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Implementing a value-driven care model for atrial fibrillation

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Chapter 1

Introduction

Epidemiology

Atrial fibrillation (AF) is the most frequently diagnosed sustained arrhythmia worldwide with an incidence rate that is continuously rising (1). Prior research has demonstrated a global prevalence of 33.5 million people, affecting 2.5% to 3.2% of populations, and an incidence of approximately five million new cases of AF annually (2). In Europe, AF affects 2–3% of the population (3). The prevalence of AF increases with age and exceeds 15% at 80 years and over (4). Currently, 8% of the world population and 13–21% of the European population is aged 65 years or older and life expectancies are expected to continue to increase. Therefore, it is expected that, in Europe, the number of people aged ≥ 55 years with AF will increase drastically from 8.8 to 17.9 million between 2010 and 2060 (1). In the Netherlands, it is expected that the total number of AF patients will rise from ~338,000 in 2020 to ~547,700 in the year 2060 **(Figure 1)** (1).

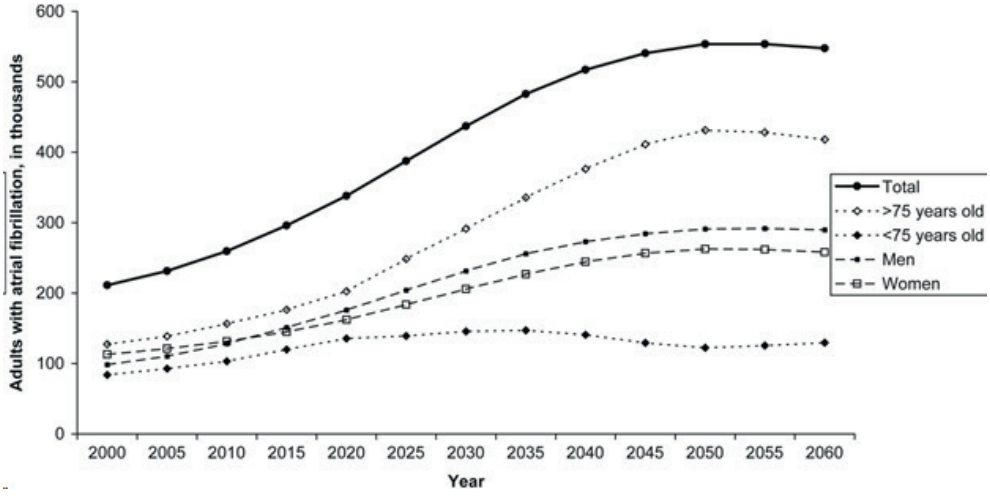

Figure 1. Projected number of adults with AF in the Netherlands between 2000 and 2060.
Krijthe et al. Euro Heart J, Volume 34, Issue 35, 14 September 2013, Pages 2746–2751

Pathophysiology

The pathophysiologic mechanisms by which aging itself increases the likelihood of AF development remain poorly understood (5). The duration of the exposure of atrial myocardium to external stressors i.e., risk factors, causing atrial myopathy, such as hypertension or obesity, most likely plays a role in the association between age and AF (5). Because most elderly patients suffer from one or more risk factors, it is almost impossible to distinguish the impact of these risk factors from true "age-related" factors. Whether atrial myopathy is primary or secondary remains unclear, but the predominant risk factors may evolve with disease progression. As AF burden progresses from paroxysmal to persistent and long-standing persistent AF, the role of atrial myopathic substrate may increase (6).

The number one risk factor for AF globally is hypertension. The higher the blood pressure, the greater the risk for an incident of AF (7). The cumulative risk of developing AF is higher in men than in women over most of their lifespan but becomes similar in older age with a comparable lifetime risk. It is unknown whether this difference is due to sex differences or just the consequence of under-diagnosed AF in women due to differences in symptom intensity and/or medical attention (2). Physical activity also plays a crucial role in AF, but this relation is far from being fully understood. In the general population, light to moderate physical activity results in reduced risk of AF, while subjects exposed to high volumes of moderate to vigorous intensity exercise during a long-lasting period appear to have an increased risk of AF (8). In one-third of all AF occurrences, surgery, infection, or myocardial infarction may account for the development of the arrhythmia (9).

The age-related increase in AF may also be related to an earlier and more frequent diagnosis across all age groups due to better awareness of the arrhythmia and its complications as well as more frequent ECG monitoring over longer periods of time (5). In addition, improved treatment, and subsequently improved survival of patients with cardiovascular disease may lead to an increase in individuals with AF over time (5).

The clinical consequences of AF, which include emboli, heart failure, and early mortality, are of utmost importance. Cerebral emboli leading to ischemic stroke and cognitive decline account for 25% to 30% of all acute ischemic strokes (2). AF is an independent risk factor of all-cause mortality and is associated with an increased risk of cardiovascular disease, with the highest absolute risk increase in patients with heart failure (HF) (10,11). The risk of stroke in patients with AF also increases with age, rising from 1.5% for those aged 50–59 years to 23.5% for those aged 80–89 years, suggesting that the elderly are particularly vulnerable to stroke when AF is present (12,13).

Treatment

Contemporary management of AF encompasses screening and diagnosis, improvement of quality of life (QoL) through rate or rhythm control, reduction of morbidity and mortality through prevention of stroke and systemic thromboembolism, as well as treatment of associated conditions (14). The ESC guidelines recommend systematic screening for patients with higher risk of stroke. In the absence of anticoagulation therapy, AF is associated with a 3- to 5-fold increased risk of stroke; furthermore, AF-related strokes are more severe (greater resource utilization, long-term disability, and mortality) than strokes of other aetiologies (15,16). The CHA_2DS_2-VASc scores have been widely used to predict the risk of stroke with Congestive heart failure, Hypertension, Age ≥ 75 years (doubled), Diabetes mellitus, Stroke (doubled), Vascular disease, Age 65 to 74 Years, and Sex category [CHA_2DS_2-VASc]. A patient with a CHA_2DS_2-VASc score of 2 or higher is regarded as high risk, and oral anticoagulation is indicated; in patients with a score of 1, the thromboembolic risk is regarded as intermediate (17). More recent evidence shows a benefit of starting anticoagulation even if only one risk factor for stroke is present, that

is, men with a CHA_2DS_2-VASc score of 1 and women with a CHA_2DS_2-VASc score of 2 (18). Stroke prevention in patients at risk, assessed by the CHA_2DS_2-VASc score, was traditionally achieved with a vitamin K-antagonist; however, direct oral anticoagulants have proven to be effective and safer alternatives. Despite overwhelming evidence for the efficacy of oral anticoagulant therapies (OAC), their value is limited by under-prescription (19), limited persistence (20) and subtherapeutic dosing (21). Additionally, left atrial appendage exclusion has emerged as a viable option in patients intolerant of anticoagulation.

The clinical choice between rate-control and rhythm-control therapies has been debated over the years. In 2002, the AFFIRM trial demonstrated that the rhythm-control strategy had no survival advantage over the rate-control strategy. Eighteen years later, EAST-AFNET 4 showed that the rhythm-control approach is better than rate control at reducing adverse cardiovasculawr outcomes in patients with a recent diagnosis of AF (22). Treatment of comorbidities and the reduction of risk factors like hypertension, diabetes mellitus, obesity and obstructive sleep apnoea should be part of any comprehensive treatment approach (23).

Economic impact

Costs associated with the medical management of AF account for 1–3% of Europe's health care expenditure (€1,073 billion in 2020) and 1–3% of the US's health care expenditure ($4,100 billion in 2020). Hospitalizations represent the major cost driver, accounting for 50–70% of total costs; stroke, sudden death, heart failure, and other complications constitute the other important cost drivers (24). More specifically, in the Dutch situation, total costs of AF are estimated to be €583 million per year, which approximately accounts for 1.3% of the Dutch health care expenditure in 2008 (25). Subsequently, the cost of managing individual AF patients is high since most estimates of the direct cost per patient-year ranged from ~$10,100 to 14,200 in the US and from ~€450 to 3,000 in Western Europe (26). In the literature, though very few national cost-of-illness estimates can be identified (26), the above-mentioned estimates are comparable with those reported from the economic analyses performed for the RACE and AFFIRM trials (27,28).

The increased proportion of older adults suffering from AF and the complications caused by AF, as described above, will have several significant consequences for Dutch public health, including increases in burden of disease, pressure on health service utilization and healthcare costs.

e-Health technologies are modernizing healthcare by using information and communication technology to support and improve healthcare and healthcare delivery. In recent years, cardiology has increasingly made use of e-health in diagnosing and treating AF patients. This can make AF care more effective and potentially provide a solution to rising cost.

Dutch AF care

To stimulate quality improvement in AF care, it is crucial to pursue the best outcomes possible for AF patients against lower or equal healthcare costs to decrease the disease burden for patients and society (29). The Dutch healthcare model for AF is a medical model that has been defined historically as a systematic process of differentiation of a disease process through observation, description, and delineation (30). This model aims to differentiate disease and promote recovery through tailored plans leading to a model best suited for acute medical care (30). AF, however, is a chronic medical condition that requires management of not only acute complications, but also management of the long-term disease processes and patient journey. The Dutch healthcare system, like many healthcare systems that follow this medical model, suffers from fragmentation of care of chronic disease processes, with lack of care coordination, duplication of services, and disproportionate resource allocation for rehabilitation (31). The Dutch fragmented AF care has, for example, resulted in distinct guidelines for primary (32) and secondary care (33). It is striking that guidelines for general practioners (GPs) and cardiologists differ with respect to antithrombotic treatment. The 2020 ESC guideline has a clear preference for direct oral anticoagulants over VKA because of their safer profile in terms of bleeding severity, while the Dutch GPs Association (NHG) considers these treatments to be equally safe. In contrast to the 2020 ESC guideline, a strong recommendation for AF screening is lacking in the NHG guideline. Yet, screening for AF in combination with the CHA_2DS_2-VASc score has been shown to improve identification of patients who are eligible for stroke prevention irrespective of the occurrence of symptoms (34). Several screening studies reported an incidence of silent AF in patients aged over 65 years ranging from 1.1 to 1.6% (17,35). Tieleman et al. 2016 (36)estimated that with a present population of 94 million people aged ≥65 years in Europe, a screening programme could potentially identify 1–1.5 million people with silent AF who generally are not treated with oral anticoagulation. At a stroke rate of 5% per year, these patients will suffer from 50,000 to 75,000 strokes. Anticoagulation prevents ischemic stroke by at least 60% and mortality by at least 25% (37). Potentially, screening programmes can have a major impact on outcomes and costs. The optimal strategy to implement a successful screening programme in primary care, however, remains to be determined (17).

Although Dutch AF care is fragmented, with different guidelines for GPs and cardiologists, guideline adherence is crucial for improving outcomes and reducing costs, since failure to adhere to published guidelines has been associated with a higher risk of thromboembolism and the combined endpoint of cardiovascular death, thromboembolism, and major bleeding (38). As a consequence, failure to adhere to guidelines generates higher costs since approximately two-thirds of AF costs are related to disease complications and patient disability **(Figure 2)** (7). It has been documented in several international registries that anticoagulation is underutilized in AF (21,39,40). In the Netherlands, comparable results were found regarding guideline adherence in

cardiologists (70%), GPs (58%) and internists (55%)(41). Although guideline adherence for AF has improved over the past years, a study by Erküner et al. 2021 (19) reported that in the Netherlands and Belgium inappropriate use of anticoagulants is observed in 14% of the AF population, which stresses the need for further attention on guideline adherence.

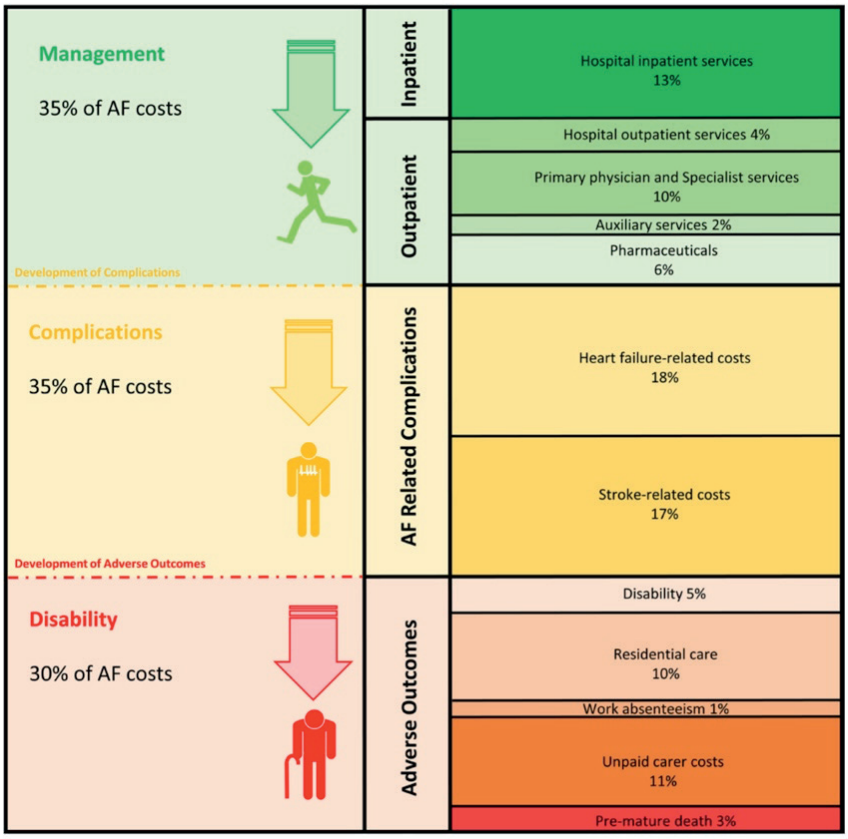

Figure 2. AF related expenditure
Pictorial breakdown of AF-related expenditure in the Australian health care system. Percentages rounded to closest integer number. Data derived from PricewaterhouseCoopers.
Bhat et al, Circ Cardiovasc Qual Outcomes. 2021;14e007411. DOI:101161/CIRCOUTCMES.120.007411

Multi-provider quality systems around chronic conditions

In the last decades the increasing prevalence of chronic disease, the increasing healthcare costs, and the fragmentation of chronic care contributed to the awareness that care for chronic patients' needs to be reorganized (42). Beginning in the 90s, disease-management programs were developed to improve health outcomes, increase patient satisfaction, improve QoL, and reduce healthcare costs (42). However, standardization was lacking, leading to a broad variety of disease management models, and long-term outcome improvement and cost reduction was often lacking (42,43). To improve patient outcomes

and to reduce healthcare costs by changing routine care delivery, the Integrated Chronic Care Model (ICCM) was developed (44). Wagner et al. advocated in the late 90s (44,45) that the ICCM should cover: 1) the entire community, 2) the healthcare system, and 3) the provider organization. The ICCM was developed to transform the healthcare system so that it meets the conditions for providing proactive, person-centred and integrated care. The ICCM strives for high-quality treatment of chronic diseases, by focusing on six interrelated elements: self-management support, delivery system design, decision support, clinical information systems, healthcare organization, and community resources (46). These elements are intended to provide a practical system for restructuring the management of chronic care, making it more efficient (process) and more effective (impact)(47). Several observational studies have examined the relationship between the presence of ICCM elements and quality of care (48). Overall, the presence of multiple ICCM elements was associated with better quality of care (49). Some elements are also seen in some examples of multi-provider quality networks around chronic conditions, such as Parkinson Net, Amyotrophic Lateral Sclerosis (ALS) Healthcare Network, Healthcare Network Dementia, and Chronic Care Network. These care networks have similar challenges, and they all strive for a long-term collaboration between independent care providers / care professionals who jointly focus on continuously improving the quality of life for people with a certain disease or condition. However, due to differences in prevalence, pathology, care and organization of the networks, there is no one-size-fits-all solution to develop and implement ICCM's for these multi-provider quality networks.

Towards integrated chronic AF care

To address problems such as fragmentation of AF care, with lack of care coordination, failure to adhere to guidelines, duplication of services, and disproportionate resource allocation for tertiary prevention, an ICCM for AF is being advised to enhance appropriate treatment and to coordinate care delivery more effectively. Although the European Society of Cardiology (ESC) guidelines in 2016 (50) emphasized the importance of integrated care and patient-reported outcomes, the best way to deliver this type of care for AF patients is still unclear (50). The Dutch Federation of Medical Specialists (FMS) is also stimulating the transition from fragmented care to an ICCM for chronic heart disease. Its vision document states that by the year 2025: "The medical specialist will, far more than at present, be able and willing to work together with other healthcare professionals. The specialist will continually consider where and by whom healthcare can best be provided. The medical specialist will be part of a flexible network of healthcare professionals in which the healthcare outcomes and the needs of the patient serve as the point of departure" (51).

According to Hendriks et al. 2021 (52) the integrated AF care approach includes four essential elements: 1) Patient participation: patients should be involved in their care, treatment, and decision-making process with a patient-centred approach; 2) Multidisciplinary team: due to the multifaceted nature of AF treatment, a multidisciplinary

team approach is recommended rather than a single healthcare professional; 3) Technology: mHealth and e-health technology is available in AF care and can be used by patients and healthcare providers; and 4) AF treatment: a comprehensive AF treatment approach is required with patient access to all treatment options, guided by evidence-based guideline recommendations. To achieve this, an ICCM for AF requires close collaboration between cardiologists, electrophysiologists, AF surgeons, GPs, AF nurses, patients, and family members (53). Because the current physician-centred care model is unsustainable given the increase in patients with atrial fibrillation, "nurse-led" care has been introduced in some ICCMs for AF, where specialized nurses are supervised by a cardiologist (54). This kind of care incorporates standardized patient education, protocol-driven diagnostic testing, and an electronic decision support system, ensuring guideline-adherent decision-making by a multidisciplinary team (52). Compared to standard care, this approach showed significant reduction in cardiovascular mortality and hospitalization, secondary to improvements in adherence to guideline-based therapies (43,55,56). This approach also showed a better cost-effectiveness in the treatment of AF (43). Until now, most nurse-led care has been operationalized and assessed for effectiveness in large academic hospitals. Most patients with AF are, however, treated by GPs in primary care or cardiologists in secondary care. The All-in trial showed that integrated care for elderly AF patients in primary care is safe and resulted in a 45% reduction in all-cause mortality when compared with usual care (57).

To change fragmented AF care into an ICCM for AF, regional collaboration is very important (53). Regional collaboration involves adapting similar procedures and activities between cooperating partners (cardiologists, nurses, and GPs), increasing the potential of collective improvements of outcomes that are most relevant for patients. To accomplish this, a multidisciplinary care pathway should jointly be developed with the focus on improving outcomes and reducing costs (53,58). Moreover, one of the key elements in value-based health care (VBHC) is regional integration of healthcare delivery systems. Patient pathways should be organized for patient groups with the same medical condition (59). This requires new forms of collaboration between healthcare professionals and providers. Besides the integration of care, the overarching goal in VBHC is improving outcomes and reducing healthcare costs.

Value-based healthcare (VBHC)

The concept of integrated care was described long before the introduction of VBHC but was not unambiguously defined and could therefore take many different forms (60). Integrated care is an important aspect within VBHC and the criteria that this care must meet are much more clearly defined. VBHC was introduced by Porter and Teisberg in 2006 as a strategy to improve healthcare systems by improving outcomes and reducing costs (61). Worldwide, VBHC is seen as an obvious strategy to solve the crisis in healthcare. Improving the performance and accountability in healthcare depends on having a shared

goal that unites the interests and activities of all stakeholders (59). The goal of VBHC is to maximize patient value, which is defined as outcomes that matter most to patients, divided by costs of healthcare delivery **(Figure 3)** (59). Besides outcomes, costs constitute the denominator in patient value. Those healthcare costs should reflect the total costs of the full cycle of care for the patients' medical condition, including all involved healthcare providers. If value improves, patients, payers, providers, and suppliers can all benefit while the economic sustainability of the healthcare system increases (59).

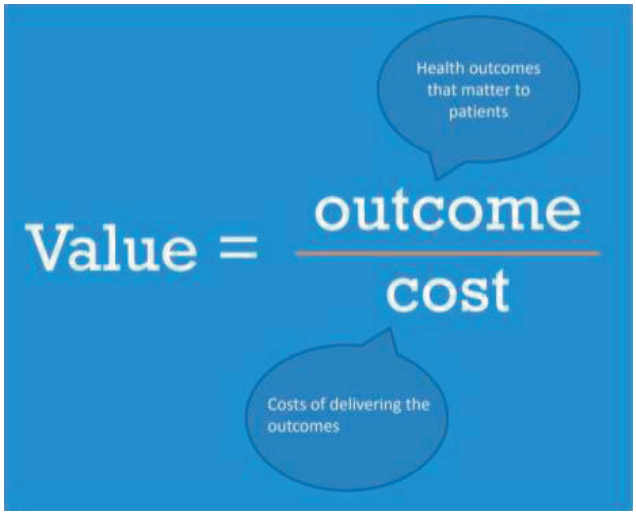

Figure 3. The value equation underpinning value Bases Health Care
Source: reprinted from VBHC presentation by Cole, D.
Retrieved from http://ahha.asn.au/sites/default/files/civicrm/contribute/files/

Porter defined and ordered outcomes in a three-tier hierarchy: Health Status Achieved or Retained, Process of Recovery, and Sustainability of Health **(Figure 4)** (59). This outcome measure hierarchy helps to understand the relation between the different outcomes by weighing their relative importance to patients. A limited set of outcome measures should be used to covering all tiers of the outcome hierarchy. The International Consortium for Health Outcomes Measurement (ICHOM) initiative recommends the shift to measuring and improving outcomes by defining standard sets of outcomes for the most common diseases. In the Netherlands, outcome measurement of interventions and institutional performance on cardiac diseases are monitored by the Netherlands Heart Registration (NHR).

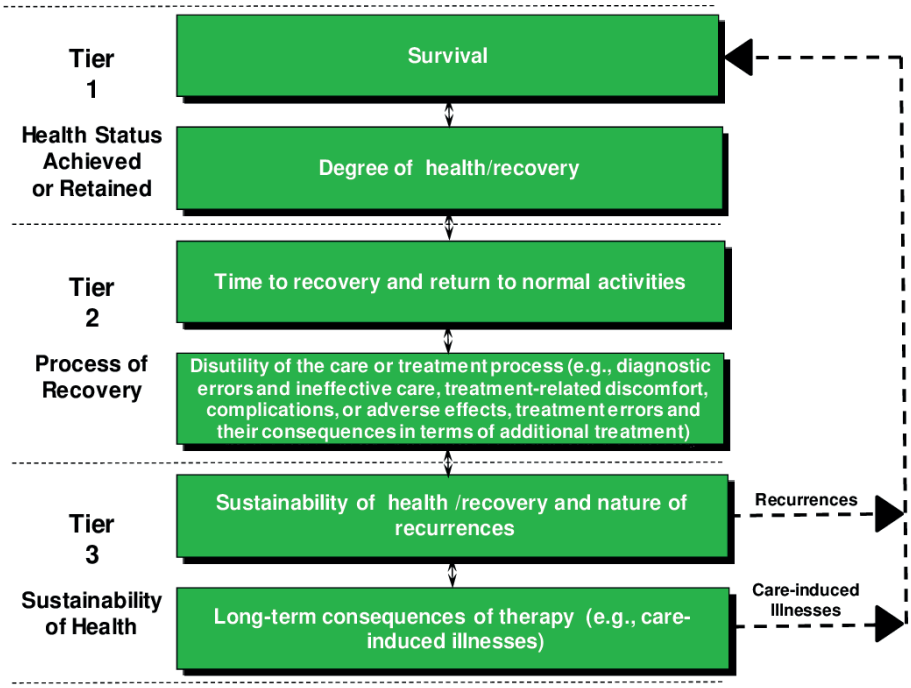

Figure 4. The outcome Measures Hierarchy
Porter et al, The strategy that will fix health care (2013) Harvard business review, 91(10, 1-19.

The success of VBHC depends on its implementation, which is why a Strategic Value Agenda was introduced **(Figure 5)** (29), consisting of the following six elements:

1. Organize into Integrated Practice Units (IPU). In an IPU, the organisation is structured around the needs of the patient group with the same condition.
2. Measure outcomes and costs for every patient. Outcomes that matter most to patients are the main goal. Costs should reflect the total costs of the full cycle of care for patients' medical conditions.
3. Move to bundled payments for care cycles. The bundled payment approach, which is best aligned with value when covering the full cycle of care, is believed to directly encourage teamwork and high-value care.
4. Integrate care delivery systems. There are huge opportunities of improving value as providers integrate systems to eliminate the fragmentation and duplication of care and to optimize the types of care delivered in each location.
5. Expand geographic reach. Superior providers for particular medical conditions should expand their geographic reach, remaining focused on value not on volume.
6. Build an enabling information technology (IT) platform. The right kind of IT system can help the parts of an IPU work with one another, enable measurement and new reimbursement approaches, and tie the parts of a well-structured delivery system together.

Implementing all six components will make value improvement easier and faster, as the components are interdependent and mutually reinforcing (29). Porter advises to start implementing VBHC by measuring outcomes, as measuring outcomes is the key element in the Value Agenda (59).

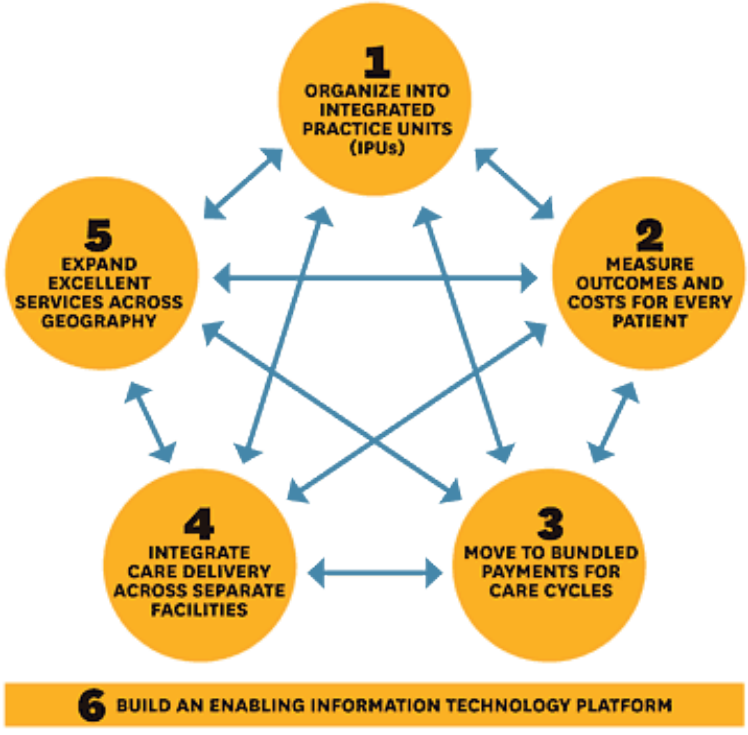

Figure 5. The Value Agenda.
Porter et al, Harvard Bus Rev 2013. The strategy that will fix health care.

To improve outcomes and lower costs, it is important to understand how various activities in the full care chain fit together in delivering care. This chain of activities that is required to deliver care is called the Care Delivery Value Chain (CDVC), and it illustrates their sequence and organisation. The CDVC can be applied as a systemic framework for assessing healthcare delivery **(Figure 6)** (29).

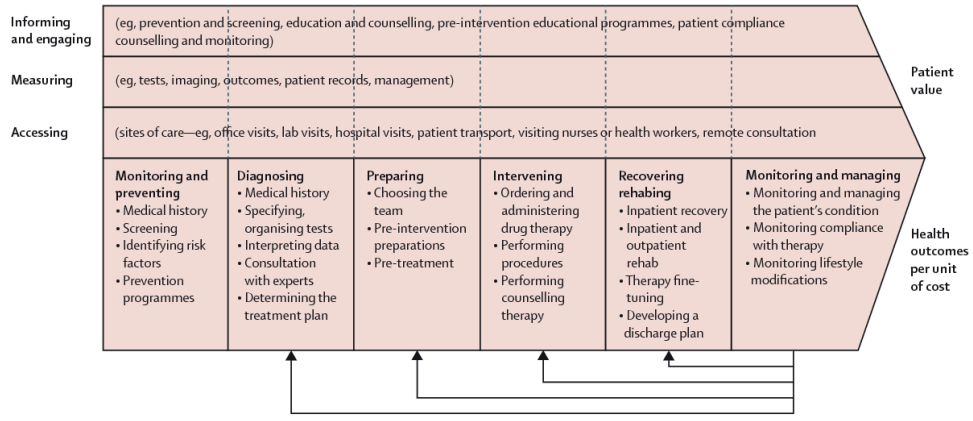

Figure 6. Care Delivery Value Chain (CDVC)
Source: Mapping processes and value chains to understand strategy in care delivery. Sastry A 2014 Retrieved from https://groundwork.mit.edu/cdvc/

Optimizing patient value can be achieved by adopting processes within the CDVC. Structure and process indicators are known to reflect elements of the CDVC that influence the outcomes that matter most to patients and can therefore be used in quality improvement projects **(Figure 7)** (29).

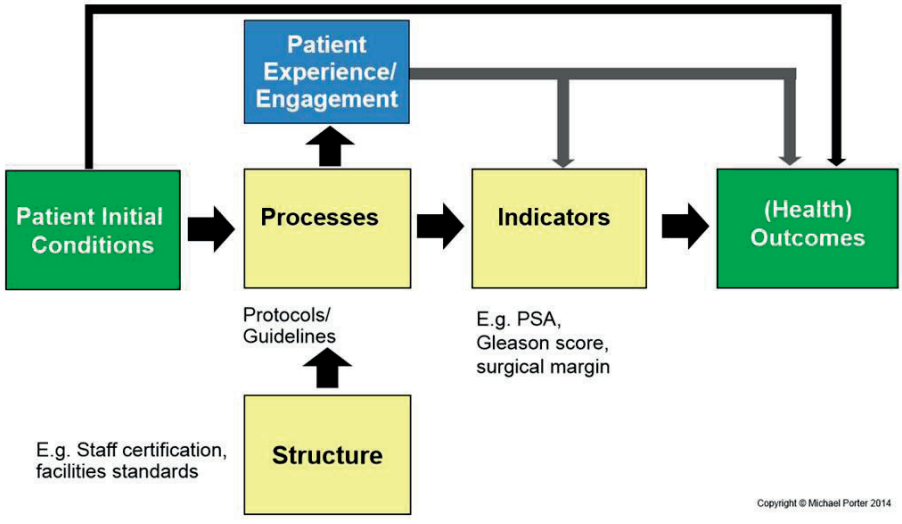

Figure 7. Measuring outcomes and costs for every patient.
http://www.hbs.edu/faculty/Publication%20Files/Website_Outcomes%20Measurement_737ae94d-f1b3-48ed-a789-025766d63670.pdf

Developing a CDVC is a critical part of VBHC as it provides a framework that can help conceptualize the organization and structure of care delivery for medical conditions.

