




The association of endometriosis with work ability and work life participation in late forties and lifelong disability retirement up till age 52: A Northern Finland Birth Cohort 1966 study

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Funding information

The study was funded by The Academy of Finland (315921, 321763), Sigrid Jusélius Foundation, The Finnish Medical Association and Ahokkaan Säätiö. NFBC1966 received financial support from University of Oulu Grant nos. 65354 and 24000692, Oulu University Hospital Grant nos. 2/97, 8/97 and 24301140, Ministry of Health and Social Affairs Grant nos. 23/251/97, 160/97, 190/97, National Institute for Health and Welfare, Helsinki Grant no. 54121, Regional Institute of Occupational Health, Oulu, Finland Grant nos. 50621, 54231 and ERDF European

Abstract

Introduction: Endometriosis may cause a deterioration of daily functioning due to related symptoms such as pain, fatigue and psychological distress. Accordingly, endometriosis may jeopardize work ability, as suggested in mainly survey-based case-control studies, including clinically established cases at fertile age. This is the first general population-level study to evaluate how endometriosis is associated with (1) self-rated work ability and sick leave dates at age 46 years, (2) registered disability and unemployment days between age 46 and 48 and (3) lifelong emergence of registered disability retirement up to age 52.

Material and methods: Endometriosis case identification was based on the Care Register for Health Care and self-reported diagnosis from a population-based birth cohort, which covers 96% of children born in Northern Finland in 1966. A total of 348 women with endometriosis and 3487 women without endometriosis were identified. Questionnaire data on Work Ability Index Score was collected at age 46. Unemployment and disability days were determined from the Social Insurance Institution of Finland and the Finnish Center for Pensions registers. Finally, each individual's first-ever granted pension decision and diagnoses were collected until age 52 years. The associations between endometriosis and work ability were assessed using logistic regression models.

Results: Endometriosis was associated with poor work ability at age 46 (odds ratio [OR] 1.62, 95% confidence interval [CI] 1.06–2.47). Furthermore, the association between endometriosis and over 10 days of absenteeism was increased (OR 1.53; 95% CI 1.05–2.23). Between ages 46 and 48, women with endometriosis had 10 days more disability days (55.5 vs 45.5, $p = 0.030$) in comparison to women without

Abbreviations: CI, confidence interval; FCP, Finnish Center for Pensions; ICD, International Classification of Diseases codes; IRR, incidence rate ratios; NFBC1966, Northern Finland Birth Cohort 1966; OR, odds ratio; SII, Social Insurance Institution.

Terhi T. Piltonen and Leena Ala-Mursula contributed equally.

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Regional Development Fund Grant no. 539/2010 A31592.

endometriosis, but 20 days less unemployment days (40.6 vs 59.2 days, $p = 0.013$). There were no differences in early retirement between the study groups until age 52. **Conclusions:** Our study showed that endometriosis associates with poor work ability at age 46. Women with endometriosis have more disability days. However, their employment rate and risk of early retirement are comparable to those of women without endometriosis at late fertile age.

KEYWORDS

disability, employment, endometriosis, register-based study, retirement, work ability

1 | INTRODUCTION

Endometriosis is a common chronic disease affecting 6%–10% of fertile-aged women.¹ Associated symptoms, such as chronic pain, fatigue and psychological distress, may impair daily functioning, even at work.^{2–5} Given that endometriosis occurs during the same years as education and career building, career development may be affected. Due to the need to promote sustainable careers in aging societies, the identification of health conditions associated with poor career outcomes is of critical importance.⁶ However, the role of chronic gynecological diseases such as endometriosis, remains poorly understood.

Previous studies suggest that the role of endometriosis on women's ability to work is undermined.^{4,7–11} Using a modified Work Ability Index (WAI), a Danish case–control study showed that women with endometriosis aged 26–35 years reported poorer work ability and more sick days than women without endometriosis.¹⁰ Other studies using the Work Productivity and Activity Impairment (WPAI) questionnaire indicate that women with endometriosis report major losses regarding hours of missed work, impairment of work tasks, productivity losses and impairment of daily life activities.^{9,11} Concerning employment status, cross-sectional case–control studies suggest that women with endometriosis are less likely to be employed and practicing their desired profession.^{4,8} A longitudinal case–control study in the USA evaluated endometriosis-related exits from the workforce and found increased risks of sick leave and short-term disability.¹² However, although previous studies quite unanimously agree that endometriosis has adverse effects on work life, the evidence remains limited, as all but one study¹² utilize self-reported data and cross-sectional designs and mainly cover the years of fertility. Moreover, all case–control studies stem from specialized clinics or patient organizations, whereas population-level studies are lacking.

