

ORIGINAL RESEARCH ARTICLE

Setting the record straight—Correcting uterine cancer incidence and mortality in the Nordic countries by reallocation of unspecified cases

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Abstract

Introduction: The incidence of and mortality from cancers of the cervix uteri and corpus uteri are underestimated if the presence of uterine cancers, where the exact topography (site of origin) is not specified, is omitted. In this paper we present the corrected figures on mortality from and incidence of cervix and corpus uteri cancers in the Nordic countries by reallocating unspecified uterine cancer deaths and cases to originate either from the corpus uteri or cervix uteri. To further validate the accuracy of reallocation, we also analyzed how well the reallocation captures the changes occurring as the result of a transition in cause of death coding in Norway that took place in 2005.

Material and Methods: This study uses data available in the NORDCAN database, which contains aggregated cancer data from all the Nordic countries for the years 1960–2016. The unspecified uterine cancer cases and deaths were reallocated to either cervix uteri or corpus uteri based on the estimated probability that follows the distribution of cases and deaths with verified topography. The estimated proportions of cases and deaths for both cancers were calculated for each combination of age group, year, and country as a proportion of cases (and deaths, respectively) with known topography. Annual age-standardized rates were calculated by direct age-adjustment.

Results: The proportions of unspecified uterine cancers were higher in the mortality data than in incidence data, with mean values for 1960–2016 ranging between 5.1% and 26.6% and between 0.2% and 6.8% by country, respectively. In the Nordic countries combined, the reallocation increased the number of cases by 4% and deaths by approximately 20% for both cancers. Finland was the only Nordic country where the mortality rate did not increase substantially after reallocation.

Abbreviations: U-NOS, uterus, not otherwise specified.

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Conclusions: The reallocation procedure had a significant impact on mortality from cancers of the cervix and corpus uteri for countries where the proportion of cancer deaths coded as uterus, not otherwise specified, is substantial. More effort to validate cause of death data with incidence data from cancer registries is warranted to avoid erroneous conclusions of temporal trends based on uncorrected cancer burden.

KEYWORDS

cancer, cervix, coding, incidence, international classification of disease, morbidity uterine neoplasms, mortality, register

1 | INTRODUCTION

Incidence and mortality are customary ways of monitoring cancer burden. However, analysis of cancers of the cervix uteri and corpus uteri is hampered by inaccuracies in cancer registration. A considerable fraction of cases, and especially deaths attributable to these cancers, are registered without exact topography (site of origin either cervix uteri or corpus uteri) only as cancer of the uterus not otherwise specified (U-NOS). It is important to distinguish between cancers of the cervix and corpus uteri because their etiology and epidemiology differ significantly because cervical cancer is preventable by human papillomavirus vaccination and screening.¹⁻³

The decrease in the incidence of and mortality from cancer of the cervix uteri are indicators for effectiveness of cancer screening. However, the cancer burden is underestimated when presence of U-NOS cancers is not accounted for. The European guidelines on cervical cancer screening recommend that the specific location of the cancer should always be given and that cancer and cause of death registries should be linked routinely to improve the quality of both registers.⁴ The linkage increases the accuracy of death records by adding data from the cancer registry and helps to identify cancer-related deaths that were not initially registered in the cancer registry. The guidelines also recommend that the percentage of uterine cancer deaths with known topography should be at least 80%. A comparison of Nordic cervical screening programs showed that Nordic countries, except Finland, fail to adhere to this recommendation.⁵

Methods exist to correct mortality by reallocating U-NOS to either cervix uteri or corpus uteri. Earlier studies have shown that reallocating U-NOS deaths increases mortality from both cancers. In the United States, 27%–41% of uterine cancer deaths in four different studies during 1950–1979 were classified as U-NOS and patient record linkage confirmed that the majority of deaths were corpus uteri in origin.⁶ Loos et al. have developed age- and time-dependent reallocation methods and showed that many differences in uterine cancer mortality between countries were explained by the varying presence of U-NOS deaths.⁷ A similar reallocation method has been applied for correcting the reported mortality for cervix and corpus uteri in all the European Union member states,^{8,9} as well as revealing a rapidly increasing corpus uteri mortality trend in Korea,¹⁰ and a halt in decreasing cervix uteri cancer mortality in Spain.¹¹

In this paper we present the corrected figures on mortality from and incidence of cervix and corpus uteri cancers in the Nordic

Key message

Reallocating unspecified uterine cancer deaths increases mortality from cancers of the cervix uteri and corpus uteri. Routine linkage between cancer and cause of death registries is needed to minimize the problem of underreporting cancer burden.

countries for the years 1960–2016 by using reallocation of U-NOS deaths and cases. To further validate the accuracy of reallocation, we analyzed how well the reallocation captures the changes occurring as the results of a transition in cause of death coding in Norway from 2005 onwards.

2 | MATERIAL AND METHODS

2.1 | Data source

This study uses data available in the NORDCAN database, which contains aggregated cancer and population data from all the Nordic countries stratified into 5-year age groups.¹² Downloadable data from all countries were available for the years 1960–2016. The cancer entities in NORDCAN are mostly based on the International Classification of Diseases, 10th revision (ICD-10).

