ORIGINAL ARTICLE

Micro- and macrovascular complications among Greenlanders and Danes with type 2 diabetes mellitus in Nuuk, Greenland

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Received 9 June 2009; Accepted 8 December 2009

ABSTRACT

Objectives. To estimate the prevalence of micro- and macrovascular complications and risk factors among Greenlanders and Danes with type 2 diabetes mellitus (T2DM) in Nuuk, Greenland.

Study design. Observational and cross-sectional study, based on a review of medical records and patient interviews.

Methods. Review of the electronic medical records and interviews obtained from T2DM patients connected to the Center of Primary Health Care in Nuuk.

Results. A total of 123 patients (81 Greenlanders and 42 Danes) with T2DM for a mean of 6 years were included. Fifty-seven percent of the Greenlanders were diagnosed within the last 3 years. Ninety-one percent of the patients had BMI≥25 kg/m², 42% had 1 or more first-degree relatives with diabetes, 43% were current smokers, 69% were categorized as leading a very physically active lifestyle and 60% described a healthy diet pattern. Sixty-eight percent of all the patients suffered from at least 1 complication – 51% neuropathy, 14% retinopathy, 10% macrovascular complication and 43% microalbuminuria. The number of complications was significantly correlated to the duration of diabetes (p=0.008) and low physical activity (p=0.037). Retinopathy was correlated to Danish ethnicity (p=0.020).

Conclusion. The majority of the Greenlandic patients (57%) were diagnosed within the last 3 years, which may indicate either the beginning of an epidemic or an increased awareness of T2DM, or both. The high prevalence of microvascular complications and risk factors such as smoking and microalbuminuria are a matter of concern. Efforts to reduce smoking and increase physical activity could be considered as prime targets for initiatives.

(Int J Circumpolar Health 2010; 69(2):195-207)

Keywords: Greenland, diabetes mellitus, type 2 diabetes, diabetic complications, lifestyle, Inuit
INTRODUCTION

Previously, type 2 diabetes mellitus (T2DM) was almost non-existent in Greenland (1). Epidemiological studies performed between 1999 and 2002 reported a high prevalence of T2DM among Greenlanders, suggesting an age standardized prevalence of diabetes among men and women of 10.8% and 9.4%, respectively (2). Furthermore, 70% of those with diabetes were undiagnosed (2). A high prevalence of diabetes has also been reported among Greenlandic migrants living in Denmark (3). Thus, the prevalence of T2DM and related complications had been predicted to increase in Greenland (4). However, the prevalence of diagnosed T2DM in Greenland is still relatively low, affecting around 2% of adults who were at or above 40 years of age at the beginning of 2008 (5). Furthermore, micro- and macrovascular complications have created a minor burden for the health care system in Greenland, although no systematic evaluation has been conducted so far. The prevalence of complications and unhealthy lifestyles among Greenlanders with T2DM are not known.

Nuuk, the capital of Greenland, has approximately 15,000 inhabitants (including 3,200 immigrants born outside of Greenland), representing around one-third of the country’s entire population (6). The Primary Health Care Center in Nuuk serves all the inhabitants of the capital. Most patients with T2DM in Nuuk are checked regularly, between 2 and 4 times a year at the Primary Health Care Center, where an electronic medical record (EMR) system serves as a database documenting the prevalence of diabetes in the population. The patients can be divided into a group of Greenlanders, a group of Danes and a group of mixed origin. This provides researchers with the ability to analyse and compare the rates of complications from T2DM as well as risk factors for each group, which may provide important information about the nature of T2DM among Greenlanders.

Thus, the aims of this study are to estimate the prevalence of micro- and macrovascular complications and other selected risk factors among Greenlanders and Danes with type 2 diabetes mellitus (T2DM) in Nuuk, Greenland, and to study the correlation between diabetic complications and the duration of diabetes, as well as the biological and lifestyle risk factors for the disease.

MATERIAL AND METHODS

Medical review and interview

Patients with T2DM can be identified in the EMR in Nuuk due to systemized record-keeping. The medical records were reviewed for information about age, gender and year of diagnosis. The latest measurements of height, weight and body mass index were taken, as well as urinary albumin/creatinine ratio (UACR) and blood lipids, including total, high and low density lipoprotein (HDL and LDL) cholesterol and triglycerides (TG). The mean of all blood pressures measured in the office within the last year was used in this study. Blood pressures were measured using an automated device (UA-787 from A&D Medical®) with an appropriate cuff on a sitting patient after approximately 5 minutes of rest. Results from the latest eye examination performed by an ophthalmologist using photography of
the retina from a dilated pupil were recorded. The results of the latest foot examination were performed by a foot therapist, including an examination of pulses in the foot (dorsalis pedis and tibialis posterior arteries). Foot sensation, including pressure (10 g monofilament), thermal (Tip Therm*) and vibration (biothesiometer, Rova Company*) modalities were recorded as well.

