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# Arrhythmias in Older People: Focusing on Atrial Fibrillation

## Epidemiology and impact on daily life

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TERESE LINDBERG

DEPARTMENT OF HEALTH SCIENCES | LUND UNIVERSITY





# Arrhythmias in Older People: Focusing on Atrial Fibrillation

**Epidemiology and impact on daily life**

Terese Lindberg



**LUND**  
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DOCTORAL DISSERTATION

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<p>Older people with arrhythmias comprise a large group requiring complex care, posing many healthcare challenges. Rapid growth of the older population demands a better understanding of the needs of this patient group. The aim of this thesis was to investigate arrhythmia prevalence, incidence, survival, and experiences from the perspective of a geriatric population (aged 60+ years), and to examine the feasibility of using the new wireless LTR ECG-BodyKom® device for arrhythmia screening. This thesis comprises four studies (I–IV) performed using data from the Swedish National Study on Aging and Care (SNAC). The results illustrate different perspectives regarding arrhythmias in the older general population. In <b>Study I</b>, 6904 subjects underwent ECG at baseline, of whom 3419 subjects (49.5%) of 66–105 years of age also underwent resting ECG at their 6-year follow-up visit. At baseline, there was a 4.9% prevalence (95% CI, 4.5–5.5) of atrial fibrillation (AF), and an 8.4% prevalence (95% CI, 7.7–9.0) of other arrhythmias, including ventricular premature complexes, supraventricular tachycardia, and supraventricular extrasystole. Additionally, 7.1% (95% CI, 6.5–7.7) exhibited a first or second degree AV block, and 1.3% (95% CI, 1.0–1.6) had a pacemaker-induced rhythm. Baseline arrhythmia presence did not significantly differ between men and women. The 6-year cumulative incidence of AF was 4.1% (95% CI, 3.5–4.9) or 6.9/1000 person-years (py) (95% CI, 5.7–8.0). Subgroup analyses revealed AF incidences of 9.9/1000 py (95% CI, 7.8–11.9) among men; 4.4/1,000 py (95% CI, 3.1–5.6) among women; 3.7/1000 py (95% CI, 2.6–4.7) in the 60- and 66-year age cohort; 8.9/1000 py (95% CI, 6.3–11.4) in the 72- and 78-year cohort; 20/1000 py (95% CI, 14.2–25.7) in the 81-, 84-, and 87-year cohort; and 18/1000 py (95% CI, 0.8–26.7) among those ≥90 years old. Incidences of AF, other arrhythmias, AV block, and pacemaker-induced rhythm were significantly higher among men, except in the oldest cohorts. <b>Study II</b> revealed that among 6904 persons (mean age, 73.9 years) the overall AF prevalence was 4.9%, which increased with age, except in the oldest subgroup. AF at baseline was associated with a hazard ratio (HR) of 1.29 (95% CI, 1.10–1.51) for death during the 10-year observation period. Cox regression analysis in persons with AF (<math>n=341</math>) revealed that men had a higher HR for death (1.57; 95% CI, 1.15–2.13) compared to women (<math>P&lt;0.01</math>). CHA2DS2-VASc score was significantly associated with 10-year death (HR=1.29/score point; 95% CI, 1.10–1.51). A total of 146 participants (146%) reported any form of oral anticoagulant (OAC) use, and 14% reported OAC treatment with warfarin. Cox regression analysis of warfarin (33.6%) and ASA (66.4%), separately, revealed that warfarin was significantly associated with survival (<math>P=0.031</math>). <b>Study III</b> revealed persistent AF in 10% and paroxysmal AF in 5.5% of the population aged ≥66 years, with no differences between younger (66–80 years) and older (&gt;80 years) subgroups. Our findings support LTR ECG-BodyKom® as a feasible method of screening for arrhythmias in older outpatient populations. This simple method requires little of the user, and participants reported high satisfaction with the equipment and a good overall experience wearing it. <b>Study IV</b> focused on geriatric experiences of living with arrhythmias. Interviews with older persons revealed one main theme: “ambivalence in the need of knowledge”. With regards to requiring lifelong medical treatment, participants expressed feelings of “it doesn’t matter, but it does matter” and “being in the hands of the healthcare system”. The participants lacked sufficient knowledge about their condition, leaving them with poor insight into their medical treatment, which, in turn, affected their daily life. They had thoughts and questions about their medical treatment, but had no opportunity to discuss these questions due to a lack of follow-up from the healthcare system. The findings of this thesis contribute to the knowledge regarding increasing arrhythmia occurrence in the older population, and the high number of untreated cases of AF. Furthermore the results demonstrate that AF is associated with increased mortality, and highlight sex-related differences in AF incidence. In line with findings from Europe and the USA, our findings show that AF incidence rapidly increases with advancing age. This thesis also highlights the present lack of knowledge and the need for follow-up and information regarding AF in the oldest old population.</p>	
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# Arrhythmias in Older People: Focusing on Atrial Fibrillation

**Epidemiology and impact on daily life**

Terese Lindberg



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“When the heart is diseased, its work is imperfectly performed: the vessels proceeding from the heart become inactive, so that you cannot feel them....if the heart trembles, has little power and sinks, the disease is advanced and death is near.” Ebers Papyrus 1500 BC



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## Abstract

Older people with arrhythmias constitute a large group requiring complex care. There remains a need to better understand the healthcare challenges of this growing population. The present thesis aimed to investigate arrhythmia prevalence, incidence, survival, and experiences from a geriatric perspective (aged 60+), and to examine the feasibility of using the new wireless long-term recording (LTR) ECG-BodyKom® device for arrhythmia screening. This thesis comprised four studies (I–IV) that used data from the Swedish National Study on Aging and Care (SNAC). The findings of these studies illustrate different perspectives of arrhythmias in the older general population. **Study I** revealed that among 6904 subjects who underwent a baseline ECG, 3419 (49.5%) subjects of 66–105 years of age also completed a resting ECG at their 6-year follow-up visit. The atrial fibrillation (AF) prevalence at baseline was 4.9% (95% CI, 4.5–5.5). Other arrhythmias were detected in 8.4% (95% CI, 7.7–9.0) of the cohort, including ventricular premature complexes, supraventricular tachycardia, and supraventricular extrasystole. Moreover, 7.1% (95% CI, 6.5–7.7) showed a first or second degree AV block, and 1.3% (95% CI, 1.0–1.6) had a pacemaker-induced rhythm. The baseline prevalence of arrhythmias did not significantly differ between men and women. The 6-year incidence of AF was 4.1% (95% CI, 3.5–4.9) or 6.9/1000 person-years (py) (95% CI, 5.7–8.0). Subgroup analyses showed incidences of 9.9/1000 py (95% CI, 7.8–11.9) among men; 4.4/1,000 py (95% CI, 3.1–5.6) among women; 3.7/1000 py (95% CI, 2.6–4.7) in the 60- and 66-year age cohort; 8.9/1000 py (95% CI, 6.3–11.4) in the 72- and 78-year cohort; 20/1000 py (95% CI, 14.2–25.7) in the 81-, 84-, and 87-year cohort; 18/1000 py (95% CI, 0.8–26.7) among those aged  $\geq 90$  years. Incidences of AF, other arrhythmias, AV block, and pacemaker-induced rhythm were significantly higher in men, except in the oldest cohorts. **Study II** found an overall AF prevalence of 4.9% among 6904 persons (mean age, 73.9 years), which increased with age except in the oldest subgroup. AF presence at baseline was associated with a hazard ratio (HR) of 1.29 (95% CI, 1.10–1.51) for death during the 10-year observation period. Cox regression analysis of persons with AF ( $n=341$ ) revealed that men had a higher HR for death (1.57; 95% CI, 1.15–2.13) compared to women ( $P<0.01$ ). CHA<sub>2</sub>DS<sub>2</sub>-VASc score was also significantly associated with 10-year death (HR=1.29/score point; 95% CI, 1.10–1.51). A total of 146 persons (42.8%) reported any oral anticoagulant (OAC) use, and only 14% received OAC treatment with warfarin. Cox regression analysis of warfarin (33.6%) and ASA (66.4%), separately, revealed that warfarin use was significantly associated with survival ( $P=0.031$ ). **Study III** revealed persistent AF in 10% of the population aged  $\geq 66$  years, and paroxysmal AF in 5.5%, with no differences between the younger (66–80 years) and older ( $>80$  years) subgroups. The results supported LTR ECG-BodyKom® as a feasible method for arrhythmia screening in older outpatient populations. This simple method requires little of the user, and participants reported high satisfaction with the equipment and a good overall experience wearing it. **Study IV** focused on geriatric experiences of living with arrhythmias. Interviews with older persons revealed one main theme: “ambivalence in the need of knowledge”. In

general, interviewees shared that their requirement of lifelong medical treatment led to experiencing feelings of “it doesn’t matter, but it does matter” and “being in the hands of the healthcare system”. The participants lacked sufficient knowledge about their condition, yielding poor insight into their medical treatment, which, in turn, affected their daily life. They had thoughts and questions about their medical treatment, but had no opportunity to ask these questions due to a lack of follow-up from the healthcare system. The findings of this thesis contribute to the knowledge regarding increasing arrhythmia occurrence in the older population, and the high number of untreated cases of AF. Furthermore the results demonstrate that AF is associated with increased mortality, and highlight sex-related differences in AF incidence. In line with findings from Europe and the USA, our findings show that AF incidence rapidly increases with advancing age. This thesis also highlights the present lack of knowledge and the need for follow-up and information regarding AF in the oldest old population.

Keywords: arrhythmia, epidemiology, incidence, long-term ECG, older people, prevalence, survival analysis

## Abbreviation list

AF	Atrial fibrillation
AV block	Atrioventricular block
BBB	Bundle branch block
CHF	Chronic heart failure
CHA2DS2-VASc	Congestive heart disease, Hypertension, Age $\geq$ 75 years, Diabetes, earlier Stroke, Vascular disease, Age $\geq$ 65, female Sex
CI	Confidence interval
CVD	Cardiovascular disease
ECG	Electrocardiogram
HR	Hazard ratio
INR	International normalized ratio
LTRE	Long-term recording ECG
NOAC	Novel oral anticoagulation therapy
OAC	Oral anticoagulation therapy
OR	Odds ratio
PSVT	Paroxysmal supraventricular tachycardia
RR	Relative risk
SBU	Swedish Agency for Health Technology Assessment and Assessment of Social Services. (Statens beredning för medicinsk och social utvärdering)
SD	Standard deviation
SNAC	Swedish National study on Aging and Care
SVT	Supraventricular tachycardia
SVES	Supraventricular extrasystole
VPC	Ventricular premature complexes

## List of publications

This thesis is based on the following papers, identified in the text by Roman numerals:

- I. Lindberg, T., Sanmartin Berglund, J., Wimo, A., Qiu, C., Bohman, D.M. & Elmståhl, S. Prevalence and incidence of arrhythmias in the older general population. Findings from the Swedish National Study on Aging and Care (SNAC) (manus)
- II. Lindberg, T., Elmståhl, S., Wimo, A., Qiu, C., Bohman, D.M. & Sanmartin Berglund, J. Prevalence and long-term survival of atrial fibrillation in older adults - findings from the SNAC study (submitted)
- III. Lindberg, T., Bohman, D.M., Elmståhl, S., Jogr eus, C. & Sanmartin Berglund, J. Prevalence of unknown and untreated arrhythmias in an older outpatient population screened by wireless long-term recording with ECG-BodyCom®. *Clinical Intervention in Aging* 2016;11 1083-1090.
- IV. Lindberg, T., Sanmartin Berglund, J., Elmståhl, S. & Bohman, D.M. Older individuals' need for knowledge and follow-up about their chronic atrial fibrillation, lifelong medical treatment and medical controls. *Scandinavian Journal of caring science*. 2016.

# Background

## Older people

Older people constitute the population showing the fastest growth in the industrialized world. While the 20th century was characterized by population growth, the 21st century will be remembered as the century of population aging (1). The United Nations estimates that about 900 million people were 60 years of age and older in 2015, representing about 12% of the global population (2). Based on medium-level growth projections, this population is expected to exceed 2 billion by 2050, which will represent close to 22% of the global population at that time. This trend is related to the increasing longevity in many parts of the world (3).

Demographic development predictions suggest that Sweden will be the country with the highest percentage of older people in its population. Ten years ago, Sweden's population was characterized by many young people and a smaller proportion of elderly individuals. However, as people are now living longer and having fewer children, the age structure has changed, yielding a population pyramid with a completely different shape. Statistics Sweden's population forecast shows that the proportion of elderly individuals is expected to increase by 30% between 2010 and 2050 (4). Under these circumstances, a quarter of the population will be 65 years of age or older in 2050. The population pyramid also shows a clear pattern of age distribution when comparing women and men, with a greater proportion of men in all age groups up to 60 years, but a majority of women in the older age groups (5). This is because, although more boys than girls are born, women live longer than men. These estimates are based on expected demographic development, advancements in medical technology, and changing expectations in the population.

The present thesis defines older people as 60–80 years of age, and the oldest old population as 81 years and older. The World Health Organization states that chronological time plays a paramount role in the developed world. Old age is considered to begin at 60 or 65 years, roughly equivalent to the retirement ages in most developed countries (6). The United Nations has used 60 years of age to represent the transition to the elderly group (2). The global population is now living to increasingly advanced ages, such that for the first time in human history, most people worldwide can expect to live into their 60s (6). The ageing process is accompanied by a loss of physiologic reserve, which can be viewed as the extra capacity built into individual organ systems, which allows them to withstand challenges, such as infection, injury, or stress. The loss of this



reserve leaves older people more vulnerable to disease (7)—especially cardiovascular diseases (CVDs), which are commonly diagnosed in older individuals and have become a leading cause of death in both developing and developed countries (8).

