

WEB MATERIAL

Endogenous Steroid Hormone Concentrations and Risk of Endometriosis in Nurses' Health Study II

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Contents

Web Tables 1–5

Web Table 1. Relative risks (and 95% confidence intervals) of laparoscopically confirmed endometriosis by quartile of plasma sex steroid hormone levels utilizing unconditional logistic regression

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	<i>P</i> for Trend ¹
Estradiol					
Follicular					
Cutpoints (pg/mL)	<27	≥27 – <40	≥40 – <59	≥59	
Cases/controls	54/164	117/166	93/168	83/165	
Multivariable ²	1.00	2.76 (1.78,4.28)	2.19 (1.38,3.46)	1.95 (1.23,3.11)	0.16
Luteal					
Cutpoints (pg/mL)	<98	≥98 – <133	≥133 – <187	≥187	
Cases/controls	89/186	104/180	106/190	78/185	
Multivariable	1.00	1.29 (0.88,1.91)	1.35 (0.92,1.99)	0.84 (0.56,1.27)	0.26
Free Estradiol					
Follicular					
Cutpoints (pg/mL)	<0.34	≥0.34 – <0.49	≥0.49 – <0.71	≥0.71	
Cases/controls	64/164	98/164	112/164	70/164	
Multivariable	1.00	1.69 (1.10,2.58)	2.23 (1.45,3.43)	1.19 (0.76,1.88)	0.86
Luteal					
Cutpoints (pg/mL)	<1.23	≥1.23 – <1.63	≥1.63 – <2.21	≥2.21	
Cases/controls	94/185	111/185	84/185	88/185	
Multivariable	1.00	1.29 (0.88,1.88)	0.87 (0.58,1.30)	0.97 (0.65,1.45)	0.50
Estrone					
Follicular					
Cutpoints (pg/mL)	<30	≥30 – <38	≥38 – <49	≥49	
Cases/controls	74/170	82/161	87/171	104/165	
Multivariable	1.00	1.17 (0.77,1.78)	1.12 (0.73,1.72)	1.49 (0.99,2.26)	0.06
Luteal					
Cutpoints (pg/mL)	<65	≥65 – <85	≥85 – <117	≥117	
Cases/controls	86/184	89/185	124/188	79/184	
Multivariate	1.00	1.08 (0.73,1.60)	1.50 (1.02,2.18)	0.86 (0.57,1.30)	0.58
Testosterone					
Cutpoints (ng/dL)	<19	≥19 – <25	≥25 – <32	≥32	
Cases/controls	109/212	144/225	91/214	97/216	
Multivariable	1.00	1.33 (0.95,1.87)	0.93 (0.65,1.35)	0.94 (0.64,1.38)	0.31
Free testosterone					
Cutpoints (ng/dL)	<0.13	≥0.13 – <0.19	≥0.19 – <0.27	≥0.27	
Cases/controls	106/208	106/208	108/209	105/208	
Multivariable	1.00	1.07 (0.74,1.53)	1.08 (0.74,1.58)	1.03 (0.68,1.55)	0.94
Progesterone					
Luteal					
Cutpoints (ng/mL)	<7	≥7 – <14	≥14 – <20	≥20	
Cases/controls	106/188	92/188	106/188	78/188	
Multivariable	1.00	0.88 (0.59,1.29)	1.16 (0.78,1.71)	0.90 (0.58,1.40)	0.94
SHBG					
Cutpoints (nmol/L)	<47	≥47 – <68	≥68 – <94	≥94	
Cases/controls	110/209	103/209	113/211	101/209	
Multivariable	1.00	1.12 (0.77,1.64)	1.18 (0.80,1.76)	1.08 (0.71,1.64)	0.81

¹ *P* values were calculated by the Wald test of a score variable that contained median values of tertiles.

² Relative risks and 95% CIs were estimated by unconditional logistic regression adjusting for age, race, infertility history, menopausal status at diagnosis, time of day and fasting status at blood draw, birth weight (not full term, <5.5, 5.5-6.9, 7.0-8.4, ≥8.5 pounds), age at menarche (<12, 12, >12 years), body mass index (BMI) at age 18 (<18.5, 18.5-22.4, 22.5-24.9, ≥25 kg/m²) and at blood draw (<22.5, 22.5-24.9, 25.0-29.9, ≥30 kg/m²), number of pregnancies >6 months (0, 1-2, >2 births), total months of breast feeding (nulliparous, 0 or <1, 1-11, 12-23, ≥24 months), time since last birth (<2, 2-3, 4-5, ≥6 years), age at first birth (<25, 25-29, 30-34, ≥35 years), smoking history (never, past,

current), oral contraceptive use (ever, never), alcohol consumption (0, 0-5, >5 g/day), diet score tertiles, physical activity (<3, 3-8, 9-17, \geq 18 METs/week), menstrual cycle length at age 18-22 (<26, 26-31, 32-39, \geq 40 days), adult menstrual cycle length (<26, 26-31, \geq 32 days), menstrual cycle pattern at age 18-22 and adult menstrual cycle pattern (very regular, regular, irregular).

