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Adenomyosis and Endometriosis in the California Teachers Study: Reproductive and Lifestyle Correlates

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Abstract

Objective—To evaluate the reproductive and lifestyle correlates of a surgically confirmed diagnosis of endometriosis or adenomyosis in a large prospective cohort.

Setting—The California Teachers Study (CTS), an ongoing prospective study of female teachers and school administrators established from the rolls of the California State Teachers Retirement System.

Patients—Diagnoses of endometriosis and adenomyosis were identified from California statewide hospital patient discharge records for CTS cohort members with no prior history of endometriosis. Women with an incident surgical diagnosis of endometriosis (n=229) or adenomyosis (n=961) were compared to disease-free women in the same age range (for endometriosis, n=43,493; for adenomyosis, n=79,495).

Main Outcome Measure(s)—Logistic regression methods were used to calculate age-adjusted and multivariable-adjusted prevalence odds ratios (POR) and associated 95 percent confidence intervals (CI) for self-reported menstrual and reproductive characteristics.

Results—Women diagnosed with endometriosis were younger than those diagnosed with adenomyosis. Factors significantly associated with endometriosis were having a mother or sister with endometriosis and nulligravidity. Factors significantly associated with adenomyosis were increasing parity, early menarche (≤10 years of age), and having short menstrual cycles (≤24 days in length). Women who were obese were also more likely to have a diagnosis of adenomyosis.

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Capsule
The epidemiologic profile of women with a surgical diagnosis of adenomyosis differs from that of women with a surgical diagnosis of endometriosis. Our results also suggest that adenomyosis but not endometriosis is associated with increased endogenous exposure to estrogen.

Conclusions—These observations provide the first epidemiologic profile of women with a surgical diagnosis of adenomyosis and indicate that this profile differs from that of women with a surgical diagnosis of endometriosis. Our results also suggest that adenomyosis but not endometriosis is associated with increased endogenous exposure to estrogen.

Keywords

Adenomyosis; endometriosis; epidemiology

Introduction

Endometriosis and adenomyosis are poorly understood diseases that affect women of reproductive age, causing pelvic pain, dysmenorrhea, and infertility. Adenomyosis occurs when the normal relationship between the basal endometrial layer and the myometrium is disrupted (1); this results in pockets of endometrial glands and stroma within the myometrium. Endometriosis is the presence of endometrial glands and stroma outside the myometrium, usually on the pelvic organs.

Endometriosis may affect as many as 10% of females during their reproductive years but precise estimates of prevalence seem to vary by population (2). Endometriosis is seen in up to 70% of women examined for chronic pelvic pain (2) and among 30-40% of women investigated for infertility, but less frequently among those undergoing tubal sterilization (3). Adenomyosis is thought to be most prevalent among women aged 35-50 years based upon pathologic examination of hysterectomy specimens in women treated surgically for menorrhagia. However, using pelvic ultrasound and magnetic resonance imaging, adenomyosis may be present but asymptomatic in a proportion of women (4).

This study aimed to evaluate the reproductive and lifestyle correlates of a surgically confirmed diagnosis of endometriosis or adenomyosis in a large prospective study (5).

Methods

Study Population and Data Collection

The California Teachers Study (CTS) is an ongoing prospective study of female teachers and school administrators established from the rolls of the California State Teachers Retirement System, as described elsewhere (5). A total of 133,479 women, ranging in age from 22 to over 90 years, completed a self-administered, baseline questionnaire in 1995-1996. In this questionnaire, members of the cohort were asked about health conditions including endometriosis, as well as reproductive history, use of hormones, physical activity, diet and alcohol intake, smoking history, and family history of health conditions including endometriosis.

Diagnoses of endometriosis and adenomyosis were identified from the California Office of Statewide Health Planning and Development (OSHPD) hospital patient discharge records for 1991 to 2003. OSHPD retains a record of each inpatient discharged from a California licensed hospital as required by the California Health and Safety Code (6) and provides up to 24 discharge diagnoses per patient for each admission. A probabilistic record linkage algorithm using social security number, date of birth and sex, was used to obtain OSHPD records for the CTS cohort. Social security numbers have been obtained for 99 percent of the CTS cohort and were validated using a checking algorithm that excludes numbers out of the possible range. Dates of birth were recorded for all CTS members; these were verified by comparing them with California State Teachers Retirement System records.

