Further detail on the androgen/androgen metabolite measurement

We used stable isotope dilution high performance LC-MS/MS to quantify the androgens and androgen metabolites, as described in Trabert et al. (reference 12 in the manuscript). For the present analyses, we performed the LC-MS/MS analysis with updated instrumentation, a Thermo TSQ™ Quantiva triple quadrupole mass spectrometer (Thermo Fisher, San Jose, CA) coupled with a NexeraXR LC system (Shimadzu Scientific Instruments, Columbia, MD). Both the chromotographer and mass spectrometer were controlled by Xcalibur™ software (Thermo Fisher, San Jose, CA). Nine stable isotope labeled unconjugated and conjugated androgens were used to account for losses during sample preparation and analysis: dehydroepiandrosterone-2,2,3,4,4-d_5, dehydroepiandrosterone sulfate-2,2,3,4,4-d_5, androstenedione-2,3,4-$^{13}C_3$, testosterone-2,3,4-$^{13}C_3$, dihydrotestosterone-16,16,17-d_3, and dihydrotestosterone sulfate-16,16,17-d_3, androsterone-2,2,4,4-d_4, androsterone glucuronide-2,2,4,4-d_4, obtained from Cerilliant Corporation (Round Rock, TX); and 5α-androstane-3α,17β-diol-17-glucuronide-16,16,17-d_3, purchased from 13C Molecular, Inc. (Fayetteville, NC).

The limits of quantitation for the unconjugated androgens and conjugated androgens were: 0.01 ng/mL for androstenedione and testosterone; 0.05 ng/mL for DHEA, DHT, and ADT; 0.1 ng/mL for 5α-androstanedione; 0.05 ng/mL for DHEAS and DHTS; 0.1 ng/mL for 3α-diol-3G, 3α-diol-17G, ADT-G, and Etio-G. There were no samples in this study with undetectable levels for any of the hormones measured. Laboratory coefficients of variation of blinded duplicate samples within and across batches were <11.0% for all hormones measured. Intraclass correlation coefficients ranged from 0.77-0.997 with a mean of 0.94 (median 0.99).

Supplemental Table 1. Odds ratios (OR) for endometrial cancer across quintiles (Q1-Q5) of circulating androgen/androgen metabolites

		Overall Models			
		Cases n=313	Controls n=354	Model 1*	Model 2†
Hormone/Metabolite	Median Concentration within quintile (nmol/L)	n(%)	n(%)	OR (95% CI)	OR (95% CI)
Parent Androgens					
DHEA					
Q1	2.1	47 (15.0)	70 (19.8)	Reference	Reference
Q2	3.6	58 (18.5)	70 (19.8)	1.44 (0.83 to 2.50)	1.36 (0.78 to 2.38)
Q3	5.0	68 (21.7)	71 (20.1)	1.58 (0.92 to 2.73)	1.54 (0.89 to 2.68)
Q4	6.8	61 (19.5)	70 (19.8)	1.42 (0.81 to 2.50)	1.37 (0.78 to 2.43)
Q5	10.7	74 (23.6)	71 (20.1)	1.85 (1.06 to 3.25)	1.67 (0.94 to 2.96)
P trend‡				0.07	0.15
DHEAS					
Q1	422.3	51 (16.3)	70 (19.8)	Reference	Reference
Q2	764.2	57 (18.2)	70 (19.8)	1.02 (0.59 to 1.78)	0.95 (0.54 to 1.67)
Q3	1156.1	69 (22.0)	71 (20.1)	1.18 (0.69 to 2.00)	1.18 (0.69 to 2.03)
Q4	1659.9	54 (17.3)	70 (19.8)	0.95 (0.54 to 1.67)	0.90 (0.51 to 1.59)
Q5	2657.9	77 (24.6)	71 (20.1)	1.31 (0.76 to 2.26)	1.20 (0.69 to 2.09)
P trend				0.36	0.53
Androstenedione§					
Q1	0.7	34 (10.9)	70 (19.8)	Reference	Reference
Q2	1.0	64 (20.4)	70 (19.8)	1.94 (1.10 to 3.41)	1.81 (1.03 to 3.20)
Q3	1.3	62 (19.8)	70 (19.8)	1.71 (0.96 to 3.06)	1.56 (0.87 to 2.81)
Q4	1.7	70 (22.4)	71 (20.1)	2.15 (1.22 to 3.78)	1.90 (1.07 to 3.36)
Q5	2.3	78 (24.9)	71 (20.1)	2.36 (1.34 to 4.16)	2.01 (1.12 to 3.60)
P trend				0.01	0.06
Testosterone					
Q1	0.3	41 (13.1)	69 (19.5)	Reference	Reference
Q2	0.4	57 (18.2)	69 (19.5)	1.33 (0.77 to 2.30)	1.30 (0.75 to 2.25)
Q3	0.6	51 (16.3)	73 (20.6)	1.03 (0.59 to 1.82)	0.96 (0.54 to 1.71)
Q4	0.7	72 (23.0)	70 (19.8)	1.84 (1.06 to 3.19)	1.66 (0.95 to 2.90)
Q5	1.0	87 (27.8)	71 (20.1)	1.91 (1.12 to 3.24)	1.55 (0.89 to 2.69)
P trend				0.01	0.08
5α Pathway					
5α-Androstanedione					
Q1	0.7	54 (17.3)	68 (19.2)	Reference	Reference
Q2	1.0	56 (17.9)	72 (20.3)	0.75 (0.44 to 1.28)	0.71 (0.42 to 1.22)
Q3	1.2	72 (23.0)	70 (19.8)	1.15 (0.68 to 1.93)	1.04 (0.62 to 1.77)
Q4	1.6	68 (21.7)	71 (20.1)	1.27 (0.75 to 2.13)	1.15 (0.68 to 1.94)
Q5	2.3	58 (18.5)	71 (20.1)	1.13 (0.66 to 1.92)	0.99 (0.57 to 1.71)
P trend				0.28	0.54
DHT					
Q1	0.1	51 (16.3)	67 (18.9)	Reference	Reference
Q2	0.2	49 (15.7)	73 (20.6)	1.03 (0.59 to 1.79)	0.96 (0.55 to 1.68)
Q3	0.2	77 (24.6)	71 (20.1)	1.68 (0.99 to 2.85)	1.54 (0.90 to 2.62)
Q4	0.2	74 (23.6)	67 (18.9)	1.58 (0.93 to 2.70)	1.36 (0.79 to 2.35)
Q5	0.3	57 (18.2)	74 (20.9)	1.04 (0.61 to 1.78)	0.94 (0.55 to 1.62)
P trend				0.74	0.93