However, for a patient-centred multi-provider quality system the entire healthcare chain needs to be involved to continuously monitor and, where possible, further improve value for the patient. Another crucial element for continuous improvement of the patient-centred multi-provider quality system is including a Plan-Do-Check-Act (PDCA) cycle on patient-relevant outcomes and healthcare costs. Since physicians are key in organizing and optimizing patient pathways and collaborate with other providers in daily healthcare delivery, a physician-driven and patient-centred approach is advised in implementing VBHC in practice (29). Physicians have the knowledge to define outcome measures, interpret the outcomes measured, and define hypotheses on how to improve outcomes by improving the process of healthcare delivery. In addition, it is crucial to take patient experience into account to improve the multidisciplinary care pathway and, thereby, outcomes (59). The collection and use of patient-reported experience measures (PREMs) for the purpose of quality improvement has become part of a relatively recent move towards more holistic, 'patient-centred' provision of care in the Netherlands and other countries. Higher levels of positive patient experience are associated with higher levels of patient safety and clinical effectiveness as well as self-reported and objective outcomes (e.g., mortality, greater adherence to treatment recommendations and lower use of additional healthcare, such as rehospitalisation and overuse of primary care) (62). Whereas patient experience is often marginalized in favour of aspects of care that are easier to quantify, patients' experience of the quality of care can provide insightful feedback to enable clinical teams to direct quality improvement efforts in areas where they are most needed. For example, the European Cancer Consumer Quality Index (ECCQI) is the first to measure and compare experiences and satisfaction of cancer patients on an international level; it may enable healthcare providers to improve the quality of cancer care (63). The CQI Audiology Care is a valid and reliable instrument to assess clients' experiences with audiology care (64). With the development of the CQI Chronic Heart Failure, an important step has been taken in making the quality of heart failure care experienced by the patients transparent in the Netherlands. This CQI can be used nationally to measure and improve the quality of heart failure care and offers health insurers a guideline when purchasing care. It gives patients valuable information and insight into the performance of hospitals based on which they can make a choice.

International examples of the implementation of VBHC

Instead of completely implementing the Value Agenda, many national and international institutions are adopting elements of VBHC in their clinical practices. One of the most well-known examples of VBHC is the Martini Klinik in Germany (65). The Martini Klinik is a leading example of outcome measurement and improvement routine. This is mainly due to three success factors: organizing care into IPUs, measuring outcomes and costs at an individual level, and engaging patients, which is essential for generating data. Moreover, the Texas Children's Hospital and the West German headache center: integrated

migraine care (66), show that VBHC not only leads to an improvement in patient outcomes (including a strong reduction in mortality for more complex and common diseases), but also to a significant reduction in healthcare costs (67). Another element in the Value Agenda is bundle payment which was first introduced at the Texas Heart Institute in 1984. Reliably assessing bundled payment models' effectiveness is difficult due to the initiative's voluntary nature (68). Current evidence suggests that the model is more effective when it is applied to surgical procedures, rather than chronic medical conditions (69). Joint replacement using bundled payment models in Medicare patients showed substantial hospital savings and reduced Medicare payments, 20.8% ($5,577) per joint replacement (70). Besides examples in secondary and/or tertiary care, Oak Street Health is one of the best international examples of VBHC in primary care. Oak Street Health provides healthcare for the elderly in medically underserved Chicago communities. It receives a fee per client that is based on the risk profile, including the entire primary care, specialist care, acute care except for IC care and admission to a clinic.

National examples of the implementation of VBHC

Numerous VBHC initiatives in the Netherlands started, like in many other countries, with measuring and improving outcomes. A Dutch example of outcome improvement using VBHC principles is Diabeter. Diabeter improves outcomes and lowers patient hospitalization for Diabetes Mellitus patients by applying e-health solutions, delivering individualized, comprehensive care, and supporting self-care management (71). Other examples are Santeon (https://www.santeon.nl/) and mProve (http://www.mprove.nu); both networks introduced multidisciplinary teams across many hospitals working together on various medical conditions to improve healthcare in the Netherlands by reaching better patient outcomes at reduced costs and sharing the knowledge and experience. Another important, Dutch example of VBHC is "VBHC at Erasmus MC" (72). A key element of VBHC at Erasmus MC is discussing outcomes of care with the patient it concerns, enabling healthcare professionals and patients to tailor the care to the patient's needs. Their aim is to provide care tailored to "what matters to patients" for 80% of the local disease burden by 2023. Outcome measures have been defined for all IPUs, of which some have resulted in an ICHOM set. Moreover, the Dutch Ministry of Healthcare has embraced VBHC as an important principle in their policy for the coming years, leading to the program called "Outcome-Oriented Care" (73). Outcomes that matter most for a patient depend on the patient's personal situation and can be different for everyone. This program stimulates healthcare professionals and patients to decide together what outcomes are most important, leading to a more personalised treatment.

Cardiac care

Although no multi-provider quality system that covers the whole patient journey has yet been developed for heart conditions, despite the urgent need caused by an enormous

increase in cardiac patients impacting both outcomes and costs, there have been some important VBHC developments in the field of cardiology in the Netherlands. Firstly, Measurably Better, currently known as NHR, is a Dutch initiative which uses patient-relevant outcomes to improve quality and transparency of care for patients with heart disease (74). NHR is a doctor-driven and patient-focused initiative with strong scientific roots that aims to improve the transparency and quality of cardiovascular care in the Netherlands, and it has become an international best practice in the implementation of VBHC (75). Another excellent Dutch example of outcome-based payment is an initiative of the insurance company CZ and the Catharina hospital Eindhoven, in which they jointly developed a model for healthcare procurement based on patient-relevant outcomes (76).

Netherlands Heart Network

The work presented in this dissertation was performed within the Netherlands Heart Network (NHN), in Southeast Brabant, which is a densely populated region in the Netherlands with 791,075 inhabitants (CBS Open data StatLine 2022). Three GP organizations representing about 450 GPs and four hospitals, including a heart centre, a hospital specialized in cardiac rehabilitation, and two general hospitals are situated in this area. In recent decades, health professionals in the Southeast Brabant region have been faced with an increasingly aging population, resulting in a sharp increase in patients with a heart disease. This trend is comparable to the aging of the population in the Netherlands **(Figure 8)** (Regionaal rapport GGD).

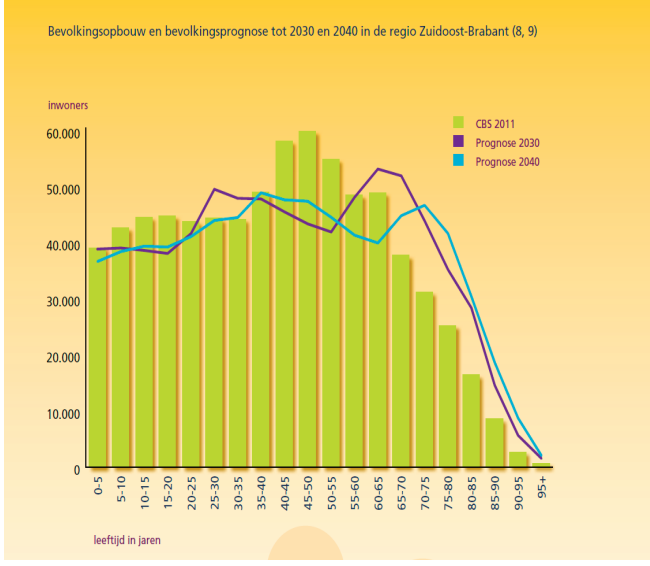

Figure 8. Population structure and population forecast in 2030 and 2040 in Southeast Brabant.
Op weg naar een gezonder Zuidoost Brabant
Regionaal rapport Volksgezondheid Toekomst Verkenning 2011, GGD.

To face the expected increase in the number of patients with heart disease, GPs, cardiologists, and cardiothoracic surgeons in Southeast Brabant initiated, in 2015, the NHN. The goal is to create a continuum of care without barriers between primary, secondary, and tertiary care by developing a regional integrated system for cardiac care with a focus on improving patient outcomes, lowering costs, and creating more patient centredness.

Besides healthcare professionals, diagnostic centres, ambulance services, home care organisations, academic centres and pharmacists were actively involved in the NHN as well. The NHN's vision is that optimal patient value can be achieved if all relevant healthcare providers in primary, secondary, and tertiary cardiac care join forces, embrace and prioritize the shared goals, and use data from daily practice to continuously improve healthcare delivery. The NHN developed a solid, evidence-based methodology to define and implement regional transmural care standards (RTA) and to measure and discuss outcomes (i.e., ICHOM datasets) and costs (i.e., aligned with health insurance companies) (61). To enable improvement of patient value in the full care cycle, multidisciplinary network teams were formed. The NHN started on a small scale with one cardiac condition, AF. Subsequently, RTAs for other common heart conditions, i.e., heart failure, coronary artery disease and aortic valvular disease, were developed, taking previous experiences into account. After implementation of the RTAs, a PDCA cycle is applied to continuously improve patient-relevant outcomes and to define improvement projects to increase value for cardiac patients. This continuous improvement cycle included the implementation of the RTA in the full care cycle. After the implementation, an audit is performed by an audit team of healthcare providers. Findings and advice were used to optimize patient value for the specific organisation. Patient-relevant outcome measures, registered by all healthcare organisations involved, are continuously extracted and analysed so that the most relevant findings can be included in the revised standard of care. Focus group interviews are organized annually to update the current standard of care. Guidelines and national standards are reviewed, and renewals are considered to update the current standard of care. Suitable innovations from leading medical industry organizations are considered for further optimalisation of the RTA. To ensure patient-centeredness, a Patient Advisory Board has been installed advising on strategy, priorities, and project plans. Based on all the input, the multidisciplinary network teams decided which improvements of the RTA were needed to improve the relevant outcomes and reduce healthcare costs **(Figure 9)** (77).

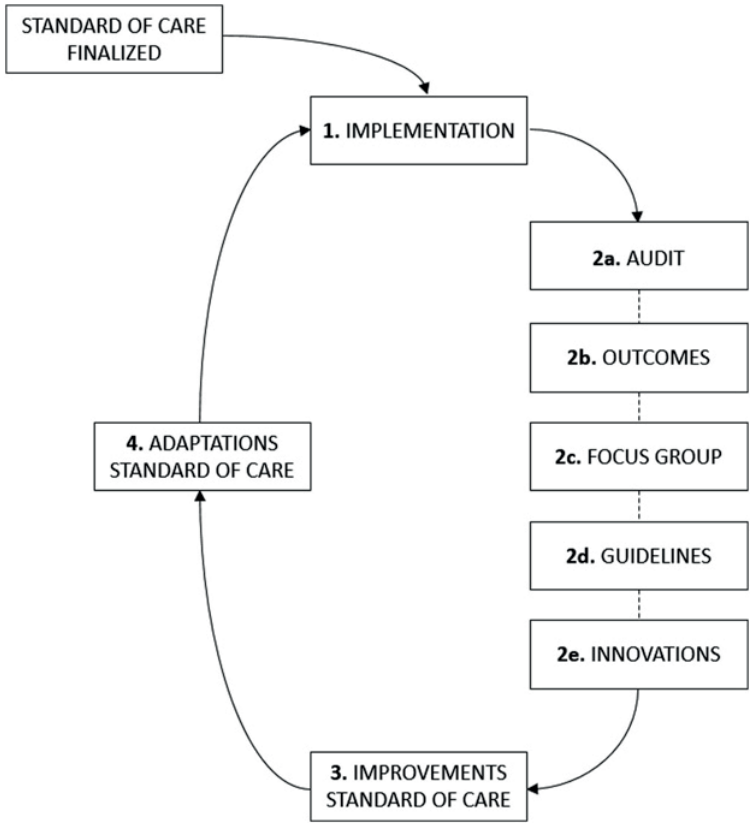

Figure 9. PDSA cycle within the NHN.
Van Veghel et al, 2020, International Journal of Healthcare Management

e-Health interventions

e-Health is defined by the World Health Organization (WHO) as "the use of information and communications technology in support of health and health-related fields" (78). It refers to forms of prevention and education, diagnostics, therapy, and care delivered through digital technology (79). Ten years ago, this was often limited to using computers to access results, basic electronic health records of teleconsultation for people living in remote areas. Today it encompasses a wide range of applications, from mobile health (mHealth) to telehealth, and is increasingly becoming the basis for all healthcare activities. e-health interventions will undoubtably play a substantial role in shaping healthcare systems in the 21st century, as has been the case in many other sectors. Globally, it is hoped that the "quadruple aim" of healthcare will be achieved with the help of e-health (i.e., reducing costs, improving patient experience, improving the work life of healthcare providers, and improving population health)(80). It is expected that e-health will lead increased patient value but also to a reduction in the large number of patients who are unintentionally harmed by medical errors and violations (81). The outcomes of digital health transformation are,

however, inconclusive and mixed (80,81). Moreover, the potential risks of implementing e-health in complex environments such as healthcare should not be ignored. If we want to maximize the benefits of e-health interventions while minimizing the risks, it is crucial to assess the development and implementation of new e-health interventions (82).

A crucial e-health intervention is the development of a common information technology platform because it could potentially improve patient value even further (59). Accurate and comprehensive care data in combination with modern analytical tools can play an important role in enabling healthcare providers to make more informed decisions, leading towards effective and cost-efficient care (83). However, the shift from care in a single unit to care across multiple units with a varying but specialized expertise and each with its own information technology platform makes it difficult to develop a comprehensive healthcare data infrastructure that captures complete care processes at individual, organizational and population levels. Besides the technical challenges of a multi-provider regional information technology platform, legal, cultural, and political constraints also exist concerning "data access" (84). The healthcare landscape is highly fragmented which prevents healthcare providers from accessing complete datasets, leaving them unable to understand and safeguard all aspects of the patient's health journey.

The above-mentioned fragmentation of the technology platforms of all healthcare organizations also applies for the Southeast Brabant region. The next step in the further development of the NHN is the implementation of a regional information technology platform. A regional information technology platform can improve AF care as it is crucial to facilitate both patients and healthcare professionals (i.e., data-sharing or e-health interventions), making automated sharing of information among providers and patients possible (avoiding duplicative tests). A regional information technology platform also creates more complete, more accurate and better structured clinical data and documentation. It also ensures automatic sorting and summarization of data, so that relevant information is presented to the clinician in context-relevant displays. The clinicians will have direct access to instant updates when needed for decision making.

Another important e-health intervention is population screening to diagnose silent atrial fibrillation, as discussed in the previous section "Dutch AF care". With the growing number of technological solutions, AF screening is expected to be easier and more widely available in the near future (85). Previous research showed that technology is no longer a limiting factor in AF screening interventions (86–88). Although the European Heart Rhythm Association (EHRA) provided practical guidelines on using digital devices to detect and manage arrhythmias, clear guidance on large-scale implementation of technology-assisted AF screening programs is still lacking (86).

Aim of the dissertation

Based on the abovementioned rationale, this dissertation aims to increase the current knowledge on how to develop, implement and evaluate an ICCM for AF patients by

using VBHC principles. The NHN's ambition is to improve patient value even further by introducing more e-health interventions. In this dissertation, we provide practical recommendations on how e-health interventions can be better implemented.

Research questions

Part 1

- Is it feasible to put VBHC principles into practice for AF patients in a multi-provider network?

Part 2

- How can real-life data from such an AF network create relevant insights for improving patient value?

Part 3

- What conditions in AF care are needed for the successful implementation of e-health interventions in such a network?

Outline of this dissertation

Part 1. Development and organization of an AF network according to VBHC principles

In chapter 2 the development of the NHN is described. The NHN is an example of a physician-driven and patient-centred collaboration of healthcare providers in primary, secondary and tertiary care based on VBHC philosophy, in which multidisciplinary networks are initiated for the most prevalent cardiac conditions, such as atrial fibrillation. In chapter 3 a stepwise methodology is presented to implement VBHC principles in the full cycle of care in a cardiac network organization, including the first results for the AF care pathway.

Part 2. Real life data from this AF network

In chapter 4 the first preliminary data from the NHN are presented on the effectiveness of outpatient AF clinics in the Southeast Brabant region. In chapters 5 and 6 we assess the association between QoL and patient-relevant outcomes including hospitalizations as a proxy for healthcare costs in AF patients. In chapter 7 we examine the relation between patient-relevant outcomes and patient experiences regarding quality of care in outpatient AF clinics.

Part 3. Successful e-health implementation in AF care

An e-health implementation guideline is presented in chapter 8, with an overview of determinants for successful implementation of e-health interventions, and in chapter 9 facilitating and inhibiting factors for implementation of AF screening interventions in primary care are evaluated.

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Part 1

Development and organization of an atrial fibrillation network according to VBHC principles

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Chapter 2

Implementing value-based healthcare principles in the full cycle of care: the pragmatic evolution of the Netherlands Heart Network

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Introduction

Rising healthcare costs and variations in healthcare quality are major challenges in global healthcare (1). In order to overcome these challenges, healthcare providers are stimulated to focus on improving patient value (1). In value-based healthcare (VBHC), several principles are defined, including measuring and improving outcomes and costs and integrating care delivery systems (1). Since physicians are able to interpret the outcome- and healthcare data and to redefine the healthcare process in a responsible way, a physician-driven and patient-centered approach is advised in implementing VBHC in practice (1). Although measuring and improving patient value in a continuous improvement cycle in an integrated care delivery system across separate facilities is expected to be highly impactful, such initiatives are still scarce (1).

Successful international examples such as the Cleveland Clinic's Heart and Vascular Institute (1), the Medicare and Medicaid bundled payment program, ICHOM (e.g., international outcome-based datasets in amongst others Cardiology) and the Netherlands Heart Registration have shown the impact on clinical outcomes for cardiac patients of implementing VBHC principles in healthcare and/or the impact of implementing value-based payment models in the field of Cardiology (2). However, a full collaboration between primary, secondary and tertiary care regarding one medical condition using VBHC as primary methodology has not been initiated yet. Therefore, in 2015 in the southeast of the Netherlands, cardiologists, cardiothoracic surgeons, and general practitioners (GPs) launched the Netherlands Heart Network (NHN) to create a regional integrated care system for cardiac patients. Besides healthcare professionals, hospital boards, diagnostic centers, ambulance services, home care organizations, academic centers and pharmacists are actively involved in the NHN as well.

Goals and Vision of the Program

The goal of the NHN is to maximize 'patient value', defined as optimal patient-relevant outcomes divided by lowest possible costs. The NHN's vision is that optimal patient value can be achieved if all relevant healthcare providers in primary, secondary and tertiary cardiac care join forces, embrace and prioritize improving patient value as the shared goal and use data from daily practice to continuously measure and improve the added value of healthcare delivery. Therefore, the NHN facilitates a platform for physicians and other healthcare providers to form multidisciplinary network teams. These physician-driven teams use a solid methodology, based on VBHC principles, to define and implement transmural care standards (i.e., care standards between all healthcare providers involved in primary, secondary and tertiary care), measure and discuss outcomes (i.e., selected by ICHOM datasets), initial conditions and costs (i.e., aligned with health insurance companies) and implement improvement projects as crucial elements of the PDSA cycle (1,3).

Local Challenges in Implementation

Before the start of the NHN, major challenges needed to be tackled, namely creating a mutual vision among healthcare providers in the full care chain and making daily practice data available to gain insights into the outcomes that matter most to patients and enable improvement. As healthcare was organized in silos, circumstances for optimal collaboration and coordination between healthcare providers were not ideal. Although the provided care and cure for patients was believed to be adequate, physicians lacked structural insights into the outcomes that matter most to patients and quality systems were only organized on institutional levels. To generate more in-depth insights for physicians, a regional quality system for continuously improving outcomes was needed. An additional challenge is that the current healthcare system is based on fee-for-service instead of fee-for-quality, which might disincentivize collaboration.

Design of the Initiative

To increase patient value in the full care cycle, the design of the NHN involves all relevant healthcare providers in the field of cardiac care in a region of approximately 800,000 inhabitants. Multidisciplinary network teams were formed around the most prevalent heart conditions. In order to ensure a mutual vision in the organizations and implement changes in daily routine, a steering group was installed including representatives of GP organizations, physicians and board members of the participating hospitals. Moreover, a program manager was employed, assisted by a methodological expert, to develop the stepwise methodology and facilitate the network teams (3).

In periodical network meetings physicians develop transmural care standards, using a stepwise methodology to optimize patient value (3). Those care standards are focused on adherence to prevailing guidelines for both cardiologists and GPs. Full attention is paid to acute stabilization of AF-patients' complications or hemodynamic comprise, detection and treatment of underlying and accompanying cardiovascular disease, stroke risk assessment and oral anticoagulation for stroke prevention, and rate and rhythm control therapy. Moreover, a nurse-led outpatient clinic is implemented in order to facilitate physicians in the optimization of guideline adherence (3). Also, AF-patients are extensively informed by the nurses about their disease and lifestyle improvement options. After completion, the care standard is implemented in practice and a continuous improvement cycle (based on insights of outcomes, new guidelines, consultation of patient panels and technological innovations) starts to ensure the optimization of patient value per medical condition. Collection of data regarding patient-relevant outcomes and initial conditions creates large real-world data (RWD) databases. Data analysis creates insights into outcomes and costs and enables the identification of potential improvement. Subsequently, disease-specific improvement projects are initiated. This stepwise methodology is a key factor in the NHN's strategy since it guides physicians to focus primarily on improving outcomes and decreasing costs by applying disease-specific protocols, processes and structures.

Via the Patients Advisory Board which advises on strategy, priorities and project plans, patients are actively involved within the NHN. Also, per medical condition a patient panel is organized to reflect on the experienced healthcare pathways and provide advice regarding improvement possibilities.

Implementation of the Initiative

The NHN can best be characterized as 'pragmatic' and 'bottom-up', initiated by highly motivated cardiologists of four large and medium-sized Dutch hospitals (fortified with regional GP organizations), and started on a small scale with one cardiac condition (i.e., AF). Subsequently, care standards for other medical conditions were developed, taking previous experiences into account. To involve all healthcare providers, a thorough communication strategy was applied via training programs, smartphone applications and periodic newsletters with up-to-date disease-specific information. After implementation of the care standards, a PDSA cycle is applied to continuously improve patient value, based on outcomes and on peer-to-peer reviews (i.e., based on tailored comparison) (4) to assess whether the agreements were implemented as intended. Then data are analyzed and periodically discussed in the network team meetings. To improve the balance between outcomes and costs per medical condition, an innovation agenda was developed to guide impactful innovations into practice. All studies in the NHN are assessed for approval by the Medical research Ethics Committee United (MEC-U). MEC-U confirmed that the Medical Research Involving Human Subjects Act does not apply to the performed studies and that therefore an official approval is not required.

At initiation, directors of the involved healthcare organizations were informed but had no formal role in the NHN. In this initial phase, funding was obtained via unrestricted grants from pharmaceutical and medical device companies. The first results of implementation of the developed care standards were appealing in terms of patient-relevant outcomes and healthcare costs (5). Consequently, this approach resulted in the support by directors of the healthcare organizations and finally in a formal collaboration agreement between all involved healthcare providers. Due to clear agreements on aims, tasks and responsibilities, this formal agreement resulted in smooth data transfer and a higher implementation power of the care standards. Moreover, health insurance companies were convinced by the impact of the NHN, resulting in an enduring partnership in which financial resources were allocated. This partnership constitutes a crucial step in creating the most relevant preconditions to implement highly impactful innovations for cardiac patients.

Success of the Initiative

The multidisciplinary networks succeeded in defining, implementing and continuously improving regional care standards for the most prevalent heart conditions in order to optimize patient value **(Figure 1)**. Audits confirm that adherence to guidelines and the completeness of the needed registrations on outcomes is >95% (5). Moreover, a

data infrastructure was built complying with the applicable laws and regulations. Large RWD databases (>3,000 patients) are created including initial conditions, outcomes and healthcare costs. It was shown that the implementation of the care standard for AF (448 patients) resulted in significantly better EHRA (European Heart Rhythm Association) scores (*B*=0.17;SEM=0.04;*p*<0.01), blood pressure levels (*B*=7.71;SEM=0.96;*p*<0.01) and a significant shift of patients with persistent to paroxysmal AF (*B*=2.93;SEM=0.40;*p*<0.01) 6 months after implementation (5). A 12 months follow-up comparison of a retrospective (N=502) and prospective cohort (N=1,045) showed significant outcome improvement regarding hospitalizations (retrospective N=263 (52.4%)/prospective N=356 (34.1%); $OR_{age\text{-}gender\ adjusted}$=0.50;95%CI 0.40-0.62;*p*<0.01) and Event Free Survival (retrospective N=278 (55.4%)/prospective N=385 (36.9%); $OR_{age\text{-}gender\ adjusted}$=0.49;95%CI 0.40-0.61;*p*<0.01). Data and study materials will not be made available to other researchers for purposes of reproducing the results or replicating the procedure.

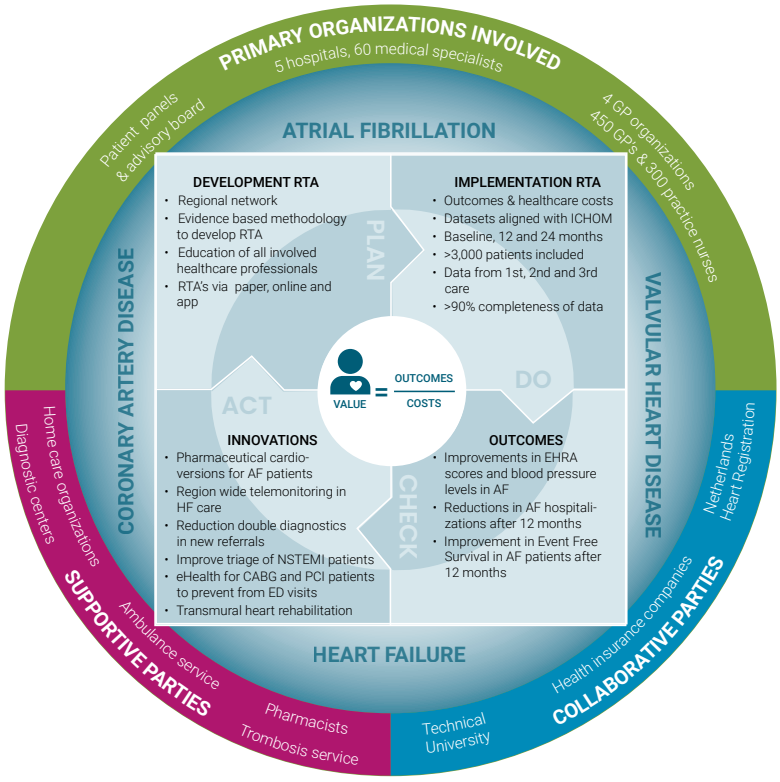

Figure 1. Procedure en Results of the Netherlands Heart Network
Figure legend: GP= General Practitioner, RTA= Regional Transmural Agreement, ICHOM= International Consortium for Health Outcomes Measurement, EHRA= European Heart Rhythm Association, AF= Atrial Fibrillation, HF= Heart Failure, NSTEMI= Non-ST-elevation myocardial infarction, CABG= Coronary Artery Bypass Grafting, PCI= Percutaneous Coronary Intervention, ED= Emergency Department

Translation to Other Settings

Processes of healthcare delivery vary between medical conditions, and healthcare systems vary between countries. However, the NHN's methodology is based on VBHC principles and the physician-driven and patient-centered approach of the NHN is independent of healthcare systems and/or medical conditions and can be used as a blueprint for other settings. Core elements such as physician leadership, formation of multidisciplinary network teams to develop regional care standards and using RWD to measure and improve outcomes should be addressed. Creating a shared vision among healthcare providers is a precondition for success. Our approach showed that it is effective to start bottom-up focusing on outcomes, taking into account initial conditions and costs by developing and implementing regional care pathways. Other initiatives are advised to consider starting on a small scale (i.e., one medical condition) and gradually extending to more medical conditions when the first hurdles are overcome. In parallel, involved healthcare providers can design collaboration agreements. In order to realize such a mutual understanding, a clear governance structure needs to be organized in which the responsibilities of the involved organizations are aligned.

Summary of the Experience, Future Directions and Challenges

The NHN is a physician-driven and patient-centered collaboration of healthcare providers in primary, secondary and tertiary care based on the VBHC philosophy, in which multidisciplinary networks are initiated for the most prevalent cardiac conditions. Following a stepwise methodology, the physicians develop and maintain transmural care standards in order to continuously improve patient value based on RWD, by using a PDSA cycle. Initially, the NHN started pragmatically with highly motivated physicians. However, due to appealing results, the healthcare institutions' directors were convinced by the potential impact of the initiative. Therefore, an administrative embedding was created in which the hospitals and GP organizations were actively involved in the NHN, and thereby acquired a guiding role within the NHN. Nevertheless, the NHN remains a physician-driven organization in which the primary focus is to increase patient value of cardiac patients in which the patient perspective is central. Next to applying a PDSA cycle based on regional care standards, outcomes and costs of healthcare delivery, an innovation agenda was developed to guide innovations into practice.

Within the innovation agenda an information technology platform is crucial to facilitate both patients and healthcare professionals (i.e., data-sharing or e-health interventions). Although such a platform will facilitate the healthcare process, it also introduces a challenge in selecting regional IT-systems that are able to facilitate and integrate healthcare processes into the full care cycle and fit the preferences of all organizations involved.

Currently, healthcare providers in the Netherlands are financed individually and paid for volume of healthcare delivery. Introducing bundled payment models might encourage

the current collaboration and facilitate the shift from a 'volume focus' towards a 'value focus'. Within the NHN, first steps have been taken by a shared saving agreement regarding the implementation of innovations. Part of this agreement contains the sustainability of the project organization of the NHN. Moreover, the health insurance companies have agreed to compensate healthcare institutions if implementing impactful innovations result in loss of income. However, for the future, fundamentally different choices must be made to arrange sustainable funding for network organizations that are valuable to patients. Although it is not yet clear how this can be organized within a network approach, a multi-provider investment seems to be a precondition.