To our knowledge, this is the first general population-level study on the association between endometriosis and work ability, including a life course approach to disability retirement. Using the unique data from the Northern Finland Birth Cohort 1966 (NFBC1966) linked to national registers, we evaluated the associations of endometriosis with (1) self-rated work ability and sick leave at the age of 46 years, (2) registered unemployment and disability days during individually determined 2-year follow-up periods starting from the 46th-year study, and (3) emergence of registered disability retirement from age 16 up to the age of 52 years.

Key message

Endometriosis associates with poor work ability but not unemployment or early retirement at late fertile age.

2 | MATERIAL AND METHODS

The NFBC1966 is a general population-based cohort consisting of 96.3% of all expected births during 1966 in Northern Finland (12 055 mothers, 12 058 live-born children, 5889 girls).¹³ In this study, we utilized: (1) the follow-up study at age 46 including postal questionnaires, (2) diagnoses from the Care Register for Health Care (CRHC) until age 46 years and (3) participation in the workforce registered by the Social Insurance Institution (SII) and the Finnish Center for Pensions (FCP) (Figure 1).

2.1 | Identification of women with endometriosis

Women with endometriosis were identified from the NFBC1966 using previously validated methodology.¹⁴ First, we used data from the CRHC, which systematically recorded all diagnoses during hospital visits between 1968 and 2012 using International Classification of Diseases (ICD) codes.¹⁵ The ICD-9 and 10 codes for endometriosis (617.1–617.9 and N80.1–N80.9, respectively) were used for case identification. ICD-8 codes were converted to ICD-9 codes and included. The age at first diagnosis was collected. Secondly, we used data from the 46th-year questionnaire mailed to all NFBC1966 participants living in Finland (5123 women; response rate 72%), including the question: "Have you ever been diagnosed with endometriosis by a physician?"; if yes, at what age, followed by a multiple choice question whether the diagnosis was based on gynecological examination, ultrasound or laparoscopy/surgery. Finally, by combining the 281 self-reported doctor-diagnosed, and the 224 register-based cases, we found a total of 348 endometriosis cases. Among the self-reported cases, 54% reported having been diagnosed by surgery, 30% by ultrasound and 8% in gynecological examination.

As a reference group, all women without a hospital-based ICD code for endometriosis and who replied "no" to having been

