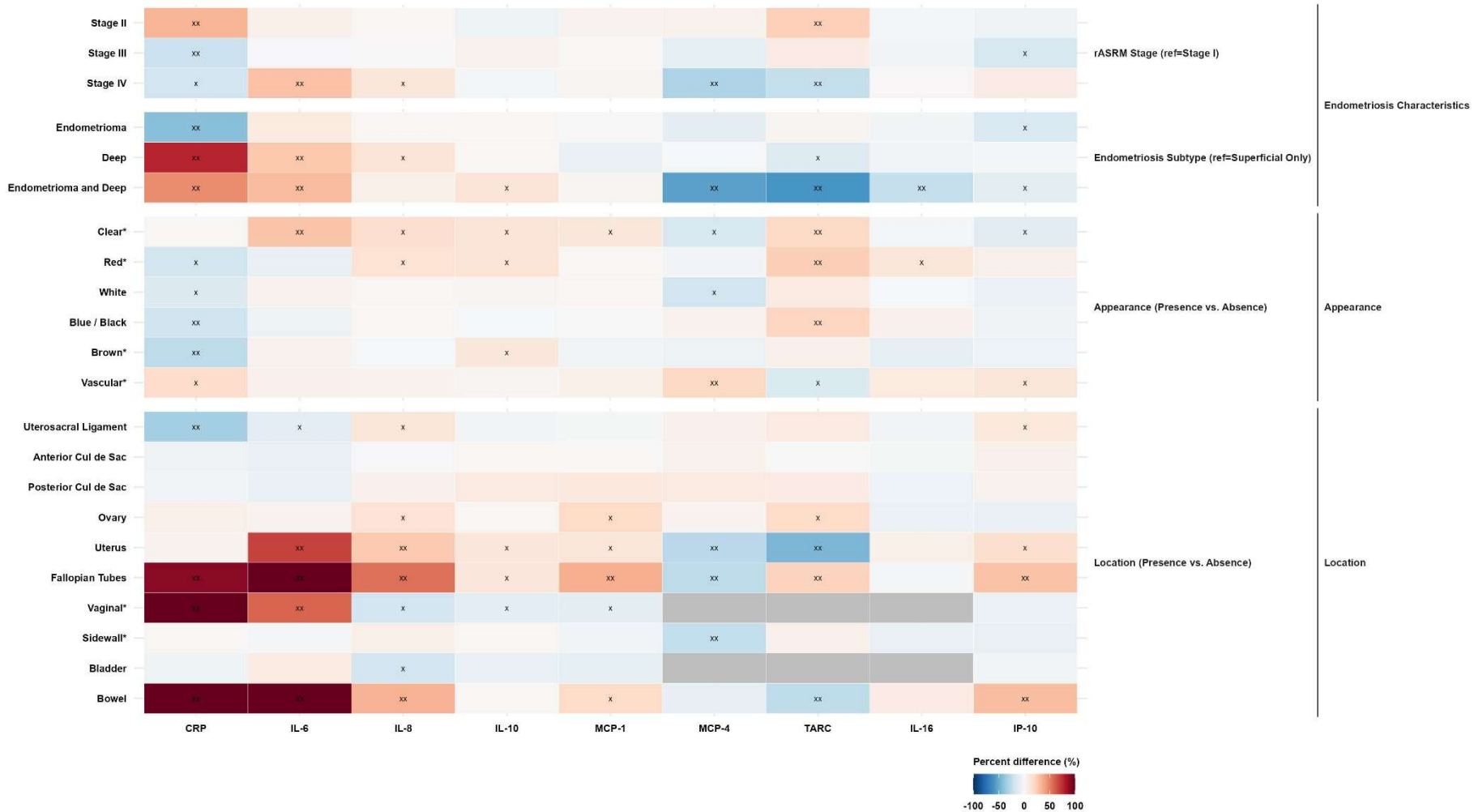


**Supplementary Figure 1. Percent difference in blood inflammatory biomarker levels by lesion characteristics restricted to those using hormones at time of blood collection.**

Reference group for rASRM stage is Stage I and reference for endometriosis subtype is superficial peritoneal, and absence of that lesion type for color and location. Models are adjusted for study site, age at blood draw, body mass index, and analgesic use. 'X' indicates >10% difference and 'XX' indicates >20% difference in inflammatory biomarker level by lesion characteristic. Asterisk ('\*') indicates the lesion characteristic was not available in the ENDO study and therefore ENDO participants were not included in those analyses. Gray squares indicate that values were missing for this marker because no participants were in the comparison group. A few measurements fell outside the scale of -100 to 100 percent change. The actual values are as follows: 639.57% increase in CRP for vaginal lesions, 106.32% increase in CRP for bowel lesions, 189.38% increase in IL-6 for fallopian tube lesions, and 102.5% increase in IL-6 for bowel lesions.



**Supplementary Table 1. Reasons for exclusion and final analytic sample size for each inflammatory marker among baseline blood samples assayed from three studies The Women's Health Study: From Adolescence to Adulthood (A2A), Endometriosis cohort studies in Oxford (ENDOX), and Endometriosis, Natural History, Diagnosis, and Outcomes (ENDO).**

Inflammation Marker	Luminex Assay Only				Ella Immunoassay and Luminex Recalibration <sup>1</sup>			Ella Immunoassay Only				
	MCP-4	TARC	IL-16	TNFAlpha	IL-8	MPC-1	IP-10	CRP	IL-1 $\beta$	IL-6	IL-10	TNFAlpha
<b>Blood samples sent to laboratory***</b>	638	638	638	637	1186	1186	1186	1186	1186	1186	1186	665
<b>Exclusions</b>												
Non-detectable levels	--	15*	--	*	*	--	*	--	**	*	*	--
Outliers <sup>2</sup>	--	1	5	9	13	4	7	--	--	6	15	2
Intra-assay batch CV>30%	--	--	--		--	--	--	42	--	--	--	--
Controls	303	296	302	299	527	526	527	508	527	526	522	309
Surgical form not completed at time of enrollment	51	51	51	51	65	65	65	58	65	64	65	18
Blood collected after surgery	5	5	5	5	14	14	14	14	14	14	14	10
Lesion details missing on surgical form	2	2	2	2	4	4	4	4	4	4	4	2
Using immune modulating drugs at time of blood draw	5	5	5	4	10	10	10	10	10	10	9	6
<b>Final analytic sample</b>	<b>272</b>	<b>263</b>	<b>268</b>	<b>267</b>	<b>553</b>	<b>563</b>	<b>559</b>	<b>550</b>	<b>566</b>	<b>562</b>	<b>557</b>	<b>318</b>

\*\*\*All 638 samples measured on the Luminex assay were from A2A, among the 1186 samples measured on the Ella assay, 957 were from A2A, 130 from NICHD, and 99 from Oxford.

