

## Prevalence of patients treated with anti-diabetic medicine in Greenland and Denmark. A cross-sectional register study

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### ABSTRACT

Diabetes mellitus is a large and growing worldwide health issue. Prior to this publication, a direct comparison of the prevalence of persons treated with anti-diabetic medicine in Greenland and Denmark has not been found. Therefore, the aim of this study is to estimate and compare the age- and gender-specific prevalence of patients treated with anti-diabetic medicine comparing Greenland and Denmark. The study was performed as a cross-sectional register study using data from population and medical registers in Greenland and Denmark. A total of 784 Greenlandic and 215,580 Danish patients treated with anti-diabetic medicine were included. The prevalence of patients aged 20–79 years treated with anti-diabetic medicine in Greenland was 2.6% (95% CI 2.4–2.8), much lower ( $p < 0.001$ ) compared to Denmark with 5.2% (95% CI 5.2–5.2). The difference was less pronounced after excluding those treated with insulin and women below 45 years treated with metformin. In conclusion, this study showed a lower prevalence of patients treated with anti-diabetic medicine in Greenland than Denmark. The main reason may be a much higher prevalence of undiagnosed diabetes in Greenland, particularly among the middle-aged. Differences in awareness of diabetes and access to continued primary healthcare may be contributing factors.

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## Introduction

Diabetes mellitus is an immense, worldwide health issue that is constantly growing. By 2030, diabetes mellitus is expected to be in the top 10 of the leading causes of disease burden worldwide [1], and it has been projected that by then 7.7% of the world's adult population will live with the disease [2]. Prior to 60 years ago, diabetes was not a health issue in Greenland, because the disease was very rarely encountered [3]. However, it has since then, particularly during the last two decades, become certain that Greenland is now on the same course as the rest of the world with its increasing prevalence of diabetes, as indicated in the latest population study showing a prevalence of 6.7% [4]. It is very remarkable that previous studies have shown a prevalence of 70% undiagnosed cases of diabetes mellitus in Greenland [5], and in the latest population study, 40% of the cases were also found to be previously undiagnosed [6]. These results have led to increased focus on the diagnosis of diabetes in Greenland [7], because underdiagnosis of the disease can mean undermedication of these patients with the

probability of an increased risk of diabetes complications [8].

The sales of anti-diabetic medicine in Greenland have been reported to be low compared with other Nordic countries [9]. However, the actual use of anti-diabetic medicine in Greenland, including age- and gender-specific trends remains unexplored. Additionally, it has been shown that the prevalence of diagnosed diabetes in Greenland is still higher among non-Greenlandic males compared with Greenlandic males, while the opposite trend was observed among females [10]. This distinguishes Greenland from other previously colonised countries, which generally have a higher prevalence of diabetes in the indigenous population compared with the non-indigenous population [11]. The majority of the non-indigenous population in Greenland consists of immigrants from Denmark [12], and there has not previously been made any direct comparison of the use of anti-diabetic medicine between Greenland and Denmark.

Therefore, the aim of this study was to estimate and compare the age- and gender-specific prevalence of

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patients in Greenland and Denmark treated with anti-diabetic medicine regardless of the indication triggering a prescription of an anti-diabetic medicine.

## Material and methods

The study was performed as a cross-sectional study using data from population and medical registers in Greenland and Denmark.

### Setting

Greenland is the largest island in the world, and the country has a population of 56,000 people located in 17 towns and approximately 60 settlements along the coast. Greenland was previously a Danish colony and is now a self-governed country as part of the Danish kingdom.

