–98.79)	85.73 (79.27–92.72)	<0.001
Androstenedione: Estrone ratio	21.94 (18.07–26.64)	34.21 (27.75–42.18)	25.02 (19.82–31.59)	<0.001
Testosterone: Estradiol ratio	162.16 (154.49–170.20)	250.15 (237.43–263.55)	192.33 (181.48–203.84)	<0.001
Free testosterone (nmol/L)	0.23 (0.20–0.27)	0.26 (0.23–0.30)	0.17 (0.14–0.20)	<0.001
Free DHT (pmol/L)	19.25 (18.57–19.96)	21.77 (20.93–22.63)	13.88 (13.29–14.50)	<0.001
Free estradiol (pmol/L)	2.08 (2.07–2.09)	1.65 (1.64–1.65)	1.47 (1.46–1.48)	<0.001

\*Calculated using the Kruskal Wallis test, Chi-Square/Fishers Exact test, and ANOVA test, as applicable. All p-values are from two-sided statistical tests. PLCO: Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial; ATBC: Alpha-Tocopherol, Beta-Carotene (ATBC) Cancer Prevention Study; CPSII: Cancer Prevention Study II Nutrition Cohort; DHEA: dehydroepiandrosterone; DHT: dihydrotestosterone; SHBG: sex hormone binding globulin.

<sup>†</sup>Standardized to 61 years, mean age among controls.

**Supplementary Table 2.** Adjusted\* odds ratios and 95% confidence intervals for associations between study-specific quartiles of circulating sex steroid hormone concentrations and esophageal and gastric cardia adenocarcinoma risk.

Hormone	Control (n)	Case (n)	OR	95% CI	P-value
DHEA, nmol/L					
Quartile 1	63	98	Referent		
Quartile 2	63	64	0.68	(0.40, 1.15)	
Quartile 3	61	49	0.50	(0.29, 0.88)	
Quartile 4	63	39	0.38	(0.21, 0.70)	
Continuous†	250	250	0.73	(0.60, 0.88)	0.001
Androstenedione, nmol/L					
Quartile 1	65	93	Referent		
Quartile 2	61	56	0.71	(0.42, 1.21)	
Quartile 3	62	50	0.63	(0.35, 1.11)	
Quartile 4	63	52	0.63	(0.36, 1.10)	
Continuous†	251	251	0.86	(0.72, 1.03)	0.09
Testosterone, nmol/L					
Quartile 1	64	84	Referent		
Quartile 2	63	63	0.95	(0.56, 1.60)	
Quartile 3	61	56	0.85	(0.49, 1.47)	
Quartile 4	63	48	0.76	(0.44, 1.29)	
Continuous†	251	251	0.91	(0.77, 1.08)	0.28
DHT, pmol/L					
Quartile 1	63	84	Referent		
Quartile 2	61	60	0.93	(0.54, 1.59)	
Quartile 3	62	52	0.85	(0.49, 1.48)	
Quartile 4	63	53	0.82	(0.47, 1.44)	
Continuous†	249	249	0.94	(0.78, 1.12)	0.46
Estrone, pmol/L					
Quartile 1	61	72	Referent		
Quartile 2	61	63	0.75	(0.44, 1.28)	
Quartile 3	63	50	0.61	(0.33, 1.11)	
Quartile 4	62	62	0.67	(0.39, 1.16)	
Continuous†	247	247	0.87	(0.73, 1.04)	0.13
Estradiol, pmol/L					
Quartile 1	61	78	Referent		
Quartile 2	63	64	0.85	(0.49, 1.47)	
Quartile 3	62	53	0.64	(0.37, 1.11)	
Quartile 4	65	56	0.62	(0.35, 1.09)	
Continuous†	251	251	0.84	(0.71, 1.00)	0.05
SHBG, nmol/L					
Quartile 1	64	79	Referent		
Quartile 2	63	47	0.57	(0.32, 1.04)	
Quartile 3	62	69	1.02	(0.62, 1.70)	
Quartile 4	64	58	0.85	(0.47, 1.53)	
Continuous†	253	253	1.00	(0.83, 1.20)	0.97
Parent estrogens, pmol/L					
Quartile 1	62	73	Referent		
Quartile 2	59	73	0.99	(0.58, 1.68)	
Quartile 3	64	34	0.36	(0.19, 0.69)	

