ORIGINAL RESEARCH

Trends in Hysterectomy Incidence Rates During 2000–2015 in Denmark: Shifting from Abdominal to Minimally Invasive Surgical Procedures

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Background: Hysterectomy (removal of the uterus) is a common surgical procedure in gynecology. Although minimally invasive surgical procedures have been introduced, hysterectomy is still associated with risk of short- and long-term complications. Given that hysterectomized women are no longer at risk of either hysterectomy or being diagnosed with endometrial or cervical cancer, it is important to describe trends in hysterectomy rates.

Objective: To describe trends in hysterectomy incidence rates overall and stratified by age, indication, and procedure.

Methods: Nationwide population-based cohort study using Danish national registries, 2000–2015, was conducted. We calculated the overall hysterectomy-corrected and age-standardized incidence rates of hysterectomy among women ≥20 years old. Incidence rates were stratified by age group, indication, and surgical procedure. We performed trend analyses using Joinpoint regression, thereby estimating the average annual percentage change (AAPC).

Results: A total of 98,484 women had a hysterectomy during the study period, corresponding to an overall age-standardized, hysterectomy-corrected hysterectomy incidence rate (SIR) of 351.1 per 100,000 person-years (95% CI 348.9;353.3). SIR of hysterectomy declined over time (AAPC −1.4; 95% CI −1.9;-1.0), which was driven by a decline in rates of benign hysterectomy (AAPC −2.1; 95% CI −2.7;-1.6). Irrespective of indication, rates of abdominal hysterectomy declined substantially during the study period and were surpassed by rates of minimally invasive procedures (ie, laparoscopy and robot-assisted laparoscopy) in 2013.

Conclusion: Hysterectomy-corrected incidence rates of benign hysterectomy declined over time. Irrespective of indication, we observed a shift in surgical procedure over time, from abdominal hysterectomy to minimally invasive surgical procedures.

Keywords: hysterectomy, incidence, surgical procedure, indication, epidemiology

Introduction

Hysterectomy is one of the most common surgical procedures in gynecology, and it may be performed due to benign or malignant disease. Hysterectomy includes the removal of the uterine corpus and typically the cervix as well. Often, hysterectomy also includes the removal of both fallopian tubes, as this may reduce subsequent risk of ovarian cancer.[1–3] Hysterectomy may also include the removal of both ovaries.[2,3] The procedure may be performed through an incision in the abdominal wall, by laparoscopy (with or without robot-assistance), or vaginally. Despite the introduction of minimally invasive procedures in the past decades,[4,5] hysterectomy

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is still associated with risk of surgical complications, including bleeding, infection, and damage to the bladder and bowels.[6] Moreover, studies show that women undergoing hysterectomy are at increased risk of physical impairment,[7] pain,[8,9] depression,[10] and cardiovascular disease.[11]

Globally, hysterectomy incidence rates vary across countries, with rates being two-fold higher in Australia and the United States compared to the Scandinavian countries.[5,12–14] The overall hysterectomy incidence is important for proper calculation of incidence rates of cervical and endometrial cancer, as only women with an intact cervix and uterine corpus, respectively, are at risk of these diseases.[2,15–20] Similarly, only women with an intact uterus are at risk of undergoing a hysterectomy.[13,21] Most previous studies have reported trends in uncorrected hysterectomy incidence rates; few have reported hysterectomy incidence rates after correcting for hysterectomy.[13,21] However, in previous studies, correction for hysterectomy was based on surveys and, therefore, results may be subject to recall bias.

Using individual-level data from high-quality nationwide registries, we provide an update on temporal trends in hysterectomy incidence rates in Denmark after correcting for hysterectomy prevalence, overall and stratified by age, indication, and surgical procedure.

Materials and Methods
Study Population and Design
We conducted a nationwide population-based cohort study in Denmark from 2000 to 2015. In Denmark, the health care system is tax-funded and all citizens have free and equal access to general practitioners and public hospitals. Using the Danish civil registration number (CPR-number), a unique code assigned to every resident at birth or immigration, it is possible to link prospectively collected individual-level data from Danish nationwide registries.[22] The CPR-number is registered in the Civil Registration System and contains information on date of birth, emigration status, vital status, and date of vital status. The Civil Registration System has virtually complete follow-up.[22] Estimates in the present study are based on the adult female population residing in Denmark at some point during the study period, 2000–2015 (N=3.55 million). Women <20 years were excluded because the risk of hysterectomy was extremely low.

