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ATRIAL FIBRILLATION IN GREENLAND

BY
NADJA ALBERTSEN

PhD Thesis 2024

AALBORG UNIVERSITY
DENMARK

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PhD Thesis 2024

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The implications of life in the polar areas have been my main research fields. Topics range from vaccinations, infectious diseases, aging and cardiac arrhythmias in Greenland to life in isolation, confinement and extreme cold in Antarctica.

Peer-reviewed publications published between 2020 and 2023 and not included in the thesis:

Ischemic Strokes Are Common Among Young Greenlanders: A Cross-Sectional Study.
Albertsen N, Hansen AS, Skovgaard N, Riahi S, Pedersen ML, Andersen S.
Stroke. 2023 Oct;54(10):e438-e439.

The influence of Scandinavian presence on Greenlandic lactase persistence.
Niclasen, S, Andersen S, **Albertsen N**, Krarup HB.
Scand J Gastroenterol. 2023 Apr;58(4):349-353.

Polypharmacy and potential drug-drug interactions among Greenland's care home residents.
Albertsen N, Sommer TG, Olsen TM, Prischl A, Kallerup H, Andersen SS.
Ther Adv Drug Saf. 2022 Jun 26;13:20420986221103918.

The prevalence of patients treated for osteoporosis in Greenland is low compared to Denmark.
Sten KA, Højgaard EE, Backe MB, Pedersen ML, Skovgaard N, Andersen S, **Albertsen N**.
Int J Circumpolar Health. 2022 Dec;81(1):207847

Who lives in care homes in Greenland? A nationwide survey of demographics, functional level, medication use and comorbidities.
Albertsen N, Olsen TM, Sommer TG, Prischl A, Kallerup H, Andersen S.
BMC Geriatr. 2021 Sep 18;21(1):500.

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Albertsen N, Lynge AR, Skovgaard N, Olesen JS, Pedersen ML
Int J Circumpolar Health. 2020 Dec,79(1):1721983.

Assessment of the effects of isolation, confinement and hypoxia on spaceflight piloting performance for future space missions - The SIMSKILL experiment in Antarctica.
Bruguera MB, Fink A, Schröder V, Bermúdez SL, Dessy E, van den Berg F, Lawson G, Dangoisse C, Possnig C, **Albertsen N**, Pattyn N, Ewald R.
Acta Astronautica. Nov 2020; 179:471-483.

Prevalence of medication-related falls in 200 consecutive elderly patients with hip fractures: a cross-sectional study.
Andersen CU, Lassen PO, Usman HQ, **Albertsen N**, Nielsen LP, Andersen S
BMC Geriatr. 2020 Mar 30;20(1):121.

Papers in submission by December 2023 (including Study IV):

High prevalence of atrial fibrillation found in the capital of Greenland when using continuous ECG monitoring: a cross-sectional study.
Albertsen N, Jensen MM, Hansen KLK, Pedersen ML, Andersen S, Brock C, Riahi S.

Quality of care among patients diagnosed with atrial fibrillation in Greenland.
Nielsen MT, Nielsen MH, Andersen S, Riahi S, Geisler UW, Pedersen ML, **Albertsen N.**

Psychological adaption in a small mixed gender and ability team undertaking a ski expedition to the South Pole. A limited observational study.
Harper P, **Albertsen N**, Koivula F.

ENGLISH SUMMARY

This PhD-project aims to investigate the prevalence of atrial fibrillation in the Greenlandic population, which comprises approximately 57,000 people. One-third of the population resides in the capital, Nuuk, while the rest live in towns along the Greenlandic coast. Greenland's climate is extreme, with vast distances between towns, and there no roads connecting them.

Over the past 70 years, living conditions in Greenland have undergone significant changes. Dietary habits have changed, the population is aging, and like elsewhere in the world, the health of the Greenlandic population is increasingly affected by lifestyle-related and chronic diseases. One of these is atrial fibrillation, a common heart rhythm disorder that can be not only uncomfortable but also increases the risk of dementia and strokes.

The thesis is structured around four studies. The first study utilizes data from the electronic medical records system, where information on patients' diseases and medications is recorded. The next study examines the prevalence of atrial fibrillation on the east coast of Greenland using a handheld device, while the third study investigates the occurrence of atrial fibrillation in Nuuk using questionnaires and heart rhythm recordings over several days. Finally, the project explores the prevalence of atrial fibrillation in patients discharged from Greenland's only hospital with a diagnosis of ischemic stroke.

The results from the first three studies suggest that the prevalence of atrial fibrillation in the Greenlandic population is likely not significantly different from that in other Nordic countries. Additionally, the occurrence follows a similar pattern as elsewhere, becoming more frequent with age and primarily affecting men. However, the fourth study finds that fewer ischemic stroke patients than previously thought have atrial fibrillation. This decline may be attributed to challenges in examining and diagnosing patients, indicating that conducting prolonged examinations for atrial fibrillation may be a general challenge in Greenland.

This dissertation contributes to the existing knowledge of cardiovascular diseases in Greenland. Further studies are recommended to expand and refine our understanding of atrial fibrillation in Greenland.

DANSK RESUME

Dette ph.d.-projekt tager udgangspunkt i den grønlandske befolkning på ca. 57.000 mennesker. En tredjedel af befolkningen bor i hovedstaden Nuuk, mens resten bor i byer langs den grønlandske kyst. Klimaet i Grønland er ekstremt, afstandene store og ingen byer er endnu forbundet med vej.

Igennem de sidste 7 årtier har levevilkårene i Grønland ændret sig markant. Blandt andet har kosten ændret sig, befolkningen bliver ældre og den grønlandske befolknings sundhedstilstand er, som andre steder i verden i dag, tiltagende præget af livsstilsrelaterede sygdomme og kroniske sygdomme. En af disse sygdomme er forkammerflimmer, også kaldet atrieflimren.

Atrieflimren er en hyppig hjerterytmeforstyrrelse, som dels kan være ubehagelig, men også øger risikoen for blandet andet demens og blodpropper i hjernen. Atrieflimren i Grønland er kun sparsomt beskrevet tidligere, men vi ved fra andre studier, at der bliver flere ældre i Grønland, ligesom sygdomme som øger risikoen for atrieflimren, bliver hyppigere. Formålet med denne afhandling er derfor at give et mere fyldestgørende indblik i forekomsten af atrieflimren i Grønland.

Afhandlingen er bygget op omkring fire studier. Det første studie tager udgangspunkt i oplysninger fra det elektroniske journalsystem, hvor patienters sygdomme og medicin registreres. Det næste studie undersøger forekomsten af atrieflimren på den grønlandske østkyst ved hjælp af optagelse foretaget med et håndholdt apparat, mens det tredje undersøger forekomsten i Nuuk ved hjælp af spørgeskemaer og hjerterytmeoptagelser foretaget over flere dage. Endelig undersøger vi forekomsten af atrieflimren hos patienter som er udskrevet fra Grønlands eneste hospital med en diagnose for blodprop i hjernen.

Resultaterne af de tre første undersøgelser peger på, at forekomsten af atrieflimren i den grønlandske befolkning næppe er væsentlig anderledes end i andre lande i Norden. Dertil har forekomsten et lignende mønster som i andre lande, nemlig at tilstanden bliver hyppigere med alderen og oftest forekommer hos mænd. Til gengæld finder det sidste studie, at færre blodproppatienter end tidligere har atrieflimren. Dette fald kan skyldes udfordringer med at undersøge, og dermed diagnosticere, patienterne, og vores resultater antyder at længerevarende undersøgelser for atrieflimren kan være en generel udfordring i Grønland.

Med denne afhandling bidrager vi til den eksisterende viden om hjertesygdomme i Grønland. Fremtidige studier anbefales for at udvide og præcisere vores kendskab til forkammerflimmer i Grønland.

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First, I would like to thank my supervisors Stig Andersen, Michael Lynge Pedersen, and Sam Riahi for building the foundation of the project, inviting me to join and offering their support and guidance over the past three years.

Next, the project would only have happened with the participants who took time out of their busy schedules to participate in the studies. Thank you for sharing your thoughts, experiences, data and, perhaps most importantly, your heart rhythms.

I would also like to thank Karen Elise Jensen's Foundation for supporting the project financially. As William E. Vaughan said: "Money won't buy happiness, but it will pay the salaries of research staff to study the problem".

I would also like to express my gratitude to my colleagues at the Department of Geriatric Medicine, Christina Brock and the Danish Center for Clinical Health Research for sharing their knowledge and ideas.

And I send a heartfelt "Qujanarussuaq" to Nuuk: The staff at Steno Diabetes Center, Queen Ingrid's Health Care Center, the Department of Internal Medicine at Queen Ingrid's Hospital and Ilisimatusarfik. Thank you for always making me feel at home for the assistance, advice and rooms offered to the project.

Thanks to Professor Chris Imray and the Inspire22 team for inviting me to join the research expedition to the South Pole, and no smaller thanks to the PhD school at Aalborg University for their support in letting me participate as my stay abroad.

A big thank you goes to my family and friends in Denmark and abroad. Thank you for your love, support, patience and, not least, for keeping me laughing and my plants alive during my stays in the Arctic and Antarctic.

Finally, thanks to the European Space Agency and Institute Polaire Français Paul-Émile Victor for giving me the job opportunity that made me fall in love with research.

Nadja Albertsen

LIST OF PUBLICATIONS

The thesis is based on the following papers, which are referred to in Roman numerals in the text. The manuscripts are appended as Appendix A to F (including supplemental material).

I. **The prevalence of atrial fibrillation in Greenland: a register-based cross-sectional study based on diagnosis codes and prescriptions of oral anticoagulants** [1]**.**
Albertsen N, Riahi S, Pedersen ML, Skovgaard N, Andersen S.
Int J Circumpolar Health. 2022 Dec;81(1):2030522.

II. **Prevalence of persistent atrial fibrillation and screening for Atrial Fibrillation in East Greenland using a single lead handheld ECG device** [2]**.**
Albertsen N, Riahi S, Pedersen ML, Noahsen P, Andersen S.
JAFIB-EP.2022,15(4):56-60.

III. **Is the pattern changing? Atrial fibrillation and screening with Holter electrocardiograms among ischemic stroke patients in Greenland from 2016 to 2021** [3]**.**
Albertsen N, Hansen AS, Skovgaard N, Pedersen ML, Andersen S, Riahi S.
J Clin Med. 2023 Aug 18;12(16):5378.

IV. **High prevalence of atrial fibrillation found in the capital of Greenland when using continuous ECG monitoring: a cross-sectional study** [4]**.**
Albertsen N, Jensen MM, Hansen KLK, Pedersen ML, Andersen S, Brock C, Riahi S.
[In submission] 2023

ABBREVIATIONS

AF	Atrial fibrillation
ATC	Anatomical Therapeutical Chemical Classification
CHA_2DS_2-VASc:	C: Congestive heart failure, H: Hypertension, A: Age ≥ 75 years, D: Diabetes, S: Stroke, V: Vascular disease, A: Age 65-74 years, Sc: Sex category
CHD	Coronary heart disease
CVD	Cardiovascular disease
ECG	Electrocardiogram
ESC	European Society of Cardiology
HF	Heart failure
ICD-10	International Classification of Diseases, 10^{th} revision
ICPC	International Classification of Primary Health Care
IHD	Ischemic Heart Disease
IS	Ischemic stroke
LDL	Low Density Cholesterol
OAC	Oral anticoagulant
QIH	Queen Ingrid's Hospital
SAH	Subarachnoid hemorrhage
SR	Sinus rhythm
T2D	Type 2 Diabetes

TABLE OF CONTENTS

CHAPTER 1. INTRODUCTION

My first trip to Greenland was on January 2nd, 2014. I was going to fill a two-month vacancy in Queen Ingrid's Health Care Center in Nuuk, and when the conclusion of the employment approached, my then-boss Jesper Olesen proclaimed "*It's a bad time to leave. Now is when it gets really good*."

Jesper was right, and I ended up staying three full years. I have since been a returning guest as a researcher, clinician and outdoor guide. Today, I'm proud to call Greenland my second home, and the land and the people far up north have helped shape my personal and professional identity. I even wrote my first scientific paper in Greenland, earning myself the somewhat unflattering nickname "Syphilis-Nadja".

Greenland has changed culturally and demographically over the past decades, and the population's health, the health care system and health research have developed with it. As chronic and lifestyle-related diseases are becoming increasingly common, they are also being described to a greater extent. Atrial fibrillation (AF) is one of these diseases.

