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Trends in the incidence rate, type and treatment of surgically verified endometriosis – a nationwide cohort study

Running headline: Finnish cohort study on endometriosis

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Conflicts of Interest statement

All authors report no conflicting interest, financial or otherwise, in relation to the present work.

Abstract

Introduction: To study the trends in incidence rate, type and surgical treatment, and patient characteristics of surgically verified endometriosis during 1987-2012. *Material and methods:* This is a register-based cohort study. We identified women receiving their first diagnosis of endometriosis in surgery from the Finnish Hospital Discharge Register (FHDR). Quality of the FHDR records was assessed bidirectionally. The age-standardized incidence rates of the first surgically verified endometriosis was assessed by calendar year. *Results:* The cohort comprises 49 956 women. The quality assessment suggested the FHDR data to be of good quality. The most common diagnosis, ovarian endometriosis (46%), was associated with highest median age 38.5 years (interquartile range 31.0, 44.8), the second was peritoneal endometriosis (40%) with median age 34.9 years (28.6, 41.7). Between 1987 and 2012, a decrease was observed in the median age (from 38.8 [32.3-43.6] to 34.0 [28.9, 41.0] years), and in the age-standardized incidence rate (from 116 [95% confidence interval; 112-120] to 45 [43-48] per 100 000 women). The proportion of hysterectomy as a first surgical treatment decreased from 38% to 19% whereas that of laparoscopy increased from 42% to 73% when comparing periods 1987-1995 to 1996-2012. *Conclusions:* This nationwide cohort of surgically verified endometriosis showed a decrease in the incidence rate and in the patient age at the time of first diagnosis even the proportion of laparoscopy has increased. The number of hysterectomies has decreased. These changes are likely to reflect the evolving diagnostics, increasing awareness of endometriosis, and effective use of medical treatment before surgery.

Key words

Endometriosis, cohort, incidence rate, register-based, surgical treatment

Abbreviations

FHDR	The Finnish Hospital Discharge Register
ICD	International Classification of Diseases
IQR	Interquartile Range

Key message

The rate of surgical treatment of endometriosis has declined, the patients are younger and the operations less radical.

Introduction

Endometriosis is a chronic inflammatory disease of the female pelvis with an estimated prevalence of 1-10% (1) and an incidence of 0.1-0.3% among fertile women (2-6). Clinical symptoms include pelvic pain, dysmenorrhea and infertility or subfertility (7). Acknowledging the usual delay of 6-12 years in diagnosing the disorder, loss of productivity and the treatments for infertility and chronic pain symptoms, the societal costs of the disease are substantial (8).

Finland has a long history of administrative data collection. Nationwide health and social registers such as the Finnish Hospital Discharge Register (FHDR) have provided an important data source for epidemiological research (9). A unique personal identity number has been issued to every resident in Finland since 1969. The use of the personal identity number secures a reliable data recording in administrative registers, and allows data linkages. Validity of FHDR with respect to different diseases has been evaluated as satisfactory to very good in numerous studies, but subsidiary diagnoses and secondary operations have often been less completely recorded and few validation studies have been published in the field of gynecology (10).

The diagnosis of endometriosis is considered definite only after surgical verification (11). In the present study, we used the FHDR to form and study a nationwide cohort of surgically verified endometriosis, and evaluated the quality of the diagnosis of endometriosis. To provide clinically important information, we divided the cohort into subgroups, and assessed demographic characteristics by the type of endometriosis. We also studied the incidence rate of the surgically diagnosed disease and the trends in the first surgical treatment.

Material and methods

The study cohort was identified from the FHDR, maintained by the National Institute for Health and Welfare and containing individual-level data on patients discharged from public and private hospitals since 1967. Day-surgeries have been included in the FHDR since 1994. The records on inpatient care in the FHDR comprise personal identity number, hospital number, admission and discharge dates, main and subsidiary diagnoses and procedure codes. In the FHDR, diagnoses have been recorded using International Classification of Diseases (ICD) revisions (ICD-8 in 1969-1986, ICD-9 in 1987-1995, and ICD-10 since 1996), and procedures using the codes of the National League of Hospitals (1986-1995), and the Nordic Medico-Statistical Committee Classification of Surgical Procedures since 1996.