Data Sources
Information on hysterectomy was collected from the Danish National Registry of Patients (DNRP). DNRP was established in 1977 and holds information on all non-psychiatric contacts at private and public hospitals in Denmark, including all in-patient admissions. Data from each contact include the patient's CPR number, type of contact (in-patient, out-patient, emergency room), treatment, surgical procedures, dates of admission and discharge, and up to 20 diagnoses coded according to the International Classification of Disease 8th edition (ICD-8) until 1993 and ICD-10 since 1994.[23]

As summarized in Supplementary Table 1, we categorized surgical procedures according to the procedure codes registered in DNRP; laparoscopy, robot-assisted laparoscopy, abdominal, vaginal, supravaginal (ie, leaving the cervix intact), and radical. A procedure was considered robot-assisted if it contained the additional procedure code (KZXX0), irrespective of the main procedure code. Of note, most robot-assisted hysterectomies had laparoscopy as the main procedure code (98%), suggestting a low conversion rate. We collected information on the primary diagnosis code for all patients to determine whether the indication for the procedure was benign or malignant (Supplementary Table 2). In the present study, borderline ovarian tumors (DD391A), cervical neoplasia (DN87*), carcinoma in situ (DD0*), and atypical endometrial hyperplasia (DD0*) were classified as malignant. The rationale behind this decision was that these diagnoses are associated with increased risk of cancer compared to benign diagnoses (eg, abnormal uterine bleeding) and, as a result, these diagnoses may be managed with the corresponding malignant diagnoses, particularly borderline ovarian tumors and atypical hyperplasia.

Statistical Analyses
We tabulated the distribution of all hysterectomies in the study period by age group, calendar year, type of procedure, and indication. We calculated the uncorrected and hysterectomy-corrected incidence rates (IR) and age-standardized incidence rates (SIR) of hysterectomy per 100,000 person-years, overall and stratified by age group (20–39, 40–54, 55+), surgical procedure (laparoscopy, robot-assisted laparoscopy, abdominal, vaginal, supravaginal, radical), and indication (benign, malignant). We conducted a sensitivity analysis in which the premalignant

diagnosis codes were classified as benign instead of malignant.

Incidence rates were age-standardized to the US 2010 female population. For the uncorrected estimates, women contributed time at-risk from January 1, 2000 or age 20 to date of hysterectomy, emigration, death, or December 31, 2015, whichever came first. For calculation of hysterectomy-corrected IR of hysterectomy, women were excluded from the population at-risk denominator if they had undergone a hysterectomy between January 1, 1977 through December 31, 1999. Since DNRP was established in 1977, some women may have undergone hysterectomy before 1977. Therefore, we made an additional correction considering the probability of hysterectomy prior to 1977 for women aged 20 or older, as described in details elsewhere.[16,18] The lifetime cumulative probability of hysterectomy used for hysterectomy-correction was performed using STATA version 15.1 (StataCorp. College Station, TX), whereas the remaining statistical analyses were undertaken using SAS, v. 9.4 (SAS Institute, Cary, NC). In this study, we mainly present hysterectomy-corrected IR and SIR, unless otherwise stated. Uncorrected rates are reported in Supplementary Table 3.

To estimate temporal trends in hysterectomy incidence rates during the study period, we calculated the average annual percentage change (AAPC) using the National Cancer Institute's Joinpoint Regression Program, version 4.8.[24]

Results

During the study period, 2000–2015, a total of 98,484 hysterectomies were registered, 74% of which were performed due to benign disease and 26% due to malignant disease (Table 1). The annual number of hysterectomies declined by 12%, from 6,252 hysterectomies in 2000 to 5,530 in 2015. Median age at hysterectomy was 49 years overall (interquartile range, IQR 43;60); 47 years (IQR 43;54) for women having a benign hysterectomy, and 61 years (IQR 50;70) for women undergoing hysterectomy due to malignant disease. Two-thirds of benign hysterectomies were performed among women aged 40–54, whereas two-thirds of malignant hysterectomies were performed among women aged 55+.

As seen in Table 1, 78 of benign hysterectomies were classified as radical (of 2,152 radical hysterectomies in total). Because radical hysterectomy is a procedure performed due to cervical cancer, we

Table 1 Number and Percentage of Hysterectomies, Stratified by Age, Calendar Year, and Surgical Procedure