DHTS					
Q1	0.4	51 (16.3)	69 (19.5)	Reference	Reference
Q2	0.8	67 (21.4)	71 (20.1)	1.12 (0.66 to 1.90)	1.05 (0.61 to 1.79)
Q3	1.1	61 (19.5)	70 (19.8)	1.25 (0.73 to 2.14)	1.23 (0.71 to 2.11)
Q4	1.6	54 (17.3)	70 (19.8)	0.99 (0.57 to 1.73)	0.96 (0.55 to 1.68)
Q5	2.2	75 (24.0)	72 (20.3)	1.27 (0.75 to 2.17)	1.18 (0.69 to 2.02)
P trend				0.51	0.68
ADT					
Q1	0.4	58 (18.5)	68 (19.2)	Reference	Reference
Q2	0.4	49 (15.7)	72 (20.3)	0.62 (0.36 to 1.07)	0.63 (0.36 to 1.08)
Q3	0.5	60 (19.2)	68 (19.2)	0.85 (0.50 to 1.44)	0.87 (0.51 to 1.49)
Q4	0.6	76 (24.3)	73 (20.6)	1.12 (0.67 to 1.88)	1.04 (0.62 to 1.76)
Q5	0.9	65 (20.8)	71 (20.1)	0.93 (0.55 to 1.57)	0.89 (0.52 to 1.52)
P trend				0.48	0.67
ADT-G					
Q1	6.9	36 (11.5)	70 (19.8)	Reference	Reference
Q2	12.8	71 (22.7)	70 (19.8)	1.97 (1.12 to 3.46)	1.94 (1.10 to 3.42)
Q3	19.7	50 (16.0)	71 (20.1)	1.31 (0.73 to 2.37)	1.17 (0.64 to 2.13)
Q4	30.5	86 (27.5)	70 (19.8)	2.11 (1.20 to 3.71)	1.91 (1.08 to 3.39)
Q5	53.0	65 (20.8)	71 (20.1)	1.34 (0.75 to 2.39)	1.19 (0.66 to 2.15)
P trend				0.88	0.80
3α-diol-3G					
Q1	0.5	31 (9.9)	70 (19.8)	Reference	Reference
Q2	1.0	60 (19.2)	70 (19.8)	1.71 (0.96 to 3.05)	1.54 (0.86 to 2.76)
Q3	1.4	87 (27.8)	71 (20.1)	2.48 (1.42 to 4.34)	2.34 (1.33 to 4.11)
Q4	2.1	58 (18.5)	70 (19.8)	1.52 (0.84 to 2.74)	1.37 (0.76 to 2.49)
Q5	3.7	72 (23.0)	71 (20.1)	1.62 (0.91 to 2.91)	1.42 (0.78 to 2.56)
P trend				0.77	0.93
3α-diol-17G					
Q1	0.5	45 (14.4)	69 (19.5)	Reference	Reference
Q2	0.8	63 (20.1)	71 (20.1)	1.29 (0.75 to 2.25)	1.27 (0.73 to 2.22)
Q3	1.2	68 (21.7)	71 (20.1)	1.07 (0.62 to 1.83)	1.02 (0.59 to 1.77)
Q4	1.8	57 (18.2)	70 (19.8)	0.89 (0.51 to 1.56)	0.84 (0.47 to 1.48)
Q5	3.0	75 (24.0)	71 (20.1)	1.13 (0.65 to 1.98)	1.04 (0.58 to 1.84)
P trend				0.93	0.67
Marker of Androgenic Activity (ADT-G + 3α-diol-3G + 3α-diol-17G)					
Q1	8.3	33 (10.5)	70 (19.8)	Reference	Reference
Q2	14.9	76 (24.3)	70 (19.8)	2.22 (1.26 to 3.93)	2.13 (1.20 to 3.77)
Q3	23.0	50 (16.0)	71 (20.1)	1.35 (0.74 to 2.46)	1.24 (0.68 to 2.27)
Q4	34.5	82 (26.2)	70 (19.8)	2.16 (1.21 to 3.85)	1.98 (1.10 to 3.54)
Q5	58.3	67 (21.4)	71 (20.1)	1.39 (0.77 to 2.52)	1.23 (0.67 to 2.23)
P trend				0.99	0.68
5β Pathway					
Etio-G					
Q1	12.3	50 (16.0)	70 (19.8)	Reference	Reference
Q2	21.7	40 (12.8)	70 (19.8)	0.87 (0.49 to 1.54)	0.86 (0.48 to 1.53)
Q3	33.6	77 (24.6)	71 (20.1)	1.54 (0.91 to 2.59)	1.46 (0.86 to 2.47)
Q4	49.0	75 (24.0)	70 (19.8)	1.54 (0.90 to 2.61)	1.44 (0.84 to 2.47)
Q5	89.7	66 (21.1)	71 (20.1)	1.23 (0.72 to 2.10)	1.13 (0.66 to 1.95)
P trend				0.36	0.57

Parent Estrogens					
Unconjugated Estradiol					
Q1	4.0	17 (5.4)	70 (19.8)	Reference	
Q2	7.5	44 (14.1)	71 (20.1)	2.75 (1.39 to 5.43)	
Q3	11.5	43 (13.7)	70 (19.8)	2.26 (1.13 to 4.51)	
Q4	17.2	83 (26.5)	71 (20.1)	4.48 (2.27 to 8.87)	
Q5	38.8	123 (39.3)	71 (20.1)	5.28 (2.64 to 10.59)	
P trend				0.0001	
Unconjugated Estrone					
Q1	29.9	32 (10.2)	70 (19.8)	Reference	
Q2	41.9	32 (10.2)	71 (20.1)	0.91 (0.49 to 1.69)	
Q3	55.2	61 (19.5)	70 (19.8)	1.59 (0.90 to 2.81)	
Q4	71.8	63 (20.1)	71 (20.1)	1.62 (0.91 to 2.89)	
Q5	115.9	122 (39.0)	71 (20.1)	2.63 (1.49 to 4.66)	
P trend				0.0001	
Ratios					
5α-Androstanedione:Androstenedione					
Q1	0.43	63 (20.1)	70 (19.8)	Reference	Reference
Q2	0.68	70 (22.4)	70 (19.8)	0.97 (0.59 to 1.62)	0.97 (0.58 to 1.63)
Q3	0.95	67 (21.4)	71 (20.1)	1.14 (0.69 to 1.90)	1.17 (0.70 to 1.96)
Q4	1.33	59 (18.8)	70 (19.8)	1.02 (0.61 to 1.71)	1.07 (0.64 to 1.81)
Q5	2.35	49 (15.7)	71 (20.1)	0.74 (0.43 to 1.27)	0.79 (0.46 to 1.36)
P trend				0.22	0.35
Unconjugated Estrone:Androstenedione					
Q1	23.4	28 (8.9)	70 (19.8)	Reference	
Q2	31.8	41 (13.1)	70 (19.8)	1.19 (0.64 to 2.23)	
Q3	41.1	74 (23.6)	71 (20.1)	2.23 (1.24 to 4.01)	
Q4	54.6	62 (19.8)	70 (19.8)	1.50 (0.81 to 2.78)	
Q5	97.8	102 (32.6)	71 (20.1)	2.18 (1.19 to 3.98)	
P trend				0.02	
DHT:Testosterone					
Q1	0.2	91 (29.1)	70 (19.8)	Reference	Reference
Q2	0.3	55 (17.6)	70 (19.8)	0.62 (0.37 to 1.04)	0.59 (0.35 to 1.00)
Q3	0.3	56 (17.9)	71 (20.1)	0.67 (0.41 to 1.11)	0.72 (0.43 to 1.20)
Q4	0.4	57 (18.2)	70 (19.8)	0.60 (0.36 to 1.01)	0.65 (0.38 to 1.10)
Q5	0.6	49 (15.7)	71 (20.1)	0.52 (0.31 to 0.88)	0.59 (0.35 to 1.01)
P trend				0.02	0.10
Unconjugated Estradiol:Testosterone§					
Q1	7.1	30 (9.6)	70 (19.8)	Reference	
Q2	12.5	35 (11.2)	70 (19.8)	1.23 (0.67 to 2.27)	
Q3	18.3	50 (16.0)	71 (20.1)	1.44 (0.79 to 2.63)	
Q4	30.4	76 (24.3)	70 (19.8)	1.84 (1.01 to 3.35)	
Q5	67.2	116 (37.1)	71 (20.1)	2.56 (1.38 to 4.75)	
P trend				0.002	

*Models for each androgen/metabolite were adjusted for gravidity, smoking status, body mass index, duration of oral contraceptive use, and age at menarche (conditioned on matching factors)

†Adjusted for factors from model 1 plus estradiol. Results not shown for models in which unconjugated estrogens were exposures

‡P for trend across quintiles of a given hormone/metabolite

§Effect estimates comparing the 5th versus 1st quintile (from model 1) that were statistically significant using a Bonferroni correction threshold of $p<0.003$.

Supplemental Table 2. Odds ratios (OR) for endometrial cancer across quintiles (Q1-Q5) of circulating androgen/androgen metabolites: heterogeneity by tumor characteristics