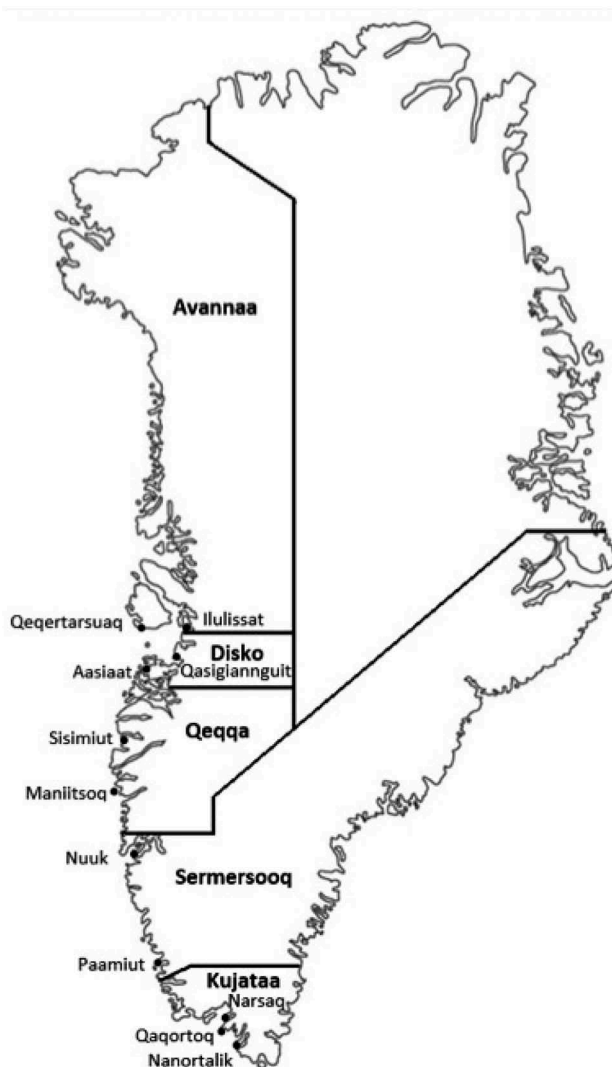
In Greenland, healthcare is free for the inhabitants. The country is divided into 5 healthcare regions covering a number of towns and settlements [13] (see Figure 1). Each town has a primary healthcare centre, whereas minor healthcare units exist in the settlements. Queen Ingrid's hospital is located in the capital, Nuuk, and provides secondary specialised healthcare for the entire country. All medicine requiring a prescription is free of charge for the population and is handed out at the pharmacies, which are located in and are part of the primary healthcare centres.

In Denmark, the healthcare system consists of a primary and a secondary sector. The primary sector consists of the general physicians, who have the authority to refer patients to the secondary sector consisting of the hospitals and other specialised medical units. These healthcare services are also free in Denmark, excluding medicine. Prescribed medicine is available at pharmacies, and there is some subsidised coverage of the expenditures from the healthcare system, but still requires some payment from the individual.

### Study population

The study included patients treated with anti-diabetic medicine, aged 20–79 years and residing in Greenland or Denmark.

In Greenland, the medical data were extracted from the electronic medical record (EMR) using data from 11 towns (see Figure 1), those which have had the new Greenlandic EMR implemented the longest. The population in these 11 towns accounted for 75.9% of the entire Greenlandic population [14]. Anyone with a prescription of anti-diabetic medicine with anatomic classification code (ATC) A10 as of July 2017 was included in the



**Figure 1.** The figure illustrates Greenland's 5 healthcare regions (Avannaa, Disko, Qeqqa, Sermersooq and Kujataa). The 11 towns included in the present study (Qeqertarsuaq, Ilulissat, Aasiaat, Qasigiannnguit, Sisimiut, Maniitsoq, Nuuk, Paamiut, Narsaq, Qaqortoq, Nanortalik) are also illustrated at the map.

Note: The remaining towns in the different healthcare regions are not shown on the map.

analysis [15]. In addition, a subgroup including all patients treated with anti-diabetic medicine excluding insulin and insulin-analogues for all age groups, and metformin for women less than 45 years old, was analysed as a proxy for prevalence of patients treated for type 2 diabetes. The population numbers in the mentioned 11 towns, as of 1st of January 2017, was extracted from Greenland's online statistics bank [14], and this was used as the background population in the study.

In Denmark, the medical data were available in an online medical register, which contains age- and gender-specific data for >99% of all sold anti-diabetic

medicine [16]. Data from 2016 were used in the analyses. The entire population from Denmark's online statistics bank as of the first quarter of 2016 was used as the background population [17].

### Statistics

The age- and gender-specific proportion of patients treated with anti-diabetic medicine in Greenland and Denmark was calculated with 95% confidence intervals. A z-score for the 2 populations was calculated to compare estimates from Greenland and Denmark using the Social Science Statistics online calculator [18]. *P*-values below 0.05 were considered significant.

The study was approved by The Ethics Committee for Medical Research in Greenland (reference 2017–06) and by The Agency for Health and Prevention in Greenland.

### Results

A total of 784 Greenlandic patients and 215,580 Danish patients treated with anti-diabetic medicine were included in the study. The study population consisted of 342 (43.6%) females and 442 (56.4%) males in Greenland and 91,123 (42.3%) females and 124,457 (57.7%) males in Denmark.