Formation of the cohort

To form the cohort of women with endometriosis, all FHDR records with endometriosis-associated diagnoses (Table 1) were identified from hospital discharges recorded during 1983-2012. Due to insufficient procedural information, we limited the study period to 1987-2012, and excluded the patients with endometriosis diagnosis between 1983-1986. We accepted the first endometriosis diagnosis recorded in the FHDR as main or subsidiary diagnosis concomitantly with any relevant gynecological surgical code (Supporting Information Table S1), and set no age limitation. The FHDR records with adenomyosis as a single diagnosis were excluded as the diagnosis could not be histologically verified. The index date was the date of the first hospital discharge satisfying these criteria.

We assessed the quality of the FHDR records with respect to the endometriosis diagnosis by performing bidirectional evaluation. First, to assess the accuracy of the FHDR information, we randomly selected 200 patients with at least one FHDR record satisfying the inclusion criteria. Restriction to Helsinki University Hospital outpatients' visits, for any reason during 2000-2014, ensured access to most of the patient files also for those with the index surgery outside Helsinki University Hospital. We compared the endometriosis diagnosis recorded for the index surgery in the FHDR to the corresponding data in the hospital records. Second, we checked whether surgeries of 168 women treated between 2004 and 2012 at Helsinki University Hospital due to deep infiltrating endometriosis, especially bowel endometriosis, were recorded in the FHDR (12), and whether the FHDR data corresponded to the records in the patient file.

Demographics and other characteristics

The demographics and other characteristics of the study population were obtained through register linkage using personal identity number. The residence was obtained from Statistics Finland and recorded according to municipal division in Finland 2012 and the statistical group of municipalities according to their degrees of urbanization and rurality by Statistics Finland in 2011. The data on the removal of the gynecological organs were obtained from the FHDR (1983-2012) to identify those who had undergone this surgery before the index day, and the number of live births from the Finnish Population Register Center. The procedure was defined as day-surgery when the admission and discharge day were the same.

According to the diagnostic codes assigned at the index surgery, the endometriosis cohort was divided into five subgroups: ovarian, peritoneal, deep infiltrating, mixed (including both ovarian and deep infiltrating), and other endometriosis (Table 1). Deep infiltrating endometriosis includes rectovaginal and bowel endometriosis from 1987 to 1995, and rectovaginal, bowel, bladder and endometriosis of the sacrouterine ligaments from 1996 to 2012. The subgroups of ovarian, deep infiltrating and mixed endometriosis were also permitted to include diagnoses of peritoneal endometriosis and/or other endometriosis. The subgroup of peritoneal endometriosis could also include diagnoses of other endometriosis but not ovarian, deep infiltrating or mixed endometriosis.

Incidence rates

To study the trends in the first surgical treatment of endometriosis, we assessed the annual age-standardized incidence rates as weighted average (World Standard Population, 1960) of the crude five-year (0-4, 4-9, 10-14, ..., 80-84, 85 or more) age-specific incidence rates calculated as the number of patients who entered the cohort within particular age group divided by the size of Finnish female population of corresponding age group (reported by Statistics Finland for the end of year). The exact 95% confidence intervals (CI) were calculated using the method based on gamma distribution (13). The results were plotted as the curve (1996 excluded as an exceptional due to change from ICD-9 to ICD-10) in the same graph with the annual frequencies of the new patients shown by endometriosis subgroups. To explore the changes in the shape of the age-specific incidence rate curves over time, we assessed and plotted the crude five-year (the first age category of 10-19 years, the last 60 years or more) age-specific incidence rates for four calendar periods (1987-1990, 1991-1995, 2001-2005, and 2011-2012).

The statistical calculations were performed using the R version 3.3.2 software (14).

Ethical approval

The study was approved by the ethics committee of the Hospital District of Helsinki and Uusimaa (238/13/03/03/2013).

Results

Figure 1 shows how the final cohort of 49 956 women with surgically verified endometriosis was formed.