Quartile 4	62	67	0.75	(0.43, 1.30)	
Continuous†	247	247	0.86	(0.72, 1.02)	0.09
Testosterone: Parent estrogens ratio					
Quartile 1	63	63	Referent		
Quartile 2	61	71	1.39	(0.83, 2.33)	
Quartile 3	61	55	1.13	(0.63, 2.01)	
Quartile 4	60	56	1.35	(0.75, 2.43)	
Continuous†	245	245	1.07	(0.89, 1.29)	0.45
Androstenedione: Estrone ratio					
Quartile 1	61	55	Referent		
Quartile 2	63	86	1.86	(1.08, 3.20)	
Quartile 3	60	60	1.32	(0.75, 2.32)	
Quartile 4	62	45	1.00	(0.53, 1.90)	
Continuous†	246	246	0.96	(0.79, 1.17)	0.71
Testosterone: Estradiol ratio					
Quartile 1	64	61	Referent		
Quartile 2	63	79	1.54	(0.90, 2.62)	
Quartile 3	61	63	1.41	(0.80, 2.49)	
Quartile 4	61	46	1.01	(0.54, 1.87)	
Continuous†	249	249	1.00	(0.82, 1.21)	0.99
Free testosterone, nmol/L					
Quartile 1	66	84	Referent		
Quartile 2	61	58	0.79	(0.47, 1.32)	
Quartile 3	62	67	1.04	(0.61, 1.76)	
Quartile 4	62	42	0.60	(0.34, 1.07)	
Continuous†	251	251	0.89	(0.75, 1.06)	0.21
Free DHT, pmol/L					
Quartile 1	64	87	Referent		
Quartile 2	59	53	0.72	(0.42, 1.25)	
Quartile 3	63	47	0.65	(0.38, 1.11)	
Quartile 4	63	62	0.92	(0.54, 1.56)	
Continuous†	249	249	0.96	(0.81, 1.14)	0.64
Free estradiol, pmol/L					
Quartile 1	62	82	Referent		
Quartile 2	61	57	0.62	(0.35, 1.08)	
Quartile 3	64	61	0.61	(0.35, 1.07)	
Quartile 4	64	51	0.45	(0.25, 0.81)	
Continuous†	251	251	0.79	(0.65, 0.95)	0.01

\*Conditional logistic regression models were conditioned on matching factors (study, age, race/ethnicity, year of blood draw, and time of blood draw) and adjusted for age (continuous), education (less than high school, high school/GED, some college/technical, college graduate), smoking status (never, current, former), number of cigarettes per day (continuous), body mass index (BMI, 18.5–25.0, 25.0–29.9, ≥30.0 kg/m<sup>2</sup>), and diabetes (yes, no). OR: odds ratio; CI: confidence interval; DHEA: dehydroepiandrosterone; DHT: dihydrotestosterone; SHBG: sex hormone binding globulin.

†Tests of linear trend were performed based on the quartile-specific score of the hormone concentrations. All p-values are from two-sided statistical tests.

**Supplementary Table 3.** Minimally adjusted\* odds ratios and 95% confidence intervals for associations between circulating sex steroid hormone concentrations and esophageal and gastric cardia adenocarcinoma risk.

Hormone	Control (n)	Case (n)	OR	95% CI
DHEA, nmol/L				
<4.02	63	84	Referent	
4.02 to < 7.36	65	73	0.67	(0.40, 1.12)
7.36 to < 12.26	65	59	0.41	(0.22, 0.77)
≥12.26	63	40	0.25	(0.12, 0.52)
P-trend†				<0.001
Continuous (log <sub>2</sub> ), per unit	256	256	0.61	(0.48, 0.78)
Androstenedione, nmol/L				
<2.40	65	78	Referent	
2.40 to < 3.32	63	42	0.52	(0.30, 0.91)
3.32 to < 5.09	64	84	1.00	(0.56, 1.77)
≥5.09	65	53	0.59	(0.31, 1.14)
P-trend†				0.69
Continuous (log <sub>2</sub> ), per unit	257	257	0.76	(0.54, 1.06)
Testosterone, nmol/L				
<12.65	65	80	Referent	
12.65 to < 16.70	64	60	0.74	(0.46, 1.20)
16.70 to < 23.11	64	70	0.84	(0.51, 1.39)
≥23.11	64	47	0.52	(0.29, 0.92)
P-trend†				0.05
Continuous (log <sub>2</sub> ), per unit	257	257	0.86	(0.68, 1.09)
DHT, pmol/L				
<923.19	65	80	Referent	
923.19 to < 1290.17	63	70	0.88	(0.55, 1.41)
1290.17 to < 1743.03	63	47	0.52	(0.30, 0.91)
≥1743.03	64	58	0.63	(0.37, 1.10)
P-trend†				0.05
Continuous (log <sub>2</sub> ), per unit	255	255	0.83	(0.65, 1.06)
Estrone, pmol/L				
<98.37	63	73	Referent	
98.37 to < 124.80	62	63	0.85	(0.50, 1.44)
124.80 to < 158.98	65	52	0.66	(0.39, 1.13)
≥158.98	63	65	0.84	(0.49, 1.44)
P-trend†				0.45
Continuous (log <sub>2</sub> ), per unit	253	253	0.91	(0.65, 1.27)
Estradiol, pmol/L				
<63.87	64	74	Referent	
63.87 to < 80.90	65	66	0.85	(0.50, 1.43)
80.90 to < 103.15	63	68	0.91	(0.54, 1.52)
≥103.15	65	49	0.63	(0.37, 1.07)
P-trend†				0.14

