

# Incidence of pancreatic cancer in Greenland 2000–2010

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**Background.** Inuit people are known to be at an increased risk of cancers usually uncommon to the western world such as cancers of the nasopharynx and salivary glands. But what is the trend regarding pancreatic cancer?

**Objective.** To determine the incidence of pancreatic cancer (PC) in Greenland compared with Denmark in the period 2000–2010.

**Study design.** Retrospective register-based study. Cases were retrieved from The Danish Cancer Register and The Greenlandic Patient Register and stratified in 5-year age intervals for each year. Age-standardized incidence ratios (SIR) for each year for Greenland compared with Denmark were calculated using the number of cases and the number of inhabitants in each 5-year age interval and in each country. The average SIR for the entire period was calculated using a weighted average.

**Results.** The study revealed a SIR of 2.38 (95% CI: 1.97–2.86;  $p < 0.0001$ ) indicating a significantly increased incidence of PC in Greenland compared with Denmark. A linear regression analysis showed no significant change in the SIR over time ( $p$  for trend 0.25) as well as no significant change isolated in Greenland ( $p$  for trend 0.8). Furthermore, the Inuit were significantly younger at the time of diagnosis (mean 62.7 vs. 70.0;  $p < 0.0001$ ).

**Conclusions.** The age-standardized incidence of PC is 138% higher in Greenland than in Denmark. A part of this could be explained by a higher prevalence of smoking and DM-2. However, the impact of genetic factors cannot be disregarded and should be subjected to further investigation.

Keywords: *pancreas; neoplasms; Greenland; epidemiology; Inuit*

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The Inuit people living in Greenland have undergone a tremendous westernization of their society starting in the early 20th century. This is exemplified by a decrease in physical activity, due to the depletion of the Greenlandic hunting traditions, tobacco smoking and unhealthy diet. Urbanization and improvement of health facilities speeded up starting in the 1950s (1,2).

At the beginning of the westernization, malignant diseases were highly uncommon, but they started to increase due to the increasing life expectancy and changes in lifestyle (3). Inuit people are known to be at an increased risk of cancers of the nasopharynx and salivary glands. These are tumours uncommon in the western populations suggesting a broad impact including environmental exposures, diet and genetics (4). However, the pattern is changing and common types of cancers in the west – such as tumours of the lung, breast and colon – are emerging in Greenland (2).

Regarding pancreatic cancer (PC), a comprehensive meta-analysis has suggested tobacco smoking, obesity, diabetes mellitus type 2 (DM-2) and chronic pancreatitis as risk factors (5). Alcohol is known to be responsible for 70–80% of all cases of pancreatitis, but it is uncertain if alcohol per se is a risk factor for PC (6,7). Besides the lifestyle factors several inherited disorders, such as HNPCC and Peutz–Jeghers, have been linked with PC (8).

In 2003, Friberg et al. investigated the patterns for several malignant diseases including PC in Greenland for the years 1973–1997 and compared the rates to those in Denmark (9). The study yielded sex-specific standardized incidence ratios (SIRs) for PC in the period 1988–1993 of 1.7 (95% CI: 1.1–2.6) for men and 1.9 (95% CI: 1.2–2.7) for women indicating an increased tendency to PC among Greenlandic Inuit. Other studies have, however, showed a tendency towards either no difference or lowered incidence for PC in general Arctic populations (10–12).

The aim of this study was to assess the impact of the aforementioned westernization of the Greenlandic community on the risk of developing PC. Rates for Greenland were compared with Denmark (as Greenland is a part of the Danish Kingdom) in the period 2000–2010.

In the year of 2000, 0.23% of all inhabitants in Denmark were born in Greenland, whereas in 2010 this was 0.26% (13). Conversely, of the people living in Greenland 12% were born outside Greenland in 2000, which decreased to 11% in 2010 (14). These numbers indicate that the populations did not change due to migration in the observation period.

### Materials and methods

Cases from Greenland were retrieved from the National Patient Register, in which all admissions to hospitals in the entire Greenland are registered, using ICD-10 code C25. Multiple registrations of a same patient were removed, including only the first duplicate record. Cases from Denmark were retrieved from The Cancer Register, in which all diagnoses of cancer in Denmark are registered. However, only the number of cases in each year and 5-year age group was available. Country-specific population data for Greenland and Denmark were collected from the National Statistical Databases, [www.stat.gl](http://www.stat.gl) and [www.dst.dk](http://www.dst.dk), respectively. Inuit are defined as people living in Greenland in this study.