Exclusions

We restricted all analyses to the 124,612 women who were California residents at baseline, since the California OSHPD data are limited to hospitalizations in California. We excluded 29,410 women who either reported a hysterectomy on the first questionnaire, or who had a hospitalization for hysterectomy prior to completing the first questionnaire in 1995-1996, and 1,922 women without a known age at menarche, thereby limiting the study to women with intact uteri who were considered to be at risk of menstrual disorders. A prior history of endometriosis was identified among 4,962 women who responded affirmatively to the question 'Have you ever had endometriosis?' asked on the baseline questionnaire. These women were excluded from all analyses. An additional 45 women were excluded because they had either an endometriosis diagnosis or an adenomyosis diagnosis recorded in the OSHPD file of hospital discharge records before joining the CTS cohort. A total of 88,273 women were potentially eligible for inclusion in the analyses of endometriosis.

Ascertainment of Endometriosis

An eligible cohort member was defined as having incident endometriosis if she had a principal, second, or third discharge diagnosis of endometriosis (ICD-9 codes 617.1-617.9 inclusive in the OSHPD database) occurring between the date she joined the cohort and December 31, 2003. We verified that the diagnosis was surgically confirmed by checking the principal and other procedures listed during the same hospitalization. We excluded 137 women whose endometriosis diagnoses were not listed among the top three on their records or whose diagnoses were not confirmed by surgery. We had a total of 229 women with a new endometriosis diagnosis, confirmed by surgery, in the cohort. These women ranged in age from 25 to 54 years; all were premenopausal at the time they joined the cohort.

All disease-free premenopausal women who were ages 25 to 54 years among the 88,273 women established as the base cohort were eligible to serve as control subjects for analyses of endometriosis (n=44,031). We excluded 538 women diagnosed with incident adenomyosis during the study from this group of eligible women, leaving 43,493 women available for analysis.

Ascertainment of Adenomyosis

An eligible cohort member was defined as having incident adenomyosis if she had a principal, second or third discharge diagnosis of uterine adenomyosis (ICD-9 code 617.0) between the date she joined the cohort and December 31, 2003. We excluded 419 women whose adenomyosis diagnosis was not among the top three on their OSHPD record or whose diagnosis was not confirmed by surgery, leaving 961 women with a surgically confirmed adenomyosis diagnosis. Sixty-three women included as adenomyosis also had a diagnosis of endometriosis.

Women who were aged 25-79 years without adenomyosis among the 88,273 women established as the base cohort were eligible to serve as control subjects for the adenomyosis analyses (n=79,495 women). We excluded from this group 166 women diagnosed with incident endometriosis during the study follow-up period, leaving 79,329 women available for analysis.

Variable Definitions

Hospitalization Characteristics: The case patients' ages at hospitalization, principal and other diagnoses, including diagnoses of fibroids and infertility, and principal and other procedures, were obtained from the same OSHPD discharge record as their endometriosis or adenomyosis diagnoses.

Participant Characteristics: All characteristics used in the statistical analyses were self-reported by cohort members on the baseline questionnaire. Age at baseline in years was calculated from

the date of birth and the date of questionnaire completion. Race/ethnicity was classified as White, Black, Latina, Asian/Pacific Islander, or other. A positive family history of endometriosis was defined as having a mother or sister with endometriosis and categorized as no, yes, or adopted/unknown.

The menstrual factors that we investigated included age at menarche (less than 10 years, 11, 12, 13, 14, or 15 years or older), time to regular periods (less than one year, one year, two or more years, or never regular/not provided) defined as the time after the first menstrual period until menstruation became regular, and length of usual menstrual cycle (after regular periods were established) in days (less than 25 days, 25-26, 27-28, 29-30, 31-32, 33 or more days, or unknown).

Women were grouped into quintiles according to their body mass index (kg/m^2) at age 18 years; body mass index at baseline was categorized as underweight ($<18.5\ kg/m^2$), normal weight ($18.5\text{-}24.9\ kg/m^2$), overweight ($25\text{-}29.9\ kg/m^2$), obese ($\geq 30\ kg/m^2$), or unknown. Women were also classified according to their use of oral contraceptives (no, yes past user, yes current user, or unknown if used).