Web Table 2. Relative risks (and 95% confidence intervals) of laparoscopically confirmed endometriosis by quartile of plasma sex steroid hormone levels among Nurses' Health Study II participants with ovulatory cycles¹

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for Trend ²
Estradiol					
Follicular					
Cutpoints (pg/mL)	<27	≥27 – <40	≥40 – <59	≥59	
Cases/controls	47/101	91/124	82/141	72/128	
Multivariable ³	1.00	1.56 (0.94, 2.58)	1.25 (0.75, 2.09)	1.09 (0.63, 1.90)	0.26
Luteal					
Cutpoints (pg/mL)	<98	≥98 – <133	≥133 – <187	≥187	
Cases/controls	61/113	93/155	98/160	67/133	
Multivariable	1.00	1.15 (0.71, 1.89)	1.18 (0.74, 1.89)	0.85 (0.51, 1.43)	0.11
Free Estradiol					
Follicular					
Cutpoints (pg/mL)	<0.34	≥0.34 – <0.49	≥0.49 – <0.71	≥0.71	
Cases/controls	54/113	82/123	99/130	57/128	
Multivariable	1.00	1.36 (0.82, 2.25)	1.64 (1.00, 2.69)	0.70 (0.40, 1.21)	0.74
Luteal					
Cutpoints (pg/mL)	<1.23	≥1.23 – <1.63	≥1.63 – <2.21	≥2.21	
Cases/controls	70/117	100/154	76/160	73/130	
Multivariable	1.00	1.11 (0.71, 1.74)	0.67 (0.42, 1.07)	0.85 (0.52, 1.40)	0.13
Estrone					
Follicular					
Cutpoints (pg/mL)	<30	≥30 – <38	≥38 – <49	≥49	
Cases/controls	60/122	72/124	75/138	85/113	
Multivariable	1.00	1.10 (0.66, 1.83)	0.85 (0.52, 1.39)	1.36 (0.83, 2.23)	0.15
Luteal					
Cutpoints (pg/mL)	<65	≥65 – <85	≥85 – <117	≥117	
Cases/controls	70/129	79/158	108/154	62/120	
Multivariate	1.00	0.89 (0.57, 1.40)	1.38 (0.88, 2.16)	0.94 (0.57, 1.57)	0.37
Testosterone					
Cutpoints (ng/dL)	<19	≥19 – <25	≥25 – <32	≥32	
Cases/controls	79/126	104/165	73/147	65/125	
Multivariable	1.00	1.16 (0.76, 1.78)	0.85 (0.54, 1.35)	0.87 (0.54, 1.40)	0.18
Free testosterone					
Cutpoints (ng/dL)	<0.13	≥0.13 – <0.19	≥0.19 – <0.27	≥0.27	
Cases/controls	83/135	89/160	86/151	63/117	
Multivariable	1.00	0.87 (0.57, 1.34)	0.94 (0.60, 1.47)	0.79 (0.47, 1.33)	0.77
Progesterone					
Luteal					
Cutpoints (ng/mL)	<7	≥7 – <14	≥14 – <20	≥20	
Cases/controls	45/52	92/170	106/163	78/179	
Multivariable	1.00	0.48 (0.27, 0.86)	0.61 (0.34, 1.10)	0.44 (0.24, 0.82)	0.31
SHBG					
Cutpoints (nmol/L)	<47	≥47 – <68	≥68 – <94	≥94	
Cases/controls	68/124	81/146	94/150	78/144	
Multivariable	1.00	1.12 (0.69, 1.79)	1.30 (0.80, 2.10)	1.11 (0.66, 1.87)	0.86

¹ Ovulatory cycles were defined as progesterone levels of ≥4 ng/mL.

² P values were calculated by the Wald test of a score variable that contained median values of tertiles.

³ Relative risks and 95% CIs were estimated by conditional logistic regression conditioned on the matching factors including age, race, infertility history, menopausal status at diagnosis, as well as month, time of day and fasting status at blood draw and further adjusted for birth weight (not full term, <5.5, 5.5-6.9, 7.0-8.4, ≥8.5 pounds), age at menarche (<12, 12, >12 years), body mass index (BMI) at age 18 (<18.5, 18.5-22.4, 22.5-24.9, ≥25 kg/m²) and at blood draw (<22.5, 22.5-24.9, 25.0-29.9, ≥30 kg/m²), number of pregnancies >6 months (0, 1-2, >2 births), total

months of breast feeding (nulliparous, 0 or <1, 1-11, 12-23, ≥ 24 months), time since last birth (<2, 2-3, 4-5, ≥ 6 years), age at first birth (<25, 25-29, 30-34, ≥ 35 years), smoking history (never, past, current), oral contraceptive use (ever, never), alcohol consumption (0, 0-5, >5 g/day), diet score tertiles, physical activity (<3, 3-8, 9-17, ≥ 18 METs/week), menstrual cycle length at age 18-22 (<26, 26-31, 32-39, ≥ 40 days), adult menstrual cycle length (<26, 26-31, ≥ 32 days), menstrual cycle pattern at age 18-22 and adult menstrual cycle pattern (very regular, regular, irregular).