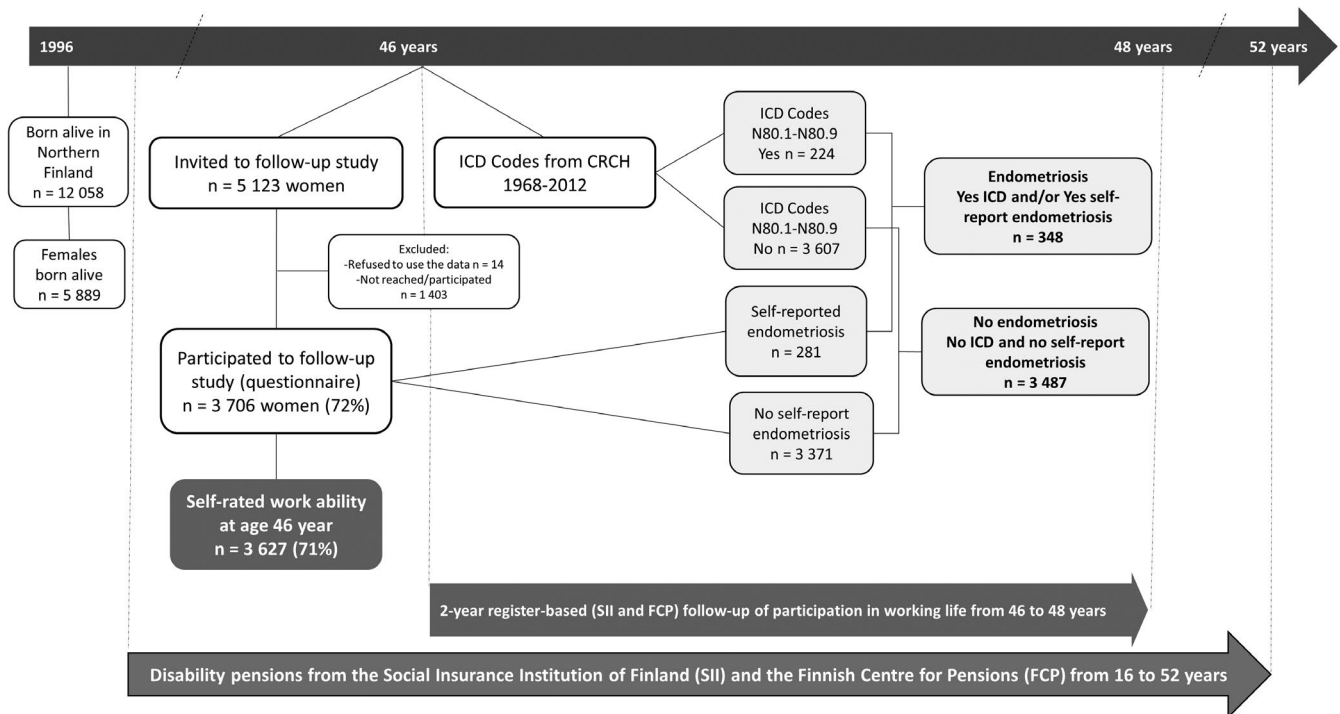


FIGURE 1 Flowchart of the data collection and study population. The population of women with endometriosis and women without endometriosis formed in the Northern Finland Birth Cohort 1966 for the present study are marked in light grey and the registers are marked in dark grey

diagnosed with endometriosis, were considered women without endometriosis ($n = 3487$). A flow chart of the study is shown in Figure 1.

2.2 | Questionnaire data on work ability

Perceived work ability at age 46 was measured with two items of the Work Ability Index, a validated tool for research.^{16,17} First, the respondents rated their current work ability (scale from 0 to 10), which we classified as good (scores 8–10) or poor work ability (0–7) based on previous studies.^{16,17} Secondly, we inquired about sickness absenteeism with the question: “How many days have you been absent from work due to health issues within the last 12 months?”, dichotomized into 0–9 and ≥ 10 or more days.

Regarding retirement intentions, answers to “Have you considered retiring before normal retirement age due to medical or other reasons?” were divided into “no retirement intention” and “intention to retire”.¹⁸

2.3 | Register data on 2-year follow-up of unemployment and disability days

The individually determined 2-year (730-day) follow-up started from the day the woman returned the 46th-year questionnaire. All days of employment and self-employment are recorded by the FCP. Based on the FCP and SII registers, each day with any type of unemployment compensation or a medically certified disability benefit was

coded either as an unemployment day or a disability day; overlaps were coded as a disability day.

Sickness allowances are registered by the SII after a deductible time of 10 weekdays, 4 weekdays for entrepreneurs. In cases of accidents, they are registered by the FCP after 4 weekdays. Sickness allowance can be paid for a year, after which eligibility for a fixed-term (rehabilitation subsidy) or permanent disability pension, either full- or part-time, is evaluated.

2.4 | Registered new disability pensions

Using the participants’ data from age 16 to 52 years in the SII and FCP registers, we determined the date and diagnoses of the first-ever disability pension of any type, either permanent or fixed-term, full- or part-time, as an indicator of long-term disability. The follow-up lasted until the end of 2018.

2.5 | Covariates

Several endometriosis-related, health-related and socioeconomic covariates were considered (Table 1). Regarding pain, the number of musculoskeletal pain sites (0–8) during the previous 12 months was illustrated using a drawing in the questionnaire. More than three pain sites was considered widespread pain based on our previous study.¹⁴ Regarding other endometriosis-related covariates, the respondents were asked about ever having used hormonal contraceptives (yes/

no) and their parity status, divided into no delivery, one to two deliveries, and three or more deliveries.