The aggregation process for NORDCAN is explained thoroughly elsewhere.¹³ Briefly, the incidence data are coded in ICD-O-3, which is then converted to ICD-10 before forming cancer entities by combining site codes. For mortality data, different versions of the ICD classification are converted to ICD-10 and site codes are combined. For a detailed overview of cancer registration procedures and changes over time in different Nordic countries, see Pukkala et al.¹⁴

In NORDCAN, cancers of the cervix uteri (C53), corpus uteri (C54), and uterus other (C55) are reported separately. The cancer entity of uterus other also contains cancer of the placenta (C58). Placenta cancer cases represent only 0.1%–0.4% of all uterine cancer cases in Sweden, Norway, and Finland and 0.1% of cancer deaths in Finland.¹⁵⁻¹⁷ Therefore efforts to correct for this were not essential.

2.2 | Statistical analyses

2.2.1 | Reallocation procedure

The U-NOS cases and deaths were reallocated to either cervix or corpus uteri based on the estimated probability that follows the distribution of cases and deaths with verified topography. To estimate corrected incidence and mortality from uterine cancers we have applied a reallocation procedure that is based on the method described by Loos et al.⁷ and applied in several other studies.^{8–11} However, we used a country-specific distribution instead of reference countries even when the proportion of U-NOS was high (over 25%), as there is considerable variation between countries. For Iceland, we used the distribution in the Nordic countries combined to reduce the volatility of temporal trends in the distribution of topography.

The ratio of both cases and deaths between cervix and corpus uteri depends on several factors. First, the ratio is age-dependent with more corpus uteri cases and deaths in older age groups.¹² Second, there are temporal trends and especially screening has substantially reduced the incidence of and mortality from cancer of the cervix uteri.³ The estimated proportions of cases and deaths for both cancers were calculated for each combination of age group, year, and country as a proportion of cases (and deaths, respectively) with known topography. Wider age groups of 0–39, 40–49, 50–59, 60–69, and 70+ years were used to reduce combinations where the ratio between cancer sites could not be calculated because of zero cases or deaths with known topography. Still, there were 85 combinations out of 2850 (84 in Iceland) where the proportion could not be calculated for a given year and age group. The missing proportions were imputed with probable values using spline functions.¹⁸ Proportions were then smoothed using locally weighted regression¹⁹ to reduce variation between years.

Finally, corrected numbers of cases and deaths were calculated for each combination of 5-year age group, year, and country by multiplying the number of cases and deaths of U-NOS by the smoothed proportion of both cancers and adding these figures to those originally reported (for each cancer site). The younger age groups (0–24) were grouped together because both cancers are very rare in these age groups.

2.2.2 | Temporal trends

Annual age-standardized rates were calculated by direct age-adjustment using the 1960 world standard as a reference population.²⁰ The age-standardized rates were smoothed using locally weighted regression.¹⁹ Smoothed age-specific trends by 5-year age groups were also estimated and are available in the Supporting Information.

The Supporting Information also includes age-standardized incidence and mortality rates for both cancers by 5-year periods with 95% confidence intervals calculated using exact method.²¹

2.2.3 | Estimation of mortality rates in Norway after reallocation of diagnoses

In Norway, the underlying cause of death was determined manually until 2005 when Automated Classification of Medical Entities (ACME) software was introduced to standardize and increase the quality of coding.^{22,23} We used this change in coding practices to assess how the reallocated mortality trend differs from the mortality that we predicted using data from the years 1990–2004. We estimated the predicted mortality for years 1990–2016 using a Poisson model that included year, age, and their interaction as explanatory variables.

2.2.4 | Statistical software

All statistical processing and analyses were done with R software (version 3.6.1)²⁴ and using EPITOOLS (0.5–10.1)²⁵ and IMPUTETS (3.0)²⁶ packages.

2.3 | Ethical approval

We have used tabulated data that is freely available on the cancer statistics database NORDCAN. According to the ethical guidelines of Finnish National Board on Research Integrity (chapter 4.2) this study did not need ethical approval.²⁷

3 | RESULTS

3.1 | Distribution of uterine cancers

The distribution of uterine cancers in the Nordic countries in 1960–2016 varied widely over the years in both cancer cases and deaths. The proportions of U-NOS cancers were higher in the mortality data than in incidence data, with mean values for years 1960–2016 ranging between 5.1% and 26.6% and between 0.2% and 6.8% by country, respectively (Table 1). In incidence data, the proportion of U-NOS cases was lowest in Iceland and highest in Sweden. The proportion of cervix uteri cancers was higher in younger age groups whereas the proportion of corpus uteri cancers increased by age (Figure 1). The proportion of cervical cancer cases and deaths also decreased over time in all the Nordic countries.

The proportion of deaths coded as cervix uteri was higher in younger age groups and in earlier years (Figure 2). The proportion of deaths due to U-NOS varied over time in all countries, but an apparent increase can be seen in Norway in the early 2000s where the proportion increased in all age groups.

The distribution between cervix and corpus uteri cancer cases and deaths varied across age groups, countries, and over time (see

TABLE 1 Summary of NORDCAN data for cancers of the uterus (C53, C54, and C55) in 1960–2016 by 10-year period. Percentages add up by 10-year period for each country for both cases and deaths, respectively

