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# Prevalence of cardiovascular and other selected diseases among Greenlanders with and without type 2 diabetes

Lise Lyngbak Klockmann [a*], Emma Marie Kragh Tøttenborg[a*], Marie Balslev Backe[b,c,d], Marit Eika Jørgensen[b,c,d,e] and Michael Lynge Pedersen[b,c,e]

[a]Department of Public Health, Aarhus University, Aarhus, Denmark; [b]Queen Ingrid's Hospital, Steno Diabetes Center Greenland, Nuuk, Greenland; [c]Greenland Center for Health Research, Institute of Health and Nature, University of Greenland, Nuuk, Greenland; [d]Department of Clinical Epidemiology, Steno Diabetes Center Copenhagen, Herlev, Denmark; [e]Department of Public Health, University of Copenhagen, Copenhagen, Denmark

**ABSTRACT**

This study aims to estimate the prevalence of cardiovascular disease, kidney disease, and other selected diseases including hypertension, atrial fibrillation, asthma, chronic obstructive lung disease, osteoarthritis, osteoporosis, psoriasis and depression among Greenlanders living in Nuuk with and without type 2 diabetes (T2D). The study was designed as a cross-sectional case-control study based on data from the electronic medical record (EMR) in Greenland. Persons with a registered T2D diagnosis in EMR and residence in Nuuk ($N = 435$) were included. The prevalence of cardiovascular disease was 17.9% among persons with T2D and significantly higher compared to the control group (10.1%). In addition, our results showed a significantly higher prevalence of ischaemic heart disease, hypertension, heart failure, atrial fibrillation, osteoarthritis and psoriasis among persons with T2D compared to the control group.Our study found a higher prevalence in five out of 10 selected diseases in regularly followed persons with T2D in Nuuk compared to unselected controls. This enlightens the importance of a broad multifaceted approach in combination of changing primary health care to focus on early detection of controllable risk factors and chronic conditions care in Artic Greenland.

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## Introduction

Type 2 diabetes (T2D) is a severe common chronic disease affecting millions of people worldwide. In 2021, the International Diabetes Federation estimated that the overall prevalence of diabetes was 537 million people with T2D accounting for 90% of diabetes cases [1].

T2D is characterised by hyperglycaemia and is associated with development of micro- and macrovascular complications. Microvascular complications are damage to small blood vessels, which can lead to nephropathy, retinopathy, and neuropathy, and can result in amputations [2]. Macrovascular complications are damage to arteries and can lead to stroke, peripheral arteriosclerosis (PA) [3], and ischaemic heart disease (IHD) with the risk of developing myocardial infarction (MI) [2]. More recently, T2D was found to be associated with several additional medical conditions including heart failure (HF) [4], atrial fibrillation (AF) [5], asthma [6], chronic obstructive pulmonary disease (COPD) [7], osteoarthritis [8], osteoporosis [9], psoriasis [10] and depression [11].

Globally, the management of multimorbidity defined as living with two or more chronic health conditions remains a challenge for health care systems designed around single conditions. Yet, awareness of co-morbidities requires that these conditions are diagnosed and preferably also labelled with the proper diagnosis code in the electronic medical record (EMR). In Greenland, several chronic conditions remain underdiagnosed [12–14]. Systematic diagnose coding has been limited to patients with diabetes, where national diabetes coding has been monitored since 2008, and patients were admitted to the department of internal medicine or the department of psychiatry at the national hospital, Queen Ingrid Hospital [15], in Nuuk. Thus, almost 40% of patients with the diagnosis atrial fibrillation were not labelled the diagnosis in 2020 [16]. However, since 2021 focus on diagnosis coding has increased [17]. Thus, in Nuuk, diagnosis coding became mandatory for physicians in Queen Ingrid Health Care Center (QIHC) and for both nurses and

**CONTACT** Lise Lyngbak Klockmann EMKTLLK@gmail.com; Emma Marie Kragh Tøttenborg emma.marie.tot@gmail.com Aarhus University, Bogensegade 9, 4tv, 8000 Aarhus, Denmark
*Lise Lyngbak Klockmann and Emma Marie Kragh Tøttenborg have contributed equally for this paper and is therefore seen as first co-authors.

physicians at Steno Diabetes Center Greenland (SDCG). This was followed by increased focus on diagnosis coding at the outpatient clinic of both internal medicine and psychiatry at QIH. Thus, in 2023, almost 80% of patients diagnosed with ulcerative colitis were labelled the proper diagnosis code at least once indicating increased focus on diagnosis coding in the outpatient clinic at department of internal medicine. Furthermore, in 2021, around 92,000 contacts were diagnosed coded in the primary health care setting in Nuuk compared to around 32,000 contacts in the rest of Greenland indicating that the most consultations are now diagnosis coded in Nuuk [17]. Consequently, focus on awareness of multi-morbidity may be facilitated in the near future.