In the first part of Chapter 2 of this thesis, I will introduce you to Greenland and Greenland's health care system. The second part includes an introduction to AF and a short description about what we knew about AF in Greenland before beginning this PhD.

Chapter 3 offers the aims of the PhD and the individual studies, and Chapter 4 follows with a description of the methods used.

The results and conclusions of each study are detailed in Chapter 5, starting with Studies 1, II and IV, as they all describe the prevalence of AF among the general population. Study III finishes the chapter describing the prevalence of AF among ischemic stroke patients in Greenland.

Chapter 6 will include a discussion of the results of the studies and some methodological considerations.

Chapter 7 finalized the thesis with a conclusion and thoughts on future perspectives for AF research in Greenland.

In the thesis, I will describe the Greenlandic population as "Greenlanders" or "the Greenlandic population" when referring to the modern-day mixed population. However, in Studies II and IV, we have included questions about the participants' parents' place of birth as a marker of Greenlandic, or Inuit, origin. When referring to these results in the text, it will be as "participants with Inuit origin".

CHAPTER 2. BACKGROUND

Greenland may be one of the most extreme and fascinating places on Earth.

Figure 2-1. A land of contrasts. Qeqertarsuaq (Disko Island). Private photo (2023).

Eighty-two per cent of the two million square kilometer island is covered in permanent ice and there are 2,700 kilometers from North to South. Most of the island is located above the polar circle, meaning the sun will not set amid summer or rise for a amid winter. The temperature dips as low as -33 C average in the North in January, and no month reaches an average temperature above 10 C [5]. Finally, the ice and mountains make travel by land difficult, and none of Greenland's towns and villages are yet connected by road, making transportation by sea and air essential [5, 6].

Greenland is a part of the Kingdom of Denmark but is self-governing to a great extent and is not a member of the European Union [7]. Greenland is divided into five districts (Figure 2-2), each with a council and at least one health care center with basic hospital facilities.

Figure 2-2. Greenland, the five districts and the locations of the towns mentioned in the thesis. Study II was conducted around Tasiilaq and Study IV in Nuuk. The image is adapted from Figure 1 in [3].

The health care system in Greenland is based on the Danish system, with free health care for all permanent residents, in addition to free prescription medicine and basic dental care. All larger towns have a health care center with facilities to perform basic diagnostics and treat common illnesses and injuries. The health care centers are staffed by at least one doctor and nurse, and often also therapists and midwives [8]. Smaller villages have health care clinics with either a nurse or a trained health care worker, supervised by nurses and doctors in the health care centers [8]. Telemedicine is implemented in all parts of Greenland and used for diagnostic support and treatment [9]. Queen Ingrid's Hospital (QIH) in Nuuk is currently the only hospital in Greenland with facilities for intensive care, advanced surgery and cancer treatment, and diagnostics such as MRIs and CT scans. Patients are therefore often transferred to Nuuk from other parts of Greenland or to Iceland or Denmark when needing more advanced treatment [8].

2.1. A UNIQUE POPULATION

Today, almost 57,000 people call Greenland their home. One-third of the population lives in the capital, Nuuk, another third in the four largest towns, and the remainder live in towns and settlements along the West, South and East Coast [10]. Approximately 87% of the population is born in Greenland [11].

The indigenous Greenlandic population is called Inuit or Kalallit and originates from North America. Isolation, genetic bottleneck events and founder populations have resulted in the Greenlandic population being genetically differentiated from any large population [12] and highly adapted to life in the Arctic. Even within Greenland, a clear genetic subdivision between people originating in East, North and West Greenland [12].

Some of the unique genetic traits are likely related to the traditional Inuit diet, which consists mainly of marine animals, fish and berries. Consequently, the diet is rich in fat and protein and low in carbohydrates and specific vitamins and minerals. Some examples of genetic adaptations are an increased ability for calcium uptake [13] and the hyperglycaemia induced by the TBC1D4 variant that is associated with an increased risk of Type 2 Diabetes (T2D) and insulin resistance today [14], which may have been an advantage before the introduction of a Western diet [15].

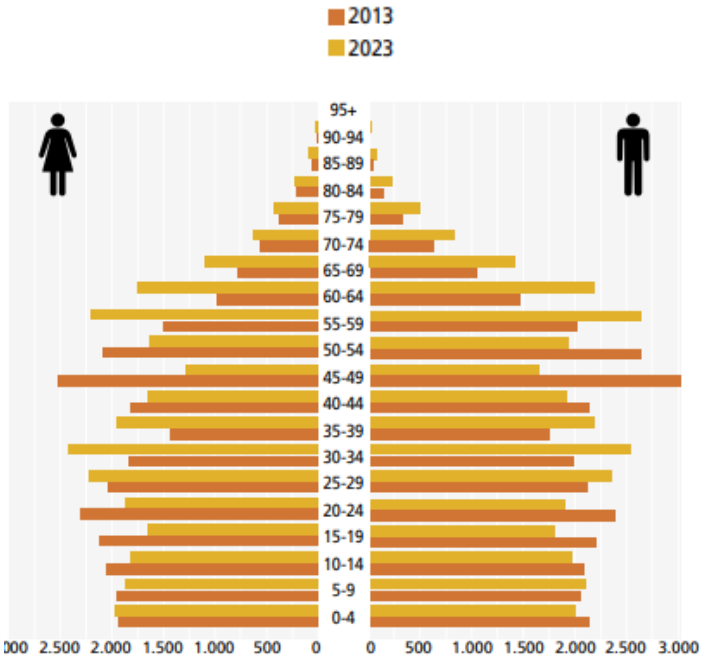
Scandinavians, mainly Danes, have had a permanent presence in Greenland since 1721 when Hans Egede created a colony close to where Nuuk is today. Today, Inuit have approximately 25% European genetic admixture, mainly Danish [16], although the percentage is lower in more remote areas such as North and East Greenland [12]. In addition, 11% of the population in 2023 were born outside of Greenland, and 64% of this fraction were born in Denmark [17]. The European presence has significantly changed the availability of different foods in Greenland, and the diet has changed from being mainly locally caught to consisting of a higher proportion of imported food. From 1953 to 2018, the diet has changed from being 45% to 21% local in settlements and from 21% to 14% local in towns [18]. This change has increased the amount of dietary fibre and decreased the amount of persistent organic pollutants in the diet; however, it has also become richer in carbohydrates and saturated fat [19, 20].

Along with the change in diet, Greenland has also undergone rapid social changes, especially since the 1950s (Figure 2-3). The average prosperity index has increased, homes are becoming less crowded and more people are taking a formal education [18]. However, the percentage of the population who rates their health as good or very good is dropping [18] and the most recent population survey indicates inequality in the Greenlandic society. The prosperity index is higher among people living in towns than among those living in remote areas, and self-rated health and food security are higher among those with a higher prosperity index [18].

Figure 2-3. A mural in central Nuuk commenting on the societal changes in Greenland. Private photo (2022).

Finally, life expectancy is increasing in Greenland but is still shorter than in most Western countries. The average life expectancy in Greenland is 71.4 years, which is ten years shorter than in Denmark [21]. Fifty-three per cent of the population are men, although most of the 80+-year-olds are women [11], and Greenlandic women are expected to live three years longer than Greenlandic men [22]. The demographic change over the past ten years is shown in Figure 2-4.

Figure 2-4. Demographic changes in Greenland from 2013 to 2023. The figure is modified from [6], page 7.



2.2. CARDIOVASCULAR DISEASE IN GREENLAND

With the changing lifestyle and increasing life expectancy, certain lifestyle- and age-related conditions have become more common in Greenland. Twenty-seven per cent of the population had a BMI above 30 kg/m2 in 2018, more than double since 1993 [18]. T2D affects nearly seven per cent of the population aged 35 years and older [18], eight per cent of the adult population are treated for hypercholesterolemia [23], and 17.5% aged 20 years and older are in medical treatment for hypertension [24]. Finally, 52% of the Greenlandic population are daily smokers [18].

All of the above predispose to cardiovascular disease, but up until the early 2000s, it was widely believed that cardiovascular disease (CVD) and coronary heart disease (CHD) were uncommon among Inuit. The main reason was an assumed protective effect among Inuit of the traditional marine diet rich in polyunsaturated fatty acids [25, 26], a theory that has later been disproved [27–29]. However, there are some indications that the prevalence of CVD has changed over time. A study from 2009 including 181 electrocardiograms (ECGs) performed among East Greenlanders from 1962 to 1964 describes ischemic changes among 3.3% of the participants only, and 12 out of 1,851 participants (0.6%) from the same study had a history of chest pain [30]. These results stand in contrast to studies based on more recent data, such as Bjerregaard et al.'s study from 2003 describing similar mortality from non-stroke CVD in Denmark and Greenland based on mortality statistics [31]. Additionally, Jørgensen et al. found that the prevalence of markers of CHD based on self-reported myocardial infarction and angina pectoris as well as ischemic changes on ECGs was 10.8% among men and 10.2% among women in 2007 among 1,316 Greenlanders with a mean age of 43.4 years; the same as in Western populations [29]. Finally, in 2022, Larsen et al. estimated the prevalence of heart failure (HF) to be around one per cent in the Greenlandic population, the same as in other high-income countries.

2.3. ISCHEMIC STROKES IN GREENLAND

However, it is undisputed that cerebral strokes are common in Greenland. Based on discharge diagnoses from QIH, Kjærgaard and Bjerregaard found that with an incidence of 86.8/100,000 person-years (not including subarachnoid hemorrhages (SAHs)), strokes were four times as common as myocardial infarction in Nuuk from 1999 to 2002 [32].

In 2010, a national strategy was implemented in Greenland with the objective of offering all patients in Greenland suspected of having suffered a stroke a standardized examination regime. Most of these examinations are only performed in QIH and require patients living outside of Nuuk to be able to travel from their hometown to the capital. The regime includes a cerebral scan, an ultrasound of the carotid arteries, an echocardiography, rehabilitation and a continuous ECG recording [33].

A few years after the implementation, Bjørn-Mortensen et al. found the age-standardized incidence of stroke survivors to be 149/100,000 person-years including SAHs in a study including patients from all parts of Greenland discharged from QIH in 2011 and 2012 [33]. No patients included in the study had recurrent events in the study period, and the results indicated a higher incidence than in Denmark [33]. Among these patients, five per cent of 139 patients with ischemic stroke (IS) had been diagnosed with AF before their stroke, but almost one-third had been given the diagnosis at the time of discharge [34]. As IS are often caused by AF, Bjørn-Mortensen et al.'s study indicated that AF may have been underdiagnosed in Greenland.

The connection between AF and IS will be described in more detail later. First, a few words about AF.

2.4. ATRIAL FIBRILLATION

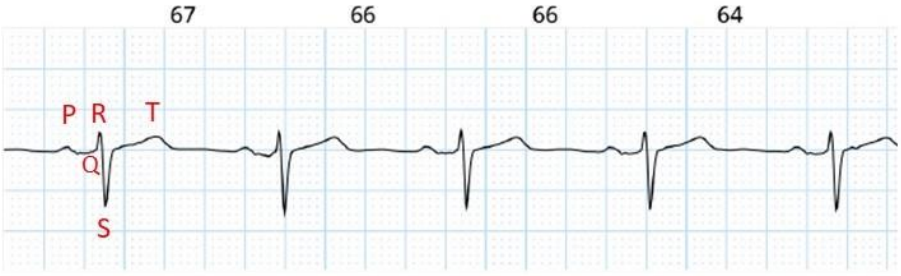
2.4.1. DEFINITION AND CLASSIFICATIONS

AF is defined as "*a supraventricular tachyarrhythmia with uncoordinated atrial electrical activation and consequently ineffective atrial contraction*" [35], page 385. AF is one of several types of arrhythmias and the most common and clinically important.

Usually, the heart beats in a so-called sinus rhythm (SR). SR is regular, and the pace is controlled by the autonomic nervous system to cope with internal and external factors, such as physical activity and stress. The electrical impulse controlling the heart's contraction begins in the built-in pacemaker, the sino-atrial (SA) node in the right atrium. From there, the impulse moves to the ventricles through the atrioventricular (AV) node, resulting in a coordinated contraction beginning in the atria and ending in the ventricles. As a result, the blood is pumped efficiently into the lungs and body.

