

1 Title: East/South East Asian Ethnicity and Moderate-to-Severe Endometriosis

2 Running Title: Ethnicity and Severe Endometriosis

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17

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23

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37

38 Précis:

39 In our tertiary referral center, East and South East Asian women were more likely than
40 Caucasians to have moderate-to-severe endometriosis.

41

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43

44 ABSTRACT

45 Study Objective: To investigate ethnic differences for moderate-to-severe endometriosis

46 Design: Analysis of a prospective registry, December 2013 – December 2016

47 (ClinicalTrials.gov # NCT02911090). Inclusion Criteria: Women presenting to tertiary

48 referral center for pelvic pain and/or endometriosis. Exclusion criteria: Age greater than
49 50, menopausal, or mixed ethnicity. Logistic regression analysis was used to obtain
50 adjusted odds ratios (aOR) and 95% confidence intervals (CI) adjusting for potential
51 confounders (e.g., age, infertility, body-mass-index (BMI), previous hormonal use and
52 previous surgery for endometriosis). (Canadian Task Force Classification II-2).

53 Setting: Tertiary referral center

54 Patient(s): A total of 1594 women with pelvic pain and/or endometriosis.

55 Intervention: None

56 Main outcome measure: Moderate-to-severe endometriosis.

57 Main Results: On logistic regression, adjusting for potential confounders, East/South
58 East Asians were 8.3 times more likely than Caucasians to have a previous diagnosis of
59 Stage III/IV endometriosis prior to referral (aOR 8.33, 95% CI 3.74–18.57); 2.7 times
60 more likely to have a palpable nodule (aOR 2.66, 95% CI 1.57-4.52); 4.1 times more
61 likely to have an endometrioma on ultrasound (aOR 4.10, 95% CI 2.68–6.26); and 10.9
62 times more likely to have Stage III/IV endometriosis at the time of surgery at our center
63 (aOR 10.87, 95% CI 4.34–27.21).

64 Conclusion: Moderate-to-severe endometriosis was more common in women with East
65 or South East Asian ethnicity in our tertiary referral center. This could be explained by
66 East/South East Asians with minimal-mild disease being less likely to seek care, or
67 genetic/environmental differences that increase the risk of more severe disease amongst
68 East/South East Asians.

69 [ClinicalTrials.gov # NCT02911090, Endometriosis Pelvic Pain Interdisciplinary Cohort

70 Data Registry, <https://clinicaltrials.gov/ct2/show/NCT02911090>, September 22, 2016 –
71 data prior to this date were incorporated into registry with institutional research ethics board
72 approval from the University of British Columbia]

73 Key words: ethnicity, endometriosis, stage, severity

74

75 INTRODUCTION

76 The Revised American Fertility Society (rAFS) classification of endometriosis (Stage I/II
77 vs. Stage III/IV) reflects the amount, depth and location of endometriosis and adhesive
78 disease present at the time of surgery (1), with consideration of the three anatomic sub-
79 types of endometriosis: superficial peritoneal endometriosis (SUP), endometrioma (OMA),
80 and deep infiltrating endometriosis (DIE) (2).

81

82 In previous studies, several factors have been found to be possibly associated with DIE
83 and OMA (and by extension, Stage III-IV disease): older age, infertility/nulliparity, lower
84 body mass index (BMI), urban (versus rural) populations, previous usage of hormonal
85 medications, previous surgery for endometriosis, more severe pain symptoms, and diet
86 and other lifestyle factors (2-10). In addition, recent studies have investigated
87 endometriosis as an inheritable complex genetic trait (11-14), with genetic associations
88 that may be stronger for more advanced stages of disease.

89

90 To our knowledge, there have not been studies that assessed ethnic differences in severity
91 of endometriosis (e.g. Stage or anatomic subtypes). Historically it was believed that

92 endometriosis was a disease confined almost exclusively to Caucasian women (15). More
93 recent population studies have had conflicting results for racial and ethnic differences in
94 the prevalence of the disease (7, 16, 17).

95

96 Our objective was to investigate the distribution of moderate-to-severe endometriosis
97 across different ethnic racial groups presenting with pelvic pain and/or infertility. Based on
98 our clinical experience, we hypothesized that East and South East Asian women in this
99 population are more likely to have moderate-to-severe endometriosis (Stage III/IV) and/or
100 the DIE/OMA phenotypes compared to Caucasians and other ethnic groups.

101

102 MATERIALS AND METHODS

103 Setting and Sample

104 This study involved an analysis of data from the prospective Endometriosis Pelvic Pain
105 Interdisciplinary Cohort (EPPIC) Data Registry (Clinicaltrials.gov # NCT02911090,
106 <https://clinicaltrials.gov/ct2/show/NCT02911090>, September 22, 2016), which is based at
107 a tertiary referral center for endometriosis and pelvic pain in British Columbia, Canada.

