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ORIGINAL RESEARCH ARTICLE

Cervical neoplasia in relation to socioeconomic and demographic factors – a nationwide cohort study (2002–2018)

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Abstract

Introduction: Cervical cancer is a major cause of mortality and morbidity. We aimed to estimate the association between sociodemographic factors and cervical neoplasia.

Material and methods: In this Swedish nationwide open cohort study, 4 120 557 women aged ≥15 years at baseline were included between January 1, 2002 and December 31, 2018. The two outcomes were cervical cancer and carcinoma in situ identified in the Swedish Cancer Register. Sociodemographic factors (age, education level, family income level, region of residency, country of origin) were the main predictors. Incidence rates per 10 000 person-years were calculated. Cox regression was used to estimate hazard ratios. Sensitivity analyses were conducted, including parity, urogenital infections, alcohol- and drug-use disorders, and chronic obstructive pulmonary disease (used as a proxy for tobacco abuse).

Results: In 38.9 million person-years of follow-up, 5781 (incidence rate: 1.5, 95% confidence interval [CI] 1.4–1.5) and 62 249 (incidence rate 16.9, 95% CI 15.9–16.1) women were diagnosed with cervical cancer and carcinoma in situ, respectively. Women from Eastern Europe had a hazard ratio of 1.18 (95% CI 1.05–1.33) for cervical cancer compared with Swedish-born women, while women from non-Western regions were inversely associated with cervical cancer and carcinoma in situ. Women with a low education level had a hazard ratio of 1.37 (95% CI 1.29–1.45) for cervical cancer compared with women with a high education level.

Conclusions: Women from the Middle East and Africa living in Sweden seem to suffer less from cervical neoplasia, whereas women with low education and women from Eastern Europe seem to suffer more from cervical cancer.

KEYWORDS
cervical cancer, cervical neoplasia, epidemiology, parity, sociodemographic factors

Abbreviations: CI, confidence interval; hr-HPV, high risk human papillomavirus; HR, hazard ratio; ICD, International Classification of Diseases; MENA, Middle East/North Africa.

1 | INTRODUCTION

Cervical cancer is a major cause of mortality and morbidity in young adult and older women. It develops almost exclusively from a high-risk human-papillomavirus (hr-HPV) infection in the cervix, which causes cervical carcinoma in situ that can progress to cancer.[1–3] Lifestyle factors, vaginal microbiological factors and common urogenital infections have been associated with oncogenic cervical infections and neoplasia.[4–10] Sociodemographic group variations in the vaginal microbiome have been suggested[4,6] and our group recently demonstrated an unequal distribution of common urogenital infections among certain sociodemographic groups in Sweden.[11,12]

All this considered, it is possible that certain sociodemographic groups of women might suffer disproportionately from cervical neoplasia, as global estimations also seem to suggest.[3] Earlier studies have also found that low socioeconomic status, immigration status, drug-use disorders and urban living are related to cervical cancer incidence in Sweden.[13–15] However, more comprehensive epidemiological studies are needed to establish the pathways and relation between sociodemographic factors and cervical neoplasia, adjusted for recently described plausible confounders such as common urogenital infections[10] and other known risk factors (eg tobacco- and drug abuse[13,16] and parity[17]). This could provide a more contextual framework regarding the prevention of this common malignancy in women. By utilizing comprehensive nationwide healthcare and sociodemographic data, we aimed to explore the relation between individual-level sociodemographic factors and cervical neoplasia in women on a national level, adjusted for several known risk factors.

Key message

Women of low education level and Eastern European origin seem to suffer disproportionately from cervical cancer, whereas women from other regions (especially Middle East and Africa) appear to be less affected. The findings can be used in cancer prevention.

2 | MATERIAL AND METHODS

2.1 | Study design, eligibility and setting

This was a Swedish nationwide open cohort study. The baseline for inclusion in the study was residence residing in Sweden for ≥15 years during the study period (2002–2018). The STROBE statement-checklist for cohort studies was considered. The research was conducted at Lund University, Sweden.

