6-14-2021 12:00 PM

Measuring the impact of atrial fibrillation on patients

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A thesis submitted in partial fulfillment of the requirements for the Master of Science degree in Epidemiology and Biostatistics

Recommended Citation

Chang, Justine, "Measuring the impact of atrial fibrillation on patients" (2021). *Electronic Thesis and Dissertation Repository*. 7839.
https://ir.lib.uwo.ca/etd/7839

Abstract

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia. Patients experience the effects of AF from early symptom onset to treatment and beyond. A previous qualitative study found AF to substantially affect patients' emotional wellbeing, social relationships, employment, and finances. Existing quality of life questionnaires do not adequately assess the AF impact. In this thesis, a new patient-reported questionnaire was developed to measure the impact of AF as experienced by patients. An exploratory factor analysis was conducted on the new questionnaire, revealing five domains: "Affect", "Social Support", "Major Life Events", "Financial Impact", and "Diagnostic Experience". Age, marital status, educational attainment, and time of last episode were significantly associated with the overall score. Female gender was associated with a worse diagnostic experience after adjusting for covariates, confirming previous qualitative findings. The new questionnaire has good internal consistency and can be used to study variables associated with the AF impact.

Keywords

Atrial Fibrillation, Measurement, Patient-Reported Outcome Measure, Patient Journey, Quality of Life, Factor Analysis

Summary for Lay Audience

The normal heart rate for adults at rest ranges from 60 to 100 beats per minute. Apart from rate, the normal heart also follows a characteristic rhythm that can be detected on an electrocardiogram. Departures from a regular rate or rhythm are referred to as arrhythmias. Atrial fibrillation (AF) is the most common sustained arrhythmia where the heart beats too fast or too slow and out of rhythm. Patients with AF can often feel their hearts pounding or racing and experience symptoms such as chest pain, shortness of breath, difficulty exercising, dizziness, and fatigue. AF can affect a patient's wellbeing as soon as they begin to experience symptoms. Previously, focus groups and interviews with patients revealed that getting a diagnosis of AF was difficult because some physicians did not take patients' symptoms seriously. It was also found that AF affected patients' emotional wellbeing, social relationships, employment, and personal finances.

We developed a questionnaire, called Mapping the Impact of Atrial Fibrillation (MAP-AF), and used it to study the life impacts of AF on patients. A statistical technique called factor analysis allowed us to determine the different areas of peoples' lives that AF impacts. By examining these areas, or "domains", we were able to see whether the MAP-AF measures what it was supposed to measure. We found five domains underlying 16 questions. They were "Affect", or mood, "Social Support", "Major Life Events", "Financial Impact", and "Diagnostic Experience". The MAP-AF allows us to calculate a total score and a score for each of the five domains for each person. We found patients who were younger, divorced or separated, completed high school or below, or experienced a recent AF episode had higher total scores and were more impacted by AF. Confirming previous findings, our results showed female patients to score higher (i.e., worse) on "Diagnostic Experience" than male patients. After our results are confirmed in a separate group of patients, the MAP-AF questionnaire can be used to study how AF affects the wellbeing of patients, identify patient needs, and improve healthcare services. Timely diagnosis and empathetic care are essential for patient-centered AF management.

Acknowledgments

I would like to express my deepest appreciation to my supervisory committee for their unwavering support of my education and career over the past two years. My academic achievements and the completion of this thesis would not have been possible without their guidance and mentoring.

First, I am greatly indebted to Dr. Mark Speechley, who was always available to share his expertise and provide invaluable suggestions for this project. The clinical perspectives provided by Dr. Lorne Gula and his critical review of my work have been very much appreciated. I am also truly grateful to Dr. Mary Runte for her kindness, encouragement, and extensive knowledge of the qualitative methodology. She inspired my interest in patient-centered research.

I wish to acknowledge all the assistance I received from Ms. Heather Weir for patient recruitment. Many thanks to the officers at the Western Research Ethics Board and the Lawson Health Research Institute for their help with the ethics application.

I cannot conclude without mentioning all the participants who contributed their valuable time to make this study possible. My sincere appreciation goes out to every one of them.

Finally, I would like to extend my gratitude towards my parents, Alan Chang and Angela Lin, and my brother, Nelson Chang, for their love, support, and belief in me.

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List of Abbreviations

AF – Atrial Fibrillation

CI – Confidence Interval

ECG – Electrocardiogram

EFA – Exploratory Factor Analysis

EM – Expectation Maximization Algorithm (Maximum Likelihood Estimation)

HF – Heart Failure

HRQoL – Health-Related Quality of Life

iPAF – Iterative Principal Axis Factoring

MAP-AF – Mapping the Impact of Atrial Fibrillation Questionnaire

N/A – non-applicable

PREM – Patient-Reported Experience Measure

PROM – Patient-Reported Outcome Measure

PVA – Pulmonary Vein Ablation

QoL – Quality of Life

SAF – Silent Atrial Fibrillation

SD – Standard Deviation

ULS – Unweighted Least Squares

Chapter 1

1 Introduction

Departures from the normal heart rate or rhythm are referred to as arrhythmias[1]. Atrial fibrillation (AF) is the most common sustained arrhythmia and is associated with symptoms such as palpitations, chest pain, dyspnea, exercise intolerance, dizziness, and fatigue[2,3]. The sometimes transient nature of AF episodes and symptoms can present challenges to diagnosis.

AF can affect a patient's wellbeing in many ways. For instance, the uncertainty associated with the onset of symptoms can create anxiety for many patients, which can be worse if physicians do not take patients' concerns and symptoms seriously. After patients are treated, their symptoms may be alleviated, but they can also experience side effects and restrictions to their lifestyle. For example, patients taking blood thinners to prevent strokes may avoid physical activities out of the fear of bleeding[4,5]. Research is needed to understand how patients experience the effects of AF.

This thesis is the quantitative phase of the two-phase mixed methods exploratory sequential design, aimed at addressing the impact of AF on patients. Our research follows the "instrument development model" of the exploratory design described by Creswell and Plano Clark (2007)[6]. In this model, qualitative data (e.g., quotes from interviews) are collected first to explore a phenomenon. The qualitative information is then used to inform the development of a measure (e.g., a questionnaire), which will be used to collect data for quantitative analysis. The qualitative and quantitative phases are connected through the development of questionnaire items[6]. This type of research design is particularly helpful for understanding and measuring subjective and latent constructs like wellbeing and quality of life.

The qualitative phase involved two studies. The first was a Canada-wide project funded by the Cardiac Arrhythmia Network of Canada (CANet). Led by Dr. Mary Runte, the project utilized focus groups, narrative interviews, and patient journey mapping to solicit the patient view of the arrhythmia impact. Patients in this study came from eight different

Canadian cities and had various arrhythmic conditions, not limited to AF. The project specifically looked at the economic, employment, social, emotional, and psychological impact of arrhythmias from symptom-onset to treatment and beyond[7]. To our knowledge, this is the first large scale project on the arrhythmia patient journey in Canada. The second study was a secondary analysis of the first study (Chang J et al., unpublished data, May 2021). It analyzed only quotes and patient journey maps of AF patients and used the results to inform concerns that are important to AF patients. The study then identified existing patient-reported measures and compared the content of these measures to themes emerged from the quotes of AF patients. Existing quality of life questionnaires were deemed inadequate for assessing the full impact of AF. The results of this (i.e., second) qualitative study will be used to develop items for a new questionnaire that will capture the AF impact in a holistic manner.

This thesis will describe the development and initial validation of a new questionnaire, Mapping the Impact of Atrial Fibrillation (MAP-AF), in a sample of AF patients in London, Ontario. The initially validated MAP-AF questionnaire will then be used for scoring, and we will explore the relationship between the MAP-AF scores and selected covariates (including demographic and clinical variables).

1.1 Objectives

The objectives of this thesis are presented below.

I. To generate items for a new questionnaire (MAP-AF) based on previous qualitative research

II. To determine the factor structure of the MAP-AF questionnaire using exploratory factor analysis and to evaluate each factor's internal consistency using Cronbach's alpha

III. To compute factor scores and an overall score that will be used for hypothesis testing and in regression models to identify important predictors

1.2 Thesis organization

This thesis is written in a monograph format. Chapter 2 is a literature review on atrial fibrillation and patient-reported measures. It includes a description of the qualitative study we previously conducted (Chang J et al., unpublished data, May 2021) that compared existing quality of life questionnaires to findings from focus groups and interviews with AF patients. The qualitative study highlights the limitations of existing questionnaires and serves as the basis for our questionnaire development.

Briefly, Chapter 3 will describe the development and validation of the MAP-AF questionnaire, and Chapter 4 will describe the analyses of the questionnaire scores. Since the methods of Chapter 4 depend entirely on the results of Chapter 3, both Chapters have their own methods and results sections.

In Chapter 3, we describe the methods and results of generating items for the new questionnaire, factor analyzing the questionnaire, and removing items with suboptimal measurement properties.

In Chapter 4, we describe the methods and results of score computation, hypothesis testing, statistical regression for model selection, and multivariable linear regression of the overall (total) score on selected predictors.

Chapter 5 will discuss the results from both Chapters 3 and 4. We will also describe the implications, strengths, and limitations of this thesis and make suggestions for future research.

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Chapter 2

2 Literature review and qualitative research

2.1 Atrial fibrillation: overview

Irregular rate or rhythm of the heart is referred to as an arrhythmia[1]. Atrial fibrillation (AF), the most common sustained cardiac arrhythmia, is associated with significant morbidity, mortality, and healthcare burden[2]. As estimated by the Global Burden of Disease project, 46.3 million individuals around the world were living with AF or atrial flutter in 2016[3]. Prevalence of AF is higher in developed countries, especially in Northern Europe and the United States (US), and lower in the Asia-Pacific area[3,4].

The incidence and prevalence of AF are expected to rise globally as a result of population aging, increasing prevalence of AF risk factors, and enhanced AF detection[2,4-6]. By 2030, 14 – 17 million individuals in the European Union are expected to have AF[2]; by 2050, 6 – 16 million individuals in the US alone are anticipated to have AF[6].

While the arrhythmia itself is not fatal, AF-related complications like heart failure (HF), tachycardia induced cardiomyopathy, and stroke put AF patients at an elevated risk of cardiovascular and all-cause mortality[2,6,7]. AF is associated with a 2- to 5-fold increase in the risk of stroke [4,6,8], and 20% – 30% of all ischemic strokes are attributable to AF[2]. Additional morbidity includes cognitive impairment (e.g., vascular dementia) and cardiovascular morbidity (e.g., cardiomyopathy, left ventricular dysfunction) [2,9].

From the Outcomes Registry for Better Informed Treatment of Atrial Fibrillation (ORBIT-AF) study, 31% of AF patients had one or more hospitalizations after a one-year follow-up[10]. Another population-based study in the US found that 1.5% of all hospitalizations listed AF as the primary cause, and 12% of all hospitalizations listed AF as a secondary cause or comorbidity[7]. The cost of emergency department visits and hospitalizations related to AF represents a significant burden on the healthcare system[2].

2.1.1 Diagnosis and classification

AF rhythm is characterized by irregular RR intervals and the absence of distinct P waves on the electrocardiogram[2,9]. In contrast, atrial flutter typically has atrial activity with a “saw tooth” morphology[2]. According to the European Society of Cardiology (ESC) guidelines, clinical AF is diagnosed when an electrocardiography (ECG) documented AF episode lasts at least 30 seconds. The standard diagnostic procedure for patients reporting AF symptoms or patients who had a recent cryptogenic stroke involves a 12-lead ECG in the clinic. If the 12-lead ECG does not indicate ongoing AF, a 24/48-hour Holter monitor or other prolonged ECG monitoring methods (e.g., 7- to 30-day event monitors) are attempted to document AF[11].

AF can be clinically classified into paroxysmal or persistent based on the duration and frequency of arrhythmic episodes[12]. According to the latest Canadian Cardiovascular Society (CCS) guidelines for AF management, paroxysmal AF is defined as “a continuous AF episode lasting longer than 30 seconds but terminating within 7 days of onset” and persistent AF as “a continuous AF episode lasting longer than 7 days but less than 1 year”[12]. Paroxysmal AF that is short-lasting and intermittent may not be present during 12-lead ECG or 24/48-hour Holter monitoring – in this case, repeated and prolonged monitoring may be necessary to diagnose AF[11]. Progression from paroxysmal to more persistent forms of AF is common when AF is left untreated[2].

Besides overt clinical AF, there is also silent atrial fibrillation (SAF), where patients are asymptomatic and unaware of their arrhythmia[4]. It is estimated that approximately one-third of all AF is asymptomatic and subclinical[4,5,13]. Despite the absence of symptoms, the prognostic impact of SAF is considered to be the same as symptomatic clinical AF[4,14]. Therefore, delays in diagnosis can allow the disease to progress to more severe forms and exacerbate the risk of stroke and other complications[12]. Unfortunately, SAF often remains undetected until a patient experiences an adverse effect of AF and presents to the emergency department with a cryptogenic stroke or congestive heart failure[4,5,15]. SAF may also be incidentally detected by implanted pacemakers or during routine physicals[4,5,15].

Recently, promising screening devices that are non-invasive (i.e., smartwatches) have been developed to enhance AF detection and expedite treatment initiation[12].

2.1.2 Symptoms

Symptoms related to AF are highly variable between individuals and in the same individuals over time[13]. The most common symptoms, however, are palpitations, chest pain, and exercise intolerance[13]. Other symptoms reported by patients include dyspnea, sleeping difficulties, dizziness, psychosocial distress, and fatigue[2,13]. In some patients, syncope and presyncope can be present[13]. Not all symptoms reported are attributable to AF because risk factors and comorbidities of AF may also produce similar symptoms[13].

Symptom severity and burden can be assessed and classified by a number of instruments. The CCS 2020 guidelines described four symptom severity scales[12]:

The European Heart Rhythm Association (EHRA) Classification and the Canadian Cardiovascular Society Severity of Atrial Fibrillation Scale (CCS – SAF) are two clinician-reported measures; the University of Toronto Atrial Fibrillation Severity Scale (AFSS) and the Atrial Fibrillation Symptom Severity and Burden (AFS/B) scale are two patient-reported measures[12].

As mentioned earlier, asymptomatic AF is considered to have the same prognostic impact as symptomatic AF[4,14]. Even if successful treatment alleviates symptoms for symptomatic patients, it may not eliminate AF or its associated stroke risk. Stroke prevention is continued in patients even after symptoms appear to be remedied. In addition, symptom alleviating treatment may not necessarily improve patients' perceived wellbeing because of side effects, hospitalizations, and other factors. Two studies found that symptom severity does not correlate well with global life satisfaction, and quality of life may be reduced even in asymptomatic individuals[5,16].

Gender and sex-based analyses in health can provide valuable insight into biological differences and potential health disparities. Using the EHRA symptom classification scale, one study found that female patients with AF reported more frequent and severe symptoms compared to male patients[17]. Regardless of gender, participants in the study most commonly experienced fatigue, dyspnea, and palpitations[17]. Similarly, Westerman and Wenger (2019)[18] reviewed four studies that all found women to be more symptomatic[17,19-21].

2.1.3 Management

Current management of AF consists of anticoagulation for stroke prevention, risk factor and comorbidity management, and rate and/or rhythm control[8,9,22-24]. Timely initiation of management is critical to reduce symptoms and complications and slow the progression of AF[4].

Following diagnosis, stroke and bleeding risk are assessed to guide decisions to anticoagulate. While the CHADS2 is the reference tool for stratifying stroke risk in clinical guidelines, the CHA2DS2-VASc score is more commonly used in clinical practice[8,25,26]. The letters "CHADS" stands for congestive heart failure, hypertension, age ≥ 75, diabetes, and stroke; and "VASc" stands for vascular disease, age 65-74, and sex category female[9,25,26]. The numeric "2" distinguishes factors with a much higher risk of stroke, for which 2 points (one additional point on the score) are warranted. A higher score on both instruments indicates a greater need for anticoagulation.

Warfarin and oral anticoagulants (OAC) effectively reduce the risk of stroke but can produce side effects such as major bleeding[8,9]. An individual with a high risk of bleeding, as assessed by scales like the HAS-BLED score, may be a candidate for percutaneous left atrial appendage occlusion instead of OAC for stroke prevention[9,27].

While stroke prevention reduces stroke-related mortality, cardiovascular mortality due to other causes is still common in anticoagulated individuals[2]. Risk factors, underlying disease, and comorbidity management are essential to reduce other causes of mortality.

Alongside stroke prevention, ventricular rate control should be initiated for recent-onset AF patients. The most common pharmacologic rate control interventions are β-blockers and non-dihydropyridine calcium channel antagonists, both of which can slow the atrial fibrillation heart rate to a target range[2,8].

Acute rhythm control may be pursued as first-line therapy for severely compromised patients. Otherwise, it is indicated when ventricular rate control fails to adequately alleviate symptoms. For patients with persistent AF, sinus rhythm can be restored by pharmacologic cardioversion (antiarrhythmic drugs) or direct current cardioversion along with a rhythm medication to maintain sinus rhythm once it is restored.

Amiodarone is both a rate and rhythm control drug[8,9]. While it is more efficacious than other antiarrhythmic drugs, it should be reserved for highly symptomatic patients because of its potential for long-term adverse side effects[8,9].

For patients who remain symptomatic despite rate and rhythm control medications, catheter ablation targeting the pulmonary veins can be considered[9]. Pulmonary vein ablation has been found to effectively restore sinus rhythm, improve quality of life, and reduce hospital admissions[8].

Atrio-ventricular nodal ablation with pacing is another type of ablation procedure. In contrast to pulmonary vein ablation, which is a form of rhythm control, atrio-ventricular nodal ablation can deliver permanent rate control without the need for rate medications[9,28]. It is an option for whom pharmacological rate control fails and rhythm control strategies are deemed inappropriate (due to their inherent risks and timeline).

AF management is complicated by concomitant conditions. The 2018 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation highlighted seven advancements in AF management, including catheter ablation for AF patients with HF and antithrombotic therapy for patients with coronary artery disease[23].

Interestingly, two review articles found sex differences in AF management[18,29]. For example, women were less likely to receive electrical cardioversion or ablation than men[17,18,29].

Overall, patients with AF face unique challenges. Patients experiencing intermittent episodes of AF may need to frequent medical centers and require prolonged monitoring for a diagnosis. Furthermore, AF symptoms are highly variable. Even in the absence of symptoms, AF is associated with increased stroke risk and complications that will require ongoing management. Patients navigating through the AF illness experience are faced with much uncertainty. We will be able to better address patient needs and preferences with a patient-centered care approach to AF management.

2.2 Patient-centered care

Patient-centered care was a new concept in medicine in the early 50s and had roots in Carl Rogers' client-centered therapy. Client-centered therapy emerged from humanistic psychology in 1951 and revolutionized the therapist-and-client relationship. Clients are to be treated as active participants in consultations, the therapist as an agent rather than an authority[30]. This approach encouraged clients to tell their own stories, believing that clients know themselves best. Medical psychoanalyst Michael Balint proposed a similar concept in the medical field, coining the term "patient-centered medicine"[31-34].

This new perspective and approach to medicine were, to a large degree, a response to the limitations of traditional medicine[31,35]. The traditional biomedical model was "illness-centered", interested primarily in localizing disease entities and resolving physiological aberrations[31,35]. During this time, physicians practicing under this illness-centered lens had difficulty helping patients who had complaints but for whom clinical investigations identified no obvious physical cause[36]. In response, Balint explained how the doctor's affective response might play a role in alleviating or exacerbating the patient's illness[31,34,36]. He further urged physicians to examine patients as whole persons when making a diagnosis or prescribing treatment [31,34].

Since Balint's pioneering work, there has been a growing interest and emphasis on patient-centered care. It is now widely acknowledged as a core value in medicine. In fact, patient-centered care is one of six establishing aims put forth by the Institute of Medicine in the US for the 21st-century healthcare system[37].

With the growing body of literature on the topic, various definitions of patient-centered care have been proposed[35,38,39]. The general consensus is that "patient-centeredness" means moving away from physician-dominated "dialogue" to actively involving participants in their own care (i.e., patient empowerment) and incorporating patient values and preferences into clinical decision making[34,37,38]. Akin to Roger's client-centered therapy, at the core of patient-centered care is the moral imperative of respecting patients as unique living beings[34,38].

We describe two popularly cited frameworks that aim to clarify the concept of patient-centered care.

In 1995, Stewart and colleagues from the Department of Family Medicine at Western University (Ontario, Canada) developed a model to define the patient-doctor relationship and guide clinical practice. Stewart's "patient-centered clinical method" was inspired by Dr. Ian R McWhinney and Dr. Joseph Levenstein and initially had six components: exploring the disease and illness experience, understanding the whole person, finding common ground, incorporating prevention and health promotion, enhancing the patient-clinician relationship, and being realistic[34]. In 2014, the framework was revised to have four components, dropping "incorporating prevention and health promotion" and "being realistic". The earliest version of the model remains one of the most cited in family medicine[33].

Mead and Bower (2000) reviewed the literature on existing patient-centered care models (including Stewart's work) and synthesized aspects of the patient-doctor relationship characterized by patient-centeredness[35]. Five key dimensions of patient-centeredness were proposed by Mead and Bower, including the biopsychosocial perspective, patient-as-person, sharing power and responsibility, therapeutic alliance, and doctor-as-person.

Several similarities can be found between the two conceptual frameworks described. We highlight one similarity in particular – understanding the illness experience – in the following section.

2.3 Understanding the disease and illness experience – an essential component of patient-centered care

Understanding the illness experience from the patient's perspective is essential for achieving patient-centered care. In both the patient-centered clinical method developed by Stewart and colleagues and the five dimensions of the patient-centered doctor-patient relationship proposed by Mead and Bower, physicians are asked to enter the patient's world.

One component of the patient-centered clinical method developed by Stewart and colleagues (2014) is exploring the patient's disease and illness experience[34]. It requires physicians to appreciate the patient's feelings about being ill, their ideas about the illness, their expectations from healthcare providers, and how the illness is affecting their functioning.