Of the 200 index surgeries selected for the accuracy assessment of the FHDR, 16 patient files could not be found (11 operated outside Helsinki University Hospital). Thus, the accuracy of the recorded operations was validated by reviewing 184 cases. Of these surgeries, 84% were performed during the ICD-10 period (1996-2012) and 78% in Helsinki University Hospital. In 179 (97%) cases the endometriosis diagnosis verified from the patient files had been correctly reported to the FHDR. In 12 (7%) cases, only one diagnostic code for endometriosis was recorded in the FHDR instead of multiple codes justified by the clinical findings, peritoneal endometriosis being the lacking code in all of them.

Among the 168 patients, who were operated for deep infiltrating endometriosis (12), 159 (94.6%) were found among the cohort identified from the FHDR. The missing nine (5.4%) cases did not have a surgical procedure code logged in the FHDR.

Description of the cohort

The baseline demographic characteristics and some determinants of reproductive health are shown in Table 2 during the two different diagnostic periods ICD-9 (1987-1995) and ICD-10 (1996-2012). The overall median age of the women at the index surgery was 36.4 (interquartile range [IQR] 29.6, 43.3), the youngest and oldest patients were 12.5 and 84.8 years-of-age, respectively. When compared ICD-9 and ICD-10 periods, the proportion of women living in urban municipalities increased from 65% to 71%, whereas the proportion of women with history of live birth decreased from 60% to 40%. The

mean (\pm standard deviation [SD]) number of births among parous women was 1.9 (\pm 0.9). The proportion of women with a history of removal of reproductive organ(s) was under 3%.

Endometriosis was defined as the main diagnosis in 63% of patients and leiomyoma the second most common. Day-surgeries accounted for 21% (n=6677) of the patients from 1994. A third of the index surgeries was performed in the Helsinki University Hospital health care district.

Table 3 shows the distribution of the women into different subgroups of endometriosis and characteristics of surgery at the time of the first surgical verification of endometriosis during ICD-9 and ICD-10. According to the diagnostic codes used at the index surgery, 46% had ovarian endometriosis, 40% peritoneal, 6% other, 5% deep infiltrating and 2% had both ovarian and deep infiltrating endometriosis. The patients with deep infiltrating endometriosis were the youngest (median age 32.9 years; IQR 28.0, 40.8) and those with ovarian the oldest (38.5; IQR 31.0, 44.8).

Trends in the first surgical treatment

The annual age-standardized incidence rates of the first surgical treatment for endometriosis decreased from 116 (95% confidence interval (CI); 112-121) to 45 (95% CI; 43-48) per 100 000 women (Figure 2). Along with the decreasing incidence rate, we observed a shift towards younger age at the first surgery from the median age of 38.8 years (IQR 32.2, 43.6) in 1987-1990 to 33.3 years (IQR 28.2, 41.3) in 2006-2010. The changes in the shape of age-specific incidence rate curves plotted for four calendar periods demonstrates the character of these changes in more detail (Figure 3).

The use of laparoscopy increased from 35% (1987-1990) to 84% (2011-2012). The hysterectomy rate at the index procedures decreased from 38% to 19% and unilateral or bilateral oophorectomy from 30% to 24% comparing ICD-9 to ICD-10. The mean age (\pm SD) at hysterectomy increased from 44.8 (\pm 5.5) to 46.8 years (\pm 6.9), and the proportion of hysterectomized women with history of live birth decreased from 80% to 69%.

Discussion

We formed, described and studied a large nationwide cohort of patients with surgically verified endometriosis (n=49 956) using the FHDR. From 1987 to 2012, the age at the first endometriosis associated surgery decreased, as did the incidence rate of surgically verified endometriosis. During the study period, surgical treatment of endometriosis via laparoscopy as first line approach has replaced most laparotomies, and the proportion of radical procedures, such as hysterectomy and/or oophorectomy, has declined.

In the present study, we focused on the first surgically verified endometriosis diagnosis. Moreover, we restricted the type of surgical procedures only to those presumed accurate. In many previous register-based studies concerning endometriosis, the diagnosis has been made either by clinical examinations, ultrasound imaging and/or surgery (15-17). However, in recent studies the diagnosis has been based only on surgical diagnoses (18,19), or been even verified histologically (3,19).