108

109 EPPIC includes demographic information, clinical history, patient reported outcomes,
110 physical exam data, objective surgical findings and surgical pathology data captured by
111 the Research Electronic Data Capture (REDCap) Database. Usage of this database for
112 data management and subsequent prospective outcomes has been previously reported
113 in the literature (18, 19). All women in the EPPIC cohort consented to participate in the

114 registry and data from December 2013 onwards were incorporated into the registry with
115 institutional research ethics approval from BC Women's Hospital and Health Center and
116 the University of British Columbia Research Ethics Board (H16-00264).

117

118 Inclusion criteria were participants in the EPPIC data registry who were seen by one of
119 the center's gynecologists for a new or re-referral between December 1st, 2013 and
120 December 31st, 2016 and consented to be included in the data registry. Women eligible
121 for the registry were new or re-referrals with pelvic pain and/or endometriosis. Excluded
122 from analysis were duplicate data entries, women who did not complete a physical exam
123 or ethnicity questionnaires, women who withdrew from the data registry prior to the date
124 of data extraction, women who were menopausal and/or over 50 years of age, and those
125 of self-reported mixed ethnicity (Figure 1).

126

127 Prior to attending an assessment with a gynecologist, women were asked to self-identify
128 their ethnicity according to the categories in Table 1. In the questionnaire, participants
129 could choose a single ethnicity or multiple ethnicities, and women who chose multiple
130 ethnicities were excluded from the analysis.

131

132 Other information collected in the EPPIC registry have been described in detail) (18,
133 19). Endometriosis data were obtained from surgical reports and/or referral letters
134 based on surgery prior to referral to our center, findings on physical exam and point-of-
135 care ultrasound at our center, and surgery performed at our center. Pain symptoms
136 were measured on a numeric rating scale of 0 – 10 across different categories;

137 dysmenorrhea, deep dyspareunia, dyschezia and chronic pelvic pain (20). Quality of life
138 assessment was evaluated with the Endometriosis Health Profile (EHP-30) (scale 0-100)
139 (21), and psychological questionnaires included the Patient Health Questionnaire (PHQ-
140 9) (scale 0-27) (22), the Generalized Anxiety Disorder scale (GAD-7) (scale 0-21) (23),
141 and the Pain Catastrophizing Scale (PCS) (scale 0-52) (24). In each of these scales a
142 higher score equates to worse quality-of-life or more severe psychological symptoms.
143 Sociodemographic and lifestyle variables of interest included self-reported age, infertility,
144 and current or ever used hormonal therapy. Rural versus urban residence was defined
145 by the Canadian Postal Code forward sortation area (FSA) system which specifies rural
146 from urban areas in Canada (25).

147

148 Data analysis

149 The primary outcome was severity of endometriosis, and was phenotyped as follows:

- 150 a) Moderate-to-severe endometriosis before referral to the center: Stage III/IV (vs.
151 Stage I/II) endometriosis at previous surgery, with the denominator being all women who
152 had surgery for endometriosis prior to referral and surgical reports with staging
- 153 b) Palpable nodule on physical exam at our center: Palpable nodule (present/absent) of
154 the pouch of Douglas or uterosacral ligaments on initial assessment, with the
155 denominator being all women who had a pelvic examination at our center
- 156 c) Ovarian endometrioma on point-of-care ultrasound at our center, performed by
157 gynecologists trained in advanced gynecologic ultrasound: Endometrioma of either ovary
158 (present/absent), with the denominator being all women who had an endovaginal
159 ultrasound examination at our center

160 d) Moderate-to-severe endometriosis at surgery at our center: Stage III/IV (vs. Stage I/II)
161 endometriosis at surgery, with the denominator being all women who subsequently
162 underwent surgery at our center and were found to have histologically confirmed
163 endometriosis.

164

165 The main explanatory variable of interest was ethnicity. As demonstrated in Figure 2
166 and the results from the chi-square post hoc tests in Table 3, East and South East
167 Asians had a higher incidence of Stage III/IV endometriosis on surgery prior to referral to
168 the center, compared to Caucasians, South Asians, and other ethnicities. Therefore, for
169 subsequent analyses, ethnicity was classified into three groups: Caucasian, East/South
170 East Asian, and Other.

171

172 Ethnicity (classified into the three groups) was then examined with respect to each of the
173 endometriosis phenotypes using Chi-square test. Other variables from EPPIC were then
174 compared between the ethnic groups to identify any potential confounders, using Chi-
175 square or ANOVA/Kruskal-Wallis test.

176

177 Logistic regression analyses were then carried out to assess the association between
178 each endometriosis phenotype and ethnicity, while controlling for potential confounders
179 (e.g. age, BMI, history of infertility, previous surgery for endometriosis and use of
180 hormonal therapy (2, 5). For each endometriosis phenotype, ethnicity was entered as a
181 categorical variable (three groups) into the logistic regression model, and each potential
182 confounding variable was also entered simultaneously into the model. Adjusted odds

183 ratios (ORs) were then calculated between ethnicity and the endometriosis outcomes,
184 adjusting for the potential confounders.