Continuous (log <sub>2</sub> ), per unit	257	257	0.70	(0.49, 1.00)
SHBG, nmol/L				
<40.93	64	74	Referent	
40.93 to < 57.92	65	66	1.08	(0.66, 1.76)
57.92 to < 73.87	63	68	0.57	(0.32, 1.01)
≥73.87	65	49	0.96	(0.55, 1.65)
P-trend†				0.45
Continuous (log <sub>2</sub> ), per unit	257	257	0.83	(0.62, 1.11)
Parent estrogens, pmol/L				
<168.83	62	73	Referent	
168.83 to < 208.17	65	71	0.93	(0.54, 1.59)
208.17 to < 259.10	63	46	0.59	(0.34, 1.02)
≥259.10	63	63	0.80	(0.47, 1.37)
P-trend†				0.24
Continuous (log <sub>2</sub> ), per unit	253	253	0.80	(0.55, 1.15)
Testosterone: Parent estrogens ratio				
<58.40	64	58	Referent	
58.40 to < 85.33	62	86	1.54	(0.93, 2.57)
85.33 to < 115.56	63	61	1.03	(0.62, 1.72)
≥115.56	62	46	0.77	(0.43, 1.38)
P-trend†				0.17
Continuous (log <sub>2</sub> ), per unit	251	251	0.90	(0.70, 1.15)
Androstenedione: Estrone ratio				
<20.62	61	65	Referent	
20.62 to < 27.32	64	59	0.85	(0.51, 1.44)
27.32 to < 38.10	64	68	0.98	(0.57, 1.71)
≥38.10	63	60	0.88	(0.50, 1.56)
P-trend†				0.78
Continuous (log <sub>2</sub> ), per unit	252	252	0.86	(0.64, 1.16)
Testosterone: Estradiol ratio				
<153.02	65	63	Referent	
153.02 to < 204.60	64	65	1.01	(0.61, 1.67)
204.60 to < 289.04	62	81	1.26	(0.77, 2.06)
≥289.04	64	46	0.70	(0.39, 1.26)
P-trend†				0.45
Continuous (log <sub>2</sub> ), per unit	255	255	0.97	(0.74, 1.27)
Free testosterone, nmol/L				
<0.20	64	81	Referent	
0.20 to < to 0.24	66	66	0.76	(0.47, 1.24)
0.24 to < 0.30	63	60	0.71	(0.43, 1.17)
≥0.30	64	50	0.56	(0.32, 0.97)
P-trend†				0.04
Continuous (log <sub>2</sub> ), per unit	257	257	0.89	(0.68, 1.17)
Free DHT, pmol/L				

<16.12	65	88	Referent	
16.12 to < 20.37	63	49	0.54	(0.33, 0.91)
20.37 to < 25.53	63	50	0.52	(0.30, 0.90)
≥25.53	64	68	0.76	(0.46, 1.26)
P-trend†				0.30
Continuous (log <sub>2</sub> ), per unit	255	255	0.94	(0.74, 1.19)
Free estradiol, pmol/L				
<1.43	65	67	Referent	
1.43 to < 1.74	63	72	1.10	(0.66, 1.84)
1.74 to < 2.23	64	71	1.06	(0.64, 1.75)
≥2.23	65	47	0.69	(0.40, 1.19)
P-trend†				0.14
Continuous (log <sub>2</sub> ), per unit	257	257	0.76	(0.53, 1.09)

\*Conditional logistic regression models were conditioned on matching factors (study, age, race/ethnicity, year of blood draw, and time of blood draw). OR: odds ratio; CI: confidence interval; DHEA: dehydroepiandrosterone; DHT: dihydrotestosterone; SHBG: sex hormone binding globulin.

†Tests of linear trend were performed based on the quartile-specific medians of the hormone concentrations. All p-values are from two-sided statistical tests.

**Supplementary Table 4.** Adjusted\* odds ratios and 95% confidence intervals for associations between circulating sex steroid hormone concentrations and esophageal and gastric cardia adenocarcinoma risk, stratified by time between blood draw and cancer diagnosis.