\*Samples below the limit of detection were extrapolated for some of the inflammatory markers: TARC – 25 cases/21 controls; IL-8 – 10 cases/4 controls; IP-10 – 1 case; IL-6 – 19 cases/13 controls; IL-10 – 45 cases/28 controls; Luminex TNFAlpha – 3 cases/2 controls. These participants are included in the main analyses but removed for sensitivity analyses

\*\*For IL-1 $\beta$ , 389 endometriosis cases and 237 controls had values below the lower limit of detection, which were incorporated into the bottom category of the categorical variable created for IL-1 $\beta$  levels

<sup>1</sup>For IL-8, MCP-1, and IP-10, 335 cases and 303 controls were assayed on the Luminex platform while 355 cases and 310 controls were assayed on the Ella Immunoassay. Samples were recalibrated between the two assays utilizing 117 samples that were run on both assays. In the final analytic sample set, 247 cases for IL-8, 247 cases for MCP-1, and 242 cases for IP-10 were run on the Luminex assay with the remaining run on Ella Immunoassay

<sup>2</sup>Outliers were detected utilizing the generalized extreme studentized deviate many-outlier detection approach

**Supplementary Table 2. Associations between endometriosis rASRM stage, lesion macrophenotype, appearance, and location and IL-1beta among endometriosis cases from A2A, ENDOX, and ENDO.**

	Interleukin-1beta (IL-1beta) level			OR (95%CI)	
	<LLD	>LLD to median	>Median	>LLD to median vs. <LLD OR (95% CI)	>Median vs. <LLD OR (95% CI)
<b>Lesion location</b>					
Uterosacral ligament					
No	260 (74%)	91 (83%)	82 (77%)	1.00 (ref)	1.00 (ref)
Yes	89 (26%)	19 (17%)	25 (23%)	0.78 (0.43, 1.40)	1.08 (0.62, 1.88)
Anterior cul de sac					
No	213 (61%)	67 (61%)	57 (53%)	1.00 (ref)	1.00 (ref)
Yes	136 (39%)	43 (39%)	50 (47%)	1.09 (0.68, 1.74)	1.31 (0.83, 2.07)
Posterior cul de sac					
No	101 (29%)	38 (35%)	29 (27%)	1.00 (ref)	1.00 (ref)
Yes	248 (71%)	72 (65%)	78 (73%)	0.89 (0.49, 1.65)	0.80 (0.43, 1.49)
Ovary					
No	296 (85%)	96 (87%)	92 (86%)	1.00 (ref)	1.00 (ref)
Yes	53 (15%)	14 (13%)	15 (14%)	0.81 (0.40, 1.67)	1.31 (0.64, 2.69)
Uterus					
No	330 (95%)	101 (92%)	98 (92%)	1.00 (ref)	1.00 (ref)
Yes	19 (5%)	9 (8%)	9 (8%)	2.00 (0.81, 4.90)	2.13 (0.87, 5.24)
Fallopian tubes					
No	336 (96%)	108 (98%)	101 (94%)	1.00 (ref)	1.00 (ref)
Yes	13 (4%)	2 (2%)	6 (6%)	0.52 (0.11, 2.43)	2.02 (0.70, 5.80)
Vagina					
No	267 (98%)	76 (99%)	88 (100%)	1.00 (ref)	--
Yes	6 (2%)	1 (1%)	0 (0%)	1.29 (0.13, 12.4)	--
Sidewall					
No	92 (34%)	23 (30%)	24 (27%)	1.00 (ref)	1.00 (ref)
Yes	181 (66%)	54 (70%)	64 (73%)	1.20 (0.68, 2.12)	1.31 (0.75, 2.28)
Bladder					
No	346 (99%)	108 (98%)	105 (98%)	1.00 (ref)	1.00 (ref)
Yes	3 (1%)	2 (2%)	2 (2%)	3.06 (0.43, 21.71)	3.57 (0.53, 24.0)
Bowel					
No	338 (97%)	108 (98%)	103 (96%)	1.00 (ref)	1.00 (ref)
Yes	11 (3%)	2 (2%)	4 (4%)	0.98 (0.20, 4.95)	1.69 (0.47, 6.02)

Odds ratio (95% confidence interval) from polytomous logistic regression model adjusted for age at blood draw (continuous), BMI (underweight, normal weight, overweight, obese), study site (A2A, ENDO, ENDOX), hormone use at time of blood draw (no, yes), and pain medication use (no, yes, missing).

**Supplementary Table 3. Associations between endometriosis rASRM stage, lesion macrophenotype, appearance, and location and inflammatory biomarker levels, stratified by pain medication use, among endometriosis cases from A2A, ENDOX, and ENDO.**

