

# Endometriosis: Incidence and Prevalence

Subjects: **Pathology**

Contributor: Antonio Sarria-Santamera

Endometriosis is a complex and heterogeneous disease. Diverse authors have tried to determine the incidence and the prevalence of endometriosis, but the results obtained show significant variability. A systematic review and meta-analysis will be conducted to produce pooled estimates of those studies and discuss the advantages and limitations of the different case definitions, data sources, and study designs that have provided incidence and prevalence figures.

endometriosis

epidemiology

incidence

prevalence

## 1. Introduction

Endometriosis is a complex clinical condition [1] characterized by the growth of endometrial-like tissue, glands, and stroma outside of the uterine cavity. Endometriosis is the leading cause of morbidity among premenopausal women, often painful and chronic, and has a negative impact on a patient's physical and emotional well-being, quality of life, and productivity, placing a significant economic and social burden on patients, their families, and society as a whole [2].

Despite extensive research [3], there remain much controversy and dilemmas regarding this complex and enigmatic disorder, related to its etiopathogenesis, diagnosis, overall clinical management, prognosis, and the epidemiology of this condition. Since the early work of Eskenazi [4], there is an overall assumption that the prevalence of endometriosis is around 10%. That study reviewed data on the epidemiology of the endometriosis population based on three publications that reported the prevalence of endometriosis in the general population: (1) Vessey revealed the prevalence of endometriosis in a group of women attending family planning clinics to be 1.8% [5]; Houston, based on data from residents in Rochester, obtained incidence ranging between 108.8 and 246.9 per 100,000 women-year and estimated an annual prevalence between 2.5 and 8.2% [6]; and Kjerulff, analyzing data from the US Health Interview Survey, obtained a self-reported prevalence of 6.9 per 1000 [7].

## 2. Discussion

The disparate results obtained in the studies analyzing the epidemiology of endometriosis, may not only be due to methodological issues and the specific limitations of the different designs and data analyzed, including case definitions and subject selection strategies, but also to the inherent heterogeneity and complexity of endometriosis.

The true incidence or prevalence of endometriosis is difficult to establish. Endometriosis is a heterogeneous clinical condition, with significant variability in terms of presentation and progression and an absence of specific biomarkers for its diagnosis and follow-up, for which imaging tests do not allow identifying all cases with sufficient sensitivity and specificity [8][9]. Since visualization by endoscopy or laparotomy and histological confirmation is required for a definitive diagnosis, as a gold standard method, compared with a less accurate diagnosis by patient history, physical examination and noninvasive tests [7][10][11] make it difficult to arrive at a definite figure for its prevalence and incidence.

The problems for the identification of the prevalence or incidence of endometriosis were already described in the Eskenazi article, with very clear recommendations on how to carry out these studies [4]. However, more than 20 years later, those recommendations to understand the epidemiology of endometriosis have not yet been put into practice, so there remain significant methodological limitations to enable a definite characterization of the population magnitude of endometriosis.

Thus, it is relevant to note how when assessing the discrepancy in the estimate identified, these are usually higher in studies with surveys and self-reported data by women [2], whereas they are lower in cohort studies in which clinical confirmation was considered or those using population-based datasets that estimate endometriosis rates based on diagnostic codes of health care utilization databases, including both ambulatory diagnosed cases and hospital discharges.

Some of the studies with self-reported data had low response rates, a serious limitation to extract valid conclusions from those reports. It would be critical to know if there were differences in the characteristics of women who responded or not to those questionnaires, but this information is not reported in those papers. Self-reported data may be subject to certain bias; it has been suggested it may have a fairly good predictive ability to have an endometriosis diagnosis [12].