Web Table 3. Relative risks (and 95% confidence intervals)¹ of laparoscopically confirmed endometriosis by quartiles of plasma sex steroid levels among subgroups in Nurses' Health Study II

	Quartile 2	Quartile 3	Quartile 4	<i>P</i> _{trend} ²	Quartile 2	Quartile 3	Quartile 4	<i>P</i> _{trend} ²	<i>P</i> _{LRT} ³
Hormone	Age at Diagnosis <45 Years (cases/controls: 16-45/27-66)				Age at Diagnosis ≥45 Years (cases/controls: 32-99/113-173)				
Follicular E2	1.33 (0.63,2.81)	0.91 (0.41,2.02)	1.36 (0.60,3.10)	0.63	3.41 (2.05,5.66)	2.86 (1.70,4.81)	2.09 (1.24,3.54)	0.22	0.08
Luteal E2	0.90 (0.44,1.83)	1.37 (0.71,2.67)	0.84 (0.42,1.66)	0.72	1.36 (0.88,2.10)	1.23 (0.79,1.91)	0.89 (0.56,1.42)	0.36	0.54
Follicular Free E2	1.26 (0.60,2.67)	1.48 (0.71,3.08)	1.13 (0.47,2.72)	0.76	1.80 (1.11,2.93)	2.42 (1.49,3.93)	1.34 (0.82,2.20)	0.63	0.72
Luteal Free E2	2.16 (1.10,4.23)	1.42 (0.69,2.92)	1.57 (0.78,3.17)	0.45	0.98 (0.64,1.51)	0.77 (0.49,1.21)	0.86 (0.55,1.34)	0.40	0.33
Follicular Estrone	1.58 (0.75,3.34)	1.04 (0.47,2.27)	1.98 (0.89,4.37)	0.16	1.06 (0.65,1.71)	1.40 (0.88,2.23)	1.60 (1.02,2.52)	0.02	0.46
Luteal Estrone	1.20 (0.60,2.41)	1.70 (0.89,3.27)	1.41 (0.70,2.84)	0.27	0.99 (0.63,1.56)	1.29 (0.83,1.99)	0.79 (0.50,1.26)	0.36	0.60
Testosterone	1.75 (0.91,3.36)	0.94 (0.48,1.86)	0.70 (0.35,1.42)	0.09	1.25 (0.85,1.83)	0.90 (0.59,1.38)	1.00 (0.65,1.52)	0.58	0.61
Free testosterone	1.40 (0.71,2.74)	0.92 (0.48,1.78)	1.19 (0.63,2.24)	0.81	0.99 (0.66,1.50)	1.16 (0.77,1.75)	1.04 (0.68,1.60)	0.77	0.52
Progesterone	0.87 (0.41,1.86)	1.23 (0.62,2.46)	0.65 (0.31,1.38)	0.39	0.86 (0.56,1.31)	0.97 (0.63,1.51)	0.85 (0.53,1.39)	0.65	0.64
SHBG	1.35 (0.71,2.55)	0.72 (0.37,1.39)	0.66 (0.35,1.26)	0.07	0.84 (0.55,1.27)	1.13 (0.76,1.68)	1.04 (0.69,1.57)	0.57	0.12
Hormone	BMI at Blood Draw <25 kg/m² (cases/controls: 24-83/44-179)				BMI at Blood Draw ≥25 kg/m² (cases/controls: 18-79/30-165)				
Follicular E2	2.26 (1.23,4.14)	1.76 (0.96,3.23)	2.08 (1.14,3.80)	0.13	3.24 (1.79,5.86)	2.90 (1.50,5.59)	1.57 (0.78,3.18)	0.40	0.36
Luteal E2	0.98 (0.60,1.61)	0.86 (0.52,1.41)	0.68 (0.41,1.13)	0.09	1.51 (0.85,2.68)	2.19 (1.24,3.88)	1.15 (0.62,2.13)	0.51	0.12
Follicular Free E2	1.37 (0.81,2.32)	1.89 (1.12,3.19)	1.26 (0.71,2.22)	0.50	1.85 (0.96,3.56)	2.30 (1.19,4.46)	1.21 (0.62,2.35)	0.91	0.81
Luteal Free E2	1.15 (0.74,1.79)	0.89 (0.55,1.45)	0.64 (0.38,1.08)	0.05	1.21 (0.64,2.27)	0.92 (0.49,1.73)	1.54 (0.84,2.80)	0.17	0.04