Two pregnancy variables incorporated responses to questions on the number of pregnancies, the outcome of each pregnancy, and the age at first full-term pregnancy. Pregnancy history was summarized as never pregnant, ever pregnant but no full-term pregnancy (FTP), and at least one FTP. We created a combined variable representing number of FTPs and age at first FTP classifying women as nulliparous, 1-2 FTP and first FTP before 25 years, 1-2 FTP and first FTP at age 25 to 29 years, 1-2 FTP and first FTP at 30 years or older, 3 or more FTP and first FTP before 25 years, or 3 or more FTP and first FTP at 25 years or older. We also considered whether women ever had difficulty becoming pregnant (no, yes, or not provided); this was defined as having tried unsuccessfully to get pregnant for at least one year. Women who had difficulty becoming pregnant were classified according to whether or not they had ever used fertility drugs for pregnancy (no, yes, or unknown). We also classified women according to whether they had breastfed (no, yes, or unknown) or had undergone a tubal sterilization (no, yes, and unknown).

Menopausal status at baseline was defined by combining information collected on age, age at last menstrual period, reason for cessation of menstrual periods, and oophorectomy status. Perimenopausal women were defined as women who had stopped menstruating within 6 months of completing the baseline questionnaire. Women who reported that their menstrual periods had stopped more than 6 months before completing the baseline questionnaire, or who had had bilateral oophorectomy were defined as postmenopausal. In addition, all women who were not already classified as premenopausal and were 55 years of age or older were considered to be postmenopausal. Menopausal status and use of hormone therapy (estrogen, combined estrogen with progestin, or mixed use of some estrogen alone and some combined estrogen with progestin) were combined into one variable, which was categorized as premenopausal, perimenopausal, postmenopausal and never used hormone therapy, postmenopausal and used estrogen-only therapy, postmenopausal and used combined hormone therapy, postmenopausal and used both estrogen and estrogen plus progestin therapy, or postmenopausal and hormone user of unknown type.

Statistical Analysis

Logistic regression methods were used to calculate age-adjusted and multivariable-adjusted prevalence odds ratios (POR) and associated 95 percent confidence intervals (CI) for each characteristic considered. We considered models where age at baseline was categorized in five-year age groups and in ten-year age groups. The models with ten-year age categories provided a better fit to the data; therefore, only results for these models are presented. To test for trend

across categories of exposure, we fit a continuous ordinal variable representing the median exposure level for each category and determined whether the coefficient for this variable differed from 1.0. The p-values we present for trend tests are 2-sided. We did not adjust the CIs associated with the PORs or the trend test p-values for multiple comparisons. All analyses were performed using SAS Version 9.1 (SAS Institute, Cary, NC).

Results

One third of the women with surgically confirmed endometriosis and almost 25% with adenomyosis were 45-49 years at the time of hospitalization (Table 1). However, 57% of the adenomyosis patients were 50 years of age or older, whereas only 16% of the endometriosis patients were. Uterine leiomyoma was the principal discharge diagnosis of 61 (26.6%) participants with endometriosis, and of 313 (32.5%) participants with adenomyosis, and was listed as one of the 24 diagnoses in the hospital discharge record of 116 (50.7%) patients with endometriosis and of 594 (61.8%) patients with adenomyosis. A concurrent infertility diagnosis was extremely rare.

We present results in tables separately for factors that reflect early characteristics which may precede the onset of either endometriosis or adenomyosis (Table 2) and those that may coexist with the diagnosis of either condition (Table 3).

Nearly all women diagnosed with surgically confirmed endometriosis were in the 30-49 year old age range at the start of the study (Table 2). Women who were aged 40 to 49 years at baseline were most likely to have a surgically confirmed diagnosis of adenomyosis. The majority of participants in this study were White; although the magnitude of the PORs for other racial ethnic groups varied somewhat, none of the 95% CI excluded 1.0. Women diagnosed with endometriosis were more likely to have a mother or sister with the disease than were women without this diagnosis (POR = 2.12, 95% CI = 1.44-3.12). A family history (mother or sister) of endometriosis was unrelated to risk of surgically diagnosed adenomyosis.