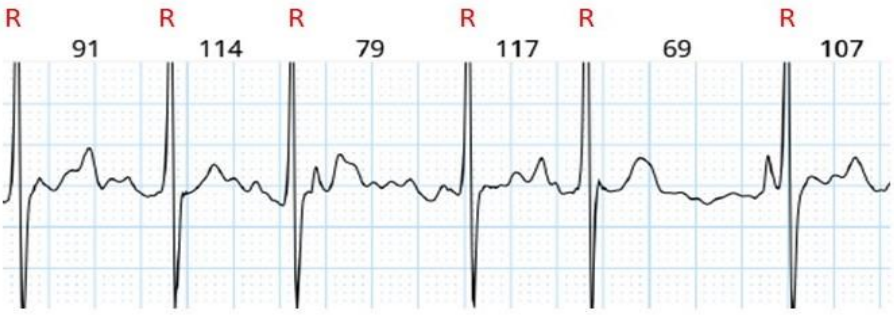
The migration of the electrical impulse can be seen on an ECG, where the P-wave indicates the depolarization of the atria, the QRS complex the depolarization of the ventricles and the T-wave indicates the repolarization of the ventricles. The PQ-interval indicates the period where the impulse moves from the atria to the ventricles, and the RR-interval describes the length of time between each contraction of the ventricles. Figure 2-4a shows an ECG from a participant from Study IV with a normal heart rhythm.

Figure 2-4a: Part of an ECG from a study participant with sinus rhythm. The numbers on top indicate the length of each RR-interval in milliseconds.



In AF, impulses from outside the SA node occur in the atria. As some of the extra impulses are conducted to the ventricles, the contraction rate of both the atria and the ventricles increases. This results in an irregular and high heart rate that can be symptomatic and uncomfortable for the affected person. An ECG showing AF is characterized by irregular RR-intervals and a lack of discernible P-waves, as shown in an ECG from a study participant with AF from Study IV in Figure 2-4b.

Figure 2-4b: Part of an ECG from a study participant with AF. The numbers on top indicate the length of each RR-interval in milliseconds.



AF is often interspersed with periods of SR, and the condition can be classified by the duration of periods with AF and treatment response or as being either asymptomatic or symptomatic. The European Society of Cardiology uses five classifications in their 2020 AF guidelines [35], as shown in Table 2-1.

Table 2-1: AF classifications and frequency of each type.

AF classification	Definition	Frequency
First diagnosed	First recording, no data on duration or symptoms	Not applicable
Paroxysmal	Terminates within 7 days of onset	20-35%
Persistent	Sustained beyond 7 days of onset	25-30%
Long-standing persistent	Sustained beyond 12 months	
Permanent	No further attempts to restore or maintain SR	45-55%

The table is based on information from [35–37].

2.4.2. EPIDEMIOLOGY AND RISK FACTORS

AF is estimated to affect between two and four per cent of the population globally, making it the most prevalent arrhythmia worldwide. The incidence is higher in developed countries [38]. and both the prevalence and incidence have been steadily increasing. In 2013, Krijthe et al. forecasted that the prevalence will double in the European Union by 2060 compared to 2010 numbers [39]. Both the age-standardized incidence and prevalence of AF have been found to increase; however, the development is more pronounced among the older age groups [39, 40].

Age is the most prominent risk factor for AF, followed by male gender and Caucasian ancestry. However, the list of risk factors for AF is long. and an overview of the most established risk factor is given in Table 2-2.

Table 2-2. Some well-established risk factors for AF.

Non-modifiable risk factors	Modifiable risk factors	
Age	Elevated blood pressure	Obesity
Male gender	Obstructive sleep apnea	Alcohol
Ethnicity and race	Smoking	Diabetes
Genetics	Hyperthyroidism	Myocardial infarction
	Left ventricular hypertrophy	Congestive heart failure

The table is based on information from [41–43].

Common to all is that they induce structural changes to the myocardium in the right atrium, affecting the function of the sinus node and the conduction of the electrical

impulses [44]. AF itself can induce changes in the myocardium, and paroxysmal AF can progress into persistent forms [44, 45].

2.4.3. ISCHEMIC STROKE AND OTHER POTENTIAL CONSEQUENCES OF ATRIAL FIBRILLATION

It is estimated that patients with AF have a five times higher risk of ischemic stroke than those without and that 15-30% of ischemic strokes are related to AF [46–48]. Most ischemic strokes among AF patients are cardioembolic, and the risk increases with age and the presence of vascular risk factors, such as hypertension, diabetes and hyperlipidemia [49, 50]. Some of the well-established risk factors are included in the CHA_2DS_2-VASc score, commonly used by clinicians to estimate an AF patient's risk of ischemic stroke and decide whether the patient should be prescribed an oral anticoagulant (OAC). The scoring system gives one or two points for the following: C: Congestive heart failure, H: Hypertension, A: Age $\geq$ 75 years (2 points), D: Diabetes, S: Stroke (2 points), V: Vascular disease, A: Age 65-74 years, Sc: Sex category (1 point if female) [51]. A score of zero for men or one for women is considered low risk with less than one per cent risk of stroke per year. Patients with higher scores are recommended OAC treatment if not contraindicated by, for example, a high risk of bleeding [52, 53]. In Greenland, three OACs are used: the Vitamin K antagonist Warfarin, the factor X_a inhibitors Rivaroxaban and, recently added, Apixaban. The factor X_a inhibitors are considered superior to Warfarin [54, 55], and the latter is only sparsely used in Greenland today [1].

AF also increases the risk of potentially debilitating conditions such as dementia [56], heart failure [57] and depression [58], and symptomatic patients often experience a decreased quality of life [59]. This affects the AF patient directly, but also means that AF constitutes a significant socioeconomic burden, making it vital to diagnose AF, preferably at a stage before severe AF-related morbidities have developed. However, AF is not always easy to catch due to its often-paroxysmal nature.

2.4.4. DIAGNOSING AND SCREENING FOR ATRIAL FIBRILLATION

Symptoms are often the trigger for examining for AF [60], and the most described symptoms of AF are palpitations, lightheadedness/dizziness, shortness of breath on exertion, syncope and fainting, fatigue, dyspnea at rest, exercise intolerance and chest discomfort/pain [61, 62]. However, as mentioned earlier, AF can be asymptomatic, and approximately 40-50% of patients do not report any symptoms [59, 63, 64]. Symptoms are more common among women, patients with paroxysmal AF, patients with heart failure, sleep apnea and chronic obstructive pulmonary disease [61]. Additionally, studies suggest that there may be seasonal variations in symptoms [62] and that certain ethnic groups are more prone to experience symptoms, for example Black patients when compared to White and Hispanic patients [64].

Diagnosing AF requires an ECG showing at least one episode of AF lasting at least 30 seconds [35]. However, when AF is suspected and not identified on a standard 30-second 12-lead ECG, other methods are recommended as they have a higher chance of capturing paroxysmal AF. Continuous ECGs, such as Holter recordings, offer the possibility to record for days to weeks, and implantable loop recorders can register for several years. Other options include intermittent use of 30-second recordings, and a 2018 review comparing the ability of portable devices to detect AF with Holter recordings found that a total of 19 minutes recorded with the intermittent devices correspond to 24 hours of Holter recording [65]. The portable handheld devices are easy to use and feasible in remote areas when detecting AF [66, 67]. Other options, such as smartwatches or app-based tools for smartphones, are readily available in most countries, as well. However, a 30-second 12-lead ECG is still required to confirm the AF diagnosis if detected on a wearable or portable device [35].

As AF is relatively common, screening has been suggested and is recommended by the European Society of Cardiology (ESC) in their 2020 AF guidelines as a Class I recommendation [35]. The are two types of screening: Opportunistic screening where persons are screened when, for example, seeing a general practitioner for some other reason. The other is systematic screening, where, for instance, certain age groups or patients with specific risk factors are invited to an examination for AF. ESC recommends opportunistic screening among people aged 65 years and older and systematic screening of patients with pacemakers and implantable loop recorders and persons aged 75 years and older [35].

2.5. ATRIAL FIBRILLATION IN GREENLAND AND AMONG OTHER INDIGENOUS POPULATIONS

Pivoting back to Greenland, AF among the Greenlandic Inuit has only been described in a few studies. Under one per cent of 181 East Greenlanders with a 30-second ECGs recorded between 1962 and 1964 had AF [30], and since then, AF has only been described among IS patients in Greenland, as described earlier in the introduction [34].

In general, the number of studies concerning AF in Indigenous populations is limited, and Katzenellenbogen et al. were unable to draw any clear conclusions on AF patterns among Indigenous populations in their review from 2015 [68].

However, some studies indicate differences in prevalence and incidence of AF when comparing Indigenous and non-Indigenous populations in the same countries. Some of these studies and the methods used are shown in Table 2-3, along with results from other studies performed among Indigenous people, including Greenland.

Table 2.3. Occurrence of AF among Indigenous populations.

Population/Country	Prevalence, Indigenous	Prevalence, non-Indigenous	Incidence, Indigenous	Incidence, non-Indigenous	Study population	Method	Publication year
Inuit/Greenland	0.6%	N/A	N/A	N/A	Age 40+, East Greenland 1962-1964 N=181	30- second ECG	2008
Métis/Canada	2.08%	1.42	0.62/100 persons	0.32/100 persons	Age 20+, Ontario N=12,550	Discharge abstracts, Insurance plans	2014
Yakutia/Russia	25% (Female) 28.2% (Male)	8.3 (Female) 20.5 (Male)	N/A	N/A	Patients with abnormal coronary arteries admitted in Yakutia 2004-2007 N=1,233	Medical records, 12-lead ECGs, Holter	2018
American Indians/USA	N/A	N/A	7.49/1000 person- years	6.89/1000 person-years	Patients admitted to hospital in California 2005-2011 N=16,442,944	Databases by diagnosis codes	2019
American Indians/USA	4.4%	6.1% Whites, 2.6% Blacks, 2.6% Hispanics, 3.4% Asians	N/A	N/A	Male US veterans N=664,754	Databases by diagnosis codes	2008
Aboriginals/Australia	296/10,000	257/10,000	N/A	N/A	Hospital admissions 2006-2016 admitted to Alice Springs Hospital N=57,056	Coded administration data	2021
Aboriginals/Australia	3%	N/A	N/A	N/A	18 years and older from communities around Alice Springs N=436	Questionnaire, clinical record review	2014
Aboriginals/Australia	2.57%	1.73%	N/A	N/A	Patients admitted in Adelaide between 2000-2009 N=14,373	Diagnosis codes	2014
Maori/New Zealand	2% (rural Māori) 1.2% (urban Māori)	1.2%	N/A	N/A	Unknown	12-lead ECG in unspecified, selected population	2013 (abstract)
Sami/Finland	4.3%	4.3%	N/A	N/A	Age 40+ N unknown*	Unknown*	2019 (abstract)*
Aboriginals/Canada	2.1%	N/A	N/A	N/A	Unknown*	Unknown*	2019 (abstract)*

**No further details on the study cited in the abstract has been found. The table is based on studies [69–78]. Abbreviations: N/A: Not applied in the study.*

More remains to be explored, described and understood about AF in Greenland. The next chapter will delve into the aims of each study included is the thesis, each focusing on exploring the prevalence of AF among persons living in Greenland.

CHAPTER 3. AIMS

The overall aim of the thesis was to estimate the frequency of AF in Greenland. We begin with the prevalence of diagnosed AF in Greenland in Study I. We then estimate the prevalence among the general population, starting with the population older than 50 years in one of the most remote areas in Greenland in Study II. In Study III, we look at AF among patients discharged from Queen Ingrid's Hospital with an IS diagnosis. Finally, we look at the prevalence of AF among the general population 50 years and older in the capital of Greenland based on continuous ECG recordings in Study IV.

The aim of each study is described in detail below:

Study I:

The aim of Study I was to estimate the prevalence of AF among the general population in Nuuk using diagnosis codes and prescribed OACs.

Study II:

Study II had two aims. First, we aimed to estimate the prevalence of AF in East Greenland based on recordings performed by a handheld single-lead ECG device. Secondly, we compared the ability of a single lead handheld ECG device with the ability of a standard 12-lead ECG device to detect AF.

Study III:

Study III had two aims. The first aim was to estimate the prevalence of AF among patients discharged from QIH from 2016 to 2021 with an ischemic stroke diagnosis. The second aim was to evaluate the standardized examination regime introduced for stroke patients using the Holter recordings performed on IS patients.