In Greenland, the prevalence of diabetes has increased since the turn of century, as a result of the increasing age and lifestyle changes caused by the transition from a traditional hunting society to a more westernised modern society [18,19]. In addition, recent studies suggest that almost one out of five diabetes cases in Greenland may be associated with genetic variants including an Inuit-specific diabetogenic TBC1D4 p. Arg684Ter variant and a frequent variant in HNF1α associated to Mature Onset Diabetes of the Young [20–22]. Consequently, the prevalence of complications from T2D and other co-morbidities among Inuit could potentially vary from T2D among Europeans and other populations. In accordance, the prevalence of retinopathy among persons with T2D in Greenland has been reported low around 10%, while neuropathy has been observed commonly, around 50% [21]. Also, the prevalence of nephropathy has been reported relatively low, around 7% among persons with diabetes in Greenland [18,21]. Furthermore, recent studies have documented no increased risk of neither cardiovascular disease nor albuminuria associated with the TBC1D4 variant [23,24]. However, the prevalence of other co-morbidities remains unexplored due to the former limited use of diagnosis coding in the health care system Greenland.

Thus, the aim of this study was to estimate the prevalence of cardiovascular disease, kidney disease, and other selected diseases including hypertension, AF, asthma, COPD, osteoarthritis, osteoporosis, psoriasis, and depression among Greenlanders living in Nuuk with and without T2D.

## Material and methods

The study was a performed as a cross-sectional case-control study based on data from the EMR in Greenland 29 March 2022.

### Setting

Greenland is the largest island in the world, and the population is sparsely distributed with approximately 56,000 people living alongside the coast in towns and small settlements.

The health care system in Greenland is divided into five regions. A regional health care centre is located in the largest town of each region and a number of local health care clinics and health stations are located in towns and settlements. Health care services and prescription medicine are offered free of charge in all of Greenland.

The capital of Greenland, Nuuk, with a population of almost 20,000 citizens, is located in the largest region: Sermersooq. Queen Ingrid's Hospital in Nuuk is the national hospital for severe situations that cannot be handled at the other regional hospitals [15]. Primary health care service for citizens of Nuuk is managed from QIHC. SDCG is responsible for management of diabetes persons in all of Greenland. Persons with T2D are offered continuous control minimum once a year including measurement of weight, height, blood pressure, and blood samples for haemoglobin A1C ($HbA_{1c}$), cholesterols and lipids. Urine is tested for albuminuria. Furthermore, persons with T2D are offered an annual foot examination and every second year they are offered an evaluation of retinal photography by an ophthalmologist.

The International Classification of Primary Health Care, second edition (ICPC-2) or International Classification of Diseases $10^{th}$ revision (ICD-10) is used at QIHC and SDCG after each consultation. International Classification of Diseases $10^{th}$ revision (ICD-10) is always used after discharge from QIH and sometimes in the outpatient clinics of the department of internal medicine and the department of psychiatry QIH. Only, persons and controls living in Nuuk were included due to the limited use of diagnosis coding outside Nuuk [17].

### Study population

The study included Greenlanders diagnosed with T2D and a permanent address in Nuuk, Greenland. Patients were considered as having T2D if diagnosed with T90 (ICPC-2) and/or E11 (ICD 10) at least one time in the EMR either as inpatient or outpatient. Patients were considered Greenlanders if born in Greenland. In total, 435 T2D persons were registered, consisting of 242 women and 193 men. The control group was found by matching gender and age within Greenlanders with a permanent address in Nuuk (242 women and 192 men). Data were extracted the same way and for the same period for both groups.

