

Global epidemiology of hysterectomy: possible impact on gynecological cancer rates

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Hysterectomy is one of the most common surgical procedures in gynecology worldwide. Not removing the proportion of women no longer at risk of gynecological cancer (ie, women who have undergone hysterectomy or oophorectomy) from the population-at-risk denominator may therefore underestimate the incidence rates of gynecological cancers.

Because hysterectomy incidence has been reported to change over time¹⁻³ and may vary considerably between countries as well as by race and age, meaningful comparison of gynecological cancer rates across populations may therefore be compromised. The impact of significant changes in the prevention and treatment of gynecological cancers, particularly vaccination and screening for cervical cancer, could be masked or misinterpreted without accurate estimation of gynecological cancer rates by removal of the hysterectomized population.

In this paper, we compare the rates, indications, and types of hysterectomy reported over time in Europe and North America based on the best available

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Despite the fact that hysterectomy is the most common surgical procedure worldwide in gynecology, national reporting of the incidence rate of gynecological cancers rarely removes the proportion no longer at risk of the disease from the population-at-risk denominator (ie, women who have had a hysterectomy). The incidence rate of gynecological cancers is thus likely underestimated. Because hysterectomy, as well as oophorectomy, incidence varies across countries, age, and over time, meaningful comparison of gynecological cancer incidence rates may be compromised. Without accurate estimates of gynecological cancer incidence rates, performed via removing the proportion of hysterectomized or oophorectomized women from the population-at-risk denominator, the impact of prevention strategies may be masked or misinterpreted. Furthermore, because national cervical cancer screening guidelines are at least in part based on the national reporting of cervical cancer incidence, it is important that the incidence rate reflects the true population at risk.

Key words: cervical cancer screening, epidemiology, gynecological cancer, hysterectomy

literature and identify data gaps that need to be considered to enable a more accurate reporting of gynecological cancer incidence rates in the future.

Hysterectomy by indication

Hysterectomy is most commonly performed because of benign disease, such as fibroids, bleeding disorders, endometriosis, and uterine prolapse. In 2000–2004, hysterectomy caused by benign disease accounted for 90% of all hysterectomies in the United States; malignant disease, such as uterine cancer, cervical cancer, and ovarian cancer, accounted for the remaining 10%.¹ Hysterectomy may also include the removal of both ovaries (bilateral oophorectomy). In 2000–2004, approximately 54% of women undergoing hysterectomy in the United States had both ovaries removed,¹ whereas the rate was much lower in Australia (30% in 2004–2005),³ Germany (12% in 2005),⁴ and Denmark (22% in 1981).⁵

The proportion of women undergoing bilateral oophorectomy concomitant with hysterectomy increases by age in most countries.^{1,5} In the United States,

37% of women aged 15–44 years had both ovaries removed concurrent with hysterectomy, and the highest proportion of concomitant oophorectomy was seen in women aged 50–54 years, peaking at 78%.¹ However, these reports vary with regard to specification of whether bilateral oophorectomy was performed at hysterectomy because of both benign and malignant disease or because of benign disease only.

It would be valuable to introduce more systematic reporting to understand not only the proportion of total hysterectomies with concomitant bilateral oophorectomy but also the fraction removed prophylactically (ie, carriers of BRCA and other women with normal ovaries) vs therapeutically (ie, women having abnormal ovaries or gynecological cancer).

Surgical procedure

Hysterectomy can be performed vaginally or abdominally or by a laparoscopic approach. Most commonly, hysterectomy includes removal of the uterine cervix, but subtotal or supracervical hysterectomy, in which the cervix is left

TABLE 1
Incidence rate of benign hysterectomy, bilateral oophorectomy, and gynecological cancer across countries

Variable	Hysterectomy	Subtotal hysterectomy	Bilateral oophorectomy	Bilateral oophorectomy	Cervical cancer ^a	Uterine cancer ^a	Ovarian cancer ^a
Country	Year	IR/100,000	Year	Subset of women with subtotal hysterectomy, %	Year	Year	Year
United States	2004	510 ^{1,b}	2004–2005	7.5 ⁶	2000–2004	2007–2011	2007–2011
					54 ¹ (benign and malignant cases)	7.8 ²³	24.6 ²²
Denmark	2007–2011	173 ²	2011	8 ¹²	1977–1981	2012	2012
					22 ⁵ (benign cases)	12.7 ²¹	23.8 ²¹
Germany	2005–2006	295 ⁸	2005–2006	4.8 ⁸	2005–2006	2010	2010
					23 ⁴ (benign and malignant cases) 12 ⁴ (benign cases)	9.3 ⁴⁹	17.7 ⁴⁹
United Kingdom	1995	355 ^{29,b}	2001	4 ⁷	1997–1999	2011	2011
					50 ⁷ (benign and malignant cases)	8.9 ²⁵	20.5 ²⁵
Australia	2004–2005	312 ³	NA	NA	2004–2005	2010	2010
					29.6 ³ (benign cases)	7.1 ²⁴	18.1 ²⁴
							2010
							10.4 ²⁴

IR, incidence rate, age standardized; NA, not available.