Regarding health-related covariates, 46th-year clinical study data on weight (kg) and height (m) were used to calculate body mass index (kg/m^2). Missing measurements were replaced with self-reported values. For health-related behavioral factors, alcohol consumption was divided into three categories: abstinence, low-risk drinking (≤ 20 g/day) and high-risk drinking (> 20 g/day). Smoking status was divided into no smoking, previous/occasional smoking and regular smoking. Physical activity was divided into low, moderate and high, depending on the amount of exercise during leisure time.¹⁶

Regarding socioeconomic factors, relationship status at age 46 was determined as marriage or cohabitation or lack thereof. Education was categorized into basic (basic or vocational school), secondary (college degree) and higher (polytechnic or university degree). The occupational status reflecting the type of work was divided into four categories: white collar, blue collar, entrepreneur and other (not working). Self-reported employment history was divided into continuous (working always or mostly on long-term or permanent contracts) or discontinuous (short- or long-term contracts with unemployment periods, mainly short-term contracts, mostly unemployed, mostly supported working, or never in paid employment). The employment status at age 46 (employment, unemployment or disability day) was obtained from the registers on the first day of the 2-year follow-up.

2.6 | Statistical analyses

Statistical analyses were performed using IBM SPSS STATISTICS 25 and R 3.6.1. Means with standard deviations (SD) for continuous variables and frequencies for categorical variables were calculated. Differences were analyzed using the independent samples *t* test or the Mann-Whitney U test. Categorical parameters were evaluated using the chi-square test. A two-sided *p* value < 0.05 was considered statistically significant.

The associations between self-reported poor work ability and sick leave among women with and without endometriosis at age 46 were analyzed with binary logistic regression models reporting odds ratios (OR) with 95% confidence intervals (CI), first unadjusted. We then separately adjusted the models for widespread pain, contraception and parity, health-related factors and socioeconomic factors. Lastly, we adjusted for all covariates. As sensitivity analysis, we replicated all models by comparing women with ICD-coded (hospital-treated) endometriosis only with those without endometriosis.

Poisson regression analyses for the prospective 2-year participation in working life were used to report incidence rate ratios (IRR) with 95% CI for unemployment and disability days for women with and without endometriosis, first unadjusted. We then separately adjusted the analyses for their employment status at the beginning of the follow-up to account for baseline disability and unemployment, followed by adjustments and sensitivity analyses analogous to those of the logistic regression models.

Finally, we used Kaplan–Meier survival analysis with Mantel–Cox estimates to estimate the lifetime emergence of disability pensions for women with and without endometriosis until 2018, when the participants turned 52. Since the number of diagnoses in individual decisions varied, only the ICD code frequencies were calculated.

2.7 | Ethical approval

This study was conducted according to STROBE guidelines for cohort studies and the principles of the Declaration of Helsinki. All participants provided written informed consent to combine the NFBC study data with the register data. The study was approved by the Ethics Committee of the Northern Ostrobothnia Hospital District (latest registration number: 94/2011) on 14 December 2011.

3 | RESULTS

Women with endometriosis experienced more widespread pain than women without endometriosis (71.4% vs 62.6%; $p = 0.002$), had used contraception more often (93.2% vs 89.2%; $p = 0.023$) and had lower parity. The mean age at first endometriosis diagnosis was 31.6 years (SD 7.3). Health behavior, socioeconomic characteristics and employment status at age 46 did not differ significantly between the two groups (Table 1).

At age 46, endometriosis was not associated with poor work ability in the unadjusted model or when considering widespread pain (Table 2). However, in the final multivariate analysis, endometriosis was associated with poor work ability (OR 1.62, 95% CI 1.06–2.47). In sensitivity analysis considering only register-based endometriosis cases ($n = 224$), the results patterned analogously, although not quite reaching statistical significance in the final model (OR 1.35, 95% CI 0.89–2.05). Moreover, women with endometriosis more often reported over 10 days' sickness absenteeism during the previous year (33.5% vs 25.4%; $p = 0.001$), as revealed by the unadjusted logistic regression (OR 1.49, 95% CI 1.17–1.90), with a slightly lower risk after adjusting for pain (OR 1.30) but a higher risk after adjusting for health-related factors (OR 1.75) and when considering all covariates (OR 1.53, 95% CI 1.05–2.23) (Table 2). In sensitivity analysis among women with registered diagnoses, the results again followed the main pattern, with slightly stronger figures (OR 1.78, 95% CI 1.26–2.51) in the final model.