## Arrhythmias

Among all types of CVDs, arrhythmias are most often responsible for sudden deaths and are indicative of other high-risk diseases (9,10). Cardiac rhythm disorders cause an estimated 400,000 deaths annually in the United States alone, and about 7 million deaths worldwide (11). Clinical and experimental studies reveal basic electrophysiological differences between genders, which likely reflect the occurrence of arrhythmias (12). Arrhythmia is the collective term for a variety of conditions that involve a heart rhythm other than sinus rhythm (13). Arrhythmia symptoms can range from normal and harmless symptoms to life-threatening symptoms of serious heart disease, such as cardiac arrest.

Arrhythmias may be classified in several ways based on different factors. They can be categorized based on heart rate, i.e. bradycardia or tachycardia. Some arrhythmias are classified based on their cause, which can include medical conditions such as hyperthyroidism, severe anemia, or lack of oxygen. Arrhythmias can be categorized as regular or irregular. An arrhythmia can also be classified based on the foci in the heart from which it originates—for example, an arrhythmia originating at the ventricular level is called a ventricular arrhythmia, while one located in the atrium is termed a supraventricular arrhythmia. Arrhythmias that occur due to changes in the heart, are called organically caused arrhythmias, while those due to changes in the autonomic system are termed functionally related arrhythmias. Finally, some arrhythmias are caused by certain pharmaceuticals, such as digitalis, diuretics, certain antiarrhythmic drugs, and some psychotropic drugs (14).

The present thesis focuses on sinus rhythms; pacemaker rhythms; atrial fibrillation (AF); atrioventricular block (AV block); bundle branch block (BBB); and several types of other arrhythmia, including ventricular premature complexes (VPC), supra ventricular tachycardia (SVT), and supraventricular extra systole (SVES).

## Atrial fibrillation

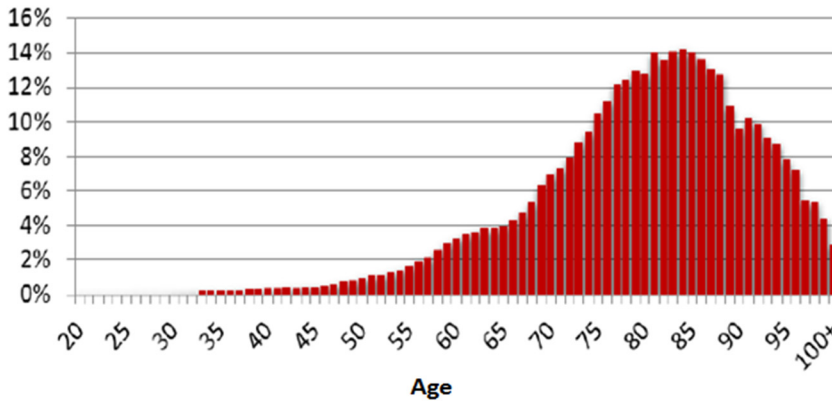
Atrial fibrillation (AF) is a supraventricular tachyarrhythmia characterized by uncoordinated atrial activation and subsequent deterioration of atrial mechanical function (15). AF involves a complete absence of sinoatrial (SA) node stimulus. Under normal conditions, SA node stimulus depolarizes the cells and causes a wave of contraction throughout the atria. Upon opening of the valves between the atria and

ventricles, up to 70% of blood within the atria falls into the ventricles, aided by gravity. The final 30% of blood is pushed from the atria into the ventricles by atrial contraction, known as the “atrial kick”. In AF, the atria are fibrillating, i.e. quivering, and the atrial kick does not occur, resulting in an at least 30% loss of blood to the arterial and coronary circulations (14). On electrocardiogram (ECG), AF is characterized by the replacement of regular P-waves with rapid oscillations or fibrillatory waves that vary in amplitude, shape, and timing, and are associated with irregular and often rapid ventricular responses when atrioventricular (AV) conduction is intact. The European Society of Cardiology (ESC) guidelines (15) provide the following consensus statement regarding simple and clinically useful definitions of AF:

- Paroxysmal AF: If the arrhythmia converts spontaneously within 7 days (most often within 24 hours).
- Persistent AF: If the arrhythmia lasts longer than 7 days but is converted by either pharmacological or direct-current cardioversion.
- Permanent AF: Long-lasting arrhythmia that does not respond to cardioversion or for which cardioversion has not been attempted.
- Recurrent AF: When a patient has had more than two AF episodes. Both paroxysmal and persistent AF can be recurrent.
- Lone AF: No universal definition exists, but usually refers to AF in the absence of any clinical or echocardiographic evidence of cardiopulmonary disease, including hypertension and diabetes, and any other known precipitating cause or illness.
- Non-valvular AF: AF in the absence of rheumatic mitral valve disease, prosthetic heart valve, or mitral valve repair.

## **Epidemiology**

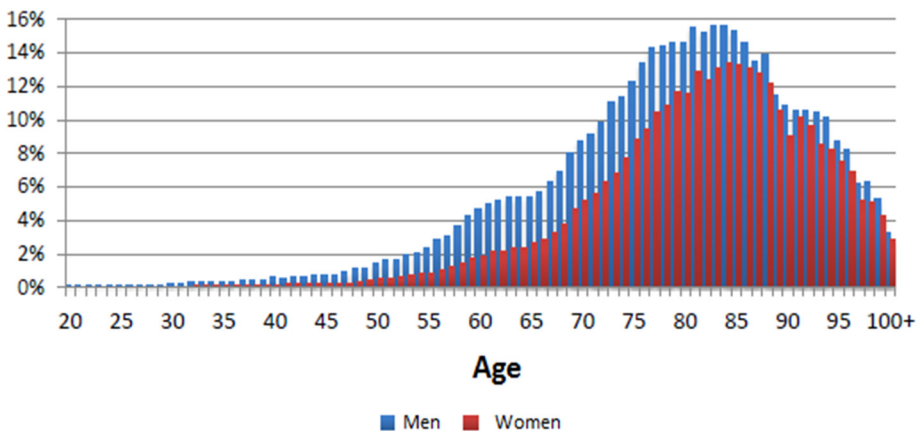
AF is the most common arrhythmia in most countries (16), and its prevalence among older persons is increasing faster than that of any other arrhythmia. Estimates suggest an AF prevalence of approximately 3% among adults ( $\geq 20$  years of age) (17,18). Higher prevalence rates are noted in older persons (19), and in persons with comorbidities, such as hypertension, heart failure, coronary artery disease, valvular heart disease, obesity, diabetes mellitus, or chronic kidney disease (20–24). In 2010, it is estimated that 20.9 million woman and 12.6 million men experienced AF worldwide, with higher incidence and prevalence rates in developed countries (25,26). Figure 1 presents the AF prevalence in Sweden in 2010 (Figure 1). Despite good progress in the management of patients with AF (15), the number of persons with AF is expected to increase in the upcoming years (27) as the older population grows.



**Figure 1.** The proportion of the population with atrial fibrillation in Sweden in 2010, stratified by age. Data were obtained from SBU Sweden (Swedish Agency for Health Technology Assessment and Assessment of Social Services) (28).

### Sex perspectives in AF

In this thesis, the term “sex” is used to refer to biologically determined differences, whereas “gender” refers to socially/culturally-derived distinctions between males and females (12). Men and women biologically differ in the normal electrophysiology of their specialized conduction system and working myocardium. Clinical and experimental studies demonstrate basic electrophysiological differences between the sexes, which is likely reflected in arrhythmia incidence. AF prevalence is lower among women in both developed and developing countries (29). Figure 2 describes the AF prevalences among men and women in Sweden in 2010.



**Figure 2.** In all age groups, atrial fibrillation is more common among men than women in Sweden. Data were obtained from SBU Sweden (Swedish Agency for Health Technology Assessment and Assessment of Social Services) (28).

Men and women show underlying hormonal differences as well as differences in autonomic tone. The sexes also show differences in responses to pharmacological and non-pharmacological arrhythmia treatment, and in the occurrence of severe complications and risk of relapse (30). A large registry study, the Euro Heart Survey, included 5333 patients (42% women) (31), and revealed that the women were older, had lower quality of life, and more commonly had hypertension, valvular heart disease, diabetes, and thyrotoxicosis. While men often had ischemic heart disease or idiopathic AF, women more commonly had symptoms, including higher incidence of heart palpitations and dyspnea. Moreover, women less frequently underwent conversion and ablation. At one year of follow-up, more women had suffered from stroke (2.2% compared with 1.2% of men) despite equivalent anticoagulation, whereas mortality did not differ between sexes.

## **Consequences and risks**

Despite good progress in the AF management, this arrhythmia remains a major cause of stroke, heart failure, sudden death, and cardiovascular morbidity worldwide (16,34). The Framingham study indicates that AF is associated with increased risk of thromboembolism, which doubles the risk of death and increases the risk of stroke by four to five times (33). AF is associated with high incidence of ischemic heart disease in men, while heart failure is more common among women (34). Women with AF also show a moderately increased risk of stroke compared with men (35).

## **Prophylactic therapy and continuous monitoring in AF**

AF management includes therapies that have prognostic impact, such as anticoagulation and treatment of cardiovascular conditions, as well as therapies that predominantly provide symptomatic benefit, such as heart rate and rhythm control (36). If these two treatment strategies are ineffective, surgical options may be considered, such as maze operations or ablation. One treatment with proven efficacy on hard endpoints (i.e. mortality, strokes, and hospitalization) is oral anticoagulation (OAC) with vitamin K antagonists (VKAs) or non-VKA oral anticoagulants (NOACs), which markedly reduces stroke and mortality in AF patients (37). VKAs (e.g. warfarin) and antiplatelet agents (e.g. aspirin) reduce the risk of stroke in patients with AF by over 60% compared with no treatment, and by 30–40% compared with low-dose aspirin. However, VKA use has several drawbacks, including the need for laboratory monitoring, increased risk of bleeding complications, and several food and drug interactions (38). The efficacy of oral anticoagulant therapy is traditionally determined by monitoring prothrombin time (PT), and determining its derived measures prothrombin ratio (PR) and international normalized ratio (INR), which reflect the extrinsic pathway of coagulation. These parameters are used to monitor warfarin dosage, liver damage, and vitamin K status (39).

An improved understanding of the blood clotting cascade has led to the development of new oral anticoagulants (NOACs) with more predictable pharmacokinetics and pharmacodynamics, thereby obviating the need for laboratory monitoring. Approved NOACs include the direct thrombin inhibitor dabigatran, and the direct Factor Xa (FXa) inhibitors rivaroxaban, apixaban, and edoxaban. These agents have been demonstrated to effectively prevent stroke/systemic embolism (SE) in AF patients (40). To date, there is insufficient evidence to preferentially recommend any specific NOAC, although the choice of agent may be influenced by patient characteristics, drug compliance and tolerability, and cost (41). The National Board in Sweden equates warfarin with NOAC (42). However, the 2016 ESC recommendations advise the use of NOAC for suitable candidates who are starting new anticoagulant treatment, based on evidence that NOAC is associated with lower mortality and reduced risk of serious bleeding, including brain hemorrhage, compared to warfarin. NOAC may also be considered for patients in whom warfarin treatment is less efficient (27).

Several scores have been developed to help determine which patients will benefit most from OAC treatment. One of the most common is the **CHA2DS2-VASc**: Congestive heart failure, Hypertension, Age  $\geq 75$  (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex category (female) (Table 1).

**Table 1.**

Guidelines for oral anticoagulation therapy based on CHA2DS2-VASc score: Congestive heart failure, Hypertension, Age  $\geq 75$  (doubled), Diabetes, Stroke (doubled), Vascular disease, Age 65–74, and Sex category (female).

	Condition	Points
<b>C</b>	Congestive heart failure (or left ventricular systolic dysfunction)	1
<b>H</b>	Hypertension: blood pressure consistently above 140/90 mmHg (or medically treated hypertension)	1
<b>A<sub>2</sub></b>	Age $\geq 75$ years	2
<b>D</b>	Diabetes mellitus	1
<b>S<sub>2</sub></b>	Prior stroke or TIA or thromboembolism	2
<b>V</b>	Vascular disease (e.g. peripheral artery disease, myocardial infarction, aortic plaque)	1
<b>A</b>	Age 65–74 years	1
<b>Sc</b>	Sex category (i.e. female sex)	1

In this scoring system, two points are assigned for a history of stroke, TIA, or other thromboembolic event; or age of  $\geq 75$ . One point each is assigned for age of 65–74 years; history of hypertension, diabetes, recent cardiac failure, and vascular disease; and female sex. The CHA2DS2-VASc score is derived from clinical trial data, and constitutes an easily remembered and utilized stroke prediction score that uses clinically available parameters to divide patients into three categories: low risk (0 points; no treatment or ASA is recommended), moderate risk (1–2 points; OAC could be considered), and high risk ( $>2$  points; OAC is recommended) (43). Patients of  $<65$  years old, and with lone AF (strictly defined irrespective of sex) do not require antithrombotic therapy (41).

# Arrhythmia detection

## **Electrocardiography (ECG)**

In general, the approaches to arrhythmia beat detection, degree assessment, and therapy selection are based on ECG—a noninvasive and low-cost method of obtaining clinical information regarding the heart by measuring the skin surface potential. Morphological changes on the ECG waveform can reveal abnormal cardiac beats, helping in arrhythmia detection (8).