### Definition of variables

Information regarding age, height, weight, body mass index (BMI), blood pressure, $HbA_{1C}$, low-density lipoprotein (LDL), high-density lipoprotein (HDL), total-cholesterol, triglyceride, estimated glomerular filtration rate (eGFR), duration of diabetes and smoking status was extracted. Only the most recent values in relation to extraction day and only data recorded standardised in the EMR or in the laboratory card were included. Age was set as age at date of extraction. BMI was calculated from recorded weight and height. Weight and height followed the defined standard guidelines where the patient wore light clothes and no other outerwear shoes. Duration of diabetes was calculated in whole years as the date of extraction minus the date by which the patient was diagnosed with T2D. For blood pressure, home blood pressure was used, and in absence of home measurement, we used consultation measurement. Blood pressure was measured using the automatic blood pressure Easy Rapid device from PiC Solutions. $HbA_{1c}$ levels and eGFR were measured in venous blood using a Tosoh G8 hPLC analyser. Blood lipids was analysed using an Architect8000 (abbott diagnostics). All analyses were performed at The Central Laboratory at Queen Ingrid's Hospital, which is a member of the Danish Quality Control System for laboratories [25].

### Definitions of cardiovascular and other diseases

In this study, diagnosis codes were used to estimate the prevalence of complications and co-morbidities. Persons were considered having T2D if one of these diagnosis codes was present at least one time in the EMR (Table 1). Likewise, persons with T2D and controls were considered to have a co-morbidity if one of these diagnosis codes was present at least one time in the EMR (Table 1). All the selected diagnoses were included whenever administered before or after the diagnosis of diabetes. Both diagnoses given to inpatients and outpatients were included. In addition, persons were considered having kidney disease if eGFR was <60 mL/min since chronic kidney is common in Greenland but rarely labelled the proper diagnosis code according to recent report diagnosis [26]. Due to technical issues, valid information on urine albumin creatinine ratio was unfortunately not available for the study.

Cardiovascular diseases were defined as having one or more of the diagnoses: stroke, PA, IHD including MI (Table 1).

### Statistical analyses

Descriptive data were analysed using means and standard deviation (SD) and values from the T2D and control group were compared using students t-test (two-tailed). In case of non-normally distributed data, medians with interquartile range (IQR) were used and compared using Mann-Whitney U Test.

The estimated prevalence of co-morbidities was determined according to gender for the T2D and control group with a 95% confidence interval (95% CI). QQ-plots were used to check for normality. Logistic regression was used to study the association between diabetes, age, gender, BMI and comorbidities and smoking. P-values below 0.05 were considered significant.

## Results

Basic characteristics of persons with T2D and the control group are shown in Table 2.

Overall, we observed a lower rate, around 50–60%, of data registrations among controls compared to 90% or above among persons with T2D.

**Table 1.** ICPC-2: the international classification of primary health care, 2nd edition, ICD-10: international classification of diseases, 10th revision.

| Disease/comorbidity | ICPC-2 | ICD-10 |
|---|---|---|
| Diabetes type 2 | T90 | E11, E12, E13, E14 |
| Stroke | K90 | I60, I61, I62, I63, I64 |
| Ischemic heart disease | K74, K75, K76 | I20-I25 |
| Acute myocardial infarction | K75 | I21 |
| Heart failure | K77 | I50, I11, I13 |
| Hypertension | K86, K87 | I11, I12, I13, I15, I16 |
| Atrial fibrillation | K78 | I48 |
| Asthma | R96 | J45 |
| Chronic obstructive lung disease | R95 | J43 |
| Osteoarthritis | L89, L90, L91 | M16, M17, M18, M19 |
| Osteoporosis | L95 | M80, M81, M82 |
| Psoriasis | S91 | L40 |
| Depression | P76 | P76 F32, f33 |