Studies that obtain prevalence or incidence estimates through automated clinical registries and calculate rates using ICD-type diagnostic codes may be subjected to the underreporting of certain diagnoses. However, it is important to note that these studies were carried out in countries and health systems with very diverse ethnic, cultural, organizational, or healthcare settings and still consistently report low incidence or prevalence figures that range between 0.1 and 0.2%. Publications reporting data exclusively from surgical cases may offer a limited view of the broad spectrum of the disease of those women who have a surgical intervention to remove endometrial tissue. Surgery is the only treatment that can completely remove the lesions associated with endometriosis. It is performed in the event of incapacitating symptoms and/or infertility. Studies based on integrated information systems include data extracted both from ambulatory care medical records, either from primary or specialized consultations, may be including cases with a clinical diagnosis and treatment for endometriosis regardless of histological or surgical confirmation.

A concern in the clinical management of endometriosis is the existence of delays in its diagnosis [13][14]. Although delays may affect women's well-being, delays would only influence incidence or prevalence if they vary across

settings, countries, or healthcare systems. If they are systematic, no effect should be assumed on incidence or prevalence. There is no evidence of the existence of variation in diagnostic delays, and the effect that this delay may have on the epidemiological burden of endometriosis is not clear [12][15], as no meta-analysis or systematic reviews investigating this question were conducted. However, single studies originating from Europe, Australia, China, and the US report diagnostic delays between 3.5 and 13 years [16][17][18][19][20], with the underrepresentation of years of diagnostic delays from Asian and African countries.

Living and working environments, along with regional and epigenetic factors, might also impact the development and manifestations of endometriosis, which were not taken into account in studies investigating the incidence and prevalence of endometriosis. Their influence needs further investigation [21][22][23][24][25][26][27].

The presence of asymptomatic endometriosis could also not be ruled out. In this case, it is generally discovered incidentally when the patient seeks medical advice due to difficulty conceiving, as a large proportion of endometriosis patients are, in fact, infertile [28][29][30]. However, if women do not experience fertility problems asymptomatic, painless endometriosis may remain undetected. Although there may be differences between clinically diagnosed endometriosis and endometriosis diagnosed from surgery and/or histology, if endometriosis is asymptomatic, it would only be possible to be diagnosed in population studies not only through interviews or questionnaires, but it would ideally require at least a gynecological examination. The closest to this approach are cohort studies, such as the Nurses' Study from the USA or the Uppsala study, in which annual incidence rates of approximately 0.2% are reported [31][32]. In the study by nurses from the Japan Nurses' Health Study [33], although the reported incidence was much higher when clinical confirmation was investigated, the figures were substantially reduced.

Given the significant variability in the diagnostic and clinical management of endometriosis, it is not surprising the significant heterogeneity identified in the meta-analysis, even considering that separate random-effects models were conducted for the different types of designs used in this review. The criteria for the diagnosis of endometriosis could vary in studies from country to country, which could explain some variations in estimates. For example, ultrasound examination and a gold standard of diagnosis laparoscopy have different positive predictive values, subsequently leading to measurement bias in the studies and increased between-study variability [8]. Apart from this, there could be other methodological heterogeneity, including sampling strategy, recruitment methods, differences in demographic characteristics of study populations (age, ethnicity, and others). Results under the assumption of a random-effects model tend to be more conservative than those obtained assuming fixed effects, resulting in broader confidence intervals.

### 3. Conclusions

Endometriosis is a heterogeneous clinical problem with significant uncertainty regarding its etiopathogenesis, diagnosis, treatment, and prognosis. It is well established that its main clinical manifestation, pain, causes a significant impact on women's quality of life and represents a significant medical and social burden because of its direct and indirect costs. This work offers a comprehensive vision of the advantages and limitations of the various

methodological approaches to provide estimates of the incidence or prevalence of endometriosis. The data already published indicates a pooled estimated prevalence of endometriosis at around 1–5% and an incidence between 1.4 and 3.5 per thousand per year. The heterogeneity in the designs and data analyzed, as well as the clinical complexity and difficulties for the diagnosis of endometriosis, may influence the variability in those estimates. As well as a necessity for improving the biomedical and clinical evidence bases for the diagnosis and clinical management of this condition, appropriately designed epidemiological studies remain necessary to provide a valid estimation of the population burden of endometriosis.

