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Cervical cancer screening in Greenland, 1997–2011: Screening coverage and trends in the incidence of high-grade cervical lesions☆

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HIGHLIGHTS

- Coverage of the Greenlandic cervical screening program was low during 1997–2011 (highest rate of 54% in 2011).
- Substantial changes in the incidence of cervical lesions was found according to calendar period and age.
- These findings suggest that improvements in the Greenlandic screening program are warranted.

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ABSTRACT

Objective. In spite of the high incidence of cervical cancer in Greenland, no assessment has been made of the impact of organized cervical screening, introduced in 1998, in relation to occurrence of high-grade cervical lesions. The objectives of the present study were to estimate coverage of the screening program and to examine possible changes in cervical intraepithelial neoplasia (CIN3) incidence in Greenland during 1997–2011 according to calendar period and age.

Methods. Using nationwide registries, we calculated age-standardized incidence rates for all women born and living in Greenland. To investigate whether possible variation in the incidence of CIN3 were related to differences in screening coverage, we further estimated relative risks of CIN3 within two years of screening among women who participated in the screening program using log-linear binomial regression.

Results. Coverage of the screening program was low during 1997–2011 with the highest level of 54% observed in 2011. Peaks in CIN3 incidence of around 300 per 100,000 person-years were observed in 1999 and between 2009 and 2011, while the incidence was lower of approximately 100 per 100,000 person-years between 2000 and 2008. During 2009–2011, the highest incidence was found among women aged 25–34 years. Similar patterns of CIN3 risk according to calendar period and age groups were observed among screened women.

Conclusions. The great variations in CIN3 incidence and low screening coverage observed during 1997–2011 suggest that improvements in the Greenlandic screening program are warranted.

1. Introduction

In Greenland, the incidence of cervical cancer has been among the world's highest during the past four decades [1–4]. The incidence peaked during 1970–1974 with a rate of approximately 60 per 100,000 person-years, while a decreasing trend has been observed since the mid-1980s [2]. Although the incidence of cervical cancer has decreased substantially with a rate reported at 25 per 100,000 person-years in 2000–2009, the incidence is still more than two-times the rate in Denmark [2].

Greenland is the world's largest island with approximately 56,000 inhabitants living in 16 towns and nearly 60 settlements, all located along the coast. The health care system is publicly funded and challenged by limited economic resources and difficulty in recruiting professionals and specialized staff, especially in the sparsely populated areas

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[5]. As a consequence, differences in health care delivery are seen across Greenland with notable differences between the smaller towns and the capital Nuuk where the national hospital is located [5]. Opportunistic cervical screening has existed in Greenland since the early 1970s, but coverage has generally been low [6]. In 1998, a national organized screening program was implemented aiming at screening women aged 20 to 70 years every three years [7]. However, no detailed evaluation of the program has yet been conducted.

Cervical screening aims at detecting precursor lesions such as cervical intraepithelial neoplasia grade 3 (CIN3) [8]. These precursor lesions develop approximately 5–10 years before the progression to invasive cervical cancer [9], and assessment of changes in the incidence of CIN3 can thus serve as a short-term effect measure of the screening program. Therefore, the objective of this study was to evaluate the Greenlandic cervical screening program by assessing possible changes in the incidence of CIN3 during 1997–2011 and according to age group among all women born and living in Greenland, and by examining the relative risk (RR) of CIN3 according to calendar year and age group among women who participated in the screening program. Moreover, the objective was to estimate coverage of the screening program.

2. Material and methods

The Civil Registration System was established in Greenland on May 1, 1972. All individuals alive and resident on that date or later have been registered and given a unique personal identification number. This registry is continuously updated and includes information on place and date of birth, sex, current and past addresses and date of death or emigration. Using this register, we established a nationwide cohort of all women who were born and at some point had lived in Greenland between January 1, 1997 and December 31, 2011. Based on the unique personal identification number used in all Greenlandic and Danish health registries, we were able to link information on cervical cancer screenings and cases of CIN3 to the women in the cohort.

All cervical smears performed in Greenland are sent to public pathology departments in Denmark for analysis. During the study period, specimens sent from Greenland to Denmark were analyzed at four different hospitals, all reporting to the Danish Pathology Register. Cytological samples sent from Greenland were analyzed at the following Danish pathology departments: Rigshospitalet University Hospital from 1960 until September 2008; Hillerød Hospital from October 2008 until August 2012; Hvidovre Hospital from September 2012 to present. Greenlandic histological samples have been analyzed at Rigshospitalet University Hospital since 1945, and Odense University Hospital during 1990–2000. The Danish Pathology Register contains information on all specimens from Danish pathology departments, including normal and abnormal cervical cytology and cervical histology (biopsies and cones) [10]. The reporting to the register has been mandatory for all public pathology departments in Denmark since 1997 [10]. We used this register to identify cervical cytological and histological samples.