Study IV:

The aim of Study IV was to estimate the prevalence of AF among the general population aged 50 years or older in Nuuk using continuous ECG recordings.

CHAPTER 4. METHODS

This chapter describes the general methodological characteristics of the four studies included in the thesis. An overview of the methods is given in Table 4-1 and more detailed information is found in the manuscripts.

Table 4-1. Overview of study characteristics.

	Study I	**Study II**	**Study III**	**Study IV**
Study design	Cross-sectional	Cross-sectional	Retrospective cohort-study/Cross-sectional	Cross-sectional
Setting	96% of Greenland 2021.	East Greenland 2019.	All of Greenland 2016-2021.	Nuuk 2022-2023.
Data source	Electronic medical records.	Handheld ECG devices and questionnaires.	Electronic medical records and Holter recordings performed between 2016 and 2020.	Questionnaires, participants' reports and continuous ECG recordings.
Date of data extraction	February 2021	N/A	April 2021 and June 2022	N/A
Study population	Patients diagnosed with AF or prescribed an OAC at the time of data extraction.	221 participants aged 50 years or older from East Greenland.	Patients given an ICD10-code for ischemic or unspecified stroke between 2016 and 2021.	Residents in Nuuk aged 50 years or older voluteering to participate.
Reference data	The Greenlandic population except Tasiilaq	The population in and around Tasiilaq aged 50 years and older	The entire Greenlandic population	Residents in Nuuk aged 50 years and older.
Recruitment of participants	Not applicable.	Invited per letter	Not applicable.	Media, social media, per phone, other PhD-project.

Abbreviations: AF: Atrial fibrillation. ECG: Electrocardiogram. ICD-10: International Classification of Diseases, 10th revision. OAC: Oral anticoagulant.

4.1. DATA SOURCES

4.1.1. THE ELECTRONIC MEDICAL RECORD SYSTEM

As mentioned in the introduction, the Greenlandic health care system is based on, and very similar to, the Danish health care system. However, an exception is the electronic medical record system (EMR). The Swedish Cambio COSMIC medical record system was introduced in Greenland in 2014 and is implemented in all parts of Greenland, except the area around Tasiilaq on the East Coast (Figure 1), where limited internet resources restrict the use to read-only. The implementation of an EMR covering 96% of Greenland's primary sector and 100% of the secondary sector not only allows easy sharing of patient data from primary to secondary care and across regions, but it also eases access to health care data from most of Greenland's primary sector for research.

The use of diagnosis codes upon discharge from QIH has been standard since the implementation of Cosmic. In recent years, an effort has been made to standardize the use of diagnosis codes in primary care to ease the transfer of information between different sectors. Today, the International Classification of Diseases and Related Health Problems 10th Revision (ICD-10) and the International Classification of Primary Care (ICPC) are used to code diagnoses. Similarly, all types of medication are registered in the EMR by their unique code from the Anatomical Therapeutic Chemical Classification System (ATC).

Using these coding systems makes it feasible to identify patients with relevant diagnoses without accessing their names, addresses or personal registration numbers. This enabled us to extract pseudonymized data from Greenlanders from 96% of Greenland diagnosed with AF or having an active prescription for one of OACs available in Study I. Similarly, data was extracted from all patients discharged from QIH between 2016 and 2021 with an IS diagnosis in Study III. The employed codes are listed in Table 4-2.

Table 4-2. Codes employed to identify patients with relevant diagnoses in the EMR for Study I and III.

	Study 1	**Study III**
ICD-10 codes	I48, I48.1, I48.2, I48.3, I48.4, I48.9	I63*, I64.9
ICPC codes	K78	Not used
ATC codes	B01AA03, B01AF01	Not used

Abbreviations: ATC: Anatomical Therapeutical Chemical Classification. ICD-10: International Classification of Diseases, 10th revision. ICPC: International Classification of Primary Health Care.

Additionally, the use of diagnosis codes and ATC codes allowed us to extract data on medication and comorbidities of the patients included in Study I and III, as well as using a prescription of an OAC as a proxy for diagnosed AF among IS patients in Study III. Based on this information, a minimum CHA_2DS_2-VASc score was also calculated in Study I; however, not all information for a full score was available. The codes used are detailed in the manuscripts [1, 3].

4.1.2. REPORTS FROM HOLTER RECORDINGS

All Holter recordings in Greenland are performed in QIH, although implementation has begun in Ilulissat, Greenland's third-largest town. The recordings performed in QIH are stored in the Novacor® program RTSoft Ultima on a computer in the outpatient clinic of the Department of Medicine and can only be accessed from that location. PDF files, including a summary and excerpts from the Holter recordings, can be exported from the program but must be either anonymized or pseudonymized before being transferred physically or digitally from the outpatient clinic.

We had access to the computer in early 2021 only, and Holter recordings performed between 2016 and 2020, but not 2021, are included in Study III.

4.1.3. SELF-REPORTED DATA: QUESTIONNAIRES

Questionnaires filled out by the participants were used to gather information on the participants in Studies II and IV. In both studies, the questionnaire included gender, age, comorbidities, smoking, alcohol consumption, medication and vitamin supplements. The participants were also asked about their parents' place of birth. As the participants in both studies were at least 50 years old and Danish immigration to Greenland was relatively limited until the 1950s, parents born in Greenland were used as a marker of Inuit origin.

In Study IV, we also asked specifically about the participants' and their families' history of diabetes, ischemic heart disease, cardiac arrhythmias, thyroid disease and hypertension, as well as the most common symptoms of AF (palpitations, irregular pulse, pauses in heart rate, chest pain when resting, shortness of breath, faintness and dizziness). Participants in Study IV were also encouraged to register any potential cardiac symptoms experienced while wearing the ePatch® (Biotel Europe AB, Sweden).

The questionnaires were discussed with each participant to ensure that the questions were understood as intended. In Study IV, participants who had answered "yes" to having a cardiac arrhythmia were asked for further details to ensure the correctness of the reply. However, neither of the questionnaires were validated before their use.

The questionnaires were written in Danish and translated into Greenlandic by a professional translator from the Greenlandic health care system.

The Danish versions of the questionnaires are appended as Appendix A (Study II), B and C (both Study IV).

4.2. ECG RECORDINGS

4.2.1. STUDY II: INSTANTCHECK®

In Study II, we used the handheld single-lead ECG device InstantCheck® (DailyCare Medical, Taiwan) to obtain 30-second ECGs from the study participants. The device works by either placing electrodes on the wrists of the participants (Figure 4-3a) or by the participant placing their thumbs on the electrodes on the panel of the device (Figure 4-3b).

Figures 4-3a and 4-3b. Placement of electrodes for InstantCheck®. Graphic made from private photo (2021).

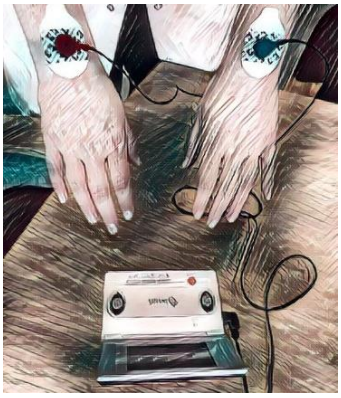


Figure 4-3a

Figure 4-3b

The device records a 30-second ECG followed by a conclusion stating whether the recording was regular, irregular or impossible to analyze [2].

The InstantCheck® has been FDA-approved [79] but not validated, and as part of Study II, we compared the recordings with standard 12-lead ECGs in both Denmark and Greenland [2].

4.2.2. STUDY IV: EPATCH®

The ePatch® is a continuous ECG recorder attachable to the chest, as pictured in Figure 4-4. The system does not require wires outside of the patch, making it easy to wear during daily activities, including exercise, showering and sleep.

The use of the ePatch® in cardiovascular diagnostics has been validated [80].

Figure 4-4. Placement of the ePatch® recorder. In this case, the participant had reinforced the patch with sports tape. Private photo (2022).

4.3. RECRUITMENT OF PARTICIPANTS

4.3.1. STUDY II

The participants in Study II were recruited in 2019 as part of a study about thyroid disease in East Greenland. All residents aged 50 years and older living in Tasiilaq (1,916 inhabitants in 2019) and Kulusuk (216 inhabitants in 2019) were invited by letter. There were no additional inclusion or exclusion criteria.

4.3.2. STUDY IV

The inclusion criteria in Study IV were age 50 years and older and residency in Nuuk. There were no additional exclusion criteria.

Participants were recruited in three different ways for Study IV. First, eligible persons in Nuuk were invited to volunteer for the project by public and social media. Information was featured in Greenlandic and Danish on the local radio and in the weekly, household-distributed newspaper in Nuuk in the Spring of 2022. Information about the study was also published on Ilisimatusarfik, the University of Greenland's homepage. This information included a video in Danish with Greenlandic subtitles describing the project and showing the material used in the study [81]. Second, a list

of names and addresses of all residents in Nuuk aged 50 years and older was provided by the local authorities, and the public online phone registry tusass.gl was used to find the phone numbers of those listed. Third, patients with T2D taking part in another PhD study were informed about the project by Steno Diabetes Center Nuuk.

4.4. DATA MANAGEMENT

Pseudonymized data was extracted from the EMR system in Greenland by a health care analyst employed by the Greenlandic Health Care System. The data was extracted to Excel (Microsoft Corp. 2017) and exported to STATA (v. 16.1, StataCorp LLC, Texas, USA).

The information from the questionnaires in Study II was entered into Excel and exported to STATA. The questionnaires in Study IV were either completed directly by the participants in RedCap (v.13.1.37, Vanderbilt University, USA) [82, 83] or completed on paper and entered into RedCap subsequently. Similarly, data from the Holter reports used in Study III was entered into RedCap and exported to STATA.

The ePatch® recordings in Study IV were pseudonymized and saved on a secure driver belonging to Aalborg University Hospital. After completion of the data collection, the files were analyzed by Biotel Europe AB as per the data processing agreement signed by Aalborg University Hospital and Biotel (case number 2022-035370). After the analysis, the reports were stored by the participant number on a secure cloud.

4.5. STATISTICAL METHODS

The studies all estimate prevalences or incidences. Prevalence is the proportion of a population affected by a specific disease or condition at a given time, and incidence is the number of persons within the population given a specific diagnosis during a specific period of time. In the thesis, prevalence is reported in per cent, and incidence is reported per 100,000 person-years.

The sample size for Study IV was calculated based on the AF prevalence found in Greenland by Kjærgaard et al. in 2009 [30] and Heeringa et al.'s estimation of AF among Caucasians from 2005 [84], as detailed in the manuscript [4].

The statistical methods used to describe and analyze data in the studies are summarized in Table 4-3 and detailed in the manuscripts.

Table 4-3. Data types and tests used in the studies.

Data type	Descriptive analyses	Tests between two groups	Tests between multiple groups	Study number
Parametric continuous data	Means and standard deviations	Student's t-test	ANOVA	I, II, III, IV
Non-parametric continuous data	Median and IQR	Wilcoxon Mann-Whitney	Kruskal-Wallis	I, II, IV
Binary data	Percentage and 95% CI	Pearson's Chi-squared	Not applied	I, II, III, IV

Abbreviations: ANOVA: Analysis of variance. CI: Confidence intervals. IQR: Interquartile range.

4.6. ETHICS AND FUNDING

The Health Research Ethics Committee Greenland approved Study I, III and IV under study number KVUG 2020-18. The data used to estimate the prevalence of AF in East Greenland in Study II was approved under study number KVUG 2018-05.

Study IV was registered at ClinicalTrials.gov with ID NCT05200676.

All studies were conducted according to the Helsinki Declaration. Participants in Study II and IV received oral and written information about the project in either Greenlandic or Danish of their own choice, and all participants in Study II and IV signed informed consent forms.

The photographs showing people in this thesis are all included with the permission of the persons pictured.

Karen Elise Jensen's Foundation funded the project.

CHAPTER 5. RESULTS

This chapter includes the results and conclusions of the four studies in the thesis.

First, the results of Studies I, II and IV are summarized, as they all estimate the prevalence of AF among the general population in Greenland, however using different methods and focusing on different geographical areas in Greenland.

The results of Study III follow and finalize the chapter.