The FHDR concerning gynecological diagnoses has been validated in few studies (10). The coverage has varied between 81-100% and the positive predictive value between 83-91% (10). The results of our validation, although limited by the small amount of verified data predominantly among patients from Helsinki University Hospital from the ICD-10 period, suggested similar quality for the FHDR concerning the first surgically verified endometriosis diagnoses. The lacking subsidiary diagnoses of the assessed files were all peritoneal endometriosis, which does not change our subdivision as subsidiary peritoneal endometriosis was already included in the ovarian, deep infiltrating and mixed endometriosis subgroups.

The median age at the first surgical procedure was 36.4 years, which is younger than that seen in the previous Nordic register-based studies. In two Swedish studies, covering years 1969-2005, the average age was 38.8 and 43.8 years, and increased to 51.4 years in 2005 (20, 21). In two Danish studies covering years 1977-2007, the average age varied between 38.6 and 40.6 years (15, 22). We included day-surgeries but excluded adenomyosis, which may explain the difference. The younger age in our study might also reflect the evolving diagnostics, increasing awareness of endometriosis, and increasing use of minimally invasive surgical approaches as treatment strategies.

The diagnostic codes for endometriosis included in the ICD classification are based on the location of endometriosis, therefore, we chose the subdivision into the three main subgroups. We excluded uterine endometriosis, in other words adenomyosis, as the diagnosis previously required histological confirmation, which we lack. The diagnosis made by ultrasound and/or magnetic resonance imaging has been rapidly evolving but was not well established during the early years of our study (24).

Few large-scale studies have divided endometriosis into subgroups. In a Swedish and a Danish study the division was ovarian, uterine and pelvic endometriosis by site (21,22). In an Icelandic study, the classification and staging was made according to the revised American Society for Reproductive Medicine (3). In a recent French study, the division was made by the “organ specific procedure” codes yielded the subgroups similar to our study: ovarian (40-50%), peritoneal (20-30%), and intestinal (10-20%) endometriosis (25). In the present study, the ovarian subgroup was the most common (46%) as in all previous studies differentiating between endometriosis subgroups (3,21,22,25).

The diagnosis of deep infiltrating endometriosis is not reliable over the 26 years of the study. Deep infiltrating endometriosis was recognized as a defined entity only in the 1990s (26,27). Making the diagnosis necessitates clinical expertise and our study concerned only the first endometriosis related surgeries (all of which were not performed for endometriosis). In addition, we classified the ICD-9 diagnosis of retrouterinal endometriosis as peritoneal disease even it might have included cases of deep infiltrating endometriosis located in this site. To ensure the validity we restricted the study to gynecological procedural codes, which could have also reduced the subgroup of deep infiltrating endometriosis. Thus, of the various subtypes of endometriosis the data on the incidence rate of ovarian endometriosis over the study period can be regarded most reliable.

The greatest decrease in the proportion of hysterectomy was seen in the age group of 40-49 years-olds; almost 70% of the first procedures included hysterectomy during the era of ICD-9, but less than 50% during ICD-10. Nevertheless, similar decrease in hysterectomy was also seen among the over 50 year-olds (from 87 to 70%). The proportion of previous live births has decreased among those who had hysterectomy. We assume that the decrease in the proportion of hysterectomy among women with surgically verified endometriosis is not only explained by the younger age of the women and their lower parity, but also by the changes in the surgical treatment of endometriosis.

Previous studies based on hospital discharge diagnoses performed in the 1980's and 1990's in Minnesota, USA revealed an endometriosis incidence of 0.13-0.19% (4,23) More recent studies, based on laparoscopic confirmation indicated an incidence of 0.3% (5). An Icelandic study with both visually verified and histologically confirmed diagnosis, during 1981-2000, reported an incidence of 0.1% (3). A similar figure of 0.14% of surgically verified endometriosis was also reported in an Italian study performed in the early 2010s, and showed a decreasing trend in the incidence (6). Thus, introduction of the laparoscopic surgery might have also increased the incidence of the procedures (2). In our study the age-standardized incidence rates of the first surgically verified endometriosis diagnosis was 0.12%, being at highest in 1987 and decreasing to 0.04% in 2012 even though more than 80% of the procedures have been lately performed via laparoscopy. The decreasing incidence is in contrast with many previous studies (3,4), but in agreement with the recent Italian study (6). Among patients entered to our cohort during the first decade, there might be those with previous operations. These prevalent endometriosis patients could have increased the median age and incidence rate during the first decade of the study even though we excluded the previous endometriosis patients from 1983 to 1986. Moreover, the restriction to relevant surgical diagnosis might also decrease our incidence rate. Increasing medical management of endometriosis may have decreased the need of surgical management, and thus the incidence rate of the surgically verified diagnosis. Moreover, the operative treatment and diagnostic procedures concerning especially fibroids (from 18% to 9% of all diagnosis here), and also female sterilization and infertility, have decreased during the years, decreasing the possibility to diagnose endometriosis as incident finding. These changing treatment trends are likely to reduce the incidence rate of surgically verified endometriosis.