**Table 2.** Basic characteristics of persons with T2D and controls.

| | Persons with T2D | | Control group | | |
|---|---|---|---|---|---|
| | Total | | Total | | |
| | Mean (SD) | N | Mean (SD) | N | p |
| Age (years) | 61 (12.0) | 435 | 62 (11.9) | 434 | 0.931 |
| Height (cm) | 164 (9.0) | 426 | 163 (9.1) | 228 | **0.025** |
| Weight (kg) | 86.7 (20.9) | 428 | 75.0 (17.7) | 240 | **<0.001** |
| BMI (kg/m [2] | 31.9 (7.1) | 426 | 27.9 (6.6) | 228 | **<0.001** |
| Blood pressure (mm Hg) | | | | | |
| – systolic | 134 (16.6) | 429 | 134 (16.9) | 243 | 0.886 |
| – diastolic | 79 (10.2) | 429 | 80 (10.0) | 243 | 0.815 |
| $HbA_{1c}$ (mmol/mol) | 53.9 (15.7) | 434 | 40.6 (3.8) | 316 | **<0.001** |
| LDL-cholesterol (mmol/l) | 2.6 (1.1) | 429 | 3.2 (1.3) | 262 | **<0.001** |
| HDL-cholesterol (mmol/l) | 1.1 (0.4) | 429 | 1.4 (0.6) | 262 | **<0.001** |
| Total-cholesterol (mmol/l) | 4.4 (1.1) | 429 | 4.9 (1.2) | 262 | **<0.001** |
| eGFR (mL/min) | 75.6 (17.3) | 433 | 76.5 (16.3) | 346 | 0.428 |
| Duration of diabetes (years) | 6 (6.0) | 431 | – | – | – |
| | *Median (IQR)* | *N* | *Median (IQR)* | *N* | *p* |
| Triglyceride (mmol/l) | 2.0 (1.7) | 429 | 1.5 (1.2) | 262 | **<0.001** |
| | *% (n)* | *N* | *% (n)* | *N* | *p* |
| Daily smokers | 38.3 (165) | 431 | 41.4 (94) | 227 | 0.435 |

Compared to the control group, persons with T2D had a significantly higher BMI (31.9 $kg/m^2$ vs. 27.9 $kg/m^2$, $p < 0.001$) and levels of $HbA_{1c}$ (53.9 vs. 40.6 mmol/mol, $p < 0.001$). In contrast, persons with T2D had lower levels of LDL-cholesterol (2.6 mmol/l vs. 3.2 mmol/l), HDL-cholesterol (1.1 mmol/l vs. 1.4 mmol/l), total-cholesterol (4.4 mmol/l vs. 4.9 mmol/l), and triglyceride (2.5 mmol/l vs. 1.9 mmol/l) compared to the control group ($p < 0.001$). The mean duration of diabetes was six years. No significant difference was observed regarding blood pressure and smoking status.

Table 3 shows the prevalence of cardiovascular and other diseases among persons with T2D compared to the control group. The prevalence of any cardiovascular disease and IHD was significantly higher among persons with T2D compared to the control group with 17.9% vs.

**Table 3.** Prevalence of and associations between co-morbidities and complications among persons with T2D and control group.

| | No adjustments | | | |
|---|---|---|---|---|
| | Persons with T2D (N = 435) % (n) (95% CI) | Control group (N = 434) % (n) (95% CI) | OR (95% CI) | P |
| Cardiovascular diseases | 17.9 (78) (14.33-21.54) | 10.1 (44) (7.30-12.98) | 1.94 (1.30-2.88) | **<0.001** |
| Stroke | 7.8 (34) (5.29-10.34) | 5.1 (22) (3.01-7.13) | 1.59 (0.91-2.76) | 0.102 |
| Ischemic heart disease | 9.0 (39) (6.28-11.65) | 4.8 (21) (2.82-6.86) | 1.94 (1.12-3.35) | **0.018** |
| Myocardial infarction | 3.2 (14) (1.56-4.88) | 3.0 (13) (1.39-4.60) | 1.08 (0.50-2.32) | 0.850 |
| Peripheral atherosclerosis | 0.9 (4) (0.02-1.82) | 0.2 (1) (0.0-0.68) | 4.02 (0.45-36.10) | 0.214 |
| ***Other diseases*** | | | | |
| Kidney disease | 12.2 (53) (9.26-15.65) | 9.0 (39) (6.47-12.08) | 1.10 (0.71-1.71) | 0.067 |
| Hypertension | 77.2 (336) (73.30-81.18) | 36.9 (160) (32.33-41.41) | 5.81 (4.32-7.82) | **<0.001** |
| Heart failure | 6.0 (26) (3.75-8.20) | 3.0 (13) (1.39-4.60) | 2.06 (1.04-4.06) | **0.037** |
| Atrial fibrillation | 10.6 (46) (7.68-13.46) | 6.0 (26) (3.76-8.22) | 1.86 (1.13-3.06) | **0.015** |
| Asthma | 9.0 (39) (6.28-11.65) | 5.5 (24) (2.81-6.84) | 1.68 (0.99-2.85) | 0.053 |
| Chronic obstructive lung disease | 15.9 (69) (12.43-19.30) | 13.4 (58) (3.56-7.93) | 1.22 (0.84-1.18) | 0.298 |
| Osteoarthritis | 13.6 (59) (10.35-16.78) | 8.5 (37) (5.90-11.15) | 1.68 (1.09-2.60) | **0.019** |
| Osteoporosis | 2.1 (9) (0.73-3.41) | 1.2 (5) (0.15-2.16) | 1.81 (0.60-5.45) | 0.290 |
| Psoriasis | 3.0 (13) (1.39-4.59) | 0.5 (2) (0.0-1.10) | 6.65 (1.49-29.67) | **0.013** |
| Depression | 2.5 (11) (1.05-4.00) | 3.5 (15) (1.74-5.17) | 0.73 (0.33-1.60) | 0.424 |

10.1% ($p < 0.001$) and 9.0% vs. 4.8% ($p = 0.018$), respectively.