Similarly, both the "biopsychosocial perspective" and "patient-as-person" dimensions of patient-centeredness proposed by Mead and Bower (2000) call for viewing patients as "experiencing individuals" rather than "objects of disease entities"[35]. Mead and Bower provided a powerful example to illustrate how one disease may affect two individuals in a completely different manner. While an office worker may be able to resume work following a leg fracture, a professional athlete may be facing an end of their career with the same injury. The distress experienced is different for the two individuals. In addition, treatments do not always alleviate suffering for patients. The side effects and threats to a patient's sense of self may be reasons why some patients decline life-saving cancer treatments. It is imperative to examine the patient's circumstances and attitudes when caring for them, as they may help physicians identify the best courses of action[35].

Undoubtedly, patients are the ones with the most experience with the disease[40]. Understanding the patient's lived experiences with illness not only helps clinicians identify patient needs and shortcomings of the healthcare system but is also a means of achieving patient-centered care.

2.4 Collecting data on the patient perspective

Attributes of patient-centered care are best evaluated using measures of the patient's perception[33]. To learn about the illness experience, we must refer to the experts on this topic – the patients themselves. Interviews and self-administered questionnaires are methods to collect information and expertise from patients.

These questionnaires are generally referred to as "patient-reported measures" and can measure a variety of concepts. There are two main groups of these measures in the literature: patient-reported outcome measures and patient-reported experience measures. The former is primarily used to evaluate the effectiveness of care, and the latter to evaluate and improve healthcare services.

2.4.1 Effects of care and PROMs

Patient-reported outcome measures (PROMs) assess the patients' perceived effects of their care. The "effects" or "outcomes" measured can range from pain level, physical functioning, symptom severity, to quality of life (QoL)[41]. Since we are interested in understanding how disease affects patients' wellbeing, we will restrict our subsequent discussion of PROMs to QoL instruments.

One context of the use of PROMs is in clinical trials. For example, a QoL questionnaire is administered to patients before and after an intervention to assess QoL changes due to treatment. The US Food and Drug Administration now recognizes QoL improvements, measured by validated instruments, as an indication or labelling claim on medical products[42,43]. It is currently the goal of many questionnaire developers to get their QoL instruments approved for use in clinical trials. For this purpose, questionnaires need to be responsive to interventions – that is, items in such questionnaires often measure aspects of QoL most responsive to health changes.

Quality of life is a theoretical construct that cannot be directly observed or measured[44]. It can be understood as "a multidimensional concept that … often involves the concept of happiness, subjective wellbeing, and the meaning given to life"[44]. Various interpretations of QoL exist, and no single definition is used consistently.

The World Health Organization Quality of Life (WHOQOL) Group in 1995 defined QoL as:

> "individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns. It is a broad ranging concept affected in a complex way

> by the person's physical health, psychological state, level of independence, social relationships and their relationship to salient features of their environment"[45].

This definition recognizes the multidimensionality of QoL and the influence of cultural and person values on one's perceived meaning of QoL[46,47]. Preliminary testing of the group's global generic QoL questionnaire, WHOQOL, revealed four domains of QoL: physical, psychological, social relationships, and environment[45]. Themes considered under "environment" include transport[ation], work satisfaction, home environment, and financial resources[45].

Another relevant concept is health-related quality of life (HRQoL), which is also what many PROMs are said to measure. Unfortunately, various interpretations of HRQoL exist, leading to substantial confusion around the term[44,48]. One definition of HRQoL is aspects of self-perceived wellbeing that are affected by the presence of disease[49]. In other words, a measure of how patients are impacted by ill-health[50,51]. However, this interpretation of HRQoL brings about another discussion – that is, what aspects of QoL are not affected by health or ill-health, especially when indirect influences are considered. Chronic illness affects almost all aspects of life. Guyatt et al. (1993) asserted that "when a patient is ill or diseased, almost all aspects of life can become health related"[52]. Moreover, different diseases have different mechanisms of affecting QoL[46]. Therefore, the recommended practice is to develop unique HRQoL questionnaires for different diseases to uncover aspects of wellbeing most impacted by the particular health problem.

Evaluating the impacts of disease on a patient's life is precisely the requisite for "exploring the disease and illness experience" – one component of Stewart's patient-centered clinical method[34].

An evaluation of existing (HR)QoL questionnaires for AF found that most were adequate at assessing physical functioning, symptoms, and psychological impacts (Chang J et al., unpublished data, May 2021). However, broader realms of wellbeing and life impacts like social relationships, employment, and personal finances were overlooked. Most questionnaires were developed for use in clinical trials instead of as a tool for routine use in the clinic.

2.4.2 Patient experience, PREMs, and patient journey mapping

Patient-reported experience measures (PREMs) typically concern patients' experiences with practical aspects of healthcare services such as wait times and patient-provider communication[41,50]. They evaluate the patient's experience or satisfaction with a particular clinical encounter (e.g., surgery or consultation) to improve healthcare delivery[53]. The majority of PREMs do not explore the patient's lived experiences and are not designed to understand how a chronic disease may affect multiple aspects of an individual's life over an extensive period of time.

To our knowledge, the only PREM for AF was adapted from the National Health Service Adult Inpatient Survey. It was used to assess patients' experiences with the catheter ablation procedures performed in England[54].

Visit-based PREMs fragment the patient experience. In reality, patients receive care from different groups and move across healthcare providers and institutions[55]. The result is healthcare providers only seeing the component of care for which they are responsible, and no single provider oversees all the steps in a patient's journey. True clinical process redesign and healthcare reform must recognize that "the patient is the only person who sees the whole journey"[55].

Another method to collect data directly from patients that overcomes the fragmentation of experiences is process mapping of the patient journey.

The patient journey is a visual tool used to understand how the patient encounters and interacts with a series of consecutive healthcare services or events[53]. McCarthy et al. (2016) developed an integrated patient journey mapping tool that can be used to evaluate management strategies for healthcare service reform[53].

Employed for a slightly different purpose, Bolz-Johnson and colleagues (2020) used patient journey mapping as a way for patients to share their expertise and experience when studying a rare syndrome called "genturis syndromes"[40]. The genetic tumour risk syndrome is difficult to diagnose and lacks effective preventative and therapeutic interventions. Stages in their journey maps were based on inherent disease stages and the clinical pathway. Their goal was to identify the needs common to the patients at each stage.

Similar to “genturis syndromes”, AF lacks effective preventative measures and can be hard to diagnose. As discussed previously, diagnosis of asymptomatic and paroxysmal AF is frequently delayed. Asymptomatic individuals may not present to the clinic until complications occur, and standard diagnostic procedures (12-lead ECG or 24/48-hour Holter monitoring) may not capture short-lasting and intermittent AF episodes right away[11,15,56]. In addition, there is much variability in the presentation of symptoms. The many uncertainties that AF patients and clinicians face, especially before a diagnosis is made, render it a candidate disease for patient journey mapping.

2.5 Atrial fibrillation patient journey

Understanding the realities and circumstances of patients is crucial to patient-centered care, will provide insight into the challenges from the patient’s perspective, and will allow clinical decisions to be made in a narrative that makes sense to patients[57]. We describe a Canada-wide qualitative study on the arrhythmia patient journey conducted by Dr. Mary Runte, a patient-partner researcher.

The project “Mapping of the Arrhythmia Patient Journey”, funded by the Cardiac Arrhythmia Network of Canada[57], is Canada’s first in-depth, comprehensive, and patient-reported record of the experiences living with arrhythmia. This study consisted of individual interviews, focus groups, and patient journey mapping that solicited the patient view of the economic, employment, social, emotional, and psychological impacts of arrhythmias[57]. The study involved patients with various arrhythmia conditions not limited to AF. Patients with confirmed cardiac arrhythmias were asked to create a map of their journey and describe the effects of their arrhythmia from the onset of symptoms to treatment and beyond. Trend lines were created to capture the changes in emotions, social relationships, employment, and finances over the course of their journeys.

Ten focus groups (91 participants) and 62 individual in-depth interviews were conducted in eight Canadian cities since August 2018. The focus groups had participants from all provinces except for Manitoba[57].

2.6 Mapping questionnaire items to the patient journey

Using the data collected from “Mapping of the Arrhythmia Patient Journey”, we conducted secondary research to evaluate whether existing PROMs, specifically (HR)QoL questionnaires for AF patients, capture important themes that emerged from the focus groups and journey maps (Chang J et al., unpublished data, May 2021).

We searched for (HR)QoL questionnaires because they approximately measure patient-perceived wellbeing impacted by AF. PROMs that assess symptom severity were not of interest, and there was only one PREM specific to AF that concerns the ablation experience. We analyzed only the transcripts and journey maps of AF patients to identify relevant concerns under each of the four themes (“Emotional”, “Social”, “Employment/Schooling”, and “Financial”). The results of thematic analysis are summarized below:

It was an emotional experience for patients, particularly women, to try to get a diagnosis for AF. Female patients reported feeling dismissed and not taken seriously when communicating their symptoms to physicians. When a diagnosis was finally confirmed, female patients expressed feeling validated. The unpredictability of episodes and symptoms left patients, regardless of gender, to experience negative emotions. These included feelings of worry, anxiety, loneliness, sadness, and fear. Women’s emotional experiences tended to be more negative than men’s.

Social support changed over the course of the patient’s journey. At the beginning of their AF journey, patients typically isolated themselves from family and friends due to feelings of embarrassment and feeling like a burden to others. Family and friends were most supportive at this time.

As patients became more comfortable with their condition following treatment, patients began to open up and seek social engagement. However, friends and family had pulled back as a result of caregiver fatigue.

AF also affected patients' personal finances. For example, patients missed work and lost potential income when they felt ill or had to attend a medical appointment. The latter was especially a burden for patients who live in rural areas and need to frequent medical centers. Patients with more severe disease may need to change careers or retire early, significantly impacting their source of income.

For patients who continued to work, work performance and relationships with colleagues can be affected by patients' conditions. The impact of AF on patient's employment and schooling was worse if institutions were not supportive or accommodating.

We mapped the items of four HR(QoL) questionnaires developed for AF patients onto the themes and subthemes presented above. This provided insight into whether existing questionnaires were adequate or if a new questionnaire was warranted to measure the AF impact in the Canadian population. We determined the latter be true. Our analysis of existing (HR)QoL questionnaires found that most were heavily focused on symptoms and physical functioning, including the ability to perform daily activities. Two questionnaires, the Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT) and the Atrial Fibrillation Quality of Life (AFQoL), addressed the impact of AF on patient's emotional wellbeing and social life. However, not all emotional- and social-related concerns found in the focus groups and journey maps were addressed. None of the four questionnaires measured AF's impact on patients' occupation, livelihood, and finances (Chang J et al., unpublished data, May 2021).

A new questionnaire that comprehensively measures the life impacts of AF along the patient journey may be beneficial for research, holistic assessments in the clinic, and for evaluating patient progress and healthcare delivery.

The above-mentioned study was conducted as part of the qualitative phase of the mixed methods exploratory design for questionnaire development (Chang J et al., unpublished data, May 2021). The quantitative phase, which concerns the development and initial validation of a new questionnaire, is based upon the qualitative and will be described in Chapter 3.

2.7 Conclusion

No PROM adequately captures the impact of AF on patients throughout the patient journey from symptom onset to post-treatment. We propose developing a new questionnaire that will comprehensively measure the AF impact, with an emphasis on the diagnostic experience, available social support, employment, and finances.

In this thesis, we describe the development and initial validation of the new questionnaire (MAP-AF) as well as the analyses of the questionnaire scores. This thesis is a quantitative investigation of the AF impact connected to earlier qualitative research through questionnaire development. The mixed methods exploratory design will allow us to gain a more comprehensive understanding of the impact AF has on patients.

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Chapter 3

3 Development of the MAP-AF questionnaire

As discussed in Chapter 2, several insights emerged from analyzing the transcripts of about 101 patients with atrial fibrillation who participated in the project “Mapping the Arrhythmia Patient Journey” (Chang J et al., unpublished data, May 2021). AF was found to impact the patients’ psychological well-being, social relationships, occupation, and personal finances. Moreover, it was more difficult for female patients to get a diagnosis for AF than males – women more frequently expressed feeling dismissed when communicating their symptoms to physicians.

Existing patient-reported outcome measures do not adequately measure these concerns brought forth by AF patients in the focus groups and interviews (Chang J et al., unpublished data, May 2021). Our goal was to develop a patient-reported questionnaire that would capture these important missing concerns and apply this questionnaire to confirm the qualitative findings and test hypotheses.

Chapter 3 summarizes the development of the Mapping the Impact of Atrial Fibrillation (MAP-AF) questionnaire. The chapter encompasses both the methods and the results of item generation, exploratory factor analysis, and item reduction. The final MAP-AF questionnaire described in this chapter was then used to develop hypotheses and plan the analyses described in Chapter 4.

3.1 Methods

3.1.1 Item generation and questionnaire design

The Mapping the Impact of Atrial Fibrillation (MAP-AF) was developed to measure the multi-faceted life impacts of AF as experienced by Canadian patients.

Thirty-five items were written to reflect the themes and concerns emerged from the transcripts of AF patients (see section 2.6 for a summary of the themes and concerns). For example, there were items about the emotional struggles of getting a diagnosis, the effects of AF on social relationships, employment, and personal finances. Furthermore, some items were tied to a specific phase in the patient journey timeline: symptom-onset/pre-diagnosis phase, peri-diagnosis phase, or post-diagnosis phase. Other items asked about general concerns and current wellbeing. The print version of the preliminary 35-item MAP-AF is available in Appendix A.

The relevance and wording of the items were discussed with a patient-partner researcher, and the final candidate items were reviewed by the committee members – including a methodologist and a clinician.

All items utilized a 7-point Likert response scale. For items 16 to 21, the response options ranged from “not at all bothered” to “extremely bothered”; for the remaining items, the response options ranged from “strongly disagree” to “strongly agree”. Except for the reverse coded items, a higher position on the scale reflects a greater experienced impact or a more negative patient experience.

Due to the coronavirus disease 2019 (COVID-19) pandemic, the preliminary 35-item MAP-AF was administered via an online survey platform – Qualtrics. The Software-as-a-Service platform uses Transport Layer Security encryption for all transmitted Internet data[1]. The study was approved by the Western University Health Sciences Research Ethics Board (HSREB) and Lawson Research. The initial approval letters and the most recent approval letter for amendments are available in Appendix B.

Using Qualtrics, we incorporated skip patterns into the questionnaire such that the occupation-related questions (items 4, 8, 9, 10, 11, 12, 17, and 18) were displayed only for participants who were currently working or worked while experiencing AF. In addition, a non-applicable (N/A) option was available for items 16, 17, 18, 19, 20, 21, 33, 34, and 35.

On Qualtrics, a textbox was available for respondents to comment on additional concerns, the questionnaire design, or the questionnaire-taking experience. The comments from respondents were used to inform some of the strengths and limitations of our study, which are discussed in Chapter 5.

Table 1. A list of the 35 items from the MAP-AF questionnaire

Item1	It was challenging for me to get a diagnosis for atrial fibrillation
Item2	My doctor did not take my symptoms seriously. I felt dismissed
Item3	My family and friends were always there for me before I was diagnosed
Item4	My symptoms before diagnosis were interfering with my ability to do my job
Item5	My diagnosis proved that my concerns were real
Item6	It felt emotionally relieving to receive my diagnosis
Item7	I felt despaired after receiving my diagnosis
Item8	Because of my symptoms, I cannot continue to work like I used to. For example, I had to work part time or retire early because of my atrial fibrillation
Item9	My symptoms negatively impacted my work performance
Item10	My condition negatively impacted the relationships I had with people at work
Item11	I had to change my career path because of my atrial fibrillation. For example, starting a new business or foregoing advancement
Item12	My employer was supportive and accommodating with regards to my atrial fibrillation
Item13	Having atrial fibrillation prompted me to rethink my life goals
Item14	As time went on, my family and friends became less supportive. For example, my family and friends expected me to be over it by now.
Item15	My atrial fibrillation affected my romantic life (dating life, relationship with partner)
Item16	The cost of ambulance services for emergencies related to my atrial fibrillation
Item17	Having to miss work (for example, taking a day off) when I experienced symptoms and felt unwell
Item18	Taking a day off or using a vacation day to attend medical appointments and examinations
Item19	The costs related to my clinic visits. For example, travelling to medical centers for appointments and paying for transportation, parking, and/or accommodations.
Item20	My ability to get insurance because this is a pre-existing condition.
Item21	The lifestyle changes that I had to make because of my atrial fibrillation
Item22	I felt satisfied with my social life
Item23	I received the social support or engagement that I need
Item24	I isolated or distanced myself from others
Item25	My family and friends did not want to be around me
Item26	I felt lonely
Item27	I worried that I would experience symptoms or episodes of atrial fibrillation again
Item28	I felt hopeless about my health
Item29	I felt optimistic about my future
Item30	I felt grateful
Item31	I felt depressed
Item32	I felt anxious
Item33	I was bothered by the cost of my atrial fibrillation (consider all costs)
Item34	I worried about my future finances because of the costs related to my atrial fibrillation
Item35	My atrial fibrillation continued to impact my work life

3.1.2 Participant recruitment

We recruited patients with AF who had a pulmonary vein ablation at the London Health Sciences Centre (LHSC).

Patients were eligible for our study if they were over the age of 18, had a pulmonary vein ablation, and were able to understand and complete an online questionnaire in English.

The MAP-AF asks questions about concerns along the patient journey and assumes patients were experiencing AF-related symptoms prior to their diagnoses. Incidentally diagnosed individuals would not be suited to answer items 1 to 5. A general treated population of AF patients would be able to look back on their experiences from symptom-onset to post-treatment and provide an overview of the AF patient journey.

Pulmonary vein ablation (PVA) is the cornerstone for most AF ablation procedures and is often pursued for patients who remain symptomatic after rate or rhythm medications[2]. By recruiting PVA patients, we could better exclude asymptomatic patients, who are more likely to be incidentally diagnosed.

Patients who were not fluent in English or not familiar with the technological requirements of the study were still eligible if they could receive assistance from another individual such as a family member.

For exploratory factor analysis, a minimum of 10 cases per item and an absolute minimum of 300 cases are recommended[3-6]. For our 35-item MAP-AF, a sample size of 350 would meet both recommendations. From the clinical database at the LHSC, we used non-probability sampling and identified 500 consecutive post-PVA patients eligible for our study.

A member within the patient’s circle of care mailed out invitation letters introducing the study and informing potential participants to expect a call from the research student. Patients were told in the letter that they had no obligation to take the call. Within three weeks of sending the letters, the student contacted all 500 patients via telephone and explained the study details outlined in the letter of information. If patients were interested, they were asked to provide their email address to receive the letter of information and a personalized link to the online questionnaire. The target sample size was 350. A participant flowchart is included in Figure 2.

Recruitment began on January 15, 2021 and continued until March 7, 2021.

3.1.3 Data collection and management

The email addresses provided by interested participants were uploaded onto Qualtrics, and personalized links were emailed to participants through Qualtric's internal mailing system.

Once the link was accessed, participants were presented with the letter of information, the 35-item MAP-AF, and a separate list of questions that collected demographic and clinical information. Participants received a reminder email two weeks before the March 7th deadline.

Implied consent was obtained from participants who submitted the online questionnaire.

The first and last names, phone numbers, and email addresses of consenting participants were collected and stored in the master list, separate from the de-identified questionnaire responses. The master list and de-identified data are linkable by a unique study ID. Both files are password protected, encrypted, and stored on Western's OneDrive (an institutionally sanctioned cloud), with access restricted to the research team. As per the protocol for Lawson Research Institute-affiliated studies, both files will be retained at Western for 15 years and securely destroyed after.

3.1.4 Demographic and clinical variables

A separate list of questions preceding the 35-item MAP-AF collected demographic and clinical information from patients (Appendix C).

Textboxes were provided for participants to indicate their age and identified gender. During data cleaning, age was recorded as the participant's current age in years as of

2021. Only two genders emerged in our sample (males and females); hence gender was treated as a binary variable in subsequent analyses.

Four Yes/No questions related to participants' employment were used to create a new variable called work status that categorized participants into three groups:

I. Currently working

II. Not currently working, but previously worked while experiencing AF

III. Never worked or never worked while experiencing AF

The remaining demographic variables were categorical and included racial/ethnic background, marital status, urban or rural residence, and educational attainment.

Five variables described the clinical characteristics of the sample: time of AF diagnosis, type of AF (paroxysmal or persistent), frequency of AF episode (i.e., irregular heart rhythm), time of last AF episode, and recent symptom severity. An additional question made possible using the online survey platform was a graphic representing a timeline of a patient journey that participants could click on, shown in Figure 1. A heatmap can then be generated, visualizing where participants perceived themselves to be on their AF journey.

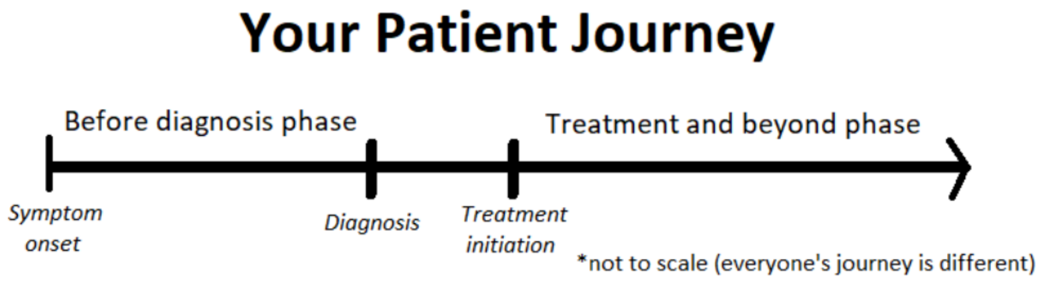


Figure 1. Patient journey timeline graphic

3.1.5 Descriptive analyses and data cleaning

The only continuous variable, age, was summarized using the mean (standard deviation) and median (interquartile range). All other demographic and clinical variables were categorical and were summarized using frequencies and percentages.

The literature review found gender differences in AF – women were more symptomatic than men, but less likely to receive an ablation[6,7]. We used bivariate analyses to compare the demographic and clinical characteristics of our male and female patients. Student’s independent t-test was used to determine whether age differed significantly between the two genders; Fisher’s exact test was used to determine whether there was an association between the other categorical variables and gender. We excluded missing values in both univariate and bivariate analyses.

The 35 item variables were assumed to be continuous from using a 7-point Likert response scale. We described for each item the number of participants who skipped, selected N/A, or did not provide a response. We also explored the missing patterns of the items. Summary statistics were then provided for the complete cases.