	Denmark		Finland		Iceland		Norway		Sweden	
	(N)	(%)	(N)	(%)	(N)	(%)	(N)	(%)	(N)	(%)
Cancer cases										
Cervix uteri (C53)										
1960–69	8836	65.7	4017	56.7	197	62.1	3660	59.5	8702	51.4
1970–79	7242	56.7	2615	39.1	143	51.1	4291	55.9	6622	40.1
1980–89	5791	46.4	1733	26.0	149	45.2	3470	46.7	5349	33.9
1990–99	4810	42.2	1550	19.4	144	39.2	3453	42.0	4759	27.2
2000–09	3860	35.9	1551	16.7	151	36.4	2948	30.9	4507	23.6
2010–2016	2604	31.5	1143	16.1	116	33.9	2283	30.2	3518	25.0
All years (1960–2016)	33 143	47.9	12 609	28.1	900	43.9	20 105	43.2	33 457	33.5
Corpus uteri (C54)										
1960–69	4256	31.7	2684	37.9	120	37.9	2268	36.9	7048	41.6
1970–79	5239	41.0	3845	57.5	136	48.6	3279	42.7	8746	52.9
1980–89	6405	51.3	4781	71.8	179	54.2	3872	52.1	9280	58.7
1990–99	6216	54.5	6297	78.7	221	60.2	4651	56.6	11 492	65.8
2000–09	6661	62.0	7621	82.0	264	63.6	6493	68	13 388	70.1
2010–2016	5493	66.5	5886	83.1	226	66.1	5209	68.8	9689	68.9
All years (1960–2016)	34 270	49.6	31 114	69.4	1146	55.9	25 772	55.3	59 643	59.7
Uterus, unspecified (C55)										
1960–69	351	2.6	384	5.4	0	0.0	220	3.6	1194	7.0
1970–79	299	2.3	231	3.5	1	0.4	101	1.3	1153	7.0
1980–89	289	2.3	147	2.2	2	0.6	94	1.3	1170	7.4
1990–99	379	3.3	152	1.9	2	0.5	111	1.4	1226	7.0
2000–09	231	2.1	120	1.3	0	0.0	112	1.2	1211	6.3
2010–2016	168	2.0	54	0.8	0	0.0	75	1.0	863	6.1
All years (1960–2016)	1717	2.5	1088	2.4	5	0.2	713	1.5	6817	6.8
Cancer deaths										
Cervix uteri (C53)										
1960–69	3394	59.3	1883	61.9	77	50.7	1497	60.9	3077	51.0
1970–79	3026	60.5	1315	51.3	50	54.9	1598	60.4	2900	47.7
1980–89	2638	56.1	991	43.9	42	45.7	1499	55.9	2162	44.0
1990–99	2004	50.1	710	32.9	47	44.8	1279	51.4	1681	36.2
2000–09	1255	42.4	577	25.7	27	31.8	888	37.8	1506	31.6
2010–2016	710	37.2	385	22.2	26	43.3	523	33.4	994	29.1
All years (1960–2016)	13 027	53.6	5861	41.9	269	46.0	7284	51.3	12 320	41.3
Corpus uteri (C54)										
1960–69	1087	19.0	894	29.4	73	48.0	721	29.3	1711	28.3
1970–79	1392	27.8	1092	42.6	41	45.1	935	35.3	1919	31.6
1980–89	1522	32.4	1173	52.0	39	42.4	1097	40.9	1657	33.7
1990–99	1359	34.0	1364	63.1	31	29.5	1108	44.6	1560	33.6
2000–09	1186	40.0	1605	71.5	34	40.0	1009	42.9	1562	32.8
2010–2016	649	34.0	1305	75.2	19	31.7	553	35.3	1197	35.0
All years (1960–2016)	7195	29.6	7433	53.1	237	40.5	5423	38.2	9606	32.2
Uterus, unspecified (C55)										
1960–69	1239	21.7	264	8.7	2	1.3	242	9.8	1250	20.7

TABLE 1 (Continued)

	Denmark		Finland		Iceland		Norway		Sweden	
	(N)	(%)	(N)	(%)	(N)	(%)	(N)	(%)	(N)	(%)
1970–79	586	11.7	158	6.2	0	0	114	4.3	1255	20.7
1980–89	540	11.5	92	4.1	11	12.0	84	3.1	1100	22.4
1990–99	639	16.0	87	4.0	27	25.7	99	4.0	1400	30.2
2000–09	522	17.6	63	2.8	24	28.2	455	19.3	1695	35.6
2010–2016	550	28.8	45	2.6	15	25.0	491	31.3	1227	35.9
All years (1960–2016)	4076	16.8	709	5.1	79	13.5	1485	10.5	7927	26.6

Figure S1). The proportion of cervix uteri cases and deaths was highest in Denmark and lowest in Finland.

3.2 | Cancer of the cervix uteri

Originally, there were 100 214 cases and 38 761 deaths reported in NORDCAN for cancer of the cervix uteri in 1960–2016 in all Nordic countries combined. After the reallocation procedure there were 104 101 cases and 46 159 deaths, which represents an increase of 4% in cases and 19% in deaths.

The differences between age-standardized incidence and mortality of cervix uteri cancer calculated with original and reallocated data are presented in Figure 3 and in Table S1. Corrected age-standardized incidence of cancer of the cervix uteri has decreased significantly between 1960 and 2016 in all the Nordic countries from approximately 15–30 cases per 100 000 women to 5–10 cases per 100 000 women depending on country. A similar decrease was seen in mortality from 6–15 deaths per 100 000 women to 1–3 deaths per 100 000 women.

Both datasets provide a similar incidence trend except for Sweden where the reallocated incidence is higher between years 1975 and 2010. For mortality data, the difference between data sets is more profound. The reallocated data produce a higher age-standardized mortality rate than original data in all countries except Finland. In Denmark, Norway and Sweden, the difference between trend lines has increased over time. In Iceland, the trend lines were identical until the end of the 1970s, when the trends diverged.