185

186 Statistical significance was set at $p < 0.05$. Missing data were excluded. The summary
187 statistics for all continuous variables are described using means and standard
188 deviations, whereas categorical variables are described using frequencies and
189 percentages. All data was analysed with the SPSS software V22.0 (IBM Corporation,
190 Armonk, NY).

191

192 Corollary analysis

193 We also compared the ethnic distribution at our center to the ethnic distribution amongst
194 females in British Columbia as reported in the 2016 Canadian census (Supplementary
195 Table 1).

196

197 Interim analysis

198 In 2015, we had conducted an interim analysis of patients recruited from December 2013
199 to April 2015. At that time, there were 264 patients with surgical staging from previous
200 surgery: 189 Caucasians, 37 East/South East Asians, and 38 of other ethnicities. The
201 prevalence of Stage III/IV disease was 43.9% (83/189) amongst Caucasians, 89.2%
202 (33/37) amongst East/South Asians, and 65.8% (25/38) amongst other ethnicities (Chi-
203 square, $p < 0.001$). Although the results were already significant at that time, indicating
204 adequate power, we continued recruitment to December 2016 in order to further

205 increase sample size. The cases in the interim sample were included in the final
206 sample, to produce the total dataset from December 2013 to December 2016. Based on
207 the data at the time of the interim analysis, our final sample size of 72 East/South East
208 Asians with previous surgical staging and 531 Caucasians/Other ethnicities with
209 previous surgical staging (see Supplementary Table 2), with $\alpha = 0.05$, provides
210 power = 100%.

211

212

213 RESULTS

214 Descriptive statistics

215 There were 1594 women who met the study criteria (Figure 1). Ethnic distribution of
216 women included is as follows: 76.2% (n=1214) of women were Caucasian, 9.1% (n=145)
217 East or South East Asian, 7.5% (n=119) were South Asian, and 7.3% (n=116) were of
218 other ethnicities (Table 2). The number of women with each of the endometriosis
219 phenotypes/outcomes is listed in Table 2. Additional demographic factors are presented
220 in Table 2.

221

222 Staging of endometriosis from previous surgical reports prior to referral was available in
223 603 patients. Of these 603 patients, 49.6% (n=299) of women had Stage I-II, versus
224 50.4% (n=304) had Stage III/IV (Table 2). Subdividing by ethnicity, we observed that
225 East/South East Asians had a higher frequency of Stage III/IV endometriosis, compared
226 to Caucasians, South Asians, and other ethnicities (Figure 2 and Table 3). Therefore, for

227 subsequent analyses, ethnic groups were divided into three groups: Caucasian,
228 East/South East Asian, and Other.

229

230 During the initial appointment at the center, 1311 patients had a pelvic examination, of
231 which 10.6% (n=139) had a palpable nodule on physical exam. A palpable nodule was
232 present in 25.4% (n=30) of East/South-East Asian women, versus 8.5% (n=85) of
233 Caucasians and 12.4% (n=24) of other ethnicities ($p<.001$) (Supplementary Table 2).

234 During the initial appointment at the center, 1559 patients had an endovaginal ultrasound
235 performed, of which 13.5% (n=210) were diagnosed with an endometrioma. An
236 endometrioma was found in 38.7% (n=55) of East/South East Asian women, versus 9.6%
237 (n=114) of Caucasians and 18.1% (n=41) of other ethnicities ($p<.001$) (Supplementary
238 Table 2).

239

240 Of women seen at the center, 375 women (23.9%) subsequently underwent surgery at
241 our center within the study time period and also had histologically confirmed endometriosis
242 (Table 2 and Supplementary Table 2). Of these, 82.9% (n=40) of East/South East Asian
243 women had Stage III-IV endometriosis, compared to 24.8% (n=71) of Caucasians and
244 54.2% (n=26) of other ethnicities ($p<.001$) (Supplementary Table 2).

245

246 Clinical characteristics

247 In Supplementary Table 3, clinical characteristics are compared between the ethnicities.

248 Interestingly, East/South East Asian women reported less pain and better quality-of-life.

249 In terms of potential confounding, of particular interest were age, history of infertility, body
250 mass index (BMI), current or previous use of hormonal treatment, previous surgery for
251 endometriosis, and geographical location, as these have been identified in previous
252 studies as risk factors for deep infiltrating endometriosis (2, 5). East/South-East Asians
253 were on average older, with lower BMI, more likely to have infertility, less likely to ever
254 have used hormonal therapy, and less likely to have had previous surgery for
255 endometriosis (Supplementary Table 3). For geographical location, only one East/South
256 East Asian patient lived in a rural location, and thus rural/urban comparisons were not
257 possible (Supplementary Table 3).