Women who had their first menstrual period at 10 years or younger had a greater likelihood of an adenomyosis diagnosis than women with later menarche (POR = 1.59, 95% CI = 1.26-2.01 relative to women with menarche at age 13 years) (Table 2). Endometriosis was not consistently associated with age at menarche; for women with menarche at age 10 years or younger, the pattern of risk (POR = 0.52, 95% CI = 0.26-1.05 relative to women with menarche at age 13 years) differed from that seen for adenomyosis. We investigated time to menstrual cycle regularity in our cohort. Establishing regular menstrual periods 12 to 23 months after menarche was associated with reduced likelihood of endometriosis (POR = 0.67, 95% CI = 0.46-0.98) and adenomyosis (POR = 0.83, 95% CI = 0.70-0.99) relative to establishing regular cycles more quickly; however, no consistent pattern was noted as the PORs were not reduced for women who established regular menstrual periods at least 24 months after menarche. Patients with adenomyosis were more likely to report menstrual cycle lengths of 24 days or less (POR = 1.46, 95% CI =1.13-1.89 relative to women with 27-28 day cycle lengths); however, no statistically significant trend in the PORs was seen.

Body mass index at age 18 years was not associated with a surgically confirmed diagnosis of either endometriosis or adenomyosis. However, women who were overweight or obese at baseline were more likely to have a diagnosis of adenomyosis than normal weight women (POR=1.30, 95% CI=1.11-1.51 for overweight and POR = 1.35, 95% CI =1.12-1.62 for obese women) (Table 3). Further, women who were underweight at baseline were less likely to have a diagnosis of adenomyosis that normal weight women (POR=0.53, 95% CI=0.30- 0.95). When we restricted the analysis to postmenopausal women, overweight and obese women were not at increased risk relative to normal weight women (POR=1.14, 95% CI=0.87-1.47 and

POR=0.95, 95% CI =0.67-1.35, respectively), whereas the risk for underweight women remained reduced (POR=0.58, 95% CI=0.21–1.57). Body mass index at baseline was not associated with a diagnosis of endometriosis.

Women diagnosed with endometriosis were less likely than women without this diagnosis to have had a full-term pregnancy (POR = 0.52, 95% CI=0.39-0.70); among women who had a term pregnancy, those with an endometriosis diagnosis were less likely to have a late pregnancy (at age 30 years or older) or to have more than 2 term pregnancies (Table 3). In contrast, women with adenomyosis were more likely to have had a full-term pregnancy (POR = 1.78, 95% CI =1.46-2.17) than to have never been pregnant, and to have their first pregnancy before age 25 years (POR=1.68 for 1-2 full term pregnancies and POR = 1.56, 95% CI = 1.25-1.93 for 3 or more term pregnancies) than to have had one to two full-term pregnancies at ages 25-29 years. Despite the fact that women with adenomyosis were likely to have term pregnancies early, they were less likely than comparison women to have breastfed their babies (POR = 0.74, 95% CI = 0.62-0.88). A similar pattern was observed for endometriosis, but because they were less likely to be parous, the number of women in the analysis was small. Despite the fact that women diagnosed with endometriosis were half as likely as comparison women to be parous, difficulty becoming pregnant and use of fertility drugs for pregnancy were not associated with the development of endometriosis. These indicators of infertility were similarly unrelated to the development of adenomyosis.

Women with a history of tubal sterilization were less likely to have a subsequent surgically confirmed endometriosis diagnosis (POR = 0.66, 95% CI = 0.42-1.04), and more likely to have a subsequent surgically confirmed diagnosis of adenomyosis (POR = 1.57, 95% CI = 1.34 - 1.84) than women who had not had this procedure (Table 3).

Oral contraceptives had been or were currently being used by the 84% of women with endometriosis and 80% of women with adenomyosis (Table 3). Current oral contraceptive users were less likely to have an endometriosis diagnosis than women who had never used oral contraceptives (POR = 0.41, 95% CI = 0.21-0.78), whereas past oral contraceptive use was associated with having an adenomyosis diagnosis (POR = 1.54, 95% CI = 1.28-1.85).

Premenopausal and perimenopausal women were substantially more likely to have a diagnosis of adenomyosis than postmenopausal women who had never used hormone therapy (Table 3). Among the 32,677 postmenopausal women, 21,000 (64%) reported using hormone therapy. Among postmenopausal women, those who used hormone therapy (estrogen alone, estrogen and progestin alone, or a mixture of both forms of therapy over time) had greater likelihood of an adenomyosis diagnosis than those who had never used hormone therapy.

Discussion

Our study investigated lifestyle and reproductive factors associated with a surgically confirmed diagnosis of endometriosis or adenomyosis in a large cohort of California teachers. Women diagnosed with endometriosis were younger than those diagnosed with adenomyosis. The correlates associated with endometriosis were having a mother or sister with endometriosis and nulligravidity. Factors associated with adenomyosis were early menarche (≤10 years of age), short menstrual cycles (≤24 days in length), parity and an early first full-term pregnancy, and obesity. Women who were premenopausal, perimenopausal or postmenopausal and had used hormone therapy were more likely to have had a subsequent adenomyosis diagnosis than postmenopausal women who had never used hormones.