The strengths of the study include the large nationwide patient cohort identified from the FHDR register, which includes virtually all inpatient discharges from Finnish hospitals, at least from the 1990s (10). In addition, the quality of the FHDR has been shown to be from good to high (9,10). The present validation results are in line with these findings. Furthermore, formation and evaluation of this cohort encourages further registry based studies assessing the potential endometriosis associated comorbidities and other health outcomes among the different subgroups of endometriosis.

We limited our study to the operated endometriosis patients, which may cause selection bias. The effect of more severe disease may be diluted as our study also includes the patients treated in day-surgery. Another limitation is that even though our study suggests the quality of the endometriosis diagnoses to be good, the differences in the quality between hospital districts, calendar periods, and endometriosis

subgroups could not be ruled out. Moreover, there is little information available on the completeness and correctness of the procedure codes. Especially, the change from ICD-9 to ICD-10 may have resulted in a significant gap regarding the separation between endometriosis groups. These limitations should be taken into account when interpreting the data, and possibly designing further studies on this cohort.

In conclusion, we have formed and described a large nationwide cohort of surgically diagnosed endometriosis covering a 26-year period from 1987 to 2012. The decrease in the incidence rate of the first surgically verified endometriosis, during both diagnostic classification periods as well as over the time, was associated with the first surgery being performed at a younger age. The number of hysterectomies has decreased and the use of laparoscopic approach increased. This is likely to reflect the evolving diagnostics, increasing awareness of endometriosis, and effective use of medical treatment as first line therapy.

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Supporting Information legend

Table S1. Accepted procedures in cohort forming as National League of Hospitals (1986-1995) and Nordic Medico-Statistical Committee Classification of Surgical Procedures (NCSP, 1996-2012).

Legends tables and figures

Table 1. International Classification of Diseases (ICD) version 9 and 10 used to form the subgroups of surgically verified endometriosis.

Table 2. Baseline characteristics of the women with surgically verified endometriosis (n=49 956). The data are presented as n (%) unless stated otherwise.

Table 3. Distribution of the women into different subgroups of endometriosis and characteristics of surgery at the time of the first surgical verification of endometriosis during ICD-9 and -10 era. The data are presented as n (%) unless stated otherwise.

Figure 1. Formation of the endometriosis cohort of the first surgically verified endometriosis. FHDR, Finnish Hospital Discharge Register. PIN, personal identity number.

Figure 2. The incidence rate (solid line) of surgically verified endometriosis (1996 excluded) and 95% confidence interval (dashed lines), and the number of patients with newly verified endometriosis according to endometriosis subgroups during 1987-2012, before and after the change in the diagnostic code system from ICD-9 to ICD-10 in 1996 (vertical line).

Figure 3. The age-specific incidence rate of the first diagnosis of surgically verified endometriosis per 100 000 women during four different time intervals.

Table 1. International Classification of Diseases (ICD) version 9 and 10 used to form the subgroups of surgically verified endometriosis.

	ICD-9	ICD-10
Ovarian ^a	6171A	N80.1
Peritoneal ^b		
- Tubal	6172A	N80.2
- Peritoneal		
- Retrouterine	6173A	N80.3
	6173B	-
Deep infiltrating ^a		
- Rectovaginal	6174A	N80.4
- Intestine	6175A	N80.5
- Bladder	-	N80.80
- Sacrouterine ligaments	-	N80.81
Mixed (ovarian and deep infiltrating) ^a	6171A+	N80.1+
	6173B/6174A/6175A	N80.4/N80.5/N80.80/N80.81
Other		
- Cicatrix cutis	6176A	N80.6
- Other specified	6178X	N80.8, N80.89
- Other unspecified	6179X	N80.9

^a Includes also possible diagnosis of peritoneal or other endometriosis in the index procedure.