2.2 | Ascertainment of the outcome variables

The two outcomes were identified in the very complete nationwide Swedish Cancer Register. This register used the 7th revision of the International Classification of Diseases (ICD-7). The first analysis was conducted on (invasive) cervical cancer; measured as ICD-7 code 171 labeled as tumor indication of malignant neoplasia of cervix uteri. The second analysis was conducted on non-invasive neoplasia of cervix uteri (in this paper: cervical carcinoma in situ); measured as the ICD-7 code 171 labeled as tumor indication of benign neoplasia of cervix uteri. Women could only be included once for each outcome during the study period. There was a 1-year wash-out period for prior diagnoses of the outcomes. About 16 100 participants (0.4%) with a history of ICD-7 code 171 in the Swedish Cancer Register prior to baseline were excluded from the study population.

2.3 | Ascertainment of predictor variables (sociodemographic factors)

Age groups were defined as een 15–24, 25–34, 35–44, 45–64 or ≥65 years of age. Educational level was based on the duration of school years attended. The following categories were used: high school education or less (≤12 years), or at least 1 year of higher education (>12 years). For those aged 15–17 years, the highest educational level of the parents was used. Family income was categorized into three groups based on a weighted average income[11] in each family: low (lowest income quartile of the study population), middle (two intermediate quartiles) and high (highest income quartile of the study population). Region of residence was categorized into three groups: residence in large cities, or residence outside large cities in Southern or Northern Sweden. Country of origin was defined as originating from any of the following countries/regions: (born in) Sweden; Eastern Europe; Western countries; Middle East/North Africa (MENA); Africa (excluding North Africa); Asia (excluding Middle East) and Oceania; or Latin America and the Caribbean. For age and country of origin, <0.0% values were missing. Values missing for education (2.5%), family income (3.5%) and region of residency (2.0%) were included in the group with the lowest level of education, low level family income, and living in large cities, respectively. The subdivisions were based on the definitions used in previous studies.[11,12]

2.4 | Ascertainment of confounding variables

Several urogenital infections share risk factors with cervical neoplasia[1–3,7,8,17,18] and some may act as co-factors[1,18] in cervical cancer development. Cystitis, bacterial vaginosis and vulvovaginal candidiasis have also been associated with cervical neoplasia.[10] Therefore, we considered urogenital infections as possible confounders in a sensitivity analysis. Similar to previous studies,[10,12] common urogenital infections were identified as an ICD-10 code of B373 ("Candidiasis of vulva and vagina"), N30 ("Cystitis"), and N768 ("Other specified inflammation of vagina and vulva"). Genital infections were defined

as upper genital tract- and Bartholin gland infection (N70-5) and urogenital herpes (A600). Drug- and tobacco-use disorders[13,16] and parity,[17] also linked to cervical neoplasia, were included in the sensitivity analyses as well. Parity was used as a continuous variable (starting from nullipara). Drug-use disorders (ICD-10 codes F11-F16, F18 and F19; suspicion or conviction of illicit drug-use activity; or having redeemed an average of >4 defined daily doses of prescribed opioids, hypnotics or sedatives for 12 months) and alcohol-use disorders (F10 and K70) were identified during the study period and used as dichotomous variables (yes or no). Tobacco smoking could not be assessed directly. Therefore, chronic obstructive pulmonary disease (J40–J47), diagnosed during the study period, was used as a proxy for significant tobacco smoking.

2.5 | Data sources

The Swedish Cancer Register[19] was used to collect data on outcomes. The Total Population Register (managed by the Swedish governmental agency Statistics Sweden) used to collect data on the predictor variables as well as emigration and death, was nearly 100% complete for the entire national population. The potential confounders were identified in the nationwide primary healthcare data, the Swedish Medical Birth Register, the Swedish Prescribed Drugs Register, the Suspicion and Crime Register, and the National Patient Register. The national medical registers have full nationwide coverage from 1987 and onward and are managed by the National Board of Health and Welfare. The coverage of the nationwide primary healthcare data varied over time and region but was based on data from 20 of the 21 administrative regions in Sweden. All linkages between the registry data were performed using the unique 10-digit personal identification number assigned to each person for their lifetime upon birth or immigration; our group had access to a pseudonymized version of this number to ensure the integrity of all individuals.