The effects of reallocation were also dependent on age as the reallocation procedure increased both incidence and mortality rates more in older age groups (see Figures S2 and S3). The most exceptional difference was in Sweden, where the age-specific mortality rate of cervix uteri cancer and corpus uteri cancer approximately doubled in recent decades in women aged 85 years or over.

3.3 | Cancer of the corpus uteri

Originally, there were 151 945 cases and 29 894 deaths reported in NORDCAN for cancer of the corpus uteri in 1960–2016 in the

Nordic countries combined. After reallocation there were 158 398 cases and 36 772 deaths which is a 4% increase in cases and 23% in deaths.

The differences between age-standardized incidence and mortality of corpus uteri cancer calculated with original and reallocated data are presented in Figure 4 and in Table S2. Corrected age-standardized incidence of cancer of the corpus uteri has increased in all the Nordic countries between 1960 and 2016 from approximately 8–12 cases per 100 000 women to 13–15 cases per 100 000 women depending on country. During the same time mortality decreased from 2–4 deaths per 100 000 women to 1–2 deaths per 100 000 women, except for Iceland where the mortality decreased from 9 per 100 000 women to approximately 1 per 100 000 women.

With reallocated data, the incidence increased slightly in Denmark and Sweden compared with original data. As with cancer of the cervix uteri, the differences between data sets were greater in mortality rates (Figures S4 and S5). Age-standardized mortality rate increased especially in Sweden for all years, whereas in Norway the difference in mortality started to increase in the early 2000s.

3.4 | The effect of changes in cause of death coding in Norway

The process of cause of death coding in Norway was changed from manual determination to automatic software in 2005. A significant drop in the original mortality rate is apparent for both cancers after the change in coding practices (Figure 5). The reallocated mortality rates were closer to the predicted mortality rates than the original rates for both cancers, but the reallocated corpus uteri cancer mortality was still lower than predicted, whereas reallocated cervix uteri cancer mortality was slightly higher than predicted.

4 | DISCUSSION

This study shows that reallocating U-NOS cases and deaths to either cervix or corpus uteri influences the incidence and mortality of both cancer sites to varying degrees. In Finland only 5%

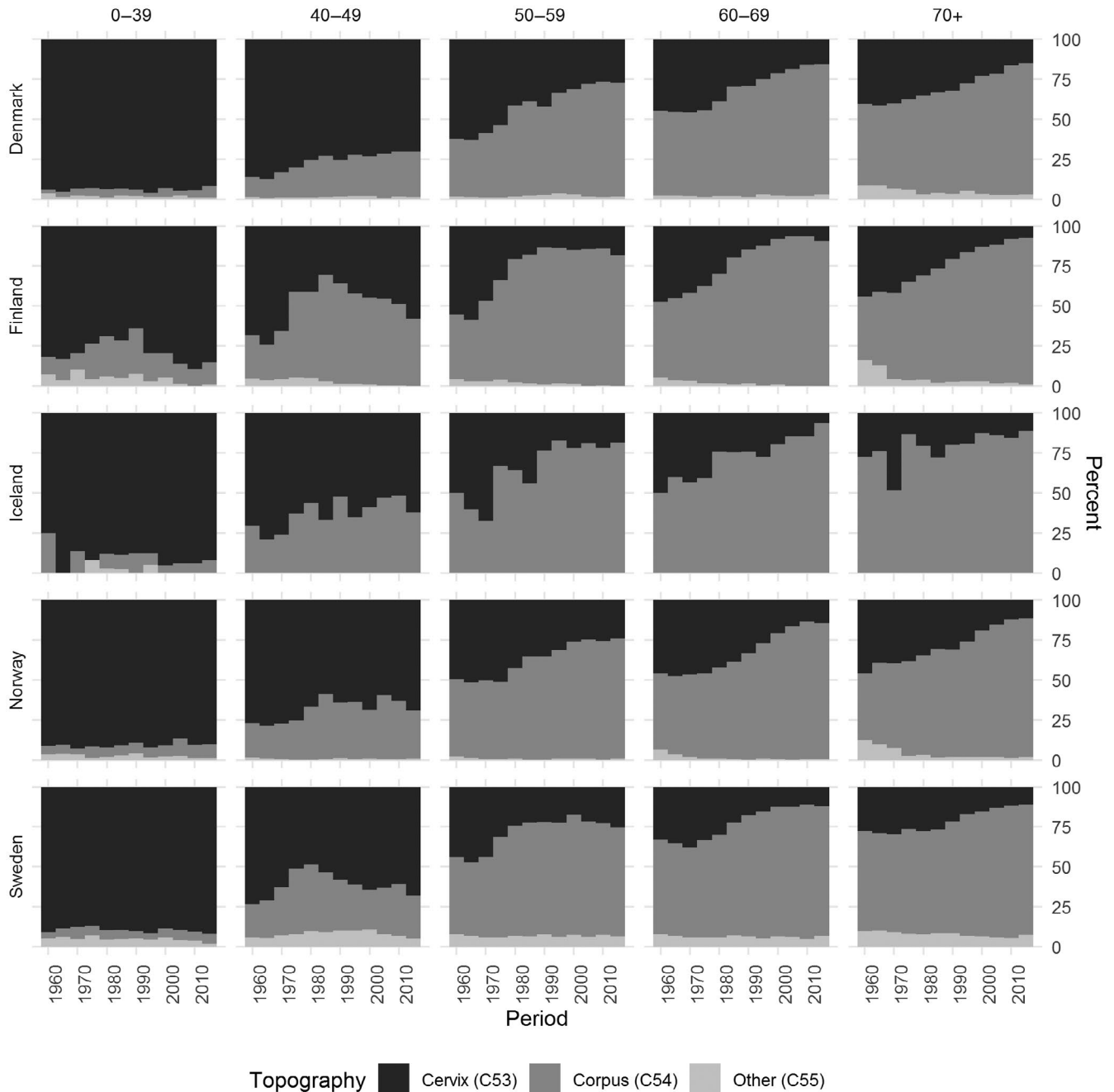


FIGURE 1 The topographical distribution of uterine cancer cases over 5-year periods by age group and country in 1960–2016