258

259 Multivariable analysis

260 Logistic regression analyses for each of the endometriosis phenotypes and ethnicity was
261 performed, controlling for potential confounders mentioned above (Table 4). East/South-
262 East Asians were 8.3 times more likely than Caucasians to have a previously documented
263 history of Stage III/IV endometriosis before referral to the center (adjusted odds ratio [aOR]
264 8.33, 95% CI 3.74 – 18.57, $p < .001$). They were also 2.7 times more likely to have a
265 palpable nodule at physical exam (aOR 2.66, 95% CI 1.57-4.52, $p < .001$), and 4.1 times
266 more likely to have an endometrioma on ultrasound (aOR 4.10, 95% CI 2.68-6.26,
267 $p < .001$). Furthermore, East/South East Asians were 10.9 times more likely to have Stage
268 III/IV endometriosis at the time of surgery by gynecologists at our center (aOR 10.87, 95%
269 CI 4.34-27.21, $p < .001$).

270

271 Corollary analysis

272 Ascertainment or referral patterns may influence our results; for example, East/South
273 East Asians with Stage I/II endometriosis may be less symptomatic and thus less likely
274 to be referred. Therefore, ethnic distribution at our center was compared to the ethnic
275 distribution amongst females in British Columbia (2016 Canadian census). Caucasian
276 women were over-represented in our center (76.2% in our sample vs. 45.6% in British
277 Columbia [BC]), while all other ethnicities were under-represented in our center vs BC:
278 East/South East Asians (9.1% vs. 32.4%), South Asians (7.5% vs. 12.8%), and other
279 ethnicities (5.1% vs. 9.1%). East/South East Asians were 3.5-fold less frequent in our
280 center, while South Asians and other ethnicities were 2-fold less frequent in our center
281 (see Supplementary Table 1).

282

283 DISCUSSION

284 In a prospective registry at a tertiary referral center for endometriosis and pelvic pain, we
285 observed significantly increased rates of moderate-to-severe endometriosis (rAFS
286 stages III-IV) in women of East and South East Asian ethnicity. The incidence of
287 endometrioma on ultrasound was also higher in the East/South East Asian group
288 compared to Caucasian and other ethnicities, as was the incidence of palpable nodule in
289 our study sample. These associations with East/South-East Asian ethnicity were
290 independent of potential confounders including age, BMI, infertility, previous surgery for
291 endometriosis, and use of hormonal medications.

292

293 One explanation for these observations may be that women of East/South East Asian
294 descent may be at increased risk of more severe, advanced stages of endometriosis.

295 However there are alternative explanations as well. For example, East/South East
296 Asians with minimal-mild endometriosis could be less symptomatic and thus not referred
297 to our center. Indeed, we found that East/South East Asian women (as well as other
298 minorities) reported less pain compared to Caucasians, and were also less frequent at
299 our center compared to the province of British Columbia as a whole (26). In addition, if
300 there is a delay in East/South East women with endometriosis seeking care, which would
301 be supported by our observation of older age in this ethnic group, then the endometriosis
302 lesions could progress over time leading to more severe disease. It is also possible that
303 a combination of these factors may lead to the observation of more frequent moderate-
304 to-severe endometriosis in East/South East women in our tertiary center.

305

306 Strengths of the study include large sample size (n = 1594) from a registry of
307 prospectively consented women in British Columbia, Canada, a province known for its
308 ethnic diversity that allows studies of ethnicity-related outcomes. In particular, we
309 compared East/South East Asian women to not only Caucasians, but other minorities
310 including South Asians, to determine that the findings were specific to East/South East
311 Asians. Other strengths include confirmation of retrospective data (previous surgical
312 staging) with prospective data (physical exam, ultrasound, and subsequent surgical
313 staging).

314

315 One limitation is that the study setting was at a tertiary referral center. Thus, the findings
316 may not be generalizable to endometriosis patients seen in the community setting or in
317 the general population. That being said, a tertiary referral center is where the clinical

318 and surgical expertise resides in order to diagnose and excise advanced stage
319 endometriosis. In future work, community or other clinical settings (e.g. infertility clinics)
320 could be included in our registry to determine whether similar ethnic differences are
321 observed in these other samples of women with endometriosis.

322

323 Previous studies have shown that infertile women are more likely to have advanced stage
324 endometriosis, as pelvic anatomy becomes distorted and pelvic adhesions and tubal
325 occlusion may impair oocyte transfer from ovary to the Fallopian tube (27, 28). Older age
326 may also be associated with DIE (3, 29). In our study, we also observed infertility and older
327 age to be associated with more severe endometriosis. Moreover, in the FEELING case-
328 control study of patients from China, Russia and France, factors associated with DIE and
329 OMA were previous use of hormonal treatments for endometriosis, previous surgery for
330 endometriosis and living in an urban area (2). In our sample, where we included ethnicity
331 as an independent variable, ever use of hormonal therapy and previous surgery for
332 endometriosis were non-significant in most of the regression models (Table 4). We were
333 unable to add geographical location into the regression models, as only one East/South
334 East Asian lived in a rural location (Supplementary Table 3).