Finally, the patients were contacted by telephone and asked if they were willing to participate in a short interview. Researchers obtained additional information about ethnicity, lifestyle factors, macrovascular complications and medical treatment from those who agreed.

**Ethnicity**
For the purposes of the study, the patients were considered Greenlanders if 3 or more of their grandparents were born in Greenland, and were considered Danes if 3 or more of their grandparents were born in Denmark. Patients with 2 grandparents born in Greenland and 2 born in Denmark were considered of mixed origin.

**Biochemical procedure**
Venous blood was analysed for lipids and glycated hemoglobin, and urine was analysed for excretion of albumin at The Central Laboratory, Queen Ingrid’s Hospital in Nuuk, using an Architecht 8000T from Abbott. The Central Laboratory is a participant of the Danish quality control system for laboratories, DEKS.

**Complications**
Information on macrovascular complications was first collected by telephone interview from patients then later confirmed by comparing interview statements to the patients’ medical records. Macrovascular complications included any history of stroke, coronary heart disease including acute myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, history of revascularization for peripheral atherosclerotic arterial disease or amputation because of ischemia in the inferior extremities. All “clinical” diagnoses and events confirmed in the physician’s notes were included. Macrovascular complications prior to the diagnosis of diabetes were also included in this study. Coronary artery disease (and other heart diseases) that did not result in any of these events were not included in this study.

The presence of a diabetic foot ulcer was defined as a medical history of non-traumatic ulcers in the foot. Peripheral neuropathy was defined as reduced or lost sensibility in the foot. No information about autonomic neuropathy was obtained in this study.

Retinopathy was characterized as background retinopathy when microaneurysms, small hemorrhages or hard exudates were described by the ophthalmologist, and as proliferative diabetic retinopathy or diabetic maculopathy when these diagnoses were used. Classification was based on the eye that was worst affected.

Microalbuminuria was defined as having a urinary albumin/creatinine ratio (UACR) above 2.5 mg/mmol in 2 consecutive urine samples, whereas a UACR exceeding 25 mg/mmol in sterile urine samples was considered to be diabetic nephropathy.

**Family history**
A family history of diabetes was defined as 1 or more first-degree relatives with diabetes mellitus.
**Smoking**
The patients were divided into current smokers and non-smokers based on their present smoking status. A combined group of current and former smokers was defined as ever smokers. No information regarding exposure to passive smoke was obtained.

**Diet**
A healthy eating pattern was defined as a diet including intake of fish at least once a week and intake of vegetables and fruits a least 3 times a week, along with an effort being made to reduce the intake of saturated fatty acids.

**Physical activity**
Self-reported physical activity at work, in leisure time and during transportation was defined as low physical activity when the daily amount of activity did not exceed 30 minutes of moderate to hard physical exercise (including working with increased breathing rate, domestic work, sports activity, bicycling and brisk walking) or 1 hour of minor exercise (including normal walking). More than 30 minutes of moderate to hard physical exercise or more than 1 hour of minor physical exercise daily was defined as high physical activity.

**Alcohol**
The self-reported average consumption of alcoholic beverages (12g of alcohol) on a weekly basis was used as an indicator of alcohol intake.

**Statistics**
Statistical analyses were performed using SPSS 17.0. Q-Q plots were used to analyse the distribution. Means and standard deviation (SD) were used to describe normal distributed parameters. Means between groups were compared with t-test. Chi-square tests were used to compare frequencies. Linear regression was used to analyse correlation between complications and other factors.

**RESULTS**

**Demographic**
A total of 152 patients with T2DM are registered in the Primary Health Care Center in Nuuk. Of these, 29 patients were excluded from the study for the following reasons: an unwillingness to participate (1), contact could not be established despite many attempts made by telephone (6), although still registered with the Center, the patient had moved from the district (2), mental illness such as schizophrenia and dementia (7), non-Greenlandic and non-Danish background (7) and mixed origin (6). In total, 123 patients (81%) were included in the study. Almost all subjects had complete data fields with numbers (n) varying from 110 to 123 (See Tables I and II).

Eighty-one patients were characterized as Greenlanders (58 women and 23 men), whereas 42 patients were characterized as Danes (7 women and 35 men). There was a difference in gender ratio between the groups (p<0.001). Clinical, demographical, biochemical and other characteristics of the patients are thus listed in subgroups in Tables I and II according to ethnicity and gender, in addition to all ethnical groups. The mean age for the whole sample is 59 years. The Danes were taller than the Greenlanders. There was no difference with regard to BMI (Table I). Ninety-one percent of all patients had BMI ≥25 kg/m² and 55% had BMI ≥30 kg/m².
Diabetes and vascular complications in Greenland

**Diabetes duration**
The mean duration of diabetes for the whole group was 6 years (6.5) with no significant differences between Danes and Greenlanders nor between the genders. However, 50% of all patients and 57% of the Greenlandic patients were diagnosed within the last 3 years (after 2005). Nineteen percent of all cases were diagnosed during 2008.

