# Differences in characteristics among 1,000 women with endometriosis based on extent of disease

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**Objective:** To determine the relationship between disease severity and patient characteristics in endometriosis.
**Design:** Cross-sectional study of self-reported survey data.
**Setting:** Academic research setting.
**Patient(s):** One thousand women in the Oxford Endometriosis Gene (OXEGENE) study.
**Intervention(s):** None.
**Main Outcome Measure(s):** Participants were assigned to one of two groups with predominantly revised AFS stage I–II (group I, n = 423) or III–IV disease (group II, n = 517). Their characteristics were compared by disease extent.
**Result(s):** Most participants were white (96%) and of reproductive age (81%). Women in group I were significantly younger on entering the study (39.9 ± 0.5 vs. 44.5 ± 0.4 years). Overall time to diagnosis did not differ between groups. The most common symptoms leading to a diagnosis were dysmenorrhea (79%) and pelvic pain (69%). In group II, subfertility (21.5% vs. 30.0%) and an ovarian mass (7.3% vs. 29.4%) more commonly led to a diagnosis, whereas dyspareunia (51.1% vs. 39.5%) was significantly more common in group I. Subfertility (41.5% vs. 53.4%) remained more common in group II throughout reproductive life, although birth and miscarriage rates were similar.
**Conclusion(s):** Pelvic pain is common to all with endometriosis and those with more extensive disease report higher rates of subfertility. Remarkably, the time to diagnosis was similar among women. (Fertil Steril® 2008;89:538–45. ©2008 by American Society for Reproductive Medicine.)

**Key Words:** Endometriosis, patient characteristics, extent of disease, pelvic pain, subfertility

Chronic pelvic pain, defined as persistent pain in the pelvis, is the most common symptom associated with endometriosis, yet there is no clear relationship between the severity of the pain experienced and the extent of disease, irrespective of which classification system is used. Researchers have found either no association between pain symptoms and disease stage (1–3) or observed a degree of association between pain and the presence of adnexal adhesions, rectal and vaginal infiltration, ovarian involvement, or endometriomas (2, 4, 5). The failure of many women with minimal endometriosis to respond to surgical treatment has led some investigators to question whether this is even a cause of pain (6), especially as it may be an incidental finding in asymptomatic women (7, 8).

The relationship between subfertility and disease stage is similarly uncertain. Some researchers have found no association between stage and subfertility (1), whereas others report that fertility decreases with increasing disease severity (9).

Although studies have reported an increased risk of other diseases among women with endometriosis (10–12), evidence is lacking as to how these other conditions are influenced by stage of disease. Women with endometriosis, regardless of stage, appear to have similar ages at menarche and menstrual patterns (13). Health and lifestyle factors, such as general health, depressive state, history of sexually transmitted diseases, or use of contraception have not been shown to differ by disease stage (1, 9), but those with milder forms of endometriosis have been reported to smoke more cigarettes per day (14). Assessing whether such factors are a cause or a consequence of the condition has been virtually impossible because of the retrospective study designs used (15), although such studies do provide a profile of the characteristics of women with different stages of disease.

The current study investigates survey responses from 1,000 women with surgically confirmed endometriosis who are participating in the Oxford Endometriosis Gene (OXEGENE) study (16). We analyzed their responses to determine whether women with extensive disease report more symptoms and more problems with their menses and reproductive

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health in general than women with milder disease. We also sought to investigate how family history, personal health, and lifestyle factors vary by extent of disease.

## MATERIALS AND METHODS

Women were recruited into the OXEGENE study, part of the International Endogene Study (17) which aims to identify susceptibility genes in endometriosis. The study design and recruitment methods have been reported previously (16). In brief, women were identified from the clinic databases of collaborating clinicians in Britain, Ireland, and the United States, or through advertisements, by the OXEGENE website, or research centers throughout the world. The sample of women used in the present analyses comprised the first 1,000 that returned the survey questionnaire. Because of the genetic focus of the OXEGENE study, many women were related to each other, such that 570 women came from 257 families and had one or more affected family members participating in the study; 430 others did not have any relatives with endometriosis who participated. In addition to providing DNA for genetic linkage and association studies, women completed a survey at study entry that included questions relating to symptoms, the diagnosis of endometriosis, menstrual and reproductive history, personal health, and lifestyle factors.