^a There is no indication that the gynecological cancer incidence rates are corrected for hysterectomy or oophorectomy incidence; ^b Hysterectomy incidence rate includes those caused by malignant disease. Hammer. *Hysterectomy and gynecological cancer incidence. Am J Obstet Gynecol* 2015.

intact, is also an option. The latter approach is not a common procedure in the United States (7.5%),⁶ in the United Kingdom (4%),⁷ and in Germany (4.8%),⁸ whereas it has been more common in the Scandinavian countries such as Sweden and Denmark during the past 20 years.^{9,10} The percentage of subtotal hysterectomies in Denmark was 22% in the period 1988–1998,⁹ but since then the rate has declined to 15% in 2008¹¹ and to 8% in 2011.¹² In Sweden 32% of hysterectomies were subtotal in 1987; thereafter the proportion declined to 18% in 2003.¹⁰

Hysterectomy incidence across countries

In the past years, several papers have been published on hysterectomy incidence rates in developed countries (Table 1). The incidence rate is very high in countries such as the United States (510 per 100,000 in 2004),¹ ranging from 430 to 100,000 for women living in the Northeast to 630 per 100,000 for those living in the South, whereas lower hysterectomy incidence rates have been reported in several European countries, including Denmark (173 per 100,000 in 2011).²

The hysterectomy incidence increases with age until age 40–50 years in which the incidence seems to peak in most countries, including Finland,¹³ Denmark,² Germany,⁸ and the United States.¹ Hysterectomy incidence is cumulative with age, and it is estimated that approximately 50% of women in the United States will have undergone hysterectomy by the age of 70–75 years.¹⁴

In some countries, the hysterectomy incidence rate has been reported to decline over time. The incidence rate has dropped in Australia (348 per 100,000 in 2000–2001 to 312 per 100,000 in 2004–2005)³ and in Denmark (from 205 per 100,000 in 1977–1981 to 173 of 100,000 in 2006–2011).² In the United States,⁶ the incidence has declined more dramatically, from 710 per 100,000 in 1980 to 660 per 100,000 in 1987 and 510 per 100,000 in 2005.^{1,15,16} This decrease is presumably owing to increased use of ablative methods, hysteroscopic

procedures, and the levonorgestrel-releasing intrauterine device for the treatment of abnormal bleeding disorders and myomas.^{17,18}

An increase in mean age at hysterectomy over the last decades has also been reported in some countries such as Denmark (from 46 years in 1977–1981 to 50 in 2006–2011)² and Sweden (from 47.3 in 1987–1990 to 52.2 in 2001–2003).¹⁰ This may indicate that conservative treatment does not completely avert hysterectomy but, to some extent, postpones it until later ages.¹⁹

The impact of hysterectomy and oophorectomy on gynecological cancer rates

The incidence rate of cervical cancer has declined significantly in developed countries after implementation of cervical cancer screening programs,²⁰ but the same phenomenon has not been seen in uterine and ovarian cancer, presumably because of the lack of an efficient screening tool.^{13,21,22} Table 1 summarizes the incidence rate of cervical, uterine, and ovarian cancer in the United States, in Australia, and in 3 European countries. As shown, the cervical cancer incidence is higher in Denmark (12.7 per 100,000)²¹ compared with the United States (7.8 per 100,000)²³ and Australia (7.1 per 100,000),²⁴ whereas the incidence of uterine and ovarian cancer is highest in the United States (24.6 per 100,000)²² and in the United Kingdom (17.1 per 100,000),²⁵ respectively.

Some studies have reported differences in the incidence of gynecological cancer when comparing hysterectomy or oophorectomy corrected and uncorrected incidence rates.^{13,14,26–30} Not surprisingly, all of the studies found that the hysterectomy or oophorectomy uncorrected incidence rates of gynecological cancers are lower than the corrected rates (Table 2).