3.1.6 Statistical analyses

All statistical analyses were performed using SAS software version 9.4 (Copyright © 2016 by SAS Institute Inc., Cary, NC, USA)[8].

3.1.6.1 Exploratory factor analysis

Factor analysis is a statistical technique used to explain a large set of observed variables (e.g., items) using a smaller number of latent variables called factors[9,10]. Exploratory factor analysis (EFA) allows items to freely load on factors. It is appropriate for determining the underlying dimensions of newly developed questionnaires. Once strong hypotheses about the factor structure exist, confirmatory factor analysis can be used to test if the items load on hypothesized factors in a new sample[9].We first investigated the factorability of our data matrix by running a principal components analysis. We examined the correlation matrix, partial correlation matrix, and Kaiser’s Measure of Sampling Adequacy (MSA) for evidence of factors underlying the items. We then ran a preliminary factor analysis to check if the squared multiple correlations (SMCs) were distant from 1, indicating an absence of singularity and multicollinearity[11].

We determined the number of factors to extract using four criteria. In addition to conventional criteria such as the eigenvalue-greater-than-1 rule (also known as Kaiser's criterion) and the scree plot, we performed parallel analysis and examined the minimum average partial, both considered more accurate than the former methods[12]. Sensitivity analyses were conducted to assess whether the suggested number of factors to extract differed when log transformations of skewed items were performed or when using an imputed dataset (using an expectation maximization algorithm to compute the maximum likelihood estimates for missing data)[13].

After several possible numbers of factors were identified, a series of factor analyses were carried out using unweighted least squares extraction and promax rotation. Unweighted least squares (ULS) is an extraction method robust to non-normal distributions, and promax rotation is a type of oblique rotation which assumes some correlation between the factors[12,14,15]. In contrast, orthogonal rotation methods assume factors are uncorrelated.

A series of sensitivity analyses was conducted to ensure the robustness of the final factor structure to missing values, skewed items, and various extraction and rotation methods.

3.1.6.2 Item reduction and internal consistency

An item was said to load on a factor if the rotated factor loading from the pattern matrix was greater or equal to 0.35. Once the items were grouped into factors, the internal consistency of each factor was assessed using Cronbach's alpha. Irrelevant items were identified as those with a low item-to-total correlation and high alpha-if-deleted values. Redundant items were removed one at a time, with Cronbach's alpha recalculated upon each deletion. Item reduction ceased when any further deletions would greatly decrease the overall internal consistency of a factor. An EFA was repeated without the deleted items to confirm the factor structure.

3.1.6.3 Inter-factor correlation

We assessed the correlation between the identified factors to see whether they seem to be measuring the same construct (i.e., the impact of AF as experienced by patients).

3.2 Results

3.2.1 Sample characteristics

Of the 319 individuals who agreed to be emailed the letter of information and the questionnaire link, 277 individuals returned the questionnaire online – a response rate of 87%. A participant flowchart is included in Figure 2.

The mean (SD) age of participants was 63.8 (8.9) years. Age ranged from 26 years to 93 years. Since the distribution of age was slightly skewed as a result of a few younger individuals, we also report the median and interquartile range of age. The median age for male patients (n=193) was 64 years with an interquartile range of 59 to 70 years; the median age for female patients (n=84) was 66 years with an interquartile range of 61 to 70 years.

Table 2 presents the demographic characteristics of male and female participants, and Table 3 presents the clinical characteristics. Overall, the majority of participants were white (95%), married (75%), diagnosed with AF more than three years ago (84%), and were unsure of their AF type (paroxysmal or persistent) (55%).

Three individuals identified themselves as Métis, First Nations, Inuit, or other Indigenous ancestries; three as Middle Eastern; and one as Asian (to avoid identifying patients, these race/ethnicity categories were grouped with the “other” category in Table 2). Participants who selected “other” (n=7) for racial and ethnic background identified themselves as Scandinavian, Greek, French Canadian, Native and White, and Dutch. A quarter of all participants were not married, of which half were divorced or separated, and another half widowed or never married. Regarding educational attainment, 28% of participants had a high school diploma or below, 35% had a college diploma or an apprenticeship or trade certificate, and 38% had completed some university or had a bachelor’s degree or higher. In terms of work status, 41% were currently working, 38% previously worked while experiencing AF, and 21% never worked or never worked while experiencing AF (Table 2). There were no students in our sample.

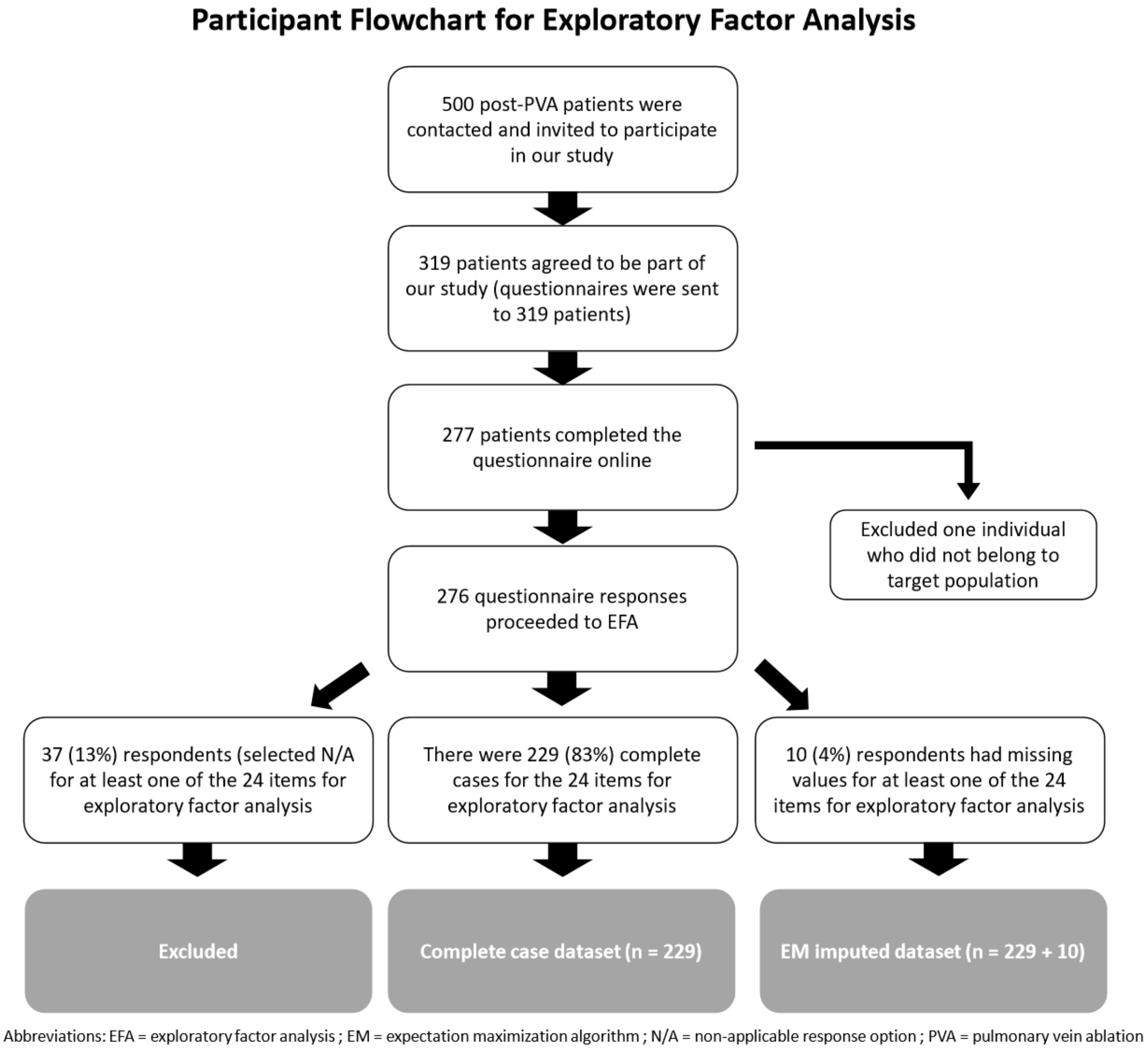


Figure 2. Participant flowchart

Table 2. Demographic characteristics of 277 participants by gender

Characteristic	Male N = 193	Female N = 84	P-value
Age			
(yr), mean (SD)	63.0 (9.3)	65.5 (7.7)	**0.03**[a]
(yr), median (IQR)	64.0 [59-70]	66.0 [61-70]	-
Race/ethnicity, n (%)			0.50[b]
White	185 (96%)	78 (93%)	
Other	8 (4%)	6 (7%)	
Marital status, n (%)			**0.003**[b]
Married	156 (81%)	53 (63%)	
Widowed	8 (4%)	13 (15%)	
Divorced	16 (8%)	7 (8%)	
Separated	4 (2%)	6 (7%)	
Never Married	9 (5%)	4 (5%)	
Education attainment, n (%)			**0.046**[b]
High school diploma or below	48 (25%)	30 (36%)	
College diploma or apprenticeship/trade certificate	72 (37%)	25 (30%)	
University below a bachelor’s degree	6 (3%)	7 (8%)	
Bachelor’s degree or higher	67 (35%)	22 (26%)	
Residence, n (%)			0.33[b]
Urban	81 (42%)	38 (45%)	
Suburban	66 (34%)	21 (25%)	
Rural	46 (24%)	24 (29%)	
Work status, n (%)			**0.02**[b]
Currently working	86 (45%)	27 (32%)	
Previously worked while experiencing AF	74 (38%)	31 (37%)	
Never worked, or never worked while experiencing AF	31 (16%)	26 (31%)	

[a] Student’s t test (equal variance assumption)

[b] Fisher’s exact test

AF = atrial fibrillation; IQR = interquartile range; SD = standard deviation

Tabled frequencies may not add up to the total sample of 277 due to the omission of missing values

P-values less than 0.05 are considered statistically significant and are bolded

Percentages may not add up to 100% due to rounding

Table 3. Clinical characteristics of 277 participants by gender

Characteristic	Male N = 193	Female N = 84	P-value*
Time of AF diagnosis, n (%)			0.96
Under 6 months ago	1 (0.5%)	0 (0%)	
6 months to under 1 year ago	1 (0.5%)	0 (0%)	
1 year to under 3 years ago	28 (15%)	14 (17%)	
3 years to under 5 years ago	50 (26%)	22 (26%)	
5 years ago, or more than 5 years ago	112 (58%)	48 (57%)	
Type of AF, n (%)			0.40
Paroxysmal	53 (27%)	30 (36%)	
Persistent	28 (15%)	12 (14%)	
Unsure	110 (57%)	42 (50%)	
Frequency of AF (irregular heart rhythm) episode, n (%)			0.06
Less than once a year	52 (27%)	15 (18%)	
Once or a few times a year	47 (24%)	13 (15%)	
Once or a few times a month	30 (16%)	23 (27%)	
Once or a few times a week	23 (12%)	11 (13%)	
Daily or constantly	32 (17%)	18 (21%)	
Time of last AF episode, n (%)			**0.01**
Today or now	8 (4%)	12 (14%)	
Within the past month	33 (17%)	21 (25%)	
1 month to under 6 months ago	29 (15%)	9 (11%)	
6 months to under 1 year ago	36 (19%)	14 (17%)	
More than 1 year ago	87 (45%)	27 (32%)	
Symptom severity as of recently, n (%)			**0.03**
Minimal to no symptoms	92 (48%)	25 (30%)	
Mild symptoms	41 (21%)	25 (30%)	
Moderate symptoms	35 (18%)	20 (24%)	
Severe symptoms	21 (11%)	14 (17%)	

*P-values were computed using Fisher's exact test

AF = atrial fibrillation

Tabled frequencies may not add up to the total sample of 277 due to the omission of missing values

P-values less than 0.05 are considered statistically significant and are bolded

Percentages may not add up to 100% due to rounding

Two-hundred and thirty-two individuals (84%) were diagnosed with AF more than three years ago, of whom 69% were diagnosed more than five years ago (Table 3). Only two individuals were diagnosed under a year ago. Slightly over half of the total sample did not know whether they had paroxysmal or persistent AF. Of patients who knew, 83 had paroxysmal AF and 40 had persistent AF. Patients in our study have had a pulmonary vein ablation procedure, and most perceived themselves to be at the “treatment and beyond” phase on a patient journey timeline (Figure 3). Many patients no longer experienced AF following successful ablations – the current AF burden in our sample was suspected to be moderate to low. In support of this, 41% last experienced an episode of AF (irregular heart rhythm) more than a year ago, and 42% indicated minimal to no recent symptoms (Table 3). Despite the reported percentages, we anticipate substantial measurement error in three clinical variables. Questions asking about the frequency of AF episodes, the time of last episode, and symptom severity were confusing to patients who no longer experienced AF. Instead of reflecting on their current AF burden, some of the patients responded in a way that reflected their past AF burden when they still had AF. Consequently, present-day AF frequency and symptom severity were likely overestimated. This is discussed in the limitations section in Chapter 5.

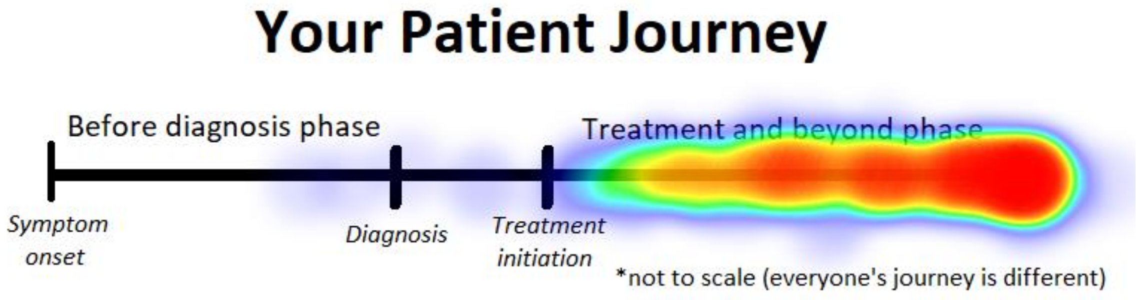


Figure 3. Heatmap visualization of the most prevalent phase

Bivariate analyses (Student’s t-test and Fisher’s exact tests) revealed statistically significant gender differences in the following variables: age, marital status, educational attainment, work status, time of last AF episode, and recent symptom severity. Compared to male patients, females in our sample were more likely to be older, less likely to be in marriage, less likely to have a bachelor’s degree or higher, less likely to have worked or be working, more likely to have experienced an AF episode recently, and more likely to have severe symptoms.

3.2.2 Item characteristics

The number of respondents who answered, skipped, missed, or selected the N/A option for each item is summarized in Table 4. Fifty-seven respondents automatically skipped the eight work-related items (items 4, 8, 9, 10, 11, 12, 17, and 18) because they never worked or never worked while experiencing AF. Alternatively stated, the work-related items did not apply to 21% of the sample. Whenever a N/A option was available (i.e., items 16, 17, 18, 19, 20, 21, 33, 34, and 35), it was always selected by at least some individuals.

Both the skip pattern and the incorporation of a N/A option were features of the questionnaire designed to reflect the non-applicability of certain items. The eleven items (marked by an asterisk in Table 4) that were considered non-applicable to greater than 10% of the total sample were removed from subsequent analyses. The remaining 24 items proceeded to factor analysis.

Our data had few missing values, ranging from none to a maximum of 6 missing values for item 12. A greater number of missing values were found for items without a N/A option, suggesting that respondents may have missed an item because the statement was not applicable, rather than simply missing by accident. Indeed, participants who had missing values often selected the N/A option when possible and appropriate. We propose that missing values could be attributed to suboptimal question wording, the nearby presence of family members, forgetfulness, or the lack of a N/A option when the question did not apply. We believe the last to be a probable explanation based on comments provided by several patients. We discuss this in greater detail in Chapter 5.

Table 4. The number of observed, non-applicable, skipped, and missing responses

Item	N	N/A	Skipped	Missing
1	276	-	-	0
2	275	-	-	1
3	275	-	-	1
4*	219	-	57	0
5	276	-	-	0
6	275	-	-	1
7	275	-	-	1
8*	218	-	57	1
9*	219	-	57	0
10*	216	-	57	3
11*	218	-	57	1
12*	213	-	57	6
13	276	-	-	0
14	275	-	-	1
15	275	-	-	1
16*	177	99	-	0
17*	177	41	57	1
18*	188	30	57	1
19	260	16	-	0
20*	230	45	-	1
21	263	13	-	0
22	276	-	-	0
23	273	-	-	3
24	276	-	-	0
25	273	-	-	3
26	275	-	-	1
27	276	-	-	0
28	276	-	-	0
29	276	-	-	0
30	273	-	-	3
31	274	-	-	2
32	273	-	-	3
33	252	24	-	0
34	252	24	-	0
35*	239	36	-	1

Skip patterns only available for items 4, 8, 9, 10, 11, 12, 17 and 18.

Non-applicable responses only available for items 16, 17, 18, 19, 20, 21, 33, 34 and 35.

*Greater than 10% of all participants skipped the item or selected the N/A option

Total number of observations sums up to 276 after removing one observation that did not belong to the target population

N = number of non-missing observations; N/A = non-applicable responses

Investigation of the missing pattern identified one respondent who missed items 1 to 3 consecutively. The respondent indicated in the textbox that they could not answer the questions because they experienced no symptoms before being diagnosed. Since we determined incidentally diagnosed patients to be out of our target population, we excluded this observation from subsequent analyses, reducing the total sample size from 277 to 276 (Figure 2).

The summary statistics of the 24 items using 276 observations are presented in Table 5. The means ranged from 1.7 for item 25 to 5.9 for item 5. Four items (3, 5, 23, and 25) had a large absolute skewness or kurtosis statistic, indicating departure from normality. Item 25 was the most severely skewed, with a skewness of 2.5 and a kurtosis of 6.8. Log transformations of the four items showed improvement only for item 25.

Table 5. Summary statistics of the 24 items for factor analysis

Item	N	N/A	Missing	For complete cases Mean ± SD	Skewness	Kurtosis
1	276	-	0	3.12 ± 2.04	0.63	-1.01
2	275	-	1	2.44 ± 1.81	1.17	0.12
3	275	-	1	5.61 ± 1.65	-1.46	1.38
5	276	-	0	5.88 ± 1.39	-1.89	3.74
6	275	-	1	5.03 ± 1.67	-0.81	-0.03
7	275	-	1	4.11 ± 1.82	-0.22	-1.01
13	276	-	0	4.54 ± 1.76	-0.42	-0.87
14	275	-	1	2.47 ± 1.63	1.10	0.29
15	275	-	1	3.58 ± 2.06	0.17	-1.45
19	260	16	0	2.47 ± 1.59	1.02	0.38
21	263	13	0	4.17 ± 1.98	0.04	-1.17
22	276	-	0	5.20 ± 1.61	-1.08	0.40
23	273	-	3	5.40 ± 1.36	-1.15	1.11
24	276	-	0	2.96 ± 1.91	0.68	-0.92
25	273	-	3	1.69 ± 1.17	2.46	6.77
26	275	-	1	2.55 ± 1.79	1.02	-0.21
27	276	-	0	4.78 ± 2.00	-0.71	-0.78
28	276	-	0	3.21 ± 1.81	0.35	-1.10
29	276	-	0	5.01 ± 1.51	-0.87	0.10
30	273	-	3	5.45 ± 1.41	-1.00	0.52
31	274	-	2	3.12 ± 1.90	0.52	-1.06
32	273	-	3	3.97 ± 1.94	-0.17	-1.29
33	252	24	0	2.71 ± 1.83	0.91	-0.47
34	252	24	0	2.67 ± 1.83	1.01	-0.14

All items utilized a 7-point Likert scale and have not been reverse scored.

The lowest value, 1, corresponds to either “strongly disagree” or “not at all bothered”. The highest value, 7, corresponds to either “strongly agree” or “extremely bothered”.

N = number of non-missing observations; N/A = non-applicable responses; SD = standard deviation

3.2.3 Exploratory factor analysis

From the initial principal components analysis with varimax rotation, Kaiser’s Measure of Sampling Adequacy (MSA) was 0.83, implying the presence of some factors that are underlying and explaining the correlations between items[11]. The SMCs were also sufficiently distant from 1, suggesting our data matrix to be absent from singularity and multicollinearity.

Before factor extraction and rotation, individuals who selected the N/A option for any of the 24 items were excluded. This resulted in 239 analyzable responses, of which 229 had no missing values (Figure 2). In addition to the complete case dataset (n=229), we created an imputed dataset using the expectation maximization (EM) algorithm – a type of maximum likelihood estimation[13].

Table 6 compares the suggested number of factors to extract from the four criteria across the various datasets (complete cases, EM imputed, complete cases with log transformation of item 25, and EM imputed with log transformation of item 25). Based on these results, we explored a 5-factor solution, a 6-factor solution, and a 7-factor solution (Appendix E, F, and G). The scree plots are available in Appendix D.

Table 6. The numbers of factors to extract as suggested by the four criteria under various conditions

Criteria	CCA	CCA with log transformation of item 25	EM imputation	EM imputation with log transformation of item 25
Kaiser's criterion	6	6	6	6
Scree plot	2 or 5 or 8	2 or 6	2 or 3 or 5 or 8	2 or 5 or 8
Parallel analysis (α=0.025)	5	5	6	6
Minimum Average Partial	4 or 5	3 or 4	4	4

The results were obtained using principal components extraction with varimax rotation

CCA = complete-case-analysis (n=229); EM = expectation maximization (a type of maximum likelihood estimation)

For each of the three possible factor solutions, eight EFAs were conducted to explore the robustness of the factor loadings to a different extraction method (i.e., iterative principal axis factoring), imputation of missing values, and log transformation of a skewed item (Appendix E, F, G). When the threshold of minimum factor loading was set to 0.35, all eight conditions produced the same factor structure. The 6-factor solution was chosen for best interpretability and parsimony.

Table 7 presents the rotated factor loadings from the pattern matrix of a 6-factor solution. The solution used a complete case analysis (n=229), unweighted least squares extraction, and promax rotation. There were no cross-loading items (items that load onto more than one factor) when the minimum factor loading was required to be at least 0.35.

