

Aalborg Universitet

Atrial Fibrillation in Greenland

Albertsen, Nadja

DOI (link to publication from Publisher): 10.54337/aau695996451

Publication date: 2024

Document Version Publisher's PDF, also known as Version of record

Link to publication from Aalborg University

Citation for published version (APA): Albertsen, N. (2024). *Atrial Fibrillation in Greenland*. Aalborg University Open Publishing. https://doi.org/10.54337/aau695996451

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
 You may freely distribute the URL identifying the publication in the public portal -

Take down policy

If you believe that this document breaches copyright please contact us at vbn@aub.aau.dk providing details, and we will remove access to the work immediately and investigate your claim.

ATRIAL FIBRILLATION IN GREENLAND

BY NADJA ALBERTSEN

PhD Thesis 2024



ATRIAL FIBRILLATION IN GREENLAND

by

Nadja Albertsen



AALBORG UNIVERSITY DENMARK

PhD Thesis 2024

Submitted:	January 2024
Main Supervisor:	Professor Stig Andersen Aalborg University Ilisimatusarfik, University of Greenland
Co-supervisors:	Professor Sam Riahi Aalborg University
	Professor Michael Lynge Pedersen Ilisimatusarfik, University of Greenland
Assessment:	Clinical Associate Professor Karina Frahm Kirk (chair) Aalborg University, Denmark
	Associate Professor Kasper Glerup Lauridsen Aarhus University, Denmark
	Professor Kristina Hermann Haugaa University of Oslo, Norway
PhD Series:	Faculty of Medicine, Aalborg University
Department:	Department of Clinical Medicine

ISSN (online): 2246-1302 ISBN (online): 978-87-94563-02-4

Published by: Aalborg University Open Publishing Kroghstræde 1-3 DK – 9220 Aalborg Øst aauopen@aau.dk

© Copyright: Nadja Albertsen

Printed in Denmark by Stibo Complete, 2024

CURRICULUM VITAE

Academic degrees:

June 2021: Master in the Anthropology of Health, Aarhus University.

June 2011: Master of Science in Medicine (MD), University of Denmark.

Research positions:

June 2022: Enrolled as a PhD student at Ilisimatusarfik (University of Greenland).

April 2020: Enrolled as a PhD student at Aalborg University.

February 2020: Clinical Assistant at Aalborg University Hospital.

August 2018 – December 2019: Research Medic, Concordia Station, Antarctica, for the European Space Agency/Institute Polaire Francais Paul-Émile Victor.

Research fields:

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.

Coverage rates of the children vaccination programme in Greenland. 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.

ACKNOWLEDGEMENTS

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 crosssectional 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 ₂ DS ₂ -VASc:	C: Congestive heart failure, H: Hypertension, A: Age \geq 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	.16
Chapter 2. Background	.17
2.1. A unique population	19
2.2. Cardiovascular disease in Greenland	21
2.3. Ischemic strokes in Greenland	21
2.4. Atrial fibrillation	22
2.4.1. Definition and classifications	22
2.4.2. Epidemiology and risk factors	24
2.4.3. Ischemic stroke and other potential consequences of atrial fibrillation	25
2.4.4. Diagnosing and screening for atrial fibrillation	25
2.5. Atrial fibrillation in Greenland and among other indigenous populations	26
Chapter 3. Aims	.29
Chapter 4. Methods	.30
4.1. Data Sources	31
4.1.1. The electronic medical record system	31
4.1.2. Reports from Holter recordings	32
4.1.3. Self-reported data: Questionnaires	32
4.2. ECG recordings	33
4.2.1. Study II: InstantCheck®	33
4.2.2. Study IV: ePatch®	34
4.3. Recruitment of participants	34
4.3.1. Study II	34
4.3.2. Study IV	34
4.4. Data management	35
4.5. Statistical methods	35
4.6. Ethics and funding	36
Chapter 5. Results	.37
5.1. Studies I, II and IV: Prevalence of atrial fibrillation in Greenland	37

5.1.1. Prevalence of atrial fibrillation in Greenland based on diagnosis and medication codes
5.1.2. Prevalence of atrial fibrillation in East Greenland 40
5.1.3. Prevalence of atrial fibrillation in Nuuk
5.2. Study III: Atrial fibrillation among ischemic stroke patients in Greenland 44
Chapter 6. Discussion47
6.1. Prevalence of atrial fibrillation in Greenland 47
6.2. Atrial fibrillation and ischemic stroke
6.3. Risk factors 50
6.4. Strengths and limitations
6.4.1. Strengths
6.4.2. Limitations
Chapter 7. Conclusion and future perspectives54
Literature list
Appendices

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].

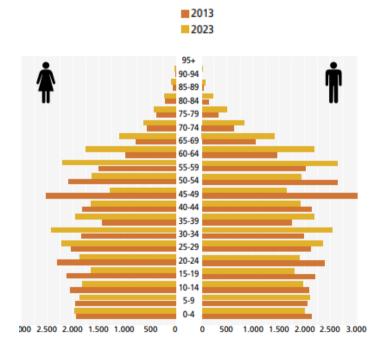
Along with the change in diet, Greenland has also undergone rapid social changes, especially since the 1950s (Figure 2-3). The average prosperity index has increased, homes are becoming less crowded and more people are taking a formal education [18]. However, the percentage of the population who rates 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.





2.2. CARDIOVASCULAR DISEASE IN GREENLAND

With the changing lifestyle and increasing life expectancy, certain lifestyle- and agerelated 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 agestandardized 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.

