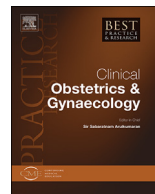




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## Risk for and consequences of endometriosis:

## Q9 A critical epidemiologic review

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## A B S T R A C T

## Keywords:

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Endometriosis affects approximately 10% of women of reproductive age. Characteristics robustly associated with a greater risk for endometriosis include early age at menarche, short menstrual cycle length, and lean body size, whereas greater parity has been associated with a lower risk. Relationships with other potential characteristics including physical activity, dietary factors, and lactation have been less consistent, partially because of the need for rigorous data collection and a longitudinal study design. Critical methodologic complexities include the need for a clear case definition; valid selection of comparison/control groups; and consideration of diagnostic bias and reverse causation when exploring demographic characteristics, medical history, and lifestyle factors. Reviewers and editors must demand a detailed

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description of rigorous methods to facilitate comparison and replication to advance our understanding of endometriosis.

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## Q11 Endometriosis prevalence and incidence

Accurate measurement of the incidence and prevalence of endometriosis is complicated by the current requirement for surgical visualization to establish a definitive diagnosis. Factors influencing referral for/acceptance of surgery and access to surgical expertise create a biased sample among those who achieve a diagnosis. Prevalence estimates vary considerably among different populations, ranging from approximately 2–4% among asymptomatic women seeking tubal ligation [1–3] to 5–50% among infertile women [4–8] and to 5–21% among women hospitalized for pelvic pain [4–8]. However, the actual prevalence of endometriosis is likely underestimated among women undergoing an elective tubal ligation and, conversely, is likely overestimated among women undergoing surgery/hospitalization for pain symptoms and/or infertility. Most recently, the ENDO study enrolled 495 women undergoing laparoscopy/laparotomy between 2007 and 2009 and 131 women from the general population to estimate the incidence of endometriosis. Approximately 41% of women scheduled to undergo laparoscopy were found to have surgically visualized endometriosis compared with approximately 11% of women from the general population visually diagnosed using magnetic resonance imaging [9].

Based on prevalence estimates of pelvic pain and subfertility in the general population, the estimated overall prevalence of endometriosis is 10% and approximately 2% for undiagnosed symptomatic disease [10]. Few studies have investigated endometriosis incidence and prevalence among adolescents. The reported prevalence of visually confirmed endometriosis among adolescents with pelvic pain ranges from 25% to 100%, with an average of 49% among adolescents with chronic pelvic pain and 75% among adolescents unresponsive to medical treatment [11].

Information about the incidence of endometriosis in the general population is limited. Two studies have reported the age-specific incidence of endometriosis diagnosis among white women in Rochester, Minnesota (Fig. 1). Houston et al. [12] reported an overall incidence of histologically confirmed endometriosis of 160.4/100,000 person-years among women aged 15–49 years between 1970 and 1979, with a peak between ages 35 and 44 years (342.3/100,000 person-years). In the same geographic region, Leibson et al. [13] observed an overall incidence rate of clinically diagnosed endometriosis of 187/100,000 person-years among women aged >15 years from 1987 to 1999, with a peak incidence between ages 25 and 34 years (380.6/100,000 person-years). Incidence patterns similar to those obtained by Leibson et al. [13] were observed in the Nurses' Health Study II (NHSII) (Fig. 1). The NHSII is a prospective cohort of 116,429 U.S. female nurses aged 25–42 years at enrollment in 1989. Between 1989 and 1999, the incidence rate of laparoscopically confirmed endometriosis was 298/100,000 person-years [14]. While the incidence peaked at ages 25–34 years (417/100,000 person-years), the decrease in incidence was more modest for women without a history of infertility, declining only after age of 44 years ( $p$ -trend<0.0001) [14].

## Methodologic issues in endometriosis-focused study design

The key methodologic issues for endometriosis discovery – whether clinical, population, or bench science – include choosing a valid (1) endometriosis case definition and (2) comparison group as well as (3) defining the appropriate etiologic window to capture the exposures, outcomes, and disease progression to address the study aims [10,15–17]. In general, case–control studies of endometriosis tend to be more vulnerable to bias owing to control selection and recall; however, these issues can occur in all study designs.

### Endometriosis case definition

There are multiple pathways through which a person with endometriosis may be diagnosed or mis/undiagnosed (Fig. 2). Some women are diagnosed due to pelvic pain, whereas others are diagnosed at

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