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Chapter 3

Introducing a method for implementing value-based healthcare principles in the full cycle of care: using atrial fibrillation as a proof of concept

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Abstract

Background:
Value Based Health Care (VBHC) is a well-known strategy in most countries, amongst whom the Netherlands, to improve patient-relevant outcomes and reduce healthcare costs. However, until now a methodology to implement VBHC principles in the full care cycle has been lacking. Therefore, this study describes a stepwise approach to implement and continuously improve patient-relevant outcomes in the total care delivery value chain.

Methods:
Key principles of VBHC are used to develop a stepwise methodology in which healthcare providers of primary, secondary, and tertiary care collaborate in a physician-driven initiative called the Netherlands Heart Network. The stepwise methodology incorporates the Plan-Do-Study-Act cycle to continuously improve patient-relevant outcomes. To outline the presented methodology, a prevalent cardiac condition (i.e. atrial fibrillation) is used as a proof of concept.

Results:
Using the stepwise methodology results in an adequate registration of patient-relevant outcomes and a structured evaluation of adherence to prevailing guidelines. Based on the followed methodology, detailed improvements are defined in order to optimize patient-relevant outcomes.

Conclusions:
The presented methodology provides a description how to implement VBHC principles in the full cycle of care. However, since this methodology is a first concept, future research should apply and assess the stepwise methodology in other fields and for different medical conditions.

Introduction

Value Based Health Care (VBHC) is a well-known strategy in healthcare (1-4) that aims to improve patient value, which is defined as outcomes that matter most to patients divided by the costs of healthcare delivery (1,3). According to Porter's outcome measurement landscape (1,5), organizing processes and structures within the healthcare setting is a precondition to realizing the best patient-relevant outcomes. To structurally measure and improve the patient value for specific medical conditions, researchers and/or healthcare providers must apply the key components of the VBHC strategy as defined by Porter (i.e. organize into integrated practice units; measure outcomes and costs for every patient; move to bundled payments for care cycles; integrate care delivery across separate facilities; expand excellent services across geography and build an enabling information technology platform) (2-4,6). Healthcare providers are advised to start the shift towards a more value-driven system by measuring and improving outcomes (6). Although various best practices are mentioned in the literature regarding some elements of the VBHC strategy, so far the focus has mostly been on measuring and improving outcomes within institutions (7-9). This leaves important parts of the total care delivery value chain unexamined. Moreover, other elements of the VBHC strategy have not been implemented and the order in which the various components will be implemented is still unclear in several healthcare systems, amongst whom the Netherlands. This lack of clarity may also be related to the diversity of healthcare systems. Currently, this limits the impact of VBHC because all dimensions of the VBHC strategy are expected to be mutually reinforcing, and should thus be examined (6).

One of the components introduced by Porter is 'integrate care delivery across separate facilities' (6). The purpose of this component is to strengthen the collaboration between healthcare professionals in primary, secondary, and tertiary care, as all involved healthcare providers contribute to the outcomes achieved and costs incurred in the treatment of all patients with the same medical condition (4,6). In such a multi-institutional network, other crucial aspects in VBHC become increasingly challenging. Valid and reliable registration of outcomes in accordance with the quality measures that matter most to patients, as well as using process and structure indicators that are interrelated to these outcomes (1) and are in accordance with (inter)national guidelines, is essential for making VBHC work in a care network. Numerous studies have indicated that adherence to guidelines within institutions has a positive impact on improving patient-relevant outcomes (10-14); such data are lacking for care networks. In addition, until now, there has been no information regarding which steps should be taken in order to improve outcomes of the full cycle of care (i.e. involving all relevant stakeholders in primary, secondary, and tertiary care) in an active multidisciplinary quality network of healthcare providers.

Atrial fibrillation is a frequently diagnosed arrhythmia in Europe (15) and it is often treated by multiple healthcare providers. Prior research by Porter (6) suggests that extensive collaboration between healthcare providers in primary, secondary, and tertiary

care may enable improvements in patient-relevant outcomes and reduce healthcare costs. However, until now such a multi-institutional quality network for atrial fibrillation care for measuring and continuously improving patient-relevant outcomes and reducing health care costs has not been initiated.

Continuous improvement of patient value using quality indicators and interrelated process and structure indicators is crucial in VBHC (1). The cycle of Deming (i.e. Plan-Do-Study-Act cycle (PDSA cycle)) may be a helpful framework to continuously update indicators in quality research (16). Integrating an outcome-based improvement cycle into VBHC has already proven to be of added value (17). Furthermore, integrating the continuous improvement of patient-relevant outcomes and related costs into a PDSA cycle, covering a multi-provider regional network, creates a unique, reproducible and structured instrument with the potential to continuously increase the patient value in the full cycle of care.

Although there are several quality models for single institutions, innovative and structured procedures to continuously improve VBHC principles in the full cycle of care are still lacking in several countries, amongst whom the Netherlands. Therefore, the goal of the present study is to introduce a stepwise methodology that is doctor driven and patient centered to implement and continuously improve patient-relevant outcomes in the total care delivery value chain. In addition, completeness of data collection on outcomes and adherence to process and structure indicators will be shown for atrial fibrillation to outline the presented methodology.

Methods

Design and setting

In the present study, a stepwise methodology is introduced using key principles of the VBHC strategy to define, implement, evaluate, and continuously improve patient-relevant outcomes and costs in the full cycle of care. This stepwise methodology is developed within a clinician driven network initiative, involving four hospitals (i.e. one heart center and three referring hospitals) and four general practitioner (GP) organizations in a suburban region in the Netherlands (i.e. South East Brabant region), called the Netherlands Heart Network (NHN) (18). The NHN is an example of an organization that facilitates the integration of care delivery facilities and aims to contribute to the continuous improvement of value for patients with a heart disease. In order to develop a VBHC network, NHN develops transmural standards of care for highly prevalent medical conditions associated with high costs and a strong need for multi-provider collaboration. The NHN provides a platform for healthcare providers to collaborate and to increase the patient value by defining transmural quality standards using VBHC principles as well as a shared PDSA cycle, in the total care delivery value chain. The participating multidisciplinary healthcare providers, consisting of providers in primary, secondary, and tertiary care (i.e. cardiologists, nurses,

GPs, pharmacists, ambulance service, home care organizations, etc.), remain responsible for the implementation of the quality standards and improvement projects within their own professional field.

In order to outline the results of this stepwise methodology, an elaboration of one highly prevalent medical condition in the field of cardiology will be illustrated in this paper, namely atrial fibrillation (i.e. arrhythmic disorder) (19).

Stepwise methodology

To be able to improve patient-relevant outcomes in the full cycle of care through a stepwise approach, a transmural standard of care is developed by healthcare providers in primary, secondary, and tertiary care. Support for the development and implementation of the transmural standard of care is increased by giving multidisciplinary healthcare providers the lead in this procedure, following a predefined roadmap concerning the following elements (**Figure 1**):

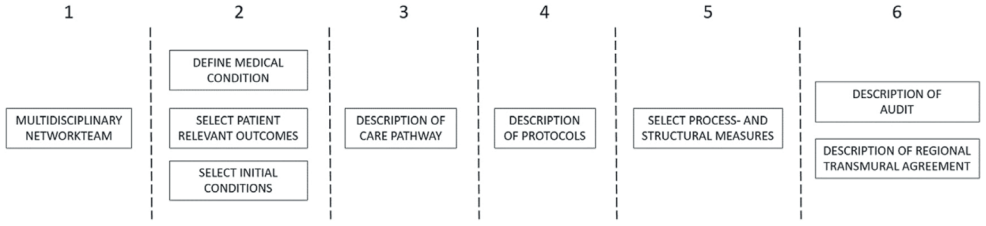

Figure 1. Stepwise methodology.

STEP 1: A *multidisciplinary network team* is formed with a delegation of multidisciplinary healthcare providers from primary (i.e. GPs and primary care nurses), secondary (i.e. cardiologists and nurses), and tertiary care (i.e. electrophysiologists and cardiac surgeons).

STEP 2: The *medical condition* is defined in which a uniform definition is described for the primary, secondary, and tertiary care process (i.e. based on prevailing medical standards and guidelines).
Subsequently, a selection is made of the *most relevant outcomes* and *initial conditions* for the medical condition. For this procedure the validated indicator sets of the Netherlands Heart Registration (20) are used.

STEP 3: A description is made of the *care delivery value chain* (CDVC) of the medical condition in which the pathway of the patient is described in the full cycle of care.

STEP 4: A description is made of the required *protocols* of essential elements in the CDVC that contribute the most to outcomes and costs.

STEP 5: A selection of *process and structure indicators* regarding elements that contribute most to managing outcomes (1) and costs is made to be able to measure the adherence to the regional standard.

STEP 6: In order to assess whether the implementation is performed as intended, an *audit* is conducted based on the quality indicators (i.e. patient-relevant outcomes, process and structure measures). In establishing the audit criteria, healthcare providers determine the norm of implementation of the various indicators. Finally, a *Regional Transmural Agreement* (RTA) is developed as a summary of the relevant steps in the transmural standard of care.

Plan – Do – Study – Act cycle

The stepwise methodology incorporates the PDSA cycle (16) in order to facilitate continuous (e.g. yearly) improvement of outcomes and costs. After the finalization of the RTA this continuous improvement cycle is started and includes the following elements (**Figure 2**):

1. The first step after the development is the implementation of the transmural standard of care in the full care cycle.

2a. Within six months after the implementation, an audit is performed by an audit team of healthcare providers. In every organization, at least two auditors assess whether the implementation is performed as intended. During the audit, amongst others, the adherence to process- and structure indicators is assessed. Afterwards, an audit report is composed with the findings and advice for the specific organization.

2b. Healthcare organizations register the patient-relevant outcome measures in the Electronic Medical Records (EMR) of the healthcare organizations. Every year the outcomes are extracted by data analysts in order to analyze the outcomes so that the most relevant findings can be included in the revised standard of care. To assess the most relevant findings statistical software packages are used.

2c. To include the opinion of patients, focus group interviews are annually organized for every medical condition. The main findings are analyzed using qualitative research techniques in order to update the current standard of care.

2d. Subsequently the guidelines and national standards are reviewed and renewals are taken into account to update the current standard of care.

2e. In addition, leading medical industry organizations are invited to pitch potential innovations for the medical condition. Suitable innovations have the potential to increase patient-relevant outcomes and reduce healthcare costs.

3. Based on all the input the multidisciplinary network team decides, supplemented with the quantitative analyses regarding the patient relevant outcomes, which improvements of the transmural standard of care are needed to improve the relevant outcomes and reduce the healthcare costs. The main improvements are selected

based on criteria relating to increasing patient value and assessing the feasibility and capacity change:

a. The improvement must concern a large group of patients;
b. The improvement needs to have an impact on the (reduction of) healthcare costs;
c. A maximum of three improvements are suggested per cycle (for every medical condition). By restricting the number of improvements, the effects can be evaluated and the implementation is more feasible;
d. At least one improvement needs to be implemented regarding the patients' perspective;
e. The improvement has to have an impact on patients' satisfaction;
f. The improvement must have an impact on the healthcare providers in primary, secondary, and tertiary care.
g. Thereafter, adaptations to the standard of care are made and the standard of care is re-implemented in practice. Healthcare providers are responsible for these adaptations and the re-implementation of the standard of care.

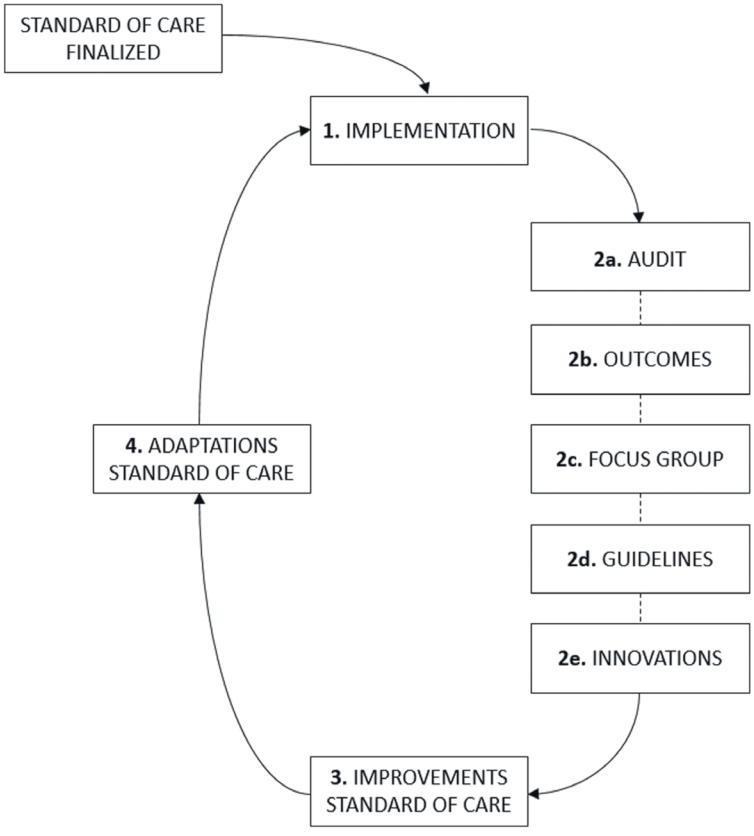

Figure 2. PDSA cycle within the NHN.

To illustrate the relationship between the stepwise methodology and the embedded VBHC principles in **Table 1** the outline is presented.

Table 1. Relationship between the stepwise methodology and the embedded VBHC principles

PDSA cycle	operationalization NHN	embedded VBHC principles

Plan	• organizing multidisciplinary networkteam
	• Defining medical condition
	• Indicating most relevant outcomes and initial conditions
	• Defining protocols
	• Indicating process-and structure indicators
	• Defining RTA
	(see **Figure 1**)
		• Organize healthcare for patient groups with the same medical condition
		• Measure and improve outcomes for each patient covering:
		  • All tiers of the outcome measure hierarchy
		  • The care delivery value chain in the full cycle of care
		• Measure and improve relevant process-and structure indicators contributing to the outcomes that matter most to patients
		• Measure and improve costs related to healthcare delivery
		• Integrate care delivery systems
		• Use a patient centered approach, involve patients in deciding what matters most
		• Let physicians lead the change

Do	• Implementation of standard of care (see **Figure 2**)	
Study	• Performing audit • Analyzing patient relevant outcomes • Organizing focus group interviews • Reviewing national guidelines and standards • Evaluating potential innovations (see **Figure 2**)	
Act	• Defining improvements to the standard of care • Adaptations towards the standard of care (see **Figure 2**)	

Results

Based on the PDSA cycle (**Figure 2**), an outline is provided below of the application of the stepwise methodology in the NHN for atrial fibrillation. Subsequently, the results of the registration density of the patient-relevant outcomes (N > 450 newly diagnosed atrial fibrillation patients) and the adherence to guidelines and protocols (i.e. based on the process and structure indicators) are illustrated in **Table 2**.

Stepwise methodology for atrial fibrillation

PLAN

To create a high-expertise multidisciplinary setting for atrial fibrillation, a network team is formed consisting of four cardiologists (from four different hospitals), two GPs (with special knowledge and interest in heart conditions), four nurses from the outpatient atrial fibrillation clinic, and a delegation from the diagnostic center. This network team has regular meetings (i.e. every six to eight weeks) and develops the transmural standard of care for atrial fibrillation. After the development and implementation, the network team is responsible for the continuous improvement of the developed care standard. In **Table 2** the main elements of the transmural standard of care are outlined. Subsequently, the RTA is developed as a final element of the transmural standard of care.

Table 2. Main elements of the transmural standard of care for atrial fibrillation and the norm- and audit scores of the outcome-, process- and structural indicators.

	Atrial fibrillation	Norm score	Audit score
1. Definition (19)	Concerns an arrhythmic disorder characterized by (1.) irregular RR interval (without the presence of a repetitive pattern), (2.) absence of P-waves on the surface ECG, and (3.) variable atrial cycle length (if visible). In addition, also an arrhythmic disorder is present when atrial fibrillation for at least 30 seconds is observed by cavitation or rhythm recording. AF is categorized into: • First diagnosed AF (i.e. AF that has not been diagnosed before, irrespective of the duration of the arrhythmia or the presence and severity of AF-related symptoms) • Paroxysmal AF (i.e. self-terminating, in most cases within 48 hours. Some AF paroxysms may continue for up to 7 days) • Persistent AF (i.e. AF that lasts longer than 7 days, including episodes that are terminated by cardioversion, either with drugs or by direct current cardioversion, after 7 days or more) • Long-standing persistent AF (i.e. continuous AF lasting for ≥1 year when it is decided to adopt a rhythm control strategy) • Permanent AF (i.e. AF that is accepted by the patient and physician)	N/A	N/A
2. Outcome measures* (21)	• EHRA score (i.e. measured by EHRA I= No symptoms; EHRA II= Mild symptoms, normal daily activities not affected; EHRA III= Severe symptoms, normal daily activity affected; EHRA IV= Disabling symptoms, normal daily activity discontinued)	90%	97,5%
	• CVA or TIA (i.e. amount of CVAs or TIAs)	90%	97,5%
	• Major bleedings (i.e. measured with the BARC-index)	90%	97,5%
	• Admissions (AF related)	90%	97,5%
	• Quality of life (i.e. measured with the validated AFEQT questionnaire (22))	90%	77,9%
	• Adverse effects of medication (i.e. percentage of patients that report serious adverse events due to rate or rhythm control medication)	90%	97,5%
3. Initial conditions (21)	• Age • Gender • Type of AF (i.e. first diagnosed AF, paroxysmal AF, persistent AF, long-standing persistent AF, permanent AF) • Comorbidities (i.e. hypertension, coronary artery disease, heart failure, peripheral artery disease, CVA, diabetes mellitus, Chronic Obstructive Pulmonary Disease, thyroid disease, obesity, valvular heart disease, OSAS) • CHA2DS2-VASc score • HAS-BLED	N/A	N/A
4. Process indicators	• Type of AF is documented	95%	98.8%
	• AF is established using ECG registration/rhythm recording	90%	97.5%
	• Choice for rate/rhythm control is documented	90%	95%
	• Echocardiogram is performed within 6 months after diagnosis	95%	98.8%
	• Results of laboratory research are documented	95%	98.8%
	• The CHA2DS2-VASc-score is documented	90%	97.5%
	• Stable AF-patients are referred to GP	90%	90%
	• For instable AF-patients the reason for outpatient follow-up is documented	90%	95%
	• AF-patients with persistent complaints are referred to a tertiary center	90%	90%
	• For all AF-patients who are registered for an ablation regarding AF, the referring hospital is informed within 7 days about the decision of the heart team	90%	96.7%
	• Time between setting the indication and the ablation is not more than 12 weeks	90%	96.7%

Table 2. Continued.

	Atrial fibrillation	Norm score	Audit score
5. Structure indicators	• In the hospital an outpatient AF clinic is operational for newly diagnosed AF-patients	90%	95%
	• The outpatient AF clinic is operated by an AF-nurse and supervised by a cardiologist	90%	97.5%
	• In the outpatient clinic the needed facilities are arranged to inform and physically examine AF-patients	100%	100%
	• A referral system is designed to refer new AF-patients by the GP	100%	100%
	• Registrations in the outpatient AF clinic are performed in an EMR	100%	100%
	• In the tertiary center the EP-team meets at least once a week to discuss AF-patients	100%	100%
	• The ECG with AF has been received from the GP	100%	90%

AF= atrial fibrillation; RR= Riva-Rocci (blood pressure); ECG= electrocardiogram; EHRA= European Heart Rhythm Association; CVA= cerebrovascular accident; TIA= transient ischemic attack; BARC= *Bleeding Academic Research Consortium; AFEQT= Atrial Fibrillation Effect on QualiTy of life; OSAS= obstructive sleep apnea syndrome; CHA_2DS_2-VASc= score for atrial fibrillation stroke risk; HAS-BLED= score for major bleeding risk; GP= general practitioner; EMR= Electronic Medical Record; EP= Electro Physiologists.*

**Detailed information regarding the definition of the outcome measures can be found elsewhere (19-21*)

DO

The healthcare providers themselves are responsible for the implementation of the transmural standard of care. The healthcare providers need to adjust their procedures (i.e. in accordance with the process and structure measures) and register the needed indicators (i.e. patient-relevant outcomes and initial conditions) in their own organizations.

STUDY

As indicated in **Figure 2**, in the STUDY phase of the PDSA cycle, several activities are performed to analyze the implementation of the transmural standard of care and information is gathered to improve the standard. The data regarding the outcome measures were registered in the Electronic Medical Records of the hospitals by the atrial fibrillation nurses. The results indicated in **Table 2** are from four hospitals in the Netherlands in which the transmural standard of care is implemented and evaluated.

Based on (inter)national guidelines, protocols, and the consensus of the healthcare professionals involved in the multidisciplinary network team, a norm score is presented for the completeness of registrations of the patient-relevant outcomes. During the audit it is assessed whether the healthcare providers have registered the outcomes as they had agreed. As indicated in **Table 2**, the EHRA score, CVA or TIA, major bleedings, atrial fibrillation related admissions, and the adverse effects of medication all score above the norm (97.5%). The quality of life score, assessed with a self-administered questionnaire (AFEQT), illustrates a score (77.9%) that is below the norm score of 90%.

To assess the adherence to guidelines, the process and structure indicators are measured. In **Table 2** the norm and audit scores for adherence to both indicators is shown. The table illustrates that only the 'ECG registrations with AF are received from the GP' score is below the set norm (90%).

In VBHC, patients are central in the healthcare process (1,6,7). Therefore, focus group interviews are performed using the stepwise methodology to receive information from patients on specific topics (i.e. experiences of the outpatient atrial fibrillation clinic, received information, communication between healthcare providers, alignment between healthcare providers, and questions regarding the aftercare process). The following are the main improvements mentioned by six patients (i.e. at least one AF patient from each of the four hospitals involved in the NHN) with atrial fibrillation participating in the focus group: *more information prior to the consultation with the outpatient atrial fibrillation clinic; information regarding referral to GP; more alignment between cardiologist and GP regarding the process of care; contact information in case of questions or medical complaints regarding patients' atrial fibrillation.*

In the yearly cycle for the transmural standard for atrial fibrillation, no new guidelines or standards were introduced. However, the literature states (23) that approximately 20% of ischemic strokes can be attributed to (undiagnosed) atrial fibrillation. For that reason, the healthcare providers in the multidisciplinary network team assessed potential innovations to detect undiagnosed atrial fibrillation patients in primary care.

ACT

In the ACT phase of the PDSA cycle for atrial fibrillation, the results, as mentioned in the STUDY phase, regarding the audit, focus group interviews, review of guidelines, pilot for potential innovations, and the results of the patient-relevant outcomes improvement projects are defined to enhance the relevant outcomes for patients diagnosed with this specific medical condition. To be able to select the most relevant improvement project, the healthcare providers within the network team used their expert opinion and statistical analyses of the outcome measures and initial conditions to assess the potential impact of improvements on the patient value of patients diagnosed with atrial fibrillation. Since the multidisciplinary network team includes the main expertise from primary, secondary, and tertiary care for a specific heart condition (i.e. in this case atrial fibrillation), the healthcare providers in the network team are mandated to select the most relevant improvements. During the selection of the most relevant improvements, the feasibility and change capacity is also taken into account, to enlarge the potential effects of the improvement. Based on the results and the criteria for selecting improvement projects for atrial fibrillation, the following improvements were defined:

- Update of the patient information folder for atrial fibrillation patients;
- Adaptations of the referral system in order to receive all ECGs of patients who were diagnosed with atrial fibrillation and referred to the hospital;
- In the diagnostic centers, other relevant healthcare providers now have the possibility to view the needed information;

- Atrial fibrillation nurses were instructed to call and remind patients to complete and send the quality of life questionnaire back to the outpatient clinic;
- Strategy to screen for undiagnosed atrial fibrillation by GPs with an innovative instrument.

The PDSA cycle is repeated annually. Therefore, during the following audit procedure it will be evaluated whether the improvement projects have resulted in better patient-relevant outcomes and reduced healthcare costs.

Discussion

In this study, a first concept of a stepwise methodology to implement and continuously increase the patient value in the full cycle of care using key principles of VBHC is presented and outlined for atrial fibrillation as a proof of concept. Based on the qualitative and quantitative audit information and the first positive results, it appears the stepwise approach is feasible for implementing VBHC principles in the total care delivery value chain when a multi-institutional network is used. Furthermore, the PDSA cycle was applied in order to continuously improve patient-relevant outcomes and to define improvement projects to increase value for cardiac patients.

The results obtained from using this stepwise methodology for atrial fibrillation suggest that it is feasible to implement VBHC principles in a network organization. Using the methodology, healthcare providers in primary, secondary, and tertiary care involved in the NHN succeeded in defining patient value in terms of outcomes and costs as a shared goal. Subsequently, they agreed on standards of care, directly eliminating cases of inefficiency and improving several parts of the care pathway, e.g. by improving communication between healthcare providers. The results show a high registration completeness of patient-relevant outcomes and a structured evaluation of adherence to prevailing guidelines (i.e. process and structure indicators). These findings are in accordance with the results presented in a study by Hendriks et al. (24) in which adherence to guidelines, by introducing a protocol-driven outpatient atrial fibrillation clinic, resulted in improved patient-relevant outcomes and reduced healthcare costs. In addition, conditions that potentially result in improved healthcare quality in the total care delivery value chain (i.e. transmural agreements, registration of main patient-relevant outcomes, adherence to guidelines, following a PDSA cycle) are included in the presented stepwise methodology, which increases the potential of improved patient-relevant outcomes. Additionally, based on Porter's outcome measurement landscape (1,5), process and structure indicators are interrelated and supportive of patient-relevant outcomes. This suggests that measuring and improving process and structure indicators in a structured manner supports the improvement of outcomes, which is the main component of the presented stepwise methodology. The implementation of the methodology in practice

has already resulted in improved patient-relevant outcomes in the field of atrial fibrillation in a suburban region in the Netherlands (25) and in the assessment of the quality of care of atrial fibrillation patients (26). However, a solid methodology in which outcomes are used for improvement projects in the full care cycle within a PDSA cycle is still lacking (27).

A crucial aspect in VBHC is that (multidisciplinary) healthcare providers are important drivers of initiatives (6). The presented stepwise methodology to implement VBHC principles in the full cycle of care focusses on the medical conditions in which healthcare providers in primary care (i.e. GPs, ambulance service, thrombosis service, pharmacists, and diagnostic centers), secondary care (i.e. cardiologists and nurses), and tertiary care (i.e. electrophysiologists and thorax surgeons) are in the lead. With this approach, the responsibility and support for both the development and implementation of the transmural standard of care stays among the healthcare providers and is free of institutional interests. It is to be expected that administrative interference in healthcare organizations enables discussions in which institutional interests (i.e. budgets or substitution of care) may be more central than the perspectives of patients.

The VBHC strategy is defined in six interrelated domains (6). Five domains support the main principle in VBHC, namely measuring and improving outcomes and related costs. In VBHC, increasing patient value should become the overarching goal for all stakeholders involved (1). As a consequence, a different line of thoughts is crucial for developing reimbursement or purchasing models that focus on value instead of volume. In the United States the MACRA legislation is introduced as a methodology to reshape the healthcare delivery, by eliminating the fee-for-service payments into a value-based payment system (28-30). Other countries, amongst whom the Netherlands, may learn from those disruptive innovations since their experiments regarding value-driven financial models are still on a basal level (31,32). Reasons may be that the implementation of VBHC principles differ due to diverse healthcare systems. As there is no hard evidence available regarding the optimal overall healthcare system, the best route for implementing VBHC principles needs to be determined. Some healthcare systems, for example in the Netherlands, lend themselves more to a doctor-driven and patient-centered approach to build a multidisciplinary value-driven network, while other healthcare systems may be better for the introduction of payment models as a first step. The best approach is still unidentified and needs to be assessed in future research.

Limitations

Despite the fact that the presented stepwise methodology has been shown to be successfully implemented, it may also have suffered from some limitations. However, in the PDSA cycle the outcomes will be evaluated and differences in outcomes may lead to improvement projects. The first focus is on the process of healthcare delivery. By focusing first on improving the care pathway, measuring and improving compliance with process and structure indicators – all of which were selected because of their proven relation

with the selected outcomes that matter most to patients – it is expected that providers will be able to increase the patient value. Although the stepwise methodology seems promising (25), the exact relationship between process, structure, and outcomes needs to be assessed in future research. As a consequence of improved outcomes, healthcare providers are also expected to be able to reduce costs, as improving the quality of care may be related to a reduction of costs (33,34).

A second limitation of the presented methodology may be that currently only patient-relevant outcomes are included. In the patient value equation, both outcomes and costs are the main aspects of VBHC. Since improving outcomes is most relevant for patients and most interesting for healthcare providers, it may be advisable to focus on outcomes first. Nevertheless, after the effectiveness of the stepwise methodology is shown regarding outcomes, healthcare costs will be assessed and become a part of the PDSA cycle in the near future.

The presented methodology seems to be an effective approach; however, it may be that the lack of support of participating organizations decreases the strength of the implementation of the transmural standards of care. Prior initiatives, such as the Children's Hospital of Philadelphia (35), have already shown to be effective with a central management. Therefore, the stepwise methodology may have even more impact in an integrated healthcare system in which other aspects of the VBHC strategy, e.g. building integrated practice units or introducing bundled payment models, can be centrally implemented.

Conclusions

A stepwise methodology is presented in order to implement VBHC principles in the full cycle of care in a cardiac network organization, including first results of implementing the proposed methodology for patients suffering from atrial fibrillation. The methodology was successfully implemented in a Dutch regional network, resulting in a high registration density of patient relevant outcomes, good adherence to the regional transmural standard and selection of first regional projects to improve outcomes and costs. Future research will be conducted to establish the impact of the presented methodology on patient value.