	C-Reactive Protein (CRP)				Interleukin-6 (IL-6)				Interleukin-8 (IL-8)			
	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)
<b>ASRM Stage</b>												
Stage I	108 (64%)	207 (74%)	1.74 (1.34, 2.25)	1.63 (1.35, 1.96)	111 (65%)	215 (74%)	1.91 (1.71, 2.13)	1.66 (1.52, 1.82)	106 (64%)	215 (75%)	6.40 (5.98, 6.86)	5.96 (5.74, 6.20)
Stage II	28 (16%)	46 (16%)	2.36 (1.44, 3.86)	1.95 (1.32, 2.89)	28 (16%)	46 (16%)	2.04 (1.65, 2.54)	1.65 (1.36, 2.00)	27 (16%)	46 (16%)	6.78 (5.94, 7.74)	5.99 (5.52, 6.50)
Stage III	19 (11%)	10 (4%)	2.03 (1.06, 3.91)	0.92 (0.37, 2.27)	19 (11%)	10 (3%)	1.68 (1.26, 2.23)	1.26 (0.81, 1.97)	18 (11%)	10 (3%)	6.73 (5.62, 8.06)	6.20 (5.13, 7.50)
Stage IV	15 (9%)	18 (6%)	2.00 (1.01, 3.96)	1.04 (0.54, 2.00)	14 (8%)	18 (6%)	2.09 (1.53, 2.85)	1.70 (1.23, 2.34)	15 (9%)	16 (6%)	6.93 (5.78, 8.30)	5.40 (4.68, 6.23)
p-trend <sup>b</sup>			0.54	0.27			0.87	0.82			0.36	0.37
p-interaction <sup>c</sup>			0.26				0.91				0.30	
<b>Endometriosis subtype</b>												
Superficial peritoneal lesion	115 (67%)	246 (86%)	1.86 (1.43, 2.41)	1.58 (1.33, 1.87)	117 (67%)	254 (87%)	1.87 (1.67, 2.09)	1.68 (1.54, 1.82)	113 (68%)	255 (88%)	6.69 (6.24, 7.18)	5.98 (5.77, 6.19)
Endometrioma	19 (11%)	11 (4%)	1.95 (1.03, 3.72)	1.25 (0.54, 2.92)	19 (11%)	11 (4%)	2.14 (1.62, 2.84)	1.47 (0.97, 2.22)	17 (10%)	10 (3%)	6.38 (5.33, 7.63)	6.18 (5.14, 7.44)
Deep	22 (13%)	13 (5%)	1.85 (1.05, 3.28)	2.49 (1.09, 5.71)	22 (13%)	13 (4%)	2.08 (1.62, 2.67)	1.53 (1.02, 2.29)	21 (13%)	12 (4%)	6.11 (5.23, 7.14)	5.44 (4.54, 6.52)
Endometrioma and Deep	16 (9%)	15 (5%)	2.18 (1.09, 4.38)	2.04 (0.96, 4.30)	16 (9%)	15 (5%)	1.95 (1.44, 2.64)	1.69 (1.17, 2.44)	16 (10%)	14 (5%)	6.56 (5.45, 7.89)	5.42 (4.61, 6.37)
p-value			0.98	0.6			0.81	0.91			0.79	0.49
p-interaction <sup>c</sup>			0.80				0.77				0.66	
<b>Lesion color</b>												
Clear												
No	30 (30%)	14 (6%)	1.45 (0.61, 3.45)	2.17 (1.02, 4.62)	31 (31%)	14 (6%)	1.65 (1.18, 2.30)	1.33 (0.92, 1.90)	31 (30%)	14 (6%)	5.31 (4.62, 6.11)	4.55 (4.00, 5.18)
Yes	69 (70%)	214 (94%)	2.04 (1.30, 3.20)	1.65 (1.37, 1.98)	70 (69%)	222 (94%)	1.74 (1.45, 2.08)	1.60 (1.47, 1.74)	71 (70%)	225 (94%)	4.40 (4.08, 4.73)	5.11 (4.96, 5.27)
p-value			0.57	0.49			0.81	0.33			0.05	0.09
p-interaction <sup>c</sup>			0.35				0.80				0.32	
Red <sup>d</sup>												
No	29 (29%)	36 (16%)	2.61 (1.51, 4.50)	1.75 (1.11, 2.76)	30 (30%)	37 (16%)	1.74 (1.39, 2.18)	1.72 (1.39, 2.13)	30 (29%)	37 (15%)	4.45 (4.05, 4.90)	4.69 (4.34, 5.06)
Yes	70 (71%)	192 (84%)	1.59 (1.13, 2.22)	1.66 (1.37, 2.02)	71 (70%)	199 (84%)	1.70 (1.48, 1.95)	1.56 (1.42, 1.70)	72 (71%)	202 (85%)	4.74 (4.47, 5.03)	5.15 (4.99, 5.32)
p-value			0.15	0.84			0.86	0.40			0.29	0.03
p-interaction <sup>c</sup>			0.45				0.49				0.82	
White												
No	123 (73%)	212 (74%)	1.89 (1.51, 2.38)	1.62 (1.35, 1.94)	124 (73%)	217 (74%)	2.01 (1.83, 2.22)	1.67 (1.53, 1.82)	117 (71%)	216 (74%)	6.73 (6.33, 7.16)	5.98 (5.76, 6.21)
Yes	46 (27%)	74 (26%)	1.73 (1.19, 2.51)	1.56 (1.14, 2.12)	47 (27%)	77 (26%)	1.66 (1.41, 1.94)	1.64 (1.42, 1.89)	47 (29%)	76 (26%)	6.31 (5.72, 6.95)	5.78 (5.43, 6.15)
p-value			0.69	0.82			0.04	0.84			0.27	0.36
p-interaction <sup>c</sup>			0.9				0.20				0.63	
Blue/black												
No	111 (66%)	213 (74%)	1.86 (1.46, 2.37)	1.72 (1.43, 2.06)	114 (67%)	221 (75%)	1.83 (1.65, 2.03)	1.70 (1.56, 1.85)	111 (68%)	221 (76%)	6.63 (6.22, 7.07)	5.94 (5.72, 6.16)
Yes	58 (34%)	73 (26%)	1.82 (1.30, 2.56)	1.32 (0.96, 1.81)	57 (33%)	73 (25%)	2.07 (1.78, 2.40)	1.55 (1.33, 1.81)	53 (32%)	71 (24%)	6.56 (5.97, 7.21)	5.89 (5.51, 6.30)
p-value			0.93	0.16			0.2	0.33			0.86	0.85
p-interaction <sup>c</sup>			0.40				0.10				0.72	
Brown <sup>d</sup>												
No	72 (73%)	171 (75%)	2.14 (1.55, 2.95)	1.74 (1.42, 2.14)	73 (72%)	178 (75%)	1.74 (1.52, 1.99)	1.55 (1.41, 1.71)	74 (73%)	181 (76%)	4.74 (4.48, 5.01)	5.12 (4.94, 5.29)
Yes	27 (27%)	57 (25%)	1.23 (0.72, 2.10)	1.48 (1.03, 2.12)	28 (28%)	58 (25%)	1.64 (1.32, 2.05)	1.67 (1.41, 1.99)	28 (27%)	58 (24%)	4.44 (4.05, 4.88)	4.96 (4.67, 5.27)
p-value			0.09	0.44			0.68	0.46			0.25	0.39
p-interaction <sup>c</sup>			0.29				0.37				0.41	
Vascular <sup>d</sup>												
No	70 (71%)	163 (71%)	1.69 (1.22, 2.36)	1.69 (1.37, 2.09)	70 (69%)	168 (71%)	1.64 (1.44, 1.88)	1.62 (1.47, 1.79)	71 (70%)	170 (71%)	4.73 (4.47, 5.01)	5.04 (4.86, 5.22)
Yes	29 (29%)	65 (29%)	2.24 (1.33, 3.76)	1.64 (1.17, 2.29)	31 (31%)	68 (29%)	1.87 (1.52, 2.30)	1.48 (1.26, 1.73)	31 (30%)	69 (29%)	4.48 (4.11, 4.89)	5.18 (4.90, 5.48)
p-value			0.38	0.88			0.31	0.33			0.32	0.41
p-interaction <sup>c</sup>			0.43				0.20				0.26	

<sup>a</sup>Geometric mean(95% CI) adjusted for age at blood draw (continuous), BMI (underweight, normal weight, overweight, obese), study site (A2A, ENDO, ENDOX), hormone use at time of blood draw (no, yes), and pain medication use (no, yes, missing).

<sup>b</sup>p-trend calculated modeling exposure variable categories as ordinal

<sup>c</sup>p-value for test of interaction for those using and not using analgesics calculated using the Wald statistic

<sup>d</sup>Red, brown, and vascular were only assessed in the A2A and ENDOX studies

**Supplementary Table 3. Associations between endometriosis rASRM stage, lesion macrophenotype, appearance, and location and inflammatory biomarker levels, stratified by pain medication use, among endometriosis cases from A2A, ENDOX, and ENDO.**