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

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

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.

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	

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

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 CHA₂DS₂-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.

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=16.447.044	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
Māori/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)*

Table 2.3. Occurrence of AF among Indigenous populations.

*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.

	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.

Table 4-1. Overview of study characteristics.

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.

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

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

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 CHA₂DS₂-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.

Data type	Descriptive analyses	Tests between two groups	Tests betwee multiple groups	en 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

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

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].

	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)
CHA2DS2-VASc- score,	2 (1;3)	4 (2;4)	< 0.01	2 (1;3)
median (IQR)				

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

* Per cent of patients without missing data. For missing data, see Table 2 in [1]. Abbreviations: AF: Atrial fibrillation. BMI: Body Mass Index. CHA₂DS₂-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 CHA₂DS₂-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.

	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)	

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

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.

2 (1.9)	0 (0)	NS	2 (0.9)
105	111 (98.2)	NS	217 (98.2)
(98.1)			
0 (0)	2 (1.8)	NS	2 (0.9)
	105 (98.1)	105 111 (98.2) (98.1) 111 (98.2)	105 111 (98.2) NS (98.1)

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 peerreviewed 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.

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	No AF	p-value
	(n=21)	(n=211)	
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 ₂ DS 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. CHA₂DS₂-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].

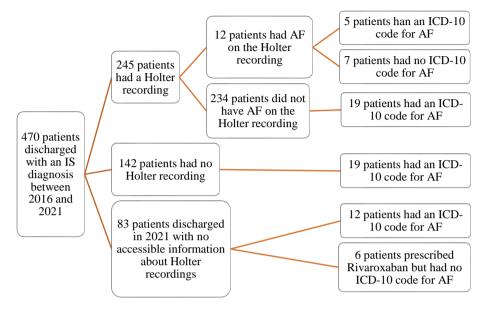
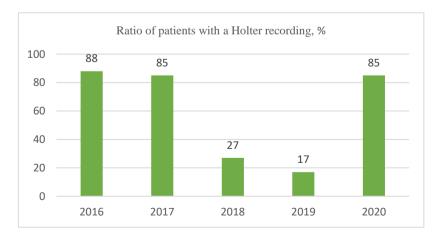


Figure 5-1. Holter recordings and AF among ischemic stroke patients.

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.

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 CHA₂DS₂-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

- [1] Albertsen N, Riahi S, Pedersen ML, et al. The prevalence of atrial fibrillation in Greenland: a register-based cross-sectional study based on disease classifications and prescriptions of oral anticoagulants. *Int J Circumpolar Health* 2022 Dec;81(1):2030522.
- [2] Albertsen N, Riahi S, Pedersen ML, Noahsen P AS. Prevalence of Persistent Atrial Fibrillation and Screening for Atrial Fibrillation in East Greenland using a Single Lead Handheld ECG Device. *JAFIB-EP* 2022;15(4):56-60.
- [3] Albertsen N, Hansen AS, Skovgaard N, et al. Is the Pattern Changing? Atrial Fibrillation and Screening with Holter Electrocardiograms among Ischemic Stroke Patients in Greenland from 2016 to 2021. J Clin Med 2023; 12: 5378.
- [4] Albertsen, Nadja; Jensen, Mads M.; Hansen, Kunuk L. K.; Pedersen, Michael L.; Andersen, Stig; Brock, Christina; Riahi S. High prevalence of atrial fibrillation found in the capital of Greenland when using continuous ECG monitoring. a cross-sectional study among the population aged 50 years and older in Nuuk. [In submission].
- [5] Génsbøl B. Naturguide til Grønland [Nature guide to Greenland]. *Gyldendal*, 2005. Pages 9-57. Danish.
- [6] Statistics Greenland. Grønland i tal 2023 [Greenland in Numbers 2022]. PxWeb [Internet], https://stat.gl/publ/da/GF/2022/pdf/Grønland i tal 2022.pdf (2022, accessed 21 November 2023). Danish.
- [7] Statsministeriet: Grønland [Greenland] [Internet], https://www.stm.dk/statsministeriet/rigsfaellesskabet/groenland/ (accessed 26 March 2023). Danish.
- [8] Niclasen B, Mulvad G. Health care and health care delivery in Greenland. *International Journal of Circumpolar Health* 2010; 69: 437–447.
- [9] Nielsen LO, Krebs HJ, Albert NM, et al. Telemedicine in Greenland: Citizens' Perspectives. *Telemd J E Health* 2017 May;23(5):441-447.
- [10] Statistics Greenland. Grønland i tal 2022 [Greenland in Numbers 2022][Internet], https://stat.gl/publ/da/GF/2022/pdf/Grønland i tal 2022.pdf (2022, accessed 21 February 2023).
- [11] Statistics Greenland. Befolkningen 1. januar efter fødested, køn, alder og tid [The population January 1st by place of birth, sex, age and time]. PxWeb.

0.

[Internet].

https://bank.stat.gl/pxweb/da/Greenland/Greenland_BE_BE01_BE0120/ BEXSTA.px/ /table/tableViewLayout1/ (accessed 27 November 2023).