Follicular Estrone	1.21 (0.72,2.03)	1.19 (0.70,2.01)	1.80 (1.08,3.01)	0.02	1.12 (0.59,2.15)	1.48 (0.79,2.77)	1.42 (0.77,2.64)	0.26	0.71
Luteal Estrone	1.16 (0.71,1.88)	1.44 (0.91,2.28)	0.83 (0.49,1.41)	0.55	0.89 (0.49,1.62)	1.30 (0.72,2.34)	1.00 (0.55,1.79)	0.85	0.64
Testosterone	1.05 (0.68,1.62)	0.87 (0.54,1.39)	0.92 (0.58,1.47)	0.57	1.86 (1.12,3.12)	1.00 (0.57,1.73)	0.84 (0.47,1.52)	0.12	0.16
Free testosterone	1.38 (0.92,2.07)	1.06 (0.67,1.67)	1.49 (0.89,2.49)	0.23	0.47 (0.23,0.95)	0.72 (0.38,1.36)	0.53 (0.28,1.00)	0.19	0.03
Progesterone	0.74 (0.44,1.24)	0.61 (0.37,0.99)	0.56 (0.33,0.93)	0.02	0.94 (0.54,1.63)	2.34 (1.30,4.19)	1.22 (0.59,2.51)	0.09	0.002
SHBG	0.63 (0.35,1.14)	0.76 (0.43,1.33)	0.67 (0.38,1.16)	0.41	1.27 (0.80,2.00)	1.26 (0.73,2.17)	1.40 (0.72,2.75)	0.24	0.24
Hormone	Nulliparous (cases/controls: 11-40/24-49)				Parous (cases/controls: 43-111/127-181)				
Follicular E2	2.30 (1.44,3.67)	1.81 (1.11,2.96)	1.62 (0.99,2.66)	0.37	4.48 (1.68,11.9)	3.07 (1.15,8.17)	2.44 (0.88,6.73)	0.53	0.66
Luteal E2	1.11 (0.74,1.69)	0.91 (0.59,1.38)	0.82 (0.53,1.27)	0.23	1.35 (0.57,3.17)	3.04 (1.34,6.91)	1.17 (0.50,2.73)	0.59	0.01
Follicular Free E2	1.45 (0.92,2.30)	1.86 (1.17,2.94)	1.16 (0.71,1.89)	0.75	2.31 (0.91,5.83)	2.61 (1.00,6.78)	1.20 (0.46,3.10)	0.65	0.63
Luteal Free E2	1.05 (0.70,1.58)	0.85 (0.55,1.33)	0.92 (0.60,1.41)	0.57	2.29 (0.99,5.29)	1.03 (0.46,2.31)	1.54 (0.66,3.63)	0.66	0.29
Follicular Estrone	1.08 (0.69,1.70)	1.09 (0.69,1.73)	1.53 (0.99,2.37)	0.04	1.74 (0.67,4.54)	2.09 (0.83,5.27)	2.01 (0.77,5.25)	0.27	0.75
Luteal Estrone	0.86 (0.56,1.32)	1.20 (0.79,1.81)	0.85 (0.55,1.31)	0.67	2.39 (1.03,5.56)	2.68 (1.19,6.05)	1.40 (0.57,3.44)	0.63	0.27
Testosterone	1.33 (0.92,1.92)	0.75 (0.50,1.14)	0.75 (0.50,1.14)	0.03	1.30 (0.60,2.80)	1.48 (0.69,3.17)	1.49 (0.67,3.34)	0.33	0.20
Free testosterone	0.86 (0.58,1.29)	0.88 (0.60,1.31)	0.93 (0.62,1.39)	0.81	2.45 (1.12,5.37)	2.28 (1.01,5.12)	1.76 (0.80,3.85)	0.46	0.09
Progesterone	0.82 (0.54,1.25)	0.94 (0.62,1.42)	0.69 (0.43,1.10)	0.19	1.38 (0.60,3.13)	1.93 (0.83,4.50)	1.72 (0.72,4.13)	0.17	0.38
SHBG	0.98 (0.66,1.45)	1.00 (0.68,1.48)	0.88 (0.59,1.32)	0.56	1.16 (0.53,2.54)	1.30 (0.63,2.69)	1.14 (0.56,2.33)	0.72	0.99
Hormone	Never Smoker (cases/controls: 40-107/102-161)				Ever Smoker (cases/controls: 14-38/42-88)				