	Interleukin-10 (IL-10)				Monocyte Chemoattractant Protein-1 (MCP-1)				Monocyte Chemoattractant Protein-4 (MCP-4)			
	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)
<b>ASRM Stage</b>												
Stage I	109 (64%)	216 (75%)	1.95 (1.82, 2.09)	1.90 (1.79, 2.00)	110 (64%)	217 (75%)	211.16 (199.55, 223.43)	191.81 (183.43, 200.58)	50 (81%)	151 (83%)	64.98 (55.47, 76.12)	75.08 (67.30, 83.76)
Stage II	27 (16%)	44 (15%)	2.06 (1.79, 2.36)	1.73 (1.54, 1.95)	27 (16%)	46 (16%)	230.84 (206.49, 258.05)	200.73 (182.28, 221.04)	9 (15%)	23 (13%)	63.46 (43.45, 92.67)	85.41 (64.28, 113.48)
Stage III	19 (11%)	10 (3%)	1.81 (1.51, 2.17)	1.49 (1.14, 1.96)	19 (11%)	10 (3%)	227.87 (197.00, 263.58)	144.11 (115.32, 180.08)	1 (2%)	1 (1%)	61.47 (19.90, 189.92)	24.44 (5.99, 99.82)
Stage IV	14 (8%)	18 (6%)	1.60 (1.32, 1.94)	1.81 (1.49, 2.20)	15 (9%)	18 (6%)	220.61 (189.43, 256.91)	167.08 (142.30, 196.17)	2 (3%)	6 (3%)	59.88 (24.21, 148.14)	38.04 (21.32, 67.85)
p-trend <sup>b</sup>			0.11	0.23			0.32	0.1			0.83	0.1
p-interaction <sup>c</sup>				0.30				0.06				0.59
<b>Endometriosis subtype</b>												
Superficial peritoneal lesion	115 (67%)	253 (87%)	1.92 (1.78, 2.06)	1.86 (1.77, 1.96)	117 (68%)	256 (87%)	218.60 (206.32, 231.62)	193.67 (185.91, 201.75)	59 (95%)	175 (96%)	62.81 (54.80, 72.00)	75.24 (67.96, 83.29)
Endometrioma	19 (11%)	11 (4%)	1.78 (1.49, 2.12)	1.92 (1.48, 2.47)	18 (10%)	11 (4%)	218.45 (188.45, 253.23)	122.50 (99.76, 150.43)	1 (2%)	3 (2%)	62.64 (21.37, 183.66)	28.37 (11.45, 70.33)
Deep	22 (13%)	12 (4%)	2.01 (1.72, 2.35)	1.72 (1.33, 2.23)	22 (13%)	13 (4%)	211.86 (186.32, 240.90)	184.92 (151.25, 226.09)	2 (3%)	3 (2%)	145.01 (67.02, 313.77)	114.96 (52.54, 251.55)
Endometrioma and Deep	15 (9%)	15 (5%)	1.98 (1.62, 2.41)	1.73 (1.38, 2.17)	16 (9%)	15 (5%)	222.61 (190.36, 260.33)	179.73 (149.80, 215.65)		2 (1%)		30.86 (10.77, 88.45)
p-value			0.73	0.86			0.96	0.0006			0.12	0.09
p-interaction <sup>c</sup>				0.61				0.006				0.56
<b>Lesion color</b>												
<b>Clear</b>												
No	29 (30%)	14 (6%)	1.92 (1.51, 2.43)	1.90 (1.53, 2.36)	31 (30%)	14 (6%)	166.25 (144.00, 191.95)	163.35 (138.40, 192.79)	6 (10%)	12 (7%)	55.07 (35.11, 86.36)	91.62 (61.12, 137.35)
Yes	69 (70%)	221 (94%)	1.99 (1.77, 2.25)	1.80 (1.71, 1.90)	71 (70%)	225 (94%)	179.15 (166.01, 193.32)	168.64 (162.15, 175.40)	56 (90%)	172 (93%)	65.63 (56.85, 75.77)	72.42 (65.33, 80.29)
p-value			0.81	0.63			0.45	0.72			0.47	0.27
p-interaction <sup>c</sup>				0.73				0.71				0.28
<b>Red<sup>d</sup></b>												
No	29 (30%)	35 (15%)	1.96 (1.69, 2.27)	1.64 (1.44, 1.87)	30 (29%)	37 (15%)	174.91 (158.91, 192.53)	170.32 (154.32, 187.96)	14 (23%)	26 (14%)	60.49 (43.25, 84.60)	82.33 (63.05, 107.49)
Yes	69 (70%)	200 (85%)	1.98 (1.80, 2.17)	1.84 (1.74, 1.94)	72 (71%)	202 (85%)	175.21 (165.13, 185.91)	167.97 (161.14, 175.08)	48 (77%)	158 (86%)	65.76 (55.85, 77.41)	72.19 (64.83, 80.38)
p-value			0.93	0.12			0.98	0.8			0.68	0.37
p-interaction <sup>c</sup>				0.31				0.87				0.56
<b>White</b>												
No	122 (73%)	218 (75%)	1.92 (1.80, 2.05)	1.85 (1.76, 1.95)	123 (72%)	219 (74%)	220.39 (209.34, 232.02)	188.04 (179.97, 196.47)	44 (71%)	134 (73%)	68.49 (58.35, 80.40)	80.44 (71.74, 90.18)
Yes	46 (27%)	74 (25%)	1.93 (1.74, 2.14)	1.85 (1.69, 2.03)	47 (28%)	77 (26%)	213.88 (196.78, 232.46)	192.11 (178.37, 206.91)	18 (29%)	50 (27%)	55.77 (43.37, 71.72)	57.83 (47.93, 69.78)
p-value			0.95	0.99			0.55	0.63			0.18	0.004
p-interaction <sup>c</sup>				0.84				0.51				0.56
<b>Blue/black</b>												
No	112 (67%)	220 (75%)	1.92 (1.80, 2.05)	1.84 (1.75, 1.95)	112 (66%)	224 (76%)	213.79 (202.51, 225.69)	189.89 (181.73, 198.40)	47 (76%)	148 (80%)	63.05 (53.86, 73.81)	74.61 (66.74, 83.41)
Yes	56 (33%)	72 (25%)	1.92 (1.74, 2.11)	1.88 (1.70, 2.07)	58 (34%)	72 (24%)	228.10 (211.40, 246.13)	186.64 (172.39, 202.08)	15 (24%)	36 (20%)	69.38 (52.32, 91.99)	69.29 (55.16, 87.04)
p-value			0.99	0.75			0.18	0.72			0.57	0.57
p-interaction <sup>c</sup>				0.60				0.31				0.40
<b>Brown<sup>d</sup></b>												
No	70 (71%)	178 (76%)	1.90 (1.73, 2.07)	1.76 (1.66, 1.87)	74 (73%)	181 (76%)	174.25 (164.59, 184.47)	168.96 (161.70, 176.54)	48 (77%)	147 (80%)	66.02 (56.44, 77.22)	73.77 (65.97, 82.50)
Yes	28 (29%)	57 (24%)	2.17 (1.88, 2.51)	1.96 (1.77, 2.17)	28 (27%)	58 (24%)	177.46 (161.50, 194.99)	166.39 (153.82, 179.99)	14 (23%)	37 (20%)	59.67 (44.29, 80.38)	72.62 (58.04, 90.88)
p-value			0.12	0.09			0.75	0.74			0.56	0.9
p-interaction <sup>c</sup>				0.80				0.56				0.58
<b>Vascular<sup>d</sup></b>												
No	68 (69%)	167 (71%)	1.89 (1.73, 2.07)	1.84 (1.73, 1.95)	71 (70%)	170 (71%)	177.19 (167.21, 187.77)	164.68 (157.44, 172.26)	39 (63%)	130 (71%)	61.64 (51.92, 73.18)	72.38 (64.24, 81.55)
Yes	30 (31%)	68 (29%)	2.16 (1.89, 2.48)	1.73 (1.57, 1.90)	31 (30%)	69 (29%)	170.49 (156.02, 186.30)	177.67 (165.46, 190.78)	23 (37%)	54 (29%)	69.73 (55.75, 87.21)	76.41 (63.40, 92.09)
p-value			0.12	0.27			0.48	0.08			0.4	0.64
p-interaction <sup>c</sup>				0.08				0.10				0.76

<sup>a</sup>Geometric mean(95% CI) adjusted for age at blood draw (continuous), BMI (underweight, normal weight, overweight, obese), study site (A2A, ENDO, ENDOX), hormone use at time of blood draw (no, yes), and pain medication use (no, yes, missing).