2.6 | Statistical analyses

Descriptive statistics on the study population, total person-years of follow-up, number of cases (first events) of the outcomes, and incidence rates per 10 000 women-years were calculated for each predictor variable. To assess the association between the predictor variables and the outcomes, Cox regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI). The study period started on January 1, 2002, and person-years were calculated from the age of 15 years or immigration (if 15 years or older at the time) to Sweden or until an outcome event, death, emigration or end of the study period (December 31, 2018). Three models were used for each of the three main predictors: Model 1, crude model; Model 2, age-adjusted; Model 3 adjusted for all sociodemographic factors. A sensitivity analysis including potential confounders was conducted. To examine whether the strength of the associations changed over time, proportionality assumptions were checked by plotting the incidence rates over time and by calculating Schoenfeld (partial) residuals – these assumptions were fulfilled. The analyses did not exclude observations with missing values. A two-tailed *P*-value of <0.05 was used to determine statistical significance. SAS software version 9.4 was used for all statistical analyses.

2.7 | Ethics statement

The study was a non-intervention nationwide register study of pseudonymized secondary data obtained from Swedish authorities after approval from the Ethical Review Board in Lund, Sweden (2012/795, date of approval February 6, 2013 and later amendments). No study-specific ethical approval was required as the present study aims were covered by this approval.

3 | RESULTS

Table 1 shows the study population, number of cases and incidence rate per 10 000 women-years. Altogether, 4 120 557 women aged 15 years or older were included in the study, with a total follow-up of around 38.9 million person-years. Table 2 shows that women aged 25–34 years at baseline had the highest risk for cervical cancer. Women with a low education level and originating from Eastern Europe showed a higher risk for cervical cancer, whereas women from the MENA region and Africa were associated with HR of 0.31 and HR 0.35, respectively, for cervical cancer in the fully adjusted models for covariates. Table 3 shows the hazard ratios for cervical carcinoma in situ associated with sociodemographic factors. The youngest groups of women (age 15–24 and 25–34) showed the highest risks for carcinoma in situ. Women with a low education level as well as those living outside larger cities had a higher risk for carcinoma in situ. All women born outside of Sweden were found to have had less carcinoma in situ, especially those born in MENA region and Africa (HR 0.32 and HR 0.31). Two sensitivity analyses were conducted (Tables S1 and S2) including urogenital infection and parity, as well as alcohol-use disorders, chronic obstructive pulmonary disease and drug-use disorders. These variables were independently associated with cervical cancer and carcinoma in situ, but the sensitivity analyses did not change the sociodemographic associations significantly.

4 | DISCUSSION

This nationwide cohort study identified 5781 and 62 249 women diagnosed with cervical cancer and carcinoma in situ (2002–2018), respectively. Findings included an almost 70% lower risk of cervical cancer and carcinoma in situ among women originating from the Middle East and Africa, in comparison with Swedish-born women. On the other hand, women originating from Eastern Europe and women with a low education level suffered higher risks of cervical

TABLE 1 Study population, number of cases and incidence rate (per 10 000 women-years) of cervical neoplasia (2002–2018)