Table 7. Rotated factor loadings from a six-factor solution using ULS extraction and promax rotation

Items	Factor 1	Factor 2	Factor 3	Factor 4	Factor 5	Factor 6
1	-0.02	0.10	0.03	0.03	**0.84**	0.11
2	0.05	0.01	-0.04	-0.05	**0.77**	0.02
3	0.08	0.28	-0.06	0.04	0.02	**0.47**
5	-0.01	-0.07	-0.04	0.07	0.03	**0.58**
6	-0.07	-0.06	0.09	-0.08	0.09	**0.67**
7	**0.41**	0.16	-0.01	0.34*	-0.06	-0.12
13	0.03	0.06	0.06	**0.61**	-0.08	0.13
14	-0.05	-0.20	-0.02	0.31	0.23	-0.23
15	-0.02	-0.18	-0.002	**0.55**	0.22	-0.001
19	0.09	-0.05	**0.46**	0.05	0.01	0.08
21	0.05	-0.03	0.08	**0.56**	-0.07	0.006
22	-0.10	**0.80**	0.008	0.03	0.14	-0.13
23	0.03	**0.78**	-0.02	0.15	-0.003	0.05
24	0.10	**-0.53**	-0.12	0.30	-0.05	-0.07
25	-0.17	**-0.45**	0.11	0.27	0.01	-0.002
26	0.20	**-0.43**	0.06	0.22	0.02	0.009
27	**0.80**	0.18	-0.04	0.09	-0.01	0.03
28	**0.75**	-0.07	0.04	0.14	0.006	0.03
29	**-0.63**	0.08	-0.13	0.16	-0.09	0.18
30	**-0.41**	0.27	0.004	0.15	-0.16	0.13
31	**0.55**	-0.34*	0.02	0.05	0.05	0.10
32	**0.78**	-0.08	-0.02	-0.03	-0.06	0.09
33	-0.02	0.02	**0.96**	0.005	-0.04	-0.002
34	0.03	-0.004	**0.80**	0.08	0.02	-0.05

Bolded factor loadings are equal to or greater than 0.35

*factor loadings above 0.32 but less than 0.35, indicating poor loading

The factor analysis was conducted using complete cases (n=229), unweighted least squares extraction, and promax rotation.

3.2.4 Item reduction and internal consistency

The internal consistency, measured using Cronbach's alpha, of the unreduced factor structure ranged from 0.6 for factor 6 to 0.86 for factor 1 (Table 8). Redundant items in a factor were identified and removed sequentially. Items 7, 30, and 29 were deleted from factor 1 in that order; item 25 was deleted from factor 2; item 7 was deleted from factor 4.

The internal consistency of the refined factors is presented in Table 9.

Table 8. Initial internal consistency of the six factors as indicated by Cronbach's alpha

Factor structure	Standardized item correlation with total	Standardized alpha-if-deleted
Factor 1 (standardized α = 0.86)		
Item 7 "I felt despaired after receiving my diagnosis"	0.36	0.87
Item 27 "I worried that I would experience symptoms or episodes of atrial fibrillation again"	0.62	0.84
Item 28 "I felt hopeless about my health"	0.79	0.81
Item 29 "I felt optimistic about my future"	0.64	0.83
Item 30 "I felt grateful"	0.51	0.85
Item 31 "I felt depressed"	0.72	0.82
Item 32 "I felt anxious"	0.72	0.82
Factor 2 (standardized α = 0.79)		
Item 22 "I felt satisfied with my social life"	0.67	0.72
Item 23 "I received the social support or engagement that I need"	0.57	0.75
Item 24 "I isolated or distanced myself from others"	0.59	0.75
Item 25 "My family and friends did not want to be around me"	0.46	0.79
Item 26 "I felt lonely"	0.57	0.75
Factor 3 (standardized α = 0.81)		
Item 19 "I was bothered by the costs related my clinic visits"	0.50	0.89
Item 33 "I was bothered by the cost of my atrial fibrillation"	0.77	0.62
Item 34 "I worried about my future finances because of the costs related to my atrial fibrillation"	0.72	0.67
Factor 4 (standardized α = 0.66)		
Item 7 "I felt despaired after receiving my diagnosis"	0.30	0.68
Item 13 "Having atrial fibrillation prompted me to rethink my life goals"	0.48	0.56
Item 15 "My atrial fibrillation affected my romantic life (dating life, relationship with partner)"	0.45	0.58
Item 21 "I was bothered by the lifestyle changes that I had to make because of my atrial fibrillation"	0.53	0.52
Factor 5 (standardized α = 0.78)		
Item 1 "It was challenging for me to get a diagnosis of atrial fibrillation"	0.64	-
Item 2 "My doctor did not take my symptoms seriously. I felt dismissed"	0.64	-
Factor 6 (standardized α = 0.60)		
Item 3 "My family and friends were always there for me before I was diagnosed"	0.35	0.58
Item 5 "My diagnosis proved that my concerns were real"	0.51	0.51
Item 6 "It felt emotionally relieving to receive my diagnosis"	0.38	0.55

Table 9. Final internal consistency of the six factors as indicated by Cronbach’s alpha

Factor structure	Standardized item correlation with total	Standardized alpha-if-deleted
Factor 1: AFFECT (standardized α = 0.87)		
Item 27 “I worried that I would experience symptoms or episodes of atrial fibrillation again”	0.63	0.87
Item 28 “I felt hopeless about my health”	0.77	0.81
Item 31 “I felt depressed”	0.71	0.83
Item 32 “I felt anxious”	0.77	0.81
Factor 2: SOCIAL SUPPORT (standardized α = 0.80)		
Item 22* “I felt satisfied with my social life”	0.69	0.70
Item 23* “I received the social support or engagement that I need”	0.60	0.75
Item 24 “I isolated or distanced myself from others”	0.57	0.76
Item 26 “I felt lonely”	0.57	0.76
Factor 3: FINANCIAL IMPACT (standardized α = 0.81)		
Item 19 “I was bothered by the costs related my clinic visits”	0.50	0.89
Item 33 “I was bothered by the cost of my atrial fibrillation”	0.77	0.62
Item 34 “I worried about my future finances because of the costs related to my atrial fibrillation”	0.72	0.67
Factor 4: MAJOR LIFE EVENTS (standardized α = 0.68)		
Item 13 “Having atrial fibrillation prompted me to rethink my life goals”	0.50	0.58
Item 15 “My atrial fibrillation affected my romantic life (dating life, relationship with partner)”	0.46	0.63
Item 21 “I was bothered by the lifestyle changes that I had to make because of my atrial fibrillation”	0.53	0.54
Factor 5: DIAGNOSTIC EXPERIENCE (standardized α = 0.78)		
Item 1 “It was challenging for me to get a diagnosis of atrial fibrillation”	0.64	-
Item 2 “My doctor did not take my symptoms seriously. I felt dismissed”	0.64	-
Factor 6 (standardized α = 0.60)		
Item 3 “My family and friends were always there for me before I was diagnosed”	0.35	0.58
Item 5 “My diagnosis proved that my concerns were real”	0.51	0.51
Item 6 “It felt emotionally relieving to receive my diagnosis”	0.38	0.55

A factor analysis was rerun after deleting items 7, 25, 29, and 30, confirming the structure presented above.

*reverse coded items

Factor 6 and its items were excluded from the final factor structure due low interpretability and the factor’s low correlation with other factors

3.2.5 Inter-factor correlation

Last, we examined the pairwise correlation between the six factors, shown in Table 10. Examining the inter-factor correlations identified factor 6 as problematic, for it had very low correlations with the other five factors. Furthermore, the three items constituting factor 6 seemed to be poorly related, making it difficult to ascribe meaning to the factor. The decision was to remove factor 6 and its items from the final factor structure.

Table 10. Inter-factor correlations between the six factors after item reduction

	Factor 1 AFFECT	Factor 2 SOCIAL SUPPORT	Factor 3 FINANCIAL IMPACT	Factor 4 MAJOR LIFE EVENTS	Factor 5 DIAGNOSTIC EXPERIENCE	Factor 6
Factor 1 AFFECT	1.00	0.53	0.40	0.44	0.27	0.07
Factor 2 SOCIAL SUPPORT		1.00	0.43	0.39	0.27	-0.15
Factor 3 FINANCIAL IMPACT			1.00	0.41	0.26	-0.005
Factor 4 MAJOR LIFE EVENTS				1.00	0.23	0.13
Factor 5 DIAGNOSTIC EXPERIENCE					1.00	0.13
Factor 6						1.00

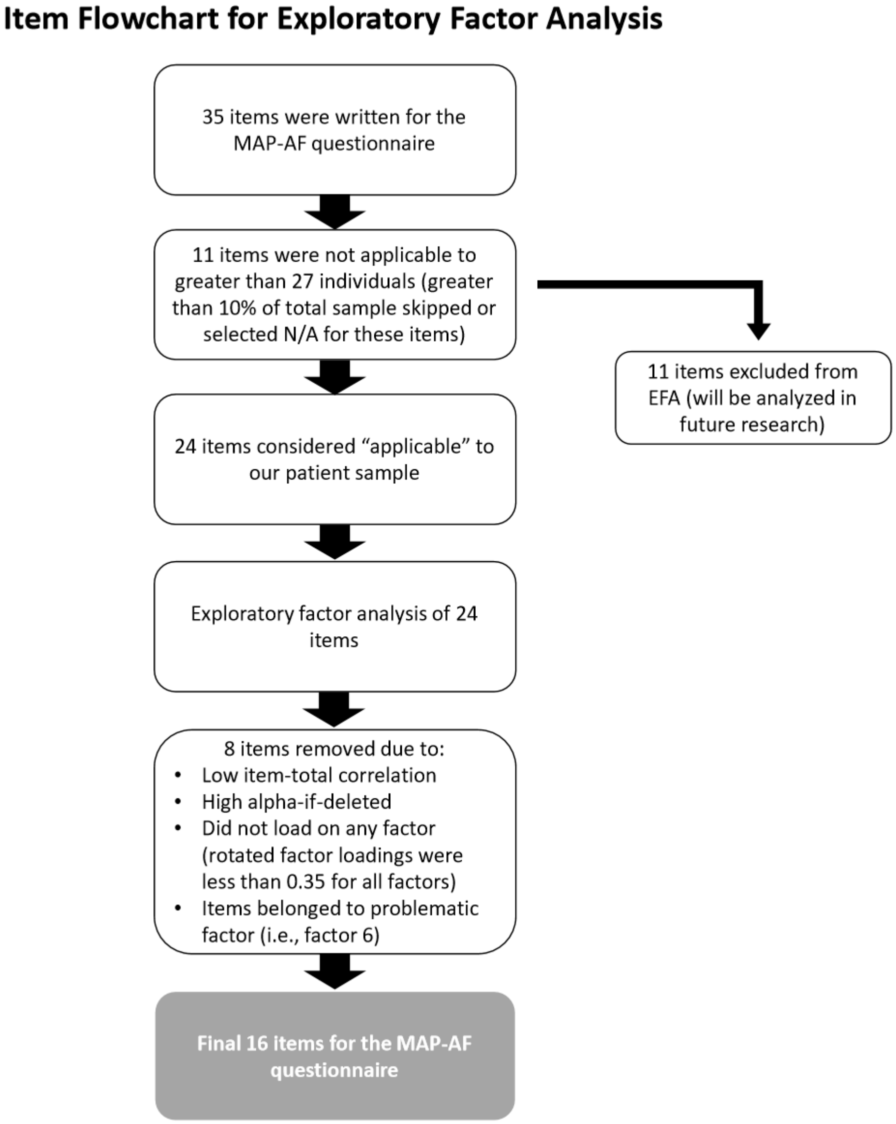
Factor 6 and its items were excluded from the final factor structure due low interpretability and the factor's low correlation with other factors

3.2.6 Final factor structure

The final MAP-AF contains five factors underlying 16 items: “Affect” (measuring feelings of anxiety, depression, hopelessness, and worries), “Diagnostic Experience” (measuring patients’ perceived difficulty of getting a diagnosis), “Social Support”, “Financial Impact”, and “Major Life Events” (Table 9). Two of the items from “Social Support” (items 22 and 23) are reverse scored. A higher overall score on the MAP-AF, calculated as the mean of all 16 items, indicates a greater experienced impact of AF or a more negative patient experience.

Figure 4 illustrates the flow of items from the 35 candidate items to the final 16 in the MAP-AF.

The next chapter describes the scoring algorithm and the analyses of the factor and overall scores of the MAP-AF. Analyses include hypothesis testing and multivariable linear regression.



Abbreviations: EFA = exploratory factor analysis; N/A = non-applicable response option; MAP-AF = Mapping the Impact of Atrial Fibrillation questionnaire

Figure 4. Item flowchart

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Chapter 4

4 Analyses of the MAP-AF scores

This chapter describes both the methods and results of the MAP-AF score analyses. Computation of the factor scores and the overall score, including the handling of missing data, is described. A priori hypotheses related to the factor scores are tested, and a multivariable linear regression is run on the overall score to identify significant predictors.

4.1 Methods

4.1.1 Factor scores

The MAP-AF has five factors underlying 16 items: “Affect” and “Social Support” each has four items, “Financial Impact” and “Major Life Events” each has three items, and “Diagnostic Experience” has two. The complete factor structure, including the specific items, can be found in Table 9 of Chapter 3.

The N/A options available for items 19, 33, and 34 from “Financial Impact” and item 21 from “Major Life Events” complicate factor score computation, along with missing values.

We first referred to the item-total correlations of the four items presented in Table 9 of Chapter 3. A low standardized item-total correlation and a high standardized alpha-if-deleted value signal an item that is less essential or potentially irrelevant for the particular factor. When examining “Financial Impact”, item 19 had the lowest item-total correlation, and when deleted, may increase the overall Cronbach’s alpha from 0.81 to 0.89. On the other hand, deleting either items 33 or 34 will reduce the overall Cronbach’s alpha significantly to the 0.6 range. Therefore, individuals selecting N/A or missing item 19 could still have a meaningful “Financial Impact” score computed. For “Major Life Events”, item 21 (with the N/A option) had the highest item-total correlation and, if deleted, would reduce the overall Cronbach’s alpha from 0.68 to 0.54. Item 21 was deemed essential to the factor – individuals selecting N/A or missing item 21 could not have a meaningful “Major Life Events” score.

The computation criteria for the factor scores are summarized in Table 11 in the results section. For the two 3-item factors, only 1 item was allowed to be missing or N/A: item 19 for “Financial Impact” and items other than item 21 for “Major Life Events”. Since “Diagnostic Experience” only had two items, both items must be non-missing for the factor score to be computed. For “Affect” and “Social Support”, at least two items needed to be non-missing for computation (50% of items should be non-missing).

If factor scores were computable, they were calculated as an arithmetic mean of the non-missing (and applicable) items. For “Social Support”, items 22 and 23 were reverse coded. The mean factor scores range from 1 to 7, where a higher score reflects a more significant impact experienced by patients.

An overall MAP-AF score was also computed as an arithmetic mean of the 16 items – if all factor scores were computable. The mean overall score was then rescaled to range from 0 to 100, where a higher score similarly indicates a worse patient experience or a greater experienced impact of AF.

4.1.2 Descriptive analysis

Factor scores were summarized statistically using mean ± SD and graphically using histograms, boxplots, and normal quantile-quantile (Q-Q) plots.

Bivariate analyses were conducted to examine the relationship between the overall score and the demographic and clinical covariates. The linear and monotonic relationships between age and the overall score were examined using the Pearson product-moment correlation and the Spearman rank-order correlation, respectively. The non-parametric Wilcoxon rank-sum test (also known as the Mann-Whitney U test or the Wilcoxon-Mann-Whitney test) was used to assess gender differences in the overall score. The non-parametric Kruskal-Wallis test was used for all other categorical covariates with more than two levels.

Non-parametric tests were selected over parametric tests because some subgroup scores were heavily skewed. This means that if the scores were normally distributed, the inferential statistics presented are more conservative.

All statistical analyses were performed using SAS software version 9.4 (Copyright © 2016 by SAS Institute Inc., Cary, NC, USA)[1].

4.1.3 Hypothesis testing

We generated seven a priori hypotheses for the five factors based on pre-existing knowledge and results from our previous qualitative work (Chang J et al., unpublished data, May 2021).

To recap our previous findings, women and patients with intermittent AF episodes had a more difficult time trying to get a diagnosis. Patients residing in rural areas incurred higher transportation costs and lost potential income when they had to miss work and travel for clinical appointments. We also discovered a pattern in social support. Family and friends were the most supportive proximally before and after patients were diagnosed. During this time, many patients withdrew socially from family and friends due to feelings of embarrassment and guilt. As patients felt more comfortable with their condition over time, they began to seek social engagement. However, friends and families had started to decrease their support as a result of caregiver fatigue.

Based on these findings, we hypothesized the following:

> I) & II) Female patients and paroxysmal patients will score higher (i.e., worse) on “Diagnostic Experience” compared to male patients and persistent AF patients, respectively
>
> III) Patients residing in rural areas will score higher on “Financial Impact” compared to patients residing in urban areas
>
> IV) Patients who were diagnosed more distantly in the past will score higher (i.e., worse) on “Social Support” than patients recently diagnosed

Three additional hypotheses were generated based on what is known in the literature:

> V) Women tend to have larger support networks than men[2]. We hypothesize female patients to score lower (i.e., better) on “Social Support” compared to male patients
>
> VI) Women tend to be more emotionally expressive than men[3] and generally experience greater anxiety and depression[4,5]. We hypothesize our female patients to score higher on “Affect” compared to male patients
>
> VII) Patients with paroxysmal AF are more likely to experience palpitations than patients with persistent AF[6]. Paroxysmal patients may experience greater anxiety due to the on and off palpitations. We hypothesize patients with paroxysmal AF to score higher on “Affect” than patients with persistent AF

Hypotheses related to gender differences were tested using the Wilcoxon rank-sum test. The Kruskal-Wallis test was used for all other hypotheses which have categorical covariates with more than two levels. If the overall Kruskal-Wallis test was statistically significant (p-value < 0.05), pairwise comparisons were made using the Dwass, Steel, Critchlow-Fligner (DSCF) method. The DSCF statistics and the associated two-sided p-value are computed based on pairwise two-sample Wilcoxon comparisons[7].

4.1.4 Using statistical regression to select predictors

By the end of Chapter 3, the MAP-AF was validated in one sample of PVA patients. Inferential analyses will remain exploratory until the MAP-AF can establish its validity across multiple samples.

For this reason, it was acceptable at our stage to select predictors based on statistical grounds.

There are three main methods for predictor selection in statistical regression: backward selection, forward selection, and stepwise selection.

Backward selection begins with a full model and deletes variables with the least significant F statistic one at a time until all variables in the model have F statistics at a specified stay significance level[8]. Vittinghoff and colleagues (2012) suggest a liberal criterion for deletion, removing only variables with p-values greater or equal to 0.2[9]. Each deletion (or addition, in forward selection) produces a new model, resulting in a sequence of models once variable movement halts. Either the last model in the sequence or the model with the best fit statistics is usually selected. The R-square statistic is one of the most common model fit statistics. An alternative tool for optimal model selection is Akaike's information criterion (AIC). The AIC measures the difference between a given model and the "true" underlying model and is a function of sample size, sum of squared errors, and the number of parameters[10]. It was shown to be superior for selecting the most optimal model in statistical regression[10].

A major limitation of both forward and stepwise selection methods is that they begin with a null model. The full model (with all predictors) may never emerge unless all candidate predictors are deemed significant. To that end, Vittinghoff et al. (2012) recommend using backward selection primarily and the other two methods for sensitivity analyses[9].

To select demographic and clinical covariates for the overall MAP-AF score, we used backward selection with a significance level for retaining predictors set at 0.20. Of all the models produced from the sequential deletion of variables, the model with the smallest AIC was selected.

Sensitivity analyses were carried out to compare results obtained from backward selection (stay significance level = 0.20), forward selection (entry significance level = 0.50), and stepwise selection (entry significance level = 0.20 and stay significance level = 0.20).

Missing values were excluded by list-wise deletion.

4.1.5 Multivariable linear regression

Based on the results of statistical regression, the final linear regression model for the overall score included age (and age-squared), gender, marital status, educational attainment, and time of last AF episode. Parameter estimates of the linear regression were obtained using the generalized linear model (GLM) procedure in SAS software since the regression (REG) procedure does not directly handle categorical predictors[11].

Age was centered to make the intercept more interpretable, and a quadratic term for age was added to improve the linearity of the continuous predictor with the overall score.

4.1.6 Model fit and diagnostics

To check model assumptions, we examined the normality of the residuals, homoscedasticity, and the linearity of age (the only continuous predictor). The adjusted coefficient of determination (adjusted R^2) reflected the model fit, and the Difference in Fits (DFFITS) was used to detect influential observations. The DFFITS statistic for an observation quantifies the change in predicted values when that observation is deleted[12]. We explored the robustness of the parameter estimates to potentially influential observations by deleting observations with the largest DFFITS five at a time.

4.1.7 Additional models

Using the same five predictors included in the main linear regression model, we ran five additional models for the five factor scores.

The factor scores were rescaled to range from 0 to 100 for better interpretability.

Significant findings are briefly summarized in the results section.

4.2 Results

4.2.1 Descriptive analysis

The number of observations, mean, and standard deviation of each factor score are summarized in Table 11. Thirteen individuals selected “N/A” for item 21, and hence, the mean score for “Major Life Events” was not computable for these individuals. Likewise, 26 individuals selected “N/A” for either item 33 or 34, reducing the number of “Financial Impact” scores to 250. “Financial Impact” had the lowest mean score (2.6 ± 1.5), and “Major Life Events” had the highest mean score (4.1 ± 1.5). The factors “Affect” and

"Major Life Events" were approximately normally distributed, whereas the other three were quite skewed. Only 244 individuals had a mean score for all five factors; thus, the overall MAP-AF score was computable for 244 individuals. The overall score on a scale of 0 to 100 had a mean of 37.8 (SD: 17.8) and ranged from 2.1 to 89.6. The distribution was positively skewed with a short tail on the left and a long tail on the right (skewness: 0.54, kurtosis: -0.11).