The questionnaire was self-administered and gathered self-reported data in women with endometriosis confirmed through operative records. Women reported retrospectively on the age at symptom onset, the type of symptoms that led to a diagnosis (e.g., pelvic pain, painful periods, infertility, ovarian tumor or mass), the age at which medical attention was first sought, and age and type of first surgery confirming the diagnosis of endometriosis. Some questions related to the timing of diagnosis with endometriosis. For instance, the survey included questions specifically on the use of contraceptives before diagnosis rather than at any time. Several questions on reproductive and other medical history inquired about their presence before, after, or both before and after diagnosis with endometriosis. Women were instructed to answer questions on their menstrual patterns at the time the diagnosis was first made. Other questions related to lifetime prevalence (e.g., ever having a pregnancy and pregnancy outcomes, ever having had infertility lasting more than 12 consecutive months, ever having had allergies, a family member with endometriosis, smoked cigarettes, or used talc as body powder).

Disease stage was assessed by one gynecologist (S.K.) from the surgical records using the revised American Fertility Society (AFS) classification system (18). Of the 1,000 women who completed the survey, 940 (94.0%) had sufficient information in their operative records to classify disease severity into four categories: stage A (revised AFS stage I); stage $A^+$ (defined as superficial ovarian disease plus some adhesions, i.e., similar to revised AFS stage II); stage B (revised AFS stage III–IV disease); and stage C (isolated rectovaginal nodules) (17). This simplified system was used because it proved difficult to assign revised AFS stage II retrospectively using the clinical records gathered from hundreds of different gynecologists. If a woman had had more than one operation, disease stage was based on the most severe findings; however, if there was ever any uncertainty about the extent of disease present, a less severe stage was always assigned. Women were excluded from the study if their operative records were unavailable or the diagnosis was questionable. In the United Kingdom, the study received approval from the regional Multi-centre Research Ethics Committee and Local Research Ethics Committees; the appropriate approval was also obtained in collaborating centers. An exemption from review by the Investigational Review Board (IRB) was granted by the Office of Human Subjects Research at the National Institutes of Health, Bethesda, Maryland, for the evaluation of this anonymized and unlinked survey.

For the purpose of analysis, the women were divided into two groups: group I (stages A and A+) and group II (stages B and C). Demographic characteristics, symptoms, diagnosis, menstrual history, reproductive health and infertility, contraception, comorbid diseases, family history, and lifestyle factors were described using frequency distributions. Overall comparisons of categorical variables were made using $\chi^2$ tests, whereas specific proportions for contingency tables with more than two rows or columns were compared using Z-tests. Post-hoc ANOVA was used to compare the number of symptoms by times to seeking medical attention and diagnosis from onset of symptoms, and time from seeking medical attention to diagnosis. Continuous variables such as subject age, and ages at and times to seeking medical attention and diagnosis were compared by the Van Der Waerden nonparametric tests as data were not normally distributed.

To account for any recall differences based on time since diagnosis, the mean time between the age at diagnosis and completion of the questionnaire was calculated and compared using nonparametric tests. Logistic regression analyses were used to control for the potential confounding of subject age and time since diagnosis when assessing the association between extent of disease and subfertility, pregnancy outcomes, use of contraception and oral contraceptive (OC) pills, and lifestyle factors. Heavy menstrual flow was also controlled for when the associations between extent of disease and use of regular tampons or overnight tampon use were assessed.

Related cases within a family may influence the frequency of the assessed characteristics in group I and group II, because it may cause dependence between individuals and the factors assessed. Therefore, all analyses were repeated using only unrelated cases, which included a randomly selected case from each family and all women without any participating relatives affected with endometriosis (total number of cases: 687 [272 in group I, 361 in group II, 54 could not be classified]).