^b Includes also possible diagnosis of other endometriosis in the index procedure.

Table 2. Baseline characteristics of the women with surgically verified endometriosis (n=49 956).

The data are presented as n (%) unless stated otherwise.

Endometriosis cohort	ICD-9 (1987-1995)	ICD-10 (1996-2012)
Number of women	23 655 (47.4)	26 301 (52.6)
Age at entry in the cohort, years, median (IQR)	38.6 (31.5-44.1)	34.3 (28.5-42.3)
Age at entry in the cohort		
10-19	165 (0.7)	361 (1.4)
20-29	4618 (19.5)	8072 (30.7)
30-39	8447 (35.7)	9597 (36.5)
40-49	8968 (37.9)	6319 (24.0)
50-59	1334 (5.6)	1650 (6.3)
60-69	95 (0.4)	244 (0.9)
70-79	28 (0.1)	46 (0.2)
80-84	0 (0.0)	12 (0.1)
Residence		
Urban municipality	15 409 (65.1)	18 814 (71.5)
Densely populated	4459 (18.9)	4081 (15.5)
Rural	3787 (16.0)	3406 (13.0)
History of live birth	14 103 (59.6)	15 880 (39.6)
Removal of reproductive organ(s)		
Uterus		
Before entry	183 (0.8)	358 (1.4)
At index day	8917 (37.7)	5108 (19.4)

Ovary/ies		
Before entry	117 (0.5)	190 (0.7)
At index day	6941 (29.3)	6165 (23.4)
<hr/>		
Index procedure type,		
Laparoscopy ^a	9916 (42.0)	19 071 (72.5)
Laparotomy	13 729 (58.0)	7230 (27.5)

IQR, Interquartile range.

^a Includes also vaginally performed operations (n=10)

Table 3. Distribution of the women into different subgroups of endometriosis and characteristics of surgery at the time of the first surgical verification of endometriosis during ICD-9 and -10 era. The data are presented as n (%) unless stated otherwise.

	Ovarian ^a		Peritoneal ^b		Deep infiltrating ^a	
	(n=23 222)		(n=20 197)		(n=2372)	
	ICD-9	ICD-10	ICD-9	ICD-10	ICD-9	ICD-10
Number of diagnosis	10 515 (44.5)	12 707 (48.3)	11 580 (49.0)	8617 (32.8)	225 (1.0)	2147 (8.2)
Age, median (years, IQR)	40.3 (33.4-45.2)	36.3 (29.6-44.3)	36.8 (30.2-42.8)	32.3 (27.0-38.4)	37.8 (30.1-43.7)	32.5 (27.8-40.1)
Laparoscopy ^c	2277 (21.7)	8538 (67.2)	7079 (61.1)	7031 (81.6)	86 (38.2)	1548 (72.1)
Laparotomy	8238 (78.4)	4169 (32.8)	4501 (38.9)	1586 (18.4)	139 (61.8)	599 (27.9)

Three most common procedures	Hysterectomy and bilateral adnex removal	Laparoscopic excision of ovarian cyst	Laparoscopy and other therapeutic procedure	Laparoscopy	Laparoscopy and other therapeutic procedure	Laparoscopy
		1720 (13.5)		1292 (15.0)		281 (13.1)
	1435 (13.6)		3313 (28.6)		36 (16.0)	
	Hysterectomy and unilateral adnex removal	Laparoscopic destruction of lesion of ovary	Laparoscopy	Laparoscopic excision or destruction of lesion of peritoneum	Hysterectomy	Laparoscopic excision or destruction of lesion of peritoneum
		1119 (8.8)	1669 (14.4)		27 (12.0)	
	902 (8.6)			1163 (13.5)		148 (6.9)
	Laparoscopy and other therapeutic procedure	Laparoscopic unilateral salpingo-oophorectomy	Hysterectomy	Laparoscopic excision or destruction of lesion of peritoneum &	Laparoscopy	Laparoscopic excision of lesion of parametrium
			1144 (9.9)		18 (8.0)	131 (6.1)
	897 (8.5)	839 (6.6)		Laparoscopic perfusion of Fallopian tube		
				489 (5.7)		

^a Includes also possible diagnosis of peritoneal and other endometriosis in the index procedure.