During the register-based 2-year follow-up, the women with endometriosis had on average 10 more disability days compared with unaffected women (55.5 vs 45.5 days; $p = 0.030$). In the Poisson regression, considering all potential confounders, women with endometriosis had a higher risk of disability days (IRR 1.35, 95% CI 1.31–1.38) (Table 3). However, the affected women had around 20 fewer unemployment days compared with unaffected women (40.6 vs 59.2 days; $p = 0.013$), as reflected in a lower risk of unemployment days (IRR 0.88, 95% CI 0.86–0.91) in the final model (Table 3). The risks for disability (IRR 1.54, 95% CI 1.50–1.57) and unemployment

	No endometriosis, n = 3487 (%/SD)	Endometriosis, n = 348 (%/SD)	p value
Widespread pain	1933 (62.6%)	222 (71.4%)	0.002
Contraception use (ever)	2958 (89.2%)	299 (93.2%)	0.023
Parity			
0	303 (9.7%)	42 (13.8%)	
1-2	1696 (54.5%)	174 (57.0%)	0.017
≥3	1111 (35.7%)	89 (29.2%)	
Self-rated health			
Good	2256 (67.4%)	223 (66.0%)	0.589
Poor	1090 (32.6%)	115 (34.0%)	
BMI	26.5 (5.3)	26.0 (5.1)	0.113
Alcohol consumption			
Abstainer	383 (11.4%)	46 (13.5%)	
Low-risk drinker	2707 (80.7%)	274 (80.6%)	0.250
At-risk drinker	264 (7.9%)	20 (5.9%)	
Smoking			
Non-smoker	1886 (53.9%)	203 (58.2%)	
Former/occasional	807 (23.1%)	69 (19.8%)	0.419
Smoker	635 (18.1%)	62 (17.8%)	
Physical activity			
Low	746 (22.2%)	65 (19.2%)	
Moderate	1376 (41.0%)	150 (44.2%)	0.351
High	1232 (36.7%)	124 (36.6%)	
Education			
Basic	210 (6.2%)	15 (4.4%)	
Secondary	2148 (63.8%)	208 (61.4%)	0.152
Tertiary	1010 (30.0%)	116 (34.2%)	
Occupational status			
White collar	1233 (37.5%)	132 (40.2%)	0.252
Blue collar	1543 (46.9%)	145 (44.2%)	
Entrepreneur	286 (8.7%)	35 (10.7%)	
Other	266 (6.9%)	16 (4.9%)	
Marital status			
Single	784 (22.4%)	70 (20.1%)	0.314
In a relationship	2715 (77.6%)	279 (79.9%)	
Employment history			
Continuous	2314 (70.6%)	242 (73.3%)	0.300
Discontinuous	963 (29.4%)	88 (26.7%)	
Employment status at age 46*			
Employment day	2860 (86.6%)	291 (86.6%)	
Unemployment day	229 (6.9%)	21 (6.3%)	0.797
Disability day	212 (6.4%)	24 (7.1%)	

TABLE 1 Characteristics of the study population in the Northern Finland Birth Cohort 1966.

Data reported as mean values (SD) or count numbers (%). Significance tests for continuous variables were performed by using the independent samples *t* test or the Mann-Whitney *U* test, as appropriate.

Two-sided *p* values <0.05 were considered statistically significant.

Differences in numbers vary in analyses as the result of missing data.

*Registered data in the beginning of the 2-year follow-up.

TABLE 2 Self-reported work ability and work absenteeism in women with endometriosis and women without endometriosis at age 46 in a population-based dataset

	Poor work ability, OR (95% CI)	Ten or more days absenteeism, OR (95% CI)
Crude OR (95% CI)	1.22 (0.92–1.62)	1.49 (1.17–1.90)
Model 1, OR (95% CI)	1.20 (0.89–1.60)	1.30 (1.01–1.69)
Model 2, OR (95% CI)	1.35 (1.01–1.82)	1.52 (1.18–1.97)
Model 3, OR (95% CI)	1.41 (1.00–1.99)	1.75 (1.29–2.36)
Model 4, OR (95% CI)	1.37 (1.02–1.83)	1.54 (1.20–1.97)
Model 5, OR (95% CI)	1.47 (1.06–2.04)	1.53 (1.05–2.23)

OR: The odds ratios were calculated per 1 unit change.

Model 1: widespread pain.

Model 2: contraceptive use, parity.

Model 3: smoking, alcohol, BMI, physical activity.

Model 4: working history, educational level, occupational status, marital status.

Model 5: All.