Hormone	<8.42 Years				≥8.42 Years			
	Control (n)	Case (n)	OR	95% CI	Control (n)	Case (n)	OR	95% CI
DHEA, nmol/L								
<4.02	41	48	Referent		19	31	Referent	
4.02 to < 7.36	28	34	0.89	(0.39, 2.00)	35	39	0.76	(0.31, 1.84)
7.36 to < 12.26	24	24	0.71	(0.26, 1.92)	40	34	0.39	(0.14, 1.10)
≥12.26	24	11	0.32	(0.09, 1.09)	39	29	0.27	(0.08, 0.86)
P-trend†				0.07				0.02
Continuous (log <sub>2</sub> )	117	117	0.78	(0.53, 1.15)	133	133	0.51	(0.33, 0.79)
Androstenedione, nmol/L								
<2.40	36	43	Referent		26	30	Referent	
2.40 to < 3.32	33	22	0.55	(0.23, 1.36)	27	20	0.53	(0.20, 1.42)
3.32 to < 5.09	26	34	1.21	(0.43, 3.38)	38	49	1.20	(0.47, 3.07)
≥5.09	24	20	0.73	(0.24, 2.19)	41	33	0.78	(0.27, 2.29)
P-trend†				0.79				0.82
Continuous (log <sub>2</sub> )	119	119	0.94	(0.56, 1.57)	132	132	0.84	(0.45, 1.54)
Testosterone, nmol/L								
<12.65	31	46	Referent		31	32	Referent	
12.65 to < 16.70	35	23	0.35	(0.14, 0.84)	27	35	1.65	(0.73, 3.75)
16.70 to < 23.11	30	31	0.69	(0.31, 1.57)	33	37	1.97	(0.80, 4.89)
≥23.11	22	18	0.43	(0.16, 1.15)	42	29	1.15	(0.43, 3.08)
P-trend†				0.26				0.95
Continuous (log <sub>2</sub> )	118	118	0.91	(0.64, 1.27)	133	133	1.05	(0.70, 1.57)
DHT, pmol/L								
<923.19	32	43	Referent		30	35	Referent	
923.19 to < 1290.17	29	32	0.91	(0.43, 1.95)	32	35	1.72	(0.74, 4.02)
1290.17 to < 1743.03	31	22	0.48	(0.20, 1.19)	32	24	1.26	(0.46, 3.45)
≥1743.03	25	20	0.48	(0.18, 1.25)	38	38	2.01	(0.77, 5.24)
P-trend†				0.08				0.25
Continuous (log <sub>2</sub> )	117	117	0.67	(0.43, 1.04)	132	132	1.44	(0.93, 2.23)
Estrone, pmol/L								
<98.37	31	36	Referent		27	33	Referent	
98.37 to < 124.80	30	27	0.96	(0.38, 2.41)	31	35	0.75	(0.33, 1.74)
124.80 to < 158.98	28	19	0.60	(0.25, 1.43)	37	33	0.61	(0.26, 1.43)
≥158.98	25	32	0.84	(0.34, 2.06)	38	32	0.58	(0.25, 1.33)
P-trend†				0.53				0.18
Continuous (log <sub>2</sub> )	114	114	0.84	(0.46, 1.51)	133	133	0.81	(0.50, 1.34)
Estradiol, pmol/L								
<63.87	31	38	Referent		28	33	Referent	
63.87 to < 80.90	34	23	0.54	(0.21, 1.36)	31	42	1.41	(0.63, 3.17)