5.1. STUDIES I, II AND IV: PREVALENCE OF ATRIAL FIBRILLATION IN GREENLAND

We start with the prevalence of AF in the 96% of Greenland covered by the same EMR, as described in Chapter 2. We then narrow our focus to the Tasiilaq area in East Greenland, where single-point ECGs were used to estimate the prevalence in Study II. Finally, the prevalence of AF in Nuuk is described based on continuous ECG recordings in Study IV.

5.1.1. PREVALENCE OF ATRIAL FIBRILLATION IN GREENLAND BASED ON DIAGNOSIS AND MEDICATION CODES

As described in Chapter 3, Study I is based on data extracted by ICD-10 and ICPC diagnosis codes for AF and ATC codes used to prescribe the types of OACs available in Greenland at the time of data extraction.

Results:

Based on ICD-10 and ICPC diagnosis codes for AF, we extracted data on 391 patients. An additional 399 patients were prescribed an OAC and therefore assumed to have been diagnosed with AF but not registered with a diagnosis code. Table 5-1 shows some of the characteristics of 790 included patients, including AF risk factors and the prevalence of competing reasons for taking an OAC. Additional information can be found in the published manuscript in Appendix A, including missing data [1].

Table 5-1. Patients diagnosed with AF in Greenland in 2021.

	Men	Women	p-value	All
Age, mean (SD)	64.6 (11.3)	68.7 (12.4)	<0.01	66.0 (11.8)
BMI, mean (SD)	31.3 (6.9)	31.2 (7.0)	0.89	31.3 (6.9)
Daily smokers, n (%) *	123 (41.4)	61 (35.3)	0.19	184 (39.2)
AF diagnosis code, n (%) *	269 (51.4)	122 (45.7)	0.13	391 (49.5)
Diabetes, n (%) *	89 (17.0)	65 (24.3)	0.01	154 (19.5)
Stroke, n (%) *	59 (11.3)	44 (16.5)	0.04	103 (13.0)
TIA, n (%) *	11 (2.1)	10 (3.8)	0.18	21 (2.7)
DVT, n (%) *	6 (1.2)	2 (0.8)	0.60	8 (1.0)
PE, n (%)*	0 (0.0)	3 (1.1)	0.02	3 (0.4)
Prosthetic heart valve, n (%) *	11 (2.1)	6 (2.3)	0.90	17 (2.2)
Warfarin, n (%) *	55 (10.5)	25 (9.4)	0.61	80 (10.1)
Rivaroxaban, n (%) *	391 (74.8)	214 (80.1)	0.09	605 (76.6)
Antidiabetics, n (%) *	64 (12.2)	39 (14.6)	0.35	103 (13.0)
Antihypertensives, n (%) *	425 (81.3)	224 (83.9)	0.36	649 (82.2)
Lipid-lowering drugs, n (%) *	247 (47.2)	114 (42.7)	0.23	361 (45.7)
Antithyroid drugs, n (%) *	3 (0.6)	14 (5.2)	<0.01	17 (2.2)
CHA_2DS_2-VASc- score, median (IQR)	2 (1;3)	4 (2;4)	<0.01	2 (1;3)

** Per cent of patients without missing data. For missing data, see Table 2 in [1]. Abbreviations: AF: Atrial fibrillation. BMI: Body Mass Index. CHA_2DS_2-VASc: C: Congestive Heart Failure, H: Hypertension, A: Age 75 and older, D: Diabetes, S: Previous stroke, V: Vascular disease, A. Age 65-74, Sc: Sex category. DVT: Deep venous thrombosis. IQR: Interquartile range. PE: Pulmonary embolism. SD: Standard deviation. TIA: Transient ischemic attack. The table is adjusted from Table 2 in [1] (Appendix A). The CHA_2DS_2-VASc score has been added for the thesis.*

The 790 patients correspond to a prevalence of AF of 1.4% in the study population, as shown in Table 5-2. The table also highlights that the prevalence increases with age and is higher among men than women in Greenland until reaching nearly the same level among those aged 70 years and older.

Table 5-2. Age-adjusted prevalences of AF in total and by gender.

	Men	Women	Total	p-value
All participants, %	1.8	1.0	1.4	<0.01
(95% CI)	(1.6;1.9)	(0.9;1.1)	(1.3;1.5)	
Age < 60 years, %	0.6	0.3	0.4	<0.01
(95% CI)	(0.5;0.7)	(0.2;0.4)	(0.4;0.5)	
Age 60-69 years, %	5.9	2.6	4.5	<0.01
(95% CI)	(5.1;6.7)	(2.0;3.3)	(3.9;5.1)	
Age > 69 years, %	11.9	10.1	11.0	0.077
(95% CI)	(10.3;13.6)	(8.6;11.8)	(9.9;12.2)	

Abbreviations: CI: Confidence Interval. The table is adjusted from Table 2 in the published manuscript [1] (Appendix A).

Conclusion:

We found a relatively low prevalence of AF in Greenland when comparing our results to Denmark and other Western countries. However, the global trend of AF becoming more common with age and being more prevalent among men until old age applies to the Greenlandic population.

5.1.2. PREVALENCE OF ATRIAL FIBRILLATION IN EAST GREENLAND

In Study II, the prevalence of AF was estimated using the handheld ECG device InstantCheck® among persons aged 50 years and older in East Greenland.

In addition, InstantCheck®'s ability to detect AF was compared to the recordings of standard 30-second 12-lead ECGs performed on patients in Nuuk, Greenland and Aalborg, Denmark.

Results:

Based on the comparison of 12-lead ECGs and InstantCheck® recordings, the sensitivity of InstantCheck® to detect AF was 100%, the specificity was 96%, the positive predictive value was 66.7% and the negative predictive value was 100% [2] (Appendix C).

A description of the 221 East Greenlanders who participated in the study is given in Table 5-3.

Table 5-3. Description of participants in Study II. For missing data, see Appendix C or [2].

	Men	**Women**	**p-value**	**Total**
Gender, n (%) *	107 (48.9)	113 (51.1)	0.79	220
Age, median (IQR)	63 (56;69)	60.5 (54;69)	0.35	61 (55;69)
BMI, mean (SD)	26.8 (4.9)	27.0 (5.7)	0.61	26.9 (5.3)
Height, mean (SD)	166.7 (8.0)	153.3 (6.1)	<0.01	159.8 (9.7)
Weight, mean (SD)	75.1 (17.3)	63.8 (14.9)	<0.01	69.2 (17.0)
Both parents born in Greenland, n (%) *	100 (93.5)	111 (98.2)	0.07	211 (95.9)
Smoking, cigarettes per day				
Never, n (%) *	11 (10.8)	4 (3.6)	0.04	15 (7.0)
Previous smoker, n (%) *	29 (28.4)	30 (27.0)	0.82	59 (27.7)
1-10, n (%) *	37 (36.3)	65 (58.6)	<0.01	15 (7.0)
11-20, n (%) *	23 (22.6)	11 (9.9)	0.01	59 (27.7)
21+, n (%) *	2 (1.9)	1 (0.9)	0.51	102 (48.9)
Thyroid disease [b]	0 (0)	0 (0)	-	34 (15.9)

Risk factors for AF				
Diabetes, n (%) *	4 (3.7)	1 (0.9)	0.16	3 (1.4)
Hypertension, n (%) *	1 (0.9)	3 (2.7)	0.34	4 (1.8)
Arrhythmia, n (%) *	1 (0.9)	0 (0)	0.30	0 (0)
Previous stroke, n (%) *	5 (4.7)	2 (1.8)	0.22	5 (2.3)
Ischemic heart disease, n (%) *	1 (0.9)	0 (0)	0.30	4 (1.8)
Heart failure, n (%) *	1 (0.9)	0 (0)	0.30	1 (0.5)

**Per cent of participants without missing data. Abbreviations: AF: Atrial fibrillation. IQR: Interquartile range. SD: Standard deviation. The table is adjusted from Table 1 in Appendix C.*

Using InstantCheck® among the 221 participants, we found a prevalence of AF of 0.9%, as shown in Table 5-4.

Table 5-4. Distribution of cardiac rhythms identified by InstantCheck® in East Greenland.

Rhythm	Men	Women	p-value	Total
Atrial fibrillation, n (%)	2 (1.9)	0 (0)	NS	2 (0.9)
Sinus rhythm, n (%)	105 (98.1)	111 (98.2)	NS	217 (98.2)
Pacemaker, n (%)	0 (0)	2 (1.8)	NS	2 (0.9)

The table is adjusted from Table 2 in Appendix C.

Conclusion:

We found a low prevalence of AF among the 221 participants aged 50 years and older. However, as the device records for 30 seconds only and each participant had a single recording, we may have missed cases of paroxysmal AF. Therefore, we concluded that the prevalence found in this study should be considered an estimation of the prevalence of persistent AF.

5.1.3. PREVALENCE OF ATRIAL FIBRILLATION IN NUUK

Study IV was conducted in Nuuk from April 2022 to January 2023 and is based on continuous ECGs recorded with ePatch® among participants aged 50 years and older from Nuuk.

The study was submitted for publication in December 2023 and has yet to be peer-reviewed by the time of submission of this thesis.

Results:

A total of 226 participants (38% men) with a mean age of 61.3 years had an analysable ECG recording and were included in the study. The inclusion of participants in the study is shown in Figure 1 in Appendix D, page 20 [4].

The median recording time of the ECGs was 4.3 days, and 85% of the participants had a recording lasting at least three days.

Before the recording, 18 participants reported in the questionnaire that they had AF. Three additional participants had AF on the recording, bringing the number of participants with AF to 21 and the prevalence of AF in the study to 9.3%. The age-adjusted prevalence is presented in Table 5-5.

Table 5-5. Age-adjusted prevalence of AF in Nuuk.

Age group	Prevalence, %	95% CI, %
50-59 years	7.2	2.7-15.1
60-69 years	8.8	4.1-16.1
70 years and older	18.2	7.0-35.5

Abbreviations: CI: Confidence interval.

Selected characteristics of the study participants by whether they had AF are shown in table 5-6. The complete list can be found in Appendix D, Table 3.

Table 5-6: Characteristics of participants with and without AF.

	AF (n=21)	No AF (n=211)	p-value
Male gender, % *	67 (14/21)	35 (72/205)	0.01
Age, years, mean (SD)	64.2 (8.7)	61.5 (6.8)	0.09
BMI, kg/m^2, mean (SD)	30.5 (4.5)	29.0 (6.0)	0.31
Active smoker, % *	20 (4/20)	25 (49/196)	0.43
Consumes alcohol weekly, % *	75 (15/20)	61 (119/195)	0.67

Systolic blood pressure, mmHg, mean (SD)	139 (15)	143 (18)	0.36
Diastolic blood pressure, mmHg, mean (SD)	83 (9)	85 (12)	0.64
Pulse, bpm, mean (SD)	75 (12)	78 (12)	0.33
Greenlandic origin, % *	85 (18/21)	85 (168/198)	0.61
Family history of cardiac disease, % *	33 (7/21)	51 (100/197)	0.10
CHA_2DS_2-VASc- score, median (IQR) **	1 (2)	1 (2)	0.41
Comorbidities, self-reported			
Atrial fibrillation, % *	86 (18/21)	0 (0/197)	<0.01
Ischemic heart disease, % *	0 (0/21)	2 (3/197)	0.74
Heart failure, % *	9.5 (2/21)	1 (1/197)	0.03
Pacemaker, % *	9.5 (2/21)	1.0 (2/197)	0.047
Hypertension, % *	48 (10/21)	32 (63/195)	0.12
Diabetes, % *	14 (3/21)	21 (41/196)	0.37
Thyroid disease, % *	10 (2/21)	7 (13/196)	0.44
Symptoms within the last 3 months before the test, self-reported, % *	63 (16/19)	74 (141/190)	0.66
Irregular pulse, % *	68 (13/19)	34 (64/190)	<0.01
Palpitations, % *	47 (9/19)	44 (83/190)	0.47
Pauses in heart rate, % *	42 (8/19)	16 (30/190)	0.01
Chest pain when resting, % *	37 (7/19)	21 (40/190)	0.10
Shortness of breath, % *	42 (8/19)	26 (49/190)	0.11
Faintness, % *	47 (9/19)	41 (77/190)	0.37
Dizziness, % *	11 (2/19)	8 (15/190)	0.47

** % (yes-sayers/total number of respondents). ** Female participants, with no other risk factors than gender, were given a score of zero. Abbreviations: BMI: Body mass Index. bpm: beats per minute. CHA_2DS_2-VASc: C: Congestive Heart Failure, H: Hypertension, A: Age 75 and older, D: Diabetes, S: Previous stroke, V: Vascular disease, A. Age 65-74, Sc: Sex category. IQR: Interquartile range. OAC: Oral anticoagulant. The table is modified from Table 3 in Appendix D.*

Conclusion:

Based on continuous ECG recordings among 226 participants from Nuuk aged 50 years and older, we found a higher prevalence of AF than in previous studies. Additionally, we saw the same trend as earlier with AF being more common among men.