- [12] Moltke I, Fumagalli M, Korneliussen TS, et al. Uncovering the Genetic History of the Present-Day Greenlandic Population. Am J Hum Genet 2015; 96: 54–69.
- [13] Sellers EAC, Sharma A, Rodd C. Adaptation of Inuit children to a low-calcium diet. *CMAJ* 2003; 168: 1141–3.
- [14] Moltke I, Grarup N, Jørgensen ME, et al. A common Greenlandic TBC1D4 variant confers muscle insulin resistance and type 2 diabetes. *Nature* 2014; 512: 190–193.
- [15] Andersen MK, Hansen T. Genetics of metabolic traits in Greenlanders: lessons from an isolated population. *Journal of Internal Medicine* 2018; 284: 464–477.
- [16] Waples RK, Hauptmann AL, Seiding I, et al. The genetic history of Greenlandic-European contact. *Curr Biol* 2021; 31: 2214–2219.
- [17] Statistics Greenland. Befolkningen 2023 [The population 2023]. PxWeb [Internet]. Available from: https://bank.stat.gl/pxweb/da/Greenland/ Greenland_BE_BE01_BE0125/BEXST8.px/table/tableViewLayout1 (accessed 5 December 2023). Danish.
- [18] Viskum C, Larsen L, Hansen CB, et al. Befolkningsundersøgelsen i Grønland 2018-Levevilkår, livsstil og helbred. Oversigt over indikatorer for folkesundheden. [The Population Survey in Greenland 2018 - Living conditions, life style and health. An overview of indicators for the public health]. Statens Institut for Folkesundhed, www.sdu.dk/sif (2019, accessed 5 November 2023). Danish.
- [19] Jeppesen C, Bjerregaard P. Consumption of traditional food and adherence to nutrition recommendations in Greenland. *Scand J Public Health* 2012; 40: 475–481.
- [20] Bjerregaard P, Dewailly E, Ayotte P, et al. Exposure of Inuit in Greenland to Organochlorines Through the Marine Diet. J Toxicol Environ Heal Part A 2001; 62: 69–81.
- [21] OECD. Health status Life expectancy at birth OECD Data. [Internet]. https://data.oecd.org/healthstat/life-expectancy-at-birth.htm (accessed 5

January 2023).

- [22] Statistics Greenland. Middellevetid efter område, fødested, køn, basis, Dødelighedsmål og tid. [Life expectancy by area, birth place, sex, basics, mortality measures and time]. [Internet]. PxWeb, https://bank.stat.gl/pxweb/da/Greenland/Greenland_BE_BE10_BE20/B EXBBDTB.px/table/tableViewLayout1/ (accessed 27 November 2023). Danish.
- [23] Bundgaard JS, Jørgensen ME, Andersen K, et al. Dyslipidemia and the preventive potential in the Greenlandic population. *Atheroscler Plus* 2023; 51: 22–27.
- [24] Nielsen MH, Backe MB, Pedersen ML. Prevalence of patients using antihypertensive medication in Greenland, and an assessment of the importance of diagnosis for the associated quality of care a cross-sectional study. *Int J Circumpolar Health* 2022; Dec;81(1):2110675.
- [25] Bjerregaard P, Pedersen HS, Mulvad G. The associations of a marine diet with plasma lipids, blood glucose, blood pressure and obesity among the Inuit in Greenland. *Eur J Clin Nutr 2000 Sep*;54(9): 732–737.
- [26] Fodor JG, Helis E, Yazdekhasti N, et al. "Fishing" for the Origins of the "Eskimos and Heart Disease" Story: Facts or Wishful Thinking? Can J Cardiol 2014; 30: 864–868.
- [27] Senftleber NK, Albrechtsen A, Lauritzen L, et al. Omega-3 fatty acids and risk of cardiovascular disease in Inuit: First prospective cohort study. *Atherosclerosis* 2020; Nov:312:28-34.
- [28] Bjerregaard P. Inuit Health in Transition Greenland Survey 2005-2010. Population sample and survey methods. 2nd revised edition. [Internet]. In: SIF Writings on Greenland, https://www.sdu.dk/da/sif/rapporter/2010/inuit health in transition greenland, nd (2005, accessed 3 November 2023).
- [29] Jørgensen ME, Bjerregaard P, Kjærgaard JJ, et al. High prevalence of markers of coronary heart disease among Greenland Inuit. *Atherosclerosis* 2008; 196: 772–778.
- [30] Kjærgaard M, Andersen S, Holten M, et al. Low occurrence of ischemic heart disease among Inuit around 1963 suggested from ECG among 1851 East Greenland Inuit. *Atherosclerosis* 2009; 203: 599–603.