of uterine cancer deaths were classified as U-NOS whereas in Sweden the proportion was almost 27% during the whole study period of 1960–2016. The increase in incidence due to reallocation of U-NOS is practically inconsequential for both cancers because U-NOS is rarely used in coding incident cases, except in Sweden where 7% of cases in 1960–2016 were classified as U-NOS. The reallocation had a significantly higher effect on mortality rates for both cancers, which means that the reported mortality figures both in national cancer statistics and in NORDCAN are underestimated, except for Finland.

The magnitude of reallocation depends on the frequency of use of the U-NOS category by clinicians, and the verification

procedures in place in cancer and cause of death registration. Linkage between these registers is recommended in the European guidelines for cervical cancer screening to verify that the cervical cancer mortality will not underestimate the true number of deaths.⁴ As Norway switched from manual to automated cause of death coding in 2005 the routine linkage between registries ceased. Currently, the Finnish Cancer Registry is the only Nordic cancer registry that re-evaluates cancer deaths by linkage to incidence data from the registry, resulting in only small changes due to reallocation in the Finnish data.¹⁴ Although most Nordic countries do not use cancer registry data for validating the cause of death, Sweden is the only country not supplementing cancer registry

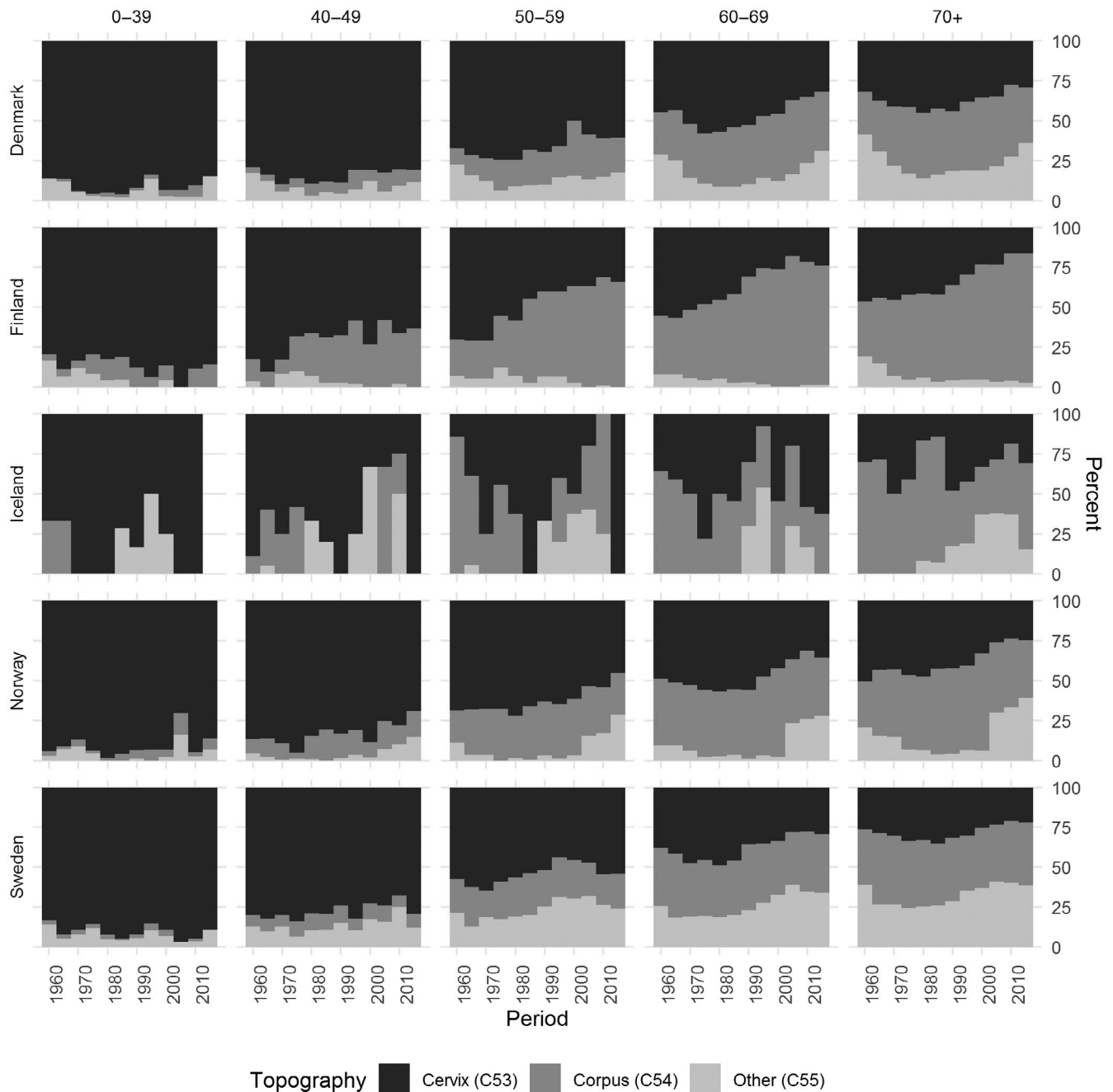


FIGURE 2 The topographical distribution of uterine cancer deaths over 5-year periods by age group and country in 1960–2016

data with cause of death registry data and it has been estimated that including these would increase the number of incident cancer cases by 4%.¹⁴ Other Nordic cancer registries include death certificate initiated cases, meaning deaths from cancer not originally reported to the cancer registry.