Table 11. Factor score computation and subsets

Factors	Number of computable scores	Mean ± SD	Range (Min, Max)	Criteria for computation
Affect	276	3.76 ± 1.61	1, 7	No more than 50% of items are missing
Social Support	276	2.73 ± 1.32	1, 6.8	No more than 50% of items are missing
Financial Impact	250	2.61 ± 1.50	1, 7	Items 33 and 34 are applicable and non-missing
Major Life Events	263	4.12 ± 1.49	1, 7	Item 21 is applicable and non-missing. Otherwise, one missing value for item 13 or item 15 is acceptable.
Diagnostic Experience	275	2.78 ± 1.76	1, 7	Both items are non-missing
Overall score	244	37.8 ± 17.8	2.1, 89.6	All factor scores are computable

Max = maximum; Min = minimum; SD = standard deviation

Bivariate analyses revealed the following covariates to be significantly associated with the overall MAP-AF score: age, gender, marital status, educational attainment, frequency of AF episode, time of last AF episode, and recent symptom severity (Tables 12 and 13). Higher (i.e., worse) scores were found in patients who were younger, female, divorced or separated, had lower educational attainment, more frequent and more recent episodes, and more severe symptoms. Patients self-identified as Métis, First Nations, Inuit, or other Indigenous ancestries had the highest overall score (59 ± 16), compared to White individuals (37.4 ± 17.8) and Middle Eastern individuals (35.9 ± 11). Nevertheless, the differences in scores between patients of various racial and ethnic backgrounds were not statistically significant (p-value: 0.11). Tables 12 and 13 present the summary statistics of the overall score in each subgroup of the categorical covariates.

Table 12. Relationship between demographic covariates and the overall score

Characteristic (n)	Overall score Mean (SD)	P-value
Age	Pearson's r: -0.11	0.08
	Spearman's r: -0.16	**0.01**
Gender		
Male (171)	35.9 (16.8)	**0.04**[a]
Female (73)	42.1 (19.4)	
Race/ethnicity		
White (232)	37.4 (17.8)	0.11[b]
Middle Eastern (Egyptian, Lebanese, Iranian) (2)	35.9 (11.0)	
Métis, First Nations, Inuit, or other Indigenous ancestry (3)	59.0 (15.9)	
Other (5)	49.6 (10.0)	
Marital status		
Married (180)	35.0 (16.9)	**0.0001**[b]
Divorced/Separated (30)	50.0 (18.4)	
Widowed/Never Married (33)	42.3 (16.8)	
Educational attainment		
High school diploma or below (68)	40.9 (20.4)	**0.004**[b]
College diploma or apprenticeship/trade certificate (87)	39.9 (16.6)	
University below a bachelor's degree (11)	43.7 (17.4)	
Bachelor's degree or higher (78)	31.8 (15.3)	
Residence		
Urban (104)	37.6 (18.4)	0.39[b]
Suburban (78)	35.8 (16.9)	
Rural (61)	40.4 (17.8)	
Work status		
Currently working (99)	38.3 (18.2)	0.67[b]
Previously worked while experiencing AF (94)	38.3 (17.4)	
Never worked, or never worked while experiencing AF (50)	35.8 (18.0)	

[a] Two-sided p-value obtained from the two-sample Wilcoxon-Mann Whitney test

[b] P-value obtained from the non-parametric Kruskal-Wallis test

P-values less than 0.05 are considered statistically significant and are bolded.

Observations with missing values are excluded from the analyses.

Cells of 1 are omitted to avoid patient identification

Table 13. Relationship between clinical covariates and the overall score

Characteristic (n)	Overall score Mean (SD)	P-value*
Time of AF diagnosis		
1 year to under 3 years ago (34)	36.7 (21.5)	0.62
3 years to under 5 years ago (61)	38.6 (17.8)	
5 years ago, or more than 5 years ago (146)	37.9 (17.0)	
Type of AF		
Paroxysmal (75)	35.7 (17.5)	0.18
Persistent (34)	36.3 (20.0)	
Unsure (134)	39.3 (17.4)	
Frequency of AF (irregular heart rhythm) episode		
Less than once a year (58)	31.6 (14.8)	**0.008**
Once or a few times a year (55)	34.5 (13.4)	
Once or a few times a month (47)	43.3 (20.6)	
Once or a few times a week (31)	44.1 (20.0)	
Daily or constantly (42)	38.3 (18.3)	
Time of last AF episode		
More than 1 year ago (96)	34.5 (17.1)	**0.0002**
6 months to under 1 year ago (47)	35.0 (15.7)	
1 month to under 6 months ago (37)	34.5 (16.1)	
Within the past month (46)	46.8 (18.6)	
Today or now (17)	47.0 (19.0)	
Symptom severity as of recently		
Minimal to no symptoms (96)	31.1 (15.8)	**<0.0001**
Mild symptoms (60)	41.2 (17.5)	
Moderate symptoms (52)	42.6 (17.4)	
Severe symptoms (32)	43.1 (19.6)	

* P-value obtained from the non-parametric Kruskal-Wallis test

P-values less than 0.05 are considered statistically significant and are bolded.

Observations with missing values are excluded from the analyses.

Since only the Spearman correlation coefficient (r: -0.16, p-value: 0.01), and not the Pearson correlation coefficient (r: -0.11, p-value: 0.08), was significant for age, we anticipate age to exhibit a non-linear but monotonic relationship with the overall score.

4.2.2 Hypothesis testing

The results of all hypothesis tests are summarized in Tables 14, 15, 16, and 17.

Hypothesis I:

Female patients scored significantly higher on “Diagnostic Experience” than male patients (difference in means: 0.66, two-sided p-value: 0.006). The null hypothesis of no difference was rejected at α = 0.05 (Table 14).

Hypothesis II:

“Diagnostic Experience” mean scores were significantly different between patients with paroxysmal AF, persistent AF, and patients who were unsure of their AF type (p-value: 0.02) (Table 14). Pairwise comparisons using the DSCF method found paroxysmal patients to score significantly higher than persistent patients on “Diagnostic Experience (two-sided p-value: 0.04).

Table 14. The effect of gender and AF type on “Diagnostic Experience”

		Diagnostic Experience Factor			
		N Obs	Mean score	SD	P-value
Gender	Male	193	2.58	1.66	0.006[a]
	Female	82	3.24	1.91	
Type of AF	Paroxysmal	83	2.86*	1.77	0.02[b]
	Persistent	39	2.22*,**	1.75	
	Unsure	151	2.88**	1.75	

[a] two-sided p-value obtained from the non-parametric Wilcoxon-Mann Whitney test

[b] p-value obtained from the non-parametric Kruskal-Wallis test

N Obs = Number of observations; SD = standard deviation

*,** statistically significant pairwise comparisons as indicated by the DSCF method

Hypothesis III:

There was no difference in the “Financial Impact” mean scores across areas of residence (p-value: 0.11). Patients residing in rural areas did not score differently on “Financial Impact” than patients residing in urban or suburban areas (Table 15).

Table 15. The effect of residence on “Financial Impact”

		Financial Impact Factor			
		N Obs	Mean score	SD	P-value
Residence	Urban	107	2.52	1.52	0.11[a]
	Suburban	79	2.48	1.44	
	Rural	63	2.91	1.53	

[a] p-value obtained from the non-parametric Kruskal-Wallis test

N Obs = Number of observations; SD = standard deviation

Hypothesis IV:

When comparing the “Social Support” mean scores across the different levels of the “time of AF diagnosis” variable, two levels were excluded because they only had one observation each (“under 6 months ago” and “6 months to under 1 year ago”). The remaining three levels analyzed were “1 year ago to under 3 years ago”, “3 years ago to under 5 years ago”, and “5 years ago or more than 5 years ago”.

The mean scores of “Social Support” decreased as the time since diagnosis became shorter. The highest score was found in patients diagnosed 5 years ago or earlier. Nevertheless, the differences in scores between the three groups were not statistically significant (p-value: 0.66) (Table 16).

Hypothesis V:

Contrary to our hypothesis, female patients scored higher on “Social Support” than male patients. However, this difference was not statistically significant (p-value: 0.87) (Table 16).

Table 16. The effect of gender and time of AF diagnosis on "Social Support"

		Social Support Factor			
		N Obs	Mean score	SD	P-value
Gender	Male	193	2.71	1.29	0.87[a]
	Female	83	2.77	1.39	
Time of diagnosis	1 to under 3 years ago	42	2.65	1.47	0.66[b]
	3 to under 5 years ago	72	2.71	1.35	
	5 years or more than 5 years ago	159	2.77	1.26	

[a] two-sided p-value obtained from the non-parametric Wilcoxon-Mann Whitney test

[b] p-value obtained from the non-parametric Kruskal-Wallis test

N Obs = Number of observations; SD = standard deviation

Hypothesis VI:

As hypothesized, female patients scored significantly higher on "Affect" than male patients (difference in means: 0.54, p-value: 0.02) (Table 17).

Hypothesis VII:

There was no difference in the "Affect" mean scores between patients with paroxysmal AF, persistent AF, and patients unsure of their AF type (p-value: 0.08) (Table 17).

Table 17. The effect of gender and AF type on "Affect"

		Affect Factor			
		N Obs	Mean score	SD	P-value
Gender	Male	193	3.60	1.58	0.02[a]
	Female	83	4.14	1.64	
Type of AF	Paroxysmal	83	3.51	1.64	0.08[b]
	Persistent	39	3.56	1.63	
	Unsure	152	3.97	1.57	

[a] two-sided p-value obtained from the non-parametric Wilcoxon-Mann Whitney test

[b] p-value obtained from the non-parametric Kruskal-Wallis test

N Obs = Number of observations; SD = standard deviation

4.2.3 Statistical regression

There were seven demographic covariates and five clinical covariates in our dataset.

Before specifying all covariates into backward statistical regression, we carefully examined three clinical covariates: frequency of AF episode, time of last AF episode, and recent symptom severity. These variables were designed to reflect participants’ current AF burden. However, they were problematic for patients who no longer experience AF following successful PVA. A few of those patients asked for clarification because they were unsure whether to approach the questions as they would in the past when they still had AF or as of now. We suspect that many patients in a similar situation may have responded in a way that reflected past AF burden. When we examined the responses participants provided, we discovered many incongruent answers that were variants of the following:

> Frequency of AF episode(s) was “every day”; time of last AF episode was “more than 1 year ago”; recent severity of symptoms was “severe”.

Based on the conflicting answers, “frequency of AF episode” and “recent symptom severity” were likely measured with substantial error. “Time of last AF episode” might be, relatively, a more accurate indicator of patients’ current AF burden post-PVA.

As a result, all but the two problematic covariates were considered for statistical regression, including age, gender, racial or ethnic background, marital status, educational attainment, residence, work status, time of AF diagnosis, AF type, and time of last AF episode.

Since age seemed to exhibit a non-linear but monotonic relationship with the overall score, a quadratic term was added to the model to improve linearity.

Table 18 summarizes the predictor selection results from backward, forward, and stepwise regression. The selected model with the smallest AIC statistic was the same for all three methods. This model contained age, age squared (age^2), marital status, educational attainment, and time of last AF episode.

Table 18. Model selection comparing three different statistical regression methods

Selection method	Selection summary	Model with the smallest AIC
Backward (stay significance level: 0.20)	Variables removed: Work status, racial/ethnic background, AF type, gender, time of AF diagnosis, residence	Age, age^2, marital status, educational attainment, time of last AF episode
Forward (entry significance level: 0.50)	Variables entered: Marital status, time of last AF episode, educational attainment, age, age2, gender, residence, time of AF diagnosis, AF type	Age, age^2, marital status, educational attainment, time of last AF episode
Stepwise (entry significance level: 0.20, stay significance level: 0.20)	Variables entered: marital status, time of last AF episode, educational attainment, age, age2	Age, age^2, marital status, educational attainment, time of last AF episode

All predictors initially specified: age, age^2, gender, racial/ethnic background, marital status, educational attainment, residence, work status, time of AF diagnosis, AF type, time of last AF episode

Number of observations used: 237

AIC = Akaike's information criterion

Gender was not selected as a predictor on statistical grounds. However, we included gender in all regression models because it was our primary predictor of interest.

4.2.4 Multivariable linear regression

The multivariable linear regression model of the overall score included the following predictors: age (centered), age^2 (centered then squared), gender, marital status, educational attainment, and time of last AF episode. The regression coefficients, p-values, and 95% confidence intervals are presented in Table 19.

The intercept was interpreted as follows. The average MAP-AF score for a patient that is male, 63.8 years old (the mean age), married, with a bachelor's degree or higher, and last experienced an AF episode more than 1 year ago is 29.8 on a scale from 0 to 100 (95% CI: 25.1 to 34.4).

Age was non-linearly related to the overall MAP-AF score. The addition of a quadratic term improved linearity, model fit, and even changed qualitative conclusions for marital status and educational attainment. Indeed, both the linear and quadratic terms for age were statistically significant and essential to the model (p-value: 0.002, 0.008, respectively).

Table 19. Multivariable linear regression of the overall score on four (or five) predictors

	Full model (n=242) Adjusted R^2: 20%			Omitting "time of last episode" (n=243) Adjusted R^2: 15%		
Predictor	β	P-value	95% CI	β	P-value	95% CI
Intercept	29.8	**<0.001**	25.1, 34.4	31.7	**<0.001**	27.5, 35.8
Age (centered)	-0.43	**0.002**	-0.69, -0.16	-0.43	**0.002**	-0.70, -0.16
Age^2 (centered then squared)	-0.02	**0.008**	-0.04, -0.01	-0.02	**0.008**	-0.04, -0.01
Gender						
Male (Ref)	-	-	-	-	-	-
Female	3.18	0.18	-1.48, 7.85	5.01	**0.04**	0.29, 9.74
Marital status						
Married (Ref)	-	-	-	-	-	-
Widowed or never married	6.63	**0.04**	0.17, 13.1	6.81	**0.04**	0.28, 13.3
Divorced or separated	12.2	**<0.001**	5.92, 18.6	13.0	**<0.001**	6.53, 19.4
Highest education attained						
Bachelor's or higher (Ref)	-	-	-	-	-	-
Some university below Bachelor's	9.44	0.07	-0.95, 19.8	8.20	0.13	-2.49, 18.9
College or trade or apprenticeship	4.47	0.08	-0.58, 9.53	5.13	0.05	-0.06, 10.3
High school or below	6.22	**0.02**	0.85, 11.6	5.91	**0.04**	0.38, 11.4
Time of last AF episode						
More than 1 year ago (Ref)	-	-	-	-	-	-
6 months to under 1 year ago	0.24	0.93	-5.50, 5.98	-	-	-
1 to under 6 months ago	-0.87	0.78	-7.03, 5.30	-	-	-
Within the past month	10.1	**<0.001**	4.38, 15.8	-	-	-
Today or now	11.6	**0.008**	3.00, 20.2	-	-	-

Missing values were excluded by list-wise deletion.

P-values less than 0.05 are considered statistically significant and are bolded

AF = atrial fibrillation; β = regression coefficient; CI = confidence interval; R^2 = coefficient of determination; Ref = Reference group for categorical variables

With each one-year increase in age, the overall score decreased by 0.43 (95% CI: -0.69 to -0.16), adjusting for all other covariates, at the point where age is 63.8 years. Past the mean age, the overall score decreases at an increasingly quicker rate for older individuals. In statistical terms, the adjusted regression coefficient for age decreases by 0.02 with every one-year increase in age (95% CI: -0.04 to -0.01).

Compared to married individuals, individuals not in marriage had a significantly higher overall score. Divorced or separated patients scored 12.2 points higher (p-value <0.001, 95% CI: 5.9 to 18.6), and widowed or never-married patients scored 6.6 points higher than married patients (p-value: 0.04, 95% CI: 0.2 to 13.1), both adjusting for age, gender, educational attainment, and time of last AF episode.

Patients who completed high school or below scored 6.2 points higher than patients with a bachelor's degree or higher (p-value: 0.02, 95% CI: 0.9 to 11.6), adjusting for age, gender, marital status, and time of last AF episode. Patients who attended university (below a bachelor's degree) or who completed college, trade, or an apprenticeship also scored higher than patients with a bachelor's degree or higher. However, these differences were not statistically significant.

Patients who last experienced an AF episode within the past month scored 10.1 points higher than those who last experienced an episode more than a year ago (p-value <0.001, 95% CI: 4.4 to 15.8), adjusting for covariates. Patients who were experiencing an episode the day of completing the questionnaire scored 11.6 points higher than patients whose last episode was more than a year ago (p-value: 0.008, 95% CI: 3.0 to 20.2), adjusting for covariates.

In terms of gender differences, female patients, on average, scored 3.2 points higher than male patients. However, this difference was not statistically significant after adjusting for age, marital status, educational attainment, and time of last episode (p-value: 0.18, 95% CI: -1.5 to 7.9).

Earlier in predictor selection (section 4.2.3), we determined "frequency of AF episode" and "recent symptom severity" to be problematic covariates with likely substantial measurement error. We assumed the variable "time of last AF episode" to be an accurate indicator of the patients' current AF burden. However, "episode" was vaguely defined on the questionnaire as "irregular heart rhythm", and what was considered an "episode" may have varied considerably between patients. When we removed this clinical covariate from the model, the qualitative conclusion for gender changed from non-significance to statistically significant (β: 5.0, p-value: 0.04, 95% CI: 0.29 to 9.74). The qualitative conclusions for other predictors remained the same. The regression coefficients, p-values, and 95% confidence intervals for the model omitting “time of last AF episode” are also included in Table 19.

4.2.5 Model fit and diagnostics

The model with predictors age, age^2, gender, marital status, educational attainment, and time of last episode had an adjusted R^2 of 20.4%. Unmeasured variables such as comorbidities and the effectiveness of treatment (i.e., success of pulmonary vein ablation) may account for a portion of the remaining 79.6% variance unexplained. Better measurement of patients’ AF characteristics, using a validated scale, would likely enhance the adjusted R^2.

The majority of the residuals fell on the diagonal line of the normal Q-Q plot, approximating a normal distribution. No evident funnel shape was found when plotting the residuals against the predicted values. Hence, there was no evidence of heteroscedasticity. The linearity between the overall score and the only continuous predictor, age, was satisfied after including a quadratic term.

We manually checked observations with a large R studentized residual or a large Cook’s D statistic and determined there were no errors in data entry and no observations with an alarming response profile.

We show the changes to the point and interval estimates after sequentially removing influential observations with large DFFITS in Table 20. Briefly, removing influential observations altered the educational landscape of the sample, changing qualitative conclusions for patients who completed college, trade, or apprenticeship and patients who completed high school or below. In addition, the p-value for gender increased from 0.18 to 0.22 after omitting five influential observations, and furthered increased to 0.47 after omitting ten observations. The adjusted R^2 was highest in the model omitting ten observations with the highest DFFITS statistics, at 22%.

Table 20. The effect of omitting influential (high DFFITS) observations on parameter estimates

	All observations (n = 242) Adjusted R^2 = 0.20			Omitting five observations (n = 237) Adjusted R^2 = 0.19			Omitting ten observations (n = 232) Adjusted R^2 = 0.22		
Predictor	β	P-value	95% CI	β	P-value	95% CI	β	P-value	95% CI
Intercept	29.8	<0.001	25.1, 34.4	30.0	<0.001	25.6, 34.5	29.8	<0.001	25.5, 34.1
Age (centered)	-0.43	**0.002**	-0.68, -0.16	-0.39	**0.004**	-0.64, -0.12	-0.45	**<0.001**	-0.70, -0.19
Age^2 (centered then squared)	-0.02	**0.008**	-0.04, -0.01	-0.02	**0.004**	-0.04, -0.01	-0.03	**<0.001**	-0.04, -0.01
Gender									
Male (Ref)	-	-	-	-	-	-	-	-	-
Female	3.18	0.18	-1.48, 7.85	2.87	0.22	-1.69, 7.43	1.62	0.47	-2.83, 6.07
Marital status									
Married (Ref)	-	-	-	-	-	-	-	-	-
Widowed or Never married	6.63	**0.04**	0.17, 13.1	6.90	**0.03**	0.56, 13.2	7.22	**0.02**	1.0, 13.4
Divorced or separated	12.2	**<0.001**	5.92, 18.6	9.98	**0.002**	3.73, 16.2	10.8	**<0.001**	4.79, 16.8
Highest education									
Bachelor’s or higher (Ref)	-	-	-	-	-	-	-	-	-
Some university below Bachelor’s	9.44	0.07	-0.95, 19.8	5.98	0.26	-4.43, 16.4	7.48	0.14	-2.55, 17.5
College or trade	4.47	0.08	-0.58, 9.53	4.38	0.08	-0.50, 9.27	4.87	**0.04**	0.11, 9.63
High school or below	6.22	**0.02**	0.85, 11.6	4.82	0.07	-0.38, 10.0	5.43	**0.04**	0.36, 10.5
Last episode									
More than 1 yr ago (Ref)	-	-	-	-	-	-	-	-	-
6 mo to 1 yr ago	0.24	0.93	-5.50, 5.98	0.33	0.91	-5.23, 5.90	0.23	0.93	-5.16, 5.62
1 to 6 mo ago	-0.87	0.78	-7.03, 5.30	-1.05	0.73	-7.06, 4.96	-1.64	0.58	-7.47, 4.20
Within the past month	10.1	**<0.001**	4.38, 15.8	11.0	**<0.001**	5.55, 16.5	9.85	**<0.001**	4.48, 15.2
Today or now	11.6	**0.008**	3.0, 20.2	10.6	**0.01**	2.13, 19.1	11.7	**0.005**	3.50, 19.9

The initial dataset had 244 observations. Two observations had missing values and were thus excluded from the linear regression models. All ten outliers were identified by the DFFITS statistic. The first five influential points with the largest DFFITS statistic were removed; and the next five were removed.

P-values less than 0.05 are considered statistically significant and are bolded.

AF = atrial fibrillation; β = regression coefficient; CI = confidence interval; R2 = coefficient of determination; Ref = Reference group for categorical variables

4.2.6 Additional models

Tables 21, 22, 23, 24, and 25 present the results from the additional models ran on the five factor scores. All factor scores were rescaled to range from 0 to 100 points.

Major findings are briefly summarized below.

Female patients scored 8.6 points higher than male patients on “Diagnostic Experience”, adjusting for age, marital status, educational attainment, and time of last AF episode (p-value: 0.04, 95% CI: 0.5 to 16.7). Older patients scored lower on “Major Life Events” and “Financial Impact” – a one-year increase in age resulted in a 0.5 point decrease in “Major Life Events” (p-value 0.01, 95% CI: -0.90 to -0.10) and a 0.83 point decrease in “Financial Impact” (p-value <0.001, 95% CI: -1.21 to -0.44), after adjustment.