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Part 2

Real life data from this atrial fibrillation network

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Chapter 4

Regional collaboration to improve atrial fibrillation care: preliminary data from the Netherlands Heart Network

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Background:
Guideline non-adherence and variations in therapeutic and diagnostic trajectories result in suboptimal atrial fibrillation (AF) treatments. Large academic and referral hospitals demonstrated positive effects of dedicated outpatient AF clinics. Although similar results have not been indicated in (small) non-academic hospitals yet, ample opportunities are present when collaboration is initiated on a regional level. Therefore, this study assesses the effectiveness of outpatient AF clinics in a collaborative region in the Netherlands.

Methods:
For this study baseline and 6 months follow-up data of a prospective cohort including newly or recently diagnosed AF-patients of 4 hospitals involved in the Netherlands Heart Network are used. From January'15 to March'16 patient relevant outcome measures (i.e. EHRA score, stroke, major bleedings, hospitalizations, serious adverse effects of medication, and mortality) are gathered. Descriptive and regression analyses are performed to assess the effectiveness of outpatient AF clinics.

Results:
In the analyses 448 AF-patients were included. After 6 months, significant improvements regarding EHRA score ($p<0.01$), hypertension ($p<0.01$), and type of AF ($p<0.01$) were indicated. Results of the patient relevant outcomes showed that AF-patients were hospitalized 23 times, no major bleedings and 2 strokes occurred. Furthermore, zero AF-patients reported serious adverse effects of medication and no AF-patients deceased.

Conclusions:
Collaboration between cardiologists in a regional setting permits further improvement of AF care. Therefore, such quality targets are not exclusively reserved to large academic or referral hospitals. Although promising, future research should put effort in measuring the effectiveness of the outpatient AF clinics also on the long run.

Abstract

Introduction

Atrial fibrillation (AF) is the most frequently diagnosed arrhythmia [1-4], affecting only in Europe over 6 million patients [5] and leading to approximately 583 million Euros of the Dutch annual healthcare expenditure [6]. Due to the ageing population, the expectation is that both the number of AF-patients and healthcare costs will increase rapidly during the coming years [1], if no further action is taken.

Optimal treatment with less cardiovascular events in AF care can be established when adherence to guidelines is increased [7-9], and variations in therapeutic and diagnostic trajectories are reduced. Prior research indicated that improved guideline adherence and providing extensive information to patients is an achievable target in cardiac care [9-11]. More specifically, an integrated approach for AF has shown to be an effective [9, 12] and cost-effective [13] solution in the treatment of AF-patients by introducing 'nurse-led care'. Compared to usual care, in nurse-led care specialized nurses perform activities to treat AF-patients using protocolled procedures supervised by a physician. Until now most nurse-led care is operationalized and assessed for effectiveness in large academic hospitals [14], assuming that this procedure is solely feasible in similar settings. However, opportunities for outpatient AF clinics in (small) non-academic hospitals may be created when collaboration is initiated on a regional level.

Regional collaboration in healthcare involves adapting similar procedures and activities between cooperating partners (i.e. cardiologists, nurses, and general practitioners (GPs)), increasing the potential of collective improvements of outcomes that are most relevant for patients. However, to establish collaboration between hospitals regarding specific cardiac conditions, patient care pathways need to be aligned. Subsequently, those patient care pathways should be implemented and evaluated for effectiveness by using similar parameters.

The aim of this study was to assess if the nurse-led care in a collaborative region of 4 non-academic hospitals in the Netherlands is effective in improving outcomes for AF-patients after 6 months of diagnosis. To assess the registration density of the nurse-led care, completeness of registrations was also evaluated as a quality measure of AF care.

Methods

Population and design

Data for the present study was gathered at baseline (T0) and 6 months follow-up (T6) of the prospective intervention group of the AF-NET study imbedded in the Netherlands Heart Network (NHN), between January 1st 2015 and March 1st 2016. In essence, the NHN is a regional, joint effort of all relevant healthcare providers in primary, secondary, and tertiary care (i.e. cardiologists, GPs, nurses, ambulance service, thrombosis service, home care organizations, pharmacists, and diagnostic centers) to improve the quality of care for

cardiac patients by organizing the total healthcare chain in an optimal way. To achieve this purpose 4 hospitals and 4 GP organizations collaborate in a densely populated area in the Netherlands (761,763 inhabitants in 2017 [15]). The participating hospitals vary in size considerably, ranging from a 5 cardiologists' practice to a high-volume heart center.

Patients included in the present study originated from the outpatient AF clinics of the 4 hospitals involved in the NHN. Patients were included in the study when they were ≥18 years, newly or recently diagnosed with atrial fibrillation, were competent to read and agree on the informed consent, and had provided written informed consent.

AF-NET study

Outpatient AF clinic

A regional care standard has been developed for AF-patients visiting the outpatient AF clinic. This standard includes a description of the care pathway, uniform definitions for AF, initial conditions, process-and structural measures, aligned protocols to treat AF-patients, and patient relevant outcome measures. Using this regional care standard, the same procedures for AF-patients were applied in the 4 collaborating hospitals. Additionally, identical patient relevant outcome measures were registered at T0 and T6.

Within the outpatient AF clinic the AF-nurse performs the required registrations and provides education for the AF-patients during a consultation of approximately 45 to 60 minutes. During the consultation, the AF-nurse makes an inventory of complaints and the general health status of the patients. The education strategy includes information about AF and the treatment options, in order to make informed decisions concerning the treatment. Furthermore, the AF-nurse explains the relevance of treatment compliance and clarifies to the patients how the follow-up procedure will continue via the cardiologist. By using this procedure cardiologists receive more detailed information regarding the patients' conditions, supporting the decision-making process and the adherence to guidelines by medical specialists. The outline of the AF-NET study is shown by the flowchart in **figure 1**. In prior research [9, 11] nurses made decisions regarding AF care themselves, leading to an essential different process than the AF-NET study.

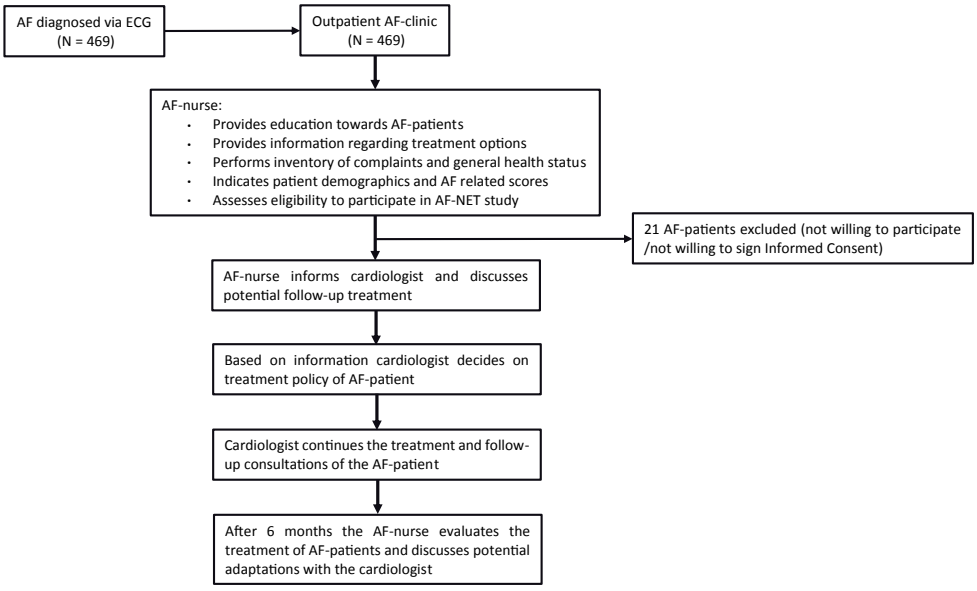

Figure 1. Flowchart of the AF-NET study

Procedure

Patients meeting the inclusion criteria visited an AF-nurse in any of the 4 hospitals. At the first visit the AF-nurse discussed the onset date of symptoms, type of symptoms, type of AF, medical history, and medication. Also, patient demographics, vital signs, stratification scores (i.e. EHRA, HAS-BLED, and CHA_2DS_2-VASc), physical exam, and ECG were noted. During the first visit the AF-NET study was explained and written informed consent of the AF-patient was obtained. All procedures at the outpatient AF clinic were supervised by a cardiologist.

AF-patients included in the AF-NET study consult the outpatient AF clinic at baseline and 6 months to evaluate the initiated treatment and the patient relevant outcome measures. During the consultations the AF-nurse registered the required data in the Medical Health Record (MHR).

Ethical approval

The protocol of the AF-NET study was submitted for approval to the Medical research Ethics Committee United (MEC-U) in the Netherlands (reference number: 14.083). The MEC-U confirmed that the Medical Research Involving Human Subjects Act does not apply to the AF-NET study and that therefore an official approval of this study by the MEC-U is not required.

Measurements

In the present study the *patient relevant outcome measures, background variables,* and the *potential comorbidities* were assessed as the main measurements.

Patient relevant outcome measures

The patient relevant outcome measures constitute the primary endpoint of the present study and are defined by Meetbaar Beter (http://www.meetbaarbeter.com/) (i.e. a Dutch organization that indicates, measures, and validates patient relevant outcome measures for cardiac patients). It includes EHRA score, stroke, major bleedings, hospitalization, adverse effects of medication, and cardiovascular death. All patient relevant outcome measures are (at least) measured after 6 months of follow-up.

EHRA score: The EHRA score, indicated by a mean score, provides an indication of the AF related symptoms during an AF episode and is indicated by 1= 'EHRA I *No symptoms*'; 2= 'EHRA II *Mild symptoms, normal daily activities not affected*'; 3= 'EHRA III *Severe symptoms, normal daily activity affected*'; 4= 'EHRA IV *Disabling symptoms, normal daily activity discontinued*' [17]. Both at T0 and T6 the EHRA score is indicated by the AF-nurse.

Ischemic stroke: The number of sudden thrombo-embolic events or focal deficits caused by focal cerebral, spinal, or retinal infarction registered in the MHR and validated by a neurologist based on computerized tomography or magnetic resonance imaging [18]. The amount of ischemic strokes of every AF-patient are measured between T0 and T6 and indicated by the AF-nurse.

Major bleedings: Percentage of patients that suffer a clinically overt bleeding associated with any of the following: fatal outcome, involvement of a critical anatomic site (intracranial, spinal, ocular, pericardial, articular, retroperitoneal, or intramuscular with compartment syndrome), fall in hemoglobin concentration >2 g/dL, transfusion of >2 units of whole blood or packed red blood cells during hospitalization, or permanent disability. All bleedings are registered by the AF-nurse between T0 and T6 using the BARC-index [19], and were only indicated as major bleedings if the BARC-index corresponded to a score of 3a, 3b, 3c, 4, 5a, or 5b.

Cardiovascular hospitalization: Percentage of patients that require inpatient hospital admission for symptomatic AF, decompensation, heart failure, myocardial infarction or coronary artery disease, hypertension, ischemic stroke, TIA, systemic embolism, major bleeding, heart valve disease, syncope, sustained VT or life-threatening adverse effects of drugs. Cardiovascular hospitalization and the days of hospitalization are indicated by the AF-nurse between T0 and T6. In the present study hospitalization is defined as unscheduled hospital admissions with an overnight stay.

Cardiovascular death: Percentage of patients that pass away due to any cardiovascular cause, such as symptomatic AF, decompensation, heart failure, myocardial infarction or coronary artery disease, hypertension, ischemic stroke, TIA, systemic embolism, major bleeding, heart valve disease, syncope, sustained VT or adverse effects of drugs. Cardiovascular death and the date of death are indicated by the AF-nurse between T0 and T6.

Serious adverse effects of medication: Percentage of patients that report serious adverse events due to rate or rhythm control medication, resulting in hospitalization with an overnight stay. The serious adverse effects of medication are registered by the AF-nurse between T0 and T6.

Background variables

The background variables in the present study include the *age* (in years), *gender* (1=male; 2=female), *Left Ventricular Ejection Fraction* (LVEF) (in %), *CHA_2DS_2-VASc* score to estimate the stroke risk (indicated by a mean score), *HAS-BLED score* to estimate major bleedings (indicated by a mean score), the *type of AF* (1= first diagnosed AF; 2= paroxysmal AF; 3= persistent AF; 4= permanent AF), *rate-control medication* (1 = Yes; 2= No), and *rhythm-control medication* (1= Yes; 2= No). *Rate-control medication* involved all medication used to reduce the rapid ventricular heart rate in AF-patients, whereas *rhythm-control medication* includes all medication to convert AF episodes to normal sinus rhythm and/or to maintain normal sinus rhythm in AF-patients.

Potential comorbidities

Potential comorbidities are measured by 1= 'Yes'; 2= 'No' and registered by the AF-nurse at T0 and T6 in the MHR. The potential comorbidities in the present study are:

Hypertension is defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg measured during 2 or more consecutive moments (during rest), and or current use of antihypertensive medication [20].

Coronary Artery Disease (CAD) is characterized as previous myocardial infarction (MI) (either ST-elevation MI or non-ST-elevation MI), percutaneous coronary or surgical coronary revascularization, or evidence of coronary atherosclerosis with the presence of a stenosis in at least one coronary artery. The stenosis should lead to a reduction of at least 50% diameter or a pressure drop (FFR) <80% [21, 22].

Heart failure is characterized by typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional

cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressures at rest or during stress [23].

Peripheral Artery Disease (PAD) is indicated by the presence of one of the following: claudicatio intermittens, amputation due to arterial insufficiency, vascular reconstruction (bypass surgery or percutaneous intervention of extremities), or documented aortic aneurysm.

Diabetes Mellitus (DM) is characterized by recurring or persistent hyperglycaemia and is diagnosed by demonstrating sober plasma glucose level ≥7.0 mmol/L (≥126 mg/dl), or plasma glucose ≥11.1 mmol/L (≥200 mg/dl) after two hours of 75g oral glucose, or symptoms of hyperglycaemia and a plasma glucose of ≥11.1 mmol/L (=200 mg/dl), or glycosylated hemoglobin (HbA1c) ≥6.5% [24, 25].

Severe renal dysfunction is characterized as chronic dialysis, renal transplantation or a serum creatinine of ≥200 mmol/L.

Severe hepatic disease is characterized as a chronic liver disease, liver cirrhosis or biochemical indicated lever dysfunction (i.e. bilirubin over twice the normal value).

Completeness of registrations

Additionally the *completeness of registrations* (in %) of the patient relevant outcome measures, background variables, and potential comorbidities is indicated as a quality measure of the outpatient AF clinic at T0 and T6. For the patient relevant outcome measures at T0 only the EHRA score is used since the other variables are not measures at T0.

Statistical analyses

To describe the study population general descriptive analyses were performed on the background variables and the potential comorbidities to indicate mean scores and percentages at T0. To assess whether the various types of AF differ regarding the background variables or potential comorbidities independent sample t-tests and chi-square tests were carried out. For the analyses the various types of AF were indicated separately as a reference group.

In addition, linear and logistic regression analyses were performed to assess potential differences between EHRA score, hypertension, and type of AF at T0 and T6. Age, gender, CHA_2DS_2-VASc, HAS-BLED, EHRA score at T0, hypertension at T0, and type of AF at T0 are included as potential confounders for these analyses. To assess potential differences in type of AF at T0 and T6, persistent AF was indicated as the reference group. For the completeness of registrations percentages were indicated on both background variables,

potential comorbidities, and patient relevant outcome measures at T0 and T6. At T6 only data was used for AF-patients of which the type of AF was registered. All analyses were performed in SPSS 21.0 and differences were indicated to be significant if $p \leq 0.05$.

Results

Basic characteristics

A total of 448 AF-patients met the inclusion criteria (95.5% of the complete sample) and were used in the analyses for the present study, also indicated in the flowchart in **Figure 1**. At baseline (**Table 1**) the mean age of the patients visiting the outpatient AF clinic was 68.3 years and most patients were male (56.7%). At inclusion the mean CHA_2DS_2-VASc-score of the AF-patients was 2.60 and the HAS-BLED-score was 1.40. In the AF-NET study hypertension is the most frequent co-morbidity (55.4%).

Table 1. Baseline characteristics

	Total (n= 448)	First diagnosed AF[a] (n= 104)	Paroxysmal AF[b] (n= 175)	Persistent AF[c] (n= 135)	Permanent AF[d] (n= 34)	*Significant difference**
Age (years ±SD)	68.3 (±10.6)	67.3 (±12.1)	66.2 (±9.9)	69.7 (±9.7)	76.2 (±8.2)	D>A,B,C
Gender (% male)	56.7	51.9	49.1	68.1	64.7	C>A,B
LVEF (% ±SD)	59 (±11.0)	62 (±9.6)	62 (±9.7)	54 (±12.4)	57 (±8.5)	A,B>C / B>D
CHA_2DS_2-VASc-score (mean)	2.60	2.62	2.26	2.90	3.09	B<C,D
HAS-BLED (mean)	1.40	1.30	1.25	1.67	1.41	C>A,B
Hypertension (% yes)	55.4	54.8	53.1	61.5	44.1	N.S.^
CAD (% yes)	9.4	12.5	5.7	11.1	11.8	B<A
Heart failure (% yes)	3.1	1.9	0.6	7.4	2.9	B<C
PAD (% yes)	5.6	1.9	6.3	8.2	2.9	C>A
DM (% yes)	13.6	16.3	8.0	14.8	29.4	B<A,D / C<D
Severe renal dysfunction (% yes)	0.2	0.0	0.0	0.7	0.0	N.S.^
Severe hepatic disease (% yes)	0.2	1.0	0.0	0.0	0.0	N.S.^
Rate-control medication (% yes)	35.3	26.0	27.4	47.8	55.9	A,B<C,D
Rhythm-control medication (% yes)	39.5	45.6	48.6	33.6	0.0	D<A,C / B>C,D

SD= standard deviation; *Significant difference if $p \leq 0.05$; ^N.S.= no significant differences

Characteristics of AF-patients

The differences in characteristics among the AF types are also indicated in **Table 1**. Patients diagnosed with permanent AF (n=34) were of higher age (mean age=76.2 years), received rate-control medication more frequently (55.9%), and had DM more often (29.4%) as compared to patients with other types of AF. Furthermore, paroxysmal

AF-patients (n=175) were male less frequently (49.1%), were diagnosed with CAD (5.7%), heart failure (0.6%), and DM (8.0%) less regularly. However, compared to other AF types, rhythm-control medication (48.6%) was most frequently prescribed to paroxysmal AF-patients.

Patient relevant outcome measures after 6 months of follow-up

In **Table 2** the data on EHRA score, hypertension, and type of AF are illustrated between T0 and T6, taking into account potential confounders. As indicated in the table the EHRA score at T0 (mean=1.93) significantly decreased (*B*=0.17; SEM=0.04; *p*<0.01) after 6 months of follow-up (mean=1.36). At T0 the percentage of patients with hypertension was 55.4%, which declined significantly (*B*=7.71; SEM=0.96; *p*<0.01) to 52.7% after 6 months of follow-up. At inclusion 30.1% of the AF-patients was diagnosed with persistent AF. The number of patients with persistent AF significantly decreased (*B*=2.93; SEM=0.40; *p*<0.01) to 12.5% at T6.

Within 6 months AF-patients were hospitalized 23 times for cardiovascular causes (of which 5 hospitalizations for symptomatic AF), 2 strokes occurred, no major bleedings were reported, and no AF-patients died due to confirmed cardiovascular causes. Furthermore, no serious adverse effects of medication were reported between T0 and T6.

Table 2. Difference in EHRA score, hypertension, and type of AF (persistent) between T0 and T6

	B	**SEM**	***P-value****
Age	<-0.01	<0.01	0.29
Gender	0.07	0.07	0.30
CHA_2DS_2-VASc-score	0.02	0.03	0.57
HAS-BLED	-0.09	0.05	0.11
EHRA score (T0)	0.17	0.04	**<0.01**
Age	0.05	0.04	0.22
Gender	-0.29	0.65	0.65
CHA_2DS_2-VASc-score	0.53	0.33	0.11
HAS-BLED	-0.99	0.65	0.13
Hypertension (T0)	7.71	0.96	**<0.01**
Age	<0.01	0.02	0.74
Gender	-0.06	0.37	0.88
CHA_2DS_2-VASc-score	-0.04	0.17	0.80
HAS-BLED	-0.03	0.28	0.90
Type AF (persistent AF) (T0)	2.93	0.40	**<0.01**

B= Unstandardized beta; *SEM*= standard error of the mean; *Significant *P*-value (≤0.05) are presented in bold

Completeness of registrations after 6 months of follow-up

The completeness of registrations by the AF-nurses at T0 and T6 is presented in **Table 3**. At T0, the completeness ranged from 99.1% to 99.8%. At T6, a high percentage of data was registered ranging from 98.6% (patient relevant outcomes), 99.0% (potential comorbidities) to 99.8% (background variables). As indicated in **Table 3**, 33 AF-patients were lost to follow-up between T0 and T6 (i.e. unable to reach despite multiple attempts,

referred to their GP without further planned contact with the AF-nurse, or withdrew their participation before T6).

Table 3. Percentages of completeness of registrations at T0 and T6

	T0 (N= 448)	T6 (N= 415)
Patient relevant outcome measures (%)	99.8%	98.6%
Background variables (%)	99.6%	99.8%
Potential comorbidities (%)	99.1%	99.0%

Discussion

Interpretation of findings

The primary aim of the present study was to assess if the nurse-led care in a collaborative region of 4 non-academic hospitals of various sizes in the Netherlands is effective in improving patient relevant outcomes after 6 months of follow-up. Due to the joint development of the regional care standard for the outpatient AF clinic significant improvements were indicated in EHRA score, hypertension, and the percentage of persistent AF-patients. Furthermore, the completeness of registrations by the AF-nurses was high ranging from 98.6% to 99.8% at both T0 and T6.

The positive influence of the outpatient AF clinic, as presented in the present study is comparable with prior research regarding outpatient AF clinics assessed in a clinical trial (academic) setting [9] and in a real-world setting [11]. Although, these prior studies reported more hospitalizations (48 [9] and 50 [11]), more major bleedings (6 [9] and 5 [11]), higher mortality rates, and a higher number of serious adverse effects of medication, the difference in measurement periods should be taken into account. While the AF-NET study presented 6 months follow-up data, the results in the study of Hendriks et.al (2012) were indicated after 22 months and in the study of Qvist et.al (2016) after 14 months of follow-up. Hence it will be most interesting to compare the data regarding the outcome measures after 12 and 24 months of follow-up. However, the preliminary data of the AF-NET study indicate that the findings are in line with prior research which endorses the hypothesis that outpatient AF clinics in collaborating, smaller hospitals may be as effective as those in (larger) academic settings.

In regular care (i.e. patients periodically consulting a medical specialist) adherence to guidelines is known to be limited [7, 9, 16]. Prior research [7-9] reported that guideline adherence results in better outcomes for AF-patients. In the present study, adherence to the prevailing guidelines is assessed by performing audits in the participating hospitals. Based on the audit results, it was concluded that the participating hospitals comply with the (inter)national AF guidelines. In addition, the effectiveness of the nurse-led care is assessed in which nurses follow protocolled procedures and inform cardiologists more in-depth regarding AF-patients' medical status. Besides a positive trend of the outcome measures, this study also reports a high registration density resulting in better decision-

making support for medical specialist. Although this information is often absent in previous studies, it underscores the notion that outpatient AF clinics employed by AF-nurses is both an effective as well as an applicable setting in non-academic hospitals.

Implication of findings

The findings of the present study indicate that multiple non-academic, and smaller hospitals are able to develop outpatient AF clinics leading to improved patient outcomes when they collaborate in a regional setting. Important aspects for achieving this improvement is (1) close collaboration between general cardiologists and electrophysiologists to define state of the art (regional) care pathways, (2) training of AF-nurses for adequate registration of relevant outcome measures and educating AF-patients, and (3) intensive cooperation with regional GPs. It is advisable for other (small) non-academic hospitals to reinforce their collaboration with referral hospitals to share knowledge and experience, and initiate outpatient AF clinics to improve and secure the quality of AF care.

Limitations

A limitation of the present study is that only a prospective intervention group was analyzed. Therefore, the results should be interpreted as mere associations between T0 and T6 regarding the efficacy of the outpatient AF clinic. Although the results indicate a positive trend of the outpatient AF clinic as compared to an equivalent research in an academic setting [9], it should be taken into account that the regular AF care may have improved during the last years. Second, data concerning the patient relevant outcome measures are only measured at T6 in this study. Therefore, no conclusion can be drawn regarding significant improvements over longer time periods. Despite significant differences in follow-up periods, the procedure and positive influence of the outpatient AF clinic on AF-patients outcomes as demonstrated in the present study are comparable with previous studies [9, 11]. Nevertheless, future research should put effort in analyzing the patient relevant outcomes at 12 and 24 months, or comparing follow-up data with similar retrospective data. A final limitation of the present study may be that the renal function was measured with the serum creatinine level instead of the currently used eGFR. Since the eGFR was not available in the participating hospitals at the moment of inclusion, this measure was not indicated in the present study. Even though the eGFR is the preferred indicator to assess renal dysfunction, the expectation is that this indicator has not affected the conclusions of the research under study.

Conclusions

Based on the provisional findings presented in this study it can be concluded that the quality of AF care can be improved in smaller and non-academic hospitals when collaboration between hospitals is reinforced by uniform standards and intensive education of AF-

patients. To continuously improve AF care collaboration with surrounding healthcare professionals (including referral hospitals and GPs) seems to provide a practicable approach by developing and implementing regional care standards for specific heart conditions.

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Chapter 5

The prognostic value of quality of life in atrial fibrillation on patient value

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Abstract

Background:
In this study, the prognostic value of AF-related quality of life (AFEQT) at baseline on Major Adverse Cardiovascular Events (MACE) and improvement of perceived symptoms (EHRA) was assessed. Furthermore, the relationship between QoL and AF-related hospitalizations was assessed.

Methods:
AF-patients diagnosed between November 2014 and October 2019 in four hospitals embedded within the Netherlands Heart Network were prospectively followed for 12 months. MACE was defined as stroke, myocardial infarction, heart failure and/or mortality. Subsequently, MACE, EHRA score improvement and AF-related hospitalizations between baseline and 12 months of follow-up were recorded.

Results:
In total, 36/687 (5.2%) AF-patients developed MACE, 190/432 (44.0%) improved in EHRA score and 189/510(37.1%) were hospitalized during 12 months of follow-up. Patients with a low AFEQT score at baseline more often developed MACE (OR(95%CI): 2.42(1.16-5.06)), more often improved in EHRA score (OR(95%CI): 4.55(2.45-8.44) and were more often hospitalized (OR(95%CI): 4.04(2.22-7.01)) during 12 months post diagnosis, compared to patients with a high AFEQT score at baseline.

Conclusions:
AF-patients with a lower quality of life at diagnosis more often develop MACE, more often improve on their symptoms and also were more often hospitalized, compared to AF-patients with a higher quality of life. This study highlights that the integration of patient-reported outcomes, such as quality of life, can be used as a prognostic indicator of the expected disease course for AF.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in adults[1, 2]. As a result of the aging population and early screening initiatives, the incidence and prevalence of AF are expected to increase in future decades with 17.9 million Europeans suffering from AF by 2060[1, 3]. The increased proportion of older adults who suffer from AF will have several impactful consequences for public health, including higher disease burden, health service utilization and health care costs[1, 4]. As a result, there is an urgent need for new strategies to improve patient-relevant outcomes and decrease healthcare costs.

AF often leads to the occurrence of various concomitant cardiovascular disorders with a prominent effect on the patients' disease burden such as major adverse cardiovascular events (MACE), a composite of myocardial infarctions (MI), stroke, heart failure and/or mortality. In AF, the occurrence of MACE is perceived as the most relevant outcome in secondary prevention[5]. In addition to MACE, AF also commonly features symptoms that influence the patients' capabilities to undertake daily activities. The extent of the patients' limitations and symptoms are routinely assessed in clinical practice using the European Heart Rhythm Association score of atrial fibrillation (EHRA) classification system[6]. Palpitations, exercise intolerance, dizziness, dyspnea at rest and chest discomfort and/or tightness are commonly experienced symptoms by AF-patients that have been shown to negatively affect the quality of life (QoL) of patients[7, 8].

As a result of concomitant cardiovascular disorders, bleedings and underlying non-cardiovascular conditions AF patients are often hospitalized[9, 10]. In general, approximately 30% of AF patients are hospitalized at least once per year, while 10% are hospitalized twice or more per year[10]. The largest part of healthcare costs for AF-patients can be accounted for by (the length of) hospitalizations and in-hospital procedures as a result of comorbidities [11–13]. Even though a relationship has been established between QoL and adverse outcomes in AF, limited information is available on the relationship between QoL at diagnosis and patient-relevant outcomes in AF during the disease trajectory. Being able to predict the occurrence of patient-relevant outcomes and hospitalizations should prove incredibly valuable for individual tailoring of AF treatment during the disease course. Focusing on patient-relevant outcomes and critically examining healthcare costs and utilization early in the disease course for new AF patients may enable medical specialists to focus on improving patient value.

Patient value is defined as patient-relevant outcomes divided by the costs of healthcare delivery and is the core philosophy of value-based healthcare (VBHC)[14]. VBHC was originally introduced by Porter and Teisberg as a strategy to improve quality in healthcare, reduce variation in outcomes that matter most to patients, raise awareness for the emerging cost crisis in healthcare and to aim for all involved parties to put patient value central[14]. By identifying potential predictors for future patient-relevant outcomes and healthcare costs early in the disease trajectory potential interventional strategies can

be employed to help reduce the burden of AF patients and potentially reduce healthcare costs. An emerging topic to estimate AF disease trajectories is the use of patient-derived outcome measures such as QoL[15]. QoL at diagnosis could potentially be an early indicator of future patient-relevant outcomes and healthcare costs[15].

Therefore, the aim of this study was to assess the association between QoL and both patient-relevant outcomes and hospitalizations as a proxy for healthcare costs in AF patients. To this end, we assessed the association between QoL as measured by the Atrial Fibrillation Effect on QualiTy-of-life (AFEQT) questionnaire, and EHRA score improvement, the occurrence of MACE and hospitalizations in Dutch AF-patients.

Methods

Study design

This prospective cohort study was performed using information from newly diagnosed AF patients between November 2014 and October 2019 in the Southeast of the Netherlands with a catchment population of approximately 800.000 inhabitants. Within this region, four non-university hospitals and approximately 350 general practitioner (GP) practices embedded within the Netherlands Heart Network (NHN) work together to improve patient-relevant outcomes and lower healthcare costs for cardiac patients across the whole healthcare chain in collaboration with all relevant healthcare providers in primary, secondary and tertiary care. Within the NHN, regional and transmural care is evaluated based on patient value according to the VBHC philosophy[16].