	Dualistic Model Type*			Stage			Grade‡		
	Type I n=271 cases	Type II n=42 cases		Stage 2 n=255 cases	Stage 3/4 n=55 cases		Grade 1/2 n=189	Grade 3/4 n=65	
Androgen/Metabolite	OR (95% CI)	OR (95% CI)	P†	OR (95% CI)	OR (95% CI)	P†	OR (95% CI)	OR (95% CI)	P†
Parent Androgens									
DHEA									
Q1	Reference	Reference	0.71	Reference	Reference	0.65	Reference	Reference	0.30
Q2	1.52 (0.85 to 2.70)	0.97 (0.34 to 2.75)		1.52 (0.85 to 2.71)	1.12 (0.43 to 2.93)		1.50 (0.79 to 2.85)	1.51 (0.57 to 3.97)	
Q3	1.61 (0.91 to 2.83)	0.89 (0.30 to 2.59)		1.60 (0.90 to 2.84)	1.15 (0.45 to 2.95)		1.76 (0.95 to 3.28)	1.51 (0.58 to 3.92)	
Q4	1.45 (0.80 to 2.60)	1.07 (0.36 to 3.17)		1.57 (0.87 to 2.83)	0.74 (0.25 to 2.22)		1.59 (0.84 to 3.02)	1.31 (0.48 to 3.60)	
Q5	1.87 (1.04 to 3.35)	1.47 (0.51 to 4.23)		1.78 (0.98 to 3.21)	1.93 (0.75 to 4.98)		1.41 (0.73 to 2.73)	2.67 (1.04 to 6.85)	
P trend§	0.09	0.43		0.12	0.21		0.57	0.04	
DHEAS									
Q1	Reference	Reference	0.56	Reference	Reference	0.21	Reference	Reference	0.49
Q2	1.14 (0.64 to 2.01)	0.72 (0.25 to 2.05)		1.25 (0.71 to 2.21)	0.47 (0.16 to 1.37)		1.15 (0.62 to 2.14)	1.00 (0.37 to 2.72)	
Q3	1.41 (0.81 to 2.45)	0.75 (0.26 to 2.13)		1.44 (0.83 to 2.53)	0.76 (0.29 to 1.99)		1.38 (0.75 to 2.52)	1.43 (0.56 to 3.66)	
Q4	1.09 (0.61 to 1.95)	0.59 (0.19 to 1.90)		1.04 (0.58 to 1.88)	0.92 (0.35 to 2.41)		1.06 (0.56 to 2.00)	1.24 (0.47 to 3.29)	
Q5	1.34 (0.75 to 2.37)	1.52 (0.56 to 4.09)		1.32 (0.74 to 2.37)	1.47 (0.59 to 3.67)		1.02 (0.54 to 1.95)	2.07 (0.82 to 5.26)	
P trend	0.45	0.32		0.62	0.12		0.80	0.08	
Androstenedione									
Q1	Reference	Reference	0.43	Reference	Reference	0.44	Reference	Reference	0.36
Q2	2.18 (1.18 to 4.01)	1.11 (0.39 to 3.19)		2.28 (1.23 to 4.22)	1.21 (0.43 to 3.46)		2.93 (1.45 to 5.93)	1.21 (0.44 to 3.38)	
Q3	2.06 (1.11 to 3.82)	1.36 (0.47 to 3.98)		2.09 (1.12 to 3.92)	1.63 (0.59 to 4.54)		2.63 (1.29 to 5.39)	1.53 (0.56 to 4.18)	
Q4	2.35 (1.28 to 4.32)	1.33 (0.47 to 3.79)		2.26 (1.21 to 4.19)	2.18 (0.82 to 5.76)		2.60 (1.27 to 5.32)	1.93 (0.74 to 5.03)	
Q5	2.60 (1.42 to 4.77)	1.10 (0.37 to 3.30)		2.61 (1.42 to 4.82)	1.35 (0.47 to 3.90)		2.68 (1.32 to 5.47)	2.09 (0.80 to 5.42)	
P trend	0.01	0.85		0.02	0.42		0.10	0.07	
Testosterone									
Q1	Reference	Reference	0.16	Reference	Reference	0.01	Reference	Reference	0.89
Q2	1.16 (0.65 to 2.07)	1.52 (0.41 to 5.58)		1.04 (0.58 to 1.86)	3.06 (0.93 to 10.10)		1.17 (0.61 to 2.22)	1.27 (0.51 to 3.16)	
Q3	0.82 (0.45 to 1.49)	2.93 (0.86 to 9.97)		0.76 (0.42 to 1.40)	3.34 (1.01 to 11.00)		0.90 (0.46 to 1.75)	0.64 (0.23 to 1.79)	
Q4	1.44 (0.81 to 2.53)	2.14 (0.61 to 7.50)		1.45 (0.82 to 2.55)	2.03 (0.58 to 7.17)		1.42 (0.76 to 2.67)	1.22 (0.49 to 3.03)	
Q5	1.74 (1.00 to 3.05)	1.98 (0.56 to 6.94)		1.79 (1.03 to 3.13)	2.09 (0.60 to 7.26)		1.78 (0.96 to 3.31)	1.35 (0.55 to 3.34)	
P trend	0.02	0.38		0.01	0.91		0.03	0.48	
5α Pathway									
5α-Androstanedione									
Q1	Reference	Reference	0.70	Reference	Reference	0.40	Reference	Reference	0.12
Q2	0.68 (0.39 to 1.18)	1.45 (0.39 to 5.32)		0.75 (0.43 to 1.30)	0.68 (0.22 to 2.13)		0.81 (0.44 to 1.49)	0.51 (0.21 to 1.28)	
Q3	0.94 (0.55 to 1.62)	2.52 (0.75 to 8.43)		0.95 (0.55 to 1.65)	1.71 (0.63 to 4.64)		0.80 (0.43 to 1.48)	1.16 (0.51 to 2.61)	
Q4	1.27 (0.73 to 2.19)	2.74 (0.80 to 9.40)		1.21 (0.70 to 2.11)	2.32 (0.85 to 6.28)		1.35 (0.74 to 2.48)	1.04 (0.44 to 2.48)	
Q5	1.08 (0.62 to 1.87)	1.84 (0.50 to 6.71)		1.13 (0.65 to 1.96)	1.25 (0.42 to 3.76)		1.31 (0.72 to 2.40)	0.56 (0.21 to 1.52)	
P trend	0.25	0.38		0.27	0.30		0.11	0.59	
DHT									
Q1	Reference	Reference	0.18	Reference	Reference	0.50	Reference	Reference	0.73
Q2	1.17 (0.66 to 2.08)	0.11 (0.01 to 0.89)		1.07 (0.60 to 1.92)	0.64 (0.23 to 1.80)		1.02 (0.54 to 1.92)	1.34 (0.53 to 3.38)	
Q3	1.49 (0.86 to 2.58)	1.50 (0.58 to 3.87)		1.58 (0.91 to 2.74)	1.21 (0.49 to 2.99)		1.29 (0.70 to 2.38)	1.34 (0.54 to 3.37)	
Q4	1.55 (0.89 to 2.70)	0.86 (0.30 to 2.45)		1.57 (0.90 to 2.76)	0.74 (0.28 to 1.97)		1.52 (0.83 to 2.79)	1.30 (0.51 to 3.30)	
Q5	1.12 (0.63 to 1.99)	1.09 (0.39 to 3.00)		1.14 (0.64 to 2.03)	1.05 (0.41 to 2.65)		1.05 (0.56 to 1.97)	1.44 (0.57 to 3.64)	
P trend	0.63	0.42		0.51	0.89		0.63	0.55	