	Total population		Cervical cancer					Cervical carcinoma in situ				
Co-variates	***n***	**%**	***n***	**%**	**IR**	**95% CI**		***n***	**%**	**IR**	**95% CI**	
Age at baseline (years)												
15–24	674 120	16.4	634	11.0	1.0	0.9	1.1	26 301	42.3	41.4	40.9	41.9
25–34	677 650	16.4	1239	21.4	1.9	1.8	2.0	21 196	34.1	32.8	32.3	33.2
35–44	635 122	15.4	1100	19.0	1.7	1.6	1.8	9613	15.4	14.7	14.5	15.0
45–64	1 174 811	28.5	1588	27.5	1.3	1.2	1.4	4657	7.5	3.8	3.7	3.9
≥65	958 854	23.3	1220	21.1	1.6	1.5	1.7	482	0.8	0.6	0.6	0.7
Educational level (years)												
≤12	2 718 970	66.0	4133	71.5	1.6	1.6	1.7	41 652	66.9	16.2	16.0	16.3
>12	1 401 587	34.0	1648	28.5	1.3	1.2	1.3	20 597	33.1	15.6	15.4	15.8
Family income												
Low	1 029 399	25.0	1281	22.2	1.4	1.4	1.5	18 373	29.5	20.7	20.4	21.0
Middle	2 060 806	50.0	3118	53.9	1.5	1.5	1.6	31 359	50.4	15.2	15.0	15.3
High	1 030 352	25.0	1382	23.9	1.5	1.4	1.5	12 517	20.1	13.3	13.1	13.5
Region of residence												
Large cities	2 270 266	55.1	3520	60.9	1.5	1.4	1.5	38 157	61.3	15.8	15.7	16.0
Southern Sweden	1 271 384	30.9	1602	27.7	1.6	1.5	1.7	15 853	25.5	16.0	15.7	16.2
Northern Sweden	578 907	14.0	659	11.4	1.3	1.2	1.4	8239	13.2	16.7	16.4	17.1
Country of origin												
Sweden (born in)	3 282 971	79.7	4873	84.3	1.5	1.5	1.6	54 067	86.9	16.8	16.6	16.9
Eastern Europe	194 473	4.7	309	5.3	1.9	1.7	2.1	2743	4.4	16.5	15.9	17.1
Western countries	242 373	5.9	333	5.8	1.6	1.4	1.8	1744	2.8	8.4	8.0	8.8
Middle East/North Africa	191 713	4.7	70	1.2	0.5	0.4	0.6	1020	1.6	7.4	7.0	7.9
Africa (excluding North Africa)	61 026	1.5	24	0.4	0.6	0.4	0.8	339	0.5	8.5	7.6	9.4
Asia (excluding Middle East) and Oceania	108 887	2.6	125	2.2	1.5	1.2	1.7	1733	2.8	20.3	19.3	21.2
Latin America and the Caribbean	39 114	0.9	47	0.8	1.3	0.9	1.6	603	1.0	16.2	14.9	17.5
Total population	**4 120 557**		**5781**		**1.5**	**1.4**	**1.5**	**62 249**		**16.0**	**15.9**	**16.1**

Abbreviations: CI, confidence interval; IR, incidence rate per 10 000 women-years; *n*, number.

cancer compared with Swedish-born women and women with high education levels. The findings remained even after adjusting for known confounders.

4.1 | Country of origin

Sweden has a high proportion of immigrants from around the globe, who are granted equal access to the universal healthcare system. However, this equal access does not necessarily facilitate a consistent equal utilization or actual access of healthcare or equality of health in the population. The findings of increased risk of cervical cancer among women originating from Eastern Europe and a lower risk among women originating from MENA regions and Africa (excluding North Africa) were in concordance with an older Swedish study and one Canadian study.[14,20] In the Swedish study, the lowest rate ratio of cervical cancer (1969–2004), in comparison with Swedish-born women, was found among women from Africa, Iran and Iraq/Arab countries and the highest rate ratio was found among women from Poland and Bosnia.[14] In the Canadian study, women originating from Russia and Ukraine had the highest rates of cervical cancer, and women from MENA, Pakistan and Iran had the lowest rates.[20] Another Swedish study found a lower incidence rate of cervical cancer (1968–2004), in comparison with Swedish-born women, among women from Western-, South Central- and Eastern Asia, Eastern Africa, Australia, New Zealand, USA and Canada.[15] However, it did not find a lower incidence rate for women originating from other parts of Africa (excluding Eastern Africa) and there was

TABLE 2 The relation between sociodemographic factors and cervical cancer ($n = 5781$)