A surgical diagnosis of endometriosis was associated with never having become pregnant among women in our cohort. This is a consistent finding in the literature (3,7). Although it is known that endometriosis can cause infertility, indicators of fertility problems were not

associated with endometriosis in our study. It is likely that women having difficulties getting pregnant seek medical attention directly, which may result in an earlier diagnosis of endometriosis. These women, who were already diagnosed with the disease before the study start, were excluded from our analyses.

Our finding that parous women, particularly those with a first birth at an early age, have a greater likelihood of an adenomyosis diagnosis is consistent with prior reports. Several prior studies have shown an increased risk of adenomyosis with increasing number of births (4, 8-9). It is possible that these associations may represent increased risks of childbirth-related trauma, with disruption of the barrier between basal endometrium and the myometrium. In particular, Leyendecker et al (10) postulate that uterine hyper peristalsis constitutes a mechanical trauma creating myometrial muscle breakages through which basal endometrial fragments may pass with accompanying development of peristromal muscular tissue leading to adenomyosis.

Substantial evidence suggests that genetic factors play an important role in the pathogenesis of endometriosis (11). In our study, women with endometriosis were more likely to have a first degree relative with the disease. Although the mode of inheritance is uncertain, linkage analysis studies are underway (12). Nevertheless, the majority of women with endometriosis do not have a mother or sister with the disease.

Age at menarche and menstrual cycle patterns have been investigated in patients with endometriosis, but there is minimal and conflicting information in patients with adenomyosis. Missmer et al (13) found an increased risk of endometriosis in women who were nulliparous, experienced early age at menarche, and had shorter menstrual cycle lengths. Alternatively late menarche (>13 years) conferred a greater risk of endometriosis in smaller case-control studies (3,14). In our study we did not find a consistent pattern of endometriosis risk associated with age at menarche or length of menstrual cycles, which may relate to our hospital discharge-based (vs. self-reported) definition of endometriosis. In the study conducted by Missmer et al., a medical record review of 131 of the 1,766 women reporting endometriosis in their study confirmed the diagnosis for 88.6% of those who reported a laparoscopic diagnosis of their disease, but for only 53.8% of those who did not report surgical confirmation (13).

Vercellini (8) and Parazzini (9) found no association between age at menarche and the diagnosis of adenomyosis made at the time of hysterectomy. However Vavilis (4) found that older age at menarche was associated with the diagnosis. Our findings of early age at menarche and short menstrual cycle length taken together suggest increased exposure to menstrual blood in patients with adenomyosis. This is significant since Takahashi et al (15) have shown that estradiol levels in menstrual blood are higher in patients with adenomyosis than in those with endometriosis or controls. Transcripts for the P450 aromatase protein, important in estrogen metabolism, have also been detected in the endometrium of patients with adenomyosis as well as endometriosis and fibroids (16). This suggests that estrogen metabolism in the endometrium of patients with adenomyosis differs from that in women without this condition resulting in a hyperestrogenic environment that may drive the disease in susceptible patients (17). Consistent with this theory are our results showing that a surgical diagnosis of adenomyosis is more likely to occur among premenopausal and perimenopausal women as well as postmenopausal women who have taken hormone therapy.

Several authors (14,18) have demonstrated an inverse relationship between body mass index and endometriosis risk. This effect may extend as far back as the intrauterine environment since fetal growth retardation has been associated with an increased risk of endometriosis (19). Our results did not demonstrate a relationship between body mass index and endometriosis; however women developing adenomyosis were significantly more likely to be overweight or

obese at baseline, although this appears restricted to premenopausal women. Body mass index at age 18 years was unrelated to adenomyosis. These findings have not been previously demonstrated in patients with symptomatic adenomyosis.

Current oral contraceptive use has been associated with lower risk of endometriosis, but past users appear to be at increased risk of this diagnosis (13,20). Our results confirm the finding for current use, but not past use. However, taken together these findings suggest that oral contraceptive use delays the diagnosis or is being used to treat patients with pelvic pain symptoms prior to a definitive surgically confirmed diagnosis. Although past use of oral contraceptives was associated with a diagnosis of adenomyosis in our study, it is not clear whether this past use was prescribed for birth control, or for symptom control of bleeding or pain.