335

336 Interestingly, although a higher proportion of East/South East Asians in our study had
337 moderate to severe endometriosis, overall they had less pain and better quality of life
338 compared to Caucasian and other ethnicity counterparts. This finding was also
339 demonstrated in the FEELING study (2), where investigators found profound differences
340 in the rate of dysmenorrhea severely impacting quality of life between the French (82%)

341 and the Chinese (44%). There have been studies showing that environmental factors,
342 lifestyle and culture may influence the rate at which pain is reported, healthcare seeking
343 behaviours across cultures, and the way in which pain is conceptualized and expressed
344 (2).

345

346 If the association between East/South East Asian ethnicity and more severe endometriosis
347 is verified in other studies, ethnic background could be considered a risk factor in the pre-
348 operative prediction of moderate-to-severe endometriosis. We observed that East/South
349 East Asians in our study sample were up to 11-times more likely to have moderate to
350 severe endometriosis at the time of our surgery, controlling for age, BMI, infertility,
351 previous surgery for endometriosis and ever usage of hormonal medications. This
352 association may be explained by genetic or environmental factors. Genome wide
353 association studies (GWAS) have identified 12 single nucleotide polymorphisms at 10
354 separate loci that were more strongly associated with Stage III/IV endometriosis than
355 Stage I/II (12), and it is plausible that these genetic loci vary between ethnicities (14).
356 Environmental factors that may differ between ethnicities include diet, employment, or
357 other psychosocial or life history variables (2). However, other population studies are
358 needed first to verify the findings observed in our tertiary referral center.

359

360 **CONCLUSION:**

361 We observed higher rates of moderate-to-severe (Stages III-IV) endometriosis in women
362 of East/South East Asian ethnicity in our tertiary referral center. Additional studies are

363 needed to replicate this finding. Our study raises the possibility that endometriosis severity
364 and/or symptomatology may vary by ethnic background.

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454 Figure legends:

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456 Figure 1: N/A

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458 Figure 2: Stage of endometriosis prior to referral to BC Women's Pelvic Pain and

459 Endometriosis tertiary referral centre (n=603).

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Patients presenting to BC Women’s Center for Pelvic Pain and Endometriosis
(tertiary care center) December 2013 to December 2016
(n = 2372)

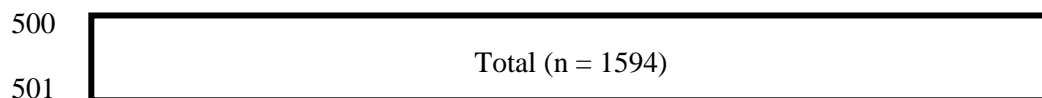


Declined research consent
or withdrew from registry (n = 380)
88% consent rate

Confirmed eligible and consented for registry



Excluded
(Age >50, Menopausal, did not complete physical exam, did not complete ethnicity question, duplicate visits, mixed ethnicity)
(n =398)



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504 **Figure 1: Inclusion/Exclusion criteria flowchart**

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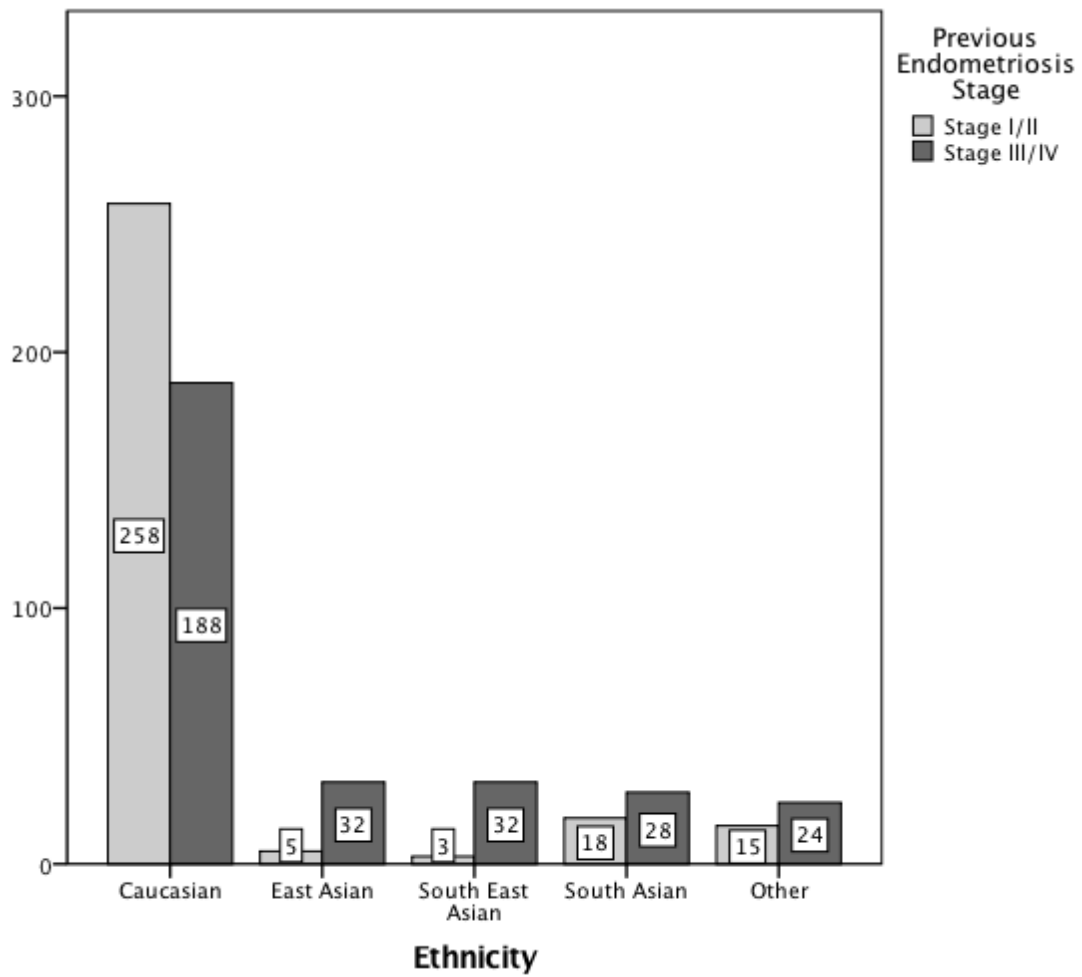
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527 **Figure 2: Ethnicity and previous stage of endometriosis**