	Model 1				Model 2				Model 3			
Covariates	**HR**	**95% CI**		***P*-value**	**HR**	**95% CI**		***P*-value**	**HR**	**95% CI**		***P*-value**
Age (ref. age ≥65 years)												
15–24	0.62	0.57	0.69	<0.0001	0.62	0.57	0.69	<0.0001	0.66	0.60	0.73	<0.0001
25–34	1.19	1.10	1.29	<0.0001	1.19	1.10	1.29	<0.0001	1.39	1.28	1.51	<0.0001
35–44	1.06	0.97	1.15	0.1883	1.06	0.97	1.15	0.1883	1.18	1.09	1.29	<0.0001
45–64	0.82	0.76	0.89	<0.0001	0.82	0.76	0.89	<0.0001	0.88	0.81	0.95	0.0007
Educational level (ref. >12 years)	1.28	1.21	1.36	<0.0001	1.37	1.29	1.45	<0.0001	1.37	1.29	1.45	<0.0001
Family income (ref. High)												
Low	0.97	0.90	1.05	0.4759	1.00	0.92	1.08	0.9884	1.03	0.95	1.12	0.4495
Middle	1.04	0.97	1.11	0.2597	1.03	0.96	1.10	0.4124	0.99	0.92	1.05	0.6531
Region of residence (ref. Large cities)												
Southern Sweden	1.09	1.02	1.15	0.0059	1.11	1.05	1.18	0.0007	1.09	1.02	1.16	0.0061
Northern Sweden	0.91	0.84	0.99	0.0258	0.93	0.85	1.01	0.0825	0.90	0.83	0.98	0.0161
Country of origin (ref. Born in Sweden)												
Eastern Europe	1.21	1.08	1.36	0.0010	1.18	1.05	1.32	0.0059	1.18	1.05	1.33	0.0051
Western countries	1.04	0.93	1.17	0.4654	1.03	0.92	1.15	0.6302	1.04	0.93	1.16	0.5159
Middle East/North Africa	0.32	0.26	0.41	<0.0001	0.31	0.25	0.39	<0.0001	0.31	0.24	0.39	<0.0001
Africa (excluding North Africa)	0.38	0.26	0.57	<0.0001	0.36	0.24	0.54	<0.0001	0.35	0.23	0.52	<0.0001
Asia (excluding Middle East) and Oceania	0.94	0.79	1.12	0.4969	0.87	0.72	1.03	0.1115	0.85	0.71	1.02	0.0753
Latin America and the Caribbean	0.83	0.62	1.10	0.1978	0.79	0.59	1.05	0.1075	0.79	0.59	1.05	0.1087

Abbreviations: CI, confidence interval; HR, hazard ratio; Model 1, univariate model; Model 2, age-adjusted model; Model 3: fully adjusted for all covariates (sociodemographic factors).

only a slightly increased incidence rate for cervical cancer among women from Central Eastern Europe.[15]

The low rates of cervical cancer among women from MENA were expected, since the incidence of cervical cancer in these countries is low,[3] which might be explained by the effect of religious beliefs and culture, which encourage low premarital sexual activity.[21] However, the low rates of cervical cancer among women originating from Africa (excluding North Africa) was unexpected, since these parts of Africa have the highest incidence rates of cervical cancer across the globe.[3] Improved healthcare and a high functioning cervical screening program in Sweden at age 23–70 years and a high compliance[22] may be possible explanations for this. Although originating from another country has, in general, been shown to increase the probability of non-attendance for screening,[23] this does not necessarily seem to cause an increased risk of cervical cancer. The low risk of cervical cancer among women originating from Africa could also be explained by the healthy migrant effect, the people migrating having better health status than their population of origin.[24] However, there was a low level of evidence for a healthy migrant effect among non-Western migrants in Sweden.[24] Furthermore, a different susceptibility to the hr-HPV types found in Sweden can be considered as a possible factor for the lower risk of cervical cancer among women from Africa and might also explain the higher risk of cervical cancer seen in other demographic sub-groups. HPV 16 and 18 are the most common hr-HPV types in all continents, but other common hr-HPV types vary across the globe.[25] In Sweden, the most common hr-HPV types in cervical cancer cases were HPV 16, 18, 45, 31, 33 and 52.[26] In Western-, Eastern- and Southern Africa the corresponding hr-HPV types were HPV 16, 18, 45 and 35.[27] Interestingly, a pooled analysis showed that women with normal cytology from sub-Saharan Africa were less likely to be infected with HPV 16 than were European women, but were more likely to be infected with HPV 35, which is less common in Europe.[28] The same pattern regarding HPV 16 prevalence was seen for high-grade squamous intraepithelial lesions and squamous cell carcinoma.[28] Another study found a higher HPV 16/18 prevalence among European women with high-grade lesions and invasive cervical cancer in comparison with African women (excluding Northern Africa).[29] These studies (together with the present study) strengthen the theory of a different susceptibility to some hr-HPV types found in Europe among women from Africa. However, studies investigating this in the native and migrating population in Europe and Sweden are needed to further confirm this theory.