Follicular E2	2.27 (1.39,3.70)	1.65 (0.99,2.75)	1.42 (0.85,2.37)	0.90	3.11 (1.42,6.82)	2.91 (1.29,6.57)	2.88 (1.25,6.64)	0.06	0.57
Luteal E2	1.31 (0.84,2.04)	1.59 (1.03,2.46)	1.02 (0.64,1.61)	0.98	0.99 (0.51,1.92)	0.67 (0.33,1.37)	0.59 (0.28,1.23)	0.10	0.16
Follicular Free E2	1.49 (0.92,2.41)	1.56 (0.97,2.51)	0.96 (0.58,1.60)	0.50	1.86 (0.85,4.10)	4.28 (1.95,9.44)	2.12 (0.94,4.77)	0.09	0.13
Luteal Free E2	1.37 (0.89,2.10)	1.07 (0.68,1.66)	1.05 (0.67,1.63)	0.82	1.05 (0.53,2.10)	0.59 (0.28,1.26)	1.06 (0.52,2.19)	0.94	0.38
Follicular Estrone	0.78 (0.48,1.27)	1.09 (0.68,1.74)	1.43 (0.90,2.27)	0.03	2.76 (1.33,5.72)	1.64 (0.74,3.61)	2.14 (0.99,4.61)	0.25	0.03
Luteal Estrone	1.09 (0.69,1.70)	1.42 (0.92,2.17)	1.15 (0.73,1.81)	0.46	1.03 (0.51,2.07)	1.35 (0.69,2.64)	0.53 (0.24,1.15)	0.12	0.26
Testosterone	1.26 (0.86,1.86)	0.95 (0.62,1.44)	1.06 (0.69,1.64)	0.83	1.59 (0.84,3.03)	0.89 (0.44,1.78)	0.75 (0.37,1.51)	0.13	0.78
Free testosterone	0.89 (0.59,1.34)	1.02 (0.68,1.55)	1.03 (0.68,1.58)	0.72	1.58 (0.80,3.12)	1.20 (0.61,2.37)	1.36 (0.68,2.69)	0.64	0.40
Progesterone	1.05 (0.67,1.64)	1.14 (0.74,1.77)	1.00 (0.62,1.62)	0.90	0.48 (0.24,0.96)	0.73 (0.37,1.46)	0.42 (0.19,0.93)	0.08	0.10
SHBG	1.05 (0.70,1.59)	1.10 (0.73,1.66)	1.07 (0.72,1.61)	0.72	0.81 (0.43,1.54)	0.83 (0.44,1.54)	0.62 (0.31,1.22)	0.19	0.52

¹All relative risks and 95% CIs were estimated by conditional logistic regression conditioned on matching factors including age, race, infertility history, menopausal status at diagnosis, month of blood draw, time of blood draw, and fasting status at blood draw with Quartile 1 as the reference group.

²*P* values were calculated by the Wald test of a score variable that contained median values of the quartiles.

³*P* values calculated from Likelihood ratio tests of the interaction terms.

Web Table 4. Relative risks (and 95% confidence intervals) of laparoscopically confirmed endometriosis by quartile of plasma sex steroid hormone levels among Nurses' Health Study II participants with follicular estradiol levels <80 pg/mL

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for Trend ¹
Estradiol					
Follicular					
Cutpoints (pg/mL)	<27	≥27 – <40	≥40 – <59	≥59	
Cases/controls	53/146	115/147	92/145	44/73	
Multivariable ²	1.00	2.40 (1.50, 3.83)	1.98 (1.22, 3.21)	1.66 (0.93, 2.96)	0.17
Luteal					
Cutpoints (pg/mL)	<98	≥98 – <133	≥133 – <187	≥187	
Cases/controls	77/137	95/150	92/166	72/139	
Multivariable	1.00	1.20 (0.75, 1.90)	1.03 (0.64, 1.66)	0.84 (0.51, 1.37)	0.27
Free Estradiol					
Follicular					
Cutpoints (pg/mL)	<0.34	≥0.34 – <0.49	≥0.49 – <0.71	≥0.71	
Cases/controls	62/151	96/139	104/145	40/72	
Multivariable	1.00	1.98 (1.22, 3.20)	2.15 (1.35, 3.45)	1.18 (0.66, 2.11)	0.48
Luteal					
Cutpoints (pg/mL)	<1.23	≥1.23 – <1.63	≥1.63 – <2.21	≥2.21	
Cases/controls	76/137	100/149	76/153	84/152	
Multivariable	1.00	1.22 (0.78, 1.91)	0.79 (0.49, 1.27)	0.87 (0.54, 1.40)	0.27
Estrone					
Follicular					
Cutpoints (pg/mL)	<30	≥30 – <38	≥38 – <49	≥49	
Cases/controls	72/151	79/142	83/139	70/82	
Multivariable	1.00	1.15 (0.72, 1.83)	1.04 (0.65, 1.66)	1.63 (0.98, 2.71)	0.07
Luteal					
Cutpoints (pg/mL)	<65	≥65 – <85	≥85 – <117	≥117	
Cases/controls	77/140	76/154	110/151	73/147	
Multivariate	1.00	0.90 (0.57, 1.40)	1.46 (0.94, 2.26)	0.77 (0.48, 1.25)	0.45
Testosterone					
Cutpoints (ng/dL)	<19	≥19 – <25	≥25 – <32	≥32	
Cases/controls	95/176	132/185	84/173	88/182	
Multivariable	1.00	1.39 (0.96, 2.02)	0.90 (0.60, 1.34)	0.93 (0.62, 1.40)	0.25
Free testosterone					
Cutpoints (ng/dL)	<0.13	≥0.13 – <0.19	≥0.19 – <0.27	≥0.27	
Cases/controls	84/157	97/172	102/172	100/181	
Multivariable	1.00	0.97 (0.65, 1.46)	1.12 (0.74, 1.70)	0.93 (0.59, 1.46)	0.79
Progesterone					
Luteal					
Cutpoints (ng/mL)	<7	≥7 – <14	≥14 – <20	≥20	
Cases/controls	94/148	83/155	94/153	69/145	
Multivariable	1.00	0.77 (0.48, 1.22)	0.94 (0.59, 1.51)	0.79 (0.47, 1.33)	0.53
SHBG					
Cutpoints (nmol/L)	<47	≥47 – <68	≥68 – <94	≥94	
Cases/controls	107/177	95/179	104/176	79/155	
Multivariable	1.00	0.94 (0.63, 1.41)	1.09 (0.72, 1.65)	0.94 (0.60, 1.49)	0.91