For each year the population and cases in both countries were divided into 5-year age groups. Age-specific rates (IR) for each age group were retrieved using the country-specific population in the age groups as person years at risk. To compare the rates, a method of indirect standardization was used, as the intention of the study was to compare only 2 population groups. To obtain the expected number of cases in the Greenlandic population, if the 2 countries had the same population age distribution, Danish age-specific rates were applied to the Greenlandic demography and summed to yield an overall standardized incidence rate expressed as per 100,000 inhabitants. A ratio (SIR) of age-adjusted rates was used to compare Greenland rates with those of Denmark.

As the number of observed cases in Greenland was relatively small (in average 10 per year) 95% confidence intervals (CIs) were calculated under the assumption that the cases followed a Poisson distribution. Trends were analysed using a linear regression model.  $p < 0.05$  was considered statistically significant.

### Results

In Denmark, a total of 9,388 cases were observed in the period 2000–2010, whereas the corresponding number in Greenland was 109 cases. Table I shows the age distribution of cases at the time of diagnosis. Inuit were significantly younger than Danes (mean  $62.7 \pm 9.9$  vs.

Table I. Age distribution of cases at the time of diagnosis

Age group	Greenland	Denmark	p-Value
	n (%)	n (%)	
0–9	0 (0)	0 (0)	–
10–19	0 (0)	1 (<1)	–
20–29	0 (0)	4 (<1)	–
30–39	1 (<1)	64 (<1)	–
40–49	10 (9)	359 (4)	–
50–59	28 (26)	1287 (14)	–
60–69	39 (36)	2739 (29)	–
70–79	29 (27)	2914 (31)	–
>79	2 (2)	2020 (22)	–
Total	109 (100)	9388 (100)	
<b>Mean (<math>\pm</math>SD)</b>	<b>62.7 (<math>\pm</math>9.9)</b>	<b>70.0 (<math>\pm</math>11.2)</b>	<b>&lt;0.0001</b>

$70.0 \pm 11.2$ ;  $p < 0.0001$ ) at the time of diagnosis. Ten percent of Inuit cases were observed before the age of 50, whereas in Denmark 5% of the cases were observed before the age of 50.

Table II shows the Danish and Greenlandic crude rates compared with the age-adjusted SIR. The p-value indicates the level of significance of the SIR for Greenland compared with Denmark.

A weighted average of the SIR for the years 2000–2010 yielded a SIR of 2.38 (95% CI: 1.97–2.86;  $p < 0.0001$ ). Thus the incidence of PC is 138% higher in Greenland than in Denmark.

A linear regression analysis showed no significant changes over the 11-year period ( $p$  for trend: 0.25) indicating that the SIR between the 2 countries has not changed since 2000. Furthermore, a linear regression

Table II. The crude rates (IR) and age-adjusted (SIR) ratios per 100,000 inhabitants for Greenland compared with Denmark year of diagnosis

Year	IR		SIR	p-Value
	Greenland (n)	Denmark (n)		
2000	14.3 (7)	13.7 (728)	2.05	0.04
2001	21.3 (12)	14.6 (783)	3.26	<0.0001
2002	14.2 (8)	14.3 (765)	2.15	0.03
2003	19.4 (11)	14.4 (775)	2.82	0.0006
2004	22.9 (13)	15.7 (849)	3.07	<0.0001
2005	17.6 (10)	15.7 (851)	2.31	0.008
2006	15.8 (9)	16.1 (870)	2.03	0.03
2007	12.4 (7)	17.1 (929)	1.42	0.35
2008	23.0 (13)	16.7 (912)	2.70	0.0003
2009	12.5 (7)	17.9 (988)	1.34	0.44
2010	21.4 (12)	17.0 (938)	2.48	0.002
<b>Average</b>	<b>17.7 (109)</b>	<b>15.7 (9388)</b>	<b>2.38</b>	<b>&lt;0.0001</b>

analysis of the rates in Greenland – after being standardized according to the Danish rates – showed no significant changes ( $p$  for trend: 0.8). Thus the age-standardized incidence of PC in Greenland is constant.

## Discussion

This study revealed a SIR of 2.38 (95% CI: 1.97–2.86;  $p < 0.0001$ ) for Greenland compared to Denmark for the period 2000–2010. This ratio has been constant throughout the entire observation period ( $p$  for trend: 0.25). The SIR corresponds to the result found by Friberg et al. in 2003 (9). This fact combined with the  $p$ -value for trend (0.25) indicates that the relative incidence rate of PC in Greenland compared with Denmark has been constant since 1988. Furthermore, we found the absolute incidence rate in Greenland to be constant in the period 2000–2010 as well ( $p$  for trend: 0.8).

The effect of tobacco smoking on PC is well documented and as much as 25% of PC is reported to be associated with tobacco smoking (5,15–17). The prevalence of daily smokers in the adult Greenlandic population is 66% (and decreasing) (18), while this number in Denmark is 21% (19) and could account, in part, to the higher rates of PC among the Greenlandic population. As an effect of the decreasing use of tobacco smoking in both countries (18,20), it is likely that a lower number of smoking-related PC will be observed in future years. However, the cessation of tobacco smoking will have to last for at least 10 years, before a reduced risk will be present (15).