**Blood pressure and biochemical results (Table I)**
The mean diastolic blood pressure among the Greenlanders (81 mmHg) was significantly lower than among the Danes (88 mmHg). No differences in mean HbA1c, total and LDL cholesterol and triglycerides was observed between the subgroups. However, mean HDL cholesterol is higher for females (1.1 mmol/l) than for males (1.0 mmol/l), p=0.001, and Danes had lower total and HDL cholesterol and higher triglycerides than the Greenlanders.

**Family history**
Forty-two percent of all the patients had at least 1 first-degree relative with diabetes mellitus.

**Lifestyle factors**
Forty-three percent of all patients were categorized as current smokers, whereas 80% of all the patients were categorized as ever smokers with no gender or ethnic differences. A lifestyle of physical activity was observed in 69% and healthy diet pattern in 60% of the patients (see Table II). The intake of alcohol was significantly higher among the males than among the females (p=0.005).

**Drug therapy (Table II)**
Twenty-four percent of the patients did not receive any blood glucose-lowering medication and were treated with lifestyle changes, whereas 72% were treated with oral hypoglycemic agents and 14% with insulin. Eighty-nine percent received lipid-lowering agents, 77% angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs) and 63% low-dose aspirin (75 mg a day).

**Diabetic complications**
Ten percent of the patients had experienced at least 1 macrovascular complication: 8 cases of stroke for 6 Greenlanders and 2 Danes, 5 cases of coronary heart disease and 1 case of amputation because of ischemia in an inferior extremity. One of the Danes and 1 of the Greenlanders had experienced both a stroke and coronary heart disease. Peripheral neuropathy was demonstrated in 51% of the patients. The frequency was higher among the males (62%) compared to the females (41%) with p=0.029.

Retinopathy was found in 17 of the patients. One Danish male with diabetes for more than 10 years was described with maculopathy and thickening of the retina. In 16 cases background retinopathy was described. Thirty-five percent of the patients with retinopathy were treated with insulin compared to 9% of the patients without retinopathy (p=0.003), and all were treated with glucose-lowering drugs compared to 72% of those without retinopathy (p=0.044). Clinical nephropathy was only demonstrated in 2 male patients. One had confirmed UACR >25 mg/mmol in sterile urine. The other patient used an indwelling catheter and the diagnosis was based on elevated serum creatinine with an estimated glomerular filtration rate of 37 ml/min/1.73m². Microalbuminuria was found in 43% of the patients.
Table I. Clinical, demographical, biochemical and other patient characteristics.

| Characteristic | Greenlanders | Danes | p | Greenlanders | Danes | p | Greenlanders | Danes | p |
|----------------|-------------|-------|---|-------------|-------|---|-------------|-------|---|
| n or variable  | males (n=23)| (n=35)|   | females (n=58)| (n=7)|   | all (n=81) | (42) |   |
| Age (years)    | 123 60 (11.3) | 59 (11.6) | 0.380 | 60 (11.6) | 52 (10.3) | 0.090 | 60 (11.4) | 57 (9.4) | 0.161 |
| Height (cm)    | 123 170 (7.6) | 179 (7.0) | <0.001 | 157 (6.9) | 166 (3.8) | 0.001 | 161 (8.8) | 177 (8.2) | <0.001 |
| Weight (kg)    | 123 86 (16.2) | 101 (15.0) | 0.001 | 76 (14.1) | 85 (15.9) | 0.146 | 79 (15.4) | 99 (16.19) | <0.001 |
| BMI            | 123 30 (5.1) | 31 (4.9) | 0.556 | 31 (5.5) | 31 (5.9) | 0.900 | 31 (5.6) | 31 (5.0) | 0.751 |
| Duration of diabetes | 123 5.1 (5.4) | 7.8 (6.6) | 0.102 | 5.7 (7.0) | 3.7 (2.9) | 0.465 | 5.5 (6.5) | 7.1 (6.3) | 0.189 |
| Blood pressure | Systolic (mmHg) | 122 132 (12.9) | 134 (12.0) | 0.653 | 131 (7.0) | 16 (1.1) | 0.957 | 132 (15.2) | 133 (11.3) | 0.577 |
| Diastolic (mmHg) | 122 82 (9.1) | 84 (8.9) | 0.036 | 80 (6.6) | 90 (4.5) | <0.001 | 81 (7.3) | 88 (6.6) | 0.006 |
| HbA1c (%)      | 121 6.6 (1.9) | 6.5 (1.5) | 0.870 | 6.6 (1.7) | 6.4 (1.4) | 0.846 | 6.6 (1.7) | 6.4 (1.5) | 0.748 |
| Cholesterol    | Total (mmol/l) | 119 4.6 (1.3) | 4.2 (1.2) | 0.394 | 5.0 (1.2) | 4.8 (1.4) | 0.132 | 4.9 (1.2) | 4.2 (1.2) | 0.020 |
| LDL (mmol/l)   | 119 2.6 (1.2) | 2.7 (1.2) | 0.804 | 2.9 (1.2) | 3.0 (1.5) | 0.551 | 2.8 (1.2) | 2.7 (1.2) | 0.793 |
| HDL (mmol/l)   | 118 1.1 (0.4) | 0.9 (0.2) | 0.019 | 1.2 (0.4) | 1.1 (0.2) | 0.111 | 1.2 (0.4) | 0.9 (0.2) | 0.001 |
| Triglycerides  | mmol/l | 115 1.4 (1.0) | 1.7 (1.0) | 0.354 | 1.7 (0.8) | 1.8 (1.0) | 0.142 | 1.6 (0.8) | 1.7 (0.9) | 0.651 |
| Beverages a week (alcohol) | 123 6 (6.2) | 7 (6.7) | 0.715 | 3 (4.6) | 5 (8.4) | 0.646 | 4.0 (5.2) | 6.3 (7.0) | 0.040 |