TABLE 3 The risk for disability and unemployment between age 46 and 48 years in women with endometriosis during a 2-year follow-up. Data from the register of Social Insurance Institution of Finland

	Disability days, IRR (95% CI)	Unemployment days, IRR (95% CI)
Crude OR (95% CI)	1.21 (1.19–1.23)	0.69 (0.67–0.70)
Adjusted with baseline employment status	1.15 (1.13–1.17)	0.65 (0.64–0.66)
Model 1, IRR (95% CI)	1.27 (1.26–1.28)	0.70 (0.69–0.70)
Model 2, IRR (95% CI)	1.42 (1.40–1.44)	0.66 (0.65–0.67)
Model 3, IRR (95% CI)	1.31 (1.28–1.34)	0.76 (0.74–0.78)
Model 4, IRR (95% CI)	1.38 (1.35–1.40)	0.79 (0.78–0.81)
Model 5, IRR (95% CI)	1.35 (1.31–1.38)	0.88 (0.86–0.91)

IRR: Incidence rate ratios were calculated per one unit change.

Model 1: widespread pain.

Model 2: contraceptive use, parity.

Model 3: smoking, alcohol, BMI, physical activity.

Model 4: working history, educational level, occupational status, marital status.

Model 5: all.

days (IRR 0.96, 95% CI 0.93–0.98) remained similar in the sensitivity analysis among women with registered endometriosis diagnoses.

At age 46, women with and without endometriosis reported retirement intentions similarly (48% vs 44.6%; $p = 0.232$). Likewise, the lifelong emergence of registered disability retirement up to the age of 52 years ($n = 18$, 5.2% vs $n = 153$, 4.4%, respectively; $p = 0.515$) did not differ in the two groups (Figure 2). In terms of diagnoses, no

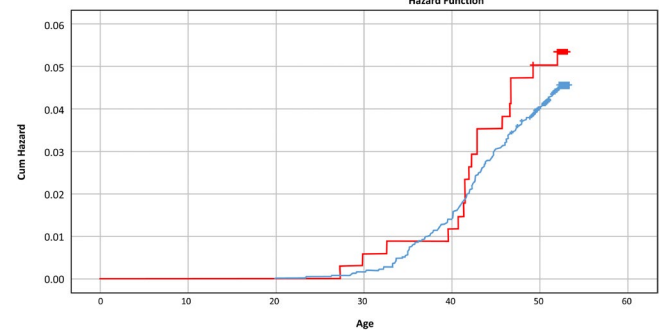


FIGURE 2 Mantel-Cox estimate for the lifetime emergence of disability pensions among women with or without endometriosis until 2018. Blue: women without endometriosis ($n = 153$, 4.4%), Red: women with endometriosis ($n = 18$, 5.2%)

decision warranting a disability pension mentioned endometriosis. The most common ICD classes in both groups were F (mental and behavioral disorders) and M (diseases of the musculoskeletal system and connective tissue) (Table S1).

4 | DISCUSSION

This unique general population-based register-linkage study supports and expands earlier evidence on endometriosis being associated with poorer work ability and sickness absenteeism, even at a late fertile age. On the other hand, we found no association between endometriosis and unemployment between the ages of 46 and 48 years or with life-long emergence of disability retirement up to age 52.

A recent review suggests that endometriosis negatively impacts women's professional lives.³ Studies based on Work Productivity and Activity Impairment surveys have estimated lower productivity at work resulting from absenteeism, presenteeism, productivity losses and activity impairments. In this study, we focused on the risk and associated factors for actual exit from the workforce. Previously, a Danish study found that associations between endometriosis and sickness absenteeism and poorer work ability were aggravated by fatigue, pain, depression and long intervals between symptom onset and diagnosis.¹⁰ In this study, endometriosis was associated with poor work ability, self-reported sickness absence and registered disability days. The fact that the associations were stronger when socioeconomic and health-related risks of work disability were considered, may reflect previous evidence of shortcomings in being diagnosed experiences by women with poorer work ability,¹⁰ linked with a lower socioeconomic status. Since our registered disability days underestimate shorter absenteeism, we conclude that endometriosis is associated with increased sickness absenteeism, even at a late fertile age.

Previous findings on the employment prospects of women with endometriosis are mixed. Some studies have found that women with endometriosis have longer professional lives compared with unaffected women.^{3,4} In contrast, a previous study showed that women with surgically confirmed endometriosis reported having considered

health in their career decisions and worked less often in their desired profession than other women.⁴ Other previous evidence suggests that women with endometriosis are highly motivated in their work.¹⁰ The fact that women with endometriosis suffer more often from infertility and have lower parity than non-affected women, may lead to greater commitment to a working career. In our study, based on full coverage of registered unemployment days, endometriosis did not predict unemployment during the 2-year follow-up.