## **Long-term recording ECG (LTRE)**

For decades, the 24-h Holter monitor has been the gold standard method for investigating patients with suspected arrhythmias, including AF, in the ambulatory setting. Many studies demonstrate the benefits of this method; however, there are some limitations regarding its use and applicability. When using a Holter monitor, the diagnostic yield ranges from only 15–39% because intermittent periods of paroxysmal AF that do not manifest during the 24-h monitoring period remain unnoticed (44,45,45–49). Event recorders and 7-day electrocardiogram (ECG) monitors have a longer measurement period and, thus, a higher diagnostic yield. However, like the 24-h Holter monitor, these devices require many cables and are therefore rather cumbersome to wear (48–50). The highest diagnostic yield is achieved with implanted devices, such as loop recorders (50). However, such monitors are costly and invasive, and are thus limited to a certain subset of patients.

While the 12-lead Holter monitor remains the “gold standard” for assessing cardiac rhythm abnormalities, there is growing interest in portable monitoring devices that enable cardiac rhythm evaluation in real-world environments, such as the workplace or home. This generates the need for new non-invasive high-quality diagnostic devices capable of monitoring for longer time periods with acceptable comfort. One such monitor that has been developed for use in heart disease patients is the BodyKom® device. The BodyKom® can be used to monitor a patient’s heart rate following discharge from the hospital, or whenever there is a heart-related health concern (51). The system includes ECG electrodes that are attached to the patient’s chest, a small portable sensor that is hung around the patient’s neck, and a smart cell phone. The monitored data are collected by the sensor and wirelessly transferred to the cell phone. The ECG data are transferred via the mobile network to a decision support system for adjustment, and then forwarded to the caregiver’s system for analysis. Rhythm monitoring data are transmitted to the phone via Bluetooth, and then transmitted across a mobile network to a caregiver who reviews the information. The data are also stored in an application, such that all data can be retrieved when necessary. By compiling all

monitoring data in a central location, this technology promotes efficient treatment, time management, and diagnosis (51).

## Living with AF

Persons who suffer from AF often feel unwell both physically and psychologically (52), which can affect several dimensions of the patient's life (53). AF is associated with many symptoms, often including a lack of energy, difficulty sleeping, breathlessness, and waking up breathless at night (54). Individuals with AF are often particularly distressed by their decreased energy and the need to slow down (55). Living with AF requires that a person make fundamental adjustments, including gradually accepting their new identity and life situation, and making lifestyle changes (55). A review of the literature reveals very few studies of this population from a caring perspective.

# Rationale

As arrhythmias are common in the older general population, it is expected that the prevalence of arrhythmias will increase over upcoming decades (56). Some types of arrhythmias have important health implications and, thus, represent a growing challenge to healthcare services (57). Atrial fibrillation (AF) is a common arrhythmia, with a reported prevalence of 1.5–3% in the general population of the developed world (16,18), and a much greater prevalence of nearly 20% within the oldest portion of the population (60,61). However, these statistics may underestimate AF prevalence, as the condition can be asymptomatic (60) and screening is not routine (61). Arrhythmia onset is often associated with other chronic diseases, and may lead to complications, including stroke (62). Early intervention can prevent or forestall negative outcomes (63), warranting further longitudinal studies to investigate arrhythmia prevalence and incidence in the general older population.

There is presently a lack of knowledge regarding the experiences of older persons living with arrhythmias. To understand and meet these person's needs, it is important to understand their experiences. Older persons with a chronic condition that negatively impacts their quality of life may suffer over long periods of time. It is important to design qualitative studies to attain increase awareness and a deeper understanding of individual experiences. The present thesis is based on the theory of "life course epidemiology" described by Kuh and Ben-Shlomo (64), in which it is considered that long-term biological, behavioral, and psychosocial processes may link adult health and disease risk to physical or social exposures during one's lifetime or even across generations. Epidemiological studies can increase our knowledge regarding the risk factors and natural history of arrhythmias, while studies from the qualitative perspective can increase our understanding about life with arrhythmias.





# Research aims

The overall aim of this thesis was to investigate the prevalence, incidence, survival, and experiences of arrhythmias from the perspective of a geriatric population (aged 60+).

Specific aims:

Study I aimed to study the prevalence and six-year incidence of arrhythmias among persons 60 years of age and older.

Study II aimed to examine the prevalence and long-term survival of AF among old adults in the general population.

Study III aimed to explore arrhythmia prevalence among 200 outpatients of >66 years of age, as well as to examine the feasibility of using the new wireless LTR ECG-BodyKom® device for arrhythmia screening.

Study IV aimed to explore and describe the lifelong medical treatment and need for medication as experienced from the perspective of older individuals living with chronic AF.



# Methodology

## Approach

To achieve the overall aims of this thesis and to explore arrhythmias in older people, both quantitative and qualitative methodologies were used. Studies I, II, and III applied a quantitative design, focusing on arrhythmia prevalence, incidence, and survival, while study IV used qualitative design with the aim of obtaining a better understanding of older people's experiences. Different approaches and methods were used to investigate older people with the intent of gathering a rich variety of information and examining different aspects of the subject. The use of a life course epidemiology approach helps bridge the gaps between biological, psychological, and social models of disease. Focusing on the phenomenon of arrhythmias in older people at both the population and individual levels promotes a deeper understanding.

Table 2 presents an overview of the four included studies.

**Table 2.**  
Overview of the included studies.

Study	I	II	III	IV
Design	Quantitative longitudinal	Quantitative longitudinal	Quantitative cross-sectional	Qualitative interviews
Sample	$n=8462$ participants $\geq 60$ years of age	$n=8462$ participants $\geq 60$ years of age	$n=200$ participants $\geq 60$ years of age	$n=11$ participants $\geq 60$ years of age
Data collection	SNAC baseline 2001–2003, and 6-year follow-up	SNAC baseline 2001–2003, and 10-year follow-up	SNAC-B 6-year follow-up	SNAC-B 6-year follow-up
Data analysis	Chi-squared test	Kaplan Meier Cox regression	Chi-squared test	Thematic analysis

# The SNAC study

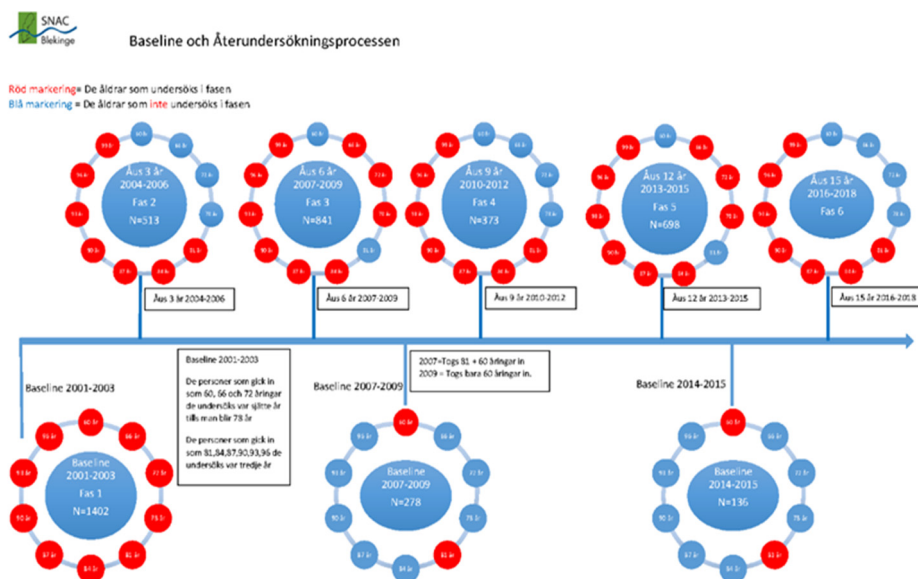
The studies in this thesis are based on data from The Swedish National Study on Aging and Care (SNAC). Health is viewed from a broad perspective, which includes medical/physical, psychological, and social well-being. SNAC collects a wide array of information, including demographic data, socioeconomic factors, physical environment, social environment, life habits, medical and psychological status, physical and cognitive functioning, and care services utilization. SNAC is a longitudinal, national, multicenter study that follows a sample of older adults stratified into various age cohorts. The study investigates patterns of health and living conditions of the Swedish population aged 60 years and older. SNAC began in 2001, and is conducted at four research centers in Sweden: SNAC-Blekinge, SNAC-Kungsholmen, SNAC-Nordanstig, and SNAC-Skåne. The characteristics of the total SNAC study sample closely reflect those of the general elderly population in Sweden. Thus, the total SNAC sample may be perceived as representative of the elderly in Sweden (65) (Figure 3).

County council	Region of Skåne					Blekinge	Stock- holm	Gävle- borg	Total SNAC	Total Sweden
	Municipality	Eslöv	Hässle- holm	Malmö	Osby	Ystad	Karls- krona	Kungs- holmen		
Population 65+:										
65+: % of total population	17	19	18	21	22	19	17	21	18	17
65-79: % of total pop.	12	13	12	14	15	13	10	15	12	12
80+: % of total pop.	5	6	6	7	7	6	7	6	6	5
Total no. of recipients of public long-term care and services	826	2253	8452	538	671	1782	2181	341	17044	258200
Recipients of care as % of all 65+	17	24	18	20	12	16	25	16	18	17
% of recipients of care:										
-living in ordinary homes	62	61	63	58	77	68	70	55	64	54
-living in special accommodation	38	39	37	42	23	32	30	45	36	46

**Figure 3.** Population and care recipients in the municipalities of SNAC and the total in Sweden. Distributions are by age in the year 2001 (65).

Persons from 10 age cohorts drawn from the National Municipality Registry were randomly selected and invited to participate in SNAC. In 2001–2004, an initial baseline survey was performed relating to the randomized selection of individuals living in different areas and aged 60, 66, 72, 78, 81, 84, 87, 90, 93, and 96 years. Potential participants received a letter inviting them to participate in SNAC 2001, and approximately 8500 individuals accepted at baseline. Reasons for non-participation included lack of willingness, feeling too ill, and could not be contacted. The data collection method was purposefully designed to construct a randomly selected sample, representing old individuals of a broad variation of ages. Participants are regularly

followed—every 6 years for younger individuals, and every 3 years for older persons. Additionally, every sixth year, new cohorts of 60-year-old and 81-year-old participants are added to the study population. At baseline, the different age groups were categorized with the intention of describing age decade values (Figure 4).



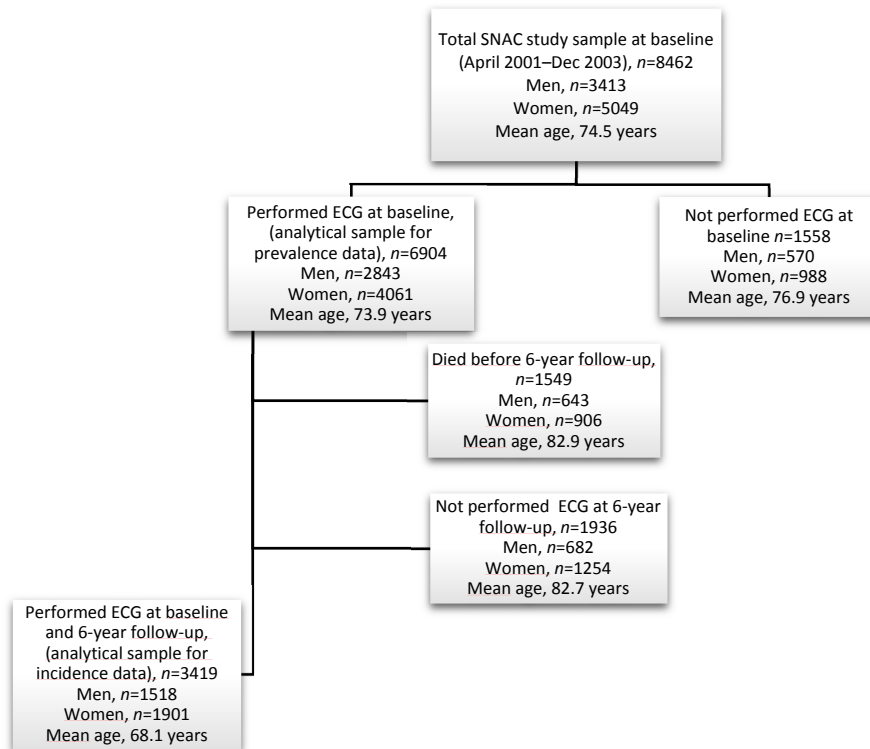
**Figure 4.** Example of SNAC cohorts from SNAB-B (Ulrika Isaksson, 2017) at baseline and during the follow-up phases.

## Study population, participants and procedure

Studies I and II are based on results collected from participants at all four centers: SNAC-Blekinge, SNAC-Kungsholmen, SNAC-Nordanstig, and SNAC-Skåne. The majority of the examinations for these studies were performed at outpatient clinics in Malmö, Kungsholmen Stockholm, Nordanstig, and Karlskrona. Studies III and IV are based on results collected from participants at SNAC-Blekinge, with most examinations performed at outpatient clinics in Karlskrona. Data were collected from physical examinations, patient records, and questionnaires, and data collection was performed in the same manner at baseline and in the follow-up phases.