Table II. Clinical, demographical, biochemical and other patient characteristics.

| Characteristic | n | Greenlanders | Danes | p | Greenlanders | Danes | p | Greenlanders | Danes | p |
|----------------|---|-------------|-------|---|-------------|-------|---|-------------|-------|---|
| n or variable  |   | males (n=23) | (n=35) |   | females (n=58) | (n=7) |   | all (n=81) | (42) |   |
| Diabetes in family | 123 | 51 | 35 | 0.212 | 36 | 57 | 0.212 | 36 | 52 | 0.077 |
| Current Smoker | 123 | 35 | 43 | 0.539 | 50 | 14 | 0.073 | 46 | 38 | 0.421 |
| Ever smoker | 123 | 83 | 74 | 0.457 | 85 | 57 | 0.078 | 84 | 71 | 0.102 |
| Low physical | 123 | 30 | 29 | 0.879 | 34 | 14 | 0.456 | 33 | 26 | 0.416 |
| Healthy eating | 123 | 61 | 49 | 0.358 | 63 | 86 | 0.247 | 63 | 54 | 0.378 |
| Drug therapy | 123 | 32 | 22 | 0.873 | 24 | 43 | 0.287 | 23 | 24 | 0.965 |
| No GLD* | 123 | 70 | 74 | 0.694 | 74 | 57 | 0.343 | 73 | 71 | 0.868 |
| ACE-inh. or ARB | 123 | 78 | 80 | 0.873 | 76 | 72 | 0.797 | 77 | 79 | 0.799 |
| Aspirin | 123 | 69 | 70 | 0.936 | 60 | 29 | 0.109 | 63 | 62 | 0.908 |
| Retinopathy | 118 | 4.3 | 21 | 0.222 | 14 | 17 | 0.189 | 11 | 21 | 0.184 |
| Neuropathy | 121 | 61 | 63 | 0.443 | 43 | 41 | 0.879 | 47 | 60 | 0.184 |
| Microalbuminuria | 110 | 40 | 35 | 0.933 | 50 | 29 | 0.362 | 47 | 34 | 0.190 |
| Macrovascular complication (%) | 123 | 9 | 9 | 0.987 | 12 | 0 | 0.331 | 12 | 7 | 0.373 |
| Stroke | 123 | 9 | 6 | 0.661 | 7 | 0 | 0.473 | 7 | 5 | 0.573 |
| Coronary heart disease** | 123 | 4 | 6 | 0.818 | 3 | 0 | 0.618 | 4 | 5 | 0.778 |
| Amputation | 123 | 0 | 0 | 0 | 2 | 0 | 0.726 | 1 | 0 | 0.470 |
| Foot ulcer | 123 | 0 | 3 | 0.336 | 2 | 0 | 0.726 | 1 | 2 | 0.690 |
| Any complication | 123 | 61 | 66 | 0.707 | 53 | 43 | 0.596 | 56 | 62 | 0.499 |

*OAH= Oral hypoglycemic agent. LLA=Lipid-lowering agent. GLD= Glucose-lowering drug.
**Coronary heart disease includes acute myocardial infarction, coronary artery bypass grafting and percutaneous coronary intervention.
A total of 68% of the patients had at least 1 complication, including microalbuminuria. Clinical, demographical, biochemical and other characteristics of the patients with and without complications are thus listed in Tables III and IV. Patients with complications were older, had had diabetes for a longer time, were less physically active and were treated with drugs more frequently than those without complications. Total and LDL cholesterol were higher for patients without complications. Patients with complications were treated with drugs more frequently than those without (see Table IV). No differences concerning smoking habits between the 2 groups where observed. However, only 1 patient with macrovascular complications had never smoked. Tables V and VI demonstrate the results of a linear regression analysis with partial regression coefficients ($\beta$), standard error (SE) and $p$ values.