<sup>b</sup>p-trend calculated modeling exposure variable categories as ordinal

<sup>c</sup>p-value for test of interaction for those using and not using analgesics calculated using the Wald statistic

<sup>d</sup>Red, brown, and vascular were only assessed in the A2A and ENDOX studies

**Supplementary Table 3. Associations between endometriosis rASRM stage, lesion macrophenotype, appearance, and location and inflammatory biomarker levels, stratified by pain medication use, among endometriosis cases from A2A, ENDOX, and ENDO.**

	Thymus and activation regulated chemokine (TARC)				Interleukin-16 (IL-16)				Interferon Protein-10 (IP-10)			
	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)
<b>ASRM Stage</b>												
Stage I	49 (82%)	146 (84%)	205.29 (165.56, 254.56)	217.56 (193.55, 244.55)	50 (81%)	149 (84%)	130.08 (117.25, 144.32)	121.50 (113.98, 129.51)	110 (64%)	215 (75%)	118.36 (107.19, 130.68)	119.26 (111.21, 127.89)
Stage II	8 (13%)	21 (12%)	318.32 (184.65, 548.74)	228.25 (166.88, 312.18)	9 (15%)	22 (12%)	119.04 (92.84, 152.62)	127.81 (108.00, 151.25)	27 (16%)	45 (16%)	130.03 (106.93, 158.12)	122.29 (105.07, 142.33)
Stage III	1 (2%)	1 (1%)	221.90 (48.23, 1020.86)	122.34 (27.88, 536.79)	1 (2%)	1 (1%)	113.40 (54.08, 237.78)	562.01 (247.58, 1275.73)	19 (11%)	10 (3%)	112.12 (86.93, 144.60)	84.09 (59.45, 118.94)
Stage IV	2 (3%)	6 (3%)	554.58 (163.63, 1879.65)	124.72 (67.86, 229.22)	2 (3%)	6 (3%)	114.81 (63.36, 208.06)	118.97 (84.81, 166.88)	15 (9%)	18 (6%)	121.48 (93.15, 158.43)	105.02 (81.82, 134.81)
p-trend <sup>b</sup>			0.08	0.16			0.47	0.52			0.91	0.24
p-interaction <sup>c</sup>				0.02				0.23				0.33
<b>Endometriosis subtype</b>												
Superficial peritoneal lesion	57 (95%)	169 (96%)	226.45 (185.27, 276.77)	216.28 (193.96, 241.18)	59 (95%)	172 (96%)	127.23 (115.91, 139.67)	122.70 (115.44, 130.43)	116 (67%)	254 (87%)	118.48 (107.16, 130.99)	119.39 (111.90, 127.38)
Endometrioma	1 (2%)	3 (2%)	238.33 (49.95, 1137.07)	128.78 (49.49, 335.14)	1 (2%)	3 (2%)	113.46 (54.43, 236.51)	160.04 (92.25, 277.64)	19 (11%)	11 (4%)	117.53 (91.62, 150.78)	89.41 (64.68, 123.60)
Deep	2 (3%)	2 (1%)	189.07 (61.83, 578.13)	182.87 (66.81, 500.56)	2 (3%)	3 (2%)	147.85 (87.28, 250.44)	152.78 (95.85, 243.52)	22 (13%)	12 (4%)	114.93 (92.11, 143.41)	133.88 (95.80, 187.11)
Endometrioma and Deep		2 (1%)		154.44 (50.89, 468.67)		2 (1%)		101.24 (53.67, 190.97)	16 (9%)	15 (5%)	137.13 (104.75, 179.51)	97.46 (73.12, 129.90)
p-value			0.95	0.71			0.82	0.49			0.74	0.17
p-interaction <sup>c</sup>				0.73				0.78				0.15
<b>Lesion color</b>												
Clear												
No	6 (10%)	11 (6%)	193.12 (102.71, 363.10)	195.84 (125.69, 305.15)	6 (10%)	12 (7%)	116.39 (86.46, 156.66)	131.61 (103.64, 167.14)	31 (31%)	13 (6%)	131.84 (97.83, 177.67)	131.73 (97.89, 177.25)
Yes	54 (90%)	166 (94%)	229.17 (186.84, 281.09)	214.24 (192.09, 238.95)	56 (90%)	169 (93%)	128.88 (117.21, 141.71)	122.94 (115.64, 130.69)	69 (69%)	223 (94%)	109.69 (93.31, 128.93)	114.75 (107.25, 122.77)
p-value			0.62	0.7			0.53	0.59			0.38	0.38
p-interaction <sup>c</sup>				0.97				0.51				0.92
Red <sup>d</sup>												
No	14 (23%)	26 (15%)	145.31 (91.64, 230.41)	191.15 (144.98, 252.01)	14 (23%)	26 (14%)	110.18 (88.63, 136.96)	118.94 (101.67, 139.14)	30 (30%)	36 (15%)	123.58 (101.22, 150.88)	109.59 (92.32, 130.09)
Yes	46 (77%)	151 (85%)	257.44 (205.31, 322.82)	217.06 (193.67, 243.28)	48 (77%)	155 (86%)	133.20 (119.82, 148.08)	124.28 (116.60, 132.46)	70 (70%)	200 (85%)	113.07 (99.75, 128.16)	116.74 (108.69, 125.38)
p-value			0.05	0.41			0.15	0.61			0.48	0.51
p-interaction <sup>c</sup>				0.46				0.57				0.31
White												
No	44 (73%)	129 (73%)	235.92 (188.37, 295.45)	210.06 (185.62, 237.71)	44 (71%)	131 (72%)	127.48 (114.50, 141.94)	124.89 (116.52, 133.87)	123 (72%)	217 (74%)	117.52 (107.58, 128.39)	119.40 (111.55, 127.80)
Yes	16 (27%)	48 (27%)	198.44 (136.47, 288.56)	221.30 (180.55, 271.24)	18 (29%)	50 (28%)	127.94 (108.08, 151.43)	119.91 (107.13, 134.21)	47 (28%)	76 (26%)	127.56 (110.53, 147.21)	112.58 (100.33, 126.34)
p-value			0.44	0.67			0.97	0.55			0.34	0.39
p-interaction <sup>c</sup>				0.34				0.68				0.20
Blue/black												
No	46 (77%)	141 (80%)	207.67 (167.18, 257.97)	210.11 (186.65, 236.51)	47 (76%)	147 (81%)	126.82 (114.27, 140.74)	123.29 (115.45, 131.65)	113 (66%)	222 (76%)	123.17 (112.22, 135.19)	119.00 (111.17, 127.38)
Yes	14 (23%)	36 (20%)	294.34 (198.23, 437.04)	224.95 (177.59, 284.95)	15 (24%)	34 (19%)	130.16 (108.00, 156.85)	124.40 (108.40, 142.77)	57 (34%)	71 (24%)	114.57 (100.37, 130.78)	113.31 (100.13, 128.22)
p-value			0.14	0.62			0.81	0.91			0.39	0.50
p-interaction <sup>c</sup>				0.23				0.92				0.85
Brown <sup>d</sup>												
No	46 (77%)	141 (80%)	231.36 (185.06, 289.25)	211.32 (187.75, 237.85)	48 (77%)	144 (80%)	132.74 (119.92, 146.93)	125.40 (117.38, 133.96)	72 (72%)	180 (76%)	117.64 (104.24, 132.75)	117.33 (108.81, 126.52)
Yes	14 (23%)	36 (20%)	206.40 (136.11, 313.00)	219.94 (173.83, 278.28)	14 (23%)	37 (20%)	111.50 (91.92, 135.25)	116.37 (102.07, 132.67)	28 (28%)	56 (24%)	112.32 (92.24, 136.78)	110.29 (96.16, 126.49)
p-value			0.64	0.77			0.13	0.32			0.7	0.44
p-interaction <sup>c</sup>				0.47				0.52				0.91
Vascular <sup>d</sup>												
No	38 (63%)	125 (71%)	234.93 (184.22, 299.58)	224.93 (198.43, 254.96)	39 (63%)	127 (70%)	125.97 (112.42, 141.16)	122.30 (113.94, 131.27)	70 (70%)	169 (72%)	115.22 (101.95, 130.21)	112.57 (104.16, 121.65)
Yes	22 (37%)	52 (29%)	209.54 (152.12, 288.64)	186.99 (153.70, 227.47)	23 (37%)	54 (30%)	130.46 (112.47, 151.32)	126.35 (113.26, 140.96)	30 (30%)	67 (28%)	118.26 (97.92, 142.84)	123.69 (109.24, 140.06)
p-value			0.58	0.12			0.72	0.63			0.82	0.21
p-interaction <sup>c</sup>				0.75				0.95				0.58

<sup>a</sup>Geometric mean(95% CI) adjusted for age at blood draw (continuous), BMI (underweight, normal weight, overweight, obese), study site (A2A, ENDO, ENDOX), hormone use at time of blood draw (no, yes), and pain medication use (no, yes, missing).