DHTS									
Q1	Reference	Reference	0.76	Reference	Reference	0.58	Reference	Reference	0.87
Q2	1.10 (0.63 to 1.93)	1.10 (0.41 to 2.97)		1.21 (0.69 to 2.13)	0.66 (0.25 to 1.75)		1.19 (0.65 to 2.18)	1.01 (0.40 to 2.53)	
Q3	1.22 (0.70 to 2.15)	1.07 (0.39 to 2.96)		1.32 (0.75 to 2.32)	0.81 (0.31 to 2.12)		1.15 (0.61 to 2.14)	1.14 (0.45 to 2.88)	
Q4	1.01 (0.56 to 1.80)	0.62 (0.19 to 2.05)		1.02 (0.57 to 1.84)	0.61 (0.21 to 1.75)		1.01 (0.53 to 1.90)	0.83 (0.31 to 2.24)	
Q5	1.21 (0.69 to 2.10)	0.79 (0.27 to 2.35)		1.12 (0.64 to 1.97)	1.15 (0.47 to 2.82)		1.01 (0.54 to 1.88)	1.45 (0.61 to 3.45)	
P trend	0.64	0.45		0.97	0.60		0.76	0.41	
ADT									
Q1	Reference	Reference	0.84	Reference	Reference	0.99	Reference	Reference	0.34
Q2	0.62 (0.35 to 1.10)	0.49 (0.16 to 1.47)		0.61 (0.34 to 1.08)	0.49 (0.18 to 1.35)		0.50 (0.26 to 0.94)	1.06 (0.43 to 2.65)	
Q3	0.86 (0.49 to 1.50)	0.76 (0.27 to 2.11)		0.88 (0.50 to 1.54)	0.74 (0.28 to 1.95)		0.87 (0.48 to 1.58)	0.81 (0.30 to 2.16)	
Q4	1.07 (0.63 to 1.83)	0.63 (0.22 to 1.78)		1.00 (0.58 to 1.73)	0.97 (0.39 to 2.38)		1.07 (0.60 to 1.91)	1.04 (0.42 to 2.61)	
Q5	0.85 (0.49 to 1.49)	0.92 (0.33 to 2.51)		0.90 (0.52 to 1.58)	0.71 (0.26 to 1.91)		0.67 (0.36 to 1.26)	1.23 (0.49 to 3.09)	
P trend	0.74	0.79		0.61	0.997		0.84	0.62	
ADT-G									
Q1	Reference	Reference	0.57	Reference	Reference	0.36	Reference	Reference	0.35
Q2	2.23 (1.22 to 4.05)	1.14 (0.40 to 3.21)		2.35 (1.28 to 4.31)	1.14 (0.42 to 3.07)		2.59 (1.29 to 5.19)	1.56 (0.62 to 3.93)	
Q3	1.61 (0.86 to 3.02)	0.61 (0.17 to 2.19)		1.62 (0.86 to 3.07)	0.90 (0.31 to 2.61)		2.15 (1.05 to 4.40)	0.86 (0.31 to 2.43)	
Q4	2.26 (1.25 to 4.06)	1.62 (0.60 to 4.35)		2.25 (1.23 to 4.10)	1.79 (0.72 to 4.47)		2.66 (1.35 to 5.24)	1.60 (0.64 to 3.98)	
Q5	1.48 (0.80 to 2.75)	1.00 (0.33 to 3.08)		1.70 (0.91 to 3.18)	0.56 (0.18 to 1.75)		1.77 (0.87 to 3.61)	0.77 (0.28 to 2.14)	
P trend	0.84	0.80		0.55	0.45		0.71	0.47	
3α-diol-3G									
Q1	Reference	Reference	0.83	Reference	Reference	0.86	Reference	Reference	0.96
Q2	2.14 (1.14 to 4.01)	1.34 (0.45 to 4.03)		2.09 (1.12 to 3.91)	1.61 (0.53 to 4.89)		2.53 (1.23 to 5.18)	1.71 (0.61 to 4.79)	
Q3	3.03 (1.65 to 5.57)	2.24 (0.80 to 6.28)		2.97 (1.62 to 5.46)	2.51 (0.87 to 7.25)		3.45 (1.72 to 6.95)	2.52 (0.94 to 6.71)	
Q4	1.72 (0.92 to 3.24)	1.09 (0.33 to 3.54)		1.54 (0.81 to 2.90)	1.97 (0.66 to 5.83)		1.96 (0.95 to 4.04)	1.46 (0.52 to 4.13)	
Q5	2.02 (1.08 to 3.78)	1.22 (0.39 to 3.88)		1.92 (1.03 to 3.60)	1.44 (0.46 to 4.47)		2.20 (1.07 to 4.55)	1.51 (0.54 to 4.22)	
P trend	0.57	0.87		0.68	0.93		0.65	0.99	
3α-diol-17G									
Q1	Reference	Reference	0.84	Reference	Reference	0.73	Reference	Reference	0.91
Q2	1.22 (0.69 to 2.17)	0.87 (0.31 to 2.45)		1.06 (0.60 to 1.89)	1.48 (0.56 to 3.93)		1.26 (0.66 to 2.39)	1.10 (0.45 to 2.69)	
Q3	1.14 (0.64 to 2.02)	0.91 (0.32 to 2.59)		1.10 (0.62 to 1.94)	1.02 (0.36 to 2.89)		1.23 (0.66 to 2.32)	0.75 (0.29 to 1.94)	
Q4	0.88 (0.49 to 1.60)	0.56 (0.17 to 1.85)		0.79 (0.44 to 1.44)	0.98 (0.35 to 2.77)		0.95 (0.49 to 1.83)	0.75 (0.29 to 1.91)	
Q5	1.02 (0.56 to 1.83)	1.18 (0.42 to 3.36)		1.04 (0.58 to 1.86)	0.79 (0.27 to 2.35)		0.98 (0.51 to 1.89)	0.80 (0.31 to 2.06)	
P trend	0.63	0.74		0.88	0.37		0.52	0.53	
Marker of Androgenic Activity (ADT-G + 3α-diol-3G + 3α-diol-17G)									
Q1	Reference	Reference	0.59	Reference	Reference	0.17	Reference	Reference	0.69
Q2	2.64 (1.43 to 4.84)	1.17 (0.42 to 3.31)		2.54 (1.38 to 4.68)	1.46 (0.54 to 3.99)		2.85 (1.41 to 5.72)	2.26 (0.86 to 5.97)	
Q3	1.68 (0.88 to 3.19)	0.76 (0.23 to 2.55)		1.63 (0.85 to 3.10)	0.95 (0.32 to 2.86)		2.02 (0.97 to 4.21)	1.13 (0.38 to 3.31)	
Q4	2.35 (1.28 to 4.31)	1.49 (0.55 to 4.06)		2.12 (1.15 to 3.91)	2.13 (0.83 to 5.46)		2.74 (1.38 to 5.47)	1.79 (0.66 to 4.82)	
Q5	1.63 (0.87 to 3.06)	0.99 (0.32 to 3.05)		1.79 (0.95 to 3.36)	0.49 (0.14 to 1.68)		1.78 (0.86 to 3.66)	1.04 (0.36 to 3.02)	
P trend	0.88	0.93		0.58	0.32		0.80	0.52	
5β Pathway									
Etio-G									
Q1	Reference	Reference	0.60	Reference	Reference	0.59	Reference	Reference	0.86
Q2	0.88 (0.48 to 1.61)	0.80 (0.26 to 2.52)		0.98 (0.53 to 1.78)	0.51 (0.16 to 1.64)		0.96 (0.49 to 1.88)	0.77 (0.28 to 2.11)	
Q3	1.75 (1.01 to 3.03)	1.44 (0.52 to 3.98)		1.81 (1.04 to 3.16)	1.51 (0.60 to 3.84)		2.01 (1.09 to 3.68)	1.43 (0.58 to 3.51)	
Q4	1.79 (1.03 to 3.11)	0.91 (0.29 to 2.83)		1.67 (0.95 to 2.94)	1.77 (0.71 to 4.41)		1.82 (0.98 to 3.37)	1.70 (0.72 to 4.04)	
Q5	1.34 (0.76 to 2.36)	1.71 (0.61 to 4.75)		1.47 (0.83 to 2.59)	1.02 (0.37 to 2.80)		1.40 (0.74 to 2.63)	1.15 (0.45 to 2.90)	
P trend	0.24	0.25		0.19	0.59		0.32	0.56	