In addition, a significantly higher prevalence was found for the following other diseases in the T2D group compared to the control group: hypertension (77.2% vs. 36.9%, $p < 0.001$), HF (6.0% vs. 3.0%, $p = 0.037$), AF (10.6% vs. 6.0%, $p = 0.015$), osteoarthritis (13.6% vs. 8.5%, $p = 0.019$) and psoriasis (3.0% vs. 0.5%, $p = 0.013$). All associations remained significant after adjusting for age and sex (data not shown).

## Discussion

The prevalence of several comorbidities including any cardiovascular disease, ischaemic heart failure, hypertension, atrial fibrillation, heart failure, osteoarthritis and psoriasis was significantly higher among persons diagnosed with T2D in Nuuk compared to controls without diabetes indicating high prevalence of multi-morbidity in this group. The prevalence of cardiovascular disease was 17.9% among persons with T2D and high compared to the control group (10.1%).

The prevalence is higher compared to a study from 2018 showing a prevalence of 12.9% among all persons with diabetes in Greenland [18]. To our knowledge, 17.9% is the highest prevalence reported among persons with T2D in Greenland and comparable to a prevalence of 16.4% in a systematic literature review with over 4.5 million persons with T2D from multiple countries [27]. The increasing prevalence may partly be explained by an increased focus on diagnosis coding and awareness of cardiovascular disease with the introduction of SDCG in Nuuk 2020. Additionally, it could be caused by an older population with diabetes and the appertaining duration of diabetes.

### *The potential role of the Greenlandic health care system*

Several explanations for the observed higher prevalence of the selected diseases could be considered. As for the cardiovascular diseases, it may partly be explained by the fact that persons with diabetes are followed regularly with stronger focus on diagnosing co-morbidities and chronic conditions. Undiagnosed chronic conditions in general are a well-documented phenomena in Greenland [13,14,28] more likely affecting the control group and thus associated with an apparent lower risk of some comorbidities. This explanation is supported by the relatively low number of controls, around 50–60%, with a registration of blood pressure, BMI, LDL cholesterol and smoking status compared to registrations on 90% or above among persons with T2D indicating less clinical focus on these risk factors among persons without diabetes.

However, it is unlikely for more severe cases of chronic conditions and acute cases as stroke and MI to be missed. Other less severe chronic conditions with a lower prevalence in the general population may have a higher risk of being neglected, which potentially would lead to detection bias.

Thus, this study suggests that persons with T2D in Nuuk have a higher prevalence of hypertension, HF, osteoarthritis, psoriasis and AF compared to non-diabetic persons, which is in line with global observations reported recently [4,5,8,10,29]. When comparing the prevalence among the T2D group from this study with global studies, they are nearly the same with 13.1% for osteoarthritis [30], 3.4% for psoriasis [31], and 5.3% for AF [32].

Regarding lipids, persons having T2D had significantly lower levels of LDL-cholesterol compared to the control group, likely due to a more frequent use of cholesterol-lowering medication among persons with T2D [18]. Similarly, no difference in mean blood pressure was observed between persons with T2D compared to controls despite higher prevalence of hypertension and higher mean BMI among persons with T2D suggesting that the risk factors have been controlled with antihypertensive drugs. Thus, the use of these drugs have reported higher than in the general population [18].

### *Potential mechanisms affecting the results*

The higher prevalence of e.g. psoriasis and osteoarthritis among the T2D group could be explained by the higher BMI among persons with T2D, since obesity is a well-established risk factor [33,34].