Procedure and population

Within the NHN, the collaborating hospitals and GP practices have developed and implemented a regional standard of care protocol aimed at guiding physicians in the management of AF patients[16]. As part of this care pathway, AF patients are educated about available treatment options and the importance of treatment compliance by specialized and trained AF-nurses. In addition, the AF-nurse registers information on patient characteristics, the patients' general health status, AF-related complaints to aid the shared decision-making process and patient counselling by medical specialists. Information includes, among others, patient demographics, patient characteristics, patient vitals, AF-related risk stratification scores, onset of symptoms, and an AF-related Quality of Life (QoL) questionnaire. AF-patients included in the study were followed-up after 12 months (T1) to record patient characteristics, the occurrence of patient-relevant outcomes and to evaluate the initiated treatment.

During the initial visit, AF-nurses also assessed study eligibility, provided information on the study, registered patient information and obtained written informed consent. Eligibility criteria for inclusion were: age ≥18 years, a new or recent diagnosis with non-valvular atrial fibrillation, competence to read and agree on the informed consent, and

provision of written informed consent. Patients with impaired cognition and the inability to understand Dutch were excluded.

Ethical approval

The protocol of the AF-NET study was submitted for approval to the Medical research Ethics Committee United (MEC-U) in the Netherlands (reference number: 14.083). The MEC-U confirmed that the Medical Research Involving Human Subjects Act does not apply to the AF-NET study and, therefore, an official approval of this study by the MEC-U is not required.

Exposure assessment and baseline measurement

Baseline characteristics were measured during the routine visit (T0) at an AF-outpatient clinic visit by dedicated AF-nurses. Among these baseline characteristics was the exposure of interest, namely the perceived QoL as measured through the AFEQT questionnaire[17]. The AFEQT is a validated and reliable 20-item questionnaire developed to quantify QoL in AF-patients across 4 conceptual domains (Symptoms, Daily Activities, Treatment Concerns and Treatment Satisfaction) using a 7-point Likert response scale[17]. The overall score is calculated using answers from the first three subdomains and ranges from 0 (severe impairment/low QoL) to 100 (no limitation/high QoL). In this study, patients were categorized into quartiles, using the upper quartile (high QoL) as the reference, based on their final AFEQT scores observed in this study (AFEQT score 0: >90.74; 1: >75.9 to ≤90.74; 2: >57.41 to ≤75.93; 3: ≤57.41).

Additionally, various other baseline characteristics were recorded, including: age, gender, CHA_2DS_2-VASc score[18], HAS-BLED score[19], Body Mass Index (BMI), diabetes mellitus (DM), hypertension, obstructive sleep apnea syndrome (OSAS), prior heart failure, malignancy, chronic lung disease, and location of AF diagnosis (General practitioner/ Hospital). Background variables were selected for use in this study based on availability and inclusion as cardiovascular risk factors in guidelines from the European Society of Cardiology (ESC)[1].

Outcome measures

The extent of AF-related symptoms was measured using the EHRA classification score of atrial fibrillation[6]. The EHRA score was used as a specific, yet simple, quantification of the functional consequences of AF. The EHRA score is a 4-point scale which ranges from low symptom severity (EHRA I: no symptoms; normal daily activity not affected) to high symptom severity (EHRA IV: disabling symptoms; normal daily activity discontinued) [6]. EHRA improvement was determined by comparing the EHRA score at 12 months of follow-up (T1) with the EHRA score at time of diagnosis (T0). Any full point improvement in EHRA score was perceived as clinically relevant, hence the use of the unmodified EHRA score during this study. MACE was defined as the composite of any MI, stroke, heart

failure and mortality between baseline and 12 months of follow-up. AF-nurses assessed whether patients were hospitalized between baseline and 12 months of follow-up by checking their hospital record during routine follow-up. If patients had any AF-related hospital visit during 12 months of follow-up, a hospitalization was recorded.

Statistical analysis

Patient characteristics at baseline were described using means, standard deviations and proportions (%). Minimally and multivariable-adjusted logistic regression analyses (Odds Ratios (ORs) and 95% confidence intervals (CIs)) were performed to assess the association between AFEQT score at baseline (T0) and the occurrence of MACE, the improvement of EHRA score, and AF-related hospitalizations between baseline (T0) and 12 months of follow-up (T1). Minimally-adjusted analyses were adjusted for categorized age and gender. In addition to categorized age and gender, in multivariable-adjusted analyses type of AF, CHA_2DS_2-VASc score, HAS-BLED score were included in all multivariable-adjusted models as a priori confounders. Potential other confounders (i.e. Overweight (BMI ≥25kg/m^2), DM, hypertension, OSAS, heart failure, malignancy, chronic lung disease and location of AF diagnosis) were added to the multivariable-adjusted model using backwards elimination ($p<0.10$). Based on this procedure DM was included in statistical models related to EHRA improvement. No additional potential confounders were included in statistical models related to MACE and hospitalizations. In sensitivity analyses in which the complete confounder subset was included, results were similar to the main analyses (data not shown). No multicollinearity was observed in tests between the CHA_2DS_2-VASc and HAS-BLED scores. As a result, all models included both CHA_2DS_2-VASc and HAS-BLED. Missing values were handled using listwise deletion on a per analysis basis using the final multivariable-adjusted model. All analyses were performed using IBM SPSS (IBM SPSS Statistics for Windows, version 26.0, IBM Corp., Armonk, NY). P-values <0.05 were considered statistically significant.

Results

Baseline characteristics of AF-patients, categorized into quartiles based on the AFEQT score ranging from low QoL (Q1) to high QoL (Q4), are presented in **Table 1**. Compared to patients with a high AFEQT score (Q4), patients with a lower AFEQT score (Q1) were more often female (Q1; 54.8% vs Q4;28.6%),more often had a CHA_2DS_2VASc score of 2+ (77.4% vs 67.5%), more often had a HAS-BLED score of 2+ (49.0% vs 40.%), had a higher prevalence of DM (15.5% vs 12.2%), were more often overweight or obese (73.9% vs 65.7%), more often had hypertension (59.4% vs 50.2%), more often had heart failure at baseline (7.5% vs 1.6%), more often had chronic lung disease (12.7% vs 7.0%) and had a lower EHRA score at baseline (mean (SD); 2.29 (0.90) vs 1.42 (0.62)). Patients in AFEQT score quartiles Q2 and Q3 less often suffered from persistent AF, compared to patients in AFEQT score quartiles Q1 and Q4 (25.4% and 25.9% vs. 37.1% and 34.0%, respectively).

Table 1. Baseline characteristics of AF-patients categorized into quartiles based on the AFEQT score at baseline.

	AFEQT score at baseline				
	First quartile (Q1) (4.63 to ≤ 57.41)	**Second quartile (Q2) (>57.41 to ≤75.93)**	**Third quartile (Q3) (>75.93 to ≤90.74)**	**Fourth quartile (Q4) (>90.74 to 100)**	**p-value**
	n (%)	**n (%)**	**n (%)**	**n (%)**	
Total*	239 (24.6%)	238 (24.5%)	248 (25.6%)	245 (25.3%)	-
Gender					
Man	108 (45.2%)	136 (57.1%)	141 (56.9%)	175 (71.4%)	
Woman	131 (54.8%)	102 (42.9%)	107 (43.1%)	70 (28.6%)	<0.001
Age					
mean (SD)	70.0 (10.4)	69.7 (9.7)	69.1 (9.6)	69.1 (9.1)	0.667
Type of AF					
Paroxysmal	132 (62.9%)	156 (74.6%)	163 (73.1%)	140 (66.0%)	
Persistent	78 (37.1%)	53 (25.4%)	60 (26.9%)	72 (34.0%)	0.024
CHA_2DS_2-VASc score (T0)					
0-1	54 (22.6%)	52 (22.3%)	66 (26.8%)	79 (32.5%)	
2+	185 (77.4%)	181 (77.7%)	180 (73.2%)	164 (67.5%)	0.037
HAS-BLED (T0)					
0-1	104 (51.0%)	120 (62.8%)	120 (60.0%)	117 (59.1%)	
2+	100 (49.0%)	71 (37.2%)	80 (40.0%)	81 (40.9%)	0.095
OSAS					
No	225 (94.1%)	229 (96.2%)	232 (93.9%)	233 (95.1%)	
Yes	14 (5.9%)	9 (3.8%)	15 (6.1%)	12 (4.9%)	0.656
Diabetes mellitus					
No	202 (84.5%)	203 (85.3%)	217 (87.5%)	215 (87.8%)	
Yes	37 (15.5%)	35 (14.7%)	31 (12.5%)	30 (12.2%)	0.663
BMI[a]					
<25	55 (26.1%)	68 (33.7%)	66 (32.8%)	70 (34.3%)	
≥25	156 (73.9%)	134 (66.3%)	135 (67.2%)	134 (65.7%)	0.239
Hypertension					
No	97 (40.6%)	103 (43.3%)	105 (42.3%)	122 (49.8%)	
Yes	142 (59.4%)	135 (56.7%)	143 (57.7%)	123 (50.2%)	0.187
Heart failure					
No	221 (92.5%)	229 (96.2%)	243 (98.0%)	240 (98.4%)	
Yes	18 (7.5%)	9 (3.8%)	5 (2.0%)	4 (1.6%)	0.002
Malignancy					
No	209 (87.4%)	210 (88.6%)	222 (89.5%)	214 (87.7%)	
Yes	30 (12.6%)	27 (11.4%)	26 (10.5%)	30 (12.3%)	0.890
Chronic lung disease					
No	207 (87.3%)	212 (89.1%)	229 (26.2%)	227 (93.0%)	
Yes	30 (12.7%)	26 (10.9%)	19 (7.7%)	17 (7.0%)	0.107
EHRA at baseline					
mean (SD)	2.29 (0.90)	1.85 (0.83)	1.69 (0.80)	1.42 (0.65)	<0.001
Location of diagnosis					
General practitioner	79 (33.6%)	62 (26.3%)	79 (32.1%)	78 (31.8%)	
Hospital	156 (66.4%)	174 (73.7%)	167 (67.9%)	167 (68.2%)	0.328

Abbreviations: SD: Standard Deviation, T0: baseline, OSAS: Obstructive Sleep Apnea Syndrome, BMI: Body Mass Index.
*Numbers may not add up to total due to missing values for individual parameters.

Occurrence of MACE during 12 months of follow-up

In total, 36 (5.2%) of all patients developed MACE during follow-up **(Table 2)**. Due to the low frequency of occurrence of MACE and the resulting limited power, AFEQT scores were assessed using the median score. In multivariable-adjusted analyses, AFEQT scores below the median (75.93) at baseline were associated with a statistically significantly increased odds of developing MACE during 12 months of follow-up, when compared to patients with AFEQT scores above the median at baseline (OR (95% CI); 2.42 (1.16-5.06)). Results for minimally-adjusted analyses were similar in direction to multivariable-adjusted analyses, albeit mildly attenuated.

Table 2. Overall associations between QoL at baseline (AFEQT) and the occurrence of MACE after 12 months of follow-up (T1).

	Total study population		MACE		
AFEQT score (T0)	**n (%)**	**n (%)**	**$OR_{minimally\text{-}adjusted}$ (95% CI)**	**$OR_{mv\text{-}adjusted}$ (95% CI)**	**p-value**
Below median (4.63 to ≤ 75.93)	339 (49.3%)	25 (7.4%)	2.55 (1.23-5.29)	2.42 (1.16-5.06)	0.018
Above median (>75.93 to 100)	348 (50.7%)	11 (3.2%)	1 (ref.)	1 (ref.)	

Minimally-adjusted models were adjusted for categorized age (<65; ≥65) and gender.
Multivariable-adjusted models were additionally adjusted for HAS_BLED (0-1; ≥2), CHA_2DS_2-VASc (0-1; ≥2), type of AF (paroxysmal/persistent). MACE was defined as the composite of any MI/stroke (n=14), heart failure (n=20) and mortality (n=8).

EHRA improvement after 12 months

In total, 190 (44.0%) AF-patients improved in EHRA-score within 12 months. A weak correlation was observed between EHRA and AFEQT at baseline (r=-0.359). Results from multivariable-adjusted analyses on the association between AFEQT score and the improvement in EHRA score after 12 months of follow-up are presented in **Table 3**. The improvement in EHRA score was statistically significant across all quartiles of AFEQT score and associations became stronger across decreasing AFEQT scores, when compared to patients in the highest AFEQT quartile (Q1 vs. Q4: OR (95% CI); 4.55 (2.45-8.44)). Results for minimally-adjusted analyses were similar in strength and direction, when compared to multivariable-adjusted analyses.

Table 3. Overall associations between QoL at baseline (AFEQT) and the improvement in symptom scores (EHRA improvement) after 12 months (T1).

	Total study population		EHRA improvement		
AFEQT score (T0)[e]	**n (%)**	**n (%)**	**$OR_{minimally\text{-}adjusted}$ (95% CI)**	**$OR_{mv\text{-}adjusted}$ (95% CI)**	**p-value**
First quartile (4.63 to ≤ 57.41)	121 (28.0%)	69 (57.0%)	4.41 (2.41-8.08)	4.55 (2.45-8.44)	<0.001
Second quartile (>57.41 to ≤75.93)	97 (22.5%)	50 (51.5%)	3.53 (1.88-6.62)	3.42 (1.80-6.53)	<0.001
Third quartile (>75.93 to ≤90.74)	116 (26.9%)	49 (42.2%)	2.44 (1.33-4.48)	2.34 (1.26-4.34)	0.007
Fourth quartile (>90.74 to 100)	98 (22.7%)	22 (22.4%)	1 (ref.)	1 (ref.)	

Minimally-adjusted models were adjusted for categorized age (<65; ≥65) and gender.
Multivariable-adjusted models were additionally adjusted for HAS_BLED (0-1; ≥2), CHA_2DS_2VASc (0-1; ≥2), type of AF (paroxysmal/persistent), Diabetes Mellitus.

Occurrence of AF-related hospitalizations during 12 months of follow-up

In total, 189 (37.1%) of all patients were hospitalized at least once during 12 months of follow-up **(Table 4)**. In multivariable-adjusted analyses, a lower AFEQT score at baseline was statistically significantly associated with an increased risk of hospitalizations in the first quartile (OR (95% CI); 4.04 (2.33-7.01)), when compared to patients with a high AFEQT score at baseline. No statistically significant association was observed between AFEQT and hospitalizations between the second, third and fourth AFEQT quartiles. Results for minimally-adjusted analyses were similar in strength and direction, when compared to multivariable-adjusted analyses.

Table 4. Overall associations between QoL at baseline (AFEQT) and AF-related hospitalizations during 12 months of follow-up (T1).

	Total study population		Hospitalizations		
AFEQT score (T0)	**n (%)**	**n (%)**	**$OR_{minimally\text{-}adjusted}$ (95% CI)**	**$OR_{mv\text{-}adjusted}$ (95% CI)**	**p-value**
First quartile (4.63 to ≤ 57.41)	141 (27.6%)	81 (57.4%)	3.86 (2.26-6.59)	4.04 (2.33-7.01)	<0.001
Second quartile (>57.41 to ≤75.93)	114 (22.4%)	39 (34.2%)	1.50 (0.85-2.64)	1.77 (0.98-3.18)	0.057
Third quartile (>75.93 to ≤90.74)	133 (26.1%)	38 (28.6%)	1.15 (0.66-2.02)	1.27 (0.71-2.25)	0.417
Fourth quartile (>90.74 to 100)	122 (22.9%)	31 (25.4%)	1 (ref.)	1 (ref.)	

Minimally-adjusted models were adjusted for categorized age (<65; ≥65) and gender.
Multivariable-adjusted models were additionally adjusted for HAS_BLED (0-1; ≥2), CHA_2DS_2-VASc (0-1; ≥2), type of AF (paroxysmal/persistent).

Discussion

The present study aimed to assess the association between QoL at baseline and the occurrence of MACE, EHRA improvement and hospitalizations during 12 months of follow-up. In short, patients with a QoL below the median more often developed MACE, compared to patients with a higher QoL. In addition, patients with a low QoL at baseline more often improved on their AF-related symptoms (EHRA score) during follow-up, compared to patients with a higher QoL. Lastly, patients with a lower QoL were more likely to be hospitalized in the first 12 months after diagnosis, compared to patients with a higher QoL.

Patient-reported outcomes (PROs), such as QoL, are increasingly employed to assess the effects of a health condition and its management on the experienced disease burden and treatment satisfaction of patients and caregivers. Naturally, most studies have primarily focused on the impact of AF on the patients' QoL[20, 21]. However, aside from evaluating the effects of the experienced disease and QoL, PROs may also hold clinical relevance for predicting future disease trajectories in routine care. QoL is a simple and easily attainable PRO that may be promising for use in risk stratification in everyday clinical practice. To our knowledge, no studies have been published regarding the association between QoL at diagnosis and the subsequent development of MACE during follow-up in a broad spectrum of AF-patients. A previous study by Pedersen et al., which examined

cardiac patients after percutaneous coronary intervention, reported that a poor QoL after PCI was related to the occurrence of MACE within 6 months after percutaneous coronary intervention, but not late MACE[22]. In our study we did not make a distinction in the timing of MACE, which may warrant further investigation in future research as we strictly assessed the occurrence of MACE within 1 year of follow-up.

In addition to MACE, the improvement in EHRA score during the year post-diagnosis was also associated with QoL at diagnosis. Patients with a lower quality of life at diagnosis also more often had a lower EHRA score at diagnosis. Which might indicate that these patients had more opportunity to improve. However, we also observed a weak correlation between AFEQT and EHRA, which indicates that the patients' perceived health burden is not always in line with the perceived burden as assessed by the doctor. As such, QoL as measured through a dedicated and specialized questionnaire for AF may provide a valuable patient-derived measure to assess the potential for improvement in the patients' perceived health burden, in conjunction with the doctor-derived EHRA classification.

Previous studies have highlighted that there may be a discordance in what patients perceive and what clinicians can detect regarding AF-symptoms[23]. For instance, physicians may underestimate or have difficulty in discriminating mild, low-level, symptoms[23, 24]. As treatment decisions are generally made based on the presence of symptoms to target improvement of AF symptoms in tandem with the expected benefits and risks for the patient, physicians could benefit from more sources of information for deciding on a course of action[23, 25]. Focus groups within the RATE-AF trial have indicated that improvement of QoL, ahead of mortality and hospitalizations, is paramount for AF patients, while patients perceive that healthcare professionals tend to steer on factors which are important to them[26]. Therefore, PROs could help with shifting the focus from symptoms and treatment options to a more patient-centered perspective in clinical care and could contribute in shared-decision making about how to treat AF. To aid this process, disease course prediction by defining traditional risk groups or by artificial intelligence featuring both traditional patient characteristics and symptoms, as well as PROs, may help making well-informed decisions on the preferred treatment regimens, identify areas of improvement and avoiding treatment for patients who are unlikely to benefit from them[27].

Direct healthcare costs for AF are primarily driven by hospitalizations, accounting for 50-70% of total costs[28]. Moreover, these costs are expected to increase in the future due to the ageing population. Therefore, identifying patient groups who have an increased likelihood of becoming hospitalized becomes more important for individualizing treatment[29]. In line with findings from this study, Schron *et al.* reported that patients' QoL was a predictor for hospitalization[15]. Notably, Schron *et al.* employed both the more general SF-36 and a cardiac-specific QoL (Quality of Life Index-Cardiac Version; QLI-CV) measure[15]. Interestingly, the more general SF-36 summary score led to statistically significant prediction of hospitalizations, while cardiac-specific QoL did not reach

statistical significance. In our study, in which we used an AF-specific questionnaire focused on Health Related QoL, QoL was statistically significantly associated with hospitalizations after 1 year, when comparing low vs. high QoL at diagnosis. There were, however, some differences regarding the confounder subsets used in the models and covered domains between the cardiac questionnaires which could explain these differences. Based on these observations QoL may potentially be used as a predictor for hospitalizations and, resultingly, AF-related healthcare costs. A reduced QoL at diagnosis may therefore be used as an indicator for additional surveillance to change treatment regimens before hospitalization occurs.

Overall, from the VBHC perspective, PROs such as QoL as measured by the AFEQT questionnaire could provide valuable opportunities to improve patient value on multiple levels by reducing the occurrence of MACE, facilitating EHRA symptom improvement and reducing AF-related healthcare costs. In addition, the routine implementation of PROMs such as the AFEQT score will empower physicians to treat more than symptoms, but also allow them to focus on patient-perceived improvements and reduction of AF disease burden. For instance, PROs in routine care could aid both clinicians and patients during patient consultations in setting realistic expectations and may aid in the process of shared decision making for treatment options, while taking account the anticipated patient-relevant outcomes and symptom improvements that fit the reported health status of the patient. Moreover, patients' will benefit from accurately reporting their perceived health status and, in turn, directly impacting their treatment options and outcomes. Furthermore, PROMs may enable machine learning-based initiatives to further refine models and assist in clinical decision making[30]. In this way, patients can attain the best outcomes for their specific medical circumstances. From a managerial perspective, the integration of more patient-centered care allows for a reduction in treatment costs (*e.g.* reduction of hospitalizations), evaluating performance (*e.g.* patient-improvement) and improving treatment satisfaction (*e.g.* shared-decision making)[31]. The integration of PROMs and personalized medicine may, therefore, prove a fruitful avenue for the evaluation of health data, performance assessment, but also for exploring new value-based initiatives[32].

This study was subject to some limitations. Firstly, information on the rate or rhythm control strategy was unavailable. Therefore, we could not control for these variables in our analyses. Secondly, all outcomes were assessed after a follow-up of 1 year. Therefore, we were unable to ascertain whether the associations differed based on the timing of the occurrence. For instance, a prior study indicated that the association between QoL and MACE could be dependent on the timing[22]. Thirdly, the number of cases in our analyses on MACE were limited. To maintain statistical power, the median was used as the AFEQT questionnaire cut-off instead of quartiles. As such, the distinction between different levels of QoL are less defined in these analyses. Lastly, statistical floor effects may have influenced the results within this study as patients with EHRA class I at baseline were unable to further improve on their symptoms. As a result, AFEQT quartiles with worse

EHRA scores at baseline may have more often been able to improve on their symptoms, likely leading to an overestimation of the strength of association.

In conclusion, AF-patients with a lower AF-specific QoL at diagnosis were more likely to develop MACE and improve on EHRA score, when compared to patients with a higher QoL at diagnosis. In addition, QoL at diagnosis was also associated with hospitalizations, which was used as a proxy for healthcare costs in this study. As such, this study highlights that the integration of PROs, such as QoL, can be used as a prognostic factor for the expected disease course for AF in daily clinical practice. The routine implementation of PROs will enable care providers to treat more than symptoms and steer on factors that are most relevant to the patient. Therefore, by combining PROs with clinical characteristics of the patient, healthcare professionals are able to provide more patient-centered care, reduce healthcare costs and, as a result, optimize patient value in routine care.

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Chapter 6

Age-dependency of EHRA improvement based on quality of life at diagnosis of atrial fibrillation

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Abstract

Background:
In this study, the relationship between AF-related quality of life (AFEQT) at baseline in AF-patients and the improvement on perceived symptoms and general state of health (EHRA score) at 12 months was assessed across predefined age categories.

Methods:
Between November 2014 and October 2019 patients diagnosed with AF de novo in four hospitals embedded within the Netherlands Heart Network were prospectively followed for 12 months. These AF-patients were categorized into quartiles based on their AFEQT score at diagnosis and EHRA score was measured at diagnosis and 12 months of follow-up. Stratified analyses were performed using age categories (<65 vs. ≥65 years; <75 vs. ≥75 years).

Results:
In total, 203/483 (42.0%) AF-patients improved in EHRA score after 12 months of follow-up. AF-patients in the lowest AFEQT quartile were more likely to improve, compared to patients in the highest AFEQT quartile (OR(95%CI):4.73 (2.63-8.50)). Furthermore, patients ≥65 years and patients <75 years at diagnosis with lower AFEQT scores at baseline were most likely to improve in EHRA score after 12 months, compared to similarly aged patients with higher AFEQT scores at baseline.

Conclusion:
The present study indicates that AF-patients with a lower quality of life at diagnosis were most likely to improve their EHRA score after 12 months. This effect was most prominent in patients ≥65 years of age and patients <75 years of age, compared to patients >65 and ≥75 years, respectively. Future research should focus on further defining characteristics of these age-groups to enable the implementation of age-tailored treatment.

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia with a profound effect on the quality of life (QoL) of patients[1–3]. AF presents itself in various forms and with various adverse outcomes, which can impact the patients' general state of health both in the short- and the long-term. Therefore, AF management requires strategies to manage the patients' physical symptoms, but also the psychological well-being[3,4]. There is great variability within the AF-patient population in the change in symptoms and response to therapy, making improvement hard to predict[5]. Therefore, assessing indicators for symptom improvement may provide valuable information for selecting appropriate treatment options in the clinic[5].

The prevalence of AF increases sharply between 60 to 65 years, after which it steadily increases until the age of 80 to 85 years[6,7]. Furthermore, age strongly influences the occurrence of AF-related symptoms and declines in functional capacity as younger patients report more dizziness and palpitations, while older patients tend to feature a greater degree of dyspnea and fatigue[8]. Underlying comorbidities have been reported as one of the most important drivers for the limiting effects of AF on physical capacity[9]. Elderly patients tend to experience more comorbidities. Moreover, age is prominently featured in various clinical risk stratification schemes routinely employed in AF management[10,11]. For instance, the CHA_2DS_2-VASc stroke risk stratification score uses age categories (<65, ≥65-74 and ≥75 years) to help guide clinicians in predicting high risk patients[10]. Therefore, it is crucial to account for the patients' age at the diagnosis of AF to obtain an accurate estimate of the predicted progression of their perceived general state of health, and subsequently tailor treatment according to the patients' predicted disease trajectory.

A widespread and simple to use method to assess and quantify symptoms related to AF is the European Heart Rhythm Association (EHRA) score. The EHRA score helps classify patients based on the limitations they experience during normal daily activity. Previous studies have indicated that this score is associated with Health Related Quality of Life (HRQoL)[12,13]. The evaluation of HRQoL by health professionals is emerging as an important factor in the assessment and follow-up of patients with AF to aid in providing patient-centered care[14]. A commonly used and validated way to determine the AF-related quality of life is the Atrial Fibrillation Effect on Quality-of-Life (AFEQT) questionnaire[15]. Based on the relationship between the score of the AFEQT questionnaire and AF-related symptoms, HRQoL at diagnosis could potentially be used to predict future improvement in AF-symptoms[12,16]. As age is a prominent factor in both the experienced symptoms at onset of AF and the disease course, we hypothesize that the relationship between HRQoL and perceived AF-symptoms differ across age-groups[5,8,9]. By establishing the relationship between age, HRQoL and AF-symptoms, patient subgroups can be identified with suboptimal health benefits during the AF disease course. In particular, insights on

vulnerable patient subgroups may help tailor AF management policies to maximize clinical outcomes based on patient characteristics and patient reported outcome measures.

Therefore, we assessed the relationship between HRQoL (AFEQT) at baseline and the improvement on perceived symptoms and general state of health (EHRA score) at 12 months in AF-patients. Furthermore, we assessed potential differences between predefined age categories in this relationship to identify patient subgroups with the greatest potential for improvement in AF-symptoms.

Methods

Study population

In this prospective cohort, patients newly diagnosed with AF in the outpatient clinics in any of the four hospitals embedded within the Netherlands Heart Network (NHN) in the time-period between November 2014 and October 2019 were included. In short, the NHN is a, joint effort of healthcare providers in primary, secondary and tertiary care in a 800.000 head population in a rural and urban region in the southeast of the Netherlands, with the aim to improve the quality of care for cardiac patients by optimizing the complete healthcare chain[17].

Patients were included in this study when they were ≥18 years, newly or recently diagnosed with non-valvular atrial fibrillation, were competent to read and agree on the informed consent, and had provided written informed consent.

Procedure

In the hospitals embedded within the NHN a regional care standard has been implemented for AF-patients who visit the outpatient AF clinic to standardize the procedures and quality of care within the region. During 45-60 minute patient consultation sessions within these outpatient AF clinics, AF-nurses provide education to the AF-patients and complete the required registrations to improve guideline adherence of cardiologists through better documentation of patient information. The education strategy contains information on available treatment options and the importance of treatment compliance, enabling patients to make well-informed decisions on their treatment. Furthermore, the AF-nurse makes an inventory of the general health status and AF-related complaints of the patient to inform the medical specialists with more detailed patient-information to support the shared decision-making process. The AF-nurses collect data on the patients' demographics, anthropometry, patient vitals, various AF-related risk stratification scores, onset of symptoms, and results from the AFEQT questionnaire on HRQoL. For this study, the AF-nurse assessed eligibility, provided information on the study and obtained written informed consent. AF-patients included in the study were followed-up after 12 months (T1) to evaluate the initiated treatment and to record patient characteristics and outcomes.

In total, 561 AF-patients had an available EHRA score at both baseline and after 12 months of follow-up. AF-patients with a missing AFEQT score (n=76) or missing information on selected confounders (CHA_2DS_2VASc: n=1; OSAS: n=1) were excluded from analyses. In total, 483 (86.1%) AF-patients with complete information were eligible for analyses.

Outcome measure

The extent of AF-related symptoms and patients' perception of their general state of health was measured using the EHRA at diagnosis (T0) and after 12 months of follow-up (T1). The EHRA score is a 4 level scale ranging from EHRA class I (no symptoms) to EHRA class IV (disabling symptoms; normal daily activity discontinued)[18]. Improvement on the perceived symptoms of AF was determined by comparing EHRA scores at 12 months of follow-up (T1) with the EHRA score at time of diagnosis (T0). Any point improvement of EHRA score was perceived as clinically relevant. Therefore, the unmodified EHRA score was used during this study. Patients with a lower EHRA score at T1, compared to T0, were categorized as EHRA improver (1), while patients with an equal or higher EHRA score at T1 compared to T0 were categorized as EHRA non-improver (0).