The number of complications including microalbuminuria or nephropathy, retinopathy, neuropathy, macrovascular complication and diabetic foot ulcers were significantly correlated to years with diabetes ($p=0.008$) and physical inactivity ($p=0.037$). The significant correlations are highlighted in Tables V and VI. Retinopathy was the only complication associated with (Danish) ethnicity ($p=0.020$).

### Table III. Clinical, demographical, biochemical and other characteristics of the patients with and without complications.

| Characteristic or variable | n   | Patients with complications | Patients without complications | p   |
|----------------------------|-----|-----------------------------|--------------------------------|-----|
| Age (years)                | 123 | 61 (9.9)                    | 55 (11.7)                      | 0.003 |
| BMI                        | 123 | 31 (5.2)                    | 32 (5.8)                       | 0.392 |
| Duration of diabetes       | 123 | 7.4 (7.1)                   | 3.3 (3.5)                      | 0.001 |
| Blood pressure             |     |                             |                                |      |
| Systolic (mmHg)            | 122 | 133 (13.2)                  | 131 (15.6)                     | 0.654 |
| Diastolic (mmHg)           | 122 | 82 (8.3)                    | 83 (7.1)                       | 0.462 |
| HbA1c (%)                  | 121 | 6.6 (1.6)                   | 6.4 (1.7)                      | 0.415 |
| Total Cholesterol          | 119 | 4.4 (1.1)                   | 5.1 (1.4)                      | 0.003 |
| LDL (mmol/l)               | 119 | 2.5 (1.0)                   | 3.3 (1.4)                      | 0.001 |
| HDL (mmol/l)               | 118 | 1.1 (0.4)                   | 1.0 (0.3)                      | 0.586 |
| Serum triglycerides (mmol/l)| 115 | 1.7 (0.9)                   | 1.6 (0.7)                      | 0.596 |
| Beverages a week (alcohol) | 123 | 4.7 (5.7)                   | 5.0 (6.4)                      | 0.733 |

### Table IV. Clinical, demographical, biochemical and other characteristics of the patients with and without complications.

| Characteristic or Variable | n   | Patients with complications | Patients without complications | p   |
|----------------------------|-----|-----------------------------|--------------------------------|-----|
| Males                      | 123 | 51                          | 38                             | 0.131 |
| Greenlanders              | 123 | 63                          | 72                             | 0.230 |
| Diabetes in family         | 123 | 37                          | 51                             | 0.096 |
| Current Smoker             | 123 | 42                          | 44                             | 0.546 |
| Ever smoker                | 123 | 82                          | 74                             | 0.222 |
| Low physical activity      | 123 | 38                          | 22                             | 0.008 |
| Healthy eating pattern     | 123 | 55                          | 72                             | 0.054 |
| Drug therapy               |     |                             |                                |      |
| No glucose-lowering drugs  | 123 | 20                          | 31                             | 0.147 |
| Oral hypoglycemic agent    | 123 | 75                          | 67                             | 0.227 |
| Insulin                    | 123 | 15                          | 10                             | 0.316 |
| ACE inhibitor or ARBs      | 123 | 85                          | 62                             | 0.005 |
| Lipid-lowering agent       | 123 | 93                          | 82                             | 0.070 |
| Aspirin                    | 123 | 70                          | 46                             | 0.009 |
| Table V. Influence of lifestyle and biological factors on all diabetic complications. |
|-----------------------------------------------|
| Dependent variable | Number of complications | Microvascular complication | Macrovascular complication |
| Factor                  | β      | SE    | p    | β      | SE    | p    | β      | SE    | p    |
| Gender                 | -0.064 | 0.208 | 0.758 | -0.109 | 0.100 | 0.278 | 0.046 | 0.071 | 0.516 |
| Ethnicity              | 0.057  | 0.233 | 0.807 | 0.009  | 0.111 | 0.934 | -0.016 | 0.079 | 0.844 |
| Age                    | 0.012  | 0.010 | 0.259 | 0.009  | 0.005 | 0.064 | 0.000  | 0.004 | 0.948 |
| Duration of diabetes   | 0.041  | 0.015 | 0.008 | 0.018  | 0.007 | 0.017 | -0.003 | 0.005 | 0.629 |
| BMI                    | 0.003  | 0.007 | 0.988 | -0.009 | 0.009 | 0.333 | 0.000  | 0.006 | 0.884 |
| Sys. BP                | 0.002  | 0.008 | 0.758 | -0.002 | 0.004 | 0.585 | 0.003  | 0.003 | 0.204 |
| Dia. BP                | 0.023  | 0.013 | 0.083 | 0.016  | 0.006 | 0.016 | -0.010 | 0.005 | 0.025 |
| HbA1c                  | 0.055  | 0.060 | 0.368 | 0.011  | 0.029 | 0.698 | -0.002 | 0.020 | 0.935 |
| Total chol.            | 0.073  | 0.150 | 0.627 | -0.080 | 0.072 | 0.265 | 0.045  | 0.051 | 0.375 |
| HDL chol.              | 0.405  | 0.297 | 0.175 | 0.323  | 0.142 | 0.025 | -0.186 | 0.101 | 0.068 |
| LDL chol.              | -0.275 | 0.141 | 0.054 | -0.083 | 0.068 | 0.220 | -0.055 | 0.048 | 0.253 |
| Triglyceride           | 0.116  | 0.116 | 0.320 | 0.076  | 0.055 | 0.174 | 0.029  | 0.039 | 0.465 |
| Current smoker         | -0.051 | 0.209 | 0.808 | -0.016 | 0.100 | 0.873 | 0.001  | 0.071 | 0.984 |
| Ever smoker            | -0.338 | 0.245 | 0.170 | -0.107 | 0.117 | 0.365 | -0.048 | 0.083 | 0.565 |
| Alcohol intake         | 0.000  | 0.018 | 0.963 | -0.007 | 0.009 | 0.440 | 0.011  | 0.006 | 0.060 |
| Physical activity      | -0.430 | 0.204 | 0.037 | -0.054 | 0.097 | 0.577 | -0.074 | 0.069 | 0.288 |
| Healthy diet           | 0.243  | 0.193 | 0.211 | 0.049  | 0.092 | 0.595 | 0.012  | 0.065 | 0.858 |