## References

1. Zondervan, K.T.; Becker, C.M.; Missmer, S.A. Endometriosis. *N. Engl. J. Med.* 2020, 382.
2. As-Sanie, S.; Black, R.; Giudice, L.C.; Valbrun, T.G.; Gupta, J.; Jones, B.; Laufer, M.R.; Milspaw, A.T.; Missmer, S.A.; Norman, A. Assessing research gaps and unmet needs in endometriosis. *Am. J. Obstet. Gynecol.* 2019, 221, 86–94.
3. Rokitansky, C.V. Ueber Uterusdrusen-Neubildung in Uterus und Ovariul Sarcomen; Carl Ueberreuter: Wien, Austria, 1860
4. Eskenazi, B.; Warner, M.L. Epidemiology of endometriosis. *Obstet. Gynecol. Clin. N. Am.* 1997, 24, 235–258.
5. Vessey, M.P.; Villard-Mackintosh, L.; Painter, R. Epidemiology of endometriosis in women attending family planning clinics. *Br. Med. J.* 1993, 306, 182–184.
6. Houston, D.E.; Noller, K.L.; MELTON III, L.J.; Selwyn, B.J.; Hardy, R.J. Incidence of pelvic endometriosis in Rochester, Minnesota, 1970–1979. *Am. J. Epidemiol.* 1987, 125, 959–969.
7. Kjerulff, K.H.; Erickson, B.A.; Langenberg, P.W. Chronic gynecological conditions reported by US women: Findings from the National Health Interview Survey, 1984 to 1992. *Am. J. Public Health* 1996, 86, 195–199.
8. Stratton, P.; Winkel, C.; Premkumar, A.; Chow, C.; Wilson, J.; Hearns-Stokes, R.; Heo, S.; Merino, M.; Nieman, L.K. Diagnostic accuracy of laparoscopy, magnetic resonance imaging, and histopathologic examination for the detection of endometriosis. *Fertil. Steril.* 2003, 79, 1078–1085.
9. Mounsey, A.; Wilgus, A.; Slawson, D.C. Diagnosis and management of endometriosis. *Am. Family Phys.* 2006, 74, 594–600.
10. Taylor, H.S.; Adamson, G.D.; Diamond, M.P.; Goldstein, S.R.; Horne, A.W.; Missmer, S.A.; Snabes, M.C.; Surrey, E.; Taylor, R.N. An evidence-based approach to assessing surgical versus clinical diagnosis of symptomatic endometriosis. *Int. J. Gynecol. Obstet.* 2018, 142.
11. Kuznetsov, L.; Dworzynski, K.; Davies, M.; Overton, C. Diagnosis and management of endometriosis: Summary of NICE guidance. *BMJ* 2017.