5.2. STUDY III: ATRIAL FIBRILLATION AMONG ISCHEMIC STROKE PATIENTS IN GREENLAND

Study III is based on data from patients discharged from 2016 to 2021 from QIH with a diagnosis code for IS or stroke without specification, as detailed in Chapter 2 and Appendix C. We had access to the Holter recordings in 2021, and the study therefore only includes recordings from 2016-2020.

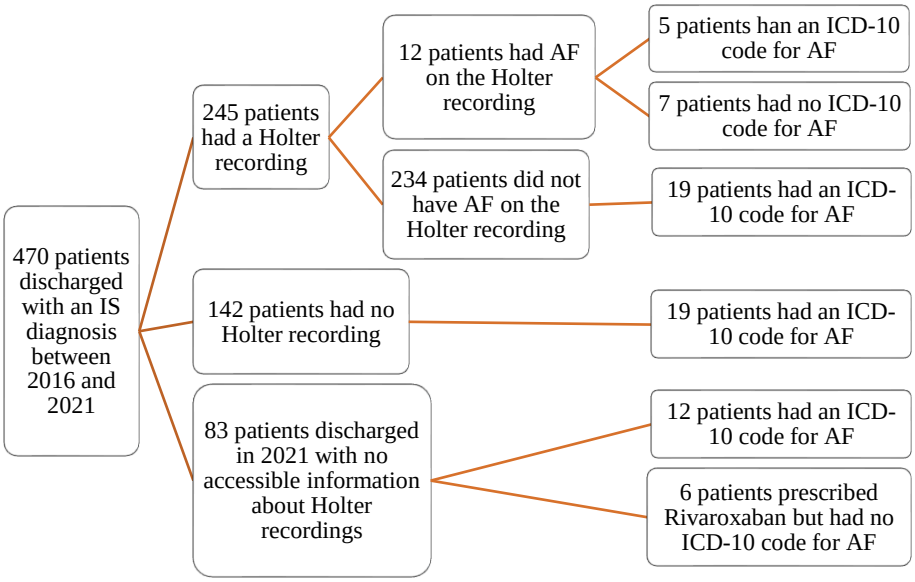
A study based on the same data describing the age-standardized incidences of IS was published in Stroke in 2023 [85], but is not included in the thesis as it did not discuss AF among the patients.

Results:

In total, 470 patients were identified as having been discharged from QIH with an IS diagnosis code between 2016 and 2021, corresponding to a mean incidence of 133/100,000/year (CI 120-147).

The mean age was 60.9 years for women and 61.0 years for men, and the latter constituted 55% of the patients. Sixty-three per cent (245) of the patients discharged between 2016 and 2020 had a Holter recording (Figure 5-1), and 69% of the recordings fulfilled the recommendation of at least 72 hours of recording [35].

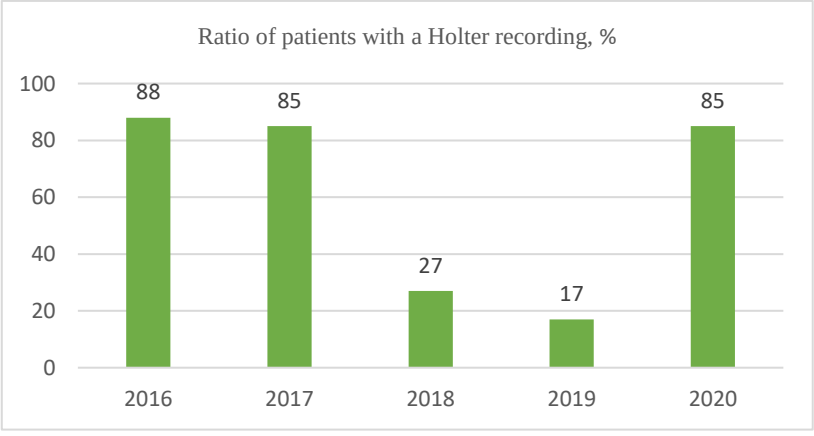
Figure 5-1. Holter recordings and AF among ischemic stroke patients.



Abbreviations: AF: Atrial fibrillation. ICD-10: International Classification of Diseases, 10th revision. The figure is from [3].

The ratio of patients with a Holter recording topped in 2016 and was at its lowest in 2018, as shown in Figure 5-3.

Figure 5-3. Ratio of IS patients with a Holter recording by year of discharge.



Based on the results of the recordings, diagnosis codes for AF and prescriptions for OACs (Warfarin and Rivaroxaban), a total of 68 patients, or 14.5% (95% CI 11.4;18.0), were estimated to have AF (Figure 5-1.. Eighty per cent of the AF patients were treated with an OAC.

Conclusion:

Compared to Bjørn-Mortensen et al.'s results from 2013, the incidence of IS remains unchanged in Greenland; however, the ratio of IS patients with AF seems to have halved from 32.4% [34] to 14.5% in our study. There are several possible explanations for the drop in the ratio of patients with AF, one being a shift in OAC treatment from Warfarin to Rivaroxaban. Another possible explanation is that AF is underdiagnosed in the study group, as the ratio of patients with a Holter recording performed according to international recommendations was low.

CHAPTER 6. DISCUSSION

AF remains the most common arrhythmia globally, and with the increasing life expectancy, the condition will likely affect an increasing number of persons in the Greenlandic population.

In Studies I, II and IV, we estimated the prevalence of AF among the general population in 96% of Greenland, East Greenland and, finally, in the capital, Nuuk. In Study III, we estimated the incidence of IS in Greenland from 2016 to 2021, and the ratio of IS patients with AF within the same period.

This chapter compares and discusses the results of the four studies. A few words on the strengths and limitations of the studies follow, including a discussion of the methods.

6.1. PREVALENCE OF ATRIAL FIBRILLATION IN GREENLAND

The prevalence of AF among people aged 50 years and older in Studies I, II and IV is summarized in Table 6-1.

Table 6-1. Prevalence of AF among participants aged 50 years and older.

Study	Method used	Prevalence, %	95% CI, %
Study I	Diagnosis and ATC codes	3.8	3.5; 4.1
Study II	Handheld 30-second ECG recordings	0.9	0.1; 3.2
Study IV	Continuous ECG recordings	9.3	5.8; 13.9

The table is based on data from [1, 2, 4]. The prevalence of AF among those aged 50 years and older is not described in [1] but has been calculated for this table. Abbreviations: CI: Confidence interval.

The estimated prevalence found in each study varies quite significantly, which may, at least to some extent, be explained by the methods used and by the included populations.

Study I was based on diagnosis codes and prescribed medication in the EMR. Therefore, the prevalence found in that study can be described as the prevalence of diagnosed AF in Greenland, as a medical professional will have assigned the patient the diagnosis code or prescribed the OAC.

Studies II and IV were both conducted among the general population, albeit in two very different locations and using different methods. In Study II, single-point 30-second ECGs were used to estimate the prevalence. As described in Chapter 2, there is a risk of missing paroxysmal AF when using this method, and, as also discussed in the manuscript [2], the estimated prevalence of 0.9% is best considered the prevalence of persistent AF in East Greenland only. Persistent AF makes up approximately 25% of AF globally [37], and if the same applies to East Greenland, the true prevalence among those aged 50 years and older would be closer to the prevalence found in Study I.

The estimated prevalence in Study I among those aged 50 years and older is less than half of the estimated prevalence in Study IV, as shown in Table 6-1. This difference may partly be attributed to undiagnosed AF in Greenland. Asymptomatic AF patients may remain unidentified unless actively screened, as subclinical AF is frequently diagnosed incidentally [60] and, emphasizing this point, one-third of the participants with previously undiagnosed AF in Study IV did not report any symptoms [4]. In addition, Holter recordings have only been available in Nuuk until recently, meaning that outside of Nuuk, there is a risk that paroxysmal AF may have been missed on the standard 12-lead ECGs used in the health care centers and stations, even among symptomatic patients.

Comparing the overall prevalence of diagnosed AF of 1.8% found in Study I to other Nordic populations, we found a prevalence lower than in Finland, where 4.1% among those 20 years and older in 2018 are diagnosed with AF [86]. In Denmark, the prevalence was 3.0% among those older than 17 years in 2018 [87] and in Norway, the cumulative prevalence from 1994 to 2014 was 3.4% [88]. In Sweden, a study from 2022 found a prevalence of 4.7%, including registrations from primary care [89], while an older study including registrations from hospitals found a prevalence ranging from 2.5% to 3.5% [90]. However, the prevalence found in Study I is similar to the estimated prevalence of 1.9%, excluding post-operative AF, found in Iceland among the population aged between 20 and 99 years of age in 2008 [40].

Comparing the prevalence of diagnosed AF to studies among other Indigenous populations based on similar methods, the prevalence of diagnosed AF in Greenland is also slightly lower than among Australian Aboriginals [78], American Indians [72] and the Canadian Métis [70] with prevalences ranging from 2.08% to 4.4% (Table 2-3 in Chapter 2).

When comparing the results from Study II to other studies estimating AF based on single ECG recordings, a prevalence of 0.8% was found in India among 450 participants [91]; however, their mean age was 31.5 years and, therefore, younger than our study group. In China, a prevalence of 1.2% was found among 11,341 participants aged 55 years and older, including participants with self-reported AF [92].

The results of Study IV can be compared to a Swedish study performed among 7,173 participants aged 75-76 years [93]. Nine per cent of the participants in that study had an AF diagnosis at the beginning of the study, and an additional three per cent were diagnosed after two weeks of screening. For comparison, eight per cent of the participants in Study IV had self-reported AF at the start and an additional 1.3% were identified as having AF based on their recording [4]. Eighty-five per cent of the participants in Study IV had recordings lasting at least the recommended 72 hours [35], but more cases of AF may have been identified had they been even longer [65, 94, 95].

6.2. ATRIAL FIBRILLATION AND ISCHEMIC STROKE

In Study III, we estimated the incidence of IS and the ratio of IS patients with AF from 2016 to 2021.

In Bjørn-Mortensen et al.'s study from 2013, the estimated incidence of IS in Greenland was 138/100,000 (95% CI 115-161) [33], which is close to the incidence of 133/100,000 (95% CI 120-147) estimated in our study. However, they found that 32% of the IS patients in 2011 and 2012 had AF [34], more than double the estimated prevalence of AF found in Study III.

As discussed in the manuscript, there may be more than one explanation for the drop [3], but it seems likely that AF may be underdiagnosed among the IS patients in our study. Between 2016 and 2020, less than half of the IS patients without a diagnosis code for AF had a Holter recording lasting at least 72 hours performed and as shown in Figure 5-2, the ratio of patients with a Holter recording was particularly low in 2018 and 2019. As already touched upon, continuous recordings increase the chance of diagnosing AF among IS patients, especially if initiated shortly after the stroke [94].

In addition, the results from Study I indicate that strokes among AF patients in Greenland are not rare events. 16.5% of the women in Study I had suffered a stroke at some point compared to 11.3% of the men. The data in Study I includes hemorrhagic strokes, but approximately 90% of strokes in Greenland are ischemic [33]. The women in Study I had a higher minimum CHA_2DS_2-VASc score than the men, and a higher risk of IS among female AF patients has been documented in studies outside of Greenland [96]. In addition, women have more often suffered a stroke by the time they are diagnosed with AF [97] and are less likely to be treated with an OAC [98]. Our data in Study I does not allow us to estimate the time between AF and IS diagnoses, but men and women were treated equally often with OACs (Table 5-1).

The risk factors for ischemic stroke overlap to a great extent with the risk factors for AF, as evidenced by the CHA_2DS_2-VASc score used to estimate the risk of stroke among AF patients [48, 52, 99, 100]. This leads us to the next part of the discussion.