| Table VI. Influence of lifestyle and biological factors on specific diabetic complications. |
|-----------------------------------------------|
| Dependent variable | Neuropathy | β    | SE    | p    | Retinopathy | β    | SE    | p    | Microalbuminuria | β    | SE    | p    |
| Factor                  | β      | SE    | p    | β      | SE    | p    | β      | SE    | p    |
| Gender                 | -0.168 | 0.105 | 0.113 | 0.018  | 0.079 | 0.817 | 0.011  | 0.119 | 0.929 |
| Ethnicity              | 0.007  | 0.117 | 0.955 | 0.204  | 0.086 | 0.020 | -0.125 | 0.134 | 0.353 |
| Age                    | 0.010  | 0.005 | 0.060 | 0.002  | 0.004 | 0.677 | 0.002  | 0.006 | 0.745 |
| Duration of diabetes   | 0.015  | 0.008 | 0.057 | 0.012  | 0.006 | 0.036 | 0.018  | 0.009 | 0.046 |
| BMI                    | 0.007  | 0.009 | 0.475 | 0.009  | 0.007 | 0.210 | -0.013 | 0.011 | 0.224 |
| Sys. BP                | 0.003  | 0.004 | 0.502 | -0.003 | 0.003 | 0.335 | -0.001 | 0.005 | 0.749 |
| Dia. BP                | 0.011  | 0.007 | 0.096 | 0.009  | 0.005 | 0.081 | 0.013  | 0.007 | 0.072 |
| HbA1c                  | 0.015  | 0.030 | 0.621 | 0.056  | 0.022 | 0.013 | -0.002 | 0.035 | 0.947 |
| Total chol.            | -0.068 | 0.076 | 0.372 | 0.098  | 0.054 | 0.074 | 0.019  | 0.091 | 0.836 |
| HDL chol.              | 0.269  | 0.150 | 0.076 | 0.127  | 0.111 | 0.257 | 0.215  | 0.175 | 0.223 |
| LDL chol.              | -0.049 | 0.071 | 0.492 | -0.117 | 0.051 | 0.025 | -0.081 | 0.082 | 0.325 |
| Triglyceride           | 0.128  | 0.058 | 0.030 | -0.025 | 0.042 | 0.350 | 0.024  | 0.073 | 0.748 |
| Current smoker         | 0.066  | 0.105 | 0.528 | -0.046 | 0.076 | 0.546 | -0.090 | 0.119 | 0.455 |
| Ever smoker            | -0.056 | 0.125 | 0.653 | -0.023 | 0.090 | 0.796 | -0.103 | 0.142 | 0.469 |
| Alcohol intake         | 0.002  | 0.009 | 0.745 | -0.013 | 0.007 | 0.044 | -0.002 | 0.010 | 0.850 |
| Physical activity      | -0.126 | 0.103 | 0.223 | 0.007  | 0.077 | 0.927 | -0.170 | 0.117 | 0.150 |
| Healthy diet           | 0.157  | 0.098 | 0.113 | 0.089  | 0.070 | 0.206 | -0.018 | 0.113 | 0.877 |
DISCUSSION