The analyses on cervical carcinoma in situ showed a lower risk among all women not born in Sweden. Women originating from

TABLE 3 The relation between sociodemographic factors and cervical carcinoma in situ ($n = 62\,249$)

	Model 1				Model 2				Model 3			
Covariates	**HR**	**95% CI**		***P*-value**	**HR**	**95% CI**		***P*-value**	**HR**	**95% CI**		***P*-value**
Age (ref. age ≥65 years)												
15–24	64.25	58.71	70.30	<0.0001	64.25	58.71	70.30	<0.0001	70.88	64.76	77.57	<0.0001
25–34	50.49	46.13	55.26	<0.0001	50.49	46.13	55.26	<0.0001	58.14	53.11	63.65	<0.0001
35–44	22.77	20.78	24.95	<0.0001	22.77	20.78	24.95	<0.0001	25.35	23.13	27.78	<0.0001
45–64	5.96	5.43	6.55	<0.0001	5.96	5.43	6.55	<0.0001	6.04	5.50	6.64	<0.0001
Educational level (ref. >12 years)	1.03	1.02	1.05	<0.0001	1.22	1.20	1.24	<0.0001	1.24	1.22	1.26	<0.0001
Family income (ref. High)												
Low	1.54	1.51	1.58	<0.0001	0.73	0.71	0.75	<0.0001	0.79	0.77	0.81	<0.0001
Middle	1.14	1.12	1.16	<0.0001	0.87	0.85	0.89	<0.0001	0.85	0.83	0.87	<0.0001
Region of residence (ref. Large cities)												
Southern Sweden	1.03	1.01	1.05	0.0035	1.11	1.09	1.13	<0.0001	1.08	1.06	1.10	<0.0001
Northern Sweden	1.08	1.05	1.10	<0.0001	1.26	1.23	1.29	<0.0001	1.22	1.19	1.25	<0.0001
Country of origin (ref. Born in Sweden)												
Eastern Europe	0.98	0.95	1.02	0.3451	0.88	0.85	0.92	<0.0001	0.95	0.91	0.99	0.0065
Western countries	0.50	0.47	0.52	<0.0001	0.83	0.79	0.87	<0.0001	0.88	0.84	0.92	<0.0001
Middle East/North Africa	0.44	0.41	0.46	<0.0001	0.29	0.27	0.31	<0.0001	0.32	0.30	0.34	<0.0001
Africa (excluding North Africa)	0.51	0.45	0.56	<0.0001	0.29	0.26	0.33	<0.0001	0.31	0.28	0.34	<0.0001
Asia (excluding Middle East) and Oceania	1.20	1.14	1.26	<0.0001	0.82	0.78	0.86	<0.0001	0.86	0.82	0.90	<0.0001
Latin America and the Caribbean	0.96	0.88	1.04	0.2923	0.74	0.68	0.80	<0.0001	0.78	0.72	0.84	<0.0001

Abbreviations: CI, confidence interval; HR, hazard ratio; Model 1, univariate model; Model 2, age-adjusted model; Model 3: fully adjusted for all covariates (sociodemographic factors).

MENA and Africa (excluding North Africa) had an almost 70% decreased risk for carcinoma in situ, which agrees with our results on cervical cancer among these women. However, the demonstration in women from Eastern Europe of a high HR for cervical cancer, indicates a slightly lower HR of 0.95 for carcinoma in situ in the fully adjusted analyses in comparison with Swedish-born women. A possible explanation for this could be that these women arrive in Sweden with an already developed invasive cervical cancer. It might also indicate that women from Eastern Europe attend cervical screenings less often and therefore precancerous lesions are not found before the development of cervical cancer. Furthermore, despite extensive adjustments and sensitivity analyses, the possibility remains that other external confounders in lifestyle and behavior may exist.