Diabetics are known to have 1.5–2 fold higher risk of developing PC than have the non-diabetics (21,22). In 2009, 28% of the Greenlandic population aged over 65 years had DM-2 – an increase from 10% in comparison with 1999 (23). In Denmark, 6% of the population more than 60 years had DM-2 in 1999 increasing to 14% in 2009 (24). Thus, the prevalence of DM-2 is twice as high in Greenland as in Denmark and could also account for some part of the findings in this study. After the time of the diagnosis, DM-2 may increase the risk of PC (21), although increases in DM-2 during 1999–2009 did not result in increases in PC during 2000–2010.

Tobacco smoking has for a long time been a part of the Greenlandic culture, but the tendency to smoke is decreasing, probably because of higher price and better educational levels (25). The higher prevalence of DM-2 in Greenland compared with Denmark is probably associated with the westernization mentioned in the Introduction section. The transition in lifestyle has led to obesity, lack of physical activity and unhealthy diet, thus increasing the risk of acquiring DM-2.

A factor less probable to be of significant contribution to our findings is chronic pancreatitis. Though expected to increase the risk of PC (26,27), a study by Tramacere et al. (28) has shown that only 5% of all cases of PC can

be related to chronic pancreatitis. Furthermore, Algul et al. (6) found that 70–80% of all cases of chronic pancreatitis is due to alcohol. Alcohol per se is probably not a risk factor, but an excessive daily intake of alcohol may lead to pancreatitis and thereby to PC (28). In Denmark, the average yearly intake per person is 11.3 L of alcohol (29) corresponding to the Greenlandic value of 11.7 L (30). The significantly increased risk of PC in Greenland found in this study is therefore not likely to be explained by a difference in alcohol intake. The consumption of alcohol has been decreasing in Greenland (since 1988), and it is possible that the incidence of PC will decrease as a long-term effect of this change of lifestyle. However, as the drinking patterns (binge drinking vs. alcoholism and intake among young vs. elderly people) in the 2 populations are not necessarily comparable and data on chronic pancreatitis are currently not available, it is very difficult to examine the influence of alcohol to the findings of this study.

It is not known how many of the observed cases that can be related to hereditary syndromes such as HNPCC and Peutz–Jeghers, but we know that hereditary PC tends to debut at a younger age (31). As the Greenlandic cases tended to be younger than the Danish cases (however, the age at diagnosis for the Danish cases is an approximation as the data on the exact ages were not available), and that twice as many cases in Greenland than in Denmark were below the age of 50, a genetic component cannot be disregarded and should be subjected to further investigations.

Also, possible risk factors including infection with microorganism *Helicobacter pylori*, liver cirrhosis through alcohol consumption and occupational exposures could all lead to an increase in the incidence of PC (32–34). Combinations of more or all of the risk factors mentioned in this article are very likely in Greenland, thus increasing the risk of PC.

The results from Greenland are associated with a certain degree of uncertainty due to the low number of observations (a total of 109 cases), though making the Greenlandic rates very vulnerable to smaller changes in the incidence. Data used in this study are from nationwide registers. The Cancer Registry in Denmark has in earlier studies shown to be very reliable (35). Both countries have free and equal access to healthcare. This should to some extent rule out the possibility of people having PC without being diagnosed. However, in sparsely populated areas of Greenland, people could have died of PC without being diagnosed. This is probably not likely in Denmark, as PC is an aggressive malignancy and cases of PC misclassified as chronic pancreatitis would quickly be apparent. Any case of a non-diagnosed PC in Greenland (where it would be more likely than in Denmark) would support the findings, as well as if there

were multiple entries of the same patient in the Danish registries thus lowering the actual Danish IR.

ICD code C25 also includes C25.4 covering endocrine tumours of the pancreas. None of these registrations were found in the Greenlandic data, whereas the incidence of endocrine pancreatic tumours in Denmark was unknown. If endocrine tumours of the pancreas had been registered in the Danish population, our estimate would have been biased towards the null-hypothesis of no difference. In that case, the SIR is underestimated.

In summary, the findings of this study suggest a significantly increased incidence of PC in Greenland compared with that in Denmark. This could be related to a higher prevalence of tobacco smoking and DM-2 in the Greenlandic population. Also, the study showed that there has been no change in the incidence ratio for Greenland compared with Denmark for the last 2 decades. To lower the incidence of PC in Greenland, prophylactic measures against these lifestyle factors could be taken into account. However, a genetic impact cannot be disregarded and should be subjected to further investigations.

### Conflict of interest and funding

The author stated no conflict of interests.

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