12. Saha, R.; Marions, L.; Tornvall, P. Validity of self-reported endometriosis and endometriosis-related questions in a Swedish female twin cohort. *Fertil. Steril.* 2017, 107.
13. Surrey, E.; Soliman, A.M.; Trenz, H.; Blauer-Peterson, C.; Sluis, A. Impact of Endometriosis Diagnostic Delays on Healthcare Resource Utilization and Costs. *Adv. Ther.* 2020, 37.
14. Kvaskoff, M.; Mu, F.; Terry, K.L.; Harris, H.R.; Poole, E.M.; Farland, L.; Missmer, S.A. Endometriosis: A high-risk population for major chronic diseases? *Hum. Reprod. Update* 2015, 21, 500–516.
15. Ghai, V.; Jan, H.; Shakir, F.; Haines, P.; Kent, A. Diagnostic delay for superficial and deep endometriosis in the United Kingdom. *J. Obstet. Gynaecol.* 2020, 40.
16. Soliman, A.M.; Fuldeore, M.; Snabes, M.C. Factors Associated with Time to Endometriosis Diagnosis in the United States. *J. Women's Health* 2017, 26.
17. O'Hara, R.; Rowe, H.; Fisher, J. Managing endometriosis: A cross-sectional survey of women in Australia. *J. Psychosom. Obstet. Gynecol.* 2020.
18. van der Zanden, M.; Arens, M.W.J.; Braat, D.D.M.; Nelen, W.L.M.; Nap, A.W. Gynaecologists' view on diagnostic delay and care performance in endometriosis in the Netherlands. *Reprod. Biomed. Online* 2018, 37.
19. Hudelist, G.; Fritzer, N.; Thomas, A.; Niehues, C.; Oppelt, P.; Haas, D.; Tammaa, A.; Salzer, H. Diagnostic delay for endometriosis in Austria and Germany: Causes and possible consequences. *Hum. Reprod.* 2012, 27.
20. Han, X.T.; Guo, H.Y.; Kong, D.L.; Han, J.S.; Zhang, L.F. Analysis of characteristics and influence factors of diagnostic delay of endometriosis. *Zhonghua fu chan ke za zhi* 2018, 53, 92–98.
21. Leibson, C.L.; Good, A.E.; Hass, S.L.; Ransom, J.; Yawn, B.P.; O'Fallon, W.M.; Melton, L.J. Incidence and characterization of diagnosed endometriosis in a geographically defined population. *Fertil. Steril.* 2004, 82, 314–321.
22. Sirohi, D.; Al Ramadhani, R.; Knibbs, L.D. Environmental exposures to endocrine disrupting chemicals (EDCs) and their role in endometriosis: A systematic literature review. *Rev. Environ. Health* 2020.
23. Upson, K. Environmental Risk Factors for Endometriosis: A Critical Evaluation of Studies and Recommendations from the Epidemiologic Perspective. *Curr. Epidemiol. Rep.* 2020, 7.
24. Olšarová, K.; Mishra, G.D. Early life factors for endometriosis: A systematic review. *Hum. Reprod. Update* 2020, 26.
25. Murvoll, K.M.; Skaare, J.U.; Jensen, H.; Jenssen, B.M. Associations between persistent organic pollutants and vitamin status in Brünnich's guillemot and common eider hatchlings. *Sci. Total Environ.* 2007, 381.

26. Zhang, S.; Gong, T.-T.; Wang, H.-Y.; Zhao, Y.-H.; Wu, Q.-J. Global, regional, and national endometriosis trends from 1990 to 2017. *Ann. N. Y. Acad. Sci.* 2020.
27. Koninckx, P.R.; Ussia, A.; Adamyan, L.; Tahlak, M.; Keckstein, J.; Wattiez, A.; Martin, D.C. The epidemiology of endometriosis is poorly known as the pathophysiology and diagnosis are unclear. *Best Pract. Res. Clin. Obstet. Gynaecol.* 2020.
28. De Ziegler, D.; Borghese, B.; Chapron, C. Endometriosis and infertility: Pathophysiology and management. *Lancet* 2010, 376, 730–738.
29. Bulletti, C.; Coccia, M.E.; Battistoni, S.; Borini, A. Endometriosis and infertility. *J. Assist. Reprod. Genet.* 2010, 27.
30. D Hooghe, T.M.; Debrock, S.; Hill, J.A.; Meuleman, C. Endometriosis and Subfertility: Is the Relationship Resolved? *Semin. Reprod. Med.* 2003, 21.
31. Leibson, C.L.; Good, A.E.; Hass, S.L.; Ransom, J.; Yawn, B.P.; O'Fallon, W.M.; Melton, L.J. Incidence and characterization of diagnosed endometriosis in a geographically defined population. *Fertil. Steril.* 2004, 82, 314–321.
32. Gao, M.; Allebeck, P.; Mishra, G.D.; Koupil, I. Developmental origins of endometriosis: A Swedish cohort study. *J. Epidemiol. Community Health* 2019, 73, 353–359.
33. Yasui, T.; Hayashi, K.; Nagai, K.; Mizunuma, H.; Kubota, T.; Lee, J.-S.; Suzuki, S. Risk profiles for endometriosis in Japanese women: Results from a repeated survey of self-reports. *J. Epidemiol.* 2015, 25, 194–203.

Retrieved from <https://encyclopedia.pub/entry/history/show/16077>