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Ethnicity Identified	Example of countries or geographic areas included*
Caucasian	Non-Indigenous North American and/or European Roots
East Asian	China, Japan, Korea, Taiwan, Mongolia
South East Asian	Vietnam, Laos, Cambodia, Thailand, Malaysia, Indonesia, Singapore, Burma, Philippines
South Asian	Pakistan, India, Nepal, Sri Lanka, Bangladesh
Middle Eastern/North African	Egypt, Iran, Iraq, Lebanon, Saudi Arabia, Syria, Turkey, United Arab Emirates and Yemen
First Nations	
Other	African, other

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538 **Table 1:** Ethnicity categories and examples of countries or geographic areas that may be included
539 within each category.

540 *Not a complete or exhaustive list

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554 **Table 2: Descriptive statistics (n=1594) of women with chronic pelvic pain/endometriosis**
555 **treated at tertiary care centre**

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Variables	%	SD / IQR	n
<u>Demographic characteristics</u>			
Age in years (mean)	34.9	7.7	(1594)
Body Mass Index (BMI) (mean)	25.3	5.9	(1567)
Household Income			
< \$20 000	13.4	-	(212)
\$20 000 - \$99 999	60.3		(962)
\$ 100 000 or more	26.1		(416)
Education			
High school or Less	15.3	-	(244)
Some college / College	62.7		(999)
Post-Graduate Degree	17.7		(282)
Other	4.1		(65)
Currently Working	72.6	-	(1150)
Infertility			
Yes	29.5	-	(469)
Never tried	42.0	-	(669)
No	28.5		(454)
Hormonal therapy			
Current use	29.0	-	(463)
Ever use	73.0		(1163)
Location			
Rural	6.3		(97)
Urban	93.7		(1443)
Previous surgery for endometriosis	39.1	-	(624)

<u>Ethnicity</u>			
Caucasian	76.2	-	(1214)
East Asian	5.4	-	(86)
South East Asian	3.7	-	(59)
South Asian	7.5	-	(119)
Hispanic	2.5	-	(40)
Afro-Caribbean	0.4	-	(6)
Middle Eastern/North African	2.1	-	(34)
First Nations	1.3	-	(21)
Other (eg. African, Fijian, etc)	0.9	-	(15)
<u>Pelvic Pain Symptoms</u> (scale 0-10)			
Dysmenorrhea (median)	7	5	(1389)
Deep Dyspareunia (median)	7	4	(1514)
Dyschezia (median)	4	6	(1594)
Chronic Pelvic Pain (median)	7	4	(1594)
<u>Quality of Life Measures</u>			
Endometriosis Health Profile (EHP-30) (mean; scale 0-100)	49.6	24.1	(1572)
Patient Health Questionnaire (PHQ-9) (mean; scale 0-27)	8.8	6.6	(1570)
			(24)
Generalized Anxiety Disorder scale (GAD-7) (mean; scale 0-21)	6.5	5.7	(1569)
Pain Catastrophizing Scale (PCS) (mean; scale 0-52)	19.6	13.6	(1569)

<u>Endometriosis</u>			
Endometriosis (pre-referral surgery) Stage I/II	49.6		(299)
Endometriosis (pre-referral surgery) Stage III/IV	50.4	-	(304)
Palpable nodule on exam	10.6	-	(139)
Endometrioma on ultrasound	13.5	-	(210)
Endometriosis Stage I/II (at current surgery, histology confirmed)	65.1	-	(244)
Endometriosis Stage III/IV (at current surgery, histology confirmed)	34.9	-	(131)