	Total n (%)	Benign n (%)	Malignant n (%)
Total	98,484 (100)	73,359 (100)	25,125 (100)
Age			
20–39	11,424 (11.6)	9,237 (12.6)	2,187 (8.7)
40–54	53,291 (54.1)	46,936 (64.0)	6,355 (25.3)
55+	33,769 (34.3)	17,186 (23.4)	16,583 (66.0)
Calendar year			
2000	6,252 (6.3)	4,831 (6.6)	1,421 (5.7)
2001	6.680 (6.8)	5,098 (6.9)	1,582 (6.3)
2002	6,980 (7.1)	5,480 (7.5)	1,500 (6.0)
2003	6,792 (6.9)	5,287 (7.2)	1,475 (5.9)
2004	6,229 (6.3)	4,760 (6.5)	1,469 (5.8)
2005	6.236 (6.3)	4,751 (6.5)	1,485 (5.9)
2006	6,138 (6.2)	4,650 (6.4)	1,488 (5.9)
2007	6,187 (6.3)	4,670 (6.4)	1,517 (6.0)
2008	5,832 (5.9)	4,257 (5.8)	1,575 (6.3)
2009	6,279 (6.4)	4,636 (6.3)	1,643 (6.5)
2010	5,489 (5.9)	4,310 (5.9)	1,539 (6.1)
2011	6,100 (6.2)	4,439 (6.1)	1,661 (6.6)
2012	5,787 (5.9)	4,123 (5.6)	1,664 (6.6)
2013	5,774 (5.9)	4.063 (5.5)	1,711 (6.8)
2014	5,869 (6,0)	4,144 (5.6)	1,725 (6.9)
2015	5,530 (5.6)	3,860 (5.3)	1,670 (6.6)
Surgical procedure			
Laparoscopic	12,249 (12.4)	9,732 (13.3)	2,517 (10.0)
Robot-assisted	3,449 (3.5)	868 (1.2)	2,581 (10.2)
Abdominal	49,208 (50.0)	32,940 (44.9)	16,268 (64.5)
Vaginal	21,890 (22.2)	20,697 (28.2)	1,193 (4.7)
Supravaginal	9,536 (9.7)	9,044 (12.3)	492 (2.0)
Radical	2,152 (2.2)	78 (0.1)	2,074 (8.2)

considered the 78 cases misclassified and excluded them from further analyses (ie IR and SIR, stratified by indication and procedure).

The overall hysterectomy-corrected SIR of hysterectomy was 351.1 per 100,000 person-years (95% CI 348.9; 353.3) (Table 2). Age-standardized incidence rates of benign hysterectomy were nearly three-fold higher than rates of malignant hysterectomy (261.7 vs 89.1 per 100,000 person-years). When stratifying by age at hysterectomy, the highest IRs were found among women aged 40–54 followed by women aged 55+, whilst women aged 20–39 had the lowest IRs (Table 2). With respect to surgical procedure, SIR of abdominal hysterectomy was highest, followed by vaginal and laparoscopic hysterectomy (Table 2).

Table 2 Overall Hysterectomy-Corrected, Age-Standardized (US 2010 Female Population) Incidence Rate per 100,000 Person-Years, Stratified by Age, Indication, and Surgical Procedure

	n	Corrected	
		IR (95% CI)	**SIR (95% CI)**
Total	98,484	343.8 (341.6;345.9)	351.1 (348.9;353.3)
Age			
20–39	11,424	107.8 (105.9;109.8)	NA
40–54	53,291	674.0 (668.3;679.7)	NA
55+	33,769	332.9 (329.3;336.4)	NA
Indication			
Benign	73,281	255.8 (254.0;257.7)	261.7 (259.8;263.6)
Malignant	25,125	87.7 (86.6;88.8)	89.1 (88.0;90.2)
Surgical procedure			
Laparoscopic	12,249	42.8 (42.0;43.5)	43.6 (42.8;44.4)
Robot-assisted	3,449	12.0 (11.6;12.4)	12.2 (11.8;12.6)
Abdominal	49,208	171.8 (170.3;173.3)	175.6 (174.1;177.2)
Vaginal	21,890	76.4 (75.4;77.4)	77.9 (76.8;78.9)
Supravaginal	9,536	33.3 (32.6;34.0)	34.2 (33.5;34.8)
Radical	2,074	7.2 (6.9;7.6)	7.3 (7.0;7.6)

Abbreviation: NA, not applicable.

Temporal Trends in Hysterectomy Incidence Rates

During the study period, overall hysterectomy-corrected SIR of hysterectomy declined from 362.9 per 100,000 person-years (95% CI 353.0;372.04) in 2000 to 307.1 per 100,000 (95% CI 299.1; 315.3) in 2015 (AAPC −1.4, 95% CI −1.9; -1.0) (Figure 1 and Supplementary Table 3). The decline was attributed to a decline in SIR of benign hysterectomy, from 279.2 (95% CI 271.4; 287.2) in 2000 to 216.2 (95% CI 209.4; 223.1) in 2015 (AAPC −2.1; 95% CI −2.7; -1.6) (Figure 2). In contrast, SIR of malignant hysterectomy increased slightly, from 83.1 (95% CI 78.8; 87.5) in 2000 to 90.9 (86.6; 95.4) in 2015 (AAPC 0.6; 95% CI 0.2; 1.0) (Figure 3). We performed a sensitivity analysis in which premalignant diagnosis codes were classified as benign instead of malignant. This resulted in an overall increase in SIR of benign hysterectomy, whereas the temporal trend was attenuated (AAPC −1.7; 95% CI −2.3; -1.2) (Supplementary Figure 1). SIR of malignant hysterectomy was lower in our sensitivity analysis compared to our main analysis, and the previously observed increase in SIR of malignant hysterectomy over calendar time was no longer observed (AAPC −0.2; 95% CI −0.6; 0.2). With respect to age, SIR of hysterectomy declined