The theory of excess body fat to create low-grade systemic inflammation and insulin resistance seems in evidence for several immunogenic diseases. It leads to pro-inflammatory cytokines increasing the risk of cardiovascular disease and AF [35], and structural damage of the joints leading to osteoarthritis [36]. In case of asthma, it can cause subsequent bronchoconstriction [6,37]. Recent research has investigated the pathophysiology of T2D regardless of being overweight, and a state of chronic hyperglycaemic have been found to induce oxidative stress and an overproduction of pro-inflammatory cytokines as seen for obesity [8,38,39]. The role of high body weight as a possible influencing factor between T2D and other comorbidities is still to be elucidated in future studies. Besides overweight, recent studies found chronic hyperglycaemia and insulin resistance to engender oxidative stress and low-grade inflammation, thus

generating inflammatory biomarkers [40]. These biomarkers have created theories upon shared inflammatory pathways between T2D and other diseases [40–42]. This knowledge calls for integrating awareness and management of multimorbidity.

Finally, the monogenic variants explaining a large part of diabetes in Greenland, may affect the associated cardiometabolic risk and comorbidities and contribute to the differences observed across the compared groups [22–24].

### *Strengths and limitations*

This is the first study comparing the prevalence of macrovascular and other selected diseases among inhabitants in Nuuk with and without T2D.

As mentioned above, the prevalence of the selected diseases among persons without T2D may be underestimated compared to persons with T2D, since persons with a T2D diagnosis in Nuuk are followed by SDCG routinely one to four times a year, in contrast to many other groups of patients with chronic conditions. However, with more than 85% of the population being in contact with the health care system at least once annually [43] with an average of five annual contacts [17], and the fact that mandatory diagnosis coding has been used in the primary clinic since 2020, the underestimation is not the full explanation of the observed difference. On the other hand, overestimation of some diagnosis may also occur since they were included if just applied once. Yet, the size of the overestimation is considered small and with no expected difference between persons with and without diabetes since the physicians at QIH are regularly trained in diagnosis coding system. Moreover, the correctness of cardiovascular diagnoses in Greenland has been found with a high validation [44].

Only persons registered in the EMR were included and no review of medical prescription or medical chart have been assessed, which could have added an extra perspective. In addition, the study population is relatively small, especially for some of the more rare diseases, thereby constraining our statistical power. Furthermore, the control group had a relatively low amount of data in contrast to persons with T2D, thus limiting the statistical power as well. Finally, the observational design of the study and the inclusion of all diagnosis applied at least once detected before or after the diagnosis of diabetes limits the possibility to draw a causal a conclusion.

### *Perspective*

In this study, we have documented high prevalence of multimorbidity among persons with T2D in Nuuk in line with a global trend. This indicates a need to increase focus on multimorbidity including organisation of care, education of health care professionals, combing guidelines with focus on multimorbidity, polypharmacy, and clinical fragility. Furthermore, we have revealed a relatively low focus on detecting common controllable risk factors like blood pressure, LDL cholesterol, and smoking among persons without diabetes. The low registration of these factors may reflect that around two third of all contacts are performed as telephone-, e-health, or administrative contacts without having the patient in the office limiting the possibility to register blood pressure [17]. Furthermore, blood pressure measurements are not always performed in the primary health care setting, and if measured sometimes registered in the text and consequently missed in the data extraction. In fact, even among patient treated with antihypertensive drugs and patients diagnosed with atrial fibrillation the registration of blood pressure measurements have been reported suboptimal in Greenland [45,46].

The combination of changing primary health care towards early detection of controllable risk factors and chronic conditions and increase knowledge about best practices of handling increasing multimorbidity seem necessary in Arctic Greenland. This may also be relevant to health care systems delivering health care service to Indigenous people living in Arctic Canada and Alaska also observing increasing rates of diabetes and other chronic conditions and higher compared to the non-Indigenous population [47–49].

In conclusion, we observed a higher prevalence of several types of comorbidities in regularly followed T2D patients in Nuuk than in unselected controls, which is in line with findings from other countries. This indicates that treatment and control of T2D patients in Greenland need to focus not only on T2D and traditional complications to diabetes, but also on related comorbidities underlining the importance of a broad multifaceted approach towards management of patients with multimorbidity including guidelines on polypharmacy [50]. Additionally, the limited data on common controllable risk factors like blood pressure and smoking calls for an increased focus on prevention in the primary health care system in Greenland.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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## Authors contribution

LLK and EMT was responsible for the study design. MLP, MEJ and MBB contributed to data analysis, description, and interpretation. MLP, MEJ and MBB reviewed draft of the manuscript and approved the final draft for submission.

## ORCID

Lise Lyngbak Klockmann http://orcid.org/0009-0002-8328-4645

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