## Study I

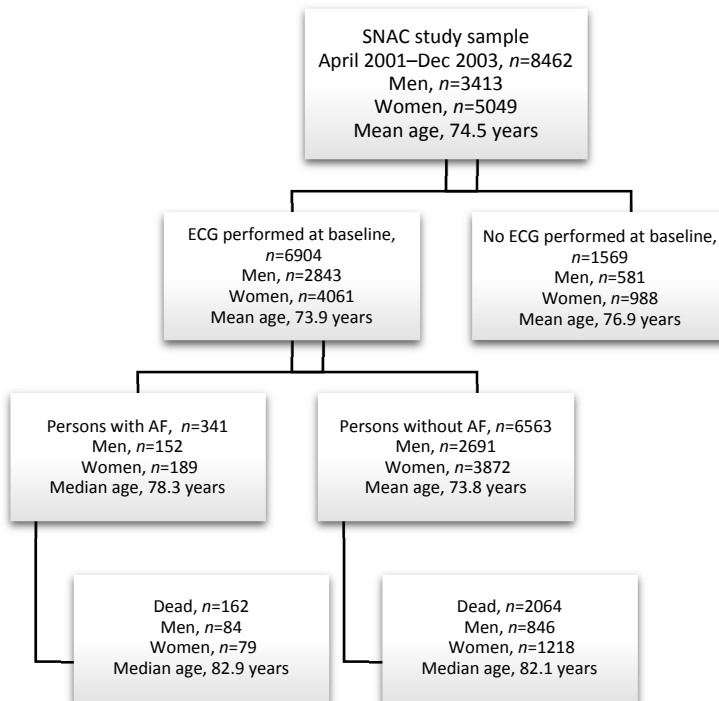
Study I included individuals of  $\geq 60$  years of age who had undergone a resting 12-lead ECG at both baseline and 6-year follow-up. All included participants underwent a medical examination and testing on two occasions, each performed by trained assessors and lasting about 3 hours. ECG data were interpreted by experts. A total of 3419 persons underwent an acceptable ECG during the physical examination at both baseline and follow-up (Figure 5).



**Figure 5.** Inclusion of participants in study I.

## Study II

Study II included persons of  $\geq 60$  years of age who underwent resting 12-lead ECG during their physical examination at baseline. A total of 6904 persons had an acceptable ECG data interpreted by experts. Among these individuals, 341 (4.9%) had AF and were analyzed in study II. During examinations, baseline sociodemographic data (age and sex) and clinical data (stroke risk factors and medication use, including antithrombotic therapy) were obtained. Follow-up of the death registry was performed after 10 years, in October 2015 (Figure 6).



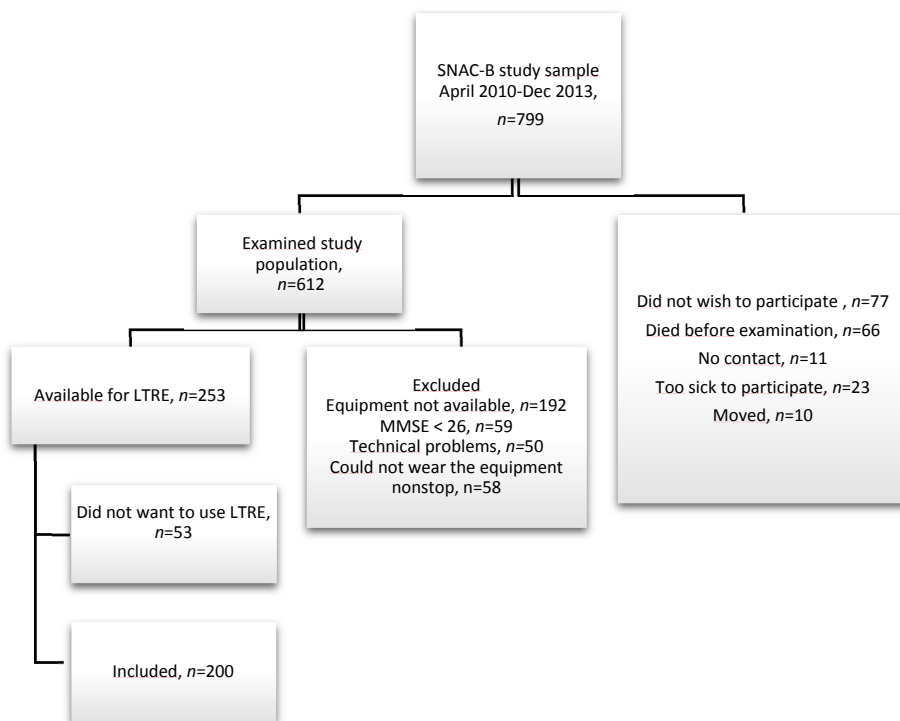
**Figure 6.** Survival of participants in study II.



## Study III

Study III included individuals of  $\geq 66$  years of age who were examined with LTR ECG. A total of 200 elderly persons (66–93 years of age) were recruited from the SNAC-B in 2010–2013 (Figure 7).

Figure 7.



Participants inclusion in study III.

## Study IV

In the quantitative study IV, an interpretive description approach was used (66). Through individual interviews, the participants were given an opportunity to share their experiences (67). In 2013, 47 individuals from SNAC-B were identified as matching the inclusion criteria: age of  $\geq 60$  years, diagnosed with chronic AF, outpatient treatment, and receiving OAC medical treatment. All 47 individuals were part of the SNAC baseline and follow-up phase 2007 cohort, and were invited to participate in this specific interview study. A total of 11 persons agreed to participate and were included in study IV (Table 3).

**Table 3.**  
Characteristics of the participants in study IV.

Interview no.	Sex, M/F	Age, years <sup>a</sup>	Social status	Living condition	Relative present, Yes/No
1	F	89	Widow	Apartment	N
2	M	84	Married	Apartment	N
3	F	89	Widow	Service housing	N
4	F	90	Widow	Own house	N
5	M	90	Married	Own house	Y
6	F	77	Widow	Apartment	N
7	M	89	Married	Service housing	Y
8	F	83	Widow	Own house	N
9	F	84	Widow	Apartment	N
10	F	69	Married	Own house	N
11	M	74	Married	Own house	N

The interviews lasted approximately 45–60 minutes, and were audio recorded and transcribed verbatim. The study sample included seven women and four men (sex differences were non-significant) (Table 4).

**Table 4.**  
Age cohorts and sex distribution of participants included in study IV.

	Total, n (%)	Men, n (%)	Women, n (%)	P value for sex differences
	11 (100)	4 (36)	7 (64)	0.704
Age cohorts				
64–80 years	3 (27)	1 (9)	2 (18)	
>80 years	8 (73)	3 (27)	5 (46)	
Interview time, min				
Mean	47.50 (SD, 24.29)			
Range	23.48–91.06			

## Data collection

Studies I and II had a longitudinal design, study III had a cross-sectional cohort design, and study IV had a qualitative design with an interpretive description approach.

### Study I

In study I, data regarding arrhythmias were attained from the ECG examination results. Baseline sociodemographic data (age and sex) and clinical data (stroke risk factors and medication use, including anticoagulant therapy) were recorded during examinations. After 6 years, the vital status of each study group participant was determined from the national death index, regardless of their last date of clinical follow-up.

### Study II

In study II, data regarding independent variable AF was attained from the ECG examination results. Baseline sociodemographic data (age and sex) and clinical data (stroke risk factors and medication use, including antithrombotic therapy) were recorded during examinations. After 10 years, in October 2015, follow-up of the death registry was conducted.

### Study III

In study III, data were collected using the wireless LTR ECG-BodyKom® (51) and questionnaires. The monitoring equipment was applied at the end of the clinical examination, usually between 11:00 am and 4:00 pm, and was removed the following day. The equipment comprised a two-channel system with five electrodes that were attached to the participant's chest, and a sensor that transmitted data to a mobile telephone via Bluetooth. The data were then transmitted across the mobile network, and transferred to a database for storage, followed by analysis using Cardio Explorer analysis software. The medical examination included collection of medical history and administration of questionnaires to gather information regarding cardiovascular risk factors, including heart failure, hypertension, diabetes, stroke, history of ischemic cardiac disease, hypo/hyperthyroidism, medical treatment for AF, and smoking habits. To examine the feasibility of the LTR ECG-BodyCom® recording duration, the study also included interviews about monitor usability. A five-point scale questionnaire was utilized, which included multiple-choice questions, such as "The equipment was easy to use", "I have been living as normal during the past day", and "Sleeping with the equipment went well".

## Study IV

In study IV, 47 individuals were sent written information about the study and an invitation to participate. Ultimately, 11 individuals agreed to participate, and were included and interviewed. All participants had received medical treatment with warfarin®, and none self-reported experiencing any adverse events due to their medical treatment. The individual interviews took place in the participants' homes between 2014 and 2015. Each participant was interviewed on only one occasion, and the mean interview duration was 47 minutes. The interviews were audio recorded and transcribed verbatim. Prior to the interview, the participant was asked to approve the use of electronic recording equipment during the interview, which was not an obstacle for any of the informants.

Interviews were conducted using an interview guide inspired by Boyce and Neale (68). The first questions addressed sociodemographic status, e.g. age, marital status, living conditions, and medical treatment. Next, the participant was asked about their experience of living with the need for lifelong medical treatment. Follow-up questions were asked to clarify and deepen their answers, for example, "Would you give me an example?" and "Would you explain that further?" The use of a structured interview guide promotes investigation of the participant's personal opinions and perspectives on a particular phenomenon (69). Although it may resemble a casual conversation, it is a professional interview with a purpose and performed using a specific technique.

The interviews were designed to be descriptive, meaning that participants were given the opportunity to describe their experiences and feelings about a certain phenomenon. The interviewer strived to obtain nuanced descriptions of a phenomenon, which could reproduce the qualitative diversity of experiences (69). In general, qualitative research seeks to attain an overall perspective, and understanding of the whole. The interviewer is subjective and involved in the research. By stimulating the narration, the interviewer becomes a co-creator of the text (70). It was intended that the interview be an open dialogue between the informant and the interviewer. The interviewer showed respect for the older person's story, while reflecting on the content of the story. Such reflection leads to use of the interviewer's imagination and creativity, and promotes the interviewer's ability and will to achieve insight into the investigated phenomenon (71). After the interview, the interviewer provided the subject with written information, including the interviewer's telephone number, and the informant was invited to call if they had questions or felt discomfort related to the interview.

# Data analysis

## Study I

In study I, the data were characterized using descriptive methods. The age- and sex-specific prevalence of overall and various arrhythmias was estimated using baseline examination, whereas we estimated the incidence of arrhythmias by following the cohort of individuals who were free of arrhythmias at baseline. Chi square test for was used in order to test significant differences between persons with arrhythmias and without arrhythmias, age and sex. Age- and sex-specific cumulative incidence and overall incidence was calculated as percent and new cases per 1000 person-years of follow-up among those whom had a sinus rhythm at baseline.

## Study II

In study II, between-group comparisons were performed using the chi-square test to investigate differences between persons with and without AF, and according to age and sex. For survival analysis, Kaplan Maier and univariate Cox proportional hazards models were used to investigate how survival was related to sex, medical history, and age among subjects with evidence of AF. Men and women were analyzed separately, except in models exploring the effect of sex on survival.

## Study III

In study III, descriptive statistical analyses were performed to obtain an overview of the data. The continuous variable age was presented as mean and standard deviation (SD). Differences between sex and age cohorts were calculated, and chi square test for significance was used to examine differences between persons with and without AF, and according to age and sex.

All statistical analyses were performed using SPSS, versions 22 and 23. The probability values (*P* values) are presented for statistically significant results. *P* values of less than 0.05 were considered significant.

## Study IV

In study IV, descriptive statistical analyses were performed to obtain an overview of the participants. The interviews were recorded and transcribed verbatim. For interpretation, the interviews were subjected to thematic analysis inspired by Braun and Clarke (72). Thematic analysis was guided by the research question: How do older people with

chronic AF experience lifelong medical treatment? In accordance with the process of Braun and Clarke, the analysis was conducted in six steps: familiarization with the data, generating initial codes, searching for themes, reviewing themes, defining and naming themes, and report generation. The data analyses process followed those steps, starting with first author transcribing, reading, and re-reading the data. The authors continuously discussed the analysis. Next, the interviews were comprehensively reviewed to identify parts that showed common patterns, with emphasis on both similarities and differences. The coding process was next. Codes with common context were combined, and checked against the material and against each other. The subsequent step included interpretation, in which the data were inductively compared and organized into themes and subthemes. In this context, inductive means that the identified themes are strongly linked to the data. After identifying themes, an effort was made to theorize the importance of the patterns, and their broader meanings and implications in relation to previous literature. Relationships were analyzed between codes, between themes and subthemes, and between levels (steps), thereby developing the main theme. Finally, representative quotations were selected for inclusion in the report.



# Ethical considerations

All studies in this thesis comply with The Declaration of Helsinki developed by the World Medical Association (WMA) (73). All participants in each study of this thesis gave their written consent. Participants were repeatedly informed that their participation was voluntarily, and that they could withdraw at any time with no consequences. The study participants' privacy was protected, and all collected data were treated with confidentiality to minimize the risk that the research could damage their social, mental, or physical integrity.

For studies I, II, and III, ethical permissions were obtained when SNAC started in 2001, from the Regional research Ethics committees at the Karolinska Institute (KI dnr 00-446) and Lund University (LU dnr 604-00, 650-00 and 744-00). Ethical permission for study IV was later granted from the regional ethical review board in Lund (LU dnr 2012/108). Written consent was obtained from all participants before the interviews. To protect the interest of the study participants and to ensure compliance with the Data Protection Act, data were anonymized and securely stored, and only the project team had access to the data.





# Summary of the results

This section presents the integrated results of the four included studies. The results of studies I and II are based on longitudinal data as well as mortality data. The results of study III are based on population-based cross-sectional data. The results of study IV are qualitative. The life course epidemiology approach used in this thesis provide a broad perspective of the results (75).

## **Prevalence and incidence**

Of the 6904 subjects who underwent a baseline ECG, 3419 (49.5%) participants between the ages of 66–105 years also completed an ECG at their 6-year follow-up visit. Due to their generally higher age, more participants were offered a home visit for their follow-up evaluation. Table 5 shows the characteristics and prevalence of arrhythmias and heart rhythms.

**Table 5.**

Characteristics of participants in study I from The Swedish National Study on Aging and Care Prevalence, and baseline prevalences of arrhythmias in men and women and in age cohorts.