among women aged 20–39 years (AAPC −1.8; 95% CI −2.6; -1.0) and women aged 40–54 (AAPC −2.0; 95% CI −2.5; -1.5), whereas rates remained unchanged for women aged 55 years and older (AAPC −0.4; 95% CI −0.9; 0.2) (Supplementary Table 3).

Trends in Type of Procedure

During the study period, we observed changes in SIR by surgical procedure (Figure 1). SIR of abdominal hysterectomy declined by 64%, from 210.5 per 100,000 person-years in 2000 to 76.2 per 100,000 person-years in 2015 (AAPC −5.6; 95% CI −7.5; -3.7), and SIR of supravaginal hysterectomy declined by 90%, from 72.3 per 100,000 person-years to 7.4 per 100,000 person-years (AAPC −12.3; 95% CI −14.1; -10.5). In contrast, SIR of laparoscopic hysterectomy increased 8-fold, from 16.9 per 100,000 person-years to 132.8 per 100,000 person-years (AAPC 21.1; 95% CI 16.5; 25.9), and robot-assisted hysterectomy increased 70-fold, from 0.7 per 100,000 person-years in 2008 to 48.8 per 100,000 person-years in 2015 (AAPC 43.6; 95% CI 20.2; 71.5).

Trends in Type of Procedure by Indication

When stratifying by procedure and indication, similar trends were observed for SIR of benign hysterectomy, with a major reduction in rates of abdominal hysterectomy (AAPC −5.9; 95% CI −7.8; -4.0) and supravaginal hysterectomy (AAPC −12.1; 95% CI −14.0; -10.1). SIR of robot-assisted hysterectomy increased 30-fold, from 0.4 per 100,000 person-years in 2008 to 11.9 per 100,000 person-years in 2015 (AAPC 44.8; 95% CI 18.5; 76.8), and SIR of laparoscopic hysterectomy increased 7-fold, from 15.0 per 100,000 person-years in 2000 to 109.7 per 100,000 person-years in 2015 (AAPC 20.4, 95% CI 15.4; 25.5) (Figure 2).

With respect to hysterectomy due to malignant disease, abdominal hysterectomy declined by 60%, from 66.6 per 100,000 person-years in 2000 to 26.9 per 100,000 person-years in 2015 (AAPC −5.0, 95% CI −6.9; -3.0). In contrast, SIR of laparoscopic hysterectomy increased 12-fold, from 2.0 per 100,000 person-years to 23.1 per 100,000 person-years (AAPC 23.8, 95% CI 17.4; 30.6), and robot-assisted hysterectomy increased 185-fold, from 0.2 per 100,000 person-years in 2008 to 37.0 per 100,000 person-years in 2015 (AAPC 42.1, 95% CI 19.8; 68.5).