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Groups	Chi-squared (degrees of freedom)	P-value
Caucasian vs. East Asian	27.076 (1)	<.001*
Caucasian vs. South East Asian	31.751 (1)	<.001*
Caucasian vs. South Asian	5.932 (1)	.015
Caucasian vs. Other	5.478 (1)	.019
East Asians vs South East Asians	.445 (1)	.505
East Asians vs South Asians	6.718 (1)	.010
East Asians vs Other	6.094 (1)	.014
South East Asians vs. South Asians	9.665 (1)	.002*
South East Asians vs. Other	8.956 (1)	.003*
South Asians vs. Other	.004 (1)	.950

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574 **Table 3: Ethnicity and previous stage of endometriosis (mutual comparisons).** Statistical
575 comparisons between ethnic groups for previous stage of endometriosis from surgical staging
576 prior to referral to our center (Stage I/II vs. Stage III/IV), as illustrated in Figure 1. Comparisons
577 are corrected for multiple comparisons (*statistical significance $p < 0.005$, due to Bonferroni
578 correction)

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Endometriosis outcome	Stage III/IV, pre-referral surgery (n = 592)			Presence of Palpable Nodule on Physical Exam (n =1283)			Presence of Endometrioma on Ultrasound (n =1521)			Stage III/IV, current surgery and histology confirmed (n = 368)		
	aOR	95% CI	p value	aOR	95% CI	p value	aOR	95% CI	p value	aOR	95% CI	p value
Ethnicity ¹												
East/South East Asian	8.33	3.74 – 18.57	<.001*	2.66	1.57 – 4.52	<.001*	4.10	2.68 – 6.26	<.001*	10.87	4.34 – 27.21	<.001*
Other	2.00	1.18 – 3.39	.010*	1.59	.96 – 2.64	.071	2.00	1.32 – 3.12	.001*	4.46	2.19 – 9.08	<.001*
Age (years, continuous variable)	1.07	1.04 – 1.11	<.001*	1.04	1.13 – 1.07	.005*	1.03	1.01 – 1.06	.016*	1.11	1.06 – 1.16	<.001*
BMI (continuous variable)	.99	.96 – 1.03	.669	.92	.88 – .96	<.001*	1.00	.97 – 1.03	.914	.99	.94 – 1.03	.577
Ever used hormonal therapy	.51	.30 – .84	.009*	1.59	1.02 – 2.48	.042	.92	.65 – 1.30	.636	.59	.32 – 1.10	.095
Infertility ²												
Yes	2.03	1.26 – 3.31	.004*	1.82	1.11 – 2.97	.017*	2.52	1.64 – 3.89	<.001*	2.57	1.27 – 5.17	.008*
Never tried	1.77	1.06 – 2.96	.028*	1.17	.69 – 2.01	.559	1.80	1.13 – 2.87	.013*	2.60	1.22 – 5.53	.013*
Previous surgery for endometriosis	-	-	-	.97	.66 – 1.44	.892	.53	.37 – .76	<.001*	.79	.46 – 1.36	.397
Household Income ³												
\$20 000 - \$99 999	1.66	.81 – 3.38	.165	1.23	.61 – 2.48	.562	1.52	.85 – 2.72	.161	.90	.37 – 2.20	.821
\$100 000 or more	1.52	.70 – 3.29	.289	1.36	.64 – 2.91	.430	1.21	.63 – 2.32	.565	.36	.13 – 1.03	.056
Education ⁴												
Some college	1.28	.71 – 2.30	.413	.73	.40 – 1.33	.306	1.62	.91 – 2.89	.102	1.68	.71 – 3.97	.234
Post-graduate degree	2.44	1.21 – 4.95	.013*	.98	.50 – 1.92	.948	1.66	.87 – 3.19	.128	1.89	.70 – 5.12	.210
Other	2.93	1.04 – 8.23	.042*	.90	.30 – 2.68	.850	1.49	.58 – 3.82	.403	5.36	1.15 – 25.01	.033*
Currently Working	1.42	.91 – 2.214	.125	1.96	1.19 – 3.21	.008*	1.84	1.22 – 2.78	.003*	1.02	.54 – 1.92	.962

¹Caucasian is the reference category.

²No infertility is the reference category.

³\$20 000 is the reference category.

⁴High school or less is the reference category.

* statistically significant p<0.05

aOR denotes adjusted odds ratio, CI denotes confidence interval, BMI(kg/m²) denotes body mass index

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Table 4 Logistic Regression Results. Adjusted odds ratios for the endometriosis outcomes.