^b Includes also possible diagnosis of other endometriosis in the index procedure.

^c Includes also vaginally performed operations (n=10).

IQR, interquartile range.

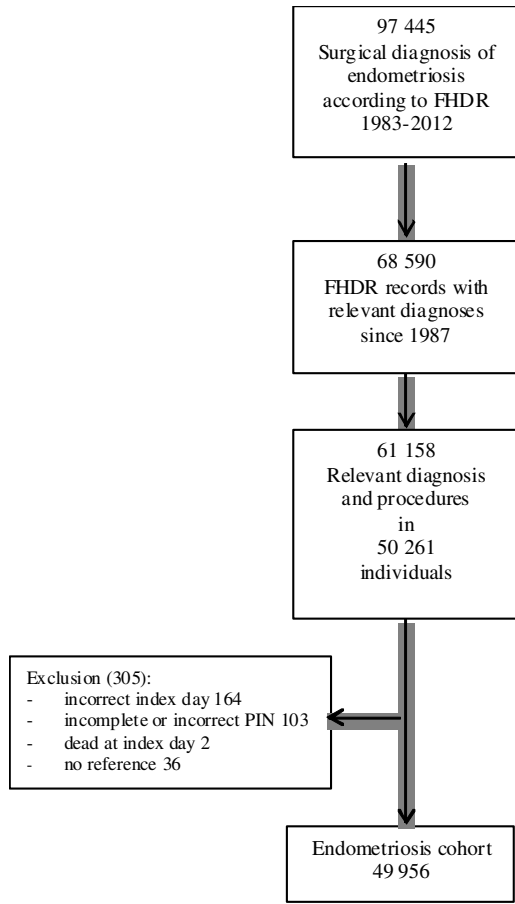


Figure 1. Formation of the endometriosis cohort of the first surgically verified endometriosis. FHDR, Finnish Hospital Discharge Register. PIN, personal identity number.