Given that mental distress and pain disorders are major causes of early retirement,^{19–21} women with endometriosis could be at risk. We found only one previous US study that used registered company-based insurance claim data to evaluate the risk of leaving the workforce, including early retirement.¹² This retrospective study showed that women with endometriosis had a greater risk of sick leave and short-term disability in the beginning of the 5-year follow-up but not of early retirement.¹² Likewise, we found no differences in reported disability retirement up to the age of 52 years between women with and women without endometriosis. Notably, no disability retirement decisions included endometriosis among the diagnoses, although endometriosis may present with or induce multisite pain syndromes impairing functioning.^{3,10} Considering the natural course of the disease, an increase in disability retirement should have occurred during the fertile years, but we found no such evidence. Since endometriosis eases off with menopause, later endometriosis-related retirement is unlikely. At present, our results suggest that endometriosis is not associated with early disability retirement.

Methodologically, our dual-source strategy to detect endometriosis cases at population level is an important starting point. Regarding validity of diagnosis, the lack of histologic/surgical confirmation may be considered a limitation; however, such an approach is not feasible in a general population setting. Instead, we were able to use reliable and comprehensive registered data on hospital-based diagnoses. To detect the remaining diagnoses, obtained in the private sector and public healthcare centers, we used questionnaires. Our instrument has been validated as a reliable method with high specificity.²² Finally, when restricting the analysis only to the hospital-based cases, the results remained largely similar. Nevertheless, if there were many undiagnosed cases among controls, our results would be underestimates. Unfortunately, the potential role of diagnostic or treatment delay on work ability cannot be assessed in our dataset, as we have no information on the time from symptom onset to diagnosis. Neither can we grasp the type of symptoms, the use and/or effectiveness of other medical therapies besides contraceptives, assisted fertility therapies or surgical treatments. Should these have mitigated losses on functioning among women with endometriosis, our results on the associations would again be underestimates. Whilst we adjusted for parity, all related factors such as infertility- or family-related absences and burdens affecting attachment to working life could not be considered.

Our data stem from a population-based unselected birth cohort covering all employment sectors, with no significant differences regarding education and occupational status between the study

groups. Nevertheless, the healthy worker effect in occupational epidemiology²³ merits consideration due to its tendency toward null in estimations. Generally, the healthiest individuals in any group are more likely to be hired and remain employed. Thus, women still employed at a late fertile age, after hardships related to endometriosis, might have the mildest phenotypes of the disease or be otherwise healthy, which might underestimate the actual effects of endometriosis. Altogether, the strengths of our study include its large representative general population sample, the wide range of covariates measured with established survey instruments, and linkage to national register data. However, our results may not be generally applicable to other countries or cultures given the unique nature of the Finnish healthcare and retirement system, representing a Nordic social welfare society setting.

For healthcare practitioners, we encourage recognition of the relevance of organizing timely care for endometriosis to promote work ability. Notwithstanding impaired work ability and the need for sick leave, it is encouraging that we found no major risks of unemployment or early disability retirement at a late fertile age. Providing this information in patient counseling might be helpful to affected women, who might face a career-related crisis due to their diagnosis and worry about their employability over the years. If possible, job modifications such as part-time or remote work during the most distressing phases should be considered.²⁴ Lastly, careful recording of endometriosis in medical certificates could serve to allocate appropriate resources for this patient group to improve diagnostics and adequate care.

5 | CONCLUSION

Women with endometriosis at a late fertile age have poorer work ability and take sick leave more frequently than unaffected women. However, the disease does not increase their risk of unemployment or disability retirement.

ACKNOWLEDGMENTS

We thank all researchers who participated in the 31st- and 46th-year studies. We also wish to acknowledge the work of the NFBC project center.

AUTHOR CONTRIBUTIONS

H-RR, LA-M, EV, TTP, OU and RA planned the study; EV, LK and H-RR statistics and figures; H-RR, OU, RA, TTP and LA-M wrote the manuscript.

CONFLICT OF INTEREST

None.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Rossi H-R, Uimari O, Arffman R, et al. The association of endometriosis with work ability and work life participation in late forties and lifelong disability retirement up till age 52: A Northern Finland Birth Cohort 1966 study. *Acta Obstet Gynecol Scand*. 2021;100:1822-1829. <https://doi.org/10.1111/aogs.14210>