Exposure assessment and background variables

Patients completed the AFEQT questionnaire at baseline to assess their perceived HRQoL. In contrast to more generic QoL questionnaires, which often include non-health related features of life, the AFEQT questionnaire focuses on AF-related HRQoL, in which the impact of AF and treatment on an individual's QoL are determined. To this end, the AFEQT is a validated and reliable questionnaire featuring 20-items targeted at AF-patients to quantify HRQoL across 4 subdomains, including symptoms, daily activities, treatment concerns and treatment satisfaction using a 7-point Likert response scale[15]. The overall AFEQT score is calculated based on the answers from the first three subdomains (18 questions) and ranges from 0 (severe impairment/low QoL) to 100 (no limitation/high QoL). Patients were categorized into quartiles ranging from low to high based on the AFEQT scores observed in this study, with the highest quartile as reference (AFEQT score; Q1: <54.63; Q2: ≥54.63-<75.00; Q3: ≥75.00-89.05; Q4: ≥89.05.

Additional background variables from patients as recorded by AF-nurses were age (0: ≥65; 1: <65years), gender (0: man; 1: woman), CHA_2DS_2VASc score at T0 (0: 0-1; 1: ≥2), HAS-BLED score at T0 (0: 0-1; 1: ≥2), body mass index (BMI; 0: <25; 1: ≥25kg/m^2), diabetes mellitus (0: yes; 1: no), hypertension (0: no; 1: yes), obstructive sleep apnea syndrome (OSAS; 0: no; 1: yes), and location of AF diagnosis (0: GP; 1: Hospital). The recorded background variables were selected based on their inclusion as cardiovascular risk factors in guidelines from the European Society of Cardiology[19].

Statistical analyses

Patient characteristics at baseline were described using general descriptive analyses on outcome measures and background variables.

In addition, multivariable-adjusted logistic regression analyses were performed to estimate Odds Ratios (ORs) and 95% confidence intervals (CIs) to assess the association between AFEQT score at baseline (T0) and the improvement of EHRA score between baseline (T0) and 12 months of follow-up (T1). Categorized age, gender, CHA_2DS_2VASc score, HAS-BLED score were included in all models as *a priori* confounders. Potential confounders (i.e. BMI, DM, hypertension, OSAS, and location of AF diagnosis) were added to the unstratified multivariable-adjusted model using backwards elimination ($p<0.10$). Based on this procedure DM and OSAS were included in all statistical models.

In separate analyses, patients were stratified into age groups (<65/≥65 years, and <75/≥75 years) based on cut-offs included in the CHA_2DS_2VASc score, a routinely employed risk prediction rule for estimating the risk of stroke in patients with non-valvular AF. Confounder subsets in stratified analyses were identical to overall analyses to maintain the comparability of models.

Furthermore, tests for multicollinearity between the CHA_2DS_2VASc and HAS-BLED scores were performed. No indications of multicollinearity were observed. In addition, sensitivity analyses were performed with the independent adjustment of models by CHA_2DS_2VASc and HAS-BLED scores which showed similar results to main analyses (data not shown). Moreover, sensitivity analyses on EHRA improvement were performed excluding patients with a score of EHRA I. Results attenuated strongly and became non-statistically significant (data not shown). Lastly, sensitivity analyses were performed to assess whether analyses could be performed to assess the relationship between the AFEQT score and decrease in EHRA score. Unfortunately, the number of patients who reported a decrease in EHRA score was too low (n=43) to obtain robust results upon further stratifying patients.

All analyses were performed using IBM SPSS (IBM SPSS Statistics for Windows, version 26.0, IBM Corp., Armonk, NY). *P*-values <0.05 were considered statistically significant.

Results

Baseline characteristics of AF-patients, categorized into quartiles based on the AFEQT score ranging from low HRQoL (Q1) to high HRQoL (Q4), are presented in **Table 1**. Patients with a lower AFEQT score were more often female (Q1: 55.0%; Q4: 26.4%), had a higher mean age (Q1: 70.6 ± 10.6; Q4: 9.4 ± 9.4) and a higher CHA_2DS_2VASc score (2+; Q1: 80.0%; Q4: 71.1%) compared to patients with a higher AFEQT score. Patients in the fourth AFEQT score quartile (Q4) more often had a higher HAS-BLED score at baseline (2+; Q1: 41.6; Q4: 47.2%) , were more often overweight or obese (Q1: 66.7%; Q4: 71.6%) and less often had a diagnosis of hypertension (Q1: 60.0; Q4: 50.4%), compared to patients in lower AFEQT quartiles. Lastly, patients in lower AFEQT quartiles more often experienced AF at the time

of completion, when compared to patients in higher AFEQT quartiles (Q1: 37.2%; Q4: 18.3%).

Table 1. Baseline characteristics of AF-patients categorized into quartiles based on the AFEQT score at baseline.

	AFEQT score at baseline			
	First quartile (Q1) (4.63 to < 54.63)	Second quartile (Q2) (≥54.63 to <75.00)	Third quartile (Q3) (≥75.00 to <89.05)	Fourth quartile (Q4) (≥89.05 to 100)
	n (%)	n (%)	n (%)	n (%)
Total	120 (100)	120 (100)	122 (100)	121 (100)
Gender				
Men	54 (45.0)	61 (50.8)	69 (56.6)	89 (73.6)
Women	66 (55.0)	59 (49.2)	53 (43.4)	32 (26.4)
Age				
mean (SD)	70.6 (10.6)	69.9 (9.6)	67.9 (9.3)	67.9 (9.4)
CHA_2DS_2VASc score (T0)				
0-1	24 (20.0)	24 (20.0)	30 (24.6)	35 (28.9)
2+	96 (80.0)	96 (80.0)	92 (75.4)	86 (71.1)
HAS-BLED (T0)				
0-1	58 (48.3)	74 (61.7)	77 (63.1)	64 (52.9)
2+	62 (41.6)	46 (38.3)	45 (36.9)	57 (47.2)
OSAS[b]				
No	115 (95.8)	117 (97.5)	115 (94.3)	119 (98.3)
Yes	5 (4.2)	3 (2.5)	7 (5.7)	2 (1.7)
Diabetes mellitus				
No	100 (83.3)	99 (82.5)	102 (83.6)	104 (86.0)
Yes	20 (16.7)	21 (17.5)	20 (16.4)	17 (14.0)
BMI				
<25	36 (33.3)	35 (34.0)	36 (36.4)	27 (28.4)
≥25	72 (66.7)	68 (66.0)	63 (63.6)	68 (71.6)
Hypertension				
No	48 (40.0)	48 (40.0)	53 (43.4)	60 (49.6)
Yes	72 (60.0)	72 (60.0)	69 (56.6)	61 (50.4)
Location of diagnosis				
GP	46 (39.0)	27 (22.7)	42 (35.0)	42 (34.7)
Hospital	72 (61.0)	92 (77.3)	78 (65.0)	79 (65.3)
Atrial fibrillation at completion of AFEQT questionnaire				
No	71 (62.8)	91 (80.5)	95 (78.5)	94 (81.7)
Yes	42 (37.2)	22 (19.5)	26 (21.5)	21 (18.3)

Improvement in EHRA score:

In total, 203 (42.0%) AF-patients improved in EHRA-score. In patients who improved in EHRA score a mean (SD) improvement of -1.31 (0.55) was observed. Results from multivariable-adjusted analyses on the association between AFEQT score and the improvement in EHRA score after 12 months of follow-up are presented in **Table 2**. Patients with a lower AFEQT score at baseline, indicating a lower HRQoL, more often improved in EHRA score, compared

to patients in the highest AFEQT quartile at baseline (Q4; **Table 2**). This association was statistically significant across the Q1-3 quartiles, and became stronger across quartiles with lower AFEQT scores. Furthermore, the mean observed EHRA improvement was larger across decreasing AFEQT quartiles, although standard deviations were relatively wide (mean (SD): Q1: -1.39 (0.55); Q2: -1.31 (0.57); Q3: -1.20 (0.50); Q4: -1.27 (0.60)).

Table 2. Overall associations with improvement of EHRA score after 12 months (T1).

	Total study population	**Improvement of EHRA score (T1)**		
AFEQT score (T0)	**n (%)**	**n (%)**	**Adj. OR (95% CI) †**	**p-value**
First quartile (4.63 to < 54.63)	120 (24.8)	70 (58.3)	**4.73 (2.63-8.50)**	**<0.001**
Second quartile (≥54.63 to <75.00)	120 (24.8)	58 (48.3)	**3.42 (1.91-6.15)**	**<0.001**
Third quartile (≥75.00 to <89.05)	122 (25.3)	49 (40.2)	**2.33 (1.30-4.18)**	**0.005**
Fourth quartile (≥89.05 to 100)	121 (25.1)	26 (21.5)	1 (Ref.)	

† Multivariable-adjusted models were corrected for age (<65; ≥65), gender (men; women), HAS_BLED (0-1; ≥2), CHA^2DS^2-VASc (0-1; ≥2), Diabetes mellitus (no; yes) and OSAS (no; yes).

Results stratified by age (<65; ≥65):

In total, 68/134 (50.7%) of the patients diagnosed with AF <65 years of age and 135/349 (38.7%) of the patients diagnosed with AF ≥65 years of age improved in EHRA score by at least one point. On average, those who improved in symptoms improved by -1.24 (0.49) and -1.34 (0.58) (mean (SD)), for age at diagnosis of <65 years and ≥65 years , respectively. Results from multivariable-adjusted analyses testing the association between AFEQT and the improvement of EHRA score after 12 months of follow-up stratified into age categories of <65 and ≥65 years are presented in **Table 3**. Results for patients aged ≥65 years at AF diagnosis were similar to unstratified analyses. However, multivariable-adjusted OR's were stronger compared to overall analyses for the first and second quartile of AFEQT score, when compared to the fourth quartile (OR (95%CI): 6.07 (2.89-12.74) and 4.75 (2.29-9.84), respectively). In patients with an AF-diagnosis before 65 years solely the first AFEQT score quartile was statistically significantly associated with an increased EHRA score, compared to the fourth AFEQT quartile (OR (95%CI): 2.77 (1.00-7.67)). Similar to overall analyses, a positive association was observed for diabetes mellitus in patients with an AF-diagnosis before 65 years of age. However, this association was not statistically significant (OR (95%CI): 3.06 (0.76-12.31)).

Results stratified by age (<75; ≥75):

In total, 138/330 (41.8%) of the AF-patients diagnosed <75 years of age and 65/153 (42.4%) of the AF-patients diagnosed ≥75 years of age improved in EHRA score by -1.31 (0.56) and -1.29 (0.52) (mean (SD)), respectively. Results from multivariable-adjusted analyses testing the association between AFEQT and the improvement of EHRA score after 12 months of follow-up stratified into age categories of <75 and ≥75 years are presented in **Table 4**. Both age groups showed similar associations to overall analyses presented in **Table 2**.

Table 3. Associations stratified by age categories (<65; ≥65 years) with improvement of EHRA score after 12 months (T1)

	Age <65				Age ≥65			
	Total study population	Improvement of EHRA score (T1)			Total study population	Improvement of EHRA score (T1)		
	n (%)	n (%)	Adj. OR (95%CI)	p-value	n (%)	n (%)	Adj. OR (95%CI)	p-value
AFEQT score (T0) †								
First quartile (4.63 to < 54.63)	33 (24.6)	20 (60.6)	**2.77 (1.00-7.67)**	0.049	87 (24.9)	50 (57.5)	**6.07 (2.89-12.74)**	**<0.001**
Second quartile (≥54.63 to <75.00)	31 (23.1)	15 (48.4)	1.54 (0.55-4.37)	0.413	89 (25.5)	43 (48.3)	**4.75 (2.29-9.84)**	**<0.001**
Third quartile (≥75.00 to <89.05)	37 (27.6)	21 (56.8)	2.30 (0.85-6.23)	0.101	85 (24.4)	28 (32.9)	**2.40 (1.13-5.10)**	**0.023**
Fourth quartile (≥89.05 to 100)	33 (24.6)	12 (36.4)	1 (Ref.)		88 (25.2)	14 (15.9)	1 (Ref.)	

† Multivariable-adjusted models were corrected gender (men; women), HAS_BLED (0-1; ≥2), CHA^2DS^2-VASc (0-1; ≥2), Diabetes mellitus (no; yes) and OSAS (no; yes).

Table 4. Associations stratified by age categories (<75; ≥75 years) with improvement of EHRA score after 12 months (T1)

	Age <75				Age ≥75			
	Total study population	Improvement of EHRA score (T1)			Total study population	Improvement of EHRA score (T1)		
	n (%)	n (%)	Adj. OR (95%CI)	p-value	n (%)	n (%)	Adj. OR (95%CI)	p-value
AFEQT score (T0) †								
First quartile (4.63 to < 54.63)	71 (21.5)	44 (62.0)	**5.46 (2.67-11.15)**	**<0.001**	49 (32.0)	26 (53.1)	**3.75 (1.31-10.71)**	**0.014**
Second quartile (≥54.63 to <75.00)	77 (23.3)	35 (45.5)	**2.80 (1.40-5.62)**	**0.004**	43 (28.1)	23 (53.5)	**4.93 (1.68-14.45)**	**0.004**
Third quartile (≥75.00 to <89.05)	96 (29.1)	40 (41.7)	**2.43 (1.25-4.73)**	**0.009**	26 (17.0)	9 (34.6)	2.11 (0.62-7.19)	0.232
Fourth quartile (≥89.05 to 100)	86 (26.1)	19 (22.1)	1 (Ref.)		35 (22.9)	7 (20.0)	1 (Ref.)	

† Multivariable-adjusted models were corrected for gender (men; women), HAS_BLED (0-1; ≥2), CHA^2DS^2-VASc (0-1; ≥2), Diabetes mellitus (no; yes) and OSAS (no; yes).

The association between improved EHRA score was the strongest in the first AFEQT score quartile, compared to the fourth AFEQT quartile in patients in the category <75 years (OR (95% CI): 5.46 (2.67-11.15)). Similar to other analyses, the strength of the association increased

across decreasing AFEQT score quartiles in stratified analyses on <75 years. This increase was less prominently visible in analyses stratified on ≥75 years at AF-diagnosis. In analyses on this stratum, the strongest association with EHRA improvement was observed in the second AFEQT quartile, when compared to the fourth. In addition, the association with EHRA improvement comparing the third and the fourth AFEQT quartile was non-significant in this stratum.

Discussion

In the present study we aimed to assess the relationship between AFEQT score at baseline in AF-patients and the improvement in EHRA score at 12 months of follow-up. In addition, we aimed to identify patient subgroups which most commonly experienced EHRA score improvement during this time period. In summary, AF patients with a lower AFEQT score at diagnosis were more likely to improve their EHRA score during follow-up, when compared to patients with a higher AFEQT score at diagnosis. In analyses stratified by age categories, patients above the age of 65 and below the age of 75 with lower AFEQT scores at baseline were most likely to improve their EHRA score between baseline and 12 months of follow-up.

The findings of this study highlight the importance of accounting for both the patients' perception of their general state of health and patient characteristics, such as age, at the moment of diagnosis to predict symptom improvement in the year post diagnosis. While the clinical value of the interrelatedness of the AFEQT questionnaire and EHRA score has been described in previous studies, little is known on the predictive value of these factors over time [12,13,16,20]. Krisai *et al.* states that patient-reported QoL might be a more robust and comprehensive patient-reported metric, when compared to symptom status, due to the stability over time independent from AF-treatment and the better prediction of future adverse cardiac events[16]. Previous studies have indicated that low QoL is associated with the prevalence of specified AF-related symptoms, such as dyspnea at rest, exercise intolerance and chest discomfort or tightness[12,16]. In light of these findings, the results from the present study indicate that patients with a low QoL may gain the most from specialized and intensive treatment regimens (e.g. multidisciplinary cardiac rehabilitation), as these patients likely experience a higher disease-burden at the onset of AF[16]. At present, most AF treatment protocols, aside from stroke prevention through anticoagulation medication use, are based on evaluating and resolving the symptomatic burden of patients[9]. Inclusion of patient-reported outcome measures into regular care, such as QoL, can provide insight on the symptomatic burden, aiding clinicians in shared-decision making prior to treatment. In addition, the availability of the HRQoL at diagnosis may help guide clinicians in setting realistic expectations of anticipated symptom improvements during patient consultations[5]. However, it remains paramount to consider the patients unique characteristics and risk factors when assessing patient-reported outcomes in the clinic to obtain an accurate estimation of patient disease progression.

Cardiovascular risk factors, such as age, are routinely employed to estimate the stroke risk of AF-patients within the CHA_2DS_2-VASc score[10,21,22]. As such, cardiovascular risk factors can be seen as important predictors for the disease course of AF. Due to the general importance of age as a predictor of stroke risk within the CHA_2DS_2-VASc score with an increase in stroke risk across increasing age cut-offs (<65, ≥65-74 and ≥75 years, respectively), similar age cut-offs were employed in this study[10]. Our results indicate that patients with a low HRQoL above 65 and below 75 years old have the greatest potential to show improvement in symptoms, when compared to patients under 65 and above 75 years of age respectively. These observations need further validation in future large-scale studies. Validation of these results will enable future research to further define patient subgroups for which symptom improvements or other cardiovascular outcomes can be predicted using patient-reported outcome measures. Using this information, treatment recommendations can be made based on the risk-stratification of patient groups by evidence-based cut-offs (e.g. by combining information on HRQoL and age) due to additional insight into the predicted disease course. This would enable clinicians to tailor treatment strategies to the expected patient-specific disease course based on both clinical and patient-reported characteristics, likely increasing the effectiveness of treatment regimens and averted negative clinical outcomes.

Besides identifying patient subgroups who are most likely to benefit from intensive treatment regimens, future studies should also focus on linking the disease course of cardiovascular patients with patient-reported predictors at diagnosis, such as HRQoL. One such cardiovascular outcome has been described in previous research by Freeman *et al.* in which EHRA score was associated with a higher risk of hospitalizations[12]. In the same study, the EHRA score was inversely correlated with AFEQT score[12]. Based on these findings we speculate that the AFEQT-derived HRQoL at diagnosis can also be used as a predictor to predict disease course of AF patients, aside from symptoms. Future research is needed to specify association between QoL at diagnosis and outcomes such as resource utilization and costs (e.g. hospitalization and treatment) and the occurrence of adverse cardiac events (e.g. MACE). Robust information on the interrelatedness of the patients' perception of their general state of health, patient-relevant outcomes and healthcare resource utilization could, in turn, provide valuable avenues for the implementation into value based healthcare[23,24]. Based on the findings from this study, patients with a low HRQoL and an age between 65 and 75 years might prove to be valuable targets for which greater health benefits can be attained through the implementation of patient-tailored treatment policies. However, further information is needed on why symptom improvements were less frequently observed in patients below 65 years and above 75 years of age. In addition, more information is needed on which treatment strategies and lifestyle recommendations are especially beneficial for these specific patient groups to provide the most optimal healthcare.

This study was subject to some limitations. Firstly, no information was available on the use of rate or rhythm control in our patient population. Due to this caveat, we were unable to discern whether there was a difference in patients within the AFEQT quartiles with regards to these treatment types. Previous studies have indicated that the presence of symptoms is associated with the selection of rate or rhythm control in AF-patients[25,26]. Furthermore, patients with an age above 75 years more often are prescribed rate control medication[25,26]. In general, patients with more prominent AF symptoms are more likely to be managed with rhythm control, which likely also leads to improved symptom control[27–29]. Not controlling for these differences in treatment may have confounded our results, because it makes it difficult to discern whether EHRA improvement has occurred either as an effect of elapsing time or treatment. Secondly, we scored patients according to the original EHRA score, instead of the modified EHRA score (mEHRA)[13,18]. Due to this, we were unable to distinguish whether patients who were not affected in their normal daily activity were either not troubled by symptoms (mEHRA class 2a) or troubled by symptoms (mEHRA class 2b)[13]. As we were mainly interested in full point improvements on the EHRA score, we do not believe that the use of the unmodified EHRA score affected our results. Furthermore, we restricted our stratified analyses to selected age categories for this study. It is likely that other patient characteristics, such as gender and BMI, may also be used to define patient subgroups that show varying associations between AFEQT and EHRA. Analyses on these subgroups was beyond the scope of this study. Moreover, statistical floor effects may have influenced the results within this study as patients with EHRA class I at baseline were unable to further improve on their symptoms. In addition, we observed that patients in lower AFEQT quartiles more often experienced AF at the time of completing the AFEQT questionnaire. Therefore, this group of patients might also have experienced more symptoms at baseline, and such, may have had more opportunity to improve. Furthermore, in stratified analyses the number of patients diagnosed <65 years of age the was limited, which may have affected the robustness of results in these particular analyses. Lastly, due to the limited number of patients who decreased in EHRA score between baseline and follow-up we were unable to assess the worsening of symptoms in this study.

In conclusion, the present study indicates that AF-patients with a lower quality of life at baseline were most likely to improve their EHRA score after 12 months. This effect was most prominent in patients ≥65 years of age and patients <75 years of age, compared to patients <65 and ≥75 years, respectively. Future research should focus on verifying these results and on further defining characteristics of patients within these age-groups to enable the implementation of age-tailored treatment. In addition, future research should elaborate on whether patient-reported outcome measures, such as QoL, can be used to predict the cardiovascular disease course.

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Chapter 7

The association between clinical outcomes and experienced quality of outpatient care among patients treated for atrial fibrillation

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Objective:
Patient-Reported Experience Measures (PREMs) are commonly used to indicate patients' experiences in atrial fibrillation (AF) care. As outcomes are the primary goal in Value-Based Health Care, questions are raised regarding whether those experiences represent AF patients' relevant outcomes. Therefore, this study aims to assess whether a questionnaire concerning AF patients' experienced quality of care is correlated with AF patients' clinical outcomes.

Materials and methods:
Data of the present study originated from a prospective cohort study performed among outpatient AF patients in the Netherlands. In October 2015, all patients were asked to complete the Consumer Quality Index (CQI) to assess their experiences with the outpatient AF clinic. Analyses are performed to assess the association between patients' experiences and clinical outcomes of AF patients (i.e. EHRA score) after three and six months of follow-up.

Results:
A total of 242 AF patients (68.8 years) met the inclusion criteria. Regarding the eight domains of the CQI, only provided information (B=3.10; p=0.01) and the physicians' communication (B=-3.12; p=0.03) were associated with improved EHRA scores at three months. After six months, EHRA score improvements were associated with only one out of eight CQI indicators, namely the information AF patients received from other healthcare providers (B=-5.15; p<0.01).

Conclusion:
An inconsistent correlation between AF patients' clinical outcomes and AF patients' PREMs was found. Although PREMs are relevant in healthcare, they cannot replace outcomes as a measure of medical care quality. For healthcare organizations, it is crucial to identify the required strategy for assessing the various aspects of the quality of services provided.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia and approximately six million patients in Europe are diagnosed with AF (1). Prior research (2-4) has indicated that quality improvements in AF care are a necessity in order to decrease the disease burden for patients and society. To indicate elements for quality improvement, self-administered Patient-Reported Experience Measures (PREMs) are often used (5,6). However, it is questionable whether AF patients' experiences are able to fully represent the quality of care provided by health professionals. According to Porter (7,8), quality of care should be assessed and improved using outcomes that matter most to patients. For that reason, this study aims to assess whether the results of a self-administered questionnaire to identify patient experiences are correlated with the AF patients' clinical outcomes as a measure of quality of care.

PREMs have been developed and tested for several domains in healthcare. Even though instruments used to measure the experience of patients are assessed to select the most suitable instrument for specific situations, these instruments face several challenges regarding their reliability, validity (6), and responsiveness in assessing changes in patients' health status (9). One instrument used to assess patients' experiences concerning the quality of Dutch hospital care is the Consumer Quality Index (CQI) (10), which was developed for inpatient hospital care, elderly care, chronic care, and outpatient hospital care (11,12). Previous research (13-15) has reported that the CQI is a reliable instrument to assess patients' perceptions. However, it is not clear whether the patients' experiences represent an objective measure for quality of care (6).

Over the last decade, Value-Based Health Care (VBHC) has received a great deal of attention as a strategy to improve healthcare (7,8). Outcome measures, the nominator of the value equation introduced as the overarching goal in healthcare, are used in VBHC to evaluate and improve quality of care. In order to assess clinical outcomes for patient groups with a specific medical condition, outcome measures are selected, measured, published and improved by many initiatives worldwide (16). In essence, improvements in patient-relevant outcomes should provide an objective indication of the quality of care provided by the involved healthcare professionals.

Although prior research has reported mixed findings on potential correlations between Patient-Reported Outcomes Measures (PROMs) and PREMs (17), there is little information on the extent to which clinical outcomes are correlated with PREMs in general, and for AF patients specifically regarding the quality assessment in healthcare. Insight into this correlation would provide opportunities to accelerate quality improvements in healthcare.

In AF care, one of the leading and internationally used health outcomes is the European Heart Rhythm Association (EHRA) score (18,19), a measure to assess AF-related symptoms. To assess the relation between patient-relevant outcomes and the PREMs, the

present study aims to indicate whether patient experiences regarding quality of care in outpatient AF clinics, measured with the CQI, are correlated with the AF patients' clinical outcome (i.e. EHRA score) at both three and six months.

Materials and methods

Population and design

In the present study baseline, three month, and six month follow-up data of AF patients are used; these patients were included in the AF-NET study between March 2015 and October 2015 when they visited the outpatient AF clinics in one of the four hospitals collaborating in the Netherlands Heart Network (NHN). The NHN (20) is a collaboration of healthcare professionals at four hospitals and four general practitioner organizations in a rural area in the Netherlands (adherence area= 760,000 inhabitants). Moreover, all AF patients who visited one of the outpatient AF clinics received a paper questionnaire from the CQI in order to assess their perceived quality of care at the outpatient AF clinics. Due to privacy legislation, no personal data was mentioned on the questionnaire. Instead a study number was used, which matched with the study number of the AF-NET study. The CQI was only distributed once (i.e. cross-sectional design) and participants were requested to return the questionnaire to their hospital using a self-addressed envelope after completion.

Patients in the present study were included if they met the following criteria: newly or recently (less than two months ago) diagnosed with AF, 18 years or older, returned the self-administered CQI, and signed the informed consent form. Excluded from participation were patients who visited the outpatient AF clinic more than six months after receiving the paper questionnaire.

AF-NET study

Patients included in the AF-NET study visited an AF nurse in any of the four hospitals. At the first visit, the AF nurse discussed the main AF measures (i.e. onset date of symptoms, type of AF, patient demographics, vital signs), stratification scores (i.e. EHRA, HAS-BLED (major bleeding risk score), and CHA_2DS_2-VASc (score for stroke prediction)). Subsequently, during the first visit the study was explained and written informed consent of the AF patients was obtained. After consultations with the AF nurse the follow-up consultations were performed by the treating cardiologist.

The protocol of the AF-NET study (including the procedure for the CQI) was submitted for approval to the Medical research Ethics Committee United (MEC-U) in the Netherlands (reference number: 14,083). The MEC-U confirmed that the Medical Research Involving Human Subjects Act does not apply to the AF-NET study and that therefore an official approval of this study by the MEC-U is not required.

Measurements

The results in the present study are based on the baseline (T0), three month (T3), and six month follow-up (T6) data of the AF-NET study and the data of the CQI. All AF patients who visited the outpatient AF clinic received the CQI within six months after their first consultation and were requested to assess their perceived quality of care at the outpatient AF clinic.

A main patient-relevant outcome in AF care is the *EHRA* score (18,19). It provides an indication of the AF-related symptoms during an AF episode. Scores range from the following: 1= 'EHRA I *No symptoms*'; 2= 'EHRA II *Mild symptoms, normal daily activities not affected*'; 3= 'EHRA III *Severe symptoms, normal daily activity affected*'; 4= 'EHRA IV *Disabling symptoms, normal daily activity discontinued*' (21). For the present study, the EHRA score is dummy coded: 'No Symptoms' (EHRA= 1) is coded by 1 and 'Symptoms' (EHRA>1) is coded by 2.

In the AF-NET study, the following patient characteristics, including their coding, are collected: *age* (based on patients' date of birth), *gender* (1= male; 2= female), *type of AF* (1= first diagnosed AF; 2= paroxysmal AF; 3= persistent AF; 4= permanent AF), *CHA_2DS_2-VASc score* to estimate stroke risk (indicated by a mean score), and *HAS-BLED score* to estimate major bleeding risk (indicated by a mean score). Furthermore, the following *co-morbidities* are indicated (and all measured by 1= Yes; 2= No):

Hypertension is defined as systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg measured during two or more consecutive moments (during rest), and/or current use of antihypertensive medication (22).

Coronary Artery Disease (CAD) is characterized as previous myocardial infarction (MI) (either ST elevation MI or non-ST elevation MI), percutaneous coronary or surgical coronary revascularization, or evidence of coronary atherosclerosis with the presence of a stenosis in at least one coronary artery (23,24). The stenosis should lead to a reduction of at least 50% diameter or a pressure drop (FFR) <80%.

Heart failure is characterized by typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) that may be accompanied by signs (e.g. elevated jugular venous pressure, pulmonary crackles and peripheral oedema) caused by a structural and/or functional cardiac abnormality, resulting in a reduced cardiac output and/or elevated intracardiac pressure at rest or during stress (25).

Peripheral Artery Disease (PAD) is indicated by the presence of one of the following: claudicatio intermittens, amputation due to arterial insufficiency, vascular reconstruction (bypass surgery or percutaneous intervention of extremities), or documented aortic aneurysm.

Cardiovascular Disease (CVD) is indicated by the occurrence of symptomatic AF, de-compensation, heart failure, myocardial infarction or coronary artery disease, hypertension, ischemic stroke, Transient Ischemic Attack (TIA), systemic embolism, major bleeding,

heart valve disease, syncope, sustained ventricular tachycardia or life-threatening adverse effects of drugs.

Diabetes Mellitus (DM) is characterized by recurring or persistent hyperglycaemia and is diagnosed by demonstrating fasting plasma glucose level ≥7.0 mmol/L (≥126 mg/dl), or plasma glucose ≥11.1 mmol/L (≥200 mg/dl) after two hours of 75 g oral glucose, or symptoms of hyperglycaemia and a plasma glucose of ≥11.1 mmol/L (=200 mg/dl), or glycosylated hemoglobin (HbA1c) ≥6.5% (26,27).

Thyroid disease is measured by the Thyroid Stimulating Hormone (TSH) and indicated to be positive if TSH ≥60 IE/ml.