- [31] Bjerregaard P, Young TK, Hegele RA. Low incidence of cardiovascular disease among the Inuit What is the evidence? *Atherosclerosis* 2003; 166: 351–357.
- [32] Kjærgaard J-J, Bjerregaard P. Incidence of myocardial and cerebral infarction in Nuuk, Greenland. *Int J Circumpolar Health* 2004:63 Suppl 2:290-1.
- [33] Bjorn-Mortensen K, Lynggaard F, Pedersen ML. Incidence of Greenlandic stroke-survivors in Greenland: A 2-year cross-sectional study. Int J Circumpolar Health 2013; Nov 22:72:22626.
- [34] Bjorn-Mortensen K, Lynggaard F, Pedersen ML. High prevalence of atrial fibrillation among Greenlanders with ischemic stroke - Atrial fibrillation found in more than 30% of cases. *Int J Circumpolar Health* 2013; Nov22:72:22628.
- [35] Hindricks G, Potpara T, Dagres N, et al. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J* 2021; Feb1;42(5):373-498.
- [36] Zoni-Berisso M, Lercari F, Carazza T, et al. Epidemiology of atrial fibrillation: European perspective. *Clin Epidemiol* 2014; 6: 213–20.
- [37] Chiang C-E, Naditch-Brûlé L, Murin J, et al. Distribution and Risk Profile of Paroxysmal, Persistent, and Permanent Atrial Fibrillation in Routine Clinical Practice. *Circ Arrhythmia Electrophysiol* 2012; 5: 632–639.
- [38] Chugh SS, Havmoeller R, Narayanan K, et al. Worldwide Epidemiology of Atrial Fibrillation: A Global Burden of Disease 2010 Study. *Circulation* 2014; Feb 25;129(8):837-47.
- [39] Krijthe BP, Kunst A, Benjamin EJ, et al. Projections on the number of individuals with atrial fibrillation in the European Union, from 2000 to 2060. *Eur Heart J* 2013, Sep;34(35):2746-51.
- [40] Stefansdottir H, Aspelund T, Gudnason V, et al. Trends in the incidence and prevalence of atrial fibrillation in Iceland and future projections. *EP Eur* 2011; 13: 1110–1117.
- [41] Elliott AD, Middeldorp ME, Van Gelder IC, et al. Epidemiology and modifiable risk factors for atrial fibrillation. *Nat Rev Cardiol* 2023; 20: 404– 417.

- [42] Schnabel RB, Yin X, Gona P, et al. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: A cohort study. *Lancet* 2015; 386: 154–162.
- [43] Benjamin EJ, Levy D, Vaziri SM, et al. Independent Risk Factors for Atrial Fibrillation in a Population-Based Cohort: The Framingham Heart Study. *JAMA J Am Med Assoc* 1994; 271: 840–844.
- [44] Falk RH. Etiology and complications of atrial fibrillation: insights from pathology studies. *Am J Cardiol* 1998; 82: 10N-17N.
- [45] de Vos CB, Pisters R, Nieuwlaat R, et al. Progression From Paroxysmal to Persistent Atrial Fibrillation. *J Am Coll Cardiol* 2010; 55: 725–731.
- [46] Romero JR, Wolf PA. Epidemiology of Stroke: Legacy of the Framingham Heart Study. *Global Heart* 2013; 8: 67–75.
- [47] Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. *Stroke* 1991; 22: 983–988.
- [48] Asplund K. High prevalence of atrial fibrillation among patients with ischemic stroke. *Stroke* 2014; 45: 2599–2605.
- [49] Paciaroni M, Agnelli G, Caso V, et al. Causes and Risk Factors of Cerebral Ischemic Events in Patients With Atrial Fibrillation Treated With Non– Vitamin K Antagonist Oral Anticoagulants for Stroke Prevention. *Stroke* 2019; 50: 2168–2174.
- [50] Hart RG, Pearce LA, Miller VT, et al. Cardioembolic vs. Noncardioembolic Strokes in Atrial Fibrillation: Frequency and Effect of Antithrombotic Agents in the Stroke Prevention in Atrial Fibrillation Studies. *Cerebrovasc Dis* 2000; 10: 39–43.
- [51] Lip GYH, Banerjee ; Amitava, Boriani G, et al. Antithrombotic Therapy for Atrial Fibrillation CHEST Guideline and Expert Panel Report. *Chest* 2018; 154: 1121–1201.
- [52] Lip GYH, Nieuwlaat R, Pisters R, et al. Refining Clinical Risk Stratification for Predicting Stroke and Thromboembolism in Atrial Fibrillation Using a Novel Risk Factor-Based Approach: The Euro Heart Survey on Atrial Fibrillation. *Chest* 2010; 137: 263–272.
- [53] Friberg L, Rosenqvist M, Lip GYH. Evaluation of risk stratification schemes for ischaemic stroke and bleeding in 182 678 patients with atrial fibrillation:

the Swedish Atrial Fibrillation cohort study. Eur Heart J 2012; 33: 1500-

1510.

- [54] Bai Y, Deng H, Shantsila A, et al. Rivaroxaban Versus Dabigatran or Warfarin in Real-World Studies of Stroke Prevention in Atrial Fibrillation: Systematic Review and Meta-Analysis. *Stroke* 2017; 48: 970–976.
- [55] Patel MR, Mahaffey KW, Garg J, et al. Rivaroxaban versus Warfarin in Nonvalvular Atrial Fibrillation. *N Engl J Med* 2011; 365: 883–891.
- [56] Dietzel J, Haeusler KG, Endres M. Does atrial fibrillation cause cognitive decline and dementia? *EP Eur* 2018; 20: 408–419.
- [57] Marijon E, Le Heuzey JY, Connolly S, et al. Causes of death and influencing factors in patients with Atrial fibrillation: A competing-risk analysis from the randomized evaluation of long-term anticoagulant therapy study. *Circulation* 2013; 128: 2192–2201.
- [58] Schnabel RB, Michal M, Wilde S, et al. Depression in Atrial Fibrillation in the General Population. *PLoS One* 2013; 8: e79109.
- [59] Freeman J V., Simon DN, Go AS, et al. Association Between Atrial Fibrillation Symptoms, Quality of Life, and Patient Outcomes. *Circ Cardiovasc Qual Outcomes* 2015; 8: 393–402.
- [60] Verbiest-van Gurp N, Uittenbogaart SB, van de Moosdijk SCM, et al. How is atrial fibrillation detected in everyday healthcare? Results of a Dutch cohort study. *Netherlands Hear J* 2023; 31: 76–82.
- [61] Freeman J V., Simon DN, Go AS, et al. Association Between Atrial Fibrillation Symptoms, Quality of Life, and Patient Outcomes. *Circ Cardiovasc Qual Outcomes* 2015; 8: 393–402.
- [62] Simantirakis EN, Papakonstantinou PE, Chlouverakis GI, et al. Asymptomatic versus symptomatic episodes in patients with paroxysmal atrial fibrillation via long-term monitoring with implantable loop recorders. *Int J Cardiol* 2017; 231: 125–130.
- [63] Kiliszek M, Uziębło-Życzkowska B, Gorczyca I, et al. Symptomatic and Asymptomatic Patients in the Polish Atrial Fibrillation (POL-AF) Registry. J Clin Med 2021; 10: 1091.
- [64] Golwala H, Jackson LR, Simon DN, et al. Racial/ethnic differences in atrial fibrillation symptoms, treatment patterns, and outcomes: Insights from