Characteristics	Total, n (%)	Sinus rhythm, n (%)	Atrial fibrillation, n (%)	Other arrhythmia, n (%)	AV block, n (%)	Pacemaker rhythm, n (%)
Total	6904 (100)	6345 (91.9)	341 (4.9)	579 (8.4)	488 (7.1)	88 (1.3)
<i>Men</i>	2843 (41.2)	2630 (92.5)	147 (5.2)	232 (8.2)	194 (6.8)	39 (1.4)
<i>Women</i>	4061 (58.8)	3715 (91.5)	194 (4.8)	347 (8.5)	294 (7.2)	49 (1.2)
Years of age						
60, 66 years	2832 (41.0)	2658 (93.9)	84 (3.0)	204 (7.2)	170 (6.0)	25 (0.9)
<i>Men</i>	1345 (47.5)	1276 (94.9)	35 (2.6)	92 (6.8)	67 (5.0)	11 (0.8)
<i>Women</i>	1487 (52.5)	1382 (92.9)	49 (3.3)	112 (7.5)	103 (6.9)	14 (0.6)
72, 78 years	1695 (24.6)	1584 (93.5)	94 (5.5)	159 (9.4)	122 (7.2)	20 (1.2)
<i>Men</i>	696 (41.0)	650 (93.4)	47 (6.8)	83 (11.9)	53 (7.6)	10 (1.4)
<i>Women</i>	999 (59.0)	934 (93.5)	47 (4.7)	96 (9.6)	69 (6.9)	10 (1.0)
81, 84, 87 years	1687 (24.4)	1528 (90.6)	124 (7.4)	172 (10.2)	140 (8.3)	31 (1.8)
<i>Men</i>	629 (37.3)	565 (89.8)	55 (8.7)	65 (10.3)	54 (8.6)	13 (2.0)
<i>Women</i>	1058 (62.7)	963 (91.0)	69 (6.5)	107 (10.1)	86 (8.1)	18 (1.7)
90+ years	690 (10.0)	638 (92.4)	39 (5.7)	44 (6.4)	56 (8.1)	12 (1.7)
<i>Men</i>	173 (25.1)	159 (91.9)	15 (8.7)	12 (6.9)	20 (11.6)	5 (2.9)
<i>Women</i>	517 (74.9)	479 (92.6)	24 (4.6)	32 (6.2)	36 (7.0)	7 (1.4)

The 6-year cumulative incidence of AF was 4.1% of the population, or 6.9/1000 person years (py). Sex subgroup analyses revealed that 6-year AF incidences were 9.9/1,000 py among men, and 4.4/1,000 py among women. Stratification by age cohorts showed AF incidences of 3.7/1000 py in the 60- and 66-year age cohort; 8.9/1000 py in the 72- and 78-year cohort; 20/1000 py in the 81-, 84-, and 87-year cohort; and 18/1000 py among those aged  $\geq 90$  years. AF incidence was significantly higher in men among all participants and in all age cohorts except for the oldest group (90+ years).

The cumulative incidence of other arrhythmia was 6.9% (11.6/1000 py) in the total sample, 14/1000 py among men, and 9.5/1000 py among women. Incidences of other arrhythmias were 8.3/1000 py in the 60- and 66-year age cohort; 17.5/1000 py in the 72- and 78-year cohort; 15.4/1000 py in the 81-, 84-, and 87-year cohort, and 18/1000 py among those aged  $\geq 90$  years. The incidence of other arrhythmias was significantly higher among men in the total sample, and in the 60- and 66-year cohort and the 72- and 78-year cohort.

AV block cumulative incidence was 7.3% (12.2/1000 py) in the total sample, 16/1000 py in men, and 8.6/1000 py in women. Analysis of age cohorts revealed AV block incidences of 8.2/1000 py in the 60- and 66-year cohort; 16.8/1000 py in the 72- and 78-year cohort; 23/1000 py in the 81-, 84-, and 87-year cohort; and 111.9/1000 py among those aged  $\geq 90$  years. AV block incidence was significantly higher among men in the total sample and in all age cohorts except for the oldest (90+ years).

The cumulative incidence of pacemaker-induced rhythm was 1.3% (2.2/1000 py) in the total sample, 2.8/1000 py in men, and 1.8/1000 py in women. Analysis by age cohorts revealed incidences of 1.0/1000 py in the 60- and 66-year cohort; 4.0/1000 py in the 72- and 78-year cohort; 4.4/1000 py in the 81-, 84-, and 87-year cohort, and 5.9/1000 py among those aged  $\geq 90$  years. The likelihood of receiving a pacemaker was significantly higher in the 72- and 78-year cohort.

## **Survival**

The study II population comprised 6904 individuals (2843 men and 4061 women) with a mean age of 73.9 years. Table 6 presents the medical history among the included and excluded participants, and among participants with and without AF.

**Table 6.**

Medical history among the included and excluded participants and among those with and without atrial fibrillation in study II.

Medical history	Total <i>n</i> =8462	ECG examination		<i>P</i> value	Atrial fibrillation		
		No <i>n</i> =1558	Yes <i>n</i> =6904		No <i>n</i> =6563	Yes <i>n</i> =341	<i>P</i> value
Death in 10 years, %	34.6	65.2	19.4	0.000	17.7	49	0.000
Smoker/former smoker, %	49.1	36.7	50.8	0.050	51.1	47	0.005
Diabetes, %	7.9	10.9	7.2	0.315	7.1	10.1	0.033
Stroke/TIA, %	8.4	15.7	6.8	0.000	6.4	14.2	0.001
Vascular disease, %	34.3	43.2	32.2	0.836	30.2	70.6	0.000
Congestive heart failure, %	5.5	7.8	5.0	0.000	4.5	14.7	0.000
Hypertension, %	28.3	30.7	27.8	0.314	32.7	24.4	0.041

Among the individuals analyzed in study II, 341 had AF. These participants were divided into age groups as shown in Table 7.

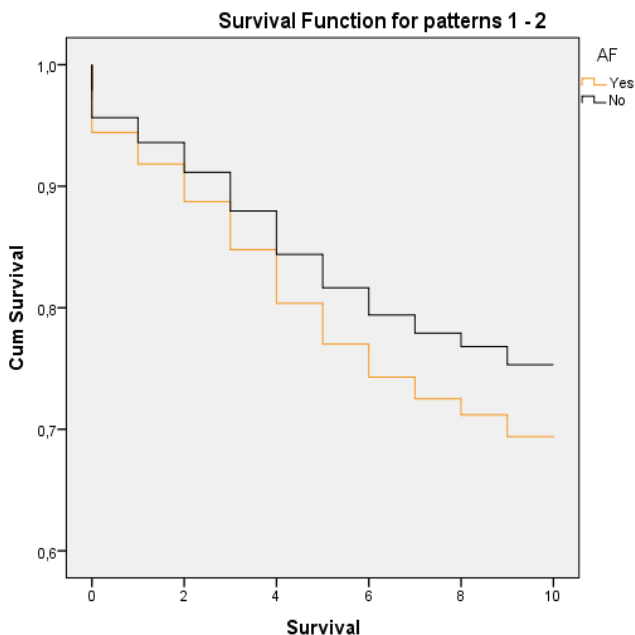
**Table 7.**

Included participants and prevalence of atrial fibrillation (AF) in study II.

Characteristics	No. of subjects	No. of persons with AF	Prevalence, % (95% CI)
Total (%)	6904	341	4.9 (4.39–5.41)
Men			
60, 66 years	1345	35	2.6 (1.7–3.4)
72, 78 years	696	47	6.6 (4.76–8.44)
81, 84, 87 years	629	55	8.7 (6.50–10.90)
90+ years	173	15	8.6 (4.4–12.8)
Total	2843	152	5.3 (4.48–6.12)
Women			
60, 66 years	1487	49	3.3 (2.39–4.21)
72, 78 years	999	47	4.7 (3.39–6.01)
81, 84, 87 years	1058	69	6.5 (5.01–7.99)
90+ years	517	24	
Total	4061	189	4.7 (4.05–5.35)

CI, confidence interval

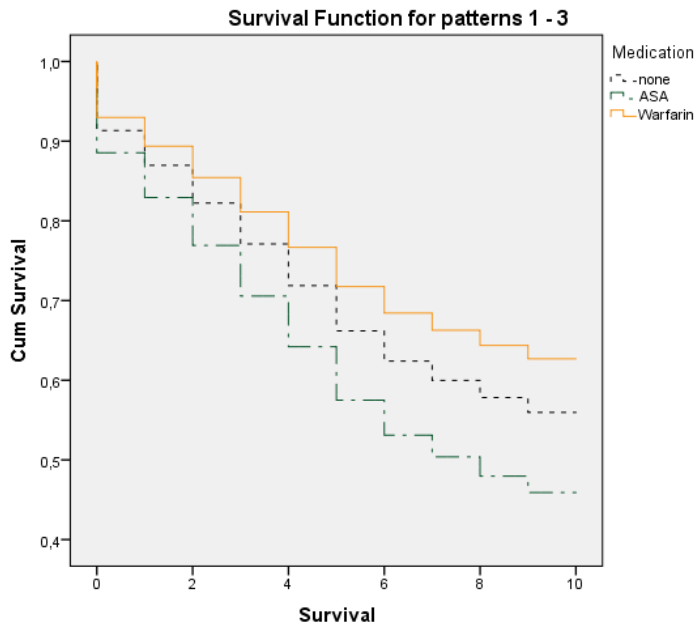
In the total study population, the overall AF prevalence was 4.9%. AF prevalence increased with age, except for in the oldest subgroup. AF at baseline showed a hazard ratio (HR) of 1.29 (95% CI, 1.10–1.51) for death during the 10-year observation period. Cox regression analysis among persons with AF ( $n=341$ ) by sex and with adjustment for age revealed that being a man showed an HR of 1.57 (95% CI 1.15–2.13;  $P < 0.01$ ). Figure 8 shows survival curves for persons with and without AF (with adjustment for age and sex).



**Figure 8.** Ten-year survival in subjects with and without atrial fibrillation, with adjustment for age and sex.

CHA<sub>2</sub>DS<sub>2</sub>-VASc score was significantly associated with 10-year death with an HR of 1.29 per score point (95% CI, 1.10–1.51).

Among the participants with AF, 146 (42.8%) reported the use of any form of anticoagulant. Individuals with higher CHA<sub>2</sub>DS<sub>2</sub>-VASc scores showed greater extents of anticoagulant use compared to those with lower scores. Cox regression analysis of persons with AF and anticoagulant use, with adjustment for CHA<sub>2</sub>DS<sub>2</sub>-VASc score, did not reveal a significant impact on survival ( $P=0.439$ ). Cox regression analysis of warfarin and ASA separately revealed that warfarin was significantly associated with survival ( $P=0.031$ ). Figure 9 shows survival curves for patients with AF ( $n=341$ ) when treated with warfarin, with ASA, and without anticoagulant use, with adjustment for CHA<sub>2</sub>DS<sub>2</sub>-VASc score.



**Figure 9.** Ten-year survival for subjects with atrial fibrillation ( $n=341$ ) who were treated with warfarin, were treated with ASA, or did not use anticoagulant therapy, with adjustment for CHA<sub>2</sub>DS<sub>2</sub>-VASc score.

## New technology: LTRE

Study III included 200 men and women. Table 8 presents their age distribution and medical history.

**Table 8.**  
Characteristics and medical history of participants in study III.

	Total, <i>n</i> (%)	Males, <i>n</i> (%)	Women, <i>n</i> (%)	<i>P</i> value for sex differences
	200 (100)	88 (44.0)	112 (56)	0.090
Age cohorts (years)				
66–80	125 (62.5)	51 (57.9)	74 (66.1)	0.040
>80	75 (37.5)	37 (42.1)	38 (33.9)	0.908
Heart failure	11 (5.5)	3 (3.4)	8 (7.1)	0.254
Hypertension	10 (5)	3 (3.4)	7 (6.2)	0.290
Diabetes	9 (4.5)	4 (4.5)	5 (4.4)	0.631
Stroke	13 (6.5)	6 (6.8)	7 (6.2)	0.860
Ischemic cardiac disease	20 (10)	11 (12.5)	9 (8.0)	0.290
Hyper/hypothyroidism	20 (10)	3 (3.4)	17 (15.1)	0.532
Smoking	10 (5)	5 (5.6)	5 (4.4)	0.661
Medical treatment (i.e. ASA and warfarin)	17 (8.5)	11 (12.5)	6 (5.3)	0.290

Screening with the LTR ECG revealed persistent AF in 10% of the outpatient population aged  $\geq 66$  years. Additionally, paroxysmal AF was detected in 5.5% of the population, with no difference between the younger (66–80 years) and older (>80 years) subgroups of elderly participants (Table 9). Moreover, all patients with paroxysmal AF had a CHA<sub>2</sub>DS<sub>2</sub>VASc score of  $\geq 2$  and were, therefore, potential candidates for follow-up and medical examination.



**Table 9.**

Heart rhythm and prevalence of arrhythmia during the analysis period in the study III population.

	Total (n=200), n (%)	95% confidence interval	Men, n (%)	Women, n (%)	P value for sex differences
Sinus rhythm	165 (82.5)	0.77–0.87	72 (85.2)	90 (80.3)	0.430
Persistent AF	20 (10)	0.06–0.14	6 (6.8)	14 (12.5)	0.393
Other rhythm	1 (0.5)	0.0–0.01	2 (1.1)	0 (0)	-
Pacemaker rhythm	3 (1.5)	0.0–0.03	2 (2.2)	1 (0.8)	-
Paroxysmal AF	11 (5.5)	0.02–0.09	4 (4.5)	7 (6.2)	-
Episodes of paroxysmal supraventricular tachycardia (>100 beats/min)	87 (43.5)	0.36–0.50	33 (37.5)	54 (48.2)	0.012

The questionnaire results suggested that the LTR ECG-BodyKom® can be considered a feasible method of screening for arrhythmias in older outpatient populations. This simple method requires little of the user, and the study participants reported high satisfaction with the equipment and a good overall experience wearing it.