The degree of underestimation depends on the hysterectomy or oophorectomy incidence and, for cervical cancer, on the proportion of subtotal hysterectomies. Hence, the difference in corrected vs uncorrected rates tended to be higher in countries with a high hysterectomy or oophorectomy incidence,

such as the United States, compared with countries with a lower hysterectomy or oophorectomy incidence, such as the United Kingdom, Germany, and Finland (Table 2).

The impact of adjusting for hysterectomy on cervical cancer incidence seems to be rather low in a Finnish study.¹³ Despite the fact that the hysterectomy incidence is similar in Finland and Germany, only a 10% increase in overall cervical cancer incidence was seen in the Finnish study when adjusting for hysterectomy prevalence compared with a 28% increase in the German study²⁶ (Table 2). This difference does not seem to be explained by a higher proportion of subtotal hysterectomies in Finland (7.3% in 1996 and 1.7% in 2006)³¹ compared with Germany (4.8% in 2005⁸).

Both studies estimated the hysterectomy prevalence based on population-based health surveys and used these data to extrapolate back in time. The German study used only 1 survey from year 2000 including 3000 women aged 40–69 years, whereas the Finnish study used 3 population-based surveys from 1981 (4000 women aged 30–99 years), 1989 (2000 women aged 45–64 years), and 1997 (3763 women aged 25–64 years). Hence, it is possible that the German study may have overestimated the hysterectomy prevalence, which subsequently causes a larger difference between hysterectomy-corrected vs uncorrected rates in the German study compared with the Finnish study.

A few studies have reported cervical cancer incidence by race. In the study by Merrill,²⁸ hysterectomy-corrected incidence rates overall were higher than the uncorrected rates, and black women had the highest incidence and American Indians/Alaska natives the lowest rates. Merrill also found that the oophorectomy-corrected rate of ovarian cancer was 23.6–35.2% higher than the uncorrected rate, depending on race.²⁸ Because the incidence rate of concomitant oophorectomy also varies considerably between races and countries, the impact of adjusting for oophorectomy will, presumably, be lower in countries with a low rate of

concomitant oophorectomy, such as Germany and Denmark (Table 1).

In contrast to Merrill's study, correction for hysterectomy incidence had a profound and differential effect on uterine cancer incidence rates by race, as reported by Stang et al²⁷ in 2014. Initially, white women were at highest risk (42.9 per 100,000 person-years in white women; 37.3 per 100,000 person-years in black women), but after adjusting for hysterectomy, black women had a higher incidence than white women (57.2 per 100,000 person-years in white women; 66.6 per 100,000 person-years in black women).²⁷ The hysterectomy-corrected rate in black women was 78% higher than the uncorrected rate.

If we are to continue to prevent gynecological cancers, it is very important to understand what may be the cause of the low incidence in one population compared with a higher incidence in another population. For example, the incidence of cervical cancer is lower in the United States (7.8 per 100,000)²³ than in Denmark (12.7 per 100,000),²¹ but currently there is no clear explanation for these differences. Both countries have implemented cervical cancer screening programs that focus on similarly aged women with similar screening interval, and the reported participation rates are almost identical in the 2 countries.^{32,33} However, the difference in cervical cancer incidence may be explained by a difference in the hysterectomy incidence in the 2 countries.

The hysterectomy incidence is much higher in the United States (510 per 100,000 in 2004¹) than in Denmark (173 per 100,000 in 2006–2011²), and the proportion of subtotal hysterectomies is much larger in Denmark than in the United States, which subsequently results in a larger proportion of women at risk of cervical cancer in Denmark compared with the United States.

A recent study found a 59% increase in the age-standardized rate of invasive cervical cancer in the United States after hysterectomy correction.¹⁴ No Danish study has yet compared hysterectomy corrected with uncorrected rates of cervical cancer; however, it seems plausible

TABLE 2

Hysterectomy-corrected vs uncorrected incidence rate of cervical and uterine cancer