CQI

CQI is a questionnaire developed by the Netherlands Institute for Health Service Research (NIVEL) and is approved to measure 'healthcare quality based on consumer experiences' (28). The CQI is partially based on the Consumer Assessment of Healthcare Providers and Systems and is reconstructed for the Dutch healthcare system. In the present study, the CQI is used to assess the quality of care for the outpatient AF clinic. This self-administered questionnaire (70 items) has been tested for reliability and validity and focuses on eight quality aspects (i.e. reception at the outpatient clinic, treatment by the physician, information provision by the physician, communication by the physician, treatment by another healthcare provider, information provision by another healthcare provider, communication by another healthcare provider, and aftercare with regard to medication) (29). In the present study, the AF nurse is indicated by the term 'another healthcare provider'.

Following the instructions of the Netherlands Institute for Health Service Research, combined quality aspects are constructed from the separate items of the CQI (i.e. scale variables) (30).

Reception at the outpatient clinic was measured by four items to assess whether the patients felt welcome at the outpatient clinic and questions regarding the reception by the desk employee of the outpatient clinic. The answer scales ranged from '1= No, not at all' to '4= Yes, completely' (Cronbach's alpha = 0.76).

Treatment by doctor was measured by three items to indicate whether the physician took time for the AF patient, listened to the AF patient, and took the AF patient seriously. The answer scales for these questions ranged from '1= No, not at all' to '4= Yes, completely' (Cronbach's alpha= 0.84).

Information provision by doctor was measured by four items to assess whether the AF patients perceived enough information regarding the medical examinations and treatment (i.e. 'Did the doctor tell you in advance why the treatment or the examination was necessary?'). The four-point answer scales for these questions ranged from '1= No, not at all' to '4= Yes, completely' (Cronbach's alpha= 0.89).

Communication by doctor was measured by three items to indicate whether the received information was tailored to the personal situation of the AF patient, whether the doctor explained the procedure in a clear way, and whether he/she had the possibility to ask the doctor questions. The four-point answer scales for these questions also ranged from '1= No, not at all' to '4= Yes, completely' (Cronbach's alpha= 0.82).

Treatment by another healthcare provider was indicated by three items assessing whether the healthcare provider took time for the AF patient, listened to the AF patient, and took the AF patient seriously. The (four-point) answer scales for these questions ranged from '1= No, not at all' to '4= Yes, completely' (Cronbach's alpha= 0.84).

Information provision by another healthcare provider was measured by four items to assess whether the AF patients received enough information regarding the medical examinations and treatment (i.e. 'Did the other healthcare provider tell you in advance why the treatment or the examination was necessary?'). The four-point answer scales for these questions ranged from '1= No, not at all' to '4= Yes, completely' (Cronbach's alpha= 0.88).

Communication by another healthcare provider was measured by three items to indicate whether the received information was tailored to the personal situation of the AF patient, whether the healthcare provider explained the procedure in a clear way, and whether he/she had the possibility to ask the healthcare provider questions. The four-point answer scales for these questions also ranged from '1= No, not at all' to '4= Yes, completely' (Cronbach's alpha= 0.83).

Aftercare with regard to medication was measured with three items to assess whether the AF patients have received information regarding the effects and side effects of their medication. The two-point answer scales for these questions ranged from '1= No' to '4= Yes' (Cronbach's alpha= 0.78).

In order to assess the association between AF patients' outcome measures (i.e. EHRA score) and their perceived quality of care, the data of the AF-NET study is merged with the data of the CQI by means of identical study numbers, used for pseudonimization of the included patients.

Statistical analyses

To describe the sample under study, descriptive statistics were used regarding the data of the AF-NET study (i.e. age, gender, type of AF, co-morbidities, CHA_2DS_2-VASc score and HAS-BLED score). In order to assess potential confounders, t-test and chi-square analyses were performed for patients with EHRA=1 and EHRA>1. Subsequently, descriptive analyses were executed to indicate the distribution of the constructed scales of the CQI. In those analyses as well, potential differences between EHRA=1 and EHRA>1 were indicated using t-test analyses.

Dummy variables are constructed to indicate improvements of the EHRA score (coded as '1') and no improvements (defined as 'equal score' or 'worsening score') of the

EHRA score (coded as '0'). Potential improvements of the EHRA score were indicated after three and six months of follow-up. In order to assess the associations between the scales of the CQI and the potential confounders, logistic regression analyses were performed on improvements of the EHRA score after three and six months. In the present study, all analyses were performed in the Statistical Package for the Social Sciences 25.0 and differences were indicated to be significant if $p \leq 0.05$.

Results

Basic characteristics

A total of 242 AF patients (mean age= 68.7 years; 56.2% male) met the inclusion criteria and were eligible for the analyses (221 AF patients were excluded due to not returning the CQI questionnaire). Most included patients (53.3%) were diagnosed with hypertension and 40.5% had paroxysmal AF. In **Table 1** the basic characteristics of the research sample are indicated for AF patients with an EHRA=1 and EHRA>1. AF patients with an EHRA=1 (n=81) are older (70.4 years; p=0.05), more often male (72.8%; p<0.01), and less often diagnosed with paroxysmal AF (27.2%; p<0.01). Moreover, AF patients with an EHRA>1 showed less CVD (7.5%; p=0.04) and lower HAS-BLED scores (1.32; p=0.03) in contrast to AF patients with no symptoms based on their EHRA score.

Table 1. Baseline characteristics

	Total (N= 242)	**EHRA[1]=1 (n= 81)**	**EHRA>1 (n= 161)**	***P*-value***
Age (mean ±SD[2])	68.74 ±9.95	70.40 ±8.52	67.90 ±10.52	**0.05**
Gender (% male)	56.2	72.8	47.8	**<0.01**
Type AF[3] (% paroxysmal AF)	40.5	27.2	47.2	**<0.01**
Hypertension (% yes)	53.3	54.3	52.8	0.75
Coronary Artery Disease (% yes)	8.3	7.4	8.7	0.73
Heart failure (% yes)	2.1	3.7	1.2	0.20
Peripheral Artery Disease (% yes)	4.5	6.2	3.7	0.38
Cardiovascular Disease (% yes)	10.3	16.0	7.5	**0.04**
Diabetes Mellitus (% yes)	14.9	19.8	12.4	0.13
COPD[4] (% yes)	7.4	7.4	7.5	0.99
Thyroid disease (% yes)	7.9	6.2	8.7	0.51
CHA_2DS_2-VASc score[5] (mean ±SD)	2.59 ±1.71	2.72 ±1.60	2.53 ±1.76	0.42
HAS-BLED[6] (mean ±SD)	1.40 ±0.82	1.56 ±0.82	1.32 ±0.80	**0.03**

*significant if $p \leq 0.05$; [1]EHRA= European Heart Rhythm Association; [2]SD= Standard Deviation; [3]AF= Atrial Fibrillation; [4]COPD= Chronic Obstructive Pulmonary Disease; [5]CHA_2DS_2-VASc score= score for stroke prediction; [6]HAS-BLED= major bleeding risk score

Self-administered questionnaire (CQI)

In **Table 2** the mean scores of the CQI are indicated for both AF patients with EHRA=1 and EHRA>1 at baseline. As shown in the table, AF patients with EHRA=1 at baseline score significantly more positively on the CQI for the following elements: treatment by the

doctor (3.91; p=0.05), information received from the doctor (3.74; p=0.03), communication received from the doctor (3.86; p=0.02), and information received from another healthcare provider (3.70; p=0.01).

Table 2. Average scores of CQI scales

	Total (N=242)	EHRA[1]=1 (n= 81)	EHRA>1 (n= 161)	*P*-value*
Reception at outpatient clinic (mean ±SD[2])	3.82 ±0.35	3.88 ±0.35	3.79 ±0.35	0.07
Treatment by doctor (mean ±SD)	3.85 ±0.36	3.91 ±0.25	3.82 ±0.41	**0.05**
Information provision by doctor (mean ±SD)	3.59 ±0.68	3.74 ±0.47	3.50 ±0.76	**0.03**
Communication by doctor (mean ±SD)	3.77 ±0.49	3.86 ±0.29	3.73 ±0.57	**0.02**
Treatment by another healthcare providers (mean ±SD)	3.84 ±0.41	3.88 ±0.35	3.82 ±0.44	0.38
Information provision by another healthcare provider (mean ±SD)	3.50 ±0.75	3.70 ±0.50	3.36 ±0.86	**0.01**
Communication by another healthcare provider (mean ±SD)	2.78 ±0.46	2.81 ±0.38	2.76 ±0.50	0.46
Aftercare with regard to medication (mean ±SD)	2.96 ±1.17	3.05 ±1.12	2.92 ±1.19	0.51

*significant if $p \leq 0.05$; [1]EHRA= European Heart Rhythm Association; [2]SD= Standard Deviation

Association between EHRA and CQI

Of the eight quality aspects of the CQI, only the information (B=3.10; p=0.05) and communication AF patients received from the doctor (B=-3.13; p=0.03) were significantly associated with improvements of the EHRA score after three months of follow-up (**Table 3**). Furthermore, improvements of the EHRA score after six months (**Table 4**) of follow-up are inversely associated with the HAS-BLED score at baseline (B=-1.39; p=0.04) and one quality aspect of the CQI, namely the information AF patients received from another healthcare provider (B=-5.15; p<0.01).

Table 3. Improvement on EHRA score after 3 months of follow-up

	B[1]	S.E.[2]	*P*-value*
Age	0.01	0.04	0.72
Gender	0.94	0.77	0.22
Type AF[3] (T0)	-0.26	0.22	0.24
Cardiovascular Disease (T0)	0.06	1.06	0.96
HAS-BLED[4] (T0)	-0.85	0.51	0.10
Reception at outpatient clinic	-1.13	1.67	0.50
Treatment by doctor	1.28	1.80	0.48
Information provision by doctor	3.10	1.59	**0.05**
Communication by doctor	-3.13	1.40	**0.03**
Treatment by another healthcare providers	-1.16	1.84	0.53
Information provision by another healthcare provider	-1.50	0.93	0.11
Communication by another healthcare provider	0.62	1.30	0.63
Aftercare with regard to medication	0.16	0.37	0.66

*significant if $p \leq 0.05$; [1]*B:* Unstandardized bèta; [2]Standard Error of the unstandardized bèta; [3]AF= Atrial Fibrillation; [4]HASBLED= major bleeding risk score

Table 4. Improvement on EHRA score after 6 months of follow-up

	B[1]	**S.E.**[2]	***P*-value***
Age	<0.01	0.04	0.99
Gender	1.73	1.08	0.11
Type AF[3] (T0)	-0.24	0.26	0.36
Cardiovascular Disease (T0)	-3.96	2.46	0.11
HAS-BLED[4] (T0)	-1.39	0.68	**0.04**
Reception at outpatient clinic	1.20	2.32	0.61
Treatment by doctor	5.29	3.31	0.11
Information provision by doctor	2.99	1.84	0.11
Communication by doctor	-1.30	2.15	0.54
Treatment by another healthcare providers	-0.27	2.25	0.91
Information provision by another healthcare provider	-5.15	1.95	**<0.01**
Communication by another healthcare provider	-0.16	2.17	0.94
Aftercare with regard to medication	-0.26	0.46	0.57

*significant if $p \leq 0.05$; [1]*B:* Unstandardized bèta; [2]Standard Error of the unstandardized bèta; [3]AF= Atrial Fibrillation; [4]HAS-BLED= major bleeding risk score

Discussion

Interpretation of findings

The present study aims to determine whether there is a correlation between patient experiences regarding the outpatient AF clinic and clinical outcomes of AF patients at both three and six months. At baseline, a significant association was found between clinical outcomes and information and communication received by a doctor or other healthcare professionals. However, follow-up results show inconsistent findings, such as a negative correlation between improvements of the EHRA score after six months of follow-up and the perceived communication from the doctor and the information AF patients received from another healthcare provider. Furthermore, the information from the doctor was positively correlated with improvements of the EHRA score after three months of follow-up.

In accordance with previous research (31,32), the present study found a significant correlation between AF patients' health outcomes and the information provided by and the communication with the doctor or other healthcare providers (i.e. AF nurse) at baseline. As reported by a review of Stewart (32), providing patients with more in-depth and tailored information is likely to result in improved health outcomes for patients. However, in the current study converse associations were found between communication by the doctor and information by the healthcare provider after three and six months of follow-up. However, this contrasting finding is difficult to explain. It may be that experience measures are strongly related to patients' first impression and do not hold over time. Measures to evaluate the quality of healthcare have been used for almost a century (33). During this period, numerous shifts and developments were reported concerning tools to assess the quality of care. Since prior research (9) has already suggested that experience

measures are less susceptible to changes in patients' health status, clinical outcomes may currently be a more valid and reliable representation of healthcare quality.

In order to assess the quality of care, previous research used either subjective (i.e. patients' experiences) (34,35) or objective measures (i.e. hard readings such as mortality, symptom scores, or diagnostic parameters) (36). Results of the present study show that both subjective and objective measures report contrasting findings regarding healthcare quality, especially in the long run. Therefore, it is crucial for organizations, also in healthcare, to identify the best or needed strategy for assessing the results of services provided. Based on the chosen strategy, the most suitable instrument, either objective or subjective, can be selected. Nevertheless, organizations often face difficulties in selecting the best-fitting strategy to assess healthcare quality (37). For that reason, indicators used in VBHC may provide a solution as they contain to indicate both objective (i.e. clinical outcomes) and subjective measures (i.e. PROMS, such as quality of life measures) that are most relevant for a specific medical condition. However, it is advisable for future research to assess whether the subjective indicators used in VBHC are also susceptible to changes over time.

Implication of findings

The findings of the present study indicate that there is a significant positive correlation between PREMs and AF patients' relevant outcomes at baseline, which implies that AF patients with limited or no AF symptoms at inclusion score higher on patient experiences such as the perceived communication and information. However, the clinical outcomes measured after three and six months of follow-up show inconsistent findings regarding AF patients' PREMs. This contradictory finding may imply that PREMs are only able to measure cross-sectional and are not able to represent clinical measures over time. Nevertheless, it is advisable for future research to assess whether this conclusion holds for other medical conditions or different patient-relevant outcomes.

The major finding of the present study is that patient experiences, measured with PREMs, do not represent AF patients' clinical outcomes over time. This implies that before assessment of quality of care is initiated, organizations should decide which strategy is needed and which instrument is most suitable to assess healthcare quality (i.e. patient-relevant outcomes or patients' experiences). If determining patients' current perceptions or opinions regarding the quality of care is the primary goal, PREMs can be used. For quality indications that remain valid over time, patient-relevant outcomes are advised.

Limitations

The presented findings should be interpreted taking into account potential limitations. One limitation was that only one patient-relevant outcome was used (i.e. EHRA score) in the present study. However, the EHRA score is an internationally validated variable in AF care (18,19) and therefore crucial to indicate AF patients' relevant outcomes. A second

limitation may be that the CQI was only measured once, while the EHRA score was measured at baseline, three months, and six months of follow-up. This may raise questions regarding the reliability and shelf life of the CQI results. However, the first question in the CQI is whether the patients had visited the outpatient clinic in the past six months. If this question was answered negatively, the patient was excluded from the analyses of the present study. Using this procedure, both AF patients' experiences and their most relevant outcome are assessed within the past six months. Finally, the CQI is a Dutch questionnaire. Therefore, one may wonder whether this questionnaire is comparable with corresponding studies. Prior research showed the CQI to be a valid and reliable (13-15) questionnaire and while the CQI is partially based on the internationally used Consumer Assessment of Healthcare Providers and Systems it is comparable with other perceived quality of care instruments. Although the CQI was not specifically designed for cardiac patients, the questionnaire was tailored for the sample under study (i.e. outpatient population) and therefore is a proper instrument for the present study sample.

Conclusion

The results of this study indicate an inconsistent correlation between PREMs of AF patients and improvements of AF patients' relevant outcomes in order to represent the quality of AF care. Although patients' experiences are crucial in healthcare, it is advisable for future research to indicate the best strategy regarding the assessment of results of services provided.

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Part 3

Successful e-health implementation

Chapter 8

Successful implementation of e-health interventions in healthcare: development of an e-health implementation guideline

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Abstract

Introduction:
e-Health interventions have the potential to improve the quality of healthcare and reduce costs. However, to implement e-health interventions successfully instruments are needed to facilitate this process. This study aims to develop an e-health implementation guideline for implementation of e-health interventions in daily practice.

Methods:
In June and July 2019 a literature research was conducted and, subsequently, a two-round Delphi study including 13 international e-health experts in the field of healthcare, ICT & technology, and research was performed. Within the Delphi study, experts scored specific determinants using an online survey. Based on mean scores and interquartile ranges (IQRs) in the online survey, consensus between the experts was assessed.

Results:
A total of five domains (i.e., Technology, Acceptance, Financing, Organizational, and Legislation & Policy) with 24 corresponding determinants were assessed by the experts. After the second Delphi round, consensus was achieved on the five domains and 23 determinants (mean scores ≥ 8; IQR ≤ 2). Only for the determinant 'Evidence-Based Medicine' was no consensus reached (mean score < 8; IQR $= 2$). Based on the 23 determinants, the e-health implementation guideline is developed for e-health implementations in healthcare in order to increase their effectiveness.

Conclusion:
The e-health implementation guideline developed in this study may help healthcare providers/researchers assess the determinants of successful e-health intervention prior to the implementation of the e-health program

Introduction

Global healthcare costs have risen rapidly, US$ 7.8 trillion in 2017, and further increases in healthcare expenditures are predicted for the coming decades (1). Solutions to reduce healthcare costs, and concurrently improve patient-relevant outcomes, are assessed in different healthcare settings using value-based healthcare (VBHC) as a primary strategy (2-5). In this regard, much attention is given to the integration of e-health into future healthcare systems in order to improve outcomes and decrease healthcare costs (6-8). However, few e-health programs have shown the desired effects on patient-relevant outcomes after implementation in practice. This may be due to the lack of successful implementation strategies and/or the inefficacy of the instruments (9,10). Previous research (11-16) concluded that personal factors (i.e., attitudes of intermediates and/or end-users) or organizational factors (i.e., strategy or organizational support) might be important determinants of the success of implementation trajectories. However, those determinants are mostly assessed during and/or after the implementation of an e-health intervention for evaluation purposes. This indicates the need for an implementation guideline for e-health interventions that can be used before the start of such interventions, in order to increase their effectiveness in practice.

The most well-known and frequently applied theoretical framework for implementing innovations in various disciplines (e.g., technology, public health, communications, economics, history, political science, and education) is the 'Diffusion of Innovations Theory' of Rogers (17), in which innovations often refer to new technologies (18). Even though this framework is widely applied, one of the main points of criticism is that it is difficult to measure the exact effect of a newly applied technology (19,20), especially in healthcare, which leads to inconsistent results. For that reason, previous studies (12,21) have suggested alternative instruments to assess the implementation of innovations or technologies in a systematic manner. The Measurement Instrument for Determinants of Innovations (MIDI) by Fleuren et al. (21,22) has shown to be a useable and generic diagnostic tool to assess the main determinants of successful implementation in healthcare and preventive care based on four domains (i.e., Innovation, Individual, Organization, and Social Political Context). Although the MIDI is a promising instrument to assess innovation in healthcare (22), factors that are crucial for e-health interventions such as finances (11,12,23), evidence-based medicine (12), and safety (11,12,23) are lacking. Those missing factors may explain the inconsistent findings regarding the effectiveness of its use in e-health interventions, and stress the importance of developing an explicit tool to guide e-health implementations (e.g., in order to increase their effectiveness) based on empirical and expert evidence.

To obtain the opinions of experts, a Delphi study has shown to be an effective methodology (24-27) to achieve consensus between expert groups on topics on which information is incomplete or unavailable (26,28). Different rounds of feedback are

organized in which international experts provide their knowledge and eventually reach consensus on the topic of attention. Useful characteristics (29) of Delphi studies include *(1)* experts respond to a specific topic in multiple feedback rounds, *(2)* a selection is made of the most useful form of communication (i.e., interview, (online) questionnaire, group decision support system), *(3)* a feedback mechanism is used, *(4)* experts with diverse backgrounds participate in the feedback rounds, *(5)* a step-by-step judgement is incorporated (i.e., insight into the other experts' feedback and the possibility to respond), and *(6)* the answers are statistically processed. Prior research (26,29) in various disciplines have already demonstrated the effectiveness and efficiency of developing (theoretical) models and/or instruments based on the results of Delphi studies, which may increase the likelihood of successfully implementing projects to support changes in healthcare.

In the present study a literature research and a Delphi study are performed with the overall objective to develop a guideline for the implementation of e-health interventions in practice. Such a newly developed guideline may support effective implementation of e-health interventions and, eventually, improve patients' outcomes and reduce healthcare costs.

Method

Study design

In the present prospective study, a literature research was performed followed by a two-round Delphi study by means of an international panel of experts from England and the Netherlands. The expert panel aimed to reach a consensus regarding the main determinants of success for implementing e-health interventions or applications in the successive Delphi rounds. Based on the consensus of the international experts, an e-health implementation guideline is developed in order to guide successful e-health implementations in healthcare. In the present study, the term 'successful e-health implementation' is used for the guideline to be developed, by which is meant that proven success factors are used for the guideline in order to increase the effectiveness of successful e-health implementations in practice.

Empirical research

Between June and July 2019 a literature research was performed to evaluate the main determinants for implementation assessed in prior research using the following data libraries: PubMed, Medline, and Google Scholar. To find potentially relevant literature, the following entry terms were used in the databases: ((implementation AND e-health) OR (implementation AND telemedicine) OR (implementation AND remote guidance) OR (implementation and screen care) NOT (early detection) NOT (early diagnosis) NOT (screening)). As indicated in **Figure 1,** this search strategy resulted in 721 potentially relevant literature sources. To select the most relevant literature on successful implementation

of e-health interventions, the titles and abstracts of these remaining publications were assessed by an independent researcher and, subsequently, a detailed assessment of the full texts was carried out, which resulted in 22 articles. Based on these articles, an overview of the main domains (i.e., Technology, Acceptance, Financing, Organizational, and Legislation & Policy) and corresponding determinants of successful e-health implementations was compiled in **Table 1**. The domains (n = 5) and determinants (n = 20) were used for the first round of the Delphi study and processed in an online questionnaire in order to rank the different domains and determinants.

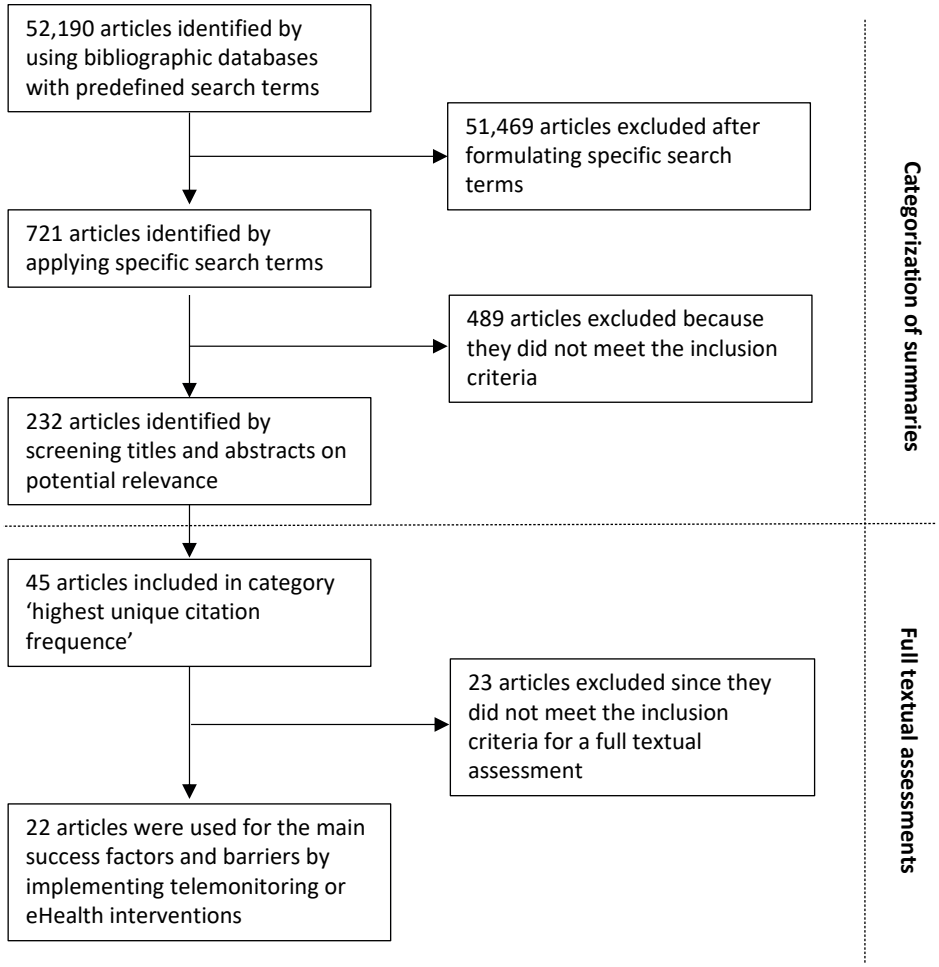

Figure 1. Results of the search strategy.

Table 1. Domains, determinants, and definitions based on the empirical research

Domain	Determinants	Definitions	References
technology	Support	User support during the use of the e-health program (i.e., installation and maintenance of the system, solving errors or problem situations).	Broens et al., 2007; Van Duijvendijk & Van den Akker, 2015
	Training	Training, at all levels, regarding the use of the e-health program (i.e., managers to interpret data, doctors to monitor vital signs, nurse to manage practical parts, patient to use the e-health program).	Boyne & Vrijhoef, 2013; Broens et al., 2007; De Vries et al., 2013
	Usability	Patients, doctors and supporting staff need to be familiar with the use and accessibility of the e-health program.	Boyne & Vrijhoef, 2013; Broens et al., 2007; Van Duijvendijk & van den Akker, 2015; Wood, Boulanger, & Padwal, 2017; De Vries et al., 2013; Asselbergs et al., 2016
	Quality	Quality of the internet connection and supporting infrastructure (i.e., equipment, data storage, and data backup).	Boyne & Vrijhoef, 2013; Broens et al., 2007; Brewster, Mountain, Wessels, Kelly & Hawley, 2014; Van Duijvendijk & van den Akker, 2015; Taylor et al., 2015; Wood, Boulanger, & Padwal, 2017
	Data Automatically	Automatic forwarding of information from the e-health program to the Electronic Medical Record (EMR).	Boyne & Vrijhoef, 2013; Asselbergs et al., 2016
	Modular Construction	Various modules can be selected based on the patients' situation, preferences, and needs.	Asselbergs et al., 2016
	View Data	Patients, nurses and/or doctors have access to the patients' information in the e-health program and can (if necessary) add additional information.	Asselbergs et al., 2016
	Setting Bandwidths	Setting bandwidths, or lower and upper limits, of physiological parameters such as blood pressure, weight, etc. per individual patient.	Asselbergs et al., 2016
	Open System	The ability of the e-health program to connect with devices (i.e., to assess physiological parameters) and to exchange data with primary, secondary, and tertiary care EMRs.	Boyne & Vrijhoef, 2013; Asselbergs et al., 2016
Acceptance	Attitude	The thoughts, opinions, and preferences of patients and/or healthcare providers regarding the e-health program.	Boyne & Vrijhoef, 2013; Broens et al., 2007; Brewster, Mountain, Wessels, Kelly & Hawley, 2014; Van Duijvendijk & van den Akker, 2015; Taylor et al., 2015
	Evidence-Based Medicine	The effectiveness of the e-health program is shown in order to convince healthcare providers and/or policy makers.	Broens et al., 2007
	Diffusion & Distribution	The presence of key users of the e-Health program to stimulate people to be involved and use the program.	Broens et al., 2007

Financing	Financing	The costs (e.g., of the e-health program and personnel costs) of using the e-health program.	Boyne & Vrijhoef, 2013; Broens et al., 2007; Wood, Boulanger, & Padwal, 2017
Organizational	Strategy	A (project) plan is made to apply the e-health program into the current organizational processes.	Boyne & Vrijhoef, 2013
	Organizational Support	Support for using the e-health program by both supporting staff, healthcare providers, and patients.	Boyne & Vrijhoef, 2013
	Available Resources	Sufficient resources to implement the e-health program (i.e., time, personnel, hardware).	Dohmen & Eijck, 2018
	Process Agreements	The presence of protocols and/or procedures to execute the e-health program (e.g., patient information or how to cope with warnings).	Boyne & Vrijhoef, 2013; Broens et al., 2007
	Organizational Change	The ability of the organization to provide changes in collaboration and (team) roles, rights and responsibilities.	Boyne & Vrijhoef, 2013; Broens et al., 2007
Legislation & Policy	Legislation & Policy	Complying with the current legislation and policy regarding e-health applications.	Broens et al., 2007
	Safety	The e-health program is safe for patients (e.g., physical safety and/or information transfer).	Boyne & Vrijhoef, 2013; Broens et al., 2007; Wood, Boulanger, & Padwal, 2017

Delphi study

The expert panel recruitment was performed by a literature search for key publications in the field of e-health implementation using PubMed, Medline, and Google Scholar as the main bibliographic databases. The corresponding authors of the key publications were contacted via email and were asked to indicate the leading experts in the field of e-health implementations. The criteria used for selecting the expert panel include 'demonstrable experience in e-health implementation in a leading position in a renowned practice or in a research position such as a professor or PhD position'. Eventually, a total of 16 of the suggested international experts met the inclusion criteria for the expert panel. They came from various fields , including healthcare, ICT & technology, and research. These 16 experts were contacted via email, of whom 13 (four had a professor degree, four a PhD degree, and five an MSc degree) agreed to participate (81.3%) in a two-round Delphi study.

In the present study, the preconditions of a Delphi study were used to generate the needed information in a structured manner. This entailed the following steps: conduct multiple feedback rounds, facilitate a communication platform for correspondence, use a feedback mechanism, pay attention to divergent interests and problem definitions, incorporate a step-by-step judgement, and perform statistical processing of the received answers (29). The expert panel received an email with a URL-link to an online questionnaire in which they were requested to score the 20 determinants for successful implementation of e-health interventions on a 10-point Likert scale (1 = not relevant at all; 10 = most

relevant). For all the determinants in the online questionnaire, a short explanation was provided to ensure the determinants were not likely to be misinterpreted.