80.90 to < 103.15	28	31	0.76	(0.32, 1.79)	35	37	1.09	(0.48, 2.49)
≥103.15	25	26	0.54	(0.21, 1.38)	39	21	0.59	(0.26, 1.35)
P-trend†			0.40				0.10	
Continuous (log <sub>2</sub> )	118	118	0.52	(0.26, 1.05)	133	133	0.77	(0.46, 1.29)
SHBG, nmol/L								
<40.93	33	36	Referent		29	32	Referent	
40.93 to < 57.92	29	34	0.91	(0.40, 2.06)	36	42	1.16	(0.53, 2.52)
57.92 to < 73.87	26	16	0.51	(0.19, 1.35)	36	27	0.94	(0.36, 2.44)
≥73.87	32	34	0.93	(0.37, 2.37)	32	32	1.51	(0.59, 3.86)
P-trend†			0.74				0.44	
Continuous (log <sub>2</sub> )	120	120	0.68	(0.40, 1.15)	133	133	1.35	(0.82, 2.22)
Parent estrogens, pmol/L								
<168.83	29	40	Referent		28	29	Referent	
168.83 to < 208.17	34	25	0.50	(0.20, 1.25)	31	45	1.20	(0.50, 2.86)
208.17 to < 259.10	27	16	0.42	(0.17, 1.05)	35	30	0.66	(0.29, 1.52)
≥259.10	24	33	0.68	(0.27, 1.74)	39	29	0.67	(0.29, 1.53)
P-trend†			0.41				0.12	
Continuous (log <sub>2</sub> )	114	114	0.68	(0.34, 1.33)	133	133	0.79	(0.46, 1.36)
Testosterone: Parent estrogens ratio								
<58.40	27	29	Referent		37	29	Referent	
58.40 to < 85.33	33	42	1.36	(0.57, 3.23)	27	42	2.95	(1.22, 7.12)
85.33 to < 115.56	24	27	1.22	(0.52, 2.88)	36	32	2.20	(0.89, 5.45)
≥115.56	28	14	0.49	(0.17, 1.41)	33	30	2.70	(0.93, 7.83)
P-trend†			0.14				0.13	
Continuous (log <sub>2</sub> )	112	112	0.96	(0.63, 1.45)	133	133	1.17	(0.80, 1.70)
Androstenedione: Estrone ratio								
<20.62	31	37	Referent		29	27	Referent	
20.62 to < 27.32	27	27	0.90	(0.37, 2.19)	36	28	1.14	(0.45, 2.89)
27.32 to < 38.10	32	23	0.73	(0.25, 2.16)	29	45	2.84	(1.07, 7.49)
≥38.10	24	27	1.15	(0.40, 3.32)	38	32	1.69	(0.61, 4.67)
P-trend†			0.60				0.27	
Continuous (log <sub>2</sub> )	114	114	1.05	(0.62, 1.79)	132	132	1.09	(0.68, 1.74)
Testosterone: Estradiol ratio								
<153.02	32	35	Referent		33	28	Referent	
153.02 to < 204.60	28	32	0.92	(0.41, 2.10)	33	30	1.34	(0.56, 3.21)
204.60 to < 289.04	32	33	0.94	(0.39, 2.24)	28	46	2.84	(1.19, 6.81)
≥289.04	24	16	0.60	(0.20, 1.74)	39	29	1.65	(0.60, 4.57)
P-trend†			0.40				0.16	
Continuous (log <sub>2</sub> )	116	116	1.05	(0.68, 1.63)	133	133	1.35	(0.83, 2.21)
Free testosterone, nmol/L								
<0.20	32	45	Referent		30	34	Referent	
0.20 to < to 0.24	38	34	0.73	(0.34, 1.56)	27	31	1.03	(0.43, 2.44)
0.24 to < 0.30	24	24	0.69	(0.30, 1.55)	36	33	1.09	(0.49, 2.41)
≥0.30	24	15	0.43	(0.17, 1.07)	40	35	1.23	(0.51, 2.95)



P-trend†			0.08				0.62
Continuous (log <sub>2</sub> )	118	118	0.99	(0.68, 1.44)	133	133	0.91 (0.58, 1.43)
Free DHT, pmol/L							
<16.12	29	50	Referent		33	35	Referent
16.12 to < 20.37	33	24	0.47	(0.22, 1.02)	28	24	1.08 (0.41, 2.83)
20.37 to < 25.53	30	20	0.40	(0.17, 0.95)	33	29	1.30 (0.52, 3.27)
≥25.53	25	23	0.57	(0.25, 1.29)	38	44	2.30 (0.95, 5.55)
P-trend†			0.13				0.04
Continuous (log <sub>2</sub> )	117	117	0.97	(0.72, 1.32)	132	132	1.39 (0.81, 2.37)
Free estradiol, pmol/L							
<1.43	31	31	Referent		30	34	Referent
1.43 to < 1.74	33	31	0.90	(0.36, 2.25)	30	40	1.12 (0.48, 2.58)
1.74 to < 2.23	28	34	1.07	(0.43, 2.67)	35	35	0.79 (0.36, 1.73)
≥2.23	26	22	0.57	(0.21, 1.57)	38	24	0.53 (0.22, 1.25)
P-trend†			0.31				0.07
Continuous (log <sub>2</sub> )	118	118	0.63	(0.30, 1.29)	133	133	0.66 (0.38, 1.14)

\*Conditional logistic regression models were conditioned on matching factors (study, age, race/ethnicity, year of blood draw, and time of blood draw) and adjusted for age (continuous), education (less than high school, high school/GED, some college/technical, college graduate), smoking status (never, current, former), number of cigarettes per day (continuous), body mass index (BMI, 18.5–25.0, 25.0–29.9, ≥30.0 kg/m<sup>2</sup>), and diabetes (yes, no). OR: odds ratio; CI: confidence interval; DHEA: dehydroepiandrosterone; DHT: dihydrotestosterone; SHBG: sex hormone binding globulin.

†Tests of linear trend were performed based on the quartile-specific medians of the hormone concentrations. All p-values are from two-sided statistical tests.

**Supplementary Table 5.** Adjusted\* odds ratio and 95% confidence intervals for associations between circulating sex steroid hormone concentrations and esophageal and gastric cardia adenocarcinoma risk, stratified by cancer site.