Variable					Cervical cancer			Uterine cancer		
Author	Country	Years	Age range, y	Race	Uncorrected IR/100,000	Corrected IR/100,000	Relative change, %	Uncorrected IR/100,000	Corrected IR/100,000	Relative change, %
Redburn and Murphy ²⁹	England and Wales	1961–1995	0–85+	All	12.6	14.4	14.3	13.4	16.2	20.9
Luoto et al ¹³	Finland	1953–2010	0–85+	All	3.8	4.2	10.5	14.6	18.8	28.8
Sherman et al ³⁰	United States	1992–2000	30–74	All	NA	NA	NA	29.2	48.7	66.8
Merrill ²⁸	United States	1998–2002	15–70+	White	11.1	15.3	37.8	32.8	56.7	72.9
				Black	14.2	22.8	60.6	24.2	46.8	93.4
				American Indians/Alaska Natives	7.3	10.6	45.2	15.9	29.6	86.2
				API	11.1	14.8	33.3	22.0	31.0	40.9
Jamison et al ⁵⁰	United States	1992–2008	50+	White	NA	NA	NA	78.8	136	72.6
				Black				60.9	115.5	89.7
				API				47.5	67.4	41.9
				Hispanic				51.0	82.3	61.3
Stang ²⁶	Germany	2003–2007	0–85+	All	9.6	12.3	28.1	17.9	26.1	45.8
Rositch et al ¹⁴	United States	2000–2009	0–85+	All	11.7	18.6	59.0	NA	NA	NA
Stang et al ²⁷	United States	2007–2010	20–80+	White non-Hispanic	7.0	8.2	17.1	42.9	57.2	33.3
				Black non-Hispanic	13.8	22.1	60.1	37.3	66.6	78.6
				Hispanic	11.3	14.5	28.3	28.6	38.8	35.7

API, Asians/Pacific Islanders; IR, incidence rate, age standardized; NA, not available.

Hammer. Hysterectomy and gynecological cancer incidence. *Am J Obstet Gynecol* 2015.

that correcting for hysterectomy would level out the difference in cervical cancer incidence between the 2 countries. Furthermore, the high proportion of concomitant oophorectomy in the United States (54% in 2000–2004)¹ compared with Denmark (22% in 1981)⁵ may also explain why the ovarian cancer incidence appears to be much higher in Denmark compared with the United States (16.9 per 100,000²¹ vs 12.3 per 100,000,³⁴ a 37% difference).

Age-specific cancer rates after correction for hysterectomy

A few studies have reported that the difference in hysterectomy corrected vs uncorrected incidence rates of cervical cancer is highest in older women because hysterectomy incidence is cumulative with age.^{13,14,26,29} These studies all found that older women were at highest risk of cervical cancer (Figure) after adjusting for hysterectomy. In

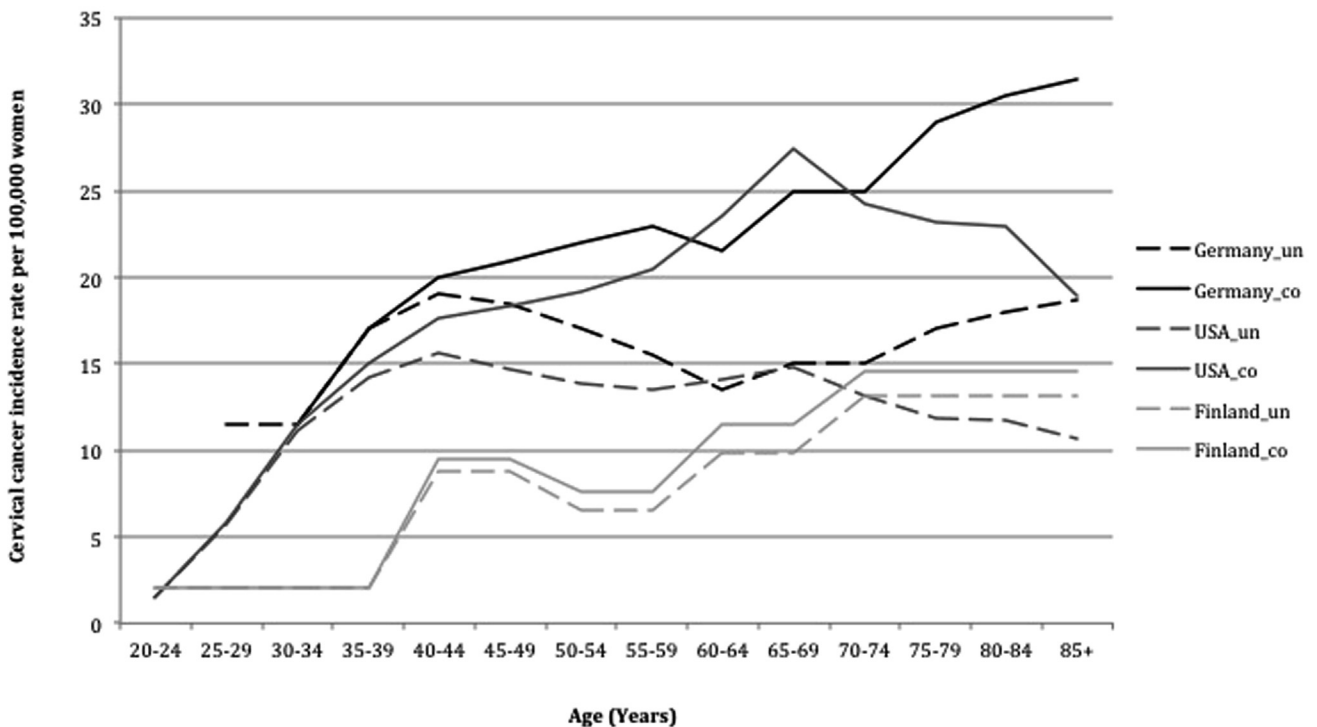
Finland, women older than 70 years had the highest cervical cancer incidence regardless of hysterectomy status,¹³ whereas a German study found a 67% increase in cervical cancer incidence in women aged 65 years or older after correction for hysterectomy prevalence.²⁶