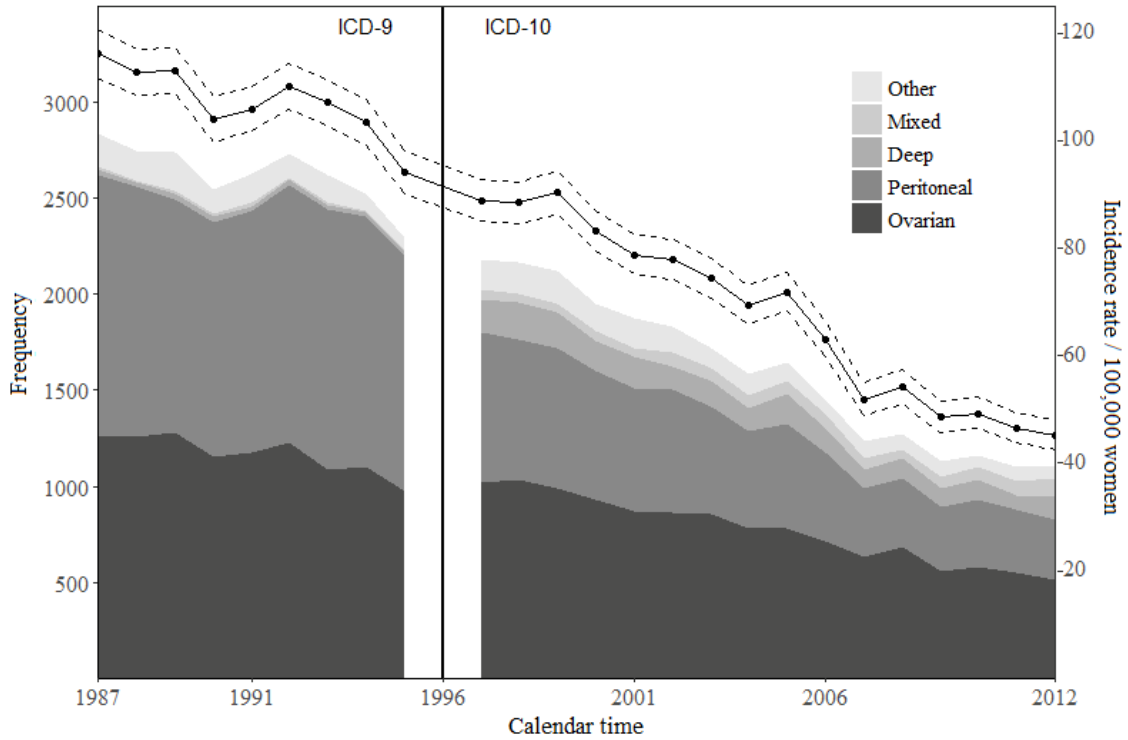


Figure 2. The incidence rate (solid line) of surgically verified endometriosis (1996 excluded) and 95% confidence interval (dashed lines), and the number of patients with newly verified endometriosis according to endometriosis subgroups during 1987-2012, before and after the change in the diagnostic code system from ICD-9 to ICD-10 in 1996 (vertical line).

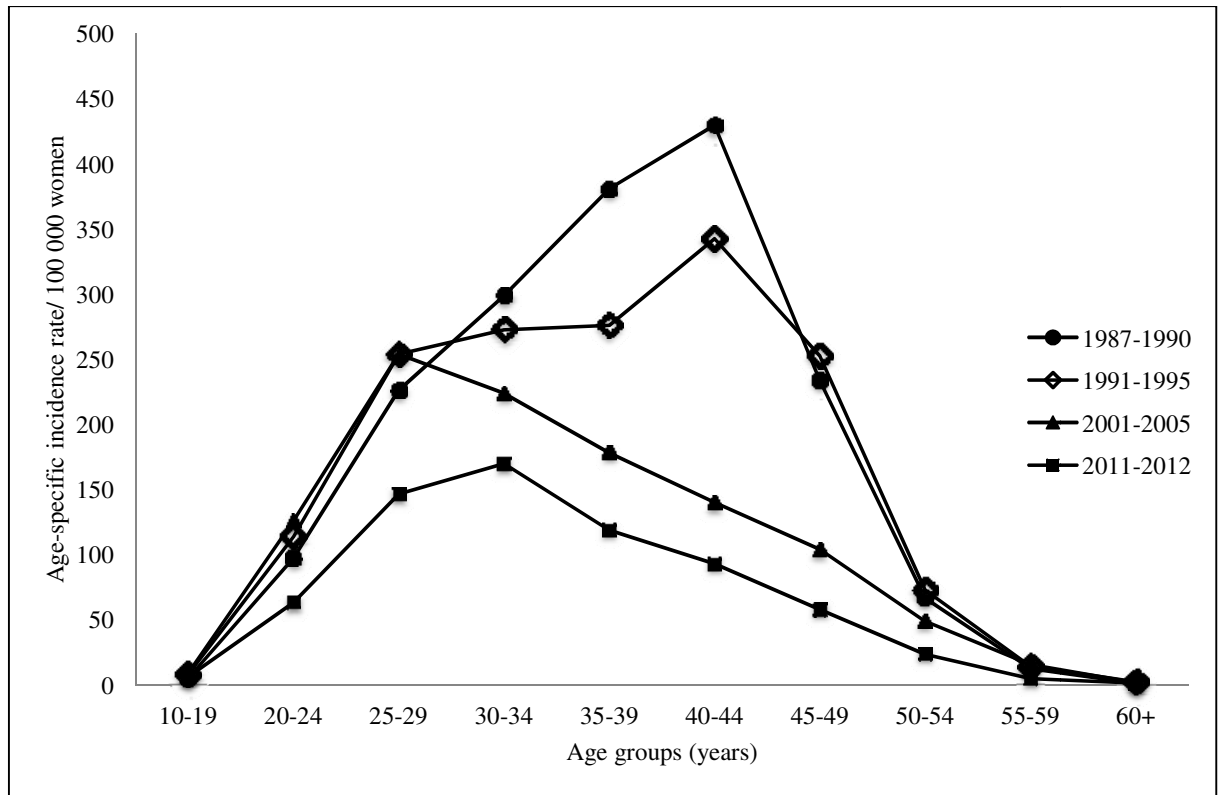


Figure 3. The age-specific incidence rate of the first diagnosis of surgically verified endometriosis per 100 000 women during four different time intervals.