Divorced or separated patients scored 10.7 points higher on “Affect” (p-value: 0.03, 95% CI: 0.96 to 20.5), 21.1 points higher on “Social Support” (p-value <0.001, 95% CI: 13.4 to 28.9), 11.9 points higher on “Major Life Events” (p-value: 0.01, 95% CI: 2.6 to 21.3), and 13.4 points higher on “Financial Impact” (p-value: 0.004, 95% CI: 4.4 to 22.3) compared to married patients, adjusting for covariates.

Compared to patients last experiencing an AF episode more than a year ago, patients last experiencing an episode within the past month scored 12.3 points higher on “Affect” (p-value: 0.005, 95% CI: 3.8 to 20.9) and patients last experiencing an episode in the past day scored 15.7 points higher on “Financial Impact” (p-value: 0.01, 95% CI: 3.3 to 28.1), after adjusting for covariates. Moreover, compared to patients with a bachelor’s degree or higher, patients with a high school education or below scored 11.5 points higher on “Affect” (p-value: 0.006, 95% CI: 3.4 to 19.6) and 10 points higher on “Financial Impact” (p-value: 0.01, 95% CI: 2.4 to 17.7), after adjustment.

Table 21. Multivariable linear regression of Affect scores

	Affect N = 274 Adjusted R^2: 7.6%		
Predictor	β	P-value	95% CI
Intercept	32.9	**<0.001**	26.3, 39.5
Age (centered)	-0.03	0.86	-0.39, 0.33
Gender			
Male (Ref)	-	-	-
Female	5.96	0.10	-1.20, 13.1
Marital status			
Married (Ref)	-	-	-
Widowed or never married	4.53	0.38	-5.52, 14.6
Divorced or separated	10.7	**0.03**	0.96, 20.5
Highest education attained			
Bachelor’s or higher (Ref)	-	-	-
Some university below Bachelor’s	6.96	0.38	-8.67, 22.6
College or trade or apprenticeship	8.69	**0.03**	1.03, 16.4
High school or below	11.5	**0.006**	3.35, 19.6
Time of last AF episode			
More than 1 year ago (Ref)	-	-	-
6 months to under 1 year ago	0.05	0.99	-8.80, 8.91
1 to under 6 months ago	1.55	0.75	-8.19, 11.3
Within the past month	12.3	**0.005**	3.81, 20.9
Today or now	5.57	0.40	-7.44, 18.6

Missing values were excluded by list-wise deletion.

P-values less than 0.05 are considered statistically significant and are bolded

AF = atrial fibrillation; β = regression coefficient; CI = confidence interval; R^2 = coefficient of determination; Ref = Reference group for categorical variables

Table 22. Multivariable linear regression of Diagnostic Experience scores

	Diagnostic Experience (n=273) Adjusted R^2: 2.6%		
Predictor	β	P-value	95% CI
Intercept	18.6	**<0.001**	11.1, 26.0
Age (centered)	-0.07	0.74	-0.47, 0.34
Gender			
Male (Ref)	-	-	-
Female	8.61	**0.04**	0.54, 16.7
Marital status			
Married (Ref)	-	-	-
Widowed or never married	4.61	0.42	-6.67, 15.9
Divorced or separated	4.74	0.40	-6.37, 15.8
Highest education attained			
Bachelor's or higher (Ref)	-	-	-
Some university below Bachelor's	4.31	0.63	-13.2, 21.9
College or trade or apprenticeship	9.03	**0.04**	0.43, 17.6
High school or below	6.89	0.14	-2.24, 16.0
Time of last AF episode			
More than 1 year ago (Ref)	-	-	-
6 months to under 1 year ago	2.74	0.59	-7.20, 12.7
1 to under 6 months ago	-1.56	0.78	-12.6, 9.46
Within the past month	5.53	0.26	-4.06, 15.1
Today or now	8.44	0.26	-6.19, 23.1

Missing values were excluded by list-wise deletion.

P-values less than 0.05 are considered statistically significant and are bolded

AF = atrial fibrillation; β = regression coefficient; CI = confidence interval; R^2 = coefficient of determination; Ref = Reference group for categorical variables

Table 23. Multivariable linear regression of Social Support scores

	Social Support (n=274) Adjusted R^2: 13%		
Predictor	β	P-value	95% CI
Intercept	21.0	**<0.001**	15.7, 26.2
Age (centered)	-0.25	0.09	-0.54, 0.04
Gender			
Male (Ref)	-	-	-
Female	-2.48	-0.39	-8.15, 3.20
Marital status			
Married (Ref)	-	-	-
Widowed or never married	7.18	0.08	-0.78, 15.1
Divorced or separated	21.1	**<0.001**	13.4, 28.9
Highest education attained			
Bachelor’s or higher (Ref)	-	-	-
Some university below Bachelor’s	13.7	**0.03**	1.34, 26.1
College or trade or apprenticeship	4.90	0.11	-1.17, 11.0
High school or below	5.99	0.07	-0.44, 12.4
Time of last AF episode			
More than 1 year ago (Ref)	-	-	-
6 months to under 1 year ago	-2.07	0.56	-9.08, 4.94
1 to under 6 months ago	-1.24	0.75	-8.96, 6.47
Within the past month	5.68	0.10	-1.09, 12.4
Today or now	8.24	0.12	-2.07, 18.5

Missing values were excluded by list-wise deletion.

P-values less than 0.05 are considered statistically significant and are bolded

AF = atrial fibrillation; β = regression coefficient; CI = confidence interval; R^2 = coefficient of determination; Ref = Reference group for categorical variables

Table 24. Multivariable linear regression of Major Life Events scores

	Major Life Events (n=261) Adjusted R^2: 4.1%		
Predictor	β	P-value	95% CI
Intercept	49.8	**<0.001**	43.0, 56.6
Age (centered)	-0.50	**0.01**	-0.90, -0.10
Age^2 (centered then squared)	-0.03	**0.02**	-0.05, -0.01
Gender			
Male (Ref)	-	-	-
Female	-1.59	0.65	-8.47, 5.28
Marital status			
Married (Ref)	-	-	-
Widowed or never married	3.24	0.51	-6.51, 13.0
Divorced or separated	11.9	**0.01**	2.57, 21.3
Highest education attained			
Bachelor’s or higher (Ref)	-	-	-
Some university below Bachelor’s	2.23	0.77	-12.6, 17.1
College or trade or apprenticeship	0.14	0.97	-7.30, 7.57
High school or below	-0.71	0.86	-8.66, 7.23
Time of last AF episode			
More than 1 year ago (Ref)	-	-	-
6 months to under 1 year ago	3.51	0.41	-4.92, 11.9
1 to under 6 months ago	0.22	0.96	-9.02, 9.47
Within the past month	8.77	**0.04**	0.29, 17.2
Today or now	12.0	0.07	-0.86, 24.9

Missing values were excluded by list-wise deletion.

P-values less than 0.05 are considered statistically significant and are bolded

AF = atrial fibrillation; β = regression coefficient; CI = confidence interval; R^2 = coefficient of determination; Ref = Reference group for categorical variables

Table 25. Multivariable linear regression of Financial Impact scores

	Financial Impact (n=248) Adjusted R^2: 16.9%		
Predictor	β	P-value	95% CI
Intercept	19.9	**<0.001**	13.4, 26.5
Age (centered)	-0.83	**<0.001**	-1.21, -0.44
Age^2 (centered then squared)	-0.04	**0.001**	-0.06, -0.01
Gender			
Male (Ref)	-	-	-
Female	4.93	0.14	-1.70, 11.6
Marital status			
Married (Ref)	-	-	-
Widowed or never married	11.1	**0.02**	1.85, 20.4
Divorced or separated	13.4	**0.004**	4.42, 22.3
Highest education attained			
Bachelor’s or higher (Ref)	-	-	-
Some university below Bachelor’s	1.95	0.80	-12.9, 16.8
College or trade or apprenticeship	2.91	0.42	-4.26, 10.1
High school or below	10.0	**0.01**	2.38, 17.7
Time of last AF episode			
More than 1 year ago (Ref)	-	-	-
6 months to under 1 year ago	-1.96	0.64	-10.2, 6.27
1 to under 6 months ago	-2.29	0.61	-11.1, 6.48
Within the past month	5.85	0.15	-2.15, 13.8
Today or now	15.7	**0.01**	3.34, 28.1

Missing values were excluded by list-wise deletion.

P-values less than 0.05 are considered statistically significant and are bolded

AF = atrial fibrillation; β = regression coefficient; CI = confidence interval; R^2 = coefficient of determination; Ref = Reference group for categorical variables

4.3 References

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Chapter 5

5 Discussion and conclusion

The summary and interpretation of the results are presented in this chapter. These include results from questionnaire development (Chapter 3) and analyses of the questionnaire scores (Chapter 4). We will also discuss the implications of the results, the strengths, and the limitations of this thesis. We conclude with suggestions for future research.

5.1 Summary of results

This thesis was built upon previous qualitative research. From focus groups with arrhythmia patients in Canada, AF was found to impact patients' mental wellbeing, social relationships, livelihood, and finances. Existing (HR)QoL questionnaires do not adequately measure the AF impact. Most questionnaires were developed to assess QoL changes before and after treatment. Therefore, their primary focus is on physical functioning, symptoms, ability to perform daily activities, and affect. This led to our proposal to develop a new questionnaire to comprehensively understand the effects of AF along the patient journey – covering broader life impacts and challenges surrounding diagnosis (a central theme of the AF patient experience).

5.1.1 Results of questionnaire development

5.1.1.1 Construct of interest

HRQoL questionnaires typically take a snapshot of the patient's physical functioning, symptoms, and psychological wellbeing over a four-week period. Validated ones are suitable for evaluating the effects of interventions during the treatment phase. Beyond this need to evaluate treatment efficacy, there is little interest in understanding QoL during symptom onset and how the disease affects multiple aspects of patients' wellbeing. This is where the MAP-AF differs from existing instruments as a patient-reported measure that addresses these gaps and recognizes the dynamics of the patient journey. The most prominent concerns of patients fluctuate over the clinical course of AF.

While the MAP-AF can be considered a measure of patient outcomes, one domain (“Diagnostic Experience”) is dedicated to measuring patients’ experiences with medical care. The international PaRIS survey, developed for patients with chronic conditions, similarly measures both important outcomes and experiences of health care in one instrument[1].

“Financial Impact” and “Social Support” are two domains of the MAP-AF that are typically considered non-health-related. Although non-health-related aspects of wellbeing are less likely to change due to medical interventions, they are nevertheless affected by disease and experienced by patients. The LupusPRO questionnaire developed by Jolly et al. (2012) measures both health-related and non-health-related aspects of QoL of systemic lupus erythematosus patients[2]. A holistic understanding of the impact of disease helps researchers and clinicians gain insight into patient needs and improve healthcare services[2].

5.1.1.2 Factor structure and internal consistency

After exploratory factor analysis and item reduction, the MAP-AF questionnaire had 16 items and five domains: “Affect”, “Social Support”, “Financial Impact”, “Major Life Events”, and “Diagnostic Experience”. Considering we did not have a priori hypotheses about the number of factors underlying the items, the factor solution came out unexpectedly clean. Results of EFA can often be quite messy, conflicting, and difficult to interpret, especially when sample sizes are small and loadings are weak[3].

When the threshold factor loading was set to 0.35, there were very few cross-loading items: two in the 5-factor solution, one in the 6-factor solution, and none in the 7-factor solution. Furthermore, the same factor solutions emerged even under different data conditions. The rotated factor loadings were robust to the factor extraction methods (ULS vs. iPAF), rotation methods (promax vs. direct oblimin), missing value imputation (CCA vs. EM), and log transformation of one skewed item (i.e., item 25). Based on parsimony and interpretability, the 6-factor structure was initially chosen as the solution for further scrutiny using measurement properties like the item-total correlation, Cronbach’s alpha, and inter-factor correlation.

The final MAP-AF had five domains because one factor (original factor 6) was deemed problematic. The three items in the factor were difficult to interpret (i.e., does not appear to reflect one unifying concept) and had low item-total correlations. The factor itself had poor internal consistency (0.70 to 0.95 considered good internal consistency)[4] and a low correlation with the other five factors. We also failed to redistribute the three items to the other established factors, ultimately resulting in our decision to remove the items from the final questionnaire.

For the remaining five factors, all except for “Major Life Events” had good internal consistency. The “Major Life Events” factor had a borderline Cronbach’s alpha of 0.68. Despite having only two items, the “Diagnostic Experience” factor was stable and had a high alpha of 0.78.

The result of EFA is sample-dependent, and one of the sample characteristics that may affect EFA results is where patients are on the patient journey. Our study recruited patients who had a pulmonary vein ablation – most patients in our sample identified themselves to be in the treatment and beyond phase, and many were “cured”.

While our post-PVA sample provided us with an overview of the patient journey, we recognize that the factor loadings and the factor structure of the MAP-AF may be different had we used a different patient sample. For example, if we administered the 35-item MAP-AF to a sample of recently diagnosed patients, the factor structure we obtain may be quite different.

5.1.2 Results of questionnaire scores

5.1.2.1 Descriptive analyses of questionnaire scores

The overall MAP-AF scores were not high for our sample – the mean was 37.8 points out of 100. Likewise, “Social Support”, “Financial Impact”, and “Diagnostic Experiences” had mean scores less than 3 on a 7-point Likert scale. “Affect” had a mean score of 3.76, and “Major Life Events” had the highest mean score of 4.12. The result is likely a consequence of a sample composed of mostly “cured” patients who no longer experience episodes and symptoms of AF. Over 80% of our patients were diagnosed more than three years ago, 41% last experienced an episode more than a year ago, and 42% experienced minimal to no symptoms recently. The perceived impact of AF may be lesser for individuals who no longer experience the condition than those who are actively experiencing the disease.

During sample selection, we recruited only patients who had a pulmonary vein ablation. Patients typically receive such a procedure if they remain symptomatic after rate and rhythm medications. By recruiting PVA patients, we would reduce the inclusion of asymptomatic patients, who are more likely to be incidentally diagnosed (and hence ill-suited for answering diagnosis-related questions). Unfortunately, we were unable to exclude all incidentally diagnosed individuals with this eligibility criteria. From patient comments, we found that several were diagnosed when presented to the emergency department for other reasons or during routine physical examinations. The inclusion of these patients likely lowered the “Diagnostic Experiences” mean scores since they would have selected “strongly disagree” for the items when in reality, the most suitable response was “non-applicable”.

5.1.2.2 Multivariable linear regression of the overall score

The total score on the MAP-AF reflects the extent to which patients have been affected by AF across all domains. Multivariable linear regression found age, marital status, educational attainment, and time of last AF episode to be associated with the overall score. Generally, patients were more impacted by AF if they were younger, divorced or separated, had lower education, or experienced more recent episodes of AF. Randolph et al. (2016) conducted similar analyses using the Atrial Fibrillation Effect on Quality of Life (AFEQT) scale and found female sex, younger age, new-onset AF, higher heart rate, and the presence of comorbidities to be significantly associated with a reduced QoL[5]. Another study also found sex differences in QoL improvements over time, in which female patients showed less improvement in AFEQT scores over 1 year than male patients[6].

Based on previous literature that found women to be more symptomatic yet less likely to be offered an ablation, we hypothesized that there would be gender differences in the AF impact[7,8]. Contrary to our expectations and different from other QoL studies, gender was not significantly correlated with the overall score in this study. Nevertheless, when time of last AF episode was tentatively excluded from the model, the effect of gender became significant (p-value went from 0.18 to 0.036). The qualitative conclusions for the other covariates remained the same. We speculate that the effect of gender on AF impact was likely confounded by disease severity and disease burden. Presumably, female patients were more impacted by AF than male patients because they experienced more frequent episodes and more severe symptoms even after pulmonary vein ablation. When disease severity was accounted for using the variable “time of last episode”, gender was no longer significant.

The four variables (age, marital status, educational attainment, and time of last AF episode) explained 20.4% of the variance of the overall score. The remaining unexplained variance could be attributed to comorbidities, treatment effectiveness, and other AF characteristics. Future studies should include valid and accurate measurements of the above variables (e.g., using validated scales to assess AF symptom severity).

5.1.2.3 Predictors

This section discusses the relationships between selected predictors and the five MAP-AF domains based on the additional analyses.

First, our results supported previous research that found women to have a more difficult time trying to get a diagnosis for AF. Scores on “Diagnostic Experience” were higher for females than males after adjusting for all covariates. Several patients also provided personal anecdotes in the comments describing how a few physicians they encountered were dismissive of their symptoms and concerns, which in many cases delayed their diagnosis or treatment and affected their care. Empathetic care was extremely important in shaping the patient experience.

Second, divorced or separated patients had the highest scores on all five domains compared to other marital statuses. Married patients were least impacted by AF; widowed or single patients consistently did better than divorced or separated patients. A study investigating the effect of divorce on mental and physical health, as measured by the Short Form 36 (SF-36), found divorce to significantly impact the wellbeing of both men and women[9].

5.2 Implications

Good measurement development practices collect qualitative data directly from the target population to generate candidate items for psychometric analysis. The MAP-AF questionnaire that assesses the impact of AF on the lives of Canadian patients was developed based on focus groups and interviews conducted across Canadian provinces. Two other PROMs developed in Canada are the University of Toronto Atrial Fibrillation Symptom Severity scale (AFSS) and the Atrial Fibrillation Effect on Quality-of-Life (AFEQT). The AFEQT is a HRQoL questionnaire developed in both the US and Canada that assesses AF symptoms, patients' ability to perform daily activities, treatment concerns, and treatment satisfaction. It has been used in clinical trials to measure QoL changes due to interventions[10,11,12]. The MAP-AF questionnaire is unlike typical HRQoL measures, as patient experiences and the impact of AF on broader realms of wellbeing were measured. Our construct of interest is most similar to the Organisation for Economic Co-operation and Development (OECD) PaRIS survey for chronic disease patients, where both patient experiences and patient outcomes are measured in one instrument[1]. Despite nuances in the construct measured, the AF impact that we assessed shares similar predictors with (HR)QoL.

Our study demonstrated a statistically significant gender bias in AF diagnoses. Previous reports of this phenomenon were from qualitative interviews[13], and we were able to support this observation with quantitative evidence. In line with results from the focus groups and patient journey maps, female patients in our study more frequently felt dismissed when communicating symptoms to physicians and found the diagnostic process to be more difficult than male patients. Unfortunately, women were also less likely to be offered or receive an ablation than men during the treatment phase[7,8]. The literature consistently reports women to experience greater symptom severity and frequency[7,8], yet they are more likely than men to experience difficulties and delays in diagnosis and treatment. One of the potential reasons for this observation is the perceived bias among healthcare providers[14]. A study found that women experiencing syncope, one of the possible symptoms of AF, were often dismissed by Emergency Medical Services as a symptom of feminine conditions like menstruation, menopause, or pregnancy[14]. Further investigation into the factors contributing to gender differences in the patient experience is warranted to achieve equitable and effective healthcare services.

5.3 Strengths and limitations

This study has several strengths, including the performance of sensitivity analyses, additional exploratory analyses, collecting patient feedback on the questionnaire, high completion rate, and survey features that allow a better understanding of missing data.

First, the results of exploratory factor analysis were robust to various data conditions. By performing sensitivity analyses, we were able to see whether conclusions would change under varying circumstances and justify our decisions.

Although the MAP-AF still needs to undergo extensive validation before its scores can be meaningfully analyzed, we conducted many additional analyses that functioned to generate hypotheses for future research.

The textbox included at the end of the online questionnaire also generated lots of qualitative data. While we did not conduct a formal analysis of the data, the comments provided by patients helped inform some of the limitations and future directions of our study.

The MAP-AF questionnaires had a high completion rate of 87% and few missing data. We show that web administration of surveys is feasible in our age demographic, which had a mean of 63.8 years and a max of 83 years. The skip patterns, N/A options, and the comment box features allowed us to categorize and better understand missing data.

A thorough investigation of missing values was done for the 24 items prior to EFA (eleven highly irrelevant items were removed). Of 277 who took the questionnaire, 14 (5.1%) individuals did not answer at least one of the 24 items. Patients' feedback suggests some of the questions did not apply to their circumstances. Patients commented on how the questionnaire made assumptions about their experiences and how some questions were difficult to answer because they no longer have AF. Some patients indicated that they did not experience symptoms before they were diagnosed, rendering them unable to answer the diagnosis-related questions. There were only four questions among the 24 items with a N/A option. There were no missing values for these four items – missing values only occurred where the N/A option was not available. Three of the 14 individuals with missing values have used the N/A option at least once. We speculate that if a N/A option existed for the items they missed, they would have selected it instead. For the remaining 11 individuals, the possible reasons for missingness were provided in the results. Briefly, these include suboptimal question wording, the nearby presence of family members, forgetfulness, and again, the lack of a N/A option when the question did not apply.

There are also limitations to this study. These include sample selection, possible recall bias, suboptimal design of clinical questions, lack of consideration for comorbidities, and the effect of the current COVID-19 pandemic on social-related questions.

First, our sample is a convenience non-probability sample of 500 consecutive post-PVA patients. Some patients were diagnosed a long time ago and no longer experienced AF. Over half of the questionnaire respondents were diagnosed more than 5 years ago, and another 30% diagnosed more than 3 years ago. Forty-one percent last experienced an episode more than a year ago, and 42% recently experienced minimal to no symptoms. Moreover, some incidentally diagnosed patients were included in our sample. For these patients, some questions were difficult to answer.

There might have been substantial recall bias for patients who were either diagnosed a long time ago or no longer experienced AF. It is also possible that the recall of memories may have depended on the success of the ablation (or other treatments).

Next, the following questions were used to ascertain the clinical characteristics of our patients:

> “how often do you have an episode of atrial fibrillation”

“when was the last time you had an episode of atrial fibrillation”

“how would you describe the severity of your symptoms as of recently”

These questions were particularly confusing for patients who no longer had atrial fibrillation. We thought these patients would have responded to the above questions with “less than one episode a year”, “last episode was more than 1 year ago”, and “minimal to no symptoms as of recently”. However, we found the questions to be suboptimally worded, such that some patients responded in a way that reflected their past AF burden when they still had AF. We thus anticipate some misclassification to be present and a greater proportion of patients with a lower AF severity and burden. In the future, a question that clarifies whether respondents are still in atrial fibrillation or not may remedy this problem. Respondents could then be directed to questions appropriate to them. Alternatively, validated symptom scales could be used to capture the clinical profile of our patients more accurately.