The corrected mortality rates for Finland and Denmark in the present study are similar to an earlier study on cervical cancer mortality in the European Union member states.⁸ The present study showed a higher corrected cervix uteri mortality for Sweden compared with earlier studies.^{7,8} This can be explained by methodological differences. The earlier studies used Finland as the reference country for Sweden for the distribution of deaths. Our analysis

(Figure S1) showed that the proportion of cervix uteri deaths is considerably lower in Finland compared with Sweden, which causes a higher number of U-NOS deaths to be reallocated to corpus uteri in the earlier studies compared with our study. Linkage between registries would be required to accurately assess how well the different reallocation rules perform.

A Swedish cervical cancer audit performed a histopathological reassessment of 89 U-NOS cancer cases reported to the cancer registry in 1999–2001, which showed that slightly more than 10% of these ($n = 11$) were of cervical origin.²⁸ The NORDCAN data included 408 U-NOS cases for the same years, 114 of which (28%) were reallocated to cervix uteri in the current study. The discrepancy in the

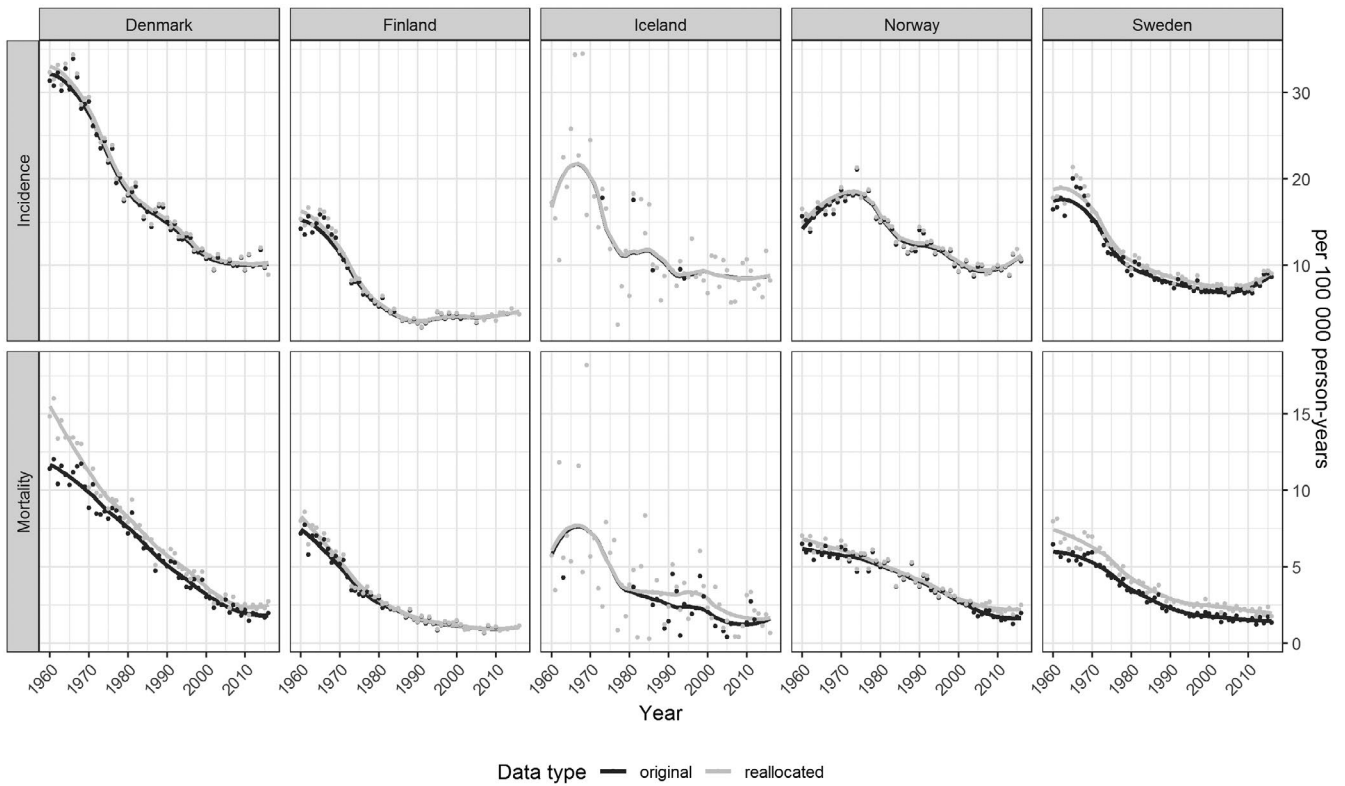


FIGURE 3 Annual age-standardized cervix uteri cancer incidence and mortality before and after reallocation in the Nordic countries during years 1960–2016. The trend line is smoothed with locally weighted regression and actual data for each year are presented as points