Parent Estrogens									
Unconjugated Estrone									
Q1	Reference	Reference	0.10	Reference	Reference	0.34	Reference	Reference	0.31
Q2	0.89 (0.45 to 1.76)	1.46 (0.50 to 4.26)		0.99 (0.51–1.93)	1.03 (0.33–3.17)		0.87 (0.41–1.85)	0.96 (0.29–3.20)	
Q3	1.68 (0.91 to 3.10)	1.18 (0.39 to 3.57)		1.52 (0.82–2.83)	1.63 (0.59–4.52)		1.33 (0.67–2.64)	2.58 (0.93–7.14)	
Q4	1.69 (0.92 to 3.12)	0.85 (0.26 to 2.75)		1.75 (0.95–3.22)	0.70 (0.22–2.30)		1.55 (0.79–3.04)	1.80 (0.63–5.16)	
Q5	2.65 (1.45 to 4.82)	1.30 (0.43 to 3.98)		2.55 (1.39–4.66)	1.77 (0.65–4.84)		2.43 (1.26–4.70)	2.25 (0.80–6.30)	
P trend	0.0001	0.86		0.0003	0.24		0.0004	0.15	
Unconjugated Estradiol									
Q1	Reference	Reference	0.01	Reference	Reference	0.12	Reference	Reference	0.36
Q2	2.95 (1.38 to 6.28)	2.27 (0.72 to 7.21)		2.68 (1.28 to 5.62)	2.90 (0.86 to 9.84)		3.97 (1.59 to 9.89)	1.85 (0.56 to 6.07)	
Q3	2.49 (1.15 to 5.39)	2.79 (0.87 to 8.98)		2.66 (1.26 to 5.60)	1.62 (0.43 to 6.09)		2.86 (1.12 to 7.32)	1.80 (0.55 to 5.93)	
Q4	5.21 (2.49 to 10.87)	1.34 (0.36 to 5.00)		4.41 (2.13 to 9.13)	3.32 (0.99 to 11.17)		5.76 (2.34 to 14.15)	3.88 (1.30 to 11.63)	
Q5	6.11 (2.88 to 12.97)	1.45 (0.39 to 5.41)		5.84 (2.78 to 12.28)	1.90 (0.53 to 6.80)		7.54 (3.03 to 18.77)	3.01 (0.96 to 9.47)	
P trend	<.0001	0.70		<.0001	0.99		<.0001	0.13	
Ratios									
5α-Androstanedione:Androstenedione									
Q1	Reference	Reference	0.23	Reference	Reference	0.63	Reference	Reference	0.24
Q2	0.87 (0.52 to 1.47)	1.47 (0.45 to 4.80)		0.80 (0.47 to 1.36)	1.71 (0.63 to 4.64)		0.92 (0.50 to 1.67)	0.86 (0.39 to 1.87)	
Q3	1.15 (0.67 to 1.95)	1.82 (0.55 to 5.99)		1.12 (0.66 to 1.91)	1.77 (0.63 to 5.02)		1.45 (0.80 to 2.62)	0.74 (0.31 to 1.76)	
Q4	0.95 (0.55 to 1.62)	1.56 (0.48 to 5.11)		0.94 (0.55 to 1.60)	1.49 (0.52 to 4.27)		1.27 (0.70 to 2.31)	0.56 (0.23 to 1.38)	
Q5	0.70 (0.40 to 1.23)	2.14 (0.68 to 6.71)		0.73 (0.41 to 1.29)	1.37 (0.47 to 3.98)		0.84 (0.44 to 1.61)	0.51 (0.20 to 1.31)	
P trend	0.21	0.24		0.34	0.97		0.64	0.11	
Unconjugated Estrone:Androstenedione									
Q1	Reference	Reference	0.39	Reference	Reference	0.80	Reference	Reference	0.37
Q2	1.44 (0.73 to 2.82)	1.18 (0.36 to 3.87)		1.50 (0.77 to 2.93)	0.94 (0.29 to 3.10)		1.81 (0.83 to 3.96)	0.65 (0.19 to 2.27)	
Q3	2.90 (1.54 to 5.44)	1.25 (0.38 to 4.08)		2.86 (1.53 to 5.37)	1.49 (0.49 to 4.53)		3.12 (1.49 to 6.53)	3.17 (1.18 to 8.52)	
Q4	1.67 (0.87 to 3.21)	1.67 (0.54 to 5.20)		1.70 (0.88 to 3.27)	1.24 (0.41 to 3.81)		1.75 (0.81 to 3.79)	1.47 (0.51 to 4.23)	
Q5	2.45 (1.30 to 4.63)	1.30 (0.40 to 4.24)		2.40 (1.27 to 4.55)	1.40 (0.47 to 4.15)		2.91 (1.38 to 6.12)	1.50 (0.53 to 4.23)	
P trend	0.04	0.74		0.06	0.49		0.03	0.69	
DHT:Testosterone									
Q1	Reference	Reference	0.92	Reference	Reference	0.68	Reference	Reference	0.47
Q2	0.62 (0.37 to 1.06)	0.81 (0.29 to 2.24)		0.67 (0.39 to 1.14)	0.54 (0.21 to 1.40)		0.65 (0.36 to 1.16)	0.43 (0.17 to 1.09)	
Q3	0.59 (0.35 to 0.99)	0.93 (0.35 to 2.48)		0.59 (0.34 to 1.00)	0.74 (0.31 to 1.77)		0.56 (0.31 to 1.01)	0.70 (0.32 to 1.56)	
Q4	0.64 (0.38 to 1.09)	0.74 (0.26 to 2.14)		0.68 (0.40 to 1.16)	0.48 (0.18 to 1.30)		0.69 (0.39 to 1.24)	0.45 (0.18 to 1.14)	
Q5	0.61 (0.36 to 1.05)	0.66 (0.22 to 1.98)		0.59 (0.34 to 1.01)	0.74 (0.30 to 1.81)		0.64 (0.35 to 1.15)	0.79 (0.35 to 1.79)	
P trend	0.13	0.48		0.10	0.57		0.24	0.74	
Unconjugated Estradiol:Testosterone									
Q1	Reference	Reference	0.02	Reference	Reference	0.60	Reference	Reference	0.92
Q2	1.61 (0.80 to 3.21)	0.65 (0.22 to 1.92)		1.42 (0.73 to 2.77)	0.71 (0.21 to 2.36)		1.28 (0.59 to 2.80)	2.32 (0.67 to 8.11)	
Q3	1.81 (0.92 to 3.55)	0.85 (0.31 to 2.32)		1.60 (0.83 to 3.07)	0.97 (0.33 to 2.84)		1.70 (0.81 to 3.54)	2.06 (0.58 to 7.33)	
Q4	2.62 (1.35 to 5.07)	0.58 (0.19 to 1.74)		2.14 (1.12 to 4.07)	1.14 (0.41 to 3.20)		2.25 (1.09 to 4.65)	3.19 (0.95 to 10.77)	
Q5	3.67 (1.87 to 7.19)	0.55 (0.17 to 1.81)		2.96 (1.53 to 5.74)	1.21 (0.42 to 3.51)		3.10 (1.48 to 6.47)	4.58 (1.34 to 15.64)	
P trend	0.0002	0.37		0.001	0.50		0.002	0.01	

Unconditional logistic regression models for each androgen/metabolite were used and adjusted for gravidity, smoking status, body mass index, duration of oral contraceptive use, and age at menarche and additionally adjusted for matching factors: age at baseline, year of blood draw, race/ethnicity, time since last menopausal hormone therapy use

*Using the "dualistic model" of endometrial cancer: Type I (adenocarcinomas, endometrioid carcinomas, mucinous tumors) and type II (serous, clear cell, other tumors).

†Chi-square P values from multinomial logistic regression models that treated the largest subgroup as the reference category and excluded non-cases

‡Limited to endometrioid tumor or adenocarcinoma cases

§P for trend across quintiles of a given hormone/metabolite

Supplemental Table 3. Odds ratios (OR) for endometrial cancer across quintiles (Q1-Q5) of circulating androgen/androgen metabolites: heterogeneity by time between blood draw and diagnosis

	Time between blood draw and diagnosis		
	<5 Years n=116 cases	≥5 n=197 cases	
Androgen/Metabolite	OR (95% CI)	OR (95% CI)	P*
DHEA			
Q1	Reference	Reference	0.27
Q2	1.50 (0.76–2.97)	1.35 (0.70–2.60)	
Q3	1.01 (0.49–2.08)	1.85 (0.99–3.47)	
Q4	1.08 (0.51–2.27)	1.62 (0.84–3.10)	
Q5	1.49 (0.72–3.08)	2.03 (1.06–3.87)	
P trend[†]	0.47	0.05	
DHEAS			
Q1	Reference	Reference	0.18
Q2	1.50 (0.75–3.02)	0.81 (0.42–1.53)	
Q3	1.46 (0.72–2.93)	1.19 (0.65–2.18)	
Q4	0.82 (0.37–1.80)	1.08 (0.58–2.02)	
Q5	1.30 (0.62–2.75)	1.34 (0.73–2.48)	
P trend	0.95	0.18	
Androstenedione			
Q1	Reference	Reference	0.64
Q2	2.50 (1.11–5.62)	1.64 (0.85–3.15)	
Q3	2.80 (1.24–6.30)	1.46 (0.75–2.85)	
Q4	2.44 (1.07–5.54)	1.93 (1.02–3.67)	
Q5	2.81 (1.25–6.34)	1.99 (1.05–3.78)	
P trend	0.06	0.05	
Testosterone			
Q1	Reference	Reference	0.98
Q2	1.13 (0.53–2.41)	1.26 (0.66–2.40)	
Q3	0.99 (0.46–2.15)	0.99 (0.51–1.91)	
Q4	1.49 (0.72–3.11)	1.52 (0.81–2.85)	
Q5	1.68 (0.82–3.46)	1.82 (0.98–3.40)	
P trend	0.08	0.03	
5α Pathway			
5α-Androstanedione			
Q1	Reference	Reference	0.37
Q2	0.73 (0.36–1.45)	0.75 (0.40–1.43)	
Q3	0.88 (0.45–1.74)	1.23 (0.67–2.26)	
Q4	0.95 (0.47–1.91)	1.77 (0.96–3.27)	
Q5	0.81 (0.40–1.66)	1.43 (0.77–2.65)	
P trend	0.82	0.05	
DHT			
Q1	Reference	Reference	0.28
Q2	1.02 (0.47–2.18)	0.94 (0.50–1.77)	
Q3	1.24 (0.60–2.59)	1.63 (0.91–2.92)	
Q4	1.84 (0.91–3.72)	1.19 (0.65–2.20)	
Q5	1.38 (0.67–2.83)	0.96 (0.51–1.80)	
P trend	0.17	0.91	