Based on the SNOMED coding system used in the Danish Pathology Register, cytological diagnoses were grouped according to the Bethesda classification. The categories included normal, atypical squamous cells of undetermined significance (ASCUS), low-grade squamous intraepithelial lesions (LSIL), and high-grade squamous intraepithelial lesions (HSIL). Histological diagnoses were categorized into the CIN nomenclature and grouped according to CIN1, CIN2, CIN3 (including diagnoses of CIN3, cervical carcinoma *in situ* and adenocarcinoma *in situ*), CIN not otherwise specified and cervical cancer [9]. All cervical cancer diagnoses recorded in the Danish Pathology Register were linked to the Danish Cancer Registry to verify the diagnosis. Cases of cervical cancer were identified in the Danish Cancer Registry using the International Classification of Diseases, 10th Revision code C53.

2.1. Screening recommendations

Between 1998 and 2009, the guidelines of the Greenlandic cervical screening program recommended to screen women aged 20–70 years. From 2010, the upper age limit of the screening interval has been reduced to 65 years. Women are invited by letter or telephone to participate in the regular screening round or follow-up examinations, carried out at local health care units in the different Greenlandic districts. After a normal cervical smear, the guidelines recommend a new smear after three years. In the event of an unsatisfactory smear or for atypia detected by smear, a new smear should be performed within three months according to the guidelines. If two consecutive smears are unsatisfactory or show atypia, the guidelines recommend that the woman is referred for a colposcopy guided biopsy. For mild to severe dysplasia (including carcinoma *in situ*) detected by smear, the recommendation is to immediately refer the woman for a colposcopy guided biopsy. In the event of mild dysplasia detected in a histological examination, the woman should be referred for a new colposcopy guided biopsy within three months. If mild dysplasia is detected in two consecutive histological examinations or if any other grades of dysplasia are detected by histology, the recommendation is to refer the woman for conization. After conization, the guidelines recommend to perform follow-up smears after three and nine months, respectively. Since 2009, HPV has been tested for after detection of abnormal smears and conization.

2.2. Statistical analysis

Using the European Guidelines for Quality Assurance in cervical cancer screening, we calculated screening coverage as the number of women in the target age group for screening (women aged 20–70 years during 1997–2009 and 20–65 years during 2010–2011) with at least one cytological sample in the preceding three-year period divided by the total number of women in the target age group for screening [11]. Only women who were born and resident in Greenland that year were included in the analysis. We also calculated the screening coverage according to age groups and place of living (town *versus* settlement) and only for the period 2009–2011. This was calculated by adding up, for each year between 2009 and 2011, the number of women with at least one cytological sample in the preceding three-year period divided by the total number of women in the target age group for screening.

To estimate incidence rates of CIN3 among all women in Greenland, women in the study cohort were followed from January 1, 1997, or date of birth, whichever occurred last, until death, emigration, or December 31, 2011, whichever occurred first. Time of residence outside of Greenland was subtracted from the calculated time at risk. Among women in the cohort, we calculated annual age-standardized incidence rates of CIN3 using WHO's World Standard Population [12]. Incident lesions were defined as those in women with no preceding CIN3 lesions within the previous 24 months.

As most cervical lesions such as CIN3 are asymptomatic, the detection is dependent on participation in the cervical screening program. In order to assess whether possible changes in the incidence of CIN3 according to calendar year and age groups were related to differences in the screening coverage, we estimated the risk of CIN3 among women who participated in the screening program. Therefore, a second cohort was established consisting of all women in the target age for screening (20–70 years) who were screened at least once between 1997 and 2011 and were born and living in Greenland at the time of screening. Women were considered screened in a given calendar year if they had at least one cytological sample during that year, and women diagnosed with CIN3 within two years of a cervical screening were included as cases. We calculated the two-year risk of CIN3 by dividing the number of CIN3 cases diagnosed within two years after a screening with the total number of screened women. Further, we estimated the relative risk of being diagnosed with CIN3 within two years after screening according to calendar year and age at screening using log-linear binomial