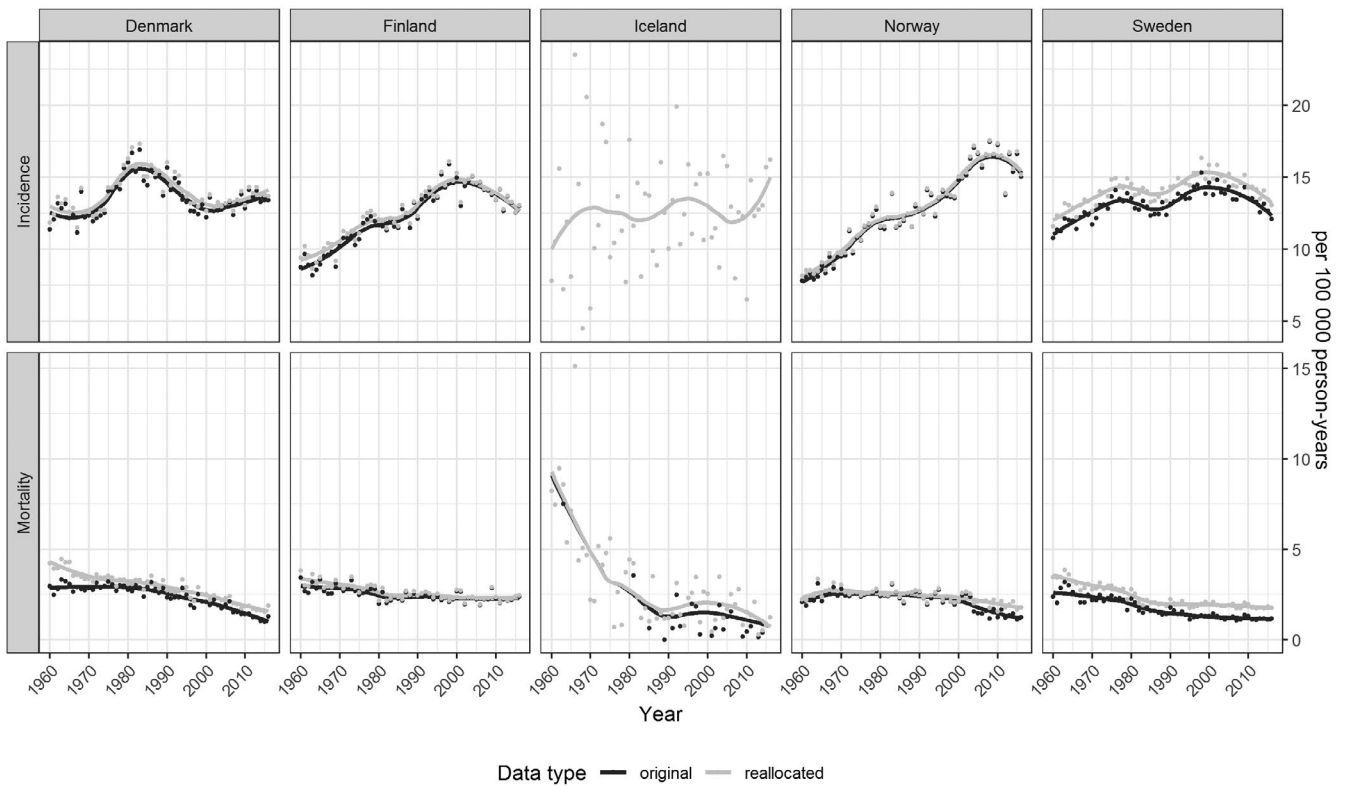


FIGURE 4 Annual age-standardized corpus uteri cancer incidence and mortality before and after reallocation in the Nordic countries during years 1960–2016. The trend line is smoothed with locally weighted regression and actual data for each year are presented as points