¹ P values were calculated by the Wald test of a score variable that contained median values of tertiles.

² Relative risks and 95% CIs were estimated by conditional logistic regression conditioned on the matching factors including age, race, infertility history, menopausal status at diagnosis, as well as month, time of day and fasting status at blood draw and further adjusted for birth weight (not full term, <5.5, 5.5-6.9, 7.0-8.4, ≥8.5 pounds), age at menarche (<12, 12, >12 years), body mass index (BMI) at age 18 (<18.5, 18.5-22.4, 22.5-24.9, ≥25 kg/m²) and at blood draw (<22.5, 22.5-24.9, 25.0-29.9, ≥30 kg/m²), number of pregnancies >6 months (0, 1-2, >2 births), total months of breast feeding (nulliparous, 0 or <1, 1-11, 12-23, ≥24 months), time since last birth (<2, 2-3, 4-5, ≥6 years),

age at first birth (<25, 25-29, 30-34, ≥35 years), smoking history (never, past, current), oral contraceptive use (ever, never), alcohol consumption (0, 0-5, >5 g/day), diet score tertiles, physical activity (<3, 3-8, 9-17, ≥18 METs/week), menstrual cycle length at age 18-22 (<26, 26-31, 32-39, ≥40 days), adult menstrual cycle length (<26, 26-31, ≥32 days), menstrual cycle pattern at age 18-22 and adult menstrual cycle pattern (very regular, regular, irregular).

Web Table 5. Relative risks (and 95% confidence intervals) of laparoscopically confirmed endometriosis by quartile of plasma sex steroid hormone levels in Nurses' Health Study II after excluding endometriosis cases within 2, 4, and 6 years of diagnosis and their matched controls