In the United States, the hysterectomy corrected cervical cancer incidence was highest in women aged 65–69 years, approximately 87% higher than the uncorrected rate.¹⁴ This pattern in age-specific cervical cancer incidence was also seen when stratifying by race.²⁷ Despite the fact that these studies report that older women have a much higher cervical cancer incidence rate than women aged 35–50 years, the age group previously believed to be at highest risk, women aged 65 years and older, are not recommended screening for cervical cancer in the United States³⁵ or in Europe.³⁶

In the most recent US guideline³⁵ on cervical cancer screening, it is stated that "cervical cancer is rare" in women aged older than 65 years.²³ Paradoxically it is estimated that 23.0% and 22.8% of cervical cancers in the United States and in Europe, respectively, occur in women aged 65 years or older.³⁷ Furthermore, it is stated in the US guideline that the current recommendations are based on the opinion of the expert panel because research regarding screening in older women is lacking. However, observational studies based on data from the United States and the United Kingdom have been published in recent years, revealing that screening women beyond the age of 65 years would continue to decrease the incidence and mortality of cervical cancer.^{38–40}

More data are needed to determine whether a substantial fraction of the cervical cancers occurring in older women is due to lack of screening

FIGURE
Cervical cancer incidence by age and country



Cervical cancer incidence by age in the United States,¹⁴ Germany,²⁶ and Finland.¹³ Hysterectomy-corrected rates (co) vs uncorrected rates (un) are shown.

Hammer. Hysterectomy and gynecological cancer incidence. *Am J Obstet Gynecol* 2015.

because of age ineligibility. If this is found to be true, consideration to extend screening beyond age 60–65 years might be warranted.

One might fear that the total number of cervical cancers will increase in the future if the screening program is not adjusted so that screening continues beyond the age of 65 years. This is based on the following factors. First, the proportion of older women diagnosed with cervical cancer may be increasing over time. For example, a Swedish study found that 5.4% of cervical cancers occurred in women older than 69 years in 1944–1957, whereas 27.3% of the total amount of cervical cancer cases in 1990–2004 were diagnosed in women older than 69 years.⁴¹ Second, the hysterectomy incidence rate is declining in several countries leaving more women at risk of cervical cancer.^{1-3,31} And third, the population of older women is anticipated to increase over time. It is projected that in 2020 and 2025, the proportion of women older than 65 years in the United States will comprise 18.3% and 20.4% of the entire female population, respectively, compared with 16.3% in 2015, an increase of 9.2 million women.⁴² Furthermore, we must keep in mind that older women are more commonly diagnosed with advanced-stage disease⁴³⁻⁴⁶ than younger women, and their mortality is therefore high.^{47,48}

Conclusion

Despite the growing evidence from previous studies, national reporting of gynecological cancer incidence rarely removes the proportion of women who have undergone hysterectomy or oophorectomy from the population-at-risk denominator. This is important when calculating incidence rates on all gynecological cancers; however, for cervical cancer it is especially important that the incidence rate reflects the true population at risk because national screening guidelines are based, in part, on national reporting of age-specific cervical cancer incidence.

Hysterectomy and oophorectomy incidence varies across populations and over time; thus, to make accurate cancer incidence estimates that allow

comparison, better hysterectomy and oophorectomy surveillance is required. Moreover, this is especially important because the vast majority of hysterectomies are performed because of benign disease, unlike other surgical procedures such as mastectomy and colectomy.

In the era of increased utilization of electronic medical records and/or national health surveillance, systematic monitoring of the incidence, type, and indication for hysterectomy and oophorectomy is not only possible, but also it is a critical parameter for accurate development and assessment of gynecological cancer prevention and control programs. ■

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