Outcomes Registry for Better Informed Treatment for Atrial Fibrillation Registry. *Am Heart J* 2016; 174: 29–36.

- [65] Ramkumar S, Nerlekar N, D'Souza D, et al. Atrial fibrillation detection using single lead portable electrocardiographic monitoring: a systematic review and meta-analysis. *BMJ Open* 2018; 8: e024178.
- [66] Macniven R, Gwynn J, Fujimoto H, et al. Feasibility and acceptability of opportunistic screening to detect atrial fibrillation in Aboriginal adults. *Aust* NZJ Public Health 2019; 43: 313–318.
- [67] Gwynne K, Flaskas Y, O'Brien C, et al. Opportunistic screening to detect atrial fibrillation in Aboriginal adults in Australia. *BMJ Open 2016*; Nov 15;6(11):e013576.
- [68] Katzenellenbogen JM, Woods JA, Teng THK, et al. Atrial fibrillation in the Indigenous populations of Australia, Canada, New Zealand, and the United States: A systematic scoping review. *BMC Cardiovasc Disord* 2015; Aug 13:15:87.
- [69] Kjaergaard M, Andersen S, Holten M, et al. Low occurrence of ischemic heart disease among Inuit around 1963 suggested from ECG among 1851 East Greenland Inuit. *Atherosclerosis* 2009; 203: 599–603.
- [70] Atzema CL, Khan S, Lu H, et al. Cardiovascular disease rates, outcomes, and quality of care in Ontario Métis: a population-based cohort study. *PLoS One*; 2015 Mar 20;10(3):e0121779.
- [71] Makharova NV, Voevoda MI, Lyutova FF, et al. Comparative analysis of clinical, electrocardiographic, angiographic and echocardiographic data of indigenous and non-indigenous residents of Yakutia with coronary artery atherosclerosis. *Int J Circumpolar Health* 2013; Aug 5:72.
- [72] Sanchez JM, Jolly SE, Dewland TA, et al. Incident Atrial Fibrillation among American Indians in California. *Circulation* 2019; 140: 1605–1606.
- [73] Borzecki AM, Keith Bridgers D, Liebschutz JM, et al. Racial Differences in the Prevalence of Atrial Fibrillation among Males. J Natl Med Assoc 2008; 100: 237–246.
- [74] Clarke N, Gallagher C, Pitman BM, et al. Atrial Fibrillation in Remote Indigenous and Non-Indigenous Individuals Hospitalised in Central Australia. *Hear Lung Circ* 2021; 30: 1174–1183.

- [75] Brown A, Carrington MJ, McGrady M, et al. Cardiometabolic risk and disease in Indigenous Australians: The heart of the heart study. *Int J Cardiol* 2014; 171: 377–383.
- [76] Martin A, Doughty RN, Chieng N, et al. Twelve Lead Electrocardiographic Findings Among Māori and non-Māori at Risk of Cardiovascular Disease in NZ. *Hear Lung Circ* 2013; 22: 569.
- [77] Poppe K, Rambaldini B, Rolleston A, et al. Atrial Fibrillation Among Indigenous Populations Globally. *Hear Lung Circ* 2019; 28: S39–S40.
- [78] Wong CX, Brooks AG, Cheng YH, et al. Atrial fibrillation in Indigenous and non-Indigenous Australians: a cross-sectional study. *BMJ Open* 2014; 4(10):e006242.
- [79] U.S. Food & Drug Administration. [Internet]. Silver Spring (MD): U.S. Department of Health & Human Services. <u>https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K</u> 062894 (accessed June 5 2021)
- [80] Saadi DB, Tanev G, Flintrup M, et al. Automatic Real-Time Embedded QRS Complex Detection for a Novel Patch-Type Electrocardiogram Recorder. *IEEE J Transl Eng Heal Med* 2015; 3: 1–12.
- [81] Ilisimatusarfik. Hjerterytmeforstyrrelser i Grønland [Cardiav Arrhythmias in Greenland]. [Internet]. Ilisimatusarfik, https://da.uni.gl/nyheder/2022/april/hjerterytmeforstyrrelser-i-groenland/. Danish.
- [82] Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: Building an international community of software platform partners. J Biomed Inform 2019; 95: 103208.
- [83] Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—A metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform 2009; 42: 377–381.
- [84] Heeringa J, Van Der Kuip DAM, Hofman A, et al. Prevalence, incidence and lifetime risk of atrial fibrillation: The Rotterdam study. *Eur Heart J* 2006; 27: 949–953.
- [85] Albertsen N, Hansen A-S, Skovgaard N, et al. Ischemic Strokes Are Common Among Young Greenlanders: A Cross-Sectional Study. Stroke 2023;

54(10):e438-e439.