Table 1 shows the estimated age- and gender-specific prevalence of patients treated with any anti-diabetic medicine in Greenland and Denmark. The total prevalence for the age group 20–79 years was 2.6% (95% CI 2.4–2.8) in Greenland and significantly lower ( $p < 0.001$ ) compared with the 5.2% (95% CI 5.2–5.2) found in Denmark. No difference in the overall prevalence, ranging from 2.1 to 3.6, was observed between 9 of the 11 towns in Greenland ( $p = 0.090$ ), whereas 2 smaller towns deviated by 1.6 and 4.5%, respectively. The age-specific prevalence was higher in Denmark compared with Greenland in all age groups except in the oldest age groups (70–79 years), where no difference was observed. The total prevalence for males aged 20–79 years was 2.7% (95% CI 2.5–3.0) in Greenland, significantly lower ( $p = 0.007$ ) than the 6.0% (95% CI 6.0–6.0) observed in Denmark. For the females, the total prevalence was 2.4% (95% CI 2.2–2.7) in Greenland and significantly lower ( $p < 0.001$ ) than the 4.4% (95% CI 4.4–4.4) observed in Denmark.

In Denmark, the total prevalence among males (6.0%) was higher ( $p < 0.001$ ) than among females (4.4%), while no significant difference ( $p = 0.072$ ) was observed among males (2.7%) and females (2.4%) in Greenland. Among males, the prevalence was higher in Denmark compared with Greenland for all age groups. Among females, the prevalence was higher in

**Table 1.** Total prevalence of patients treated with anti-diabetic medicine in Greenland and Denmark.

Age, years	Males, % (95 %-CI) (n/N)			Females, % (95 %-CI) (n/N)			Total, % (95 %-CI) (n/N)			p (z-score)
	GRL	DK	p (z-score)	GRL	DK	p (z-score)	GRL	DK		
20–44	0.4 (0.3–0.6) (33/7,793)	1.3 (1.3–1.3) (11,956/ 920,000)	<0.001 (–6.82)	0.5 (0.4–0.7) (39/7,248)	1.5 (1.5–1.5) (13,448/ 895,845)	<0.001 (–6.73)	0.5 (0.4–0.6) (72/ 15,041)	1.4 (1.4–1.4) (25,404/ 1,815,845)	<0.001 (–9.60)	
45–49	1.3 (0.8–2.0) (22/1,677)	4.0 (3.9–4.1) (8,174/203,825)	<0.001 (–5.62)	1.0 (0.6–1.7) (15/1,438)	2.9 (2.8–3.0) (5,795/ 199,814)	<0.001 (–4.19)	1.2 (0.8–1.6) (37/3,115)	3.5 (3.4–3.5) (13,969/ 403,639)	<0.001 (–6.93)	
50–54	3.0 (2.3–3.9) (64/2,106)	6.1 (6.0–6.2) (12,454/ 204,442)	<0.001 (–5.84)	2.3 (1.7–3.1) (42/1,833)	4.2 (4.1–4.3) (8,467/ 201,332)	<0.001 (–4.07)	2.7 (2.2–3.2) (106/ 3,939)	5.2 (5.1–5.2) (20,921/ 405,774)	<0.001 (–6.98)	
55–59	3.6 (2.8–4.6) (64/1,754)	8.5 (8.4–8.7) (15,323/ 179,791)	<0.001 (–7.29)	3.3 (2.4–4.4) (47/1,422)	5.5 (5.4–5.7) (9,971/ 179,683)	<0.001 (–3.69)	3.5 (2.9–4.2) (111/ 3,176)	7.0 (7.0–7.1) (25,294/ 359,474)	<0.001 (–7.79)	
60–64	6.3 (5.0–7.8) (77/1,223)	11.0 (10.9–11.2) (18,347/ 166,766)	<0.001 (–5.25)	5.4 (4.1–7.1) (53/975)	7.0 (6.8–7.1) (11,850/ 170,093)	0.061 (–1.87)	6.0 (5.0–7.0) (130/ 2,198)	9.0 (8.9–9.1) (30,197/ 336,859)	<0.001 (–4.99)	
65–69	9.2 (7.2–11.3) (75/819)	13.3 (13.1–13.4) (22,343/ 168,573)	<0.001 (–3.45)	8.7 (6.6–11.2) (53/612)	8.4 (8.3–8.5) (14,737/ 175,775)	0.803 (0.25)	8.9 (7.5–10.5) (128/ 1,431)	10.8 (10.7–10.9) (37,080/ 344,348)	0.026 (–2.22)	
70–74	11.0 (8.6–13.8) (64/583)	15.5 (15.3–15.7) (21,803/ 140,598)	0.003 (–3.02)	11.2 (8.5–14.4) (53/474)	10.0 (9.8–10.1) (15,118/ 151,845)	0.373 (0.89)	11.1 (9.2–13.1) (117/ 1,057)	12.6 (12.5–12.7) (36,921/ 292,443)	0.128 (–1.52)	
75–79	14.9 (11.0–19.5) (43/289)	15.8 (15.6–16.0) (14,057/89,001)	0.667 (–0.43)	14.2 (10.3–18.8) (40/282)	11.2 (11.0–11.4) (11,737/ 104,872)	0.112 (1.59)	14.5 (11.7–17.7) (83/571)	13.3 (13.2–13.5) (25,794/ 193,873)	0.390 (0.87)	
Total	2.7 (2.5–3.0) (442/ 16,244)	6.0 (6.0–6.0) (124,457/ 2,072,996)	<0.001 (–17.58)	2.4 (2.2–2.7) (342/ 14,284)	4.4 (4.4–4.4) (91,123/ 2,079,259)	<0.001 (–11.58)	2.6 (2.4–2.8) (784/ 30,528)	5.2 (5.2–5.2) (215,580/ 4,152,255)	<0.001 (–20.62)	