Hormone	Combined EA/GCA				Esophageal Adenocarcinoma			Gastric Cardia Adenocarcinoma			Ratio of the Odds Ratios	
	Control (n)	Case (n)	OR	95% CI	Case (n)	OR	95% CI	Case (n)	OR	95% CI	ROR	95% CI
DHEA, nmol/L												
<4.02	69	83	Referent		46	Referent		37	Referent		Referent	
4.02 to < 7.36	67	73	0.95	(0.54, 1.70)	30	0.91	(0.46, 1.81)	43	0.95	(0.48, 1.90)	0.96	(0.45, 2.02)
7.36 to < 12.26	64	59	0.60	(0.30, 1.19)	18	0.73	(0.30, 1.77)	41	0.53	(0.24, 1.18)	1.39	(0.53, 3.61)
≥12.26	65	40	0.37	(0.18, 0.78)	10	0.45	(0.16, 1.26)	30	0.34	(0.14, 0.81)	1.31	(0.43, 4.01)
P-trend†				0.003			0.11			0.004		0.49
Continuous (log <sub>2</sub> )	265	255	0.68	(0.52, 0.88)	104	0.70	(0.50, 0.99)	151	0.67	(0.49, 0.90)	1.05	(0.73, 1.52)
Androstenedione, nmol/L												
<2.40	72	78	Referent		45	Referent		33	Referent		Referent	
2.40 to < 3.32	61	42	0.76	(0.42, 1.40)	19	0.67	(0.32, 1.41)	23	0.81	(0.39, 1.69)	0.83	(0.36, 1.93)
3.32 to < 5.09	65	84	1.66	(0.85, 3.25)	31	2.10	(0.92, 4.79)	53	1.44	(0.65, 3.20)	1.46	(0.59, 3.58)
≥5.09	65	53	1.19	(0.56, 2.50)	10	0.90	(0.32, 2.57)	43	1.25	(0.53, 2.95)	0.72	(0.24, 2.20)
P-trend†				0.33			0.45			0.39		0.97
Continuous (log <sub>2</sub> )	263	257	1.01	(0.69, 1.50)	105	0.98	(0.60, 1.59)	152	1.04	(0.66, 1.65)	0.94	(0.55, 1.60)
Testosterone, nmol/L												
<12.65	69	80	Referent		43	Referent		37	Referent		Referent	
12.65 to < 16.70	65	59	0.92	(0.53, 1.61)	26	1.04	(0.52, 2.09)	33	0.86	(0.44, 1.68)	1.20	(0.56, 2.60)
16.70 to < 23.11	64	70	1.11	(0.63, 1.95)	26	1.18	(0.58, 2.41)	44	1.10	(0.57, 2.12)	1.08	(0.50, 2.32)
≥23.11	66	47	0.75	(0.40, 1.40)	10	0.53	(0.21, 1.31)	37	0.86	(0.42, 1.76)	0.62	(0.23, 1.64)
P-trend†				0.47			0.30			0.84		0.42
Continuous (log <sub>2</sub> )	264	256	0.92	(0.71, 1.20)	105	1.03	(0.73, 1.47)	151	0.86	(0.63, 1.16)	1.21	(0.83, 1.76)
DHT, pmol/L												
<923.19	70	79	Referent		46	Referent		33	Referent		Referent	
923.19 to < 1290.17	64	70	1.30	(0.74, 2.27)	35	1.42	(0.73, 2.78)	35	1.28	(0.65, 2.51)	1.11	(0.53, 2.34)
1290.17 to < 1743.03	64	48	0.80	(0.44, 1.45)	12	0.44	(0.19, 1.02)	36	1.19	(0.60, 2.37)	0.37	(0.15, 0.92)