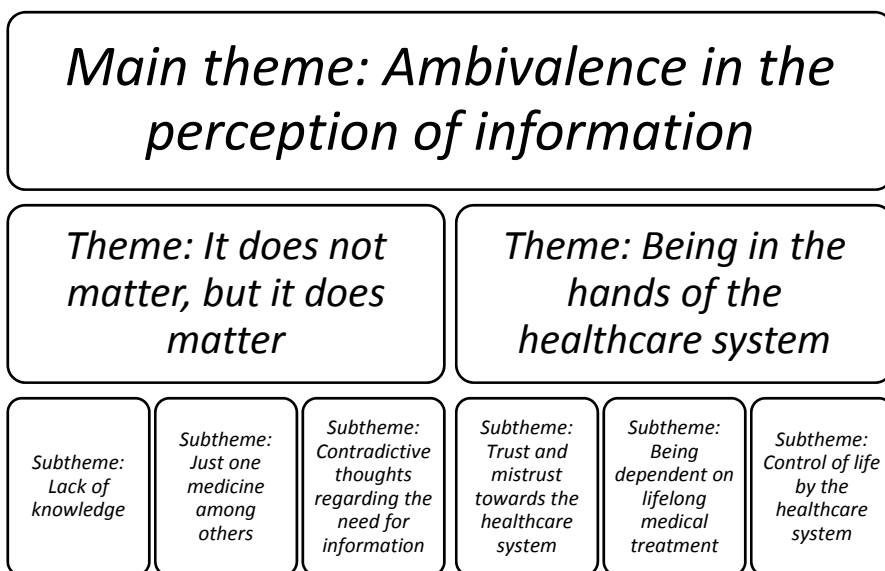
### **Living with AF: lifelong medical treatment**

The results of study IV revealed two themes. In general, the need for lifelong medical treatment was found to involve experiencing feelings of “it doesn’t matter, but it does matter” and “being in the hands of the healthcare system”. These two themes combined to form the core theme of “ambivalence in the perception of information”.

One main finding in study IV was that older individuals living with chronic AF desire additional information. The participants expressed contradictory thoughts regarding whether their medical treatment impacted their daily lives. On one hand, informants stated that their lives were not affected by their need for lifelong medical treatment. However, behind this positive spirit, they expressed concerns. For example, they stated that they lacked and, therefore, needed additional information and support at different levels in their daily lives. The interviewed older persons reported that they had to reschedule their activities of daily living due to the healthcare system. They also described reducing their day-to-day activities which impacted their feelings of independence.

Another main finding of this study was the need for increased follow-up for older people living with chronic AF. The participants expressed their feelings that no one from the healthcare organization seemed to care about their disease and medical condition. Aside

from the PK tests, there was no regular monitoring or follow-up information. If they wanted their heart condition checked or to discuss their medical treatment, they had to call to make an appointment with the doctor. The participants lacked sufficient knowledge about their AF, such that they had poor insight into their medical treatment, which, in turn, affected their daily life. Moreover, the participants had thoughts and questions about their medication, but had no opportunity to get answers due to the lack of follow-up from the healthcare system (Figure 10).



**Figure 10.** Main theme, themes, and subthemes identified in study IV.



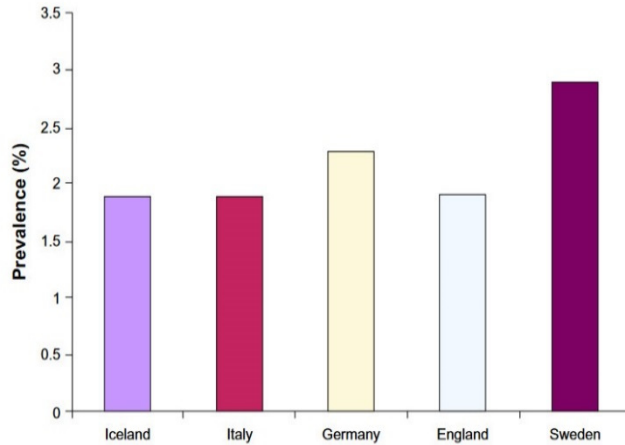
# Discussion

## General discussion of the results

This thesis used a large data set from the general population in Sweden to assess different perspectives regarding arrhythmias in persons of  $\geq 60$  years of age. The findings confirm that arrhythmias are common within the general older population (studies I, II, and III) and demonstrate that AF negatively impacts survival (study II) and daily life (study IV). The results of this thesis can be used to help improve outcomes in older persons with AF, especially with regards to developing new methods for care and treatment.

### Prevalence and incidence

From a clinical point of view, AF is a key arrhythmia. The results of this thesis confirm that AF seems to be common among older persons in Sweden. In studies I and II, screening with a resting ECG revealed an overall 4.9% prevalence of AF among persons of  $\geq 60$  years of age. In study III, screening with the LTR ECG showed a 10% prevalence of persistent AF and 5.5% prevalence of paroxysmal AF in participants of  $\geq 66$  years of age. Other studies report AF prevalence rates of approximately 1.5–3% among the general population in the developed world (16,18). Earlier studies from Sweden have reported prevalence rates of between 2.9% and 3.9% (76,77). Hendrikx et al. (78) performed opportunistic screening with intermittent handheld ECG registration over four weeks, and reported a 3.8% rate of previously undiagnosed AF within a Swedish population ( $n=928$ ) of relatively healthy and young out-of-hospital patients having at least one additional risk factor for stroke. Countries that are similar to each other show variations in AF prevalence. Zoni-Berisso et al. (2014) reviewed studies from Iceland, Italy, Germany, England, and Sweden and reported that Sweden showed the highest AF prevalence rate compared to the other countries. This may be because Sweden has an older population, as well as a better competence to suspect and diagnose AF, compared to the other analyzed countries (Figure 11).



**Figure 11.** Atrial fibrillation prevalence rates in European countries (Zoni-Berisso, Lercari, Carazza, Domenicucci, & others, 2014).

Table 10 presents the varying estimates of AF prevalence from the literature review. However, earlier studies were hindered by several limitations, such as restricted age ranges, and were mostly based on data from registries or hospital populations. The variable prevalence rates may also depend on the methods used for AF identification and validation. Overall, these limitations may reduce the generalizability of the results. Taken together, these factors leave some uncertainty regarding the actual AF prevalence in the general population, and highlight the need for investigating AF in different settings.

**Table 10.**

Prevalence of atrial fibrillation (AF) in different settings and countries: a summary of major literature.

Author/year	Setting Location	Age, years	Mean age, years	n (% women)	AF diagnosis	Prevalence, %
Andersson et al, 2012, Sweden (76)	Journals/Auricula registry	>35	74.3	65532 (42.6)	Resting ECG or Holter	3.9
Norberg et al, 2013, Sweden (80)	Patient registry	>30	77	75945 (43)	Resting ECG	3.0
Friberg et al, 2013, Sweden (77)	Patient registry	>20	75.2	7232006 (45)	Resting ECG	2.9
Herringa et al, 2006, The Netherlands (81)	Population-based cohort	>55	59.5	6808 (59)	History of AF diagnosis or resting ECG	5.5
Schnalbel et al, 2012, Germany (16)	Population study	35–74	52.2	5000 (50.6)	History of AF diagnosis or resting ECG	2.5
Wilke et al, 2012, Germany (82)	Insurance registry, AF diagnoses	All ages	73.1	8298896 (44.5)	History of AF diagnosis	2.1
Murphy et al 2007, Scotland (83)	General practitioners	>45	-	362155 (49)	ECG	9.4
Stefansdottir et al, 2011, Iceland (84)	Database with AF diagnoses	>20	73	145907	Resting ECG	2.0
Cea-Calvo et al, 2007, Spain (85)	Physician list of patients	>60	71.9	7108 (53.6)	History of AF diagnosis or resting ECG	8.5
Bonhorst et al, 2010, Portugal (86)	Population study	>40	58	10447 (55)	Resting ECG	2.5
Go et al, 2001, USA (87)	Data from a health maintenance organization	>60	71.2	3 million	ECG diagnosis of AF	3.8

The results in this thesis demonstrated that AF prevalence was strongly associated with age. Similarly, Zoni-Berisso et al. (2014) reported that AF prevalence was 0.12–0.16% among persons younger than 49 years, 3.7–4.2% among those of 60–70 years of age, and 10–17% among those  $\geq 80$  years of age. In the literature, the oldest old group is rarely analyzed separately. Our analysis showed that the AF prevalence among persons  $\geq 90$  years of age was lower compared to that in the next previous age group (77). Consistent with these findings, Andersson, Löndahl, Abdon, & Terent (2012) report a rising AF prevalence with age, but with a reduced prevalence in the oldest old group. Similar to our findings, the Rotterdam study (81) reported an increasing AF prevalence with age; however, the age-matched prevalence in our study was significantly lower in the oldest age group. This finding may have been caused by survival effects, leaving the healthiest to survive to the highest ages, and the fact that AF presence might have been missed due to the oldest participants living in assisted care homes.

Limited data are available regarding AF incidence among older persons, especially in the oldest old subgroup. Therefore, study I included evaluation of the 6-year incidence of AF in the older adult population, including in the oldest old subgroup (90+ years of age). Table 11 presents examples of AF incidences from different countries.

**Table 11.**  
Atrial fibrillation incidence rates in study I and in four other studies.

	This study, Sweden	Framingham study (88), USA	Rotterdam study (81)	Murphy (83), Scotland	Wilke (82), Germany
Age group	$\geq 60$	$\geq 40$	$\geq 55$	45–84	All ages
Overall	6.9	2.0	9.9	0.9	4.1
Men all				1.0	4.3
60, 66 years	5.9				7.5
65–74 years				3.8	
72, 78 years	12				
81, 84, 87 years	27	38	25.4		
>85 years				8.6	
90+ years	33				37.2
Women all				0.8	3.8
60, 66 years	1.7				4.3
65–74 years				2.7	
72, 78 years	6				
81, 84, 87 years	14	31.4	16.2		
>85 years				7.4	
90+ years	14				29.0

One of the first investigations of AF incidence was in the Framingham study, which reported an overall AF incidence of 2/1000 py among persons aged 32–65 years (89). A more recent population study from Scotland reports an AF incidence ranging from

3.8/1000 among persons aged 65–74 years, to 8.6/1000 in those aged  $\geq 85$  years (83). A German study reported an AF incidence of 4.4/1000 py among men and 3.9/1000 py among women (82). Additionally, the Rotterdam study reported an overall incidence of 9.9/1000 py (81). Similar to the findings of this thesis, all previous results show the strong negative association with age. During the 6 years of follow-up in this thesis, 4.1% of the study population developed AF. The overall AF incidence was 6.9/1000 py, and incidence increased with age, except in the subgroup of participants  $\geq 90$  years of age. Our findings that AF incidence rapidly increased with advancing age, are in line with results from both Europe (81,83) and the USA (90), which describe a lifetime risk at 80 years of age of 22.7% for men and 21.6% among women (79). The present AF prevalence is more than double the prevalence reported just one decade earlier, and it is predicted that the number of persons with AF will likely increase 2.5-fold over the next 50 years, reflecting the growing proportion of elderly individuals (87).

## Survival

AF is associated with premature death (91,92), which was confirmed in study II. Of the study population with AF, nearly half (49%) were dead within ten years. Persons without AF showed a mean survival time of approximately 2.5 times longer compared to persons with AF, corresponding to a 72% lower risk of 10-year death for persons without AF. Overall AF-associated mortality was higher in men. Other studies have reported that AF is independently associated with a two-fold increased risk of all-cause mortality in women, and a 1.5-fold increase in men (91,93,94). The dissimilarity between our results and the findings from prior studies may be related to several aspects, including comorbidity differences between men and women, frequency of warfarin treatment in men and women, and the fact that our study design was randomized and population based and included subjects both with and without an AF diagnosis. As the population ages, it grows more important to understand the sex differences in arrhythmias that commonly afflict the elderly (95) to ensure optimal treatment of both men and women (35). Our results support the principle that successful research and primary preventive measures will have to focus on specific target groups. It is essential to shift the focus from disease prevention to prevention of increased disease risk. The life course epidemiological approach to chronic disease utilizes a multidisciplinary framework to understand the importance of time and timing with regards to associations between exposures and outcomes at both the individual and population levels. Life-course epidemiology conceptual models may prove useful as frameworks for investigating the determinants of recurrent risk (96).

Despite improved management of persons with AF, arrhythmia remains a major cause of stroke, heart failure, sudden death, and cardiovascular morbidity worldwide (15). AF is also reportedly associated with increased risk in individuals with underlying cardiovascular disease, stroke, and diabetes (97). Study II revealed that mean CHA<sub>2</sub>DS<sub>2</sub>-VASc score was higher among persons with AF, indicating greater comorbidity in those



with AF. It was further shown that CHA<sub>2</sub>DS<sub>2</sub>-VASc score was associated with increased risk of death during the 10-year observation period, with an average of a 28.5% increase per point. Compared to women, men with AF had a lower mean CHA<sub>2</sub>DS<sub>2</sub>-VASc score, and others have reported that AF is associated with higher incidence of ischemic heart disease in men while heart failure is more common among women (34).