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	British Columbia*		Tertiary Referral Center	
	%	N	%	N
Caucasian	45.6	545,625	76.2	1,214
East/South-East Asian	32.4	387,325	9.1	145
South Asian	12.8	153,425	7.5	119
Other	9.1	108,960	5.1	82
Total		1,195,335		1,594

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608 **Supplementary Table 1: Comparison of ethnic distributions among all women in the**
609 **province of British Columbia (BC) vs women attending tertiary referral center for pelvic**
610 **pain in (BC)**

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Endometriosis outcome	Caucasian		East/ South East Asian		OR (95% CI)**	Other		OR (95% CI)**	Total n	p-value
	%	n	%	n		%	n			
Endometriosis Stage (pre-referral surgery)									603	
Stage I/II	57.8	(258)	11.1	(8)	11.0 (5.1-23.4)	38.8	(33)	2.2 (1.3-3.5)		<.001*
Stage III/IV	42.2	(188)	88.9	(64)		61.2	(52)			
Palpable nodule on Pelvic Exam									1311	
No	91.5	(915)	74.6	(88)	3.7 (2.3-5.9)	87.6	(169)	1.5 (0.9-2.5)		<.001*
Yes	8.5	(85)	25.4	(30)		12.4	(24)			
Endometrioma on Ultrasound									1559	
No	90.4	(1076)	61.3	(87)	6.0 (4.0-8.8)	81.9	(186)	2.1 (1.4-3.1)		<.001*
Yes	9.6	(114)	38.7	(55)		18.1	(41)			
Endometriosis Stage (current surgery, histologically confirmed)									375	
Stage I/II	75.2	(215)	17.1	(7)	14.7 (6.2-34.6)	45.8	(22)	3.6 (1.9-6.7)		<.001*
Stage III/IV	24.8	(71)	82.9	(34)		54.2	(26)			

Supplementary Table 2: Unadjusted associations between ethnicity and endometriosis outcomes.

* statistically significant $p < 0.05$, chi-square test

** odds ratio and 95% Confidence Intervals, Caucasian is reference category

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642 **Supplementary Table 3: Ethnicity and demographic characteristics, pain symptoms and**
 643 **quality of life (n=1594)**

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Ethnicity	Caucasian		East/South East Asian		Other		p- value
	% / M	n	% / M	n	% / M	n	
Demographic characteristics							
Age (in years, mean)	33.9	(1214)	37.7	(145)	34.4	(235)	<.001*
Household Income							
< \$20 000	12.7	(154)	9.7	(14)	19.1	(45)	.004*
\$20 000 - \$99 999	59.7	(723)	71.0	(103)	57.9	(136)	
\$ 100 000 or more	27.6	(334)	19.3	(28)	23.0	(54)	
Education							
High school or Less	16.6	(201)	4.8	(7)	15.3	(36)	<.001*
Some college / College	63.4	(768)	72.4	(105)	54.0	(127)	
Post-Graduate Degree	15.9	(192)	20.0	(29)	26.0	(61)	
Other	4.1	(50)	2.8	(4)	4.7	(11)	
Currently Working	73.8	(891)	78.3	(112)	63.4	(147)	<.001*
Body Mass Index (kg/m ² , mean)	25.4	(1193)	23.3	(144)	25.8	(230)	<.001*
Infertility							
Yes	25.8	(313)	48.3	(70)	36.6	(86)	<.001*
Never tried	44.2	(536)	35.2	(51)	34.9	(82)	
No	29.9	(363)	16.6	(24)	28.5	(67)	
Hormonal therapy							
Current use	29.8	(362)	24.8	(36)	27.7	(65)	.402

Ever use	75.1	(912)	58.3	(84)	71.1	(167)	<.001*
Location							
Rural	7.0	(82)	0.7	(1)	6.2	(14)	.016*
Urban	93.0	(1094)	99.3	(139)	93.8	(211)	
Previous surgery for endometriosis							
No	57.9	(704)	74.5	(108)	67.7	(159)	<.001*
Yes	42.1	(511)	25.5	(37)	32.3	(76)	
Pelvic Pain Symptoms							
Dysmenorrhea (mean)	6.2	(1044)	5.8	(133)	6.7	(212)	.046*
Deep dyspareunia (mean)	6.1	(1167)	4.5	(134)	6.2	(213)	<.001*
Dyschezia (mean)	4.4	(1214)	3	(145)	4.4	(235)	<.001*
Chronic Pelvic Pain (mean)	6.2	(1214)	4.7	(145)	5.6	(235)	<.001*
Quality of Life**							
EHP-30 (mean; scale 0-100)	49.6	(1199)	44.5	(143)	53.0	(231)	.004*
PHQ-9 (mean; scale 0-27)	8.9	(1197)	6.8	(143)	9	(231)	<.001*
GAD-7 (mean; scale 0-21)	6.6	(1197)	5.8	(143)	6.4	(230)	.235
PCS (mean; scale 0-52)	19.1	(1197)	22.0	(143)	21.1	(230)	.014*

645 * statistically significant $p < 0.05$

646 **EHP denotes Endometriosis Health profile, PHQ denotes Patient Health Questionnaire, GAD
647 denotes Generalized Anxiety Disorder scale, PCS denotes Pain Catastrophizing Scale

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