- [86] Lehto M, Haukka J, Aro A, et al. Comprehensive nationwide incidence and prevalence trends of atrial fibrillation in Finland. *Open Hear* 2022; 9: e002140.
- [87] Hegelund ER, Kjerpeseth LJ, Mortensen LH, et al. Prevalence and Incidence Rates of Atrial Fibrillation in Denmark 2004–2018. *Clin Epidemiol* 2022; Volume 14: 1193–1204.
- [88] Kjerpeseth LJ, Igland J, Selmer R, et al. Prevalence and incidence rates of atrial fibrillation in Norway 2004–2014. *Heart* 2021; 107: 201–207.
- [89] Lilja J, Själander A, Själander S. Prevalence of atrial fibrillation and reasons for undertreatment with oral anticoagulants. *J Thromb Thrombolysis*. Epub ahead of print 13 September 2023. DOI: 10.1007/s11239-023-02890-y.
- [90] Friberg L, Bergfeldt L. Atrial fibrillation prevalence revisited. *J Intern Med* 2013; 274: 461–468.
- [91] Singh M, Agarwal A, Sinha V, et al. Application of handheld tele-ECG for health care delivery in rural India. *Int J Telemed Appl*; 2014; 2014;981806.
- [92] GZ S, L G, XZ W, et al. Prevalence of atrial fibrillation and its risk factors in rural China: a cross-sectional study. *Int J Cardiol* 2015; 182: 13–17.
- [93] Svennberg E, Engdahl J, Al-Khalili F, et al. Mass Screening for Untreated Atrial Fibrillation. *Circulation* 2015; 131: 2176–2184.
- [94] Sposato LA, Cipriano LE, Saposnik G, et al. Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and metaanalysis. *Lancet Neurol* 2015; 14: 377–387.
- [95] Stahrenberg R, Weber-Krüger M, Seegers J, et al. Enhanced Detection of Paroxysmal Atrial Fibrillation by Early and Prolonged Continuous Holter Monitoring in Patients With Cerebral Ischemia Presenting in Sinus Rhythm. *Stroke* 2010; 41: 2884–2888.
- [96] Kassim NA, Althouse AD, Qin D, et al. Gender differences in management and clinical outcomes of atrial fibrillation patients. *J Cardiol* 2017; 69: 195– 200.
- [97] O'Neal WT, Alam AB, Sandesara PB, et al. Sex and racial differences in cardiovascular disease risk in patients with atrial fibrillation. *PLoS One*; 14.

Epub ahead of print 1 September 2019. DOI: 10.1371/journal.pone.0222147.

- [98] Kassim NA, Qin D, Richards T, et al. Abstract 18038: Gender Differences in Anticoagulation and Stroke Outcomes in Atrial Fibrillation. *Circulation*; 132.
 Epub ahead of print 10 November 2015. DOI: 10.1161/circ.132.suppl_3.18038.
- [99] Wolf PA, Abbott RD, Kannel WB. Atrial Fibrillation: A Major Contributor to Stroke in the Elderly: The Framingham Study. *Arch Intern Med* 1987; 147: 1561–1564.
- [100] Freedman B, Potpara TS, Lip GYH. Stroke prevention in atrial fibrillation. *Lancet* 2016; 388: 806–817.
- [101] Noahsen P, Rex KF, Bülow Pedersen I, et al. Adaptation to a High Iodine Intake in Greenland Inuit Suggested by Thyroid Disease Pattern. *Thyroid* 2021; 31: 1850–1857.
- [102] Nielsen MH, Backe MB, Pedersen ML. Prevalence of patients using antihypertensive medication in Greenland, and an assessment of the importance of diagnosis for the associated quality of care a cross-sectional study. *Int J Circumpolar Health* 2022; 81(1):2110675.
- [103] Wilke T, Groth A, Mueller S, et al. Incidence and prevalence of atrial fibrillation: An analysis based on 8.3 million patients. *Europace* 2013; 15: 486–493.
- [104] Chalazan B, Mol D, Darbar FA, et al. Association of Rare Genetic Variants and Early-Onset Atrial Fibrillation in Ethnic Minority Individuals. JAMA Cardiol 2021; 6(7):811-819.
- [105] Nakano Y. Genome and atrial fibrillation. *J Arrhythmia* 2023; 39: 303–309.
- [106] Jørsboe E, Andersen MK, Skotte L, et al. An LDLR missense variant poses high risk of familial hypercholesterolemia in 30% of Greenlanders and offers potential of early cardiovascular disease intervention. *Hum Genet Genomics* Adv 2022; 3: 100118.
- [107] Althubaiti A. Information bias in health research: definition, pitfalls, and adjustment methods. *J Multidiscip Healthc* 2016; 211.
- [108] Sousa VD, Rojjanasrirat W. Translation, adaptation and validation of instruments or scales for use in cross-cultural health care research: a clear and user-friendly guideline. *J Eval Clin Pract* 2011; 17: 268–274.