Discussion

In the present study, we found an age-standardized, hysterectomy-corrected incidence rate of hysterectomy of
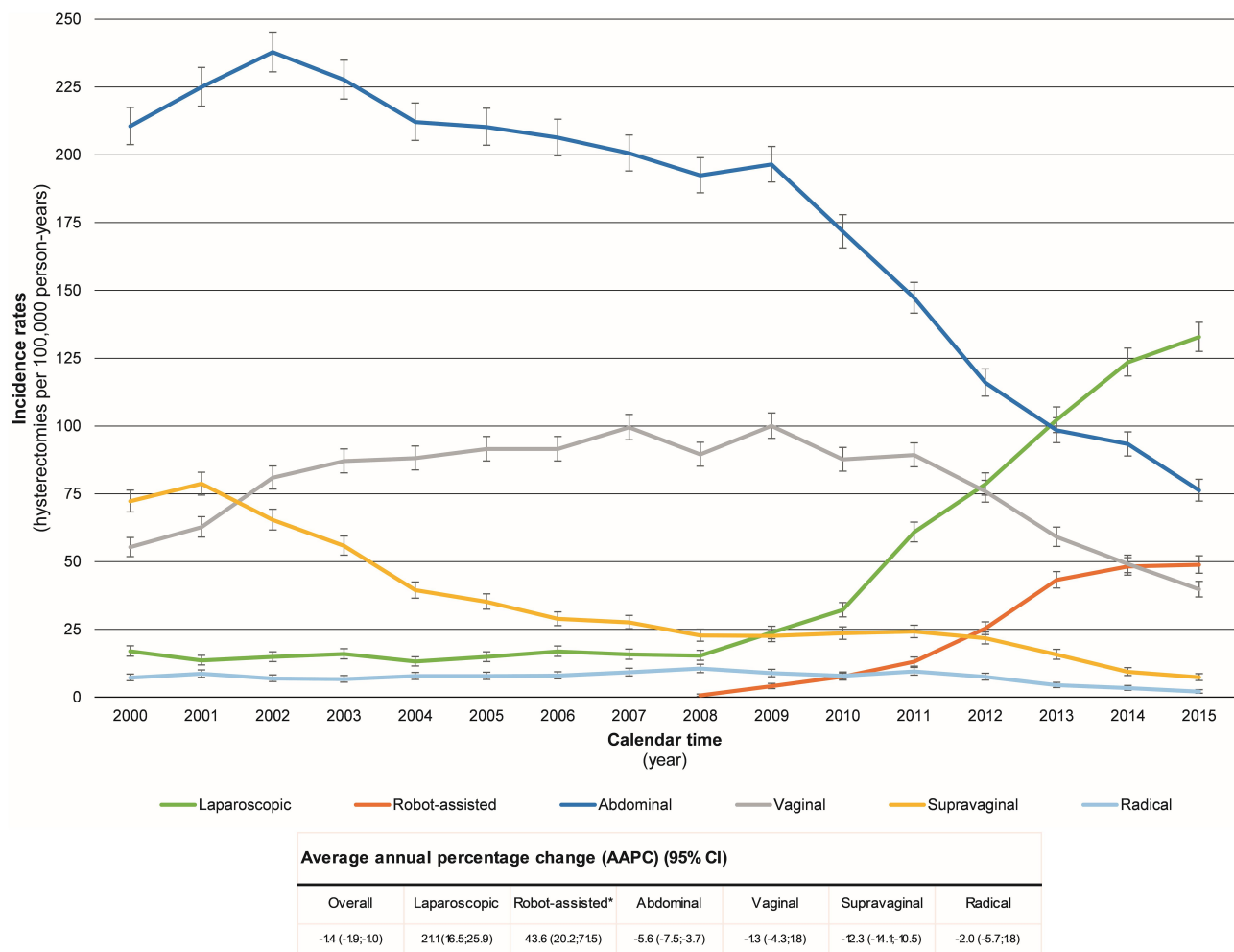
Figure 1 Age-standardized (US 2010 female population) hysterectomy-corrected incidence rates of hysterectomy over calendar time and corresponding average annual percentage change stratified by surgical procedure.
Note: *Based on SIR from 2008 to 2015 since no robot-assisted hysterectomy was performed prior to 2008.