4.2 | Other sociodemographic factors

Low education level was independently associated with both cervical cancer and carcinoma in situ, which agrees with previous studies.[13,30] Reasons for this might be lower attendance for cervical screening,[23] higher frequency of tobacco smoking (https://www.folkhalsomyndigheten.se/fu-tobaksrokning) and increased risk of urogenital infections.[10–12] On the other hand, middle and low family income were inversely associated with carcinoma in situ compared with high family income. This might reflect the lower screening attendance rates seen in women with low income.[23] However, even though lower attendance for screening ought to indicate a higher risk of cervical cancer, family income did not influence the risk of cervical cancer in our study. This is contradictory to an earlier epidemiological cervical cancer study from Denmark[30] and warrants further study.

4.3 | Strengths and weaknesses

To our knowledge, this is the first nationwide study on the association between sociodemographic factors and cervical neoplasia, adjusted for common urogenital infections as well as other known risk factors. The strengths of this present study are that it involved data from validated nationwide registers, and the consistency between our results and previous findings strengthens the validity of our data sources. For example, the incidence rates and bimodal age distribution of cervical cancer were in line with previous incidence studies in Scandinavia[10,31] and as expected in the lower range of the estimated global incidence rate[3] of cervical cancer. Furthermore,

considering the long follow-up period and the severity of cervical cancer, underdiagnosis is unlikely. In addition, our data extend from 2002 to 2018, and offers newer data than previous similar studies. Importantly, Sweden has experienced a high level of immigration in the years following the previous studies,[14,15] significantly increasing the groups of women of foreign origin and increasing the generalizability of our findings in regard to country of origin and cervical neoplasia. Furthermore, our study was the first, to our knowledge, to include both invasive cervical cancer and carcinoma in situ, adjusted for several known confounders. The most important limitations in this study were that we did not have access to vaccination data. Another limitation is that many women do not seek healthcare for urogenital infections, leading to an underestimation of those cases, as we only capture those that are registered in the medical records. Moreover, although several of the urogenital infections used in the sensitivity analysis share sexual risk behavior as a risk factor with cervical cancer, sexual behavior and other lifestyle factors could not be assessed due to the nationwide nature of our data.

4.4 | Generalizability and implications

Even though cervical cancer is a large global burden,[3] our findings suggest that foreign-born women (other than Eastern European women) seem to have a lower risk of cervical cancer compared with Swedish-born women. Therefore, if cervical cancer preventive programs aim to increase their focus on country of origin, knowledge of national findings and not global trends are necessary to provide a more contextual prevention of this common malignancy. Our findings also support that cervical screening programs ought to increase the effort to reach young women with low education level and those women suffering from high morbidity of urogenital infections (other than vulvovaginitis) as well as drug- and tobacco-related disorders.[10,13,16,18]

5 | CONCLUSION

This large nationwide study suggests that country of origin and low education levels are useful predictors in identifying women at increased risk of cervical cancer even in the presence of universal cervical screening programs. Women who originated from the Middle East and Africa had a considerably lower risk for cervical cancer compared with Swedish-born and other immigrant women in Sweden. More studies on the specific causal mechanisms behind these associations are needed.

AUTHORS' CONTRIBUTION

All authors have approved the final version of the manuscript. Concept: FJ. Development of idea: All authors. Design: FJ and XL. Critical revision and approval of design: AS, KS and CB. Funding and resources: FJ and KS. Access and acquisition of data: KS. Analysis and statistics: XL. Tables: XL and FJ. Interpretation of data: All authors. Literature search: FJ, AS and CB. Drafting of manuscript: FJ and AS with assistance from CB. Critical revision of the manuscript for intellectual content: All authors.

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CONFLICT OF INTERESTS

The authors have stated explicitly that there are no conflicts of interest in connection with this article. All authors have completed the ICMJE uniform disclosure form at www.icmje.org/disclosure-of-interest/.

DATA AVAILABILITY

Owing to the nationwide nature of the data collected for this study, data cannot be made openly available due to legal concerns. Further information regarding the health registries is available from the Swedish National Board of Health and Welfare: https://www.socialstyrelsen.se/en/statistics-and-data/registers/ and Kristina Sundquist. The code used in the analysis can be provided upon request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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