<sup>b</sup>p-trend calculated modeling exposure variable categories as ordinal

<sup>c</sup>p-value for test of interaction for those using and not using analgesics calculated using the Wald statistic

<sup>d</sup>Red, brown, and vascular were only assessed in the A2A and ENDOX studies

**Supplementary Table 3. Associations between endometriosis rASRM stage, lesion macrophenotype, appearance, and location and inflammatory biomarker levels, stratified by pain medication use, among endometriosis cases from A2A, ENDOX, and ENDO.**

	Tumor necrosis factor (TNF)- $\alpha$ (ELLA assay)				Tumor necrosis factor (TNF)- $\alpha$ (Luminex assay)			
	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)
<b>ASRM Stage</b>								
Stage I	66 (56%)	81 (64%)	8.17 (7.66, 8.71)	8.55 (8.07, 9.07)	49 (82%)	149 (83%)	6.93 (6.33, 7.58)	7.26 (6.90, 7.64)
Stage II	20 (17%)	26 (20%)	8.34 (7.43, 9.36)	8.34 (7.53, 9.24)	8 (13%)	23 (13%)	6.93 (5.52, 8.70)	6.46 (5.66, 7.37)
Stage III	18 (15%)	8 (6%)	7.87 (6.91, 8.96)	7.10 (5.84, 8.63)	1 (2%)	1 (1%)	7.28 (3.85, 13.75)	4.23 (2.21, 8.11)
Stage IV	14 (12%)	12 (9%)	7.45 (6.50, 8.54)	8.89 (7.55, 10.46)	2 (3%)	6 (3%)	6.83 (4.10, 11.39)	7.79 (5.96, 10.18)
p-trend <sup>b</sup>			0.27	0.78			0.98	0.54
p-interaction <sup>c</sup>			0.64				0.58	
<b>Endometriosis subtype</b>								
Superficial peritoneal lesion	66 (55%)	100 (77%)	8.22 (7.69, 8.79)	8.59 (8.13, 9.06)	57 (95%)	173 (96%)	6.95 (6.41, 7.54)	7.18 (6.84, 7.52)
Endometrioma	18 (15%)	7 (5%)	8.07 (7.10, 9.16)	8.95 (7.31, 10.96)	1 (2%)	3 (2%)	7.26 (3.87, 13.60)	5.91 (3.88, 9.00)
Deep	20 (17%)	10 (8%)	7.62 (6.79, 8.54)	8.48 (7.00, 10.26)	2 (3%)	3 (2%)	6.27 (4.00, 9.84)	5.93 (4.13, 8.52)
Endometrioma and Deep	16 (13%)	13 (10%)	8.29 (7.27, 9.47)	7.24 (6.19, 8.46)		2 (1%)		9.11 (5.60, 14.84)
p-value			0.71	0.21			0.9	0.36
p-interaction <sup>c</sup>			0.23				0.70	
<b>Lesion color</b>								
<b>Clear</b>								
No	27 (57%)	5 (7%)	6.98 (5.92, 8.22)	7.05 (5.39, 9.22)	6 (10%)	12 (7%)	7.84 (6.09, 10.09)	8.17 (6.78, 9.83)
Yes	20 (43%)	68 (93%)	6.99 (5.67, 8.63)	7.58 (7.10, 8.10)	54 (90%)	170 (93%)	6.84 (6.30, 7.42)	7.09 (6.76, 7.43)
p-value			0.99	0.61			0.32	0.15
p-interaction <sup>c</sup>			0.41				0.81	
<b>Red<sup>d</sup></b>								
No	17 (36%)	14 (19%)	7.55 (6.52, 8.75)	7.23 (6.12, 8.53)	14 (23%)	26 (14%)	6.67 (5.53, 8.05)	6.75 (5.97, 7.63)
Yes	30 (64%)	59 (81%)	6.68 (6.01, 7.42)	7.62 (7.09, 8.20)	46 (77%)	156 (86%)	7.01 (6.39, 7.70)	7.22 (6.87, 7.59)
p-value			0.23	0.58			0.66	0.32
p-interaction <sup>c</sup>			0.27				0.53	
<b>White</b>								
No	85 (73%)	99 (76%)	8.19 (7.78, 8.63)	8.32 (7.90, 8.76)	43 (72%)	134 (74%)	7.43 (6.82, 8.10)	7.39 (7.01, 7.79)
Yes	32 (27%)	31 (24%)	8.27 (7.60, 9.00)	8.88 (8.09, 9.75)	17 (28%)	48 (26%)	5.81 (5.06, 6.66)	6.54 (5.98, 7.14)
p-value			0.85	0.23			0.004	0.02
p-interaction <sup>c</sup>			0.51				0.22	
<b>Blue/black</b>								
No	73 (62%)	88 (68%)	8.07 (7.63, 8.53)	8.40 (7.95, 8.88)	46 (77%)	146 (80%)	7.18 (6.57, 7.84)	7.19 (6.83, 7.57)
Yes	44 (38%)	42 (32%)	8.47 (7.88, 9.11)	8.55 (7.87, 9.29)	14 (23%)	36 (20%)	6.19 (5.27, 7.27)	7.02 (6.32, 7.79)
p-value			0.3	0.74			0.12	0.69
p-interaction <sup>c</sup>			0.63				0.22	
<b>Brown<sup>d</sup></b>								
No	32 (68%)	46 (63%)	6.80 (6.18, 7.49)	7.63 (7.03, 8.28)	46 (77%)	146 (80%)	7.00 (6.40, 7.67)	7.29 (6.92, 7.67)
Yes	15 (32%)	27 (37%)	7.39 (6.41, 8.52)	7.40 (6.64, 8.24)	14 (23%)	36 (20%)	6.70 (5.66, 7.93)	6.64 (5.99, 7.36)
p-value			0.36	0.66			0.66	0.12
p-interaction <sup>c</sup>			0.28				0.68	
<b>Vascular<sup>d</sup></b>								
No	37 (79%)	54 (74%)	6.97 (6.37, 7.63)	7.49 (6.95, 8.07)	38 (63%)	129 (71%)	6.83 (6.19, 7.54)	7.07 (6.69, 7.47)
Yes	10 (21%)	19 (26%)	7.03 (5.88, 8.41)	7.72 (6.79, 8.77)	22 (37%)	53 (29%)	7.11 (6.25, 8.09)	7.36 (6.75, 8.03)
p-value			0.94	0.69			0.63	0.44
p-interaction <sup>c</sup>			0.64				0.97	

<sup>a</sup>Geometric mean(95% CI) adjusted for age at blood draw (continuous), BMI (underweight, normal weight, overweight, obese), study site (A2A, ENDO, ENDOX), hormone use at time of blood draw (no, yes), and pain medication use (no, yes, missing).