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P for Trend ¹
2 Years					
Estradiol					
Follicular					
Cutpoints (pg/mL)	<27	≥27 – <40	≥40 – <59	≥59	
Cases/controls	51/161	115/163	90/163	84/164	
Multivariable ²	1.00	2.33 (1.49, 3.65)	1.91 (1.20, 3.02)	1.75 (1.09, 2.80)	0.20
Luteal					
Cutpoints (pg/mL)	<98	≥98 – <133	≥133 – <187	≥187	
Cases/controls	84/179	104/182	100/181	79/179	
Multivariable	1.00	1.20 (0.80, 1.82)	1.17 (0.77, 1.78)	0.81 (0.52, 1.27)	0.21
Free Estradiol					
Follicular					
Cutpoints (pg/mL)	<0.34	≥0.34 – <0.49	≥0.49 – <0.71	≥0.71	
Cases/controls	63/161	96/161	110/161	68/161	
Multivariable	1.00	1.63 (1.04, 2.55)	2.04 (1.31, 3.17)	1.02 (0.64, 1.62)	0.68
Luteal					
Cutpoints (pg/mL)	<1.23	≥1.23 – <1.63	≥1.63 – <2.21	≥2.21	
Cases/controls	92/180	108/180	83/180	84/180	
Multivariable	1.00	1.13 (0.77, 1.68)	0.78 (0.52, 1.17)	0.78 (0.51, 1.19)	0.11
Estrone					
Follicular					
Cutpoints (pg/mL)	<30	≥30 – <38	≥38 – <49	≥49	
Cases/controls	73/166	80/158	84/169	103/162	
Multivariable	1.00	1.14 (0.74, 1.76)	0.96 (0.62, 1.47)	1.37 (0.90, 2.09)	0.14
Luteal					
Cutpoints (pg/mL)	<65	≥65 – <85	≥85 – <117	≥117	
Cases/controls	82/180	87/182	119/177	80/182	
Multivariate	1.00	1.03 (0.68, 1.55)	1.55 (1.04, 2.31)	0.85 (0.55, 1.34)	0.56
Testosterone					
Follicular					
Cutpoints (ng/dL)	<19	≥19 – <25	≥25 – <32	≥32	
Cases/controls	104/202	134/218	89/206	95/203	
Multivariable	1.00	1.26 (0.89, 1.79)	0.87 (0.59, 1.27)	0.93 (0.63, 1.37)	0.36
Free testosterone					
Follicular					
Cutpoints (ng/dL)	<0.13	≥0.13 – <0.19	≥0.19 – <0.27	≥0.27	
Cases/controls	103/198	99/199	101/199	103/199	
Multivariable	1.00	0.97 (0.67, 1.40)	0.99 (0.68, 1.46)	0.95 (0.63, 1.45)	0.86
Progesterone					
Luteal					
Cutpoints (ng/mL)	<7	≥7 – <14	≥14 – <20	≥20	
Cases/controls	105/183	87/183	106/183	74/183	
Multivariable	1.00	0.77 (0.51, 1.17)	0.96 (0.63, 1.48)	0.69 (0.43, 1.10)	0.21
SHBG					
Follicular					
Cutpoints (nmol/L)	<47	≥47 – <68	≥68 – <94	≥94	
Cases/controls	102/200	93/200	112/199	101/201	
Multivariable	1.00	1.07 (0.72, 1.59)	1.29 (0.87, 1.91)	1.19 (0.77, 1.82)	0.38
4 Years					
Estradiol					
Follicular					
Cutpoints (pg/mL)	<27	≥27 – <41	≥41 – <60	≥60	
Cases/controls	44/134	97/140	81/136	63/137	
Multivariable ³	1.00	2.19 (1.35, 3.57)	1.88 (1.15, 3.07)	1.59 (0.94, 2.68)	0.43

Luteal					
Cutpoints (pg/mL)	<98	≥98 – <134	≥134 – <186	≥186	
Cases/controls	71/149	91/155	77/147	66/150	
Multivariable	1.00	1.20 (0.77, 1.87)	1.05 (0.67, 1.64)	0.79 (0.48, 1.28)	0.19
Free Estradiol					
Follicular					
Cutpoints (pg/mL)	<0.34	≥0.34 – <0.50	≥0.50 – <0.72	≥0.72	
Cases/controls	54/135	84/136	90/136	55/136	
Multivariable	1.00	1.60 (0.97, 2.65)	1.91 (1.18, 3.09)	0.97 (0.57, 1.64)	0.64
Luteal					
Cutpoints (pg/mL)	<1.24	≥1.24 – <1.65	≥1.65 – <2.23	≥2.23	
Cases/controls	78/150	88/150	69/151	70/150	
Multivariable	1.00	1.19 (0.77, 1.83)	0.72 (0.46, 1.13)	0.77 (0.48, 1.23)	0.10
Estrone					
Follicular					
Cutpoints (pg/mL)	<30	≥30 – <38	≥38 – <49	≥49	
Cases/controls	63/138	67/133	70/142	85/137	
Multivariable	1.00	0.98 (0.60, 1.59)	0.87 (0.54, 1.41)	1.25 (0.79, 1.99)	0.25
Luteal					
Cutpoints (pg/mL)	<66	≥66 – <85	≥85 – <117	≥117	
Cases/controls	66/148	73/152	98/151	69/150	
Multivariate	1.00	1.02 (0.65, 1.60)	1.53 (0.98, 2.38)	0.89 (0.55, 1.45)	0.75
Testosterone					
Cutpoints (ng/dL)	<19	≥19 – <25	≥25 – <32	≥32	
Cases/controls	92/176	102/170	73/171	80/167	
Multivariable	1.00	1.31 (0.89, 1.93)	0.87 (0.57, 1.31)	1.02 (0.68, 1.55)	0.61
Free testosterone					
Cutpoints (ng/dL)	<0.14	≥0.14 – <0.19	≥0.19 – <0.26	≥0.26	
Cases/controls	86/163	79/164	78/164	89/163	
Multivariable	1.00	0.91 (0.60, 1.38)	0.88 (0.57, 1.38)	0.99 (0.63, 1.56)	0.95
Progesterone					
Luteal					
Cutpoints (ng/mL)	<8	≥8 – <14	≥14 – <21	≥21	
Cases/controls	90/152	74/151	97/153	47/152	
Multivariable	1.00	0.69 (0.44, 1.09)	0.98 (0.62, 1.55)	0.43 (0.25, 0.74)	0.01
SHBG					
Cutpoints (nmol/L)	<47	≥47 – <67	≥67 – <92	≥92	
Cases/controls	87/164	70/164	90/165	86/164	
Multivariable	1.00	0.98 (0.63, 1.53)	1.28 (0.82, 1.99)	1.29 (0.80, 2.07)	0.22