Demographics
The majority of the Greenlandic patients (57%) were diagnosed within the last 3 years, indicating increasing incidences of diabetes mellitus, and 68% of all patients suffered from at least 1 complication. The increase may be the beginning of an epidemic of T2DM in Greenland that has more or less been predicted (4). However, increased awareness of the disease may be part of the explanation of increased incidence of T2DM. The WHO criteria (7) for diagnosing diabetes was implemented in July 2008, and an ongoing Greenland diabetes program has probably also contributed to an increased awareness of the disease in the general population and in the health care system. The complications resulting from diabetes may have led to diagnosis in some cases. The relatively high prevalence of microvascular complications supports the thesis that an increased awareness of diabetes is part of the explanation for the increasing number of new patients. Increasing prevalence of diabetes has been reported among other Indigenous peoples in the circumpolar regions (8–11). The prevalence has been considered higher for Alaska Natives than for Alaskan Inuit (8). However, the increase in prevalence has been highest among the Inuit (8,12). National surveys in Greenland have demonstrated increased frequency of overweight citizens (BMI≥25 kg/m²) in the period from 1993 to 2007 (13). The frequency is higher among females than males (13). It is a likely possibility that the prevalence in Greenland will rise in proportion to the Alaskan Inuit (8).

In this study, the majority of the Greenlanders were females while the opposite is the case for Danes. The prevalence of diabetes among Greenlandic females has been reported as being higher than for Greenlandic males (5). The majority of migrants in Greenland are Danish males living in Nuuk (6). The difference in gender ratio is thus to be expected. However, the gender ratio difference is a limitation of this study. While the group of Greenlandic and Danish males is quite equal in number, there is great difference between the females, with only 7 Danish females compared to 58 Greenlanders. This may camouflage differences between Greenlandic and Danish females.

Patients are considered to be overweight if they have a BMI≥25 kg/m². Ninety-one percent of the patients in this study fell into that category. This percentage is much higher than the norm for the adult population in Greenland based on results from the 2005–2007 population survey, where 54% were reported to have BMI≥25 kg/m² (13). For the adult population in Denmark, 44% have BMI≥25 kg/m² and 11% had BMI≥30 kg/m² (14). It confirms the role of obesity as a major risk factor for diabetes in Greenland.

Blood pressure and biochemical results
The diastolic blood pressure levels were lower among Greenlanders than Danes, which has been reported among healthy Greenlanders and Danes using 24-hour blood pressure measurements (15). The mean levels for HbA1c are quite acceptable for all groups, and are currently at levels comparable with those reported in Alaska after implementation of the special Native diabetes program (16). Fifty-two percent of their diabetes patients had HbA1c<7.0% as the last value
measured within 1 year (16) compared to this study, where 72% of all the patients had HbA1c<7.0% and 9% had HbA1c >9.0 %. The low values may also reflect that the diabetes population as a whole is still “young,” with a mean diabetes duration of only 6 years. Surprisingly, patients with complications had lower levels of serum total and LDL cholesterol in this study. This may reflect the fact that the patients with known complications are treated more intensively and more frequently than those without complications (see Table IV).

**Family history and ethnicity**
Almost half of all the patients in this study (42%) had 1 or more first-degree relatives with diabetes mellitus, with no gender or ethnical differences. This indicates that genetic factors play a role in the development of diabetes among Greenlanders as they do among other peoples. Similar results have been reported among other Inuit populations. Impaired glucose intolerance among 3 Alaskan Inuit populations has been reported to be associated with age, family history of diabetes and obesity (10).

**Smoking**
Forty-three percent of all patients were current smokers. This is lower than reported in the general adult population in Greenland, where 66% of adults were smokers (13). The opposite has been reported in Native American and Alaska Native groups, were patients with diabetes were more likely to be smokers (29.8%) than those without diabetes (18.8 %) (17). Nevertheless, the frequency is somewhat lower than what was found among the patients in this study.

Eighty percent of the patients were ever smokers, and thus more than half of the ever smokers had quit smoking. However, the frequency of smoking among patients with diabetes is still very high. Smoking has been reported to be linked to the development of diabetes (18), micro- and macrovascular complications and impaired metabolic control (19–21). We found no significance between smoking and diabetic complications. This may be due to the relatively low number of patients in this study combined with the high rate of exposure, which provides limited power for this analysis.

**Lifestyle**
High physical activity exceeding 30 minutes a day was observed for 69% of the patients, which is lower than the results found in the general population in Greenland where 86% of the adults were reported to have at least 30 minutes of physical activity daily (13). In Denmark, 27% of the adult population report moderate to hard physical activity for at least 4 hours a week in their leisure time, while 13% report being inactive (14). The relatively high number of patients with high physical activity represented in this study and in the population survey in Greenland (13) may reflect that physical activity at work and during transportation was included in addition to physical activity in leisure time (13). Sixty percent of the patients express a healthy eating pattern, with no differences between the subgroups. No differences concerning weekly alcohol intake were observed between the subgroups. The majority of the patients thus seemed to have focus on lifestyle factors, but improvements for the last third of the patients may need more attention.
Drug therapy