6.3. RISK FACTORS

Studies I, II and IV include a baseline description of the study populations, including some of the most common risk factors for AF, such as age, gender, smoking, hypertension, diabetes and ischemic heart disease [1, 2, 4].

With only two participants having AF in Study II, it is difficult to compare the risk factor profile between those with and without AF in Study II, as well as comparing the two AF patients to patients in other studies. However, comparing all participants in Study II with the general Greenlandic population of the same age, diabetes [18], hyperthyroidism [101], hypertension [102] and IHD [29] were less common among the participants in Study II than in the general population of the same age [2]. Consequently, part of the low prevalence estimated in that study could be explained by a healthy study population and not only the method used.

In contrast, comparing the participants in Study IV with the general population, we found that a higher proportion of participants were women and had diabetes [4]. However, there was no difference in the ratio of AF patients and non-AF with diabetes in the study. The only risk factors more prevalent in the AF group were male gender, HF and having a pacemaker [4].

Study I included 790 Greenlandic patients with AF and offers the best comparison between men and women with AF in Greenland of the three studies. Among the patients younger than 70 years, the patients were more often male, but women generally had more risk factors as they were older, and more often had diabetes and hyperthyroidism than men [1].

In both Study I and IV, the prevalence of AF increased with age, which is consistent with other studies, where the prevalence among the oldest is estimated to be between 10 and 25% [87, 103], a range similar to what we found in Studies I and IV. The age-related increase in prevalence is likely due to an accumulation of risk factors with age [103]. Similarly, the gender differences found in Studies I and IV are also found globally [43, 103]. Generally, women's longer life expectancy is considered the main reason for this age-related change in gender distribution among the eldest AF patients [87].

Finally, as listed in Table 2-2 in Chapter 2, genetics is also considered a risk factor for AF. More than 100 AF-related genes have been detected, some increasing the risk of early-onset AF [104, 105]. These studies have primarily been conducted among Europeans [105], but it is well-established that the Greenlandic Inuit are genetically predisposed to hypercholesterolemia and diabetes, both risk factors for AF [14, 106]. If the estimated prevalence in Study IV is correct, Greenland has a high prevalence of AF among those younger than 60 years when compared to Europe [87, 103], and,

similarly, Greenland has a high incidence of IS among the young, with 33% of patients being younger than 55 years [85].

Our studies do not offer the possibility to estimate if the Greenlandic population of Inuit origin is predisposed to AF, but we found no difference in AF prevalence between participants of Greenlandic origin and others in Study IV.

6.4. STRENGTHS AND LIMITATIONS

The strengths and limitations are discussed in detail in the manuscripts. However, the most significant are listed below:

6.4.1. STRENGTHS

The main strength of Study I and III is the use of the EMR, allowing us to include most of the Greenlandic population with a relevant diagnosis. For Study II, comparing the results of InstantCheck® with 12-lead ECGs increased the reliability of the results, as well as having a consultant cardiologist review the recordings, as described in the manuscript [2]. In cases of doubt, ECGs were also consulted with a consultant cardiologist in Study III and IV [3,4].

6.4.2. LIMITATIONS

A colleague once told me, "*The quality of the result you get out when doing research is only as good as the information you put in*".

This subchapter presents some general methodological considerations, starting with the risks of bias in the studies and ending with the limitations of cross-sectional studies.

Bias:

The studies that form the backbone of this thesis rely on participant-reported information and data from electronic sources, such as the EMR. This means the risk of information bias must be considered [107]. Information bias is a type of error that occurs when something is not measured or classified correctly, and it can be divided into several subtypes of bias, as done below.

Self-reporting bias and recall bias:

Studies II and IV are based on self-reported data collected from questionnaires. This method creates a risk of self-reporting and recall bias. We managed this risk as much as possible by following up on the questionnaires. For example, all participants who had answered "yes" to having an arrhythmia were asked for further details when they

were informed about their ePatch® result after the analyses in Study IV. However, participants who answered "no" but should have replied "yes" may have been missed.

Collecting data in a setting different from your native culture is a challenge that should also be considered. Careful adaptation and validation of instruments such as questionnaires are recommended to ensure that the questions are understood and answered as intended in order to reduce information bias [108, 109]. Our questionnaires were developed in Danish and translated to Greenlandic by a Greenlandic translator recommended by the Greenlandic Health Care System; however, they were not validated with forward and back translation as recommended in the literature [108, 109]. Instead, there was a translator available for all sessions and phone calls to help minimize unclarities and questions; however, it is a point that could be improved upon in future studies.

Classification bias:

In Studies I and III, data was extracted from the EMR based on diagnosis codes and prescribed medications. This method relies on good registration praxis in the hospital and the health care centers included in the studies, as patients who are misclassified or not classified will skew the results. Registration in the EMR is a focus point in Greenland, and a study from 2018 found a 99% correspondence between information in the EMR and CVD diagnoses given between 2001 and 2013 in QIH and 2007 and 2013 in the health care centers [110]. This indicates that diagnosis codes in Greenland can be trusted as being assigned correctly; however, the number of patients not given a diagnosis code when relevant remains in the dark. This is especially relevant in Study III, where patients outside Nuuk must be transported to QIH for cerebral scans. In addition, we chose to use OAC prescriptions as a proxy for AF in Study I, thereby possibly classifying patients as having AF when they are, in fact, treated for other conditions.

Selection bias:

Selection bias could be a factor in Studies II and IV. In Study II, all eligible participants were invited directly to join the study, but we have no data on those who chose not to participate. Therefore, we may have tested a more select portion of the population in East Greenland than intended. As discussed in section 6.3., our results indicate that the study population was healthier than the background population, which may cause an underestimation of AF.

In Study IV, selection bias may have caused an overestimation of AF. All eligible participants were invited through the media, and most contacted the research team themselves to participate. Only a few were invited directly, either by phone or when seen in Steno Diabetes Center Nuuk in relation to a different study. Our data shows that the latter caused an overrepresentation of patients with diabetes in Study IV

compared to the general population of the same age (21% vs 10-15%) [18]. In addition, eight per cent of the participants reported having AF at the start, which is double that of the ratio of diagnosed patients 50 years and older found in Study I (Table 6-1).

Study Designs:

There are several different study designs within medical research, each with strengths and limitations. Systematic reviews and meta-analyses are generally considered to provide the highest level of evidence, followed by randomized controlled trials and then observational studies, including cohort studies, cross-sectional studies and case reports [111].

Cross-sectional studies:

All studies in the thesis are cross-sectional studies, meaning that they focus on a study population at a specific point in time. The main limitation of cross-sectional studies is the inability to describe changes in the study population over time, making it challenging to identify associations between outcomes and risk factors. In addition, when conducting cross-sectional studies in a small population such as Greenland, there is a chance that the outcome is rare, as in Study II and IV, which challenges the identification of associations even further [112].

Cohort-studies:

Study III was conducted as a retrospective cohort study when estimating the incidence of IS in Greenland between 2016 and 2021. One of the main limitations of retrospective cohort studies is the lack of control over data registration [113], and, as mentioned in Study IV, the uncertainty regarding when AF diagnosis codes were given to the IS patients rendered an estimation of AF incidence too uncertain to include.

CHAPTER 7. CONCLUSION AND FUTURE PERSPECTIVES

The PhD project aimed to estimate the frequency of AF in Greenland, and with the four studies in this thesis, we have gained insight into the epidemiology of AF in different regions of Greenland.

The prevalence estimates of AF among individuals aged 50 years and older vary across the studies, reflecting differences between the populations and the methodologies used. Study I, relying on diagnosis codes and prescribed medication, offers a glimpse into diagnosed AF cases in Greenland. Study II highlights the prevalence of persistent AF and the potential challenges in capturing paroxysmal AF using single ECG recordings. In contrast, Study IV, employing continuous ECG recordings in Nuuk, reveals a higher prevalence of AF than the other two studies, emphasizing the importance of monitoring over time. However, all three studies are limited by the methods used. The results of Study II may be an underestimation, whereas Study IV may overestimate the prevalence, and there is a risk of both in Study I. Therefore, it seems likely that the actual prevalence of AF in Greenland lies between the estimations of Study I and IV, close the prevalence found in other Nordic countries.

Based on our results, age and gender are the most prominent risk factors for AF in Greenland, as seen elsewhere. However, prospective cohort studies and larger studies comparing AF patients with non-AF Greenlanders could shed a clearer light on the association between risk factors, including genetic components, and the development of AF in Greenland.

The connection between AF and IS is explored in Study III, where the incidence of IS and the ratio of IS patients with AF are estimated. The results suggest that AF among IS patients in Greenland is underdiagnosed, and, as Study II, it highlights the diagnostic challenges in Greenland. The need to expand and adapt the diagnostic instruments to the Greenlandic health care system and culture should be another focus point for future studies, as well as screening for AF among the older age groups of the Greenlandic population could be considered.

Our studies offer some of the first insights into AF in Greenland and the foundation for future studies and interventions. The remaining part of the iceberg has yet to be revealed.

Figure 8-1. A boat passing a steaming iceberg close to Qeqertarsuaq (Disko Island). Private photo (2023).

LITERATURE LIST

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APPENDICES

Appendix A. Questionnaire, Study II

Grønland d._____2018

Deltager nr. _____

SPØRGESKEMA

Til undersøgelsen af
struma og stofskiftelidelser, vitamin D og kalkstofskifte og leverbetændelse
i Grønland

Stig Andersen
Paneeraq Noahsen
Karsten Fleischer Rex
Hans Chr. Florian Sørensen
Gert Mulvad
Henrik Krarup

1

SPØRGESKEMA

1. DEMOGRAFI:

   a. Er du født i Grønland Ja☐ Nej☐

   b. Er din far født i Grønland Ja☐ Nej☐

   c. Er din mor født i Grønland Ja☐ Nej☐

   d. Er du

      i. Mand ☐

      ii. Kvinde ☐

   e. Hvor gammel er du _____ år

   h. Hvor længe har du boet i Nuuk:

      fra 19___ til 2018; i alt: _____ år.

   i. Hvor har du boet før:

      By:_____ fra 20___ til 20___ ; i alt: _____ år.

      By:_____ fra 19___ til 19___ ; i alt: _____ år.

      By:_____ fra 19___ til 19___ ; i alt: _____ år.

      By:_____ fra 19___ til 19___ ; i alt: _____ år.

2. LIVSSTIL

   a. Hvor ofte er dit **hovedmåltid**:

      i. Grønlandsk: _____ gange om ugen

      ii. Dansk: _____ gange om ugen (7 i alt)

   b. Hvad drikker du til maden:

      i. Mælk ☐

      ii. Vand ☐

iii. Øl ☐

iv. Andet ☐

c. **Hvor meget ryger du:**

i. aldrig (Gå til punkt d.)

ii. holdt op - Jeg røg fra 19___ til 19___ .

Jeg ryger:

Cigaretter:

iii. 1-10 ☐

iv. 11-20 ☐

v. flere end 20 ☐

Pibe:

vi. Antal gram pr uge: _____

Andet:

vii. Hvad _____

viii. Hvor meget _____

d.	**Jeg drikker (alkohol):**	**NU**	**Tidligere**
i.	Aldrig	☐	☐
ii.	0-7 genstande pr uge	☐	☐
iii.	8-14 genstande pr uge	☐	☐
iv.	15-21 genstande pr uge	☐	☐
v.	mere end 21 genstande pr uge	☐	☐

e.	Hvor **godt taler du**	**Grønlandsk:**	**Dansk**:
i.	Uden besvær	☐	☐
ii.	Nogenlunde	☐	☐
iii.	Vanskeligt	☐	☐
iv.	Slet ikke ☐	☐	

3. SYGDOMME:

a. Er der struma eller stofskiftesygdom i din familie?

Ja ☐ Nej ☐ Ved ikke ☐

Hvis ja: Hvem Hvilken type sygdom:

Mor _____

Far _____

Bror _____

Søster _____

Anden _____

b. Har du, eller har du haft stofskiftesygdom?

Ja ☐ Nej ☐ Ved ikke ☐

Hvis ja, var dit stofskifte da:

Højt☐ Lavt ☐ Ved ikke ☐

c. Har du, eller har du haft struma?

Ja ☐ Nej ☐ Ved ikke ☐

d. Er du i, eller har du fået behandling for struma?

Ja ☐ Nej ☐ Ved ikke ☐

Hvis ja, da hvilken behandling:

(a) Medicin

(b) Radio-Jod

(c) Opereret

(d) Andet

e. Får du medicin for stofskiftet nu?