In addition to the above limitations, some patients had multiple arrhythmias and comorbidities that made it difficult to attribute their reduced wellbeing to a particular source like AF. For example, patients with both AF and atrial flutter found it difficult to discern the effects between the two arrhythmias. Some of the other comorbidities that were present in our sample include cardiomyopathy, supraventricular tachycardia, chronic obstructive pulmonary disease, obstructive sleep apnea, and erectile dysfunction. A few patients stated that their comorbidities had a greater impact on their life than their AF. Comorbidities likely explain a portion of the variance in the MAP-AF scores, but they were not measured in this study.

Questionnaire data was collected during the COVID-19 pandemic when lockdowns and social distancing were imposed. The focus groups and patient journey mapping were conducted during pre-pandemic times. The pandemic may have skewed responses to questions about patients' social relationships and social life satisfaction. Some, not all, patients answered as if the pandemic did not exist (i.e., what life would be like in pre-pandemic times).

Last, we did not factor analyze employment-related questions because they were not applicable to greater than 10% of our patient population. Our next steps would be to conduct a separate EFA on all 35 items using a smaller subset of 159 participants to whom employment-related questions applied.

5.4 Improvements of the MAP-AF

In addition to addressing the limitations described above, we also summarize patients' feedback and suggestions for improvement.

In the comments section, many patients described their personal experiences and mentioned concerns unaddressed by the MAP-AF.

First, the MAP-AF did not adequately explore the stress of the treatment phase, which primarily comes from negative experiences with the healthcare system and the side effects or ineffectiveness of treatment. Many patients mentioned the long waitlist for an ablation – a patient described getting cardioverted seven times while waiting for an ablation. These patients signed up for an ablation in many cases because the side effects of medications were intolerable. For example, the physical functioning and energy levels of some patients deteriorated, and many were unable to pursue their desired lifestyle. The difficulty of getting an ablation, an appointment, or a referral can greatly delay treatment and worsen prognosis. Patients also mentioned the inconsistent approaches to management from the many physicians they see and inconsistent experiences in emergency departments. However, not all patients' experiences were negative. Several patients expressed that the empathetic and compassionate care they received outweighed any costs or inconveniences associated with their condition and treatment. This further reinforces the importance of considering both experiences with practical aspects of care (i.e., patient experiences) and effects of care (i.e., patient outcomes).

Second, patients described additional effects of AF that were not outlined in the MAP-AF. These included the effect of AF on their sleep and their fulfillment of their sexual lives. Most frequently mentioned was the inability to perform their desired level of physical activity. This significantly affected the patient's health, autonomy (e.g., unable to drive a car and go shopping alone), and social life. Even for patients who had a successful ablation and were able to return to an active lifestyle, they worried about whether AF would return due to them being active again.

In general, there was considerable uncertainty surrounding AF, which produced anxiety for many patients.

5.5 Conclusion and future directions

The MAP-AF questionnaire was developed and initially validated in a sample of post-pulmonary vein ablation patients with AF in London, Ontario. The questionnaire contains 16 items and five domains: “Affect”, “Social Support”, “Major Life Events”, “Financial Impact”, “Diagnostic Experience”. Younger age, being divorced or separated, having a lower education, and experiencing more recent episodes were associated with a more negative patient journey. While the effect of gender on overall AF impact appears to be confounded by the time of last AF episode, gender was nevertheless an important predictor for the patient’s diagnostic experience. Confirming previous qualitative findings, female patients were more likely to have their symptoms dismissed and report having a more difficult time trying to get a diagnosis than male patients. Healthcare professionals should increase their awareness of the challenges associated with symptom onset and their own affective responses to patients presenting with palpitations and other AF symptoms. Timely diagnosis and treatment initiation are goals shared by both patients and physicians.

Our study demonstrates the importance of studying both patient experiences and outcomes of care. More research is needed to understand the lived experiences of patients with AF – a condition that is associated with a lot of uncertainties. The next steps for this study include revising the MAP-AF based on patient feedback (e.g., expanding the questionnaire to cover employment effects and treatment impacts) and administer the new questionnaire in a separate sample to obtain more evidence supporting the validity of the measure to assess the AF patient experiences and promote better AF management.

5.6 References

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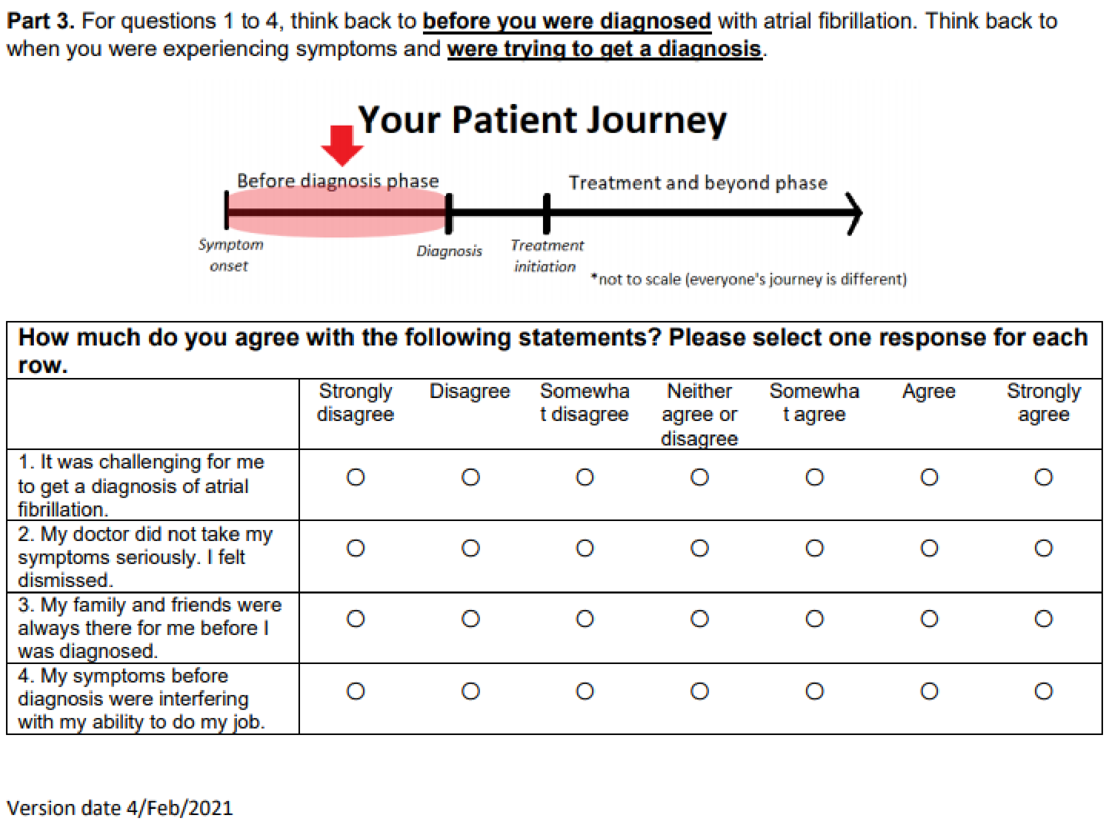
Appendices

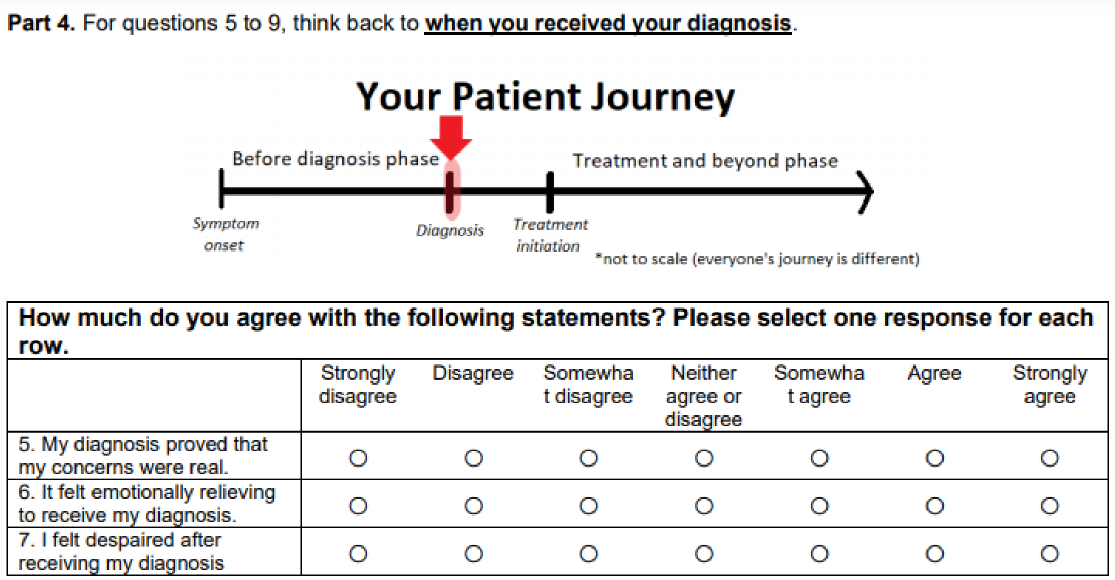
Appendix A: Preliminary 35-item MAP-AF questionnaire



Part 3. For questions 1 to 4, think back to **before you were diagnosed** with atrial fibrillation. Think back to when you were experiencing symptoms and **were trying to get a diagnosis**.

How much do you agree with the following statements? Please select one response for each row.							
	Strongly disagree	Disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Agree	Strongly agree
1. It was challenging for me to get a diagnosis of atrial fibrillation.	○	○	○	○	○	○	○
2. My doctor did not take my symptoms seriously. I felt dismissed.	○	○	○	○	○	○	○
3. My family and friends were always there for me before I was diagnosed.	○	○	○	○	○	○	○
4. My symptoms before diagnosis were interfering with my ability to do my job.	○	○	○	○	○	○	○

Version date 4/Feb/2021

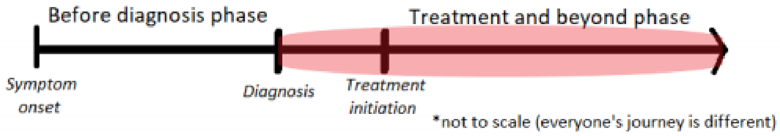


Part 4. For questions 5 to 9, think back to **when you received your diagnosis**.

How much do you agree with the following statements? Please select one response for each row.							
	Strongly disagree	Disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Agree	Strongly agree
5. My diagnosis proved that my concerns were real.	○	○	○	○	○	○	○
6. It felt emotionally relieving to receive my diagnosis.	○	○	○	○	○	○	○
7. I felt despaired after receiving my diagnosis	○	○	○	○	○	○	○

Part 5. For questions 8 to 18, think about how atrial fibrillation has been impacting your life **after you were diagnosed**.

Your Patient Journey



How much do you agree with the following statements as they relate to your atrial fibrillation? Please select one response for each row.							
	Strongly disagree	Disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Agree	Strongly agree
8. Because of my symptoms, I cannot continue to work (or stay in school) like I used to. For example, I had to work part time or retire early because of my atrial fibrillation.	○	○	○	○	○	○	○
9. My symptoms negatively impacted my work (or school) performance.	○	○	○	○	○	○	○
10. My condition negatively impacted the relationships I had with people at work or school (including co-workers, boss, peers, teachers).	○	○	○	○	○	○	○
11. I had to change my career path because of my atrial fibrillation. For example, starting a new business or foregoing advancement	○	○	○	○	○	○	○
12. My employer (or school) was supportive and accommodating with regards to my atrial fibrillation.	○	○	○	○	○	○	○
13. Having AF prompted me to rethink my life goals.	○	○	○	○	○	○	○
14. As time went on, my family and friends became less supportive. For example, my family or friends expected me to be over it by now.	○	○	○	○	○	○	○
15. My atrial fibrillation affected my romantic life (dating life, relationship with partner)	○	○	○	○	○	○	○

Part 6. This part asks about **<u>your feelings in general</u>**. How much were you **<u>bothered</u>** by the following **<u>as they occurred</u>** in your atrial fibrillation journey?

In general, how much were you bothered by the following? Please select one response for each row.

	Not at all bothered	Hardly bothered	Slightly bothered	Moderately bothered	Quite bothered	Very bothered	Extremely bothered	N/A
16. The cost of ambulance services for emergencies related to my atrial fibrillation	○	○	○	○	○	○	○	○
17. Having to miss work (for example, taking a day off) when I experienced symptoms and felt unwell.	○	○	○	○	○	○	○	○
18. Taking a day off or using a vacation day to attend medical appointments and examinations	○	○	○	○	○	○	○	○
19. The costs related my clinic visits. For example, travelling to medical centers for appointments and paying for transportation, parking, and/or accommodations.	○	○	○	○	○	○	○	○
20. My ability to get insurance because this is a pre-existing condition. For example, travel insurance, medical insurance…	○	○	○	○	○	○	○	○
21. The lifestyle changes that I had to make because of my atrial fibrillation.	○	○	○	○	○	○	○	○

Part 7. For questions 22 to 35, think about your life right now. How have you felt over the **<u>past week</u>**?

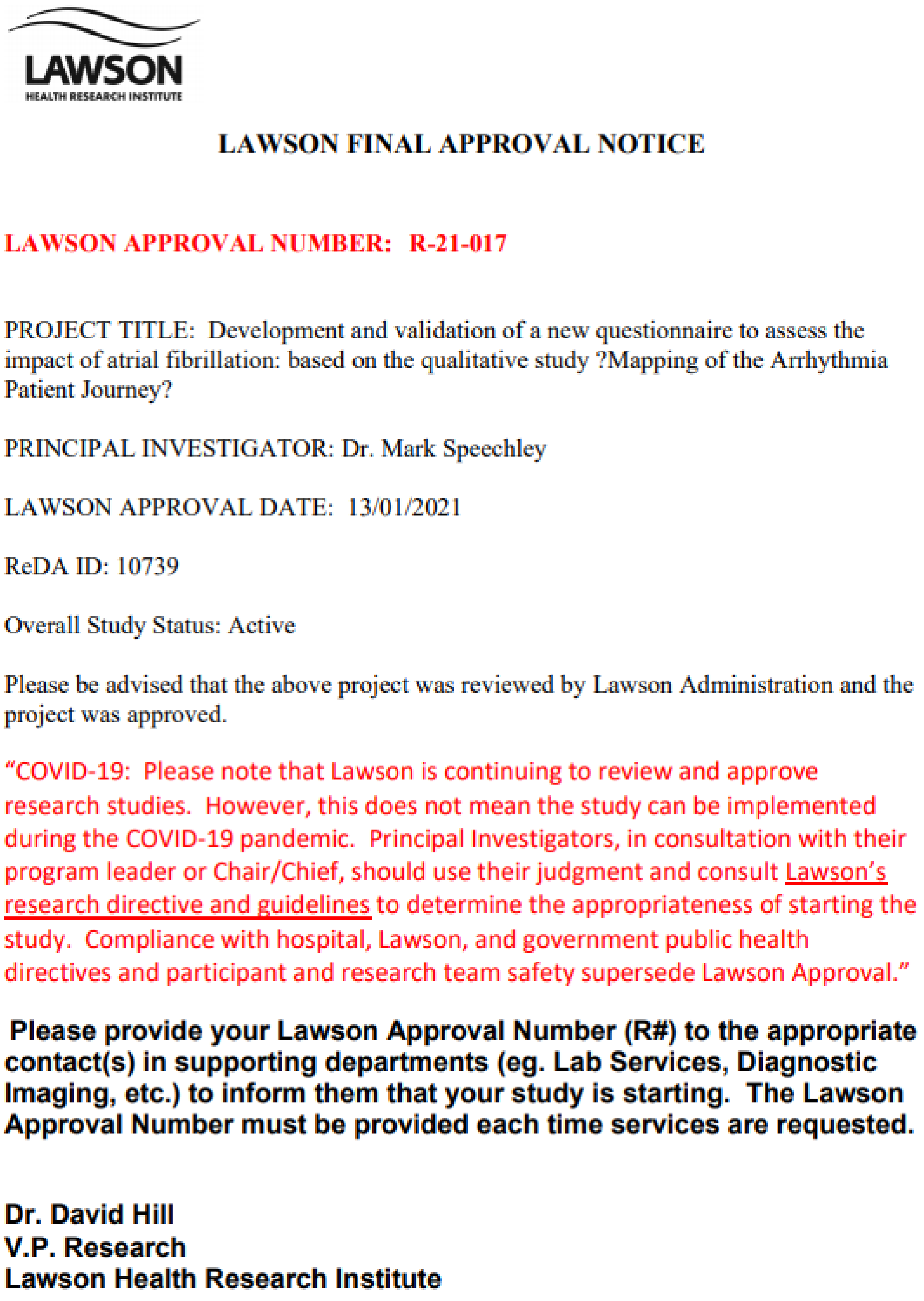
How much do you agree with the following statements? Please select one response for each row.

	Strongly disagree	Disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Agree	Strongly agree
22. I felt satisfied with my social life.	○	○	○	○	○	○	○
23. I received the social support or engagement that I need.	○	○	○	○	○	○	○
24. I isolated or distanced myself from others.	○	○	○	○	○	○	○
25. My family and friends did not want to be around me.	○	○	○	○	○	○	○
26. I felt lonely.	○	○	○	○	○	○	○
27. I worried that I would experience symptoms or episodes of atrial fibrillation again.	○	○	○	○	○	○	○
28. I felt hopeless about my health	○	○	○	○	○	○	○

29. I felt optimistic about my future	○	○	○	○	○	○	○	
30. I felt grateful	○	○	○	○	○	○	○	
31. I felt depressed	○	○	○	○	○	○	○	
32. I felt anxious	○	○	○	○	○	○	○	
	Strongly disagree	Disagree	Somewhat disagree	Neither agree or disagree	Somewhat agree	Agree	Strongly agree	N/A
33. I was bothered by the cost of my atrial fibrillation. (consider all costs)	○	○	○	○	○	○	○	○
34. I worried about my future finances because of the costs related to my atrial fibrillation	○	○	○	○	○	○	○	○
35. My atrial fibrillation continued to impact my work life (or school life)	○	○	○	○	○	○	○	○

Part 8. Please specify if there are other concerns resulting from your atrial fibrillation that were unaddressed by this questionnaire (optional):

Appendix B: Ethics approval letters



LAWSON
HEALTH RESEARCH INSTITUTE

LAWSON FINAL APPROVAL NOTICE

LAWSON APPROVAL NUMBER: R-21-017

PROJECT TITLE: Development and validation of a new questionnaire to assess the impact of atrial fibrillation: based on the qualitative study ?Mapping of the Arrhythmia Patient Journey?

PRINCIPAL INVESTIGATOR: Dr. Mark Speechley

LAWSON APPROVAL DATE: 13/01/2021

ReDA ID: 10739

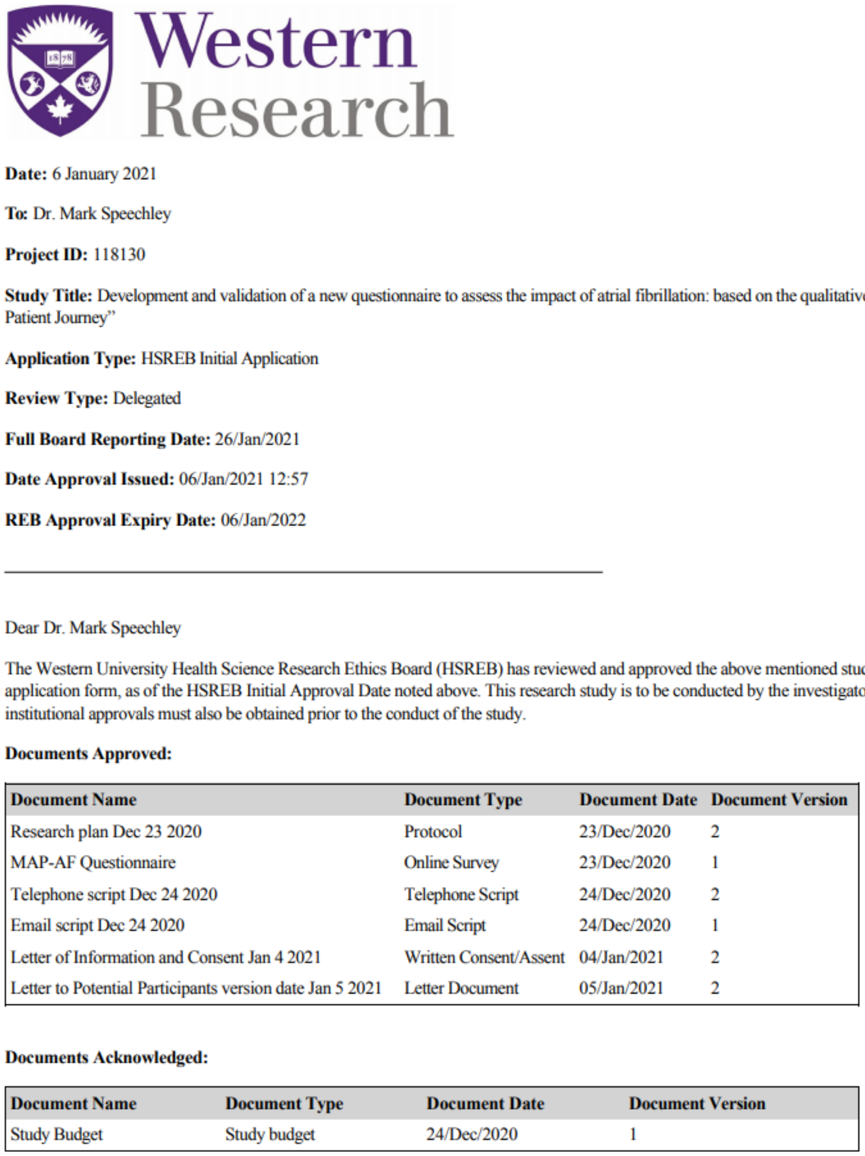
Overall Study Status: Active

Please be advised that the above project was reviewed by Lawson Administration and the project was approved.

"COVID-19: Please note that Lawson is continuing to review and approve research studies. However, this does not mean the study can be implemented during the COVID-19 pandemic. Principal Investigators, in consultation with their program leader or Chair/Chief, should use their judgment and consult Lawson's research directive and guidelines to determine the appropriateness of starting the study. Compliance with hospital, Lawson, and government public health directives and participant and research team safety supersede Lawson Approval."