<sup>b</sup>p-trend calculated modeling exposure variable categories as ordinal

<sup>c</sup>p-value for test of interaction for those using and not using analgesics calculated using the Wald statistic

<sup>d</sup>Red, brown, and vascular were only assessed in the A2A and ENDOX studies

Supplementary Table 4. Associations between endometriosis lesion locations and inflammatory biomarker levels, stratified by pain medication use, among endometriosis cases from A2A, ENDOX, and ENDO

	Interferon Protein-10 (IP-10)				Tumor necrosis factor (TNF)- $\alpha$ (ELLA assay)				Tumor necrosis factor (TNF)- $\alpha$ (Luminex assay)			
	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)	Using analgesics N (%)	Not using analgesics N (%)	Using analgesics Geometric mean <sup>a</sup> (95% CI)	Not using analgesics Geometric mean <sup>a</sup> (95% CI)
Uterosacral ligament												
No	131 (76%)	242 (83%)	117.85 (108.08, 128.50)	116.00 (108.73, 123.76)	88 (73%)	107 (82%)	8.04 (7.62, 8.48)	8.54 (8.12, 8.98)	49 (82%)	154 (85%)	6.88 (6.31, 7.50)	7.15 (6.80, 7.52)
Yes	42 (24%)	51 (17%)	124.89 (106.84, 146.00)	125.45 (108.54, 144.99)	32 (27%)	23 (18%)	8.28 (7.56, 9.08)	8.03 (7.15, 9.02)	11 (18%)	28 (15%)	7.18 (5.98, 8.63)	7.17 (6.37, 8.07)
p-value			0.53	0.34			0.59	0.36			0.68	0.96
p-interaction <sup>b</sup>			0.91				0.23				0.77	
Anterior cul de sac												
No	116 (67%)	159 (54%)	122.01 (111.22, 133.86)	111.96 (103.33, 121.32)	91 (76%)	76 (58%)	8.13 (7.71, 8.56)	8.54 (8.04, 9.08)	30 (50%)	94 (52%)	7.40 (6.62, 8.26)	7.17 (6.73, 7.65)
Yes	57 (33%)	134 (46%)	114.60 (100.17, 131.13)	124.64 (114.18, 136.06)	29 (24%)	54 (42%)	8.02 (7.29, 8.82)	8.32 (7.73, 8.96)	30 (50%)	88 (48%)	6.50 (5.82, 7.26)	7.13 (6.68, 7.62)
p-value			0.46	0.08			0.82	0.60			0.12	0.91
p-interaction <sup>b</sup>			0.11				0.66				0.16	
Posterior cul de sac												
No	77 (45%)	66 (23%)	114.04 (100.70, 129.14)	112.46 (95.18, 132.89)	66 (55%)	50 (38%)	8.05 (7.53, 8.60)	7.74 (7.00, 8.56)	10 (17%)	19 (10%)	7.94 (6.46, 9.75)	7.53 (6.45, 8.79)
Yes	96 (55%)	227 (77%)	124.11 (111.27, 138.43)	119.13 (110.63, 128.28)	54 (45%)	80 (62%)	8.16 (7.58, 8.80)	8.93 (8.31, 9.59)	50 (83%)	163 (90%)	6.75 (6.19, 7.35)	7.11 (6.77, 7.47)
p-value			0.36	0.58			0.80	0.06			0.17	0.50
p-interaction <sup>b</sup>			0.97				0.82				0.39	
Ovary												
No	135 (78%)	271 (92%)	119.87 (109.78, 130.89)	118.98 (111.93, 126.49)	86 (72%)	112 (86%)	7.89 (7.47, 8.34)	8.54 (8.13, 8.96)	56 (93%)	179 (98%)	7.08 (6.53, 7.67)	7.17 (6.84, 7.51)
Yes	38 (22%)	22 (8%)	118.29 (98.63, 141.86)	101.74 (80.46, 128.66)	34 (28%)	18 (14%)	8.66 (7.89, 9.51)	7.92 (6.97, 9.02)	4 (7%)	3 (2%)	5.18 (3.62, 7.40)	6.45 (4.40, 9.45)
p-value			0.90	0.21			0.11	0.30			0.11	0.59
p-interaction <sup>b</sup>			0.31				0.06				0.57	
Uterus												
No	156 (90%)	285 (97%)	119.30 (110.25, 129.09)	118.37 (111.57, 125.58)	105 (88%)	124 (95%)	8.13 (7.75, 8.54)	8.36 (7.99, 8.74)	58 (97%)	179 (98%)	6.96 (6.43, 7.54)	7.14 (6.81, 7.48)
Yes	17 (10%)	8 (3%)	121.61 (94.94, 155.78)	93.12 (64.98, 133.43)	15 (13%)	6 (5%)	7.89 (6.91, 9.00)	10.68 (8.63, 13.23)	2 (3%)	3 (2%)	6.17 (3.92, 9.73)	8.20 (5.69, 11.82)
p-value			0.89	0.20			0.67	0.03			0.61	0.46
p-interaction <sup>b</sup>			0.26				0.03				0.53	
Fallopian tubes												
No	168 (97%)	286 (98%)	118.56 (109.95, 127.84)	118.24 (111.45, 125.44)	115 (96%)	124 (95%)	8.05 (7.69, 8.43)	8.45 (8.07, 8.85)	60 (100%)	181 (99%)	--	--
Yes	5 (3%)	7 (2%)	156.87 (100.52, 244.80)	94.11 (63.67, 139.11)	5 (4%)	6 (5%)	9.31 (7.46, 11.64)	8.36 (6.72, 10.42)	0 (0%)	1 (1%)	--	--
p-value			0.23	0.26			0.21	0.93			--	--
p-interaction <sup>b</sup>			0.10				0.23				--	
Vagina												
No	101 (98%)	235 (100%)	115.46 (104.39, 127.69)	115.83 (108.47, 123.69)	48 (96%)	72 (99%)	6.81 (6.25, 7.43)	7.57 (7.10, 8.07)	60 (100%)	182 (100%)	--	--
Yes	2 (2%)	1 (0%)	99.22 (46.55, 211.47)	75.00 (23.35, 240.89)	2 (4%)	1 (1%)	7.00 (4.43, 11.08)	5.92 (3.14, 11.18)	0 (0%)	0 (0%)	--	--
p-value			0.70	0.47			0.91	0.46			--	--
p-interaction <sup>b</sup>			0.85				0.40				--	
Sidewall												
No	31 (30%)	71 (30%)	119.91 (98.98, 145.25)	124.46 (110.45, 140.23)	21 (42%)	22 (30%)	6.82 (5.96, 7.80)	7.55 (6.69, 8.51)	13 (22%)	54 (30%)	6.98 (5.83, 8.35)	6.99 (6.42, 7.61)
Yes	72 (70%)	165 (70%)	113.11 (100.12, 127.80)	112.01 (103.59, 121.12)	29 (58%)	51 (70%)	6.82 (6.09, 7.65)	7.55 (6.98, 8.15)	47 (78%)	128 (70%)	6.92 (6.32, 7.57)	7.22 (6.84, 7.63)
p-value			0.63	0.15			0.99	0.99			0.93	0.52
p-interaction <sup>b</sup>			0.75				0.95				0.56	
Bladder												
No	172 (99%)	291 (99%)	119.61 (110.98, 128.89)	117.66 (110.95, 124.77)	119 (99%)	128 (98%)	8.09 (7.73, 8.46)	8.49 (8.12, 8.88)	60 (100%)	182 (100%)	--	--
Yes	1 (1%)	2 (1%)	105.97 (38.35, 292.82)	108.52 (52.64, 223.73)	1 (1%)	2 (2%)	10.38 (6.21, 17.36)	6.17 (4.28, 8.90)	0 (0%)	0 (0%)	--	--
p-value			0.82	0.83			0.34	0.09			--	--
p-interaction <sup>b</sup>			0.98				0.07				--	
Bowel												
No	167 (97%)	289 (99%)	119.22 (110.49, 128.63)	117.13 (110.43, 124.24)	116 (97%)	128 (98%)	8.12 (7.76, 8.50)	8.46 (8.08, 8.85)	59 (98%)	180 (99%)	6.93 (6.41, 7.50)	7.12 (6.80, 7.45)
Yes	6 (3%)	4 (1%)	128.35 (84.46, 195.04)	156.54 (87.90, 278.76)	4 (3%)	2 (2%)	7.53 (5.76, 9.83)	8.05 (4.76, 13.64)	1 (2%)	2 (1%)	6.80 (3.69, 12.55)	11.35 (7.35, 17.54)
p-value			0.73	0.33			0.58	0.86			0.95	0.04
p-interaction <sup>b</sup>			0.65				0.56				0.20	