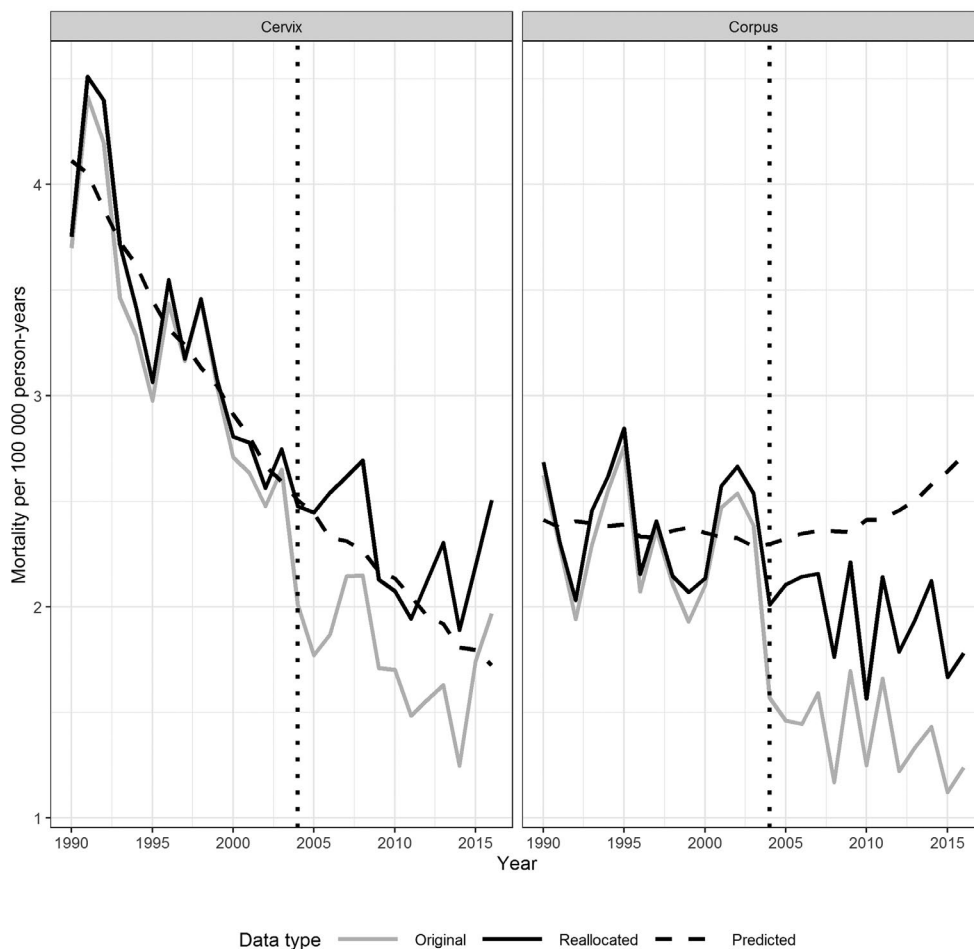


FIGURE 5 Cervix uteri and corpus uteri cancer mortality in Norway for years 1990–2016. The grey line is original data reported in NORDCAN and the black line is the reallocated mortality rate without smoothing. The black dashed line was predicted using a Poisson model with reallocated mortality data from 1990 to 2004. The vertical dotted line marks the change to automated cause of death coding

number of cases is explained by the fact that sarcomas and other non-epithelial cancers were excluded in the audit because screening is not effective against them, whereas in the WHO classification of cervix uteri cancer these are included.²⁹ The comparison of audit and reallocated data suggests, however, that at least for epithelial U-NOS cancers registered in Sweden, the reallocation slightly overestimates the proportion allocated to cervix uteri.

The prevalence of hysterectomies should also be considered when analyzing uterine cancer burden. Hysterectomy-corrected and age-adjusted incidence rates of cervix and corpus uteri cancers in Finland have been estimated to be 11% and 29% higher, respectively, during 1953–2010.³⁰ In Denmark, the incidence rate of cervix uteri cancer was estimated to be 6% higher when taking hysterectomies into account.³¹ The incidence of hysterectomies was 350–400 per 100 000 women in Finland until the early 2000s but has since decreased to rates that are similar to those of other Nordic countries, at around 150–200 per 100 000 women, as the result of the availability of more conservative treatment.^{32,33} Uterus-conserving treatments for women with gynecological conditions may cause an unintended increase in the incidence of corpus uteri cancer.

Our results also raise the question of whether the presence of U-NOS deaths introduces bias to studies on screening or vaccination effectiveness. If the proportion of U-NOS deaths is higher in un-screened or underscreened women, the effectiveness of screening is underestimated in case-control or cohort studies as some of the cervix uteri deaths are attributed to U-NOS. Research on whether U-NOS cancer deaths correlate with screening activity is therefore warranted.

The strength of our study is that the data originate from Nordic cancer registries with comparatively high completeness and quality. The data in NORDCAN are also harmonized because identical rules are applied to the convertible data for each country. The cancer entity of U-NOS in NORDCAN includes the rare cancer of the placenta, which is a minor weakness, but unlikely to influence the results, because the proportion of these cases and deaths range only between 0.1% and 0.4%.

The assumption that U-NOS cases and deaths follow the same distribution as those with known topography is uncertain. To our knowledge, there are two studies on U-NOS cancer deaths that have used a linkage between cause of death data and either cancer registry or hospital records. Both studies support our

assumption that the distribution of U-NOS deaths approximately follows the distribution of uterine cancer deaths with known topography.^{6,34} The use of year- and age-specific distribution data therefore improves the estimates, but it is plausible that the real topography distribution in U-NOS cancers is skewed towards either of the cancer sites. We performed a sensitivity analysis to see how much the reallocated mortality rate estimates change if the proportions of cancer deaths used for reallocation change by 10 percentage points in either direction. Even such marked changes in proportions had only a minor effect on the range of rates (see Figure S6). In the analysis we performed on Norwegian data before and after the change in cause of death coding, reallocation seemed to slightly underestimate corpus uteri cancer mortality. An unpublished study on Swedish U-NOS mortality, which used a linkage between Cause of Death Register and Swedish Cancer Registry data for the years 1997–2011, also found that most U-NOS deaths were registered in the cancer registry as corpus uteri in origin and only 7% were due to cervical carcinomas (Bengt Andrae, personal communication). It is therefore likely that a larger proportion of U-NOS deaths should be reallocated to corpus uteri rather than cervix uteri.

The definitive solution to correcting incidence and mortality rates for cancers of the corpus uteri and cervix uteri would be to validate the registry using patient records. This requires substantial resources and would need to be done regularly. A more feasible improvement would be to routinely validate cause of death data using cancer registry data to correct any discrepancies. Using patient records should be considered if uncertainty remains after such linkage.

5 | CONCLUSION

The reallocation of U-NOS deaths has a significant impact on mortality from cancers of the cervix uteri and corpus uteri in countries where the proportion of cancer deaths coded as U-NOS is substantial. More effort to validate cause of death data with incidence data from cancer registries is warranted, to avoid erroneous conclusions of temporal trends based on uncorrected cancer burden.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

SL conceptualized the research objective. VP collected the data, performed the statistical analyses and visualizations, and drafted the manuscript. SH provided statistical support for the analyses. SH, AA, JH, and SL discussed the results and critically reviewed the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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