Please provide your Lawson Approval Number (R#) to the appropriate contact(s) in supporting departments (eg. Lab Services, Diagnostic Imaging, etc.) to inform them that your study is starting. The Lawson Approval Number must be provided each time services are requested.

Dr. David Hill
V.P. Research
Lawson Health Research Institute



Date: 6 January 2021

To: Dr. Mark Speechley

Project ID: 118130

Study Title: Development and validation of a new questionnaire to assess the impact of atrial fibrillation: based on the qualitative study "Mapping of the Arrhythmia Patient Journey"

Application Type: HSREB Initial Application

Review Type: Delegated

Full Board Reporting Date: 26/Jan/2021

Date Approval Issued: 06/Jan/2021 12:57

REB Approval Expiry Date: 06/Jan/2022

Dear Dr. Mark Speechley

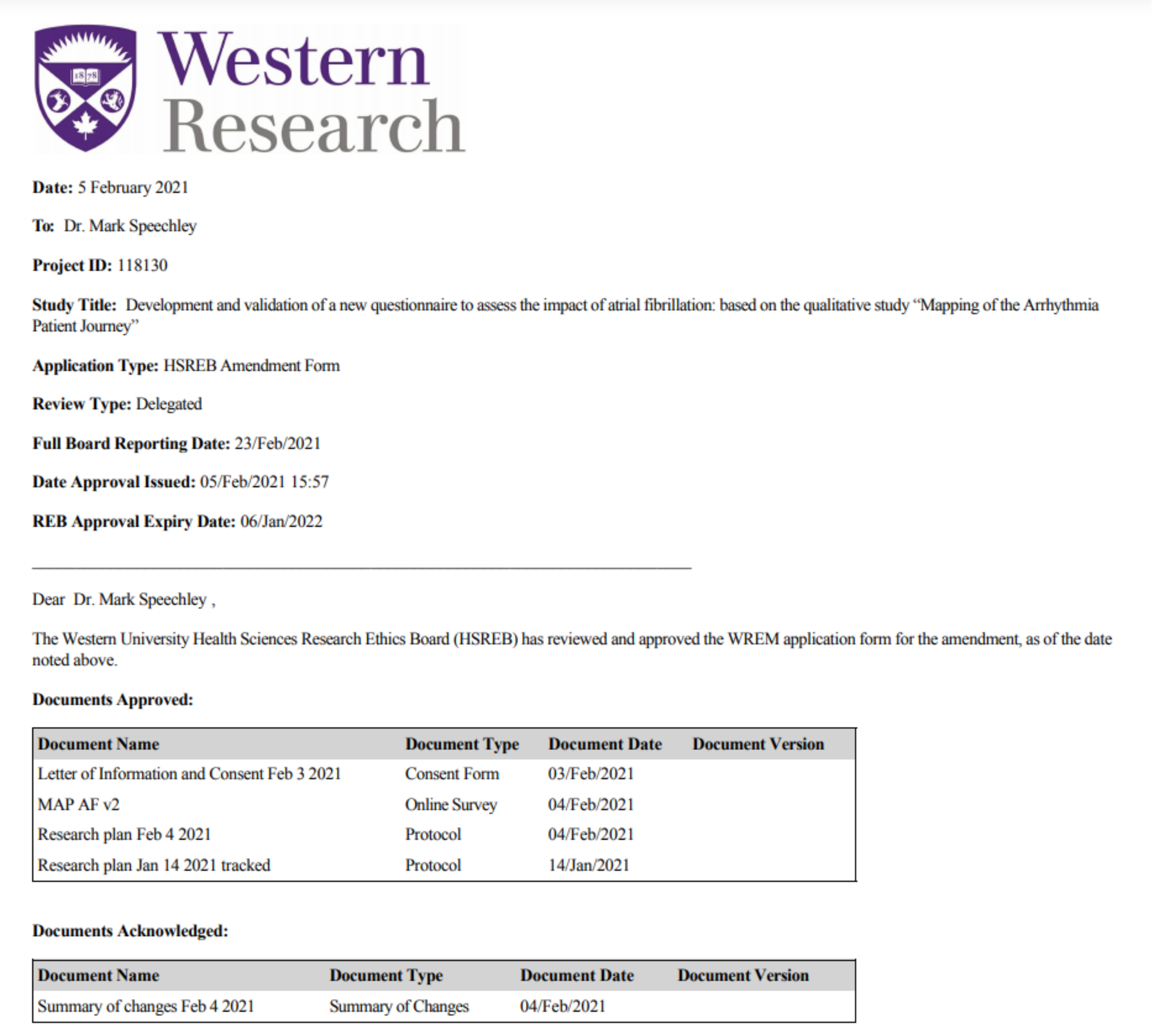
The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above mentioned study as described in the WREM application form, as of the HSREB Initial Approval Date noted above. This research study is to be conducted by the investigator noted above. All other required institutional approvals must also be obtained prior to the conduct of the study.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
Research plan Dec 23 2020	Protocol	23/Dec/2020	2
MAP-AF Questionnaire	Online Survey	23/Dec/2020	1
Telephone script Dec 24 2020	Telephone Script	24/Dec/2020	2
Email script Dec 24 2020	Email Script	24/Dec/2020	1
Letter of Information and Consent Jan 4 2021	Written Consent/Assent	04/Jan/2021	2
Letter to Potential Participants version date Jan 5 2021	Letter Document	05/Jan/2021	2

Documents Acknowledged:

Document Name	Document Type	Document Date	Document Version
Study Budget	Study budget	24/Dec/2020	1



Western Research

Date: 5 February 2021

To: Dr. Mark Speechley

Project ID: 118130

Study Title: Development and validation of a new questionnaire to assess the impact of atrial fibrillation: based on the qualitative study "Mapping of the Arrhythmia Patient Journey"

Application Type: HSREB Amendment Form

Review Type: Delegated

Full Board Reporting Date: 23/Feb/2021

Date Approval Issued: 05/Feb/2021 15:57

REB Approval Expiry Date: 06/Jan/2022

Dear Dr. Mark Speechley ,

The Western University Health Sciences Research Ethics Board (HSREB) has reviewed and approved the WREM application form for the amendment, as of the date noted above.

Documents Approved:

Document Name	Document Type	Document Date	Document Version
Letter of Information and Consent Feb 3 2021	Consent Form	03/Feb/2021	
MAP AF v2	Online Survey	04/Feb/2021	
Research plan Feb 4 2021	Protocol	04/Feb/2021	
Research plan Jan 14 2021 tracked	Protocol	14/Jan/2021	

Documents Acknowledged:

Document Name	Document Type	Document Date	Document Version
Summary of changes Feb 4 2021	Summary of Changes	04/Feb/2021	

Appendix C: Demographic and clinical questions

1. What is your age?

Please enter a value

2. What is your gender?

I identify as _______ (free text entry)

3. Please specify your racial or ethnic background
   - ☐ Black (African, Caribbean, North American)
   - ☐ East Asian (Chinese, Japanese, Korea)
   - ☐ Southeast Asian (Filipino, Vietnamese)
   - ☐ Métis, First Nations, Inuit, or other Indigenous ancestry
   - ☐ Latin American
   - ☐ Middle Eastern (Egyptian, Lebanese, Iranian)
   - ☐ White (European, North American)
   - ☐ South Asian (Indian, Pakistani, Bangladeshi, Sri Lankan)
   - ☐ Other race or ethnicity: please specify _________

4. What is your marital status?
   - ☐ Married
   - ☐ Widowed
   - ☐ Divorced
   - ☐ Separated
   - ☐ Never married

5. What is the highest degree or level of school you have completed? If currently enrolled, highest degree received.
   - ☐ No certificate, diploma, or degree
   - ☐ High school diploma
   - ☐ Apprenticeship or other trades certificate
   - ☐ College diploma
   - ☐ University below bachelor's
   - ☐ Bachelor's degree or higher

6. Do you currently reside in an urban area or a rural area?
   - ☐ Urban
   - ☐ Suburban
   - ☐ Rural

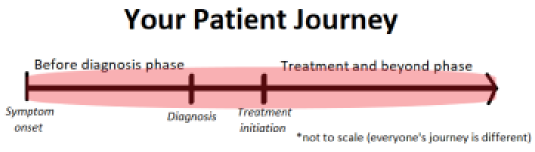
7. Have you ever worked? This includes any type of employment outside of housework.
   - ☐ Yes
   - ☐ No

8. If you answered "Yes" to Question 7, are you currently working?
   - ☐ Yes
   - ☐ No

Version date 4/Feb/2021

9. If you answered “No” to Question 7, are you a student?
- ☐ Yes
- ☐ No

10. If you answered “No” to Question 8, were you ever working during your journey with atrial fibrillation? Your journey begins when you are experiencing symptoms of atrial fibrillation and continues to where you are right now.
- ☐ Yes
- ☐ No



Part 2. The following questions ask about your atrial fibrillation.

11. When were you diagnosed with atrial fibrillation?
- ☐ Under a month ago
- ☐ 1 month to under 6 months ago
- ☐ 6 months to under a year ago
- ☐ 1 year to under 3 years ago
- ☐ 3 years to under 5 years ago
- ☐ 5 years ago or more than 5 years ago

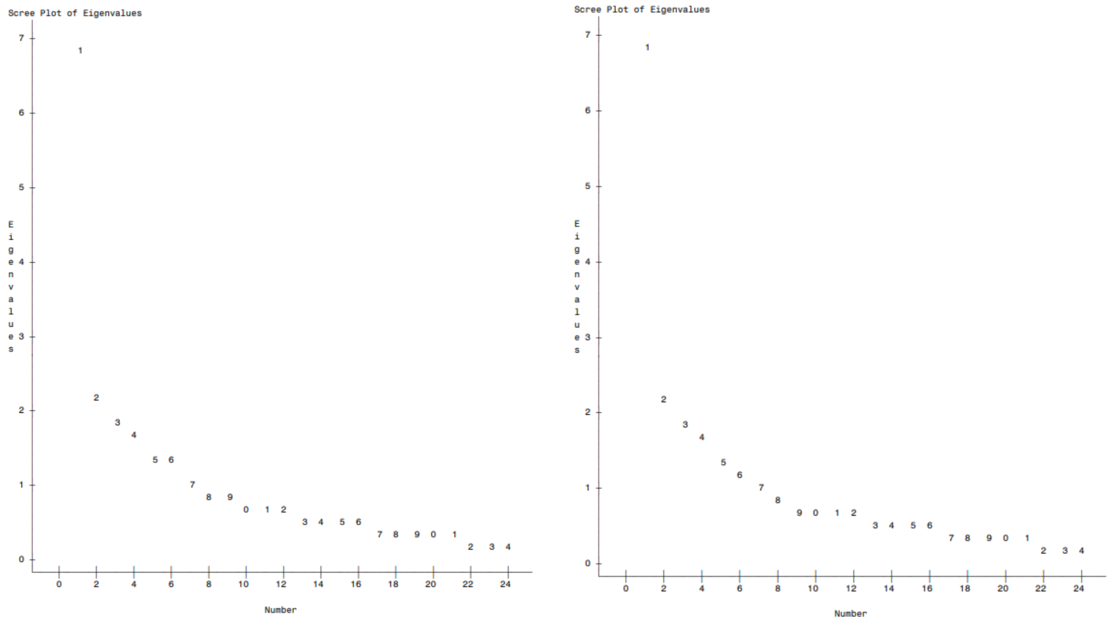
12. What type of atrial fibrillation do you have?
- ☐ Paroxysmal
- ☐ Persistent
- ☐ I am not sure

13. **How often** do you have an episode of atrial fibrillation (an episode of irregular heart rhythm)? Choose one option that best describes your situation.
- ☐ Less than once a year
- ☐ Once a year
- ☐ A few times a year
- ☐ Once a month
- ☐ A few times a month
- ☐ Once a week
- ☐ A few times a week
- ☐ Everyday
- ☐ I am constantly in atrial fibrillation

14. When was the **last time** you had an episode of atrial fibrillation?
- ☐ I am currently in atrial fibrillation or I had an episode today
- ☐ Within the past week
- ☐ Within the past month
- ☐ 1 month to under 6 months ago
- ☐ 6 months to under 1 year ago
- ☐ 1 year ago or more than 1 year ago

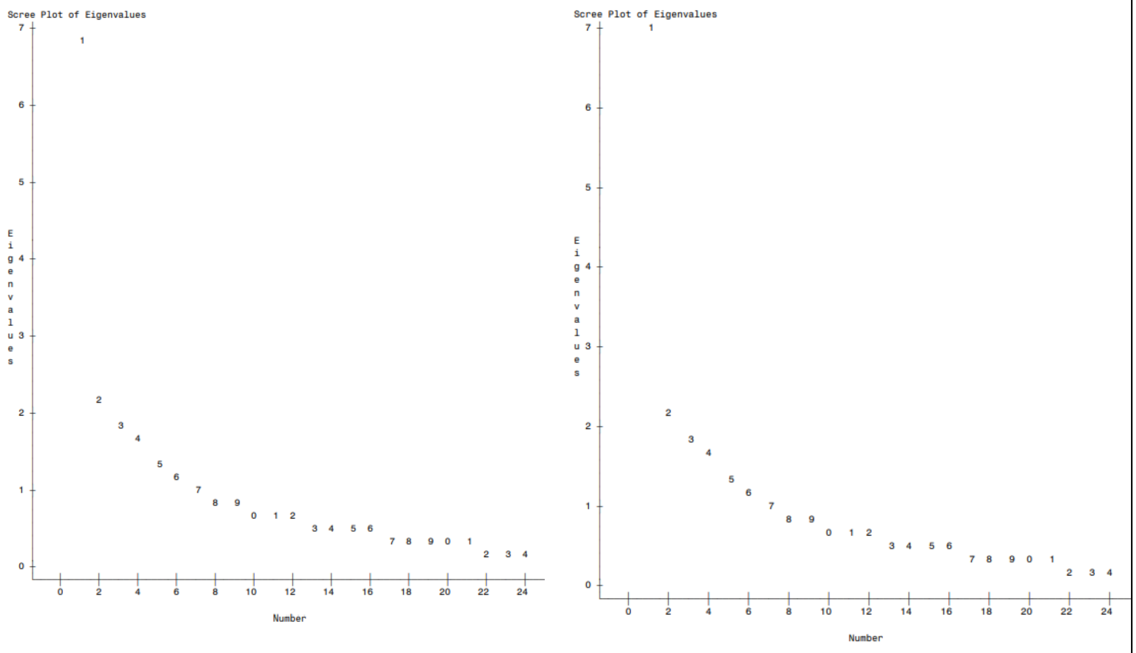
15. How would you describe the severity of your symptoms **as of recently**? Common symptoms include palpitations, shortness of breath, chest pain, and lightheadedness (dizziness).
- ☐ Minimal to no symptoms
- ☐ Mild symptoms
- ☐ Moderate symptoms
- ☐ Severe symptoms

Appendix D. Scree plots from four different datasets



CCA

CCA with log transformed item 25



EM imputed dataset

EM with log transformed item 25

CCA = complete case analysis (n = 229); EM = expectation maximization imputation

Appendix E. Rotated factor pattern solutions of a five-factor extraction under various conditions

Factor	iPAF Promax CCA	iPAF Promax EM imputation	ULS Promax CCA	ULS Promax EM imputation	iPAF Promax CCA Log(item 25)	iPAF Promax EM imputation Log(item 25)	ULS Promax CCA Log(item 25)	ULS Promax EM imputation Log(item25)
1	7, 27, 28, 29, 30, 31, 32	7, 27, 28, 29, 30, 31, 32	7, 27, 28, 29, 30, 31, 32	7, 27, 28, 29, 30, 31, 32	7, 27, 28, 29, 30, 31, 32	7, 27, 28, 29, 30, 31, 32	7, 27, 28, 29, 30, 31, 32	7, 27, 28, 29, 30, 31, 32
2	13[b], 14, 15, 21, 22, 23[b], 24 ,25, 26	13[b], 14, 15, 21, 22, 23[b], 24,25, 26	13[b], 14, 15, 21, 22, 23[b], 24 ,25, 26	13[b], 14 ,15, 21, 22, 23[b], 24, 25, 26	13[b], 14, 15, 21, 22, 23[b], 24 ,25, 26	13[b], 14, 15, 21, 22, 23[b], 24 ,25, 26	13[b], 14, 15, 21, 22, 23[b], 24 ,25, 26	13[b], 14, 15, 21, 22, 23[b], 24 ,25, 26
3	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34
4	1, 2	1, 2	1, 2	1, 2	1, 2	1, 2	1, 2	1, 2
5	3, 5, 6, 13[b], 23[b]	3, 5, 6, 13[b], 23[b]	3, 5, 6, 13[b], 23[b]	3, 5, 6, 13[b], 23[b]	3, 5, 6, 13[b], 23[b]	3, 5, 6, 13[b], 23[b]	3, 5, 6, 13[b], 23[b]	3, 5, 6, 13[b], 23[b]

The cells indicate items with a rotated factor loading of greater than 0.35 on the particular factor.

[a] Item has a rotated factor loading greater than 0.32, but less than 0.35 – indicating poor loading on the particular factor.

[b] Cross-loading items (items that load on more than one factor)

CCA = complete-case-analysis; EM = expectation maximization (maximum likelihood estimation) imputation; iPAF = iterative principal axis factoring; ULS = unweighted least squares

Interpretation: Extraction methods iPAF and ULS produced identical conclusions; EM imputation did not differ from CCA; log transformation did not produce differences

Appendix F. Rotated factor pattern solutions of a six-factor extraction under various conditions

Factor	iPAF Promax CCA	iPAF Promax EM imputation	ULS Promax CCA	ULS Promax EM imputation	iPAF Promax CCA Log(item 25)	iPAF Promax EM imputation Log(item 25)	ULS Promax CCA Log(item 25)	ULS Promax EM imputation Log(item25)
1	7[b], 27, 28, 29, 30, 31[b], 32	7[b], 27, 28, 29, 30, 31[b], 32	7[b], 27, 28, 29, 30, 31[b], 32	7[b], 27, 28, 29, 30, 31[b], 32	7[b], 27, 28, 29, 30, 31[b], 32	7[b], 27, 28, 29, 30, 31[b], 32	7[b], 27, 28, 29, 30, 31[b], 32	7[b], 27, 28, 29, 30, 31[b], 32
2	22, 23, 24, 25, 26, 31[ab]	22, 23, 24, 25, 26, 31[ab]	22, 23, 24, 25, 26, 31[b]	22, 23, 24, 25, 26, 31[ab]	22, 23, 24, 25[b], 26, 31[ab]	22, 23, 24, 25[b], 26, 31[ab]	22, 23, 24, 25[b], 26, 31[ab]	22, 23, 24, 25[b], 26, 31[ab]
3	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34
4	7[ab], 13, 15, 21	7[b], 13, 15, 21	7[ab], 13, 15, 21	7[b], 13, 15, 21	7[ab], 13, 14[a], 15, 21, 25[ab]	7[b], 13, 14[a], 15, 21, 25[ab]	7[ab], 13, 14[a], 15, 21, 25[ab]	7[b], 13, 14[a], 15, 21, 25[ab]
5	1, 2	1, 2	1, 2	1, 2	1, 2	1, 2	1, 2	1, 2
6	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6

The cells indicate items with a rotated factor loading of greater than 0.35 on the particular factor.

[a] Item has a rotated factor loading greater than 0.32, but less than 0.35 – indicating poor loading on the particular factor.

[b] Cross-loading items (items that load on more than one factor)

CCA = complete-case-analysis; EM = expectation maximization (maximum likelihood estimation) imputation; iPAF = iterative principal axis factoring; ULS = unweighted least squares

Interpretation: Extraction methods iPAF and ULS produced identical conclusions; EM imputation strengthened the loading of item 7 on Factor 4; log transformation of item 25 added two poor loading items, item 14 and item 25, to Factor 4.

Appendix G. Rotated factor pattern solutions of a seven-factor extraction under various conditions

Factor	iPAF Promax CCA	iPAF Promax EM imputation	ULS Promax CCA	ULS Promax EM imputation	iPAF Promax CCA Log(item 25)	iPAF Promax EM imputation Log(item 25)	ULS Promax CCA Log(item 25)	ULS Promax EM imputation Log(item25)
1	7, 27, 28, 29, 30[ab], 31, 32	7, 27, 28, 29, 30[ab], 31, 32	7, 27, 28, 39, 30[ab], 31, 32	7, 27, 28, 39, 30[ab], 31, 32	7, 27, 28, 29, 30[ab], 31, 32	7, 27, 28, 29, 30[ab], 31, 32	7, 27, 28, 29, 30[ab], 31, 32	7, 27, 28, 29, 30[ab], 31, 32
2	22, 23, 30[ab]	22, 23, 24[a], 30[ab]	22, 23, 30[ab]	22, 23, 24[ab], 30[ab]	22, 23, 30[b]	22, 23, 24[ab], 30[ab]	22, 23, 30[b]	22, 23, 24[ab], 30[ab]
3	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34	19, 33, 34
4	14, 15[ab], 24, 25, 26	14, 15[ab], 24[b], 25, 26	14, 15[ab], 24, 25, 26	14, 15[ab], 24[b], 25, 26	14, 15[ab], 24, 25, 26	14, 15[ab], 24[b], 25, 26	14, 15[ab], 24, 25, 26	14, 15[ab], 24[b], 25, 26
5	13, 15[b], 21	13, 15[b], 21	13, 15[b], 21	13, 15[b], 21	13, 15[b], 21	13, 15[b], 21	13, 15[b], 21	13, 15[b], 21
6	1, 2	1, 2	1, 2	1, 2	1, 2	1, 2	1, 2	1, 2
7	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6	3, 5, 6

The cells indicate items with a rotated factor loading of greater than 0.35 on the particular factor.

[a] Item has a rotated factor loading greater than 0.32, but less than 0.35 – indicating poor loading on the particular factor.

[b] Cross-loading items (items that load on more than one factor)

CCA = complete-case-analysis; EM = expectation maximization (maximum likelihood estimation) imputation; iPAF = iterative principal axis factoring; ULS = unweighted least squares

Interpretation: iPAF and ULS produced identical conclusions; EM imputation added a poor loading item 24 to Factor 2; log transformation of item 25 increased the factor loading of item 30 for Factor 2 under CCA

Curriculum Vitae

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