One of the strengths of our study is its prospective design and the large number of women in the analyses, which gave us substantial statistical power to detect associations. This is the first large cohort study to examine epidemiological factors for adenomyosis. Recall bias was also minimized by the assessment of lifestyle and reproductive factors before disease diagnosis. Furthermore, with the use of OSHPD records we have accurate surgical diagnoses of endometriosis and adenomyosis, and access to information on concurrent diagnoses. Because we confined our analyses to patients with surgical diagnoses, our results may not be applicable to women with endometriosis and adenomyosis that is less severe or asymptomatic and does not require surgery. In addition our results are based on a population that is largely non-Hispanic white and results may not be applicable to other racial groups. Although we excluded women reporting a prior history of endometriosis and with any discharge diagnosis of endometriosis or adenomyosis in the five years prior to initiating our study, it is possible that our control groups still included women with a prior surgical diagnosis of endometriosis or adenomyosis. However, given the low rates of surgical diagnosis of these diseases during our 8 year follow-up period (0.5% for endometriosis and 1.2% for adenomyosis); this is unlikely to have influenced our conclusions.

Currently no reproducible diagnostic test exists for either adenomyosis or endometriosis despite the increasing sophistication of both ultrasound and magnetic resonance imaging. The creation of a set of diagnostic criteria via consensus may enable future research to investigate these diseases in younger populations.

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Table 1

Selected characteristics of the hospitalization at the time of the endometriosis or adenomyosis diagnosis, among California Teachers Study participants, from the California Office of Statewide Health Planning and Development patient discharge records, 1995-2003

	Endometriosis diagnosis (*n*=229)		Adenomyosis diagnosis (*n*=961)	
	n	**%**	***n***	**%**
Age at diagnosis (years)				
25-29	1	0.4	3	0.3
30-34	17	7.4	11	1.1
35-39	37	16.2	45	4.7
40-44	59	25.8	129	13.4
45-49	77	33.6	224	23.3
50-54	36	15.7	215	22.4
55-59	2	0.9	98	10.2
60-64	-	-	92	9.6
65-69	-	-	70	7.3
70-74	-	-	39	4.1
75-79	-	-	30	3.1
80-84	-	-	4	0.4
85-89	-	-	1	0.1
Principal hospitalization diagnosis				
Uterine Leiomyoma	61	26.6	313	32.5
Adenomyosis	27	11.8	311	32.4
Endometriosis	85	37.1	16	1.7
Genital prolapse or incontinence	2	0.9	99	10.3
Malignant neoplasm	4	1.8	62	6.4
Benign ovarian mass	13	5.7	38	4.0
Pelvic inflammatory disease	4	1.8	22	2.3
Endometrial hyperplasia	2	0.9	19	2.0
Excessive or frequent menstruation	5	2.2	15	1.6
Other	26	11.4	66	6.9
Concurrent diagnosis of uterine fibroids				
No	113	49.3	367	38.2
Yes	116	50.7	594	61.8
Concurrent diagnosis of infertility				
No	226	98.7	958	99.7
Yes	3	1.3	3	0.3

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Table 2

Multivariable-adjusted prevalence odds ratios for surgically-diagnosed endometriosis and adenomyosis according to baseline characteristics that would precede disease development in the California Teachers Study.