6 Years

Estradiol					
Follicular					
Cutpoints (pg/mL)	<27	≥27 – <41	≥41 – <59	≥59	
Cases/controls	30/87	58/90	52/91	43/89	
Multivariable ³	1.00	2.16 (1.17, 4.00)	2.14 (1.11, 4.13)	1.96 (0.99, 3.87)	0.20
Luteal					
Cutpoints (pg/mL)	<96	≥96 – <132	≥132 – <184	≥184	
Cases/controls	41/95	57/95	54/97	40/95	
Multivariable	1.00	1.32 (0.72, 2.43)	1.27 (0.69, 2.34)	0.80 (0.42, 1.54)	0.31
Free Estradiol					
Follicular					
Cutpoints (pg/mL)	<0.36	≥0.36 – <0.50	≥0.50 – <0.72	≥0.72	
Cases/controls	39/88	48/89	64/89	31/89	
Multivariable	1.00	1.68 (0.87, 3.24)	2.70 (1.42, 5.13)	0.87 (0.44, 1.72)	0.59
Luteal					
Cutpoints (pg/mL)	<1.22	≥1.22 – <1.62	≥1.62 – <2.18	≥2.18	

Cases/controls	57/95	48/96	42/96	45/95	
Multivariable	1.00	0.64 (0.35, 1.17)	0.52 (0.29, 0.94)	0.58 (0.31, 1.10)	0.10
Estrone					
Follicular					
Cutpoints (pg/mL)	<30	≥30 – <38	≥38 – <48	≥48	
Cases/controls	44/85	34/93	50/90	55/90	
Multivariable	1.00	0.61 (0.32, 1.19)	0.94 (0.51, 1.73)	1.04 (0.57, 1.89)	0.39
Luteal					
Cutpoints (pg/mL)	<66	≥66 – <84	≥84 – <112	≥112	
Cases/controls	45/94	43/97	55/95	50/96	
Multivariate	1.00	0.74 (0.41, 1.34)	1.07 (0.60, 1.89)	0.88 (0.48, 1.63)	0.95
Testosterone					
Cutpoints (ng/dL)	<19	≥19 – <25	≥25 – <31	≥31	
Cases/controls	52/105	62/109	48/108	55/109	
Multivariable	1.00	1.35 (0.81, 2.24)	0.99 (0.58, 1.69)	1.12 (0.65, 1.94)	0.97
Free testosterone					
Cutpoints (ng/dL)	<0.14	≥0.14 – <0.18	≥0.18 – <0.26	≥0.26	
Cases/controls	47/100	50/101	52/101	54/101	
Multivariable	1.00	0.97 (0.54, 1.75)	1.13 (0.61, 2.09)	1.09 (0.59, 2.02)	0.73
Progesterone					
Luteal					
Cutpoints (ng/mL)	<8	≥8 – <14	≥14 – <20	≥20	
Cases/controls	60/96	48/95	50/96	35/96	
Multivariable	1.00	0.65 (0.35, 1.18)	0.66 (0.34, 1.27)	0.38 (0.18, 0.82)	0.02
SHBG					
Cutpoints (nmol/L)	<46	≥46 – <66	≥66 – <90	≥90	
Cases/controls	52/100	39/101	51/101	61/101	
Multivariable	1.00	0.96 (0.51, 1.78)	1.22 (0.64, 2.33)	1.51 (0.80, 2.88)	0.13

¹ P values were calculated by the Wald test of a score variable that contained median values of tertiles.

² Relative risks and 95% CIs were estimated by conditional logistic regression conditioned on the matching factors including age, race, infertility history, menopausal status at diagnosis, as well as month, time of day and fasting status at blood draw and further adjusted for birth weight (not full term, <5.5, 5.5-6.9, 7.0-8.4, ≥8.5 pounds), age at menarche (<12, 12, >12 years), body mass index (BMI) at age 18 (<18.5, 18.5-22.4, 22.5-24.9, ≥25 kg/m²) and at blood draw (<22.5, 22.5-24.9, 25.0-29.9, ≥30 kg/m²), number of pregnancies >6 months (0, 1-2, >2 births), total months of breast feeding (nulliparous, 0 or <1, 1-11, 12-23, ≥24 months), time since last birth (<2, 2-3, 4-5, ≥6 years), age at first birth (<25, 25-29, 30-34, ≥35 years), smoking history (never, past, current), oral contraceptive use (ever, never), alcohol consumption (0, 0-5, >5 g/day), diet score tertiles, physical activity (<3, 3-8, 9-17, ≥18 METs/week), menstrual cycle length at age 18-22 (<26, 26-31, 32-39, ≥40 days), adult menstrual cycle length (<26, 26-31, ≥32 days), menstrual cycle pattern at age 18-22 and adult menstrual cycle pattern (very regular, regular, irregular).