Denmark compared with Greenland in the younger age groups, while no difference was observed for the older age groups, those above 60 years old.

Table 2 shows the prevalence of patients treated with anti-diabetic medicine, excluding insulin and insulin analogues for all age groups, and metformin for women younger than 45 years old. Still, the overall prevalence (20–79 years) was higher in Denmark, 4.4%, compared with 2.3% in Greenland ( $p < 0.001$ ). However, the difference, 2.1%, was less pronounced than in the comparison of prevalence of those using any anti-diabetic medicine, 2.6%. Among males, the prevalence was higher in Denmark in all age groups except the age group of those 75–79 years. Among females, the prevalence was higher in Greenland in the youngest age group (20–44 years) while the opposite was observed in the middle age groups (45–59 years). Furthermore, no difference was observed in the older age groups among females.

## Discussion

The prevalence of patients treated with anti-diabetic medicine in Greenland was 2.6% and was much lower compared with the 5.2% observed in Denmark. The same tendency, but less pronounced, 2.3% versus 4.4%, was observed for the prevalence of patients

treated with anti-diabetic medicine excluding insulin and insulin analogues for all age groups, and excluding metformin for women less than 45 years old. The lower prevalence in Greenland than in Denmark was observed for both genders in most age groups with the oldest age groups as an exception. A higher prevalence of anti-diabetic medicine prescribed in Greenland was observed only among females aged 20–45 years old, and only after excluding insulin and metformin.

## Strengths and limitations

The major strength of this study is that the entire population of Denmark and a major part of the population in Greenland was included. Additionally, this was the first study comparing these data from Greenland and Denmark. Still, the absolute number of patients in the younger Greenlandic age groups was small and results must be interpreted with some reservations.

Also, limitations were introduced in the selection of the Greenlandic study population, which included the entire population of the 11 previously mentioned towns in Greenland, thus accounting for 75.9% of the Greenlandic population. The prevalence of diabetes has previously been reported higher in settlements than in towns [19]. Thus, in this study where only towns were

**Table 2.** Prevalence of patients treated with anti-diabetic medicine, excluding insulin and insulin analogues for all age groups and metformin for women less than 45 years old, in Greenland and Denmark.