- [109] Wild D, Grove A, Martin M, et al. Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: Report of the ISPOR Task Force for Translation and Cultural Adaptation. *Value Heal* 2005; 8: 94–104.
- [110] Tvermosegaard M, Rønn PF, Pedersen ML, et al. Validation of cardiovascular diagnoses in the Greenlandic Hospital Discharge Register for epidemiological use. *Int J Circumpolar Health* 2018; 77(1):1422668.
- [111] Wallace SS, Barak G, Truong G, et al. Hierarchy of Evidence Within the Medical Literature. *Hosp Pediatr* 2022; 12: 745–750.
- [112] Wang X, Cheng Z. Cross-Sectional Studies. Chest 2020; 158: S65–S71.
- [113] Song JW, Chung KC. Observational Studies: Cohort and Case-Control Studies. *Plast Reconstr Surg* 2010; 126: 2234–2242.

APPENDICES

Appendix A. Questionnaire, Study II	68
Appendix B. Demographic questionnaire Study IV	76
Appendix C. ePatch questionnaire Study IV	84

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.	DEM	OGRAFI:							
	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								
		Hvor længe har du boet i Nuuk:							
	h.	fra 19 til 2018; i alt: år.							
		Ira 19 ul 2018, 1 alt: ar.							
	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.	LIVS								
	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 🗆

2

	iii.	Øl 🗆						
	iv.	Andet 🗆						
c.	Hvor r	neget ryger du:						
	i.	aldrig		(Gå til	punkt d.)		
	ii.	holdt op	- Jeg ro	øg fra 1	9 til	19		
	Jeg ry	ger:						
	Cigare	tter:						
	iii.	1-10 🗆						
	iv.	11-20 🗆						
	v.	flere end 20 \square						
	Pibe:							
	vi.	Antal gram pr u	ige:					
	Andet:							
	vii.	Hvad						
	viii.	Hvor meget						
d.	Jeg dr	ikker (alkohol):			NU	Tidlige	re	
	i.	Aldrig						
	ii.	0-7 genstande p	or uge					
	iii.	8-14 genstande pr uge 15-21 genstande pr uge						
	iv.							
	v.	mere end 21 ge	nstande p	r uge				
e.	Hvor g	odt taler du		Grønl	andsk:	Dansk:		
	i.	Uden besvær						
	ii.	Nogenlunde						
	iii.	Vanskeligt						
	iv.	Slet ikke						
SYGD	OMME:							
a.	Er der	struma eller stofs	kiftesygd	om i din	familie?			
			Ja 🗆		Nej [Ved ikke	

Hvis ja: Hvem Hvilken type sygdom:

3.

3

APPENDIX A. QUESTIONNAIRE, STUDY II

	Mor Far Bror Søster Anden			
b.	Har du, eller har du haft	stofskiftesygdor	n?	
		Ja 🗆	Nej 🗆	Ved ikke 🛛
	Hvis ja, var dit s	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 l	behandling for s	truma?	
		Ja 🗆	Nej 🗆	Ved ikke 🛛
	Hvis ja, da hvill	en behandling:		
	(a)	Medicin		
	(b)	Radio-Jod		
	(c)	Opereret		
	(d)	Andet		
c.	Får du medicin for stofsk	tiftet nu?		
		Ja 🗆	Nej 🗆	
	Hvis ja, da hvill	en medicin:		
f.	Får du anden medicin?			
		Ja 🗆	Nej 🗆	
	Hvis ja, da hvill	cen:		
	(1)			
	(2)			
	(3)			
	(4)			
	(5)			
		4		

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

g.	Tager du vitamintablette	ar?				
	(a)	Aldrig				
	(b)	Af og til				
	(c)	Kun om vinterer	n 🗆			
	(d)	Daglig				
	Hvis ja, indeho	lder de da:				
	Jod	Ja 🗆	Nej		Ved ikke	
	Vitamin D	Ja 🗆	Nej		Ved ikke	
h.	Tage du regelmæssigt na	aturmedicin?				
		Ja 🗆	Nej			
	Hvis ja, indeho	lder det da:				
	Jod/ tang	Ja 🗆	Nej		Ved ikke	
	Vitamin D	Ja 🗆	Nej		Ved ikke	
j.	Fejler du, eller har du tie	lligere fejlet noget	alvor	ligt:		

	År	Indlagt	Diagnose / Symptomer
		Ja Nej	
i.	19		
ii.	19		
iii.	19		
iv.			
v.	20		

vi. 20_

- fortsættes -

Hvor ofte spiser eller drikker du følgende? Tænk især på				a de sidste 3 måneder.				
				4-6	1-3	2-3	1	
				gange	gange	gange	gang	
			hver	om	om	om	om	
			dag	ugen	ugen	måned	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
	c.	rensdyr, moskusokse, hard	e1	2	3	4	5	6
	f.	lam	1	2	3	4	5	6
	g	færdiglavede middagsrette	er					
		(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
	1.	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
	0.	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 ofte spiser eller drikker du følgende? Tænk især på de sidste 3 måneder.

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 lønarbe	ide 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?