Twenty-four percent of the patients did not receive any blood glucose-lowering drugs and were treated with lifestyle changes alone, whereas 72% were treated with oral hypoglycemic agents and 14% with insulin. This level of treatment can be compared to the baseline values for a study of 160 patients with T2DM and persistent microalbuminuria randomized to either conventional therapy or intensive therapy (22). They reported baseline values for the group in conventional therapy at 26% (no glucose-lowering drugs), 61% (oral hypoglycemic agent) and 14% (insulin). At the end of observation (mean treatment period 7.8 years) only 5% did not receive any glucose-lowering drug and 42% where treated with insulin. Eighty-nine percent of the patients in this study received lipid-lowering agents, which is comparable with the intensive group at the end of the follow-up where 84% received statins and 2% fibrates (22). Seventy-seven percent were being treated with ACE inhibitors or ARBs and 63% with low-dose aspirin (75 mg a day) compared to 91% and 85% in the intensive group at the end of observation (22).

The patients in Nuuk thus seemed to be treated quite intensively according to the guidelines, taking into account that the patients in Nuuk have had diabetes for shorter time periods and not all of them have had persistent microalbuminuria as in the other study (22).

Complications

Despite a relative short diabetes duration, 68% of the patients had at least 1 complication. This could indicate a delay in diagnosis. The number of complications was associated with duration of diabetes and low physical activity. This could indicate that healthy lifestyle with physical activity may influence the development of complications positively, but may also reflect that some of the patients with complications are less able to be physically active. Recently, a study on diabetic rats has suggested a protective effect from swimming exercise on diabetic peripheral neuropathy (23). A possible preventive effect of exercise on the development of diabetic complications needs greater attention in the future. Stroke has been reported to be more frequent among Inuit than Natives with diabetes (8). Furthermore, females had a higher stroke incidence than males (8). The total number of patients with macrovascular complications in this study is low and limits the possibility to make a final conclusion for Greenlandic diabetes patients. The number of macrovascular complications among Greenlanders with diabetes is not fully described in this study, since any fatal complication is obviously not included in the prevalent diabetes population in Nuuk. Follow-up on macrovascular complication is important for the future. Two cases of diabetic foot ulcers (1 Dane and 1 Greenlander) do not allow any final conclusions there, either.

Retinopathy was demonstrated in 14% of the patients (almost exclusively background retinopathy) and was correlated to duration of diabetes, Danish ethnicity, higher HbA1c, lower LDL cholesterol and lower alcohol consumption. Greenlanders may be less prone to retinopathy than Danes. However, the small number of patients with retinopathy limits the strength of this statement. The United Kingdom Prospective Diabetes Study reports a frequency of retinopathy at 22% after 6 years with diabetes (24).

Patients with retinopathy had significantly higher levels of HbA1c than patients without,
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and they were more likely to be treated with insulin. A high level of HbA1c is a well-established risk factor for developing retinopathy in patients with T2DM (24). High HbA1c seems to be a risk factor for retinopathy among Greenlanders as well. Peripheral neuropathy was demonstrated in 51% of the patients. While the frequency was higher for males than for females, no ethnic differences were observed. Peripheral sensory neuropathy has recently been documented as being associated to retinopathy in Swedish diabetes patients (25). They also demonstrated a higher risk of peripheral vascular disease among patients with neuropathy and no retinopathy (25). Neuropathy is also one of the factors in developing diabetic foot ulcers (26), and the high rates of neuropathy gives rise to concern for future development of retinopathy, peripheral vascular disease and diabetic foot ulcers.

No patients with end-stage renal disease were found. However, microalbuminuria was found in 43% of the patients. Microalbuminuria is a well-established risk factor for cardiovascular disease (27–28) and the high frequency is a matter of concern for the future development of complications among patients. The relatively intense therapy with ACE inhibitors and ARBs seems to be indicated. Among Alaska Natives, end-stage renal disease is reported to be lower than rates among other Native Americans. Alaska Natives had the highest incidence, while the Inuit had the lowest incidence (11).

Conclusion
The majority of the Greenlandic patients (57%) where diagnosed within the last 3 years. However, 68% of all the patients suffered from at least 1 complication. The number of complications was significantly correlated to the duration of diabetes (p=0.008) and physical inactivity (p=0.037). Smoking is frequent among the patients (43%). The majority of the patients seemed to follow a healthy lifestyle, but the possibility of further improvements should be explored. The prevalence of complications did not seem to differ much between Greenlanders and Danes. Retinopathy was, however, correlated to Danish ethnicity. The increase in patients with T2DM and the high number of patients with risk factors like smoking and microalbuminuria requires ongoing attention. Efforts to reduce smoking rates should be considered.

Acknowledgements
We want to express our thanks to Novo Nordisk A/S for their generous financial support, and to our dear colleagues Knut Borch-Johnsen and Karin Ladefoged for their skilful help and advice and our dear colleague Peter Bjerregaard for his inspiration and assistance with the questionnaire.

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