Age, years	Males, % (95 %-CI) (n/N)			Females, % (95 %-CI) (n/N)			Total, % (95 %-CI) (n/N)		
	GRL	DK	p (z-score)	GRL	DK	p (z-score)	GRL	DK	p(z-score)
20–44	0.2 (0.1–0.3) (16/7,793)	0.7 (0.6–0.7) (6,142/920,000)	<0.001 (–5.00)	0.2 (0.1–0.4) (16/7,248)	0.1 (0.1–0.1) (884/895,845)	0.001 (3.28)	0.2 (0.1–0.3) (32/ 15,041)	0.4 (0.4–0.4) (7,026/ 1,815,845)	<0.001 (–3.43)
45–49	1.1 (0.6–1.7) (18/1,677)	3.1 (3.0–3.1) (6,251/203,825)	<0.001 (–4.73)	0.9 (0.5–1.5) (13/1,438)	2.3 (2.2–2.3) (4,538/199,814)	<0.001 (–3.47)	1.0 (0.7–1.4) (31/3,115)	2.7 (2.6–2.7) (10,789/ 403,639)	<0.001 (–5.80)
50–54	2.6 (1.9–3.3) (54/2,106)	5.1 (5.0–5.2) (10,393/ 204,442)	<0.001 (–5.25)	2.1 (1.5–2.8) (38/1,833)	3.5 (3.5–3.6) (7,119/201,332)	<0.001 (–3.38)	2.3 (1.9–2.9) (92/3,939)	4.3 (4.3–4.4) (17,512/ 405,774)	<0.001 (–6.10)
55–59	3.5 (2.7–4.4) (61/1,754)	7.4 (7.2–7.5) (13,240/ 179,791)	<0.001 (–6.22)	3.0 (2.2–4.1) (43/1,422)	4.8 (4.7–4.9) (8,642/179,683)	0.002 (–3.14)	3.3 (2.7–4.0) (104/ 3,176)	6.1 (6.0–6.2) (21,882/ 359,474)	<0.001 (–6.61)
60–64	6.1 (4.8–7.5) (74/1,223)	9.8 (9.6–9.9) (16,295/ 166,766)	<0.001 (–4.37)	5.1 (3.8–6.7) (50/975)	6.2 (6.0–6.3) (10,490/ 170,093)	0.177 (–1.35)	5.6 (4.7–6.7) (124/ 2,198)	8.0 (7.9–8.0) (26,785/ 336,859)	<0.001 (–3.99)
65–69	8.4 (6.6–10.5) (69/819)	12.0 (11.7–12.1) (20,079/ 168,573)	0.002 (–3.07)	8.5 (6.4–11.0) (52/612)	7.5 (7.4–7.6) (13,191/ 175,775)	0.352 (0.93)	8.4 (7.0–10.0) (121/ 1,431)	9.7 (9.6–9.8) (33,270/ 344,348)	0.124 (–1.54)
70–74	10.2 (8.0–13.0) (60/583)	14.0 (13.8–14.2) (19,638/ 140,598)	0.010 (–2.56)	10.5 (8.0–13.7) (50/474)	9.0 (8.8–9.1) (13,599/ 151,845)	0.226 (1.21)	10.4 (8.6–12.4) (110/ 1,057)	11.3 (11.3–11.5) (33,237/ 292,443)	0.327 (–0.98)
75–79	13.1 (9.5–17.6) (38/289)	14.0 (13.8–14.2) (12,456/89,001)	0.682 (–0.41)	12.8 (9.1–17.2) (36/282)	9.9 (9.7–10.1) (10,379/ 104,872)	0.107 (1.61)	13.0 (10.3–16.0) (74/571)	11.8 (11.6–11.9) (22,835/ 193,873)	0.384 (0.87)
Total	2.4 (2.1–2.6) (390/ 16,244)	5.0 (5.0–5.0) (104,494/ 2,072,996)	<0.001 (–15.35)	2.1 (1.9–2.4) (305/ 14,284)	3.7 (3.7–3.7) (77,033/ 2,079,259)	<0.001 (–9.91)	2.3 (2.1–2.5) (695/ 30,528)	4.4 (4.4–4.4) (181,527/ 4,152,255)	<0.001 (–34.68)

included, the prevalence of patients treated with anti-diabetic medicine in Greenland can possibly be underestimated. However, since only 15% of the population lives in settlements, the size of the underestimation was expected to be of less significance.

Furthermore, it must be noted that the EMR, from which information on the Greenlandic patients has been drawn, has been implemented only recently – from 2015 to 2017 – and, therefore, it cannot be excluded that there might be some patients with diabetes who have received a prescription of anti-diabetic medicine prior to the implementation of the EMR in their town. Some towns have only had the new EMR system for the last several months of the mentioned time span. This would also cause a trend towards an underestimation of the prevalence. However, these certain towns were chosen because they had the longest running implementation of the new Greenlandic EMR – at least 4 months – and, therefore, offered a higher certainty that all patients with diabetes had received a prescription *after* the implementation, which overall lowered the risk of underestimation.