			4-6	1-3	2-3	1	
			gange	gange	gange	gang	
		hver	om	om	om	om	
		dag	ugen	ugen	måned	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?	1	Ja 🗆		Nej 🗆		
Er din far født i Grønlan	d? .	Ja 🗆		Nej 🗆		
Er din mor født i Grønla	nd?	Ja 🗆		Nej 🗆		
Hvor gammel er du?:					år	
Hvor længe har du boet	i nuværen	de by: _			_år	
I hvilken by er du født:					_	
LIVSSTIL						
Højde:						
Vægt:						
ТОВАК						
Ryger du, eller har du re	øget, cigare	tter?				
Ja:	1-5 daglig	gt 🗆	6-10 dag	gligt 🗆	11-15 dagligt 🗆	16-20 dagligt 🗆
	Flere end	l 20 dag	ligt 🗆			
Nej:	Tidligere	ryger				
	Hvor mar	nge år:		Årstal	for ophør:	
	Aldrig					
Ryger du andet end ciga	aretter?					
Hvis ja,	, angiv hvad	l og hvo	r meget:			

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 me	dlemmer af din familie hjertesyge	dom?
□ Ja, jeg har □ Ja, familiemedlem (hvem):		Ja, familiemedlem (hvem):	1
🗆 Nej		□ Ved ikke	
	Hvis ja:	3	
	Årstal f	or diagnose:	
Hjerte		ytmeforstyrrelse	
	(f.eks. f	orkammerflimmer/atrieflimren)	
	Hjertes	vigt	
	Blodpro	op i hjertet	
	Pacema	aker	
	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: ______

	🗆 Ja, jeg	g har	🗆 Ja, familiem	edlem (hvem	ı):		
	🗆 Nej		U Ved ikke				
		<u>Hvis ja:</u>					
		Årstal f	or diagnose:				
		For højt	tstofskifte				
		For lavt	stofskifte				
		Ved ikk	e				
Har du eller medlemmer af din familie sukkersyge (diabetes)?							
	🗆 Ja, jeg	g har	🗆 Ja, familiem	edlem (hven	n):		
	🗆 Nej		Ved ikke				
		<u>Hvis ja:</u>					
		Årstal f	or diagnose:				
		Type 1	diabetes:				
		Type 2	diabetes:				
		Ved ikk	e:				
Har du	andre syg	gdomme	?	Ja 🗆	Nej 🗆		
	hvilke?						
1.	Sygdom:					_Årstal for	diagnose:
2.	Sygdom:					_Årstal for	diagnose:
3.	Sygdom:_					_Årstal for	diagnose:
4.	Sygdom:					_Årstal for	diagnose:

Har du eller medlemmer af din familie stofskiftesygdom?

Har du	tidligere været	t indlagt?	Ja 🗆	Nej 🗆
Hvis ja	, hvorfor?			
1.	Årsag:			Årstal:
2.	Årsag:			Årstal:
3.	Årsag:			Årstal:
4.	Årsag:			Årstal:
SYMPT	OMER PÅ URE	GELMÆSSIG HJERTI	ERYTME	
Har du inden for de sidste 3 måneder oplevet nogle af følgende symptomer:				
Forner	nmelse af UREG	ELMÆSSIG puls:		
		Ja 🗆	Nej 🗆	
	Hvis ja, hvor o	ofte:		
	Dagligt	Ugentligt	Månedligt	Sjældnere
	Andet:			
Forner	nmelse af HJER	TEBANKEN i hvile el	ler ved normal ak	tivitet, f.eks. gang
		Ja 🗆	Nej 🗆	
	Hvis ja, hvor o	ofte:		
	Dagligt	Ugentligt	Månedligt	□ Sjældnere
	Andet:			
Fornemmelse af PAUSE I HJERTERYTMEN:				
		Ja 🗆	Nej 🗆	
	Hvis ja, hvor d	ofte:		
	Dagligt	Ugentligt	🗆 Månedligt	□ Sjældnere

APPENDIX B. DEMOGRAPHIC QUESTIONNAIRE STUDY IV

BRYSTSMERTER i hvile eller ved normal aktivitet, f.eks. gang				
		Ja 🗆	Nej 🗆	
	Hvis ja, hvor ofte	e:		
	Dagligt	Ugentligt	Månedligt	□ Sjældnere
	Andet:			
ÂNDEN	ØD i hvile eller ve	d normal aktivitet	, f.eks. gang	
		Ja 🗆	Nej 🗆	
	Hvis ja, hvor ofte	e:		
	Dagligt	Ugentligt	Månedligt	□ Sjældnere
	Andet:			
<u>SVIMM</u>	ELHED:			
		Ja 🗆	Nej 🗆	
	Hvis ja, hvor ofte	e:		
	Dagligt	Ugentligt	Månedligt	□ Sjældnere
	Andet:			
BESVIMELSE:				
		Ja 🗆	Nej 🗆	
	Hvis ja, hvor ofte	e:		
	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:
		Hyppighed:
4.	Navn:	Dosis:
		Hyppighed:
5.	Navn:	Dosis:
	Årsag:	Hyppighed:
6.	Navn:	Dosis:
		Hyppighed:
7.	Navn:	Dosis:
		Hyppighed:
8.	Navn:	Dosis:
	Årsag:	

Tager du vitamintabletter?

Aldrig			
Af og til			
Kun om vinter	en 🗆		
Dagligt			
<u>Hvis ja, indeho</u>	older de da:		
bol	Ja 🗆	Nej 🗆	Ved ikke
Vitamin D	Ja 🗖	Nej 🗆	Ved ikke
Navn på vitam	inpille:		

Tager du regelmæssigt naturmedicin?

Ja 🗆	Nej 🗆		
Hvis ja, indeho	lder det da:		
Jod/ tang	Ja 🗖	Nej 🗆	Ved ikke
Vitamin D	Ja 🗆	Nej 🗆	Ved ikke 🛛
Navn på kostti	lskud:		

TAK FOR DIN DELTAGELSE

Appendix C. ePatch questionnaire Study IV

Symptomske	ema	
Deltagernum	imer:	 _
E-patchnumn	mer:	 _
Påsætningstic	dspunkt:	
Afleveringsti	idspunkt:	
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