351.1 per 100,000 person-years. We observed a decline in SIR of hysterectomy during the study period, which was driven by a decline in SIR of benign hysterectomy. Of note, regardless of indication, SIR of abdominal hysterectomy declined substantially over calendar time, while minimally invasive procedures like laparoscopic hysterectomy and robot-assisted hysterectomy increased, surpassing the SIR of abdominal hysterectomy at the end of our study period.
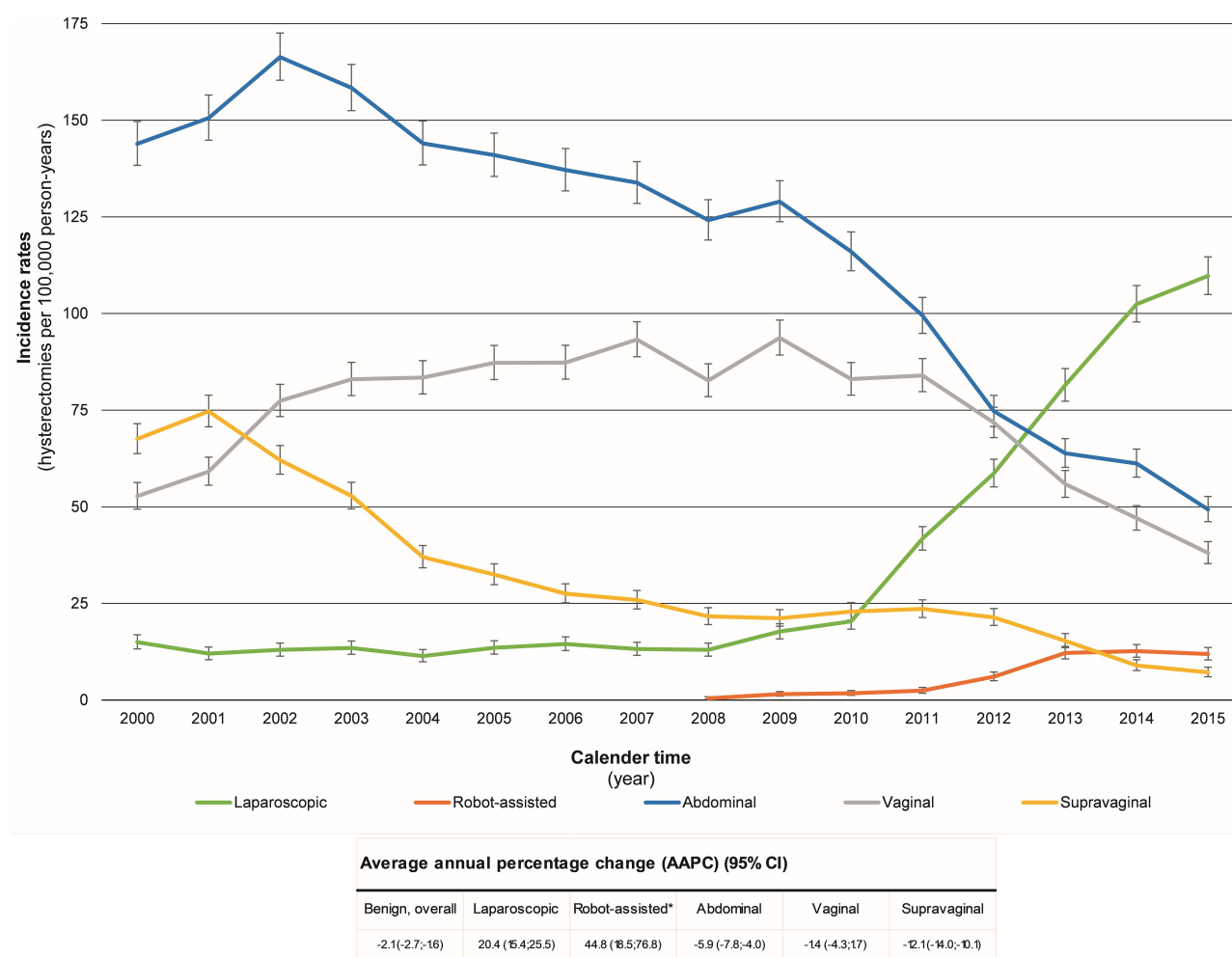
Overall Hysterectomy Incidence Rate

In general, hysterectomy incidence rates in our study were comparable to results reported in the Nordic countries, but lower than rates in the UK, Germany, US, and Australia.[2,12,13,21,25] Our findings of a temporal decline in hysterectomy incidence rates are consistent with previous US, Australian, and European studies.[5,12,13,25,26] However,

most of the previous studies reported incidence rates of hysterectomy without correction for previous hysterectomy. Furthermore, the study populations differ by age of women included and by indication for hysterectomy, with most studies reporting incidence rates of benign hysterectomy. Consequently, it is difficult to perform a meaningful comparison of hysterectomy incidence rates across countries. Only a few studies have reported hysterectomy incidence rates after correcting for hysterectomy and reported similar findings as in our study. However, these studies corrected for hysterectomy using data on hysterectomy status derived from surveys and are therefore subject to recall bias.[13,21]

Hysterectomy Due to Benign Disease

The observed overall decline was a result of declining incidence rates of benign hysterectomy, as reported in previous studies.[5,12,26,27] This decline may be explained

Figure 2 Age-standardized (US 2010 female population) hysterectomy-corrected incidence rates of hysterectomy over calendar time and corresponding average annual percentage change among women with benign disease, stratified by surgical procedure.
Note: *Based on SIR from 2008 to 2015 since no robot-assisted hysterectomy was performed prior to 2008.

by the introduction of conservative treatment options for fibromas and abnormal uterine bleeding, such as hormonal intrauterine device, ablation, and hysteroscopic resection of the endometrium and/or fibromas. By opting for conservative treatment, women avoid potential surgical complications like bleeding, infection, and damage to the bladder and bowels,[6] and long-term risks, such as physical and mental impairment,[7,10] post-surgical pain,[8,9] and cardiovascular disease.[10,11] On the other hand, an increasing number of women will have an intact cervix and uterine corpus and will therefore be at risk of developing cervical and endometrial cancer in the future.[2,16,28–30] Thus, a recent modeling study has projected an increase in cervical cancer incidence rates in the US in the future, particularly at older ages, after considering temporal changes in cervix-removing hysterectomy.[31]

Hysterectomy Due to Malignant Disease

Incidence rates of hysterectomy due to malignant disease not only reflect incidence rates of gynecological cancers, such as cervical and endometrial cancer, but also the stage of disease. When diagnosed at an early stage, hysterectomy is a crucial part of the treatment.[32,33] In our sensitivity analysis, where we classified premalignant diagnosis codes as benign, we found that the previously observed temporal increase in the incidence rate of malignant hysterectomy disappeared. This might imply that the previously observed increase in hysterectomy incidence rates when combining premalignant and malignant diagnosis codes was primarily driven by an increase in hysterectomy due to premalignant disease.