Furthermore, the comparison of the Greenlandic and the Danish population must be made with some reservations, since the patients in Greenland were identified through the medical register as all patients who were prescribed anti-diabetic medicine, while in Denmark, the number of patients was identified through individual *purchases* of anti-diabetic medicine. There is the risk that some patients in Denmark who had received a prescription of anti-diabetic medicine, never actually purchased their medicine at the pharmacy, which would cause a missing inclusion in this study. A previous study of primary non-adherence in general practice in Denmark has shown that 4.0% of patients in Denmark, of those who have been diagnosed with diabetes, do not pick up their anti-diabetic medicine when a new treatment is prescribed [20]. If a similar trend remains after the initiation of the treatment, this would cause an underestimation of the number of patients in Denmark.

Also, not all patients diagnosed with diabetes are treated with anti-diabetic medicine. Thus, in both Denmark and Greenland, around a quarter of patients diagnosed with diabetes do not receive anti-diabetic medicine [21,22]. Thus, a prevalence based on anti-diabetic medicine will tend to underestimate the prevalence of diagnosed diabetes. On the other hand, some anti-diabetic medication, metformin for PCO and GLP-1 analogues for obesity, may be prescribed even though unrelated to diabetes thus leading to overestimation. However, the sub-analysis excluding insulin for

all and metformin among younger women minimises the effect of this overestimation.

In summary, there is a risk of underestimating the number of patients with diabetes in both Greenland and Denmark in studies based on anti-diabetic medicine prescriptions. Still, the age- and gender-specific comparison of prevalence of patients treated with anti-diabetic medicine can provide some valuable information about diabetes management in Greenland.

### **Prevalence**

The lower prevalence of patients treated with anti-diabetic medicine in Greenland compared with Denmark may reflect differences both in the healthcare systems and between the populations.

First of all, awareness of diabetes and access to continued primary healthcare may be due to the differences in the 2 healthcare systems. In Denmark, diabetes care is provided by private practitioners – often those with a long-term relation to the patient – or in specialised diabetes clinics and hospitals. In contrast, most towns in Greenland are staffed with physicians working only a short time in Greenland. Thus, obviously, acute conditions will be more in their focus than the long-term managing of chronic conditions and preventive medicine, including screening for undetected diabetes. Furthermore, diabetes used to be a seldom-occurring disease in Greenland and the attention given to the diabetes found among Greenlanders may not yet be widespread among all short-term healthcare workers. This may in part explain the lower use of anti-diabetic medicine in Greenland despite the high prevalence of diabetes reported in population surveys. The most recently reported prevalence of undiagnosed diabetes in Greenland is around 40% [4]. This is remarkably higher than the 24% recently reported in Denmark [23]. Thus, this difference, certainly, also contributes to the differences observed in prevalence of prescribed anti-diabetic medicine between Denmark and Greenland.

Also, other systematic differences in the delivery of healthcare between Greenland and Denmark are suggested in the presented results. Among young females, 20–44 years old, the prevalence of patients treated with any anti-diabetic medicine was higher in Denmark than in Greenland, while the opposite was observed when excluding insulin and metformin. Because metformin is primarily used for polycystic ovary syndrome (PCO) in this age and gender group, the observation indicates higher focus on PCO in Denmark compared with Greenland, where only 1 department of gynaecology exists, located in Nuuk. Furthermore, all pregnant

women in Greenland, but not in Denmark, are routinely tested for diabetes in the first trimester using glycosylated haemoglobin. This may contribute to explaining the higher prevalence of women treated for diabetes in Greenland in the age group 20–44 years old.

Second, the difference observed may partly be explained by a higher prevalence of type 1 diabetes in Denmark compared with Greenland. Thus, the difference was less pronounced after excluding insulin in the analysis. This is in-line with a former study indicating low prevalence of type 1 diabetes in Greenland [24].

In particular, no difference was observed in the older age groups in the sub-analysis. This could indicate that the prevalence of undiagnosed and untreated diabetes in Greenland is of a lesser magnitude among the elders compared with the middle aged.

In conclusion, this study has shown a lower prevalence of patients treated with anti-diabetic medicine in Greenland compared with Denmark. The main reason may be a much higher prevalence of undiagnosed diabetes in Greenland, in particular among the middle aged. Differences in awareness of diabetes, as well as access to continued primary healthcare, may contribute and will need further attention in Greenland.

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