≥1743.03	65	58	1.00	(0.54, 1.85)	12	0.58	(0.24, 1.38)	46	1.43	(0.71, 2.89)	0.40	(0.16, 1.02)
P-trend†			0.62			0.05			0.39		0.01	
Continuous (log <sub>2</sub> )	263	255	0.98	(0.74, 1.29)	105	0.86	(0.60, 1.22)	150	1.12	(0.80, 1.56)	0.76	(0.51, 1.14)
Estrone, pmol/L												
<98.37	68	73	Referent		38	Referent		35	Referent		Referent	
98.37 to < 124.80	63	65	0.80	(0.46, 1.40)	24	0.66	(0.32, 1.36)	41	0.90	(0.48, 1.71)	0.73	(0.34, 1.57)
124.80 to < 158.98	66	52	0.69	(0.39, 1.21)	24	0.85	(0.42, 1.74)	28	0.60	(0.31, 1.19)	1.42	(0.64, 3.15)
≥158.98	63	65	0.82	(0.47, 1.44)	17	0.56	(0.26, 1.21)	48	0.97	(0.51, 1.83)	0.58	(0.26, 1.30)
P-trend†			0.46			0.24			0.80		0.36	
Continuous (log <sub>2</sub> )	260	255	0.91	(0.64, 1.30)	103	0.88	(0.56, 1.39)	152	0.93	(0.62, 1.40)	0.94	(0.58, 1.54)
Estradiol, pmol/L												
<63.87	65	73	Referent		29	Referent		44	Referent		Referent	
63.87 to < 80.90	67	67	0.96	(0.57, 1.62)	29	1.23	(0.62, 2.47)	38	0.83	(0.45, 1.51)	1.49	(0.71, 3.13)
80.90 to < 103.15	65	69	1.08	(0.64, 1.82)	21	0.94	(0.45, 1.95)	48	1.11	(0.62, 1.99)	0.84	(0.39, 1.81)
≥103.15	65	49	0.74	(0.42, 1.30)	26	1.18	(0.57, 2.44)	23	0.52	(0.27, 1.02)	2.25	(1.00, 5.07)
P-trend†			0.45			0.89			0.20		0.25	
Continuous (log <sub>2</sub> )	262	258	0.80	(0.54, 1.18)	105	0.95	(0.57, 1.58)	153	0.71	(0.46, 1.11)	1.33	(0.77, 2.30)
SHBG, nmol/L												
<40.93	66	70	Referent		35	Referent		35	Referent		Referent	
40.93 to < 57.92	68	77	1.16	(0.68, 1.97)	40	1.66	(0.86, 3.19)	37	0.88	(0.46, 1.66)	1.90	(0.92, 3.91)
57.92 to < 73.87	66	44	0.75	(0.42, 1.34)	13	0.60	(0.27, 1.37)	31	0.83	(0.43, 1.64)	0.72	(0.30, 1.76)
≥73.87	65	67	1.21	(0.67, 2.16)	17	0.91	(0.41, 2.01)	50	1.38	(0.71, 2.70)	0.66	(0.29, 1.52)
P-trend†			0.76			0.37			0.24		0.08	
Continuous (log <sub>2</sub> )	265	258	0.99	(0.72, 1.36)	105	0.94	(0.62, 1.41)	153	1.05	(0.72, 1.53)	0.89	(0.57, 1.40)
Parent estrogens, pmol/L												
<168.83	66	72	Referent		33	Referent		39	Referent		Referent	
168.83 to < 208.17	66	74	0.95	(0.55, 1.61)	31	1.06	(0.53, 2.11)	43	0.89	(0.48, 1.64)	1.19	(0.57, 2.48)
208.17 to < 259.10	65	46	0.61	(0.35, 1.08)	17	0.63	(0.29, 1.34)	29	0.59	(0.31, 1.13)	1.07	(0.46, 2.45)
≥259.10	63	63	0.83	(0.47, 1.46)	22	0.86	(0.40, 1.83)	41	0.80	(0.43, 1.51)	1.07	(0.49, 2.36)
P-trend†			0.27			0.41			0.31		0.99	
Continuous (log <sub>2</sub> )	260	255	0.85	(0.57, 1.27)	103	0.88	(0.52, 1.48)	152	0.83	(0.52, 1.31)	1.06	(0.61, 1.85)
Testosterone: Parent estrogens ratio												
<58.40	67	59	Referent		29	Referent		30	Referent		Referent	