Temporal Changes in Type of Procedure

We found a shift in surgical procedures over time, with abdominal hysterectomy being the most common procedure
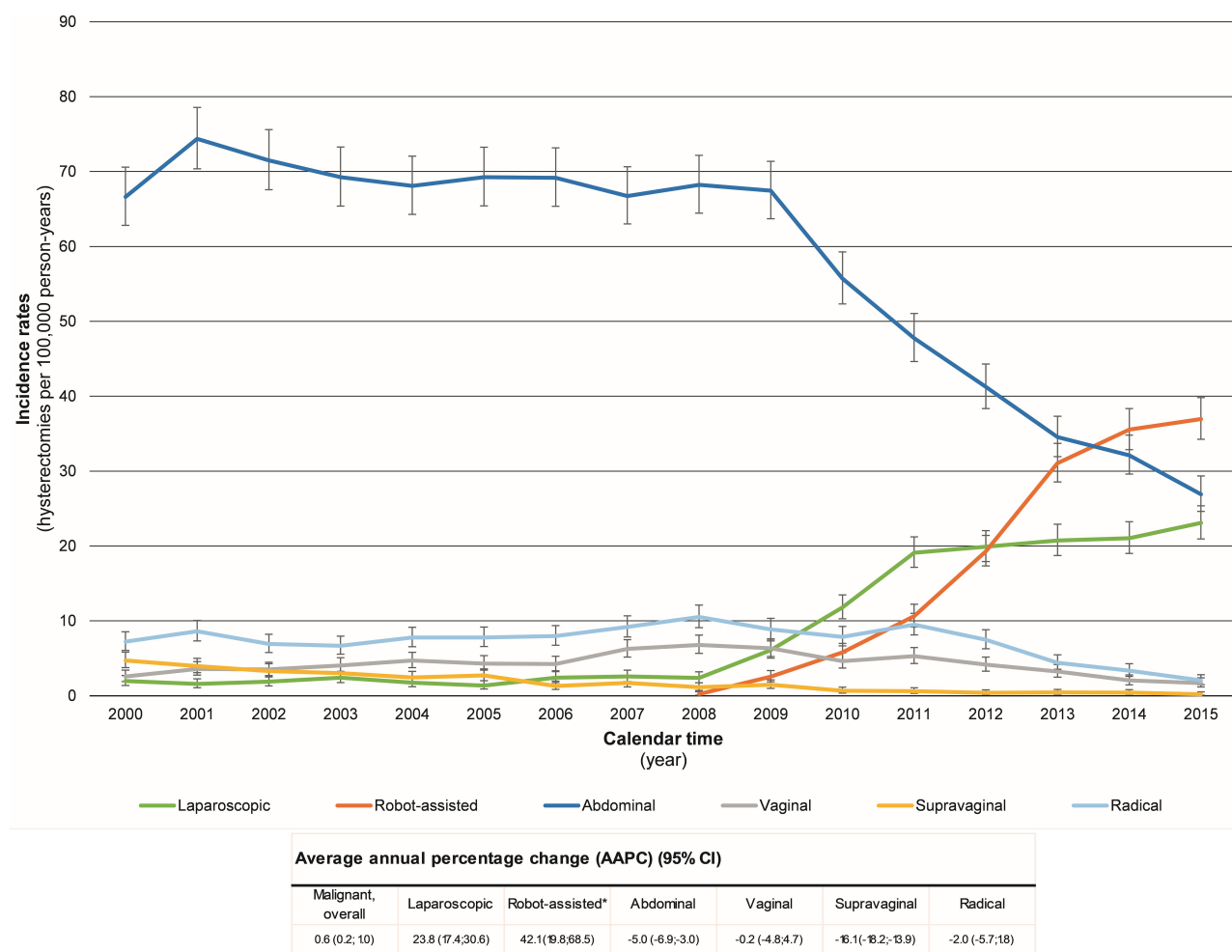
Figure 3 Age-standardized (US 2010 female population) hysterectomy-corrected incidence rates of hysterectomy over calendar time and corresponding average annual percentage change among women with malignant disease, stratified by surgical procedure.
Note: *Based on SIR from 2008 to 2015 since no robot-assisted hysterectomy was performed prior to 2008.

during 2000–2012 and minimally invasive hysterectomy being the leading procedure since 2013. Our findings, showing a rise in minimally invasive procedures over time, are consistent with previous findings in the same study period.[5,13,14,27] Studies from Australia,[13] the US,[12] and Finland[27] showed a decline in rates of abdominal hysterectomies and a rise in rates of minimal invasive procedures. However, in the Australian and the US studies, abdominal hysterectomy was still the most common procedure.