DHTS			
Q1	Reference	Reference	0.20
Q2	0.81 (0.40–1.66)	1.34 (0.73–2.48)	
Q3	0.90 (0.44–1.85)	1.44 (0.77–2.67)	
Q4	0.85 (0.41–1.78)	1.02 (0.53–1.95)	
Q5	1.28 (0.65–2.52)	1.06 (0.57–1.99)	
P trend	0.32	0.66	
ADT			
Q1	Reference	Reference	0.40
Q2	0.39 (0.18–0.84)	0.76 (0.41–1.40)	
Q3	0.80 (0.40–1.61)	0.87 (0.47–1.61)	
Q4	0.88 (0.45–1.71)	1.08 (0.60–1.95)	
Q5	0.90 (0.46–1.78)	0.83 (0.45–1.54)	
P trend	0.42	0.91	
ADT-G			
Q1	Reference	Reference	0.64
Q2	2.67 (1.23–5.82)	1.64 (0.86–3.12)	
Q3	1.53 (0.65–3.58)	1.32 (0.67–2.58)	
Q4	2.78 (1.29–6.01)	1.75 (0.94–3.29)	
Q5	1.51 (0.65–3.49)	1.28 (0.67–2.47)	
	0.90	0.80	
3α-diol-3G			
Q1	Reference	Reference	0.78
Q2	1.94 (0.86–4.38)	1.97 (1.00–3.89)	
Q3	2.77 (1.27–6.05)	2.84 (1.47–5.48)	
Q4	1.73 (0.76–3.92)	1.48 (0.74–2.95)	
Q5	2.25 (1.01–5.00)	1.62 (0.81–3.22)	
P trend	0.27	0.89	
3α-diol-17G			
Q1	Reference	Reference	0.91
Q2	1.01 (0.49–2.10)	1.24 (0.66–2.33)	
Q3	1.19 (0.58–2.42)	1.03 (0.54–1.95)	
Q4	0.74 (0.34–1.59)	0.87 (0.45–1.68)	
Q5	1.03 (0.49–2.16)	1.03 (0.54–1.96)	
P trend	0.84	0.74	
5β Pathway			
Etio-G			
Q1	Reference	Reference	0.39
Q2	0.65 (0.29–1.47)	1.01 (0.53–1.94)	
Q3	1.99 (1.01–3.92)	1.52 (0.83–2.80)	
Q4	1.47 (0.72–2.98)	1.74 (0.95–3.19)	
Q5	1.26 (0.61–2.61)	1.46 (0.79–2.70)	
P trend	0.42	0.18	
Marker of Androgenic Activity (ADT-G + 3α-diol-3G + 3α-diol-17G)			
Q1	Reference	Reference	0.44
Q2	3.29 (1.50–7.24)	1.78 (0.93–3.42)	
Q3	1.41 (0.58–3.43)	1.45 (0.74–2.86)	
Q4	2.71 (1.22–6.01)	1.82 (0.96–3.46)	
Q5	1.73 (0.74–4.05)	1.32 (0.68–2.59)	
P trend	0.93	0.89	

Parent Estrogens			
Unconjugated Estrone			
Q1	Reference	Reference	0.53
Q2	1.02 (0.44–2.34)	0.98 (0.46–2.10)	
Q3	1.14 (0.51–2.54)	1.90 (0.97–3.75)	
Q4	1.56 (0.73–3.36)	1.51 (0.75–3.02)	
Q5	1.95 (0.91–4.14)	2.75 (1.41–5.36)	
P trend	0.03	0.001	
Unconjugated Estradiol			
Q1	Reference	Reference	0.92
Q2	2.54 (0.98–6.62)	2.85 (1.26–6.47)	
Q3	2.03 (0.75–5.51)	2.75 (1.20–6.26)	
Q4	4.22 (1.66–10.74)	4.13 (1.85–9.22)	
Q5	4.80 (1.85–12.47)	4.93 (2.18–11.18)	
P trend	0.003	0.002	
Ratios			
5α-Androstanedione:Androstenedione			
Q1	Reference	Reference	0.38
Q2	0.67 (0.34–1.33)	1.11 (0.62–1.98)	
Q3	1.15 (0.60–2.22)	1.21 (0.66–2.21)	
Q4	0.79 (0.40–1.57)	1.15 (0.63–2.09)	
Q5	0.56 (0.27–1.17)	1.05 (0.56–1.95)	
P trend	0.16	0.99	
Unconjugated Estrone:Androstenedione			
Q1	Reference	Reference	0.71
Q2	1.08 (0.46–2.50)	1.64 (0.77–3.50)	
Q3	1.87 (0.85–4.09)	3.16 (1.55–6.43)	
Q4	1.10 (0.48–2.52)	2.13 (1.02–4.44)	
Q5	1.65 (0.75–3.62)	2.72 (1.33–5.57)	
P trend	0.24	0.06	
DHT:Testosterone			
Q1	Reference	Reference	0.64
Q2	0.68 (0.35–1.32)	0.63 (0.35–1.12)	
Q3	0.52 (0.26–1.04)	0.69 (0.40–1.22)	
Q4	0.65 (0.33–1.29)	0.66 (0.37–1.18)	
Q5	0.75 (0.39–1.46)	0.54 (0.30–0.99)	
P trend	0.52	0.09	
Unconjugated Estradiol:Testosterone			
Q1	Reference	Reference	0.43
Q2	1.81 (0.75–4.36)	0.97 (0.46–2.03)	
Q3	1.41 (0.57–3.47)	1.43 (0.72–2.83)	
Q4	2.38 (1.01–5.57)	1.64 (0.83–3.25)	
Q5	3.45 (1.45–8.22)	2.16 (1.08–4.35)	
P trend	0.003	0.02	

Unconditional logistic regression models for each androgen/metabolite were used and adjusted for gravidity, smoking status, body mass index, duration of oral contraceptive use, and age at menarche and additionally adjusted for matching factors: age at baseline, year of blood draw, race/ethnicity, time since last menopausal hormone therapy use

*Chi-square P values from multinomial logistic regression models that treated the largest subgroup as the reference category and excluded non-cases

†P for trend across quintiles of a given hormone/metabolite

Supplemental Table 4. Odds ratios (OR) for endometrial cancer across quintiles (Q1-Q5) of circulating androgen/androgen metabolites: modification by age at blood draw and body mass index (BMI)