58.40 to < 85.33	65	87	1.83	(1.05, 3.18)	35	1.53	(0.75, 3.11)	52	2.05	(1.08, 3.89)	0.74	(0.35, 1.58)
85.33 to < 115.56	63	61	1.40	(0.79, 2.48)	25	1.50	(0.71, 3.19)	36	1.36	(0.69, 2.66)	1.11	(0.48, 2.55)
≥115.56	65	46	1.12	(0.60, 2.11)	14	0.94	(0.39, 2.25)	32	1.26	(0.62, 2.60)	0.74	(0.29, 1.92)
P-trend†			0.88			0.88			0.97		0.91	
Continuous (log <sub>2</sub> )	260	253	0.97	(0.73, 1.27)	103	1.04	(0.73, 1.47)	150	0.92	(0.67, 1.26)	1.13	(0.78, 1.62)
Androstenedione: Estrone ratio												
<20.62	64	66	Referent		35	Referent		31	Referent		Referent	
20.62 to < 27.32	69	59	1.25	(0.71, 2.20)	23	1.15	(0.56, 2.38)	36	1.30	(0.66, 2.54)	0.89	(0.40, 1.97)
27.32 to < 38.10	65	69	1.59	(0.87, 2.89)	28	1.85	(0.87, 3.95)	41	1.44	(0.71, 2.91)	1.29	(0.56, 2.94)
≥38.10	62	60	1.50	(0.78, 2.88)	17	1.38	(0.58, 3.32)	43	1.56	(0.74, 3.27)	0.89	(0.35, 2.25)
P-trend†			0.22			0.34			0.28		0.97	
Continuous (log <sub>2</sub> )	260	254	1.09	(0.78, 1.52)	103	1.05	(0.69, 1.61)	151	1.11	(0.75, 1.63)	0.95	(0.60, 1.50)
Testosterone: Estradiol ratio												
<153.02	69	63	Referent		34	Referent		29	Referent		Referent	
153.02 to < 204.60	64	65	1.14	(0.65, 2.01)	31	1.21	(0.60, 2.46)	34	1.13	(0.57, 2.23)	1.07	(0.49, 2.36)
204.60 to < 289.04	64	82	1.59	(0.90, 2.81)	26	1.39	(0.66, 2.92)	56	1.77	(0.91, 3.43)	0.79	(0.35, 1.76)
≥289.04	65	46	0.96	(0.50, 1.85)	14	0.94	(0.38, 2.31)	32	1.02	(0.48, 2.18)	0.92	(0.35, 2.44)
P-trend†			0.81			1.00			0.66		0.73	
Continuous (log <sub>2</sub> )	262	256	1.03	(0.74, 1.44)	105	1.08	(0.71, 1.63)	151	1.02	(0.70, 1.50)	1.05	(0.69, 1.61)
Free testosterone, nmol/L												
<0.20	70	81	Referent		41	Referent		40	Referent		Referent	
0.20 to < to 0.24	66	65	0.95	(0.55, 1.64)	24	0.83	(0.42, 1.67)	41	1.03	(0.55, 1.92)	0.81	(0.39, 1.71)
0.24 to < 0.30	63	60	0.91	(0.52, 1.58)	26	1.06	(0.52, 2.15)	34	0.81	(0.42, 1.56)	1.31	(0.60, 2.85)
≥0.30	65	50	0.74	(0.41, 1.34)	14	0.70	(0.31, 1.59)	36	0.76	(0.39, 1.49)	0.92	(0.38, 2.24)
P-trend†			0.32			0.58			0.31		0.78	
Continuous (log <sub>2</sub> )	264	256	0.90	(0.68, 1.19)	105	1.13	(0.73, 1.74)	151	0.78	(0.56, 1.07)	1.45	(0.92, 2.30)
Free DHT, pmol/L												
<16.12	70	88	Referent		46	Referent		42	Referent		Referent	
16.12 to < 20.37	64	49	0.72	(0.41, 1.26)	21	0.70	(0.35, 1.43)	28	0.77	(0.40, 1.48)	0.92	(0.42, 2.01)
20.37 to < 25.53	65	50	0.73	(0.42, 1.28)	23	0.94	(0.46, 1.92)	27	0.64	(0.33, 1.25)	1.46	(0.65, 3.27)
≥25.53	64	68	0.97	(0.55, 1.70)	15	0.60	(0.27, 1.34)	53	1.20	(0.63, 2.26)	0.50	(0.22, 1.16)
P-trend†			0.98			0.39			0.52		0.19	
Continuous (log <sub>2</sub> )	263	255	0.96	(0.72, 1.29)	105	0.98	(0.70, 1.38)	150	0.96	(0.69, 1.34)	1.02	(0.74, 1.40)

Free estradiol, pmol/L

<1.43	67	68	Referent		22	Referent		46	Referent		Referent	
1.43 to < 1.74	66	72	1.01	(0.60, 1.69)	30	1.36	(0.66, 2.80)	42	0.85	(0.47, 1.52)	1.61	(0.75, 3.44)
1.74 to < 2.23	64	71	0.97	(0.57, 1.64)	25	1.02	(0.48, 2.18)	46	0.94	(0.52, 1.68)	1.09	(0.50, 2.40)
≥2.23	65	47	0.69	(0.38, 1.25)	28	1.30	(0.59, 2.87)	19	0.42	(0.21, 0.86)	3.08	(1.27, 7.45)
P-trend†				0.23			0.69			0.04		0.04
Continuous (log <sub>2</sub> )	262	258	0.79	(0.53, 1.17)	105	1.03	(0.60, 1.78)	153	0.66	(0.42, 1.03)	1.58	(0.88, 2.81)

\*Unconditional logistic regression models were adjusted for age (continuous), race/ethnicity (white, other), study year of blood draw (continuous), parent study (PLCO, ATBC, CPSII), education (less than high school, high school/GED, some college/technical, college graduate), smoking status (never, current, former), number of cigarettes per day (continuous), body mass index (BMI, 18.5–25.0, 25.0–29.9, ≥30.0 kg/m<sup>2</sup>), and diabetes (yes, no). EA: esophageal adenocarcinoma; GCA: gastric cardia adenocarcinoma; OR: odds ratio; CI: confidence interval; DHEA: dehydroepiandrosterone; DHT: dihydrotestosterone; SHBG: sex hormone binding globulin.

†Tests of linear trend were performed based on the quartile-specific medians of the hormone concentrations. All p-values are from two-sided statistical tests.