Patients with AF show an average annual stroke rate of about 1.5%, and the annualized death rate is around 3% among AF patients receiving anticoagulation treatment (98). Stroke is about equally common in paroxysmal AF as in permanent AF, which is about twice the rate seen in the general population (99). Death due to stroke can be largely mitigated by anticoagulation (100). It is estimated that 40–60% of persons with AF receive protective anticoagulant treatment (101), with such treatment being more common in patients with permanent AF than those with paroxysmal AF. Thus, it is important to increase anticoagulant use among paroxysmal AF patients in accordance with current guideline recommendations (99). One systematic review demonstrates OCA underuse among AF patients with an elevated risk of stroke, highlighting the need for improved therapies to prevent stroke in cases of AF (102). Among participants with permanent AF, 14% reported OAC use in studies I and II, and 45% reported OAC use in study III. No OAC usage was reported among persons with paroxysmal AF in study III. These findings might be related to the fact that we screened a random population sample, as the participants who were unaware of their AF likely had not received previous anticoagulation treatment. These results highlight the high proportion of persons living with a risk of stroke.

Treating older people with AF presents challenges for many reasons, including the need to evaluate the balance between the risk of stroke vs. the risk of bleeding. This leads many clinicians to underuse anticoagulation in older people (103). In the present thesis, individuals with higher CHA<sub>2</sub>DS<sub>2</sub>-VASc scores had more often received anticoagulant treatment compared to those with lower scores. However, Cox regression analysis showed that warfarin use was significantly associated with survival, while overall anticoagulant use was not. This is in line with previous reports that adjusted-dose warfarin and antiplatelet agents reduce stroke by approximately 60% and 20%, respectively, among patients with AF, and that warfarin is substantially more efficacious (by approximately 40%) than antiplatelet therapy (104).

With regards to intervention development, the life course perspective can provide several fundamental considerations. Thus, life course research can potentially provide valuable guidance in developing strategies to improve population health (105). Coordinated efforts are needed to face the increasing challenge of optimizing stroke prevention and rhythm management in persons with AF. Since stroke incidence increases with age and doubles in successive age decades, stroke morbidity and mortality will likely increase in the future as the elderly segment of the population continues to grow (33).

## New technology: LTRE

The increasing prevalence of arrhythmias, especially AF, carries a need for advanced diagnostic tools to improve the functionalities of the current gold standard Holter system. The most important aspects in need of improvement are increased measurement time and equipment miniaturization to favor patient comfort. AF is the cause of 20–30% of all strokes, and that a growing number of patients with stroke are diagnosed with ‘silent’ paroxysmal AF (27). Methods of detecting arrhythmias include resting ECG, LTRE, and Holter ECGs. Each of these techniques have been extensively tested and are used in clinical environments (106). Holter monitors are often considered the standard method (109,110,111) even though they are less sensitive than implantable devices (47) and do not offer the possibility of real-time analysis like, e.g. the BodyCom® (109). New LTR ECG methods can reportedly be used to diagnose arrhythmias, including AF, with high sensitivity (110). Their ease of use facilitates arrhythmia screening, and may also help to improve quality of care within the older population. Easier long-term screening may be useful for identifying high-risk patients with clinically significant arrhythmias that require immediate admission to the cardiology ward. In this thesis (study III), LTRE demonstrated satisfactory quality, with relatively negligible disturbances from artifacts. Nearly half of the study population used the device for  $\geq 18$  hours without problems (Table 12).

**Table 12.**  
Recording time with the long-term recording electrocardiogram equipment.

Duration of recording	Total (n=200), n (%)	Men, n (%)	Women, n (%)
<6 h	16 (8)	5 (2.5)	11(5.5)
>6–12 h	41 (20.5)	18 (9)	23 (11.5)
>12–18 h	44 (22)	27 (13.5)	17 (8.5)
>18 h	99 (49.5)	38 (19)	61 (30.5)

The arrhythmia identification in study III was consistent with that reported with other LTRE (10,111). This simple method requires little of the user and thus may be useful in screening for arrhythmias in the older population. Questionnaire interviews with the participants in this thesis revealed their high rates of satisfaction with the equipment, and their good overall experience wearing it. The 2012 ESC focused update states the following: “Diagnosing AF before the first complications occur is a recognized priority for the prevention of strokes (15) and therefore recommend that, in patients aged 65 years or over, opportunistic screening for AF by pulse palpation, followed by recording of an ECG to verify diagnosis, should be considered for the early detection of AF.”

The ease of use of LTRE devices not only facilitates arrhythmia screening, but may also help to improve quality of care for the older population. Screening may help with the identification of high-risk patients with clinically significant arrhythmias that require immediate admission to the cardiology ward. In its 2011 position paper on palpitations,

the European Heart Rhythm Association emphasizes the importance of excluding AF as the underlying cause of symptoms in patients with palpitations of unknown origin (15). The ultimate value of a life course approach will depend on its success in elucidating new mechanisms and disease pathways, and on its ability to explain social, geographical, and temporal patterns of disease distribution (75).

### **Living with AF: lifelong medical treatment**

Life-long treatment often requires a great deal of sacrifice from the patient at an individual level (112). Studies of AF prevalence have been performed, but it is critical to also examine the individual perspective of living with AF. Prior quantitative studies have examined the experience of living with AF, revealing that persons with AF generally report lower health-related quality of life compared with healthy controls (113). However, these studies are limited in their ability to tell “a patients story,” leaving a need for qualitative studies (114).

The individual interviews in this thesis (study IV) revealed that older persons lacked knowledge about their condition, leaving them with poor insight into their medical treatment, which, in turn, affected their daily life. Further studies are needed to attain improved information about chronic AF and its treatment (115). With regards to another chronic disease, data show high satisfaction (80%) with information provided at diabetes diagnosis. It is proposed that clinicians providing a diagnosis of a chronic disease, such as diabetes, should be aware of patient variability with regards to their need for emotional support and information preferences. Clinicians should therefore ask patients for their preferences, offer choices when available, and be willing to provide more information about treatment and to increase patient involvement in discussions about therapy. It is clear that more resources and education must be provided to both older persons and healthcare providers to achieve best practice and greater treatment adherence (116). The strategies used in diabetes care can be transferred to persons living with chronic AF. In the care of persons with arrhythmias, especially AF, it is important to consider the person’s subjective experiences of their daily life situation. The participant in this thesis had thoughts and questions about their medication, but had no opportunity to ask their questions due to a lack of follow-up from the healthcare system. Even if we are facing a paradigm shift in the medical therapy (117) of chronic AF, there remains a need for follow-up in these persons. Living with chronic AF requires that the individual make fundamental adjustments, including lifestyle changes and efforts to put their new life situation into context and meaning (118).

The National Board of Health and Welfare in Sweden (119) emphasizes the importance of patients having frequent and prolonged contact with the healthcare system. In this thesis, the participants agreed that no one from the healthcare organization seemed to care about their disease or medical condition, and that their care lacked regular monitoring or follow-up information, except for PK tests. This finding highlights the need to provide more information to older individuals (120) about their specific

condition, to achieve person-centered care and to promote general health among older persons. The knowledge from this thesis could be used to develop on-going support and educational programs for persons suffering from AF, for example, nursing-led multidisciplinary programs (114).

## Methodological considerations

### Dropouts

This thesis had several limitations. Characteristics of the study sample, including sex, age, medical history, and death rate, differed between the individuals who underwent an ECG at baseline and those who were excluded from the analysis. Excluded individuals had overall higher rates of morbidity and mortality compared to those included in the analysis. Attrition is a main limitation in longitudinal studies, especially in investigations including older people since the dropouts may have specific characteristics that affect the outcome, i.e. they may be sicker than the participants who remain in the study. Based on the dropout analysis in this thesis, it is reasonable to assume that the sample included in this thesis was younger and healthier sample compared to the general elderly Swedish population, and thus the AF prevalence was probably underestimated (Table 13).

**Table 13.**  
Description and medical history of the included and excluded study samples.

Medical history	Total, n=8473	No ECG performed, n=1569	ECG performed, n=6904	Without AF, n=6560	With AF, n=344
Dead in 10 years	34.6%	65.2%	19.4%	17.7%	49%
Smoker/former smoker	49.1%	36.7%	50.8%	51.1%	47%
Diabetes	7.9%	10.9%	7.2%	7.1%	10.1%
Stroke/TIA	8.4%	15.7%	6.8%	6.4%	14.2%
Ischemic heart disease	34.3%	43.2%	32.2%	30.2%	70.6%

The dropouts were generally older than the participants included in these studies. Despite efforts such as offers of home visits, selection bias cannot be omitted, which affects the external validity and generalizability of the study results.

## Reliability and validity in studies I, II, and III

To evaluate the quality of the research methods in term of factors that may interfere with the results and conclusions, we address the **reliability** and **validity** of studies I, II, and III (121).

### Reliability

Data from SNAC was used to answer the research questions in all studies. Reliability often refers to the consistency of the measurements, both between measurements and over time. (122). SNAC is a longitudinal, national, multicenter study that follows a sample of age-stratified older adults, divided into various age cohorts. All examinations are performed by trained staff using the same techniques over time. In studies I and II, a standard 12-lead resting ECG was performed, which is a common method used in healthcare and has been shown to be reliable when interpreted by experts (nurses and physicians). It is a noninvasive and low-cost method that can provide clinical information regarding the heart through measurement of the skin surface potential. Morphological changes on the ECG waveform reflect abnormal cardiac beats and can lead to arrhythmia detection (8). All ECG data used in this thesis were analyzed by experts.

Notably, in studies I and II, a standard resting 12-lead ECG was used for AF diagnosis. Previous reports (123) demonstrate that up to 25% of cases of AF are asymptomatic, and that many cases of paroxysmal AF are not detected using a traditional ECG. This suggests that AF rates were underestimated in studies I and II. In study III, the quality of the LTRE data was satisfactory, with relatively negligible disturbances from artefacts. The identification of arrhythmias using LTRE was consistent with reported values with other long-term ECGs (59,113). This simple method requires little of the user, and thus may be useful for arrhythmia screening in the older population.

Researchers must actively work with their preconceptions, and contemplate their own understanding. By reflecting on why certain research questions are asked, how they are developed, and why specific methods are chosen to answer these questions, the researcher likely adds an additional dimension to the study (124). In this thesis, pre-understanding emerged from the experience of interacting with people with arrhythmias in our work in healthcare settings. This pre-understanding was used to interpret the alternation between past and future in a non-linear view of life.

## Validity

Internal validity refers to the extent to which an outcome is explained by the independent variable, and the extent to which it was affected by alternative factors (125). To establish internal validity, one must establish that the relationship between the independent and dependent variables is not excessively influenced by alternative factors. Data collection methods may impact study results (126). In studies I, II, and III, data were collected by trained staff. Most clinical examinations were performed at the centers, where each subject was examined by a physician, a registered nurse, and a psychologist, who were organized into teams for data collection. Each examination lasted approximately four to six hours. When a participant was unable to come to the center, the examining teams administered the same question protocol at the participant's home/homecare center. When necessary, proxy interviews with relatives were conducted. Internal validity also refers to whether the instruments in a study are reliable, valid and measure what they are intend to measure. To reduce instrumentation as a threat to internal validity, internationally well-established instruments were used during the examinations whenever possible (65). Although data were collected by several persons, all research assistants were educated in how to utilize the standardized instruments and questionnaires.

*External validity* refers to the extent to which a result can be generalized to another population, setting, or set of circumstances (121). External validity is assessed based on the extent to which a causal relationship remains valid despite variations in sample characteristics, settings, multi-treatment interference, novelty effects, or measurement timing. In this thesis, data were derived from a large cohort of older people (the Swedish National study on Aging and Care). This study includes four research centers that collect data in four different areas of Sweden, and is supported by the national and local governments and by research councils and universities. The SNAC is intended to build reliable, comparable, longitudinal databases that provide a representative sample of the Swedish population (65). One implicit aim of these studies was to generalize the results to the target population—the general elderly population. Notably, all of the studies harbored a selection bias related to loss of study participants between baseline and follow-up. Non-participant analyses were performed. There was a notable healthy survivor effect, as the oldest and most ill participants had died or could not participate in the follow-up. Hence, our results may have underestimated the arrhythmia prevalence and incidence in the older population.

Populations around the world are rapidly ageing. In this context, health must be viewed from a broad perspective that includes medical/physical, psychological, and social health. In this thesis, a life course perspective is employed to identify determinants of good or poor health within an elderly population. Both current and past exposures to potential determinants are considered, as well as the cumulative effects due to chains of events that old individuals have experienced during their lifetime. Importantly, in SNAC, information is recorded regarding demographic data, socioeconomic factors,

physical environment, social environment, life habits, medical and psychological status, physical and cognitive functioning, and care services utilization (65).

*Construct validity* refers to the degree to which a test measures what it is supposed to be measuring (127). Construct validity can be lessened by attention and contact with the participants in a study, single operations or narrow stimulus sampling, researchers' expectations, and cues from the experimental situation (121). Threats to construct validity in these studies included the fact that the older persons gave subjective answers to questions regarding what medications they were using (including anticoagulant therapy) and whether they had suffered, for example, congestive heart failure, hypertension, diabetes, earlier stroke, or vascular disease. These questions were answered during the examinations and, therefore, the analyzed data were self-reported, meaning that the frequencies of these conditions may have been underestimated.

*Statistical conclusion validity* refers to the statistical methods and their influence on the conclusions reached regarding the experimental conditions and their effects (121). This can also be described as type I and type II errors. Type I error is the risk of falsely rejecting a true null hypothesis (128). The tests used in our studies were carefully selected for their ability to answer to the research questions. Statistical calculations were performed by multiple researchers and were compared. For all studies, the significance level was set at  $P < 0.05$ , meaning that each test carried only a 5% probability of falsely rejecting the null hypothesis (Type I error). Type II error is the risk of failing to reject the null hypothesis when it is false, and is determined by sample size and power. The large sample sizes in studies I and II reduced the risk of type II errors, and the detected statistically significant differences indicate that type II errors were not an issue.