	Age			BMI (kg/m^2)			
	<60 years n=192	≥60 Years n=475		<25 n=235	25 to 29.9 n=194	≥30 n=236	
Androgen/Metabolite	OR (95% CI)	OR (95% CI)	P*	OR (95% CI)	OR (95% CI)	OR (95% CI)	P*
Parent Androgens							
DHEA							
Q1	Reference	Reference	0.29	Reference	Reference	Reference	0.001
Q2	10.92 (1.11 to 107.58)	1.27 (0.70 to 2.29)		3.13 (0.95 to 10.35)	1.67 (0.62 to 4.50)	0.62 (0.22 to 1.77)	
Q3	10.27 (1.09 to 96.48)	1.40 (0.77 to 2.55)		4.52 (1.35 to 15.08)	1.59 (0.56 to 4.51)	0.67 (0.26 to 1.72)	
Q4	17.06 (1.87 to 155.84)	1.03 (0.54 to 1.96)		14.55 (4.09 to 51.80)	1.19 (0.42 to 3.36)	0.31 (0.11 to 0.82)	
Q5	15.14 (1.73 to 132.36)	1.61 (0.82 to 3.15)		5.52 (1.65 to 18.46)	1.51 (0.52 to 4.44)	1.02 (0.37 to 2.78)	
P trend†	0.04	0.30		0.01	0.79	0.84	
DHEAS							
Q1	Reference	Reference	0.41	Reference	Reference	Reference	0.07
Q2	2.48 (0.48 to 12.85)	1.06 (0.59 to 1.92)		2.06 (0.76 to 5.61)	1.41 (0.51 to 3.91)	0.33 (0.11 to 0.97)	
Q3	6.01 (1.21 to 29.96)	1.10 (0.61 to 1.98)		2.62 (0.96 to 7.17)	0.97 (0.37 to 2.52)	0.72 (0.25 to 2.11)	
Q4	4.62 (0.98 to 21.89)	0.78 (0.41 to 1.48)		2.93 (1.01 to 8.53)	1.42 (0.53 to 3.83)	0.25 (0.08 to 0.76)	
Q5	4.33 (0.99 to 18.87)	1.26 (0.65 to 2.44)		3.39 (1.20 to 9.59)	1.01 (0.36 to 2.82)	0.51 (0.18 to 1.48)	
P trend	0.17	0.72		0.03	0.90	0.53	
Androstenedione							
Q1	Reference	Reference	0.93	Reference	Reference	Reference	0.56
Q2	3.80 (0.63 to 22.83)	1.77 (0.95 to 3.30)		2.59 (0.93 to 7.20)	1.69 (0.61 to 4.67)	1.11 (0.38 to 3.28)	
Q3	3.33 (0.60 to 18.56)	1.83 (0.93 to 3.60)		2.02 (0.63 to 6.47)	2.57 (0.92 to 7.20)	1.13 (0.40 to 3.15)	
Q4	3.82 (0.65 to 22.43)	2.11 (1.13 to 3.95)		4.79 (1.70 to 13.47)	1.71 (0.58 to 4.99)	1.22 (0.45 to 3.32)	
Q5	4.20 (0.75 to 23.67)	2.16 (1.14 to 4.08)		3.01 (1.05 to 8.63)	2.18 (0.77 to 6.21)	2.19 (0.78 to 6.13)	
P trend	0.29	0.03		0.04	0.28	0.08	
Testosterone							
Q1	Reference	Reference	0.17	Reference	Reference	Reference	0.09
Q2	1.56 (0.52 to 4.67)	1.16 (0.60 to 2.27)		2.45 (0.82 to 7.26)	0.77 (0.28 to 2.09)	0.86 (0.29 to 2.49)	
Q3	1.21 (0.44 to 3.36)	0.85 (0.42 to 1.74)		2.93 (0.93 to 9.24)	1.14 (0.42 to 3.12)	0.33 (0.12 to 0.91)	
Q4	1.03 (0.37 to 2.85)	1.77 (0.91 to 3.44)		3.57 (1.24 to 10.32)	0.96 (0.35 to 2.64)	0.90 (0.32 to 2.51)	
Q5	0.76 (0.24 to 2.34)	2.37 (1.25 to 4.46)		4.87 (1.67 to 14.24)	0.97 (0.37 to 2.54)	1.15 (0.42 to 3.19)	
P trend	0.36	0.001		0.005	0.87	0.28	
5α Pathway							
5α-Androstanedione							
Q1	Reference	Reference	0.998	Reference	Reference	Reference	0.03
Q2	0.65 (0.24 to 1.77)	0.76 (0.40 to 1.47)		2.41 (0.85 to 6.86)	0.96 (0.35 to 2.63)	0.25 (0.09 to 0.67)	
Q3	1.02 (0.39 to 2.65)	1.10 (0.58 to 2.08)		2.84 (1.00 to 8.12)	0.68 (0.26 to 1.79)	0.81 (0.31 to 2.15)	
Q4	1.48 (0.56 to 3.92)	1.35 (0.71 to 2.58)		5.44 (1.94 to 15.26)	0.98 (0.38 to 2.53)	0.55 (0.20 to 1.50)	
Q5	0.92 (0.34 to 2.50)	1.15 (0.60 to 2.20)		1.90 (0.67 to 5.39)	1.31 (0.51 to 3.38)	0.98 (0.34 to 2.83)	
P trend	0.72	0.30		0.27	0.42	0.28	
DHT							
Q1	Reference	Reference	0.94	Reference	Reference	Reference	0.04
Q2	1.40 (0.42 to 4.72)	0.91 (0.48 to 1.71)		1.30 (0.40 to 4.25)	0.79 (0.28 to 2.21)	1.06 (0.40 to 2.80)	
Q3	2.31 (0.78 to 6.83)	1.33 (0.72 to 2.46)		3.79 (1.24 to 11.60)	1.12 (0.46 to 2.72)	1.09 (0.43 to 2.74)	
Q4	1.89 (0.63 to 5.69)	1.42 (0.75 to 2.67)		1.60 (0.50 to 5.07)	1.52 (0.59 to 3.96)	1.50 (0.58 to 3.88)	
Q5	1.39 (0.45 to 4.25)	1.03 (0.54 to 1.95)		3.36 (1.05 to 10.75)	0.78 (0.31 to 1.92)	0.56 (0.21 to 1.46)	
P trend	0.78	0.62		0.07	0.87	0.31	

DHTS							
Q1	Reference	Reference	0.31	Reference	Reference	Reference	0.34
Q2	0.42 (0.12 to 1.49)	1.43 (0.78 to 2.62)		2.05 (0.74 to 5.66)	0.54 (0.21 to 1.41)	1.62 (0.59 to 4.48)	
Q3	1.07 (0.34 to 3.43)	1.22 (0.66 to 2.25)		2.26 (0.81 to 6.32)	0.97 (0.38 to 2.46)	0.95 (0.34 to 2.65)	
Q4	0.73 (0.25 to 2.14)	1.10 (0.56 to 2.17)		2.22 (0.78 to 6.31)	0.52 (0.19 to 1.40)	0.80 (0.29 to 2.20)	
Q5	1.27 (0.44 to 3.69)	1.15 (0.61 to 2.16)		2.87 (0.99 to 8.31)	0.65 (0.24 to 1.73)	0.93 (0.37 to 2.37)	
P trend	0.30	0.95		0.09	0.42	0.43	
ADT							
Q1	Reference	Reference	0.71	Reference	Reference	Reference	0.73
Q2	0.83 (0.27 to 2.57)	0.55 (0.30 to 1.04)		0.49 (0.18 to 1.33)	0.36 (0.13 to 1.00)	0.77 (0.29 to 2.06)	
Q3	1.67 (0.56 to 4.93)	0.67 (0.35 to 1.26)		1.22 (0.47 to 3.14)	0.74 (0.28 to 1.98)	0.75 (0.28 to 1.98)	
Q4	1.48 (0.54 to 4.04)	0.89 (0.48 to 1.65)		0.79 (0.32 to 1.96)	0.82 (0.32 to 2.11)	1.46 (0.55 to 3.87)	
Q5	1.20 (0.43 to 3.35)	0.77 (0.41 to 1.46)		0.62 (0.23 to 1.63)	0.83 (0.31 to 2.17)	0.83 (0.31 to 2.19)	
P trend	0.66	0.92		0.51	0.62	0.88	
ADT-G							
Q1	Reference	Reference	0.48	Reference	Reference	Reference	0.73
Q2	3.12 (0.62 to 15.59)	2.02 (1.10 to 3.71)		2.00 (0.76 to 5.26)	2.28 (0.80 to 6.53)	1.92 (0.63 to 5.83)	
Q3	3.44 (0.70 to 16.82)	1.32 (0.68 to 2.56)		2.20 (0.74 to 6.56)	1.01 (0.35 to 2.87)	0.98 (0.33 to 2.94)	
Q4	6.89 (1.54 to 30.80)	1.63 (0.88 to 3.04)		3.77 (1.34 to 10.60)	1.98 (0.73 to 5.36)	1.10 (0.40 to 3.05)	
Q5	3.21 (0.73 to 14.09)	1.26 (0.64 to 2.49)		2.06 (0.65 to 6.56)	1.40 (0.49 to 4.01)	0.99 (0.36 to 2.71)	
P trend	0.52	0.95		0.19	0.87	0.46	
3α-diol-3G							
Q1	Reference	Reference	0.40	Reference	Reference	Reference	0.56
Q2	8.17 (1.41 to 47.38)	1.70 (0.89 to 3.24)		3.39 (1.27 to 9.05)	0.96 (0.34 to 2.71)	2.41 (0.72 to 8.08)	
Q3	11.43 (2.06 to 63.34)	2.37 (1.26 to 4.45)		4.39 (1.65 to 11.70)	1.10 (0.41 to 2.97)	4.91 (1.46 to 16.48)	
Q4	6.85 (1.31 to 35.93)	1.22 (0.62 to 2.43)		2.44 (0.85 to 7.05)	1.16 (0.42 to 3.24)	1.28 (0.40 to 4.10)	
Q5	10.76 (2.01 to 57.57)	1.29 (0.65 to 2.54)		2.26 (0.78 to 6.62)	0.86 (0.28 to 2.59)	2.37 (0.78 to 7.24)	
P trend	0.11	0.69		0.50	0.81	0.91	
3α-diol-17G							
Q1	Reference	Reference	0.96	Reference	Reference	Reference	0.55
Q2	2.15 (0.57 to 8.10)	1.05 (0.57 to 1.94)		1.62 (0.70 to 3.77)	1.20 (0.43 to 3.33)	0.42 (0.11 to 1.58)	
Q3	1.52 (0.43 to 5.46)	1.06 (0.57 to 1.97)		1.19 (0.47 to 3.03)	0.90 (0.34 to 2.35)	0.56 (0.16 to 1.98)	
Q4	1.30 (0.37 to 4.58)	0.78 (0.40 to 1.52)		1.08 (0.38 to 3.12)	0.46 (0.17 to 1.26)	0.57 (0.16 to 2.05)	
Q5	1.55 (0.46 to 5.21)	0.99 (0.51 to 1.93)		1.46 (0.52 to 4.07)	0.81 (0.29 to 2.23)	0.63 (0.18 to 2.17)	
P trend	0.94	0.74		0.73	0.31	0.82	
Marker of Androgenic Activity (ADT-G + 3α-diol-3G + 3α-diol-17G)							
Q1	Reference	Reference	0.55	Reference	Reference	Reference	0.63
Q2	3.39 (0.68 to 16.92)	2.40 (1.29 to 4.46)		2.14 (0.82 to 5.57)	2.71 (0.95 to 7.76)	2.18 (0.71 to 6.70)	
Q3	3.25 (0.65 to 16.17)	1.41 (0.72 to 2.77)		2.23 (0.74 to 6.67)	0.95 (0.33 to 2.71)	1.42 (0.45 to 4.49)	
Q4	6.13 (1.35 to 27.76)	1.69 (0.90 to 3.19)		3.60 (1.28 to 10.18)	2.15 (0.80 to 5.83)	1.17 (0.41 to 3.36)	
Q5	3.00 (0.67 to 13.36)	1.40 (0.71 to 2.80)		1.70 (0.52 to 5.55)	1.35 (0.47 to 3.90)	1.28 (0.45 to 3.62)	
P trend	0.65	0.94		0.37	0.998	0.61	
5β Pathway							
Etio-G							
Q1	Reference	Reference	0.44	Reference	Reference	Reference	0.20
Q2	1.21 (0.32 to 4.63)	0.83 (0.44 to 1.59)		1.39 (0.47 to 4.07)	1.07 (0.38 to 3.05)	0.63 (0.21 to 1.86)	
Q3	4.40 (1.32 to 14.73)	1.40 (0.77 to 2.56)		3.59 (1.33 to 9.67)	2.57 (0.89 to 7.43)	0.75 (0.30 to 1.86)	
Q4	4.98 (1.51 to 16.45)	1.24 (0.67 to 2.32)		3.66 (1.27 to 10.52)	1.90 (0.70 to 5.22)	1.01 (0.39 to 2.63)	
Q5	2.70 (0.87 to 8.42)	1.27 (0.67 to 2.40)		2.06 (0.73 to 5.82)	3.41 (1.14 to 10.20)	0.59 (0.24 to 1.46)	
P trend	0.23	0.34		0.25	0.02	0.38	