When choosing a surgical procedure, it is important to consider the patient's comorbidity (BMI, diabetes, smoking status, medical illnesses, American Society of Anesthesiologists' (ASA) classification of Physical Health, etc.), history of abdominal or vaginal surgery, and the indication. Although complications following benign hysterectomy are rare, several studies show that laparoscopic hysterectomy is superior with respect to risk

of bleeding, thromboembolic events, infection, and quality of life.[6,26,34–37] Minimally invasive procedures may be performed as an outpatient procedure, thereby reducing the length of hospital stay and lowering the costs.[26,35,38–40] On the other hand, the learning curve for laparoscopic hysterectomy is steep, and studies suggest that the risk of bowel and ureter injuries is higher in laparoscopic hysterectomy compared to abdominal hysterectomy.[6,41,42] Currently, robot-assisted hysterectomy is comparable to laparoscopic hysterectomy regarding complications and operating time,[43] albeit the costs associated with robot-assisted hysterectomy are higher.[44]

With regard to hysterectomy performed due to malignant disease, it has recently been questioned whether minimally invasive procedure is the correct choice of procedure for cervical cancer, as studies report that minimally invasive radical hysterectomy is

associated with shorter disease-free survival and higher mortality compared to laparotomy.[32,45] However, with respect to surgical treatment for endometrial cancer, no difference in disease-free survival has been observed when comparing robot-assisted and abdominal hysterectomy.[33]

Strengths and Limitations

When interpreting our results, some limitations should be taken into consideration. Since DNRP was established in 1977, we were unable to retrieve data on hysterectomies performed prior to this date. Instead, we had to rely on a modelling approach to estimate the cumulative lifetime probability of hysterectomy for the hysterectomy correction. As described in previous studies, this method has been found to be very robust.[16,18] Given that hysterectomy incidence rates and type of procedure vary across countries, our results may not be generalizable to other populations or countries. In our indication and procedure-stratified analyses, we excluded 78 benign radical hysterectomies due to the risk of misclassification. Radical hysterectomy includes the removal of the parametrium on both sides and the upper part of the vagina in addition to the corpus and cervix uteri, and is usually performed in patients with cervical cancer. Unfortunately, we were unable to determine whether they were misclassified by procedure or indication. However, as the number of benign radical hysterectomy accounted for less than 0.1% of all hysterectomies in the study period, this potential misclassification has minimal impact on our findings.

The strength of this study is the nationwide and population-based design in a tax-funded health care system with virtually complete follow-up.[22] The use of surgical procedure codes from DNRP to estimate hysterectomy prevalence, instead of relying on survey data as reported in previous studies,[13,21] reduces the risk of recall bias in our study. Moreover, we were able to collect information on indication and surgical procedure at an individual level, allowing us to perform a sensitivity analysis where we classified premalignant diagnoses as malignant. Our rationale was that these diagnoses are associated with increased risk of cancer and, therefore, are managed differently. Finally, correcting for hysterectomy, so that only women with an intact uterus contributed time at-risk during the study period, resulted in more accurate hysterectomy incidence rates.

Conclusions

Hysterectomy-corrected SIR of hysterectomy declined from 2000 to 2015, which was driven by declining SIR of benign hysterectomy. Irrespective of indication, the surgical procedure shifted from abdominal hysterectomy to minimally invasive surgical procedures during our study period.

Abbreviations

AAPC, average annual percentage change; CPR-number, civil registration number; DNRP, Danish National Registry of Patients; IQR, interquartile range; IR, incidence rate; SIR, standardized incidence rate.

Data Sharing Statement

Restrictions apply for the availability of these data, which were used under the license of this study. Data are available from the authors with the permission of the Danish Data Protection Agency.

Ethical Approval and Informed Consent

This study was approved by the Danish Data Protection Agency (record number 1-16-02-150-17, approved April 24, 2017). According to the Danish legislation, approval from the Ethics Committee is not required for registry-based research.

Author Contributions

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval for the version to be published; and agreed to be accountable for all aspects of the work.

Disclosure

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