## Trustworthiness of study IV

To ensure methodological credibility in the qualitative study IV, attention was paid to quality based on the four criteria of **trustworthiness**: **credibility**, **transferability**, **dependability**, and **confirmability** (129).

### **Trustworthiness**

*Credibility* refers to the truth of the presented data and its interpretation. To increase the credibility of study IV, and to prevent distortion of the data analysis and misinterpretation of the participants' intentions, we presented the results together with quotations. The selected quotations are intended to clarify the participants' statements, and to enable the reader to make their own analysis. Both men and women of varying ages contributed to sample variation, further supporting the credibility of the results.

Credibility cannot be achieved without *reliability* (129). In qualitative research, the researcher tends to be closely linked to the research instrument, and is typically involved in both the investigation and the interpretation of the results. During the interviews, it was emphasized that participants were guaranteed confidentiality (130). Furthermore, the reliability of data collection was strengthened by having the same person conduct all interviews using the same approach. Data material reliability was strengthened because all interviews were recorded on a Dictaphone and printed verbatim. This choice was made to enable interviews to be reviewed and checked to ensure that no nuances and details were missed. All interviews were conducted in a relaxed atmosphere, making it easier for the interviewer to ask follow-up questions when necessary. However, it was sometimes difficult to ask the “right” follow-up questions and some important information may have been lost because the interviewer had no prior experience in conducting interviews. It is also possible that preconceptions about the answers might have steered the narrative in some cases. After several interviews, the interviewer surmised which areas would be affected, and may have formed follow-up questions thereafter (131). However, this type of effect would not have influenced the results such that they were unusable (68). Data were collected using a thematic interview guide inspired by Boyce and Neale (2006). This guide ensured that the interviews were conducted with the same aim, and was helpful when interviewing participants who had a tendency to discuss topics that were not relevant to the study aim. Morse & Field (1995) used the term *dross rate* to describe irrelevant information, which can be high if the interviewer has difficulty getting the participants to stick to the topic. The interview guide was an important tool for keeping the discussion focused on the purpose of the study.

*Transferability* of a study’s findings describes the extent to which the results can be transferred to or applied in other units and groups. As the number of people with chronic AF is growing, our present findings will be useful for helping caregivers understand and support patients with this debilitating condition.





# Conclusions and suggestions for further work

The growing consensus among international health organizations, national policymakers, research funders, and scientists is that ageing itself must be studied from an interdisciplinary and life course perspective, to inform intervention strategies (133). The findings of this thesis contribute to the knowledge regarding increasing arrhythmia occurrence in the older population, and the high number of untreated cases of AF, which pose healthcare challenges. The results demonstrate that AF is associated with increased mortality, and highlight sex-related differences in AF incidence. In line with findings from Europe and the USA, our findings show that AF incidence rapidly increases with advancing age. This thesis also highlights the present lack of knowledge regarding AF in the oldest old population.

AF is associated with an up to five-fold higher risk of stroke, and about 6,000 people with AF suffer a stroke each year in Sweden. However, this risk can be significantly reduced by early diagnosis and proper medical treatment. Therefore, it is critical for the healthcare community to recognize the importance of preventive screening. The European Society of Cardiology has published guidelines recommending opportunistic AF screening for men and women over 65 years of age, in other words, the screening of individuals over 65 years old who seek care. Such screening differs from the systematic screening that has been evaluated and recommended by the National Board in Sweden. In the latter screening method, everyone within a defined group (in this case, 75-year-olds) is invited to the study. However, the National Board finds that several important questions remain unanswered, including the ages and groups that are optimal for this kind of screening, the ideal method for screening, and whether screening is cost-effective. Therefore, the National Board awaits further research (119). Compared with routine practice, both systematic and opportunistic screening for AF similarly increase the rate of detection of new cases. The cost of systematic screening is significantly greater than that of opportunistic screening from the perspective of the health service provider (134).

Technological advancements make it possible to conduct screening and follow-up of patients diagnosed with AF, and to thus facilitate improved healthcare resource use. There are clearly large benefits of identifying individuals with undiagnosed AF. Such identification would reduce suffering, lower the stroke incidence, and be cost-effective for healthcare. It is essential to also develop effective strategies for arrhythmia prevention and treatment.

The negative impacts of AF on survival and daily life emphasize the need for follow-up examinations, and of offering AF-related information to individuals with arrhythmias. There also exists a clear need to develop AF clinics in the format of nursing-led multidisciplinary programs. The ESC (27) recommends and provides tailored information and education to AF patients to enable them to better manage their AF. Persons with AF should be able to play a central role in their own care process. As AF treatment requires lifestyle changes and adherence to chronic therapy, sometimes without an immediately tangible benefit, the patient population with AF must understand their responsibilities in the care process.

# Sammanfattning på svenska

## Bakgrund

De äldre utgör den snabbast växande andelen av befolkningen i västvärlden och hjärtproblem är den mest växande diagnosen hos äldre personer. Den här avhandlingens huvudsyfte var att epidemiologiskt undersöka prevalensen, incidensen och överlevnaden samt upplevelsen av att leva med arytmier ur ett geriatriskt perspektiv (äldre 60+). För att möta den våg av äldre samt ge svar på hur framtida behov av vård och behov kommer att se ut och hur den bäst skall tillgodoses behövs förståelse och kunskap om sjukdomar som drabbar äldre.

## Kontext

Avhandlingsarbetet är baserat på data från -The Swedish National study on Aging and Care – SNAC. Studien har tillkommit genom initiativ från regeringen. SNAC stöds förutom av regeringen också av de kommuner och landsting som medverkar i studien. SNAC drivs på fyra ställen i Sverige och har områdesvis individbaserad insamling av uppgifter, som dels beskriver åldrandet, hälsan och uppkomsten av omsorgsbehoven ur social, medicinsk och psykologisk synvinkel, dels registrerar vilka insatser den enskilde erhåller från kommunernas äldreomsorg och landstingens hälso- och sjukvård. Även uppgifter som belyser vilka insatser anhöriga och frivilligorganisationer gör samlas in. Uppgifterna läggs in i en longitudinell databas. Syftet med SNAC är att göra det möjligt att följa individer och vårdinsatser i området över tiden för att därmed kunna studera hur vård- och omsorgsbehoven utvecklas, hur väl de täcks och vilket resultat insatserna ger ur ett helhetsperspektiv. Detta är som regel inte möjligt inom traditionell äldreforskning, där man vanligen studerar begränsade frågeställningar i mer avgränsade projekt så som kliniska studier avseende arytmier hos äldre personer vilket enbart speglar de personer som är sjuka och vårdade. Med hjälp av studier som min avhandling ser vi hur den äldre befolkningen ser ut, har för behov och ger oss en vägledning i hur en väl fungerande äldreomsorg som inom ramen för tillgängliga resurser tillgodoser de äldres behov på bästa möjliga sätt. Till de två första studierna användes data från hela SNAC, med 6904 deltagare och i studie III och IV använde data från SNAC-Blekinge, med 1402 deltagare.

## Resultat

Syftet med delstudie I var att kartlägga samt beskriva prevalens och incidens (6år) av arytmier hos den äldre befolkningen (60 år och äldre) urvalet var SNAC probander 60+ som hade genomfört viloeckg vid både baseline undersökningen samt 6 årsuppföljningen. Data innefattade 6904 personer och 3419 (49.5 %) av de här personerna i åldern 66-105 år genomförde även ett EKG vid 6 årsuppföljningen. Förekomsten av förmaksflimmer (FF) visade sig vara 4.9 % och en prevalens på 8.3% av deltagarna hade episoder av andra arytmier. Vidare visar resultaten att första och andra gradens AV-block fanns hos 7 % medan 1.2 % av deltagarna hade pacemaker. Det fanns ingen signifikant skillnad mellan män och kvinnor i baseline avseende prevalensen av arytmier. 6 års incidensen av FF var 4.1 % hos deltagarna, eller 6.9 / 1000 personår. För män och kvinnor respektive visade den sig vara 9.9/1000 personår och 4.4/1000 personår, Incidensen av FF, andra arytmier, AV-block och pacemaker var generellt signifikant högre hos män förutom i de äldsta ålderskohorterna.

Syftet med delstudie II var att undersöka överlevnaden hos befolkningen 60+ med FF vid 10 år uppföljningen. Urvalet var SNAC probander 60+ Datainsamling gjordes med hjälp av vilo-EKG samt medicinsk undersökning. Studiepopulationen utgjordes av 6904 personer (2843 män och 4061 kvinnor) med en medelålder på 73,9 år. FF innebar en HR på 1.29 (95 % CI 1.10 -1.51) för dödsfall under 10 årsobservationsperioden. Ålder gav en HR 1.11 (95 % CI 1.10 -1.11) per år för död. Cox regressionsanalys hos personer med FF (n = 341) uppdelat på kön (åldersjusterad) gav en HR 1.57 (95 % CI 1.15 -2.13) för män ( $P < 0.01$ ). Vilket innebär en lägre överlevnad för män. CHA<sub>2</sub>DS<sub>2</sub>-Vasc poäng visade sig ha signifikant negativ påverkan på överlevnad med en HR 1.29 / poäng (95 % CI 1.10 -1.51). Antikoagulantia behandling (warfarin eller ASA) användes av 42.8 % av deltagarna med FF och det visade sig inte vara signifikant ( $P = 0.439$ ) för överlevnad. Endast 14 % hade warfarin och analyser av warfarin och ASA separat visade att warfarin var signifikant associerat med överlevnad ( $P = 0.031$ ).

Syftet med delstudie III var att beskriva prevalensen av arytmier hos äldre personer som använt långtids-EKG (LTRE) i form av ny teknik. Studiepopulationen utgjordes av 200 SNAC- B probander 66+ som undersöktes mellan 2010-2013. Data samlades in med hjälp av BodyKom® (24 timmars EKG). Som ett andra delsyfte undersöktes även hur användningen av BodyKom® upplevdes ur patientperspektiv? Här fick probanderna svara på en enkät om hur de hade upplevt användningen av BodyKom®. Resultatet visade att persisterande förmaksflimmer (FF) förekom hos 10 % av deltagarna i åldrarna  $\geq 66$  år. Paroxysmal FF upptäcktes hos 5.5 % av deltagarna och resultatet visade ingen skillnad mellan de yngre (66-80 år) och äldre ( $> 80$  år) deltagare. Dessutom hade alla personer med paroxysmal FF ett CHA<sub>2</sub>DS<sub>2</sub>VASc poäng  $\geq 2$  och var därför potentiella kandidater för uppföljning och läkarundersökning. Resultaten från enkäten visade att LTRE-BodyKom® kan betraktas som en möjlig metod för att screena för arytmier i äldre populationer. Denna metod kräver lite av användaren, och deltagarna rapporterade

hög tillfredsställelse med utrustningen och ansåg att det var enkelt att använda utrustningen.

Syftet med delstudie IV var att undersöka och beskriva hur äldre personer (60+) med kroniskt förmaksflimmer upplever livslång medicinsk behandling och behovet av medicinska kontroller. Detta var en kvalitativ studie med interpretive descriptive design. Urvalet bestod av intervjuer med 11 SNAC-B probander med kroniskt förmaksflimmer och medicinskbehandling (warfarin) 60+ som samlades in under 2014-2015. I resultatet framkom ett huvudtema: "ambivalens i behovet av kunskap" som visar att livslång medicinsk behandling och behovet av medicinska kontroller i allmänhet innebar en upplevelse av känslan "det spelar ingen roll, men det spelar roll" och " att vara i händerna på sjukvården ". De äldre personer saknade kunskap om sin sjukdom, vilket genererade dålig insikt i den medicinska behandling och detta i sin tur påverkade deras dagliga liv. De hade tankar och frågor om den medicinska behandling, men saknade möjlighet att ställa frågor på grund av bristande uppföljning från hälso- och sjukvården.

## **Sammanfattning**

Sammanfattningsvis visar denna avhandling att arytmier och då framför allt förmaksflimmer (FF) påverkar både den fysiska och psykiska hälsan hos äldre personer. Den ökande förekomsten av arytmier i den äldre befolkningen, liksom det stora antalet obehandlade fall av FF utgör även en utmaning för sjukvården. Resultaten visar att endast 14 % av personerna med FF hade antikoagulantibehandling i form av warfarin. Sedan tidigare vet vi att FF är associerat med högre risk för stroke, men denna risk kan reduceras genom tidig diagnos och rätt behandling. Resultaten visar också att överlevnaden skiljer sig mellan individer med och utan FF. Män dör tidigare än kvinnor och betydande riskfaktorer såsom hjärtsvikt, hypertoni och ischemisk hjärtsjukdom har betydelse för överlevnad hos personer med FF. Den tekniska utvecklingen underlättar screening av personer med FF och den ger sjukvården möjligheter att minska både kostnader och stroke incidens med personligt lidande som följd. För att minska den negativa påverka på det dagliga livet hos personer som har fått diagnosen FF behövs uppföljning och information, exempelvis genom flimmermottagningar.



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# Arrhythmias in Older People: Focusing on Atrial Fibrillation

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As arrhythmias are common in the older general population, it is expected that the prevalence of arrhythmias will increase over upcoming decades. Some types of arrhythmias such as atrial fibrillation (AF) have important health implications and, thus, represent a growing challenge to healthcare services. We know that persons who suffer from AF often feel unwell both physically and psychologically but there is presently a lack of knowledge regarding the experiences of older persons living with this condition. The findings of this thesis contribute to the knowledge regarding increasing arrhythmia occurrence in the older population, and the high number of untreated cases of AF. Furthermore the results demonstrate that AF is associated with increased mortality, and highlight sex-related differences in AF incidence. In line with findings from Europe and the USA, our findings show that AF incidence rapidly increases with advancing age. This thesis also highlights the present lack of knowledge and the need for follow-up regarding AF in the oldest old population.