Parent Estrogens							
Unconjugated Estrone							
Q1	Reference	Reference	0.58	Reference	Reference	Reference	0.50
Q2	1.31 (0.38 to 4.55)	0.95 (0.46 to 1.95)		1.05 (0.40 to 2.74)	0.91 (0.32 to 2.57)	2.01 (0.36 to 11.24)	
Q3	1.46 (0.46 to 4.65)	1.73 (0.88 to 3.38)		1.45 (0.60 to 3.49)	0.89 (0.31 to 2.59)	3.97 (0.95 to 16.69)	
Q4	1.39 (0.41 to 4.77)	1.77 (0.91 to 3.45)		2.17 (0.84 to 5.62)	1.44 (0.52 to 4.01)	1.64 (0.41 to 6.63)	
Q5	1.84 (0.57 to 5.92)	3.02 (1.55 to 5.88)		3.34 (1.22 to 9.16)	1.30 (0.47 to 3.60)	4.45 (1.17 to 16.95)	
P trend	0.32	0.0002		0.01	0.38	0.03	
Unconjugated Estradiol							
Q1	Reference	Reference	0.60	Reference	Reference	Reference	0.98
Q2	3.09 (0.69 to 13.78)	2.77 (1.29 to 5.94)		3.90 (1.55 to 9.81)	1.34 (0.38 to 4.73)	2.47 (0.27 to 22.19)	
Q3	3.57 (0.74 to 17.35)	2.39 (1.10 to 5.18)		3.38 (1.24 to 9.20)	1.22 (0.35 to 4.22)	2.22 (0.31 to 15.83)	
Q4	6.43 (1.42 to 29.19)	3.88 (1.83 to 8.22)		4.37 (1.49 to 12.85)	2.01 (0.61 to 6.56)	5.03 (0.76 to 33.26)	
Q5	4.82 (1.05 to 22.04)	5.87 (2.67 to 12.87)		7.26 (2.17 to 24.30)	2.56 (0.73 to 9.05)	5.08 (0.81 to 31.96)	
P trend	0.32	<.0001		0.01	0.08	0.07	
Ratios							
5α-Androstanedione:Androstenedione							
Q1	Reference	Reference	0.96	Reference	Reference	Reference	0.07
Q2	0.90 (0.38 to 2.13)	0.86 (0.45 to 1.66)		1.64 (0.62 to 4.37)	0.45 (0.16 to 1.25)	0.85 (0.37 to 1.96)	
Q3	1.46 (0.56 to 3.80)	1.07 (0.57 to 2.01)		1.40 (0.53 to 3.68)	1.31 (0.49 to 3.52)	1.02 (0.42 to 2.50)	
Q4	0.96 (0.36 to 2.58)	0.94 (0.50 to 1.77)		1.27 (0.49 to 3.28)	0.36 (0.13 to 0.98)	2.43 (0.90 to 6.57)	
Q5	0.60 (0.19 to 1.90)	0.80 (0.42 to 1.51)		0.82 (0.30 to 2.29)	0.86 (0.31 to 2.41)	0.66 (0.26 to 1.66)	
P trend	0.42	0.49		0.41	0.96	0.68	
Unconjugated Estrone:Androstenedione							
Q1	Reference	Reference	0.05	Reference	Reference	Reference	0.99
Q2	0.91 (0.29 to 2.90)	1.88 (0.86 to 4.08)		1.28 (0.48 to 3.41)	1.02 (0.33 to 3.11)	1.59 (0.38 to 6.69)	
Q3	1.72 (0.59 to 5.03)	3.45 (1.65 to 7.24)		2.26 (0.93 to 5.53)	1.93 (0.64 to 5.79)	3.69 (0.94 to 14.53)	
Q4	2.64 (0.85 to 8.14)	1.59 (0.74 to 3.42)		1.60 (0.53 to 4.80)	0.97 (0.33 to 2.87)	2.23 (0.62 to 7.99)	
Q5	1.26 (0.42 to 3.77)	3.13 (1.49 to 6.58)		2.20 (0.77 to 6.26)	1.25 (0.40 to 3.87)	2.73 (0.81 to 9.23)	
P trend	0.80	0.02		0.19	0.94	0.35	
DHT:Testosterone							
Q1	Reference	Reference	0.39	Reference	Reference	Reference	0.63
Q2	0.77 (0.26 to 2.33)	0.62 (0.34 to 1.12)		1.12 (0.41 to 3.07)	0.39 (0.16 to 0.98)	0.56 (0.23 to 1.36)	
Q3	1.23 (0.43 to 3.52)	0.50 (0.27 to 0.91)		1.09 (0.42 to 2.78)	0.52 (0.20 to 1.34)	0.41 (0.17 to 0.97)	
Q4	1.48 (0.53 to 4.14)	0.48 (0.26 to 0.89)		0.85 (0.32 to 2.24)	0.53 (0.21 to 1.35)	0.55 (0.22 to 1.38)	
Q5	1.05 (0.36 to 3.12)	0.53 (0.29 to 0.98)		0.53 (0.19 to 1.46)	0.83 (0.32 to 2.20)	0.48 (0.20 to 1.18)	
P trend	0.65	0.03		0.15	0.98	0.14	
Unconjugated Estradiol:Testosterone							
Q1	Reference	Reference	0.64	Reference	Reference	Reference	0.23
Q2	1.54 (0.35 to 6.75)	1.33 (0.66 to 2.69)		1.19 (0.51 to 2.81)	1.37 (0.44 to 4.29)	0.32 (0.04 to 2.82)	
Q3	1.78 (0.41 to 7.66)	1.46 (0.74 to 2.88)		1.52 (0.61 to 3.78)	1.17 (0.39 to 3.52)	0.51 (0.08 to 3.36)	
Q4	3.95 (0.91 to 17.14)	1.61 (0.83 to 3.13)		4.31 (1.46 to 12.74)	1.62 (0.57 to 4.57)	0.52 (0.08 to 3.26)	
Q5	3.49 (0.81 to 15.05)	2.80 (1.39 to 5.63)		1.41 (0.46 to 4.29)	2.29 (0.71 to 7.37)	1.16 (0.19 to 6.97)	
P trend	0.12	0.003		0.33	0.13	0.01	

Unconditional logistic regression models for each androgen/metabolite were used and adjusted for gravidity, smoking status, body mass index (age stratified models), duration of oral contraceptive use, and age at menarche and additionally adjusted for matching factors: age at baseline (age and BMI stratified models), year of blood draw, race/ethnicity, time since last menopausal hormone therapy use

*Chi-square P values from the cross-product interaction terms between the modifiers of interest and hormone exposures

†P for trend across quintiles of a given hormone/metabolite