Ja ☐ Nej ☐

Hvis ja, da hvilken medicin: _____

f. Får du anden medicin?

Ja ☐ Nej ☐

Hvis ja, da hvilken:

(1) _____

(2) _____

(3) _____

(4) _____

(5) _____

4

(6) _____
(7) _____
(8) _____
(9) _____
(10) _____

g. Tager du vitamintabletter?

(a) Aldrig ☐
(b) Af og til ☐
(c) Kun om vinteren ☐
(d) Daglig ☐

Hvis ja, indeholder de da:

Jod	Ja ☐	Nej ☐	Ved ikke ☐
Vitamin D	Ja ☐	Nej ☐	Ved ikke ☐

h. Tage du regelmæssigt naturmedicin?

Ja ☐ Nej ☐

Hvis ja, indeholder det da:

Jod/ tang	Ja ☐	Nej ☐	Ved ikke ☐
Vitamin D	Ja ☐	Nej ☐	Ved ikke ☐

j. Fejler du, eller har du tidligere fejlet noget alvorligt:

	År	Indlagt Ja	Indlagt Nej	Diagnose / Symptomer
i.	19__	☐	☐	_____
ii.	19__	☐	☐	_____
iii.	19__	☐	☐	_____
iv.	____			_____
v.	20__			_____

vi. 20__ _____

- fortsættes -

Hvor ofte spiser eller drikker du følgende? Tænk især på de sidste 3 måneder.

		hver dag	4-6 gange om ugen	1-3 gange om ugen	2-3 gange om måned	1 gang om måned	aldrig
a.	sælkød	1	2	3	4	5	6
b.	hvalkød	1	2	3	4	5	6
c.	fugl	1	2	3	4	5	6
d.	fisk	1	2	3	4	5	6
e.	rensdyr, moskusokse, hare	1	2	3	4	5	6
f.	lam	1	2	3	4	5	6
g	færdiglavede middagsretter (forårsruller, dåsemad o.l.)	1	2	3	4	5	6
h.	kartofler	1	2	3	4	5	6
i.	andre grøntsager	1	2	3	4	5	6
j.	smør	1	2	3	4	5	6
k.	ost	1	2	3	4	5	6
l.	æg.....	1	2	3	4	5	6
m.	frisk frugt	1	2	3	4	5	6
n.	sødmælk, yoghurt, ymer ...	1	2	3	4	5	6
o.	sodavand…….....	1	2	3	4	5	6
p.	saft	1	2	3	4	5	6
q.	øl vin spiritus	1	2	3	4	5	6
r.	tang	1	2	3	4	5	6

Hvor meget har du inden for de sidste 12 måneder selv været på fangst eller fiskeri eller været med på fangst eller fiskeri?

er fanger/fisker	1
driver erhvervsmæssig fangst/fiskeri i kombination med lønarbejde	2
er fanger/fisker en stor del af fritiden	3
går lejlighedsvis på fangst/fiskeri	4
går aldrig på fangst/fiskeri	5

Hvor ofte har du de sidste 3 måneder spist et hovedmåltid, der stammer fra din egen eller din families fangst eller fiskeri?

hver dag	1
flere gange om ugen	2
en gang om ugen	3
et par gange om måneden	4
en gang om måneden	5
mindre end en gang om måneden	6
aldrig	7

Hvor ofte spiser du grønlandsk mad på de forskellige årstider?

		hver dag	4-6 gange om ugen	1-3 gange om ugen	2-3 gange om måned	1 gang om måned	aldrig
sommer	1	2	3	4	5	6	
efterår	1	2	3	4	5	6	
vinter	1	2	3	4	5	6	
forår	1	2	3	4	5	6	

Appendix B. Demographic questionnaire Study IV

SPØRGESKEMA

Til undersøgelse af hjerterytmeforstyrrelser i Grønland

Nadja Albertsen

Stig Andersen

Sam Riahi

Michael Lynge Pedersen

SPØRGESKEMA

DEMOGRAFI:

Er du:

Mand ☐ Kvinde ☐

Er du født i Grønland? Ja ☐ Nej ☐

Er din far født i Grønland? Ja ☐ Nej ☐

Er din mor født i Grønland? Ja ☐ Nej ☐

Hvor gammel er du?: _____ år

Hvor længe har du boet i nuværende by: _____ år

I hvilken by er du født: _____

LIVSSTIL

Højde: _____

Vægt: _____

TOBAK

Ryger du, eller har du røget, cigaretter?

Ja: 1-5 dagligt ☐ 6-10 dagligt ☐ 11-15 dagligt ☐ 16-20 dagligt ☐

Flere end 20 dagligt ☐

Nej: Tidligere ryger ☐

Hvor mange år: _____ Årstal for ophør: _____

Aldrig ☐

Ryger du andet end cigaretter?

Hvis ja, angiv hvad og hvor meget: _____

2

ALKOHOL

Indtag af alkohol:	NU	Tidligere
Aldrig	☐	☐
0-7 genstande pr uge	☐	☐
8-14 genstande pr uge	☐	☐
15-21 genstande pr uge	☐	☐
Flere end 21 genstande pr uge	☐	☐

SYGDOMME:

Har du eller medlemmer af din familie hjertesygdom?

☐ Ja, jeg har ☐ Ja, familiemedlem (hvem): _____

☐ Nej ☐ Ved ikke

Hvis ja:

Årstal for diagnose: _____

Hjerterytmeforstyrrelse ☐

(f.eks. forkammerflimmer/atrieflimren)

Hjertesvigt ☐

Blodprop i hjertet ☐

Pacemaker ☐

Anden hjertesygdom, ved ikke hvilken ☐

Har du eller medlemmer af din familie forhøjet blodtryk (hypertension) eller får medicin for det?

☐ Ja, jeg har ☐ Ja, familiemedlem (hvem): _____

☐ Nej ☐ Ved ikke

Hvis ja, årstal for diagnose: _____

Har du eller medlemmer af din familie stofskiftesygdom?

☐ Ja, jeg har ☐ Ja, familiemedlem (hvem): _____

☐ Nej ☐ Ved ikke

Hvis ja:

Årstal for diagnose: _____

For højt stofskifte ☐

For lavt stofskifte ☐

Ved ikke ☐

Har du eller medlemmer af din familie sukkersyge (diabetes)?

☐ Ja, jeg har ☐ Ja, familiemedlem (hvem): _____

☐ Nej ☐ Ved ikke

Hvis ja:

Årstal for diagnose: _____

Type 1 diabetes: ☐

Type 2 diabetes: ☐

Ved ikke: ☐

Har du andre sygdomme? Ja ☐ Nej ☐

Hvis ja, hvilke?

1. Sygdom:_____Årstal for diagnose: _____
2. Sygdom:_____Årstal for diagnose: _____
3. Sygdom:_____Årstal for diagnose: _____
4. Sygdom:_____Årstal for diagnose: _____

Har du tidligere været indlagt? Ja ☐ Nej ☐

Hvis ja, hvorfor?

1. Årsag:_____Årstal: _____
2. Årsag:_____Årstal: _____
3. Årsag:_____Årstal: _____
4. Årsag:_____Årstal: _____

SYMPTOMER PÅ UREGELMÆSSIG HJERTERYTME

Har du inden for de sidste 3 måneder oplevet nogle af følgende symptomer:

Fornemmelse af UREGELMÆSSIG puls:

Ja ☐ Nej ☐

Hvis ja, hvor ofte:

☐ Dagligt ☐ Ugentligt ☐ Månedligt ☐ Sjældnere

☐ Andet: _____

Fornemmelse af HJERTEBANKEN i hvile eller ved normal aktivitet, f.eks. gang

Ja ☐ Nej ☐

Hvis ja, hvor ofte:

☐ Dagligt ☐ Ugentligt ☐ Månedligt ☐ Sjældnere

☐ Andet: _____

Fornemmelse af PAUSE I HJERTERYTMEN:

Ja ☐ Nej ☐

Hvis ja, hvor ofte:

☐ Dagligt ☐ Ugentligt ☐ Månedligt ☐ Sjældnere

☐ Andet: _____

BRYSTSMERTER i hvile eller ved normal aktivitet, f.eks. gang

Ja ☐ Nej ☐

Hvis ja, hvor ofte:

☐ Dagligt ☐ Ugentligt ☐ Månedligt ☐ Sjældnere

☐ Andet: _____

ÅNDENØD i hvile eller ved normal aktivitet, f.eks. gang

Ja ☐ Nej ☐

Hvis ja, hvor ofte:

☐ Dagligt ☐ Ugentligt ☐ Månedligt ☐ Sjældnere

☐ Andet: _____

SVIMMELHED:

Ja ☐ Nej ☐

Hvis ja, hvor ofte:

☐ Dagligt ☐ Ugentligt ☐ Månedligt ☐ Sjældnere

☐ Andet: _____

BESVIMELSE:

Ja ☐ Nej ☐

Hvis ja, hvor ofte:

☐ Dagligt ☐ Ugentligt ☐ Månedligt ☐ Sjældnere

☐ Andet: _____

MEDICIN OG KOSTILSKUD

Tager du fast, lægeordineret medicin?

Ja ☐ Nej ☐

Hvis ja, skriv venligst navn på medicin, dosis (f.eks. 50 mg), årsag (f.eks. forhøjet blodtryk) og hyppighed (f.eks. 2 gange om dagen)?

1. Navn:_____ Dosis: _____
   Årsag: _____ Hyppighed: _____
2. Navn:_____ Dosis: _____
   Årsag: _____ Hyppighed: _____
3. Navn:_____ Dosis: _____
   Årsag: _____ Hyppighed: _____
4. Navn:_____ Dosis: _____
   Årsag: _____ Hyppighed: _____
5. Navn:_____ Dosis: _____
   Årsag: _____ Hyppighed: _____
6. Navn:_____ Dosis: _____
   Årsag: _____ Hyppighed: _____
7. Navn:_____ Dosis: _____
   Årsag: _____ Hyppighed: _____
8. Navn:_____ Dosis: _____
   Årsag: _____ Hyppighed: _____

Tager du vitamintabletter?

Aldrig ☐

Af og til ☐

Kun om vinteren ☐

Dagligt ☐

Hvis ja, indeholder de da:

Jod Ja ☐ Nej ☐ Ved ikke ☐

Vitamin D Ja ☐ Nej ☐ Ved ikke ☐

Navn på vitaminpille: _____

Tager du regelmæssigt naturmedicin?

Ja ☐ Nej ☐

Hvis ja, indeholder det da:

Jod/ tang Ja ☐ Nej ☐ Ved ikke ☐

Vitamin D Ja ☐ Nej ☐ Ved ikke ☐

Navn på kosttilskud: _____

TAK FOR DIN DELTAGELSE

8

Appendix C. ePatch questionnaire Study IV

Symptomskema

Deltagernummer:
_____

E-patchnummer:
_____

Påsætningstidspunkt:_____

Afleveringstidspunkt:_____

Afleveres på:

( ) DIS

( ) Naturinstituttet

( )
Andet:_____

Lev som du plejer – men undgå at sænke apparatet i vand.

Du kan være aktiv, sove og leve som du plejer, når du har apparatet på. Du må IKKE bade eller svømme med apparatet på, da den ikke må sænkes i vand. Du må derimod gerne tage brusebad, men undgå at bruse direkte på apparatet.

Notér, hvis du har symptomer fra hjertet

Hvis du oplever, at din hjerterytme ændrer sig eller du oplever andre symptomer fra hjertet, vil vi bede dig om at notere det på anfaldsskemaet på bagsiden af dette ark med dato og tidspunkt.

Efter undersøgelsen

Når måleperioden er afsluttet, skal du tage apparatet af ved at tage fat i den nederste del af klæbemærket og ryk det forsigtigt af huden. Fjern ikke apparatet fra klæbestrimlen. Fold de klæbede overflader sammen og læg apparatet i den medgivne pose sammen med anfaldsskema.

Herefter afleveres posen som aftalt ved påsætning af apparatet.

Svar på undersøgelsen

Du får svar på din undersøgelse, når alle undersøgelser i forskningsprojektet er foretaget og analyseret. Der kan derfor gå flere måneder. Hvis du oplever bekymrende symptomer fra hjertet i denne periode, er det derfor vigtigt at du kontakter din læge.

Dato	**Klokken**	**Symptomer**	**Aktivitet**