	Endometriosis diagnosed during study 1995-2003			Adenomyosis diagnosed during study 1995-2003		
	No endometriosis	**Endometriosis**	**Multivariable adjusted POR (95% CI)*[a]**	**No adenomyosis**	**Adenomyosis**	**Multivariable adjusted POR (95% CI)*[a]**
Age at baseline (years)						
25-29	4754	15	0.57 (0.33, 0.99)	4772	9	0.10 (0.05, 0.19)
30-39	14201	87	1.08 (0.81, 1.42)	14287	137	0.50 (0.41, 0.61)
40-49	20862	122	1.0	23129	441	1.0
50-59	3447	5	0.25 (0.10, 0.61)	17324	208	0.64 (0.54, 0.76)
60-69	-	-	-	11753	123	0.57 (0.47, 0.70)
70-79	-	-	-	7103	43	0.34 (0.24, 0.46)
Race/Ethnicity						
White	35963	192	1.0	67235	825	1.0
Black	976	7	1.38 (0.65, 2.97)	1921	20	0.82 (0.53, 1.29)
Latina	2992	14	0.88 (0.51, 1.52)	3860	58	1.26 (0.96, 1.66)
Asian/Pacific Island	1994	11	1.11 (0.60, 2.04)	3162	33	0.83 (0.58, 1.18)
Other	1339	5	0.70 (0.29, 1.71)	2190	25	0.95 (0.64, 1.43)
Mother or sister with endometriosis						
No	39610	194	1.0	73264	886	1.0
Yes	2788	30	2.12 (1.44, 3.12)	3763	62	1.25 (0.96, 1.63)
Adopted	866	5	1.19 (0.49, 2.92)	1341	13	0.84 (0.49, 1.47)
Age at menarche (years)						
≤10	2891	9	0.52 (0.26, 1.05)	5229	101	1.59 (1.26, 2.01)
11	6412	41	1.08 (0.74, 1.59)	11829	139	1.00 (0.81, 1.22)
12	12162	59	0.83 (0.59, 1.16)	21432	268	1.07 (0.91, 1.27)
13	12991	75	1.0	23561	276	1.0
14	5319	30	1.00 (0.65, 1.53)	9911	113	1.00 (0.81, 1.27)

	Endometriosis diagnosed during study 1995-2003			Adenomyosis diagnosed during study 1995-2003		
	No endometriosis	Endometriosis	Multivariable adjusted POR (95% CI)*[a]	No adenomyosis	Adenomyosis	Multivariable adjusted POR (95% CI)*[a]
≥15	3489	15	0.78 (0.44, 1.36)	6406	64	0.89 (0.68, 1.18)
*P*trend			.68			.004
Time to regular menstrual periods						
<12 months	19931	120	1.0	39330	495	1.0
12-23 months	8909	36	0.67 (0.46, 0.98)	16107	170	0.83 (0.70, 0.99)
≥24 months	11189	60	0.92 (0.67, 1.26)	16795	232	1.10 (0.93, 1.29)
Never regular, unknown	3235	13	1.09 (0.48, 2.46)	6136	64	0.95 (0.64, 1.41)
*P*trend			.88			.18
Length of menstrual cycle (days)						
≤24	1993	17	1.47 (0.88, 2.47)	3932	68	1.46 (1.13, 1.89)
25-26	3746	10	0.46 (0.24, 0.88)	7261	89	1.08 (0.86, 1.36)
27-28	18246	105	1.0	34744	410	1.0
29-30	10294	57	0.97 (0.70, 1.35)	18159	232	1.10 (0.93, 1.29)
31-32	3710	23	1.09 (0.69, 1.72)	5721	76	1.08 (0.84, 1.39)
≥33	2435	8	0.57 (0.27, 1.19)	3395	35	0.82 (0.58, 1.17)
Unknown	2840	9		5156	51	
*P*trend			.70			.13
Body mass index at age 18 (kg/m^2)						
≤19.1	8361	44	0.85 (0.57, 1.28)	14999	178	0.98 (0.79, 1.20)
19.2-20.2	8468	41	0.79 (0.52, 1.20)	15396	189	0.98 (0.80, 1.21)
20.3-21.3	8189	50	1.0	14854	187	1.0
21.4-23.0	7888	30	0.63 (0.40, 0.99)	14262	187	1.04 (0.85, 1.28)
≥23.1	9286	56	1.01 (0.69, 1.48)	15738	194	0.96 (0.78, 1.17)
Unknown	1072	8		3119	26	
*P*trend			.50			.49

*POR, prevalence odds ratio; CI, confidence interval.

[a] Adjusted for the other variables in the table.

Table 3

Multivariable-adjusted prevalence odds ratios for surgically-diagnosed endometriosis and adenomyosis according to baseline reproductive and hormonal characteristics in the California Teachers Study