<sup>a</sup>Geometric mean(95% CI) adjusted for age at blood draw (continuous), BMI (underweight, normal weight, overweight, obese), study site (A2A, ENDO, ENDOX), and hormone use at time of blood draw (no, yes).

<sup>b</sup>p-value for test of interaction for those using and not using analgesics calculated using the Wald statistic

**Supplemental Table 5. Associations between endometriosis rASRM stage, lesion macrophenotype, appearance, and location and IL-1beta, stratified by pain medication use, among endometriosis cases from A2A, ENDOX, and ENDO.**

	Using pain medication			Not using pain medication			Using pain medication		Not using pain medication	
	IL-1beta <LLD	IL-1beta >LLD to median	IL-1beta >Median	IL-1beta <LLD	IL-1beta >LLD to median	IL-1beta >Median	>LLD to median vs. <LLD OR (95% CI) <sup>a</sup>	>Median vs. <LLD OR (95% CI) <sup>a</sup>	>LLD to median vs. <LLD OR (95% CI) <sup>a</sup>	>Median vs. <LLD OR (95% CI) <sup>a</sup>
<b>ASRM Stage</b>										
Stage I	68 (65%)	21 (64%)	22 (61%)	132 (76%)	44 (70%)	42 (76%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Stage II	11 (11%)	7 (21%)	10 (28%)	27 (16%)	12 (19%)	7 (13%)	1.74 (0.55, 5.52)	3.42 (1.15, 10.23)	1.21 (0.54, 2.68)	0.80 (0.31, 2.06)
Stage III	16 (15%)	2 (6%)	1 (3%)	6 (3%)	3 (5%)	1 (2%)	0.35 (0.06, 2.00)	0.53 (0.05, 5.06)	1.54 (0.31, 7.73)	0.66 (0.06, 6.65)
<b>Lesion location</b>										
<b>Uterosacral ligament</b>										
No	76 (72%)	28 (82%)	29 (81%)	144 (82%)	58 (88%)	44 (79%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	29 (28%)	6 (18%)	7 (19%)	31 (18%)	8 (12%)	12 (21%)	0.68 (0.24, 1.92)	0.85 (0.31, 2.30)	0.75 (0.32, 1.76)	1.38 (0.62, 3.05)
p-het							0.62			
<b>Anterior cul de sac</b>										
No	71 (68%)	25 (74%)	21 (58%)	102 (58%)	35 (53%)	26 (46%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	34 (32%)	9 (26%)	15 (42%)	73 (42%)	31 (47%)	30 (54%)	0.91 (0.35, 2.34)	1.21 (0.52, 2.82)	1.34 (0.74, 2.44)	1.71 (0.90, 3.23)
p-het							0.78			
<b>Posterior cul de sac</b>										
No	48 (46%)	18 (53%)	12 (33%)	35 (20%)	18 (27%)	14 (25%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	57 (54%)	16 (47%)	24 (67%)	140 (80%)	48 (73%)	42 (75%)	0.84 (0.32, 2.17)	0.90 (0.33, 2.43)	0.71 (0.27, 1.87)	0.53 (0.19, 1.49)
p-het							0.17			
<b>Ovary</b>										
No	79 (75%)	28 (82%)	30 (83%)	164 (94%)	59 (89%)	52 (93%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	26 (25%)	6 (18%)	6 (17%)	11 (6%)	7 (11%)	4 (7%)	0.63 (0.20, 2.00)	1.47 (0.43, 5.02)	1.56 (0.50, 4.90)	1.03 (0.27, 3.83)
p-het							0.52			
<b>Uterus</b>										
No	96 (91%)	29 (85%)	33 (92%)	173 (99%)	63 (95%)	52 (93%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	9 (9%)	5 (15%)	3 (8%)	2 (1%)	3 (5%)	4 (7%)	2.70 (0.70, 10.35)	1.60 (0.36, 7.15)	3.74 (0.58, 24.25)	8.33 (1.36, 51.03)
p-het							0.12			
<b>Fallopian tubes</b>										
No	102 (97%)	33 (97%)	34 (94%)	170 (97%)	66 (100%)	54 (96%)	1.00 (ref)	1.00 (ref)	--	1.00 (ref)
Yes	3 (3%)	1 (3%)	2 (6%)	5 (3%)	0 (0%)	2 (4%)	1.13 (0.10, 12.57)	3.80 (0.54, 26.86)	--	1.45 (0.25, 8.50)
p-het							0.94			
<b>Vagina</b>										
No	59 (97%)	16 (100%)	28 (100%)	142 (99%)	51 (100%)	45 (100%)	--	--	--	--
Yes	2 (3%)	0 (0%)	0 (0%)	1 (1%)	0 (0%)	0 (0%)	--	--	--	--
p-het										
<b>Sidewall</b>										
No	22 (36%)	6 (38%)	4 (14%)	43 (30%)	14 (27%)	15 (33%)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	39 (64%)	10 (63%)	24 (86%)	100 (70%)	37 (73%)	30 (67%)	0.78 (0.21, 2.86)	3.18 (0.87, 11.63)	1.15 (0.56, 2.36)	0.84 (0.41, 1.74)
p-het							0.11			
<b>Bladder</b>										
No	104 (99%)	34 (100%)	36 (100%)	174 (99%)	66 (100%)	55 (98%)	--	--	--	--
Yes	1 (1%)	0 (0%)	0 (0%)	1 (1%)	0 (0%)	1 (2%)	--	--	--	--
p-het										
<b>Bowel</b>										
No	102 (97%)	33 (97%)	34 (94%)	172 (98%)	66 (100%)	55 (98%)	1.00 (ref)	1.00 (ref)	--	1.00 (ref)
Yes	3 (3%)	1 (3%)	2 (6%)	3 (2%)	0 (0%)	1 (2%)	1.93 (0.16, 23.81)	3.07 (0.41, 23.22)	--	1.53 (0.12, 19.38)
p-het							0.92			

<sup>a</sup>Odds ratio (95% confidence interval) from polytomous logistic regression model adjusted for age at blood draw (continuous), BMI (underweight, normal weight, overweight, obese), study site (A2A, ENDO, ENDOX), and hormone use at time of blood draw (no, yes).