	Endometriosis during study 1995-2003			Adenomyosis during study 1995-2003		
	No endometriosis	Endometriosis	Multivariable adjusted POR (95% CI)*[a]	No adenomyosis	Adenomyosis	Multivariable adjusted POR (95% CI)*[b]
Pregnancy history						
Never pregnant	10554	79	1.0	16831	116	1.0
Ever pregnant, no full-term pregnancy	3711	20	0.65 (0.40, 1.07)	4965	50	1.30 (0.93, 1.81)
At least one full-term pregnancy	28543	130	0.52 (0.39, 0.70)	55711	791	1.78 (1.46, 2.17)
*P*trend			<.001			<.001
Number of full-term pregnancies and age at first						
Nulliparous	14265	99	1.22 (0.88, 1.68)	21802	166	0.68 (0.55, 0.83)
1-2 full-term pregnancies, first at age <25 years	4052	25	0.98 (0.61, 1.56)	8846	186	1.68 (1.37, 2.06)
1-2 full-term pregnancies, first at age 25-29 years	9789	62	1.0	16258	206	1.0
1-2 full-term pregnancies, first at age ≥30 years	8467	31	0.54 (0.35, 0.84)	12716	145	0.83 (0.67, 1.03)
≥3 full-term pregnancies, first at age <25 years	2506	7	0.43 (0.20, 0.94)	9027	159	1.56 (1.25, 1.93)
≥3 full-term pregnancies, first at age ≥25 years	3729	5	0.20 (0.08, 0.50)	8858	95	0.90 (0.70, 1.15)
Ever had difficulty becoming pregnant						
No	35181	183	1.0	63007	750	1.0
Yes	7372	45	1.17 (0.84, 1.62)	13863	201	1.11 (0.95, 1.31)
Unknown	255	1		637	6	
Ever used fertility drugs for pregnancy						
No	40129	214	1.0	74002	900	1.0
Yes	2679	15	1.05 (0.62, 1.79)	3505	57	1.16 (0.88, 1.53)

	Endometriosis during study 1995-2003			Adenomyosis during study 1995-2003		
	No endometriosis	**Endometriosis**	**Multivariable adjusted POR (95% CI)*[a]**	**No adenomyosis**	**Adenomyosis**	**Multivariable adjusted POR (95% CI)*[b]**
Ever breastfed[c]						
No	6680	37	1.0	15963	225	1.0
Yes	25574	113	0.72 (0.43, 1.20)	44713	616	0.74 (0.62, 0.88)
Ever had tubal ligation						
No	36806	205	1.0	66342	732	1.0
Yes	5630	21	0.66 (0.42, 1.04)	10234	212	1.57 (1.34, 1.84)
Unknown	372	3	1.50 (0.48, 4.71)	931	13	1.31 (0.75, 2.28)
Oral contraceptive use						
No	6565	35	1.0	21819	175	1.0
Yes, past user	29427	179	1.17 (0.81, 1.69)	47947	718	1.54 (1.28, 1.85)
Yes, current user	5967	13	0.41 (0.21, 0.78)	6479	47	1.08 (0.76, 1.51)
Unknown	849	2		1262	17	
Menopausal status						
Premenopausal	42808	229		42862	624	4.72 (3.22, 6.91)
Perimenopausal			-	2269	32	3.40 (2.10, 5.51)
Postmenopausal, no hormone therapy use			-	11349	43	1.0
Postmenopausal, estrogen use only			-	3330	25	2.09 (1.27, 3.43)
Postmenopausal, estrogen plus progestin use only			-	13853	163	2.87 (2.04, 4.02)
Postmenopausal, mixed hormone therapy use			-	3560	69	4.93 (3.37, 7.21)
Postmenopausal, unknown hormone therapy use			-	284	1	0.92 (0.13, 6.73)
Body mass index (kg/m^2)						
Underweight (<18.5)	1335	6	0.86 (0.38, 1.96)	2159	12	0.53 (0.30, 0.95)
Normal weight (18.5-24.9)	26946	140	1.0	45036	501	1.0
Overweight (25-29.9)	8531	55	1.26 (0.92, 1.72)	17770	258	1.30 (1.11, 1.51)

	Endometriosis during study 1995-2003			Adenomyosis during study 1995-2003		
	No endometriosis	**Endometriosis**	**Multivariable adjusted POR (95% CI)*[a]**	**No adenomyosis**	**Adenomyosis**	**Multivariable adjusted POR (95% CI)*[b]**
Obese (≥30)	5224	23	0.83 (0.53, 1.29)	10112	162	1.35 (1.12, 1.62)
Unknown	772	5		2430	24	
*P*trend			.86			<.001

*POR, prevalence odds ratio; CI, confidence interval.

[a]Adjusted for age, race, family history of endometriosis, time to regular menstrual periods, and length of menstrual cycle.

[b]Adjusted for age, race, age at menarche, time to regular menstrual periods, and length of menstrual cycle.

[c]Among parous women.