First round

In July 2019, the 13 international experts who agreed to participate in the Delphi study received an email invitation to complete the online questionnaire. In the questionnaire, they were asked to score all determinants, with answer options ranging from '1 = not relevant at all' to '10 = most relevant'. In this first round, the expert panel was also asked to indicate if important determinants and/or literature references were missing with regard to assessing the implementation of e-health interventions. To monitor if all the experts had completed the online questionnaire, they were asked to enter their name in one of the questions. If a participant had not completed the questionnaire before August 2019, that participant received an email reminder. In total, 12 experts filled out the online questionnaire (response rate = 92.3%). Of the experts who completed the first round of the Delphi study, four had a professor degree, three a PhD degree, and five an MSc degree.

For the results of the first round, median and mean scores were calculated to assess the relevance of the determinants (see **Table 2**). To inform the expert panel of the scored relevance on the different determinants, the mean scores of the first Delphi round were added to all the items in the online questionnaire for the second round (i.e., divergent consensus). Furthermore, the important determinants that the expert panel indicated were missing in the first round were incorporated into the online questionnaire for the second round.

Second round

In October 2019, the 13 experts who originally agreed to participate in the Delphi study received an email invitation with a request to complete the online questionnaire for the second Delphi round. In this questionnaire, all the determinants of the first round were mentioned along with their mean scores and the additional determinants suggested by the expert panel. Similar to the first round, the experts scored the determinants on a 10-point Likert scale, ranging from '1 = not relevant at all' to '10 = most relevant'. If the questionnaire was not completed by November 2019, the expert received an email reminder. In total, 13 experts filled out the online questionnaire of the second round (response rate = 100%). Four of the experts who completed the online questionnaire had a professor degree, four a PhD degree, and five an MSc degree.

To assess the relevance of the individual determinants, in the second round the median and mean scores were calculated again. Subsequently, the interquartile range (IQR) score was assessed in order to calculate the agreement between the experts regarding the relevance of the determinants. Prior research (24,26,30) has found that the IQR in earlier Delphi studies was effectively able to assess the consensus between experts. In essence, the IQR is the difference between the 25^{th} and 75^{th} percentile. The smaller the IQR score,

the higher the degree of consensus between the experts in the panel. According to prior literature (26,31), an IQR of 2 or less combined with a mean score higher than 8 represents good consensus between experts using a 10-point Likert scale. Based on the results of the second round in the present study, determinants were indicated as relevant if the mean score was higher than 8 and the IQR was 2 or less, as this combination represents consensus between the experts (24,30,31). Determinants that met those criteria were used in the development of the instrument to guide implementation of e-health interventions. For the analyses in both the first and second Delphi rounds, SPSS 25.0 was used.

Results

First round

In **Table 2** the results of the first round, regarding median and mean scores, are shown. Usability (mean = 9.33), Support (mean = 9.25), Training (mean = 9.17), Process Agreements (mean = 9.17), Strategy (mean = 9.08), and Organizational Change (mean = 9.08) score highest on the mean scores, indicated by the expert panel (n = 12). The lowest scoring determinant in the first round is Evidence-Based Medicine, with a mean score of 6.75. Besides scoring the individual determinants, experts were also asked to suggest other important determinants. 'Evaluation' (i.e., review the effects and costs of the new e-health program and assess potential adjustments), 'Patient Characteristics' (i.e., identifying suitable patients or patient groups to participate in the e-health program based on predefined inclusion and exclusion criteria), 'Multidisciplinary Team' (i.e., involving multiple disciplines such as medicine, nursing sciences, psychology, ethics, computer sciences to increase the implementation success), and 'Upscaling' (i.e., the extent to which the e-health program can be scaled up to larger and/or other patient groups) were suggested as important determinants to take into account in the second round of the Delphi study.

Second round

The results of the second round are also presented in **Table 2**. In all but one of the 24 determinants scored by the expert panel consensus was obtained (mean score ≥ 8; IQR ≤ 2). For the determinant Evidence-Based Medicine, no consensus was reached (mean score < 8; IQR = 2). Based on the results regarding the five domains (i.e., Technology, Acceptance, Financing, Organizational, and Legislation & Policy) and 23 corresponding determinants a guideline for the implementation of e-health interventions has been developed (**Table 3**). In the **Supplementary file,** the full e-health implementation guideline to be used in practice is shown.

Table 2. Results of Round 1 & Round 2 of the Delphi study

		Round 1			Round 2			
Domain	**Determinants**	**N**	**Md**	**Mean**	**N**	**Md**	**Mean**	**Iqr**
technology	Support	12	9	9,25	13	10	9,31	1
	Training	12	9	9,17	13	9	9,07	1
	Usability	12	9,5	9,33	13	10	9,69	1
	Quality	12	8,5	8,67	13	9	8,08	1
	Data Automatically	12	9	8,92	13	9	8,85	2
	Modular Construction	12	8	8,00	13	9	8,62	1
	View Data	12	9	8,75	13	9	9,00	1
	Setting of Bandwidths	12	9,5	8,83	13	9	9,00	1
	Open System	12	9	8,83	13	9	9,00	2
	Evaluation*	-	-	-	13	9	8,62	1
Acceptance	Attitude	12	8	8,25	13	8	8,00	1
	Evidence Based Medicine	**12**	**7**	**6,75**	**13**	**7**	**6,77**	**2**
	Diffusion & Distribution	12	9	8,42	13	9	8,77	1
	Patient Characteristics*	-	-	-	13	9	7,85	2
Financing	Financing	12	8,5	8,33	13	9	8,69	1
Organizational	Strategy	12	9	9,08	13	9	8,85	2
	Organizational Support	12	9	8,92	13	9	8,77	2
	Available Resources	12	8	8,42	13	9	8,62	1
	Process Agreements	12	9	9,17	13	9	8,92	1
	Organizational Change	12	9,5	9,08	13	10	9,15	1
	Multidisciplinary Team*	-	-	-	13	9	8,54	1
	Upscaling*	-	-	-	13	9	8,85	1
Legislation & Policy	Legislation & Policy	12	8	8,08	13	8	8,38	1
	Safety	12	9	9,00	13	9	9,23	1

*New determinants addressed in the first Delphi round and assessed by the expert panel in the second Delphi round

Table 3. Domains and determinants of the e-health implementation guideline

Domain	**Determinant**	**Operationalization**	**Absent**	**Present**
technology	Support	Support is available for users both during and after implementation of the e-health intervention.		
	Training	Users are trained on the use of the e-health intervention.		
	Usability	Patients are familiar with the use of an e-health intervention. Supporting staff and/or doctors are able to operate the e-health intervention and have easy access to the system.		
	Quality	The internet connection and supporting infrastructure is of good quality.		
	Data Automatically	Information can be forwarded automatically from the e-health program to the Electronic Medical Record (EMR).		
	Modular Construction	Various modules can be selected based on the patients' situation, preferences, and needs.		
	View Data	Patients, nurses and/or doctors have access to the patients' information in the e-health program, and can (if necessary) add additional information.		

	Setting Bandwidths	It is possible to set bandwidths, or lower and upper limits, of physiological parameters such as blood pressure, weight, etc. per individual patient.
	Open System	The e-health program is able to connect with devices (i.e., to assess physiological parameters) and to exchange data with primary, secondary, and tertiary care EMRs.
	Evaluation	Effects and costs of the new e-health program are reviewed and potential adjustments can be assessed.
Acceptance	Attitude	Positive thoughts, opinions, and preferences of patients and/or healthcare providers regarding the e-health program.
	Diffusion & Distribution	The presence of key-users of the e-health program to stimulate people to be involved and use the program.
	Patient Characteristics	Suitable patients or patient groups are identified to participate in the e-health program based on predefined inclusion and exclusion criteria.
Finance	Financing	Available budget (e.g., of the e-health program and personnel costs) for using the e-health program.
Organizational	Strategy	A (project) plan is made to apply the e-health program in the current organizational processes.
	Organizational Support	Support for using the e-health program by both supporting staff, healthcare providers, and patients.
	Available Resources	Sufficient resources are available to implement the e-health program (i.e., time, personnel, hardware).
	Process Agreements	Protocols and/or procedures are present to execute the e-health program (e.g., patient information or how to cope with warnings).
	Organizational Change	The organization is able to provide changes in collaboration and (team) roles, rights and responsibilities.
	Multidisciplinairy Team	Multiple disciplines are involved, such as medicine, nursing sciences, psychology, ethics, and computer sciences, to increase the implementation success.
	Upscaling	The e-health program can be scaled up to larger and/or other patient groups.
Legislation & Policy	Legislation & Policy	Complying with the current legislation and policy regarding e-health applications.
	Safety	The e-health program is safe for patients (e.g., physical safety and/or information transfer).

Discussion

The present study aimed to develop a guideline for the implementation of e-health interventions, in order to increase their effectiveness, by means of a literature research and a two-round Delphi study. After the two-round Delphi study, consensus was reached on five domains and 23 corresponding determinants (mean scores ≥ 8; IQR ≤ 2). Concerning the determinant 'Evidence-Based Medicine', no consensus was reached by the experts (mean score < 8; IQR = 2). Based on the 23 determinants, a guideline for successful implementation of e-health interventions was developed.

In accordance with prior research (12), the experts reached a consensus on the domains Technology, Acceptance, Financing, Organizational, and Legislation & Policy. However, in other studies (21,22) different terminology was used for these domains (e.g., Innovation, Individual, Organization, and Socio-Political Environment), and in numerous prior studies (11,21,22) the domain Financing was absent. This may be explained by the fact that the purpose of these studies was to develop an instrument to assess the implementation process afterwards rather than a framework to guide the implementation of e-health interventions. In the present empirical research, the domains and determinants are mainly based on prior systematic reviews, which increases the likelihood that the most relevant domains and determinants were included. The experts' consensus in the Delphi study offers further support regarding the relevance of these domains and determinants. Nevertheless, additional determinants were suggested by the experts (e.g., Evaluation, Patient Characteristics, Multidisciplinary Team, and Upscaling) for guiding the implementation of e-health interventions in order to increase their effectiveness. Besides the determinants that were derived from the literature search, the determinants were also deemed relevant based on the consensus reached by the experts in the second round.

No consensus was reached regarding the determinant Evidence-Based Medicine. Already in the first round of the Delphi study the experts indicated this determinant was the least important, giving it the lowest mean score (mean score= 6.75). In prior research (17), it is concluded that information concerning the effectiveness of an innovation (e.g., relative advantage) is a crucial factor to convince end-users and intermediaries to implement new innovations. Although the determinant Evidence-Based Medicine is defined similarly in the current study, the experts considered it to be less relevant. Based on the quantitative results of the present research, the reason for this scoring cannot be determined; a qualitative research (i.e., face-to-face or focus group) would be necessary to assess the reason for this scoring.

Based on the results of the literature research and Delphi study, a guideline for the implementation of e-health programs was developed (see **Table 3**). To assess the presence or absence of determinants in the implementation guideline, a binary score is used which is known to be less complex and just as reliable as using a Likert scale (32). Furthermore, it may be that hierarchy between the items in the e-health implementation guideline is present and of influence. In this research, an IQR ≤ 2 represented consensus between the participating experts (24,30,31). Although a higher degree of consensus is illustrated by smaller values, it does not represent a higher degree of importance between specific determinants. In a study by Broens et al. (12), 'Acceptance' is mentioned as the most reported and assessed domain in prior research; however, it does not represent the most dominant domain in the field of e-health. Therefore, future research should assess the presented guideline for e-health interventions in prospective studies, in order to indicate the potential hierarchy of the presented domains and determinants.

In the present study, 20 determinants were selected by means of an extensive literature search. After the first feedback round by experts, four important determinants (i.e., Evaluation, Patient Characteristics, Multidisciplinary Team, and Upscaling) were added. However, in the second Delphi round, no consensus was reached for one determinant (i.e., Evidence-Based Medicine). This illustrates that, also for the participating experts, e-health implementations are complex and include a variety of variables to take into account. This complexity was also stressed by Stanimirović and Vintar (33) regarding national success factors in the development of e-health interventions (i.e., strong political commitment, support, and advocacy). Moreover, based on the inconsistent findings in prior systematic reviews (34,35) regarding e-health implementations in practice, it is stressed that extensive research is needed for effective implementation strategies. This may imply that the presented e-health implementation guideline is suitable for a qualitative assessment of the implementation strategy. For a quantitative assessment, the instrument needs to be validated and periodically recalibrated to increase the potential of improving e-health implementation strategies. Although further research is needed, the developed e-health implementation guideline contributes to the current knowledge because it provides a concrete checklist to guide e-health interventions or applications in practice using the main determinants of effective implementation. Use of the developed guideline is expected to increase the effectiveness of implementation of e-health interventions in practice.

Limitations

Despite the fact that the literature research and the Delphi study were executed in a structural manner, the development of the instrument to guide e-health interventions in practice may have been subject to methodological restrictions. First, only 13 of the 16 invited international experts (81.3%) participated in the Delphi study. For that reason, the consensus which was reached between the experts in the present Delphi study may not be completely representative for all experts in the field of e-health, since both the 'demand side' and 'supply side' of e-health interventions needs to be highlighted. Second, one might argue that the time interval between the first (July 2019) and second round (October 2019) was too long. Within a Delphi study, experts respond to questions and statements (26,29) in successive rounds with similar follow-up periods. However, it is expected that time intervals have had a minimal impact in Delphi research. Based on the mean values in the first and second round, as shown in **Table 2**, differences in mean scores between the two rounds are minimal, which indicates that the time interval had no or minimal influence on the results. A final limitation of the present study may be that the developed guideline to increase the effectiveness of e-health interventions in practice is based on empirical research and expert consensus by means of a Delphi study. The international validity, reliability, and practical applicability of the instrument needs to be assessed in future prospective studies (i.e., RCTs or cohort research).

Conclusion

In the present study an e-health implementation guideline is developed in order to increase the effectiveness of the selection and implementation of e-health interventions in daily practice. Although the presented instrument has a strong methodological basis, it is recommended to assess the validity, reliability, and applicability of the e-health implementation guideline in future prospective research.

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Chapter 9

Regional implementation of atrial fibrillation screening: benefits and pitfalls

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Abstract

Introduction:
Despite general awareness that screening for atrial fibrillation (AF) could reduce health hazards, large-scale implementation is lagging behind technological developments. As the successful implementation of a screening programme remains challenging, this study aims to identify facilitating and inhibiting factors from healthcare providers' perspectives.

Methods:
A mixed-methods approach was used to gather data among practice nurses in primary care in the southern region of the Netherlands to evaluate the implementation of an ongoing single-lead ECG-based AF screening programme. Potential facilitating and inhibiting factors were evaluated using online questionnaires (N= 74 / 75%) and 14 (out of 24) semi-structured in-depth interviews (58.3%). All analyses were performed using SPSS 26.0.

Results:
In total, 16,682 screenings were performed on an eligible population of 64,000 and 100 new AF cases were detected. Facilitating factors included 'receiving clear instructions' (mean ± SD; 4.12 ± 1.05), 'easy use of the ECG-based device' (4.58 ± 0.68) and 'patient satisfaction' (4.22 ± 0.65). Inhibiting factors were 'time availability' (3.20 ± 1.10), 'insufficient feedback to the practice nurse' (2.15 ± 0.89), 'absence of coordination' (54%), and the 'lack of fitting policy' (32%).

Conclusion:
Large-scale regional implementation of an AF screening programme in primary care resulted in a low participation of all eligible patients. Based on the perceived barriers by healthcare providers, future AF screening programmes should create preconditions to fit the intervention into daily routines, appointing an overall project lead and a GP as a coordinator within every GP practice.

Introduction

Prevalence rates of atrial fibrillation (AF) are sharply increasing due to the ageing population. In 2010, 8.8 million adults in the European Union were estimated to suffer from AF, and this number is expected to more than double by the year 2060 (1-3). Accordingly, clinical outcomes (e.g., stroke, systemic embolism and all-cause mortality) are extensive and healthcare costs will further increase in the upcoming years (4-7). In a recent multicentre randomised controlled trial called STROKESTOP, screening for atrial fibrillation showed a small net benefit compared with standard of care, indicating that screening is safe and beneficial in older populations (8). In contrast, a comparable randomised controlled trial in four centres in Denmark (LOOP-trial) showed no significant reduction in the risk of stroke or systemic arterial embolism (9). Whereas other studies found AF screening to detect undiagnosed patients (6), improve clinical outcomes and decrease overall costs (5, 6), the success of current atrial fibrillation (AF) screening programmes varies (10). For instance, previous AF screening programmes in the Netherlands have indicated that the diagnostic yield largely depends on the context of screening (8, 11-14). The D_2AF study has highlighted that the number of newly detected AF in cardiovascular risk management programmes does not substantially increase with the implementation of extensive screening methods (12). Moreover, the participation rate of eligible individuals is often substantially lower than intended (15).

With the growing number of technological solutions, AF screening is expected to be easier and more widely available in the near future (10). In recent years, devices such as mobile phones, wrist-worn wearables, and single-lead handheld ECG-based screening devices have been proven to accurately detect AF (5, 16-18), showing that technology is no longer a limiting factor in screening interventions. Despite rapid technological advances, studies on opportunistic AF screening in primary care and community screening are scarce (12, 19). Frequently used screening methods include systematic and opportunistic screening strategies. Opportunistic screening (20) mandates that a healthcare professional check explicitly for AF during routine consultations in the entire population, while systematic screening (20) is based on specific criteria such as age. Currently, it is unclear which AF screening strategy should be applied in clinical practice (21, 22). Moreover, clear guidance on large-scale implementation of technology-assisted AF screening programs is lacking. Whereas the European Heart Rhythm Association (EHRA) provided practical guidelines on using digital devices to detect and manage arrhythmias (18), advice on how to implement the most appropriate screening strategy was not provided. In prior research on the implementation of health interventions, various generic factors that can positively or negatively affect an implementation process were found such as the complexity and clarity of the intervention or innovation, user knowledge about the intervention, self-efficacy, and organisational elements such as staff turnover or financial resources and legislation (23). Screening interventions in other medical fields (e.g., cancer) revealed

inhibiting factors for implementation such as unfavourable attitudes from the healthcare provider and limited resources (24, 25). Specifically for AF screening programmes, more research is needed on implementation strategies to determine how to integrate optimal diagnostic methods in daily work routines (26).

This study aims to assess facilitating and inhibiting factors among healthcare providers directly involved in the screening process by evaluating the implementation of a large-scale opportunistic AF screening programme in a unique real-world primary care setting. In particular, we focused on the healthcare provider's perspective, as the healthcare professionals' opinion (e.g., knowledge, attitude and time) is critical to identify barriers and facilitators for implementation.

Methods

Population and design

In order to answer the research question, this study evaluates a large regional AF screening programme. To this end, a distinction is made between the participation in the screening programme and the evaluation of the screening programme. The screening programme refers to the AF screening programme, and the evaluation of the screening programme refers to the cross-sectional study with the healthcare providers (practice nurses).

Screening programme

A total of 85 GP practices (39.9% of the total GP practices in the southeast of the Netherlands with approximately 800,000 residents) received an ECG-based screening device. Inclusion criteria were, sufficient time for AF screening during the diabetes mellitus (DM) and cardiovascular risk management (CVRM) programmes, the willingness of the practice nurse to receive training and register data, and the willingness of GPs to take charge of the diagnostic process when necessary. In these practices, a total of 90,000 patients participated in the DM and CVRM programmes, with 1-4 visits per patient per year. Further instructions were to only include elderly patients (65 years and older) and exclude patients with AF. Practice nurses used an ECG-based screening device (MyDiagnostick) to assess high-risk cardiac patients from the DM and CVRM programmes for undiagnosed AF between August 2018 and December 2020. In a prior study, the MyDiagnostick showed a 100% sensitivity and a 96% specificity for detecting AF and was described as easy to use and suitable for opportunistic AF screening (27).

Evaluation of the implementation of the screening programme

The present study evaluates facilitating and inhibiting factors of implementing a screening intervention for AF patients in primary care using a mixed-methods approach consisting of online questionnaires and semi-structured in-depth interviews. Practice nurses who participated in the AF screening programme were approached to participate

in an online questionnaire and subsequently asked to participate in a telephone-based semi-structured in-depth interview.

Procedure

Training practice nurses

Prior to the screening programme, practice nurses received instructions from project coordinators who visited the GP practices. The instructions contained information on using the MyDiagnostick (e.g., registration process by sending e-mail and processing information). Subsequently, multiple training moments were planned to inform practice nurses, GPs and other stakeholders with detailed procedural instructions.

Screening routine

Practice nurses were instructed to ask patients to hold the ECG-based screening device for 60 seconds. If the device detected AF (i.e., displayed by a red light), a second reading was performed. If a second red light was displayed, validation with a 12-leads ECG was performed and assessed by a cardiologist. In addition, practice nurses determined the CHA_2DS_2-VASc and HAS-BLED risk score, kidney function and medication intake, supervised by the GP, based on the patient's medical record. This information was sent to the cardiologist for confirmation and policy regarding anticoagulation or referral to the hospital. In addition, the cardiologist provided advice on the anticoagulation policy and on further diagnostics and treatment, such as whether or not they should be referred to a cardiologist.

Evaluation of facilitators and barriers of the screening programme

A total of 98 practice nurses were invited, and all provided informed consent and approved of their answers being used for research purposes. Facilitators and inhibitors to implementing the ECG-based screening programme were evaluated by gathering data from practice nurses via online questionnaires and semi-structured in-depth interviews. Practice nurses were invited to participate in the online questionnaires in February 2021 via e-mail. The participating practice nurses received two reminders (biweekly) via e-mail to complete the online questionnaire before March 2021. Furthermore, in the final question of the questionnaire, practice nurses were asked whether they were willing to participate in a semi-structured in-depth interview. Practice nurses who agreed to participate received an invite in April 2021. The interviews were conducted within two weeks via phone and (voice) recorded for data analysis and subsequently anonymised.

Measurements

Online questionnaire

The online questionnaire is based on the validated Measurement Instrument for Determinants of Innovations (MIDI) (20). The questions were based on a 5-point Likert

scale (1: 'totally disagree' to 5: 'totally agree') and subdivided into four domains. The first domain, Innovation (Cronbach alpha = 0.77), referring to the ECG-based screening device, assessed seven different determinants (e.g., procedural clarity and correctness based on factual knowledge). Secondly, the User (Cronbach alpha = 0.78) refers to the practice nurse and contains ten determinants (e.g., personal benefits of the intervention and personal drawbacks). Thirdly, the Organisation (Cronbach alpha = 0.71) refers to the GP practice and contains 11 determinants (e.g., staff capacity, availability and feedback to the user). The last domain, consisting of only one question, was the Socio-political context which refers to compliance with the GP practice's legislation and regulations. In the present study, the MIDI was adapted to fit the purpose of the present study, which is common when using the MIDI (23, 28) (e.g., some questions have binary or three answer options). A full version of the online questionnaire is provided in Appendix 1.

Semi-structured in-depth interviews

The semi-structured in-depth interviews were also adapted from the MIDI questionnaire based on the online questionnaire responses. During the telephone interviews, practice nurses were asked to briefly describe how and by whom the ECG-based screening device was used in their GP practice and how many times a week. In addition, concerning the domain of Innovation, they were asked to indicate the advantages and disadvantages of using the ECG-based screening device. An example question for the domain User was 'Do you think that the ECG-based screening device fits well within the current guidelines and protocols for patients within the CVRM or DM consultation hours?'. For the domains Organisation and Socio-political context, practice nurses were asked whether they felt the GP practices supported the use of the ECG-based screening device and whether the AF screening programme fit well within their GP practices policy. For the complete list of the semi-structured in-depth interview questions, see Appendix 2.

Statistical analysis

The online questionnaire was analysed per domain using basic descriptive statistics (i.e., percentage, means and standard deviation) with IBM SPSS, version 26.0 (29). Mean and standard deviation was displayed for every determinant per domain (mean ± SD), using a scale from 1-5 with higher scores indicating higher satisfaction. In addition, questions phrased from negative to positive were recoded, and for the binary questions the percentage of 'yes' responses will be presented. Finally, the internal reliability of the determinants was assessed with Cronbach's alpha coefficient.

Audio recordings of the semi-structured in-depth interviews were analysed, summarised and stored by an independent researcher. The transcripts were coded deductively, and the researchers reached a consensus on the chosen broad themes (30). The insights obtained from the semi-structured in-depth interviews were used to support the interpretation of the quantitative data.

Results

From the approximated 64,000 patients participating in the DM and CVRM programmes who were eligible for AF screening, the ECG-based device was held 16,682 times between August 2018 and December 2020 and for 245 (1.5%) there was an indication of AF. After validation with a 12-leads ECG, AF was confirmed in 100 patients (0.6%). As detailed in the flowchart in **Figure 1**, 98 practice nurses were invited to complete the online questionnaire to evaluate the implementation of the screening programme. A total of 74 (76%) practice nurses completed the online questionnaire, and 24 practice nurses agreed to participate in a semi-structured in-depth interview; 15 completed the interviews (62.5%). Due to a corrupt audio recording 14 interviews were available for analysis.

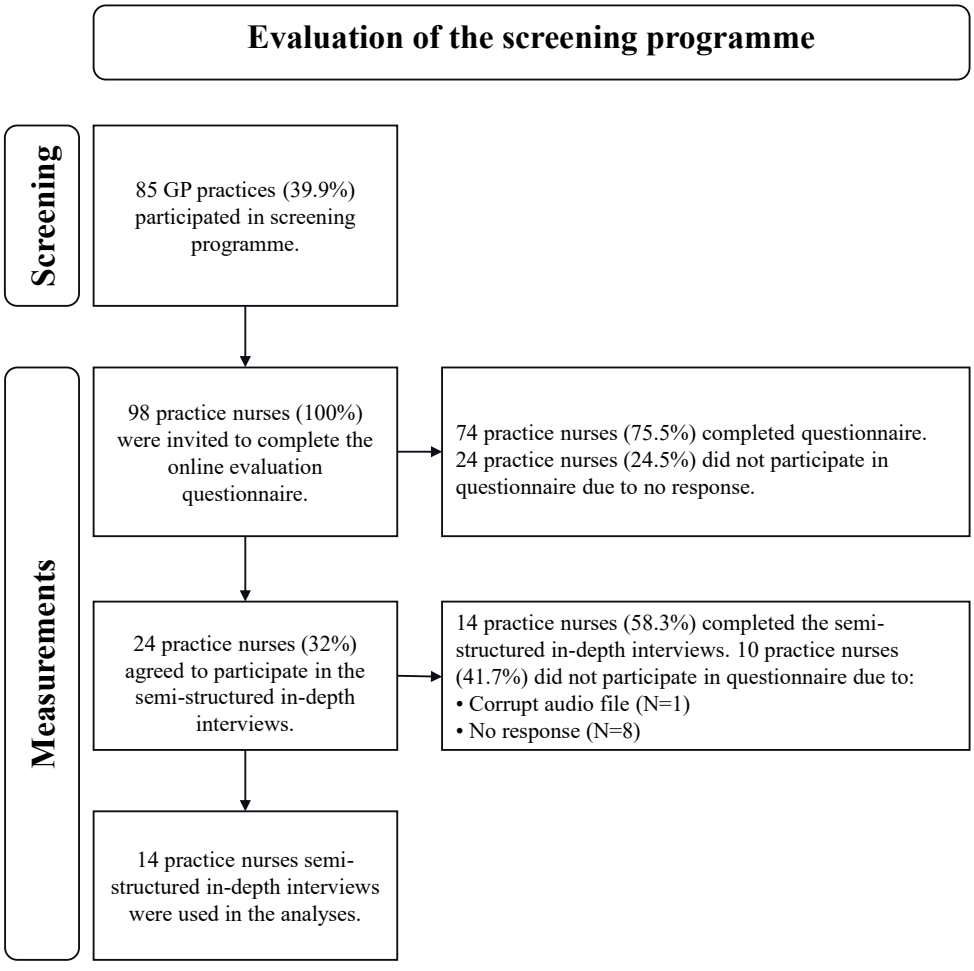

Figure 1. Flowchart detailing the GP practices and practice nurses that participated in the screening and the evaluation of the implementation of the screening.

Facilitators and barriers per domain

Innovation

The results of the questionnaires are displayed in **Table 1**. Regarding the domain innovation, practice nurses reported the instructions about the intervention to be clear (mean ± SD; 4.12 ± 1.05). Furthermore, all practice nurses in the semi-structured in-depth interviews (n = 14) reported an overall positive experience with the instructions. In addition, the practice nurses found the ECG-based screening device uncomplicated (4.58 ± 0.68) and relevant to patients (4.09 ± 0.85). However, the visibility of outcomes was rated lower (3.19 ± 1.12) due to the fact that no additional information is displayed on the device except a red or green light.

User

Highly rated determinants within the domain User were satisfaction (4.22 ± 0.65), patient cooperation (4.45 ± 0.58) and use and knowledge (4.28 ± 0.61). Yet, half of the practice nurses (44.6%) lacked colleagues who used the ECG-based screening device as intended. In addition, practice nurses reported personal drawbacks from using the ECG-based screening device during consultations (3.20 ± 1.10), such as time available to integrate the intervention into their daily work routine, which was confirmed in the interviews. In addition, the interviewees (n = 5) experienced difficulty with the time it took to register a patient (35.7%). For example, in the interviews, a practice nurse stated, 'The MyDiagnostick does not take more time than pulse palpating, but the procedure afterwards [Is time consuming]'.

Organisation and Socio-political context

In 27 (31.7%) GP practices, agreements about the use of the device were made in strategic plans, work plans or otherwise. In about half (45.8%) of the participating GP practices a coordinator was appointed for the use of the ECG-based screening device. The majority of the GP practices (57.6%) experienced difficulties during the screening due to changing circumstances such as cutbacks, staff changes or the simultaneous deployment of other innovations in their organisation. Furthermore, most practices (44,6%) had only one practice nurse trained in the ECG-based screening device, so there was no substitute available in their absence (2.70 ± 0.98), nor were there regular internal meetings about the intervention's progress. In addition, practice nurses were generally dissatisfied with the lack of feedback about the screening process (2.15 ± 0.89), which was confirmed in the semi-structured in-depth interviews by 35.7% of the interviewees (n = 5). Legislation and regulations were not perceived as an important barrier (3.76 ± 0.57).

Table 1. Means (M or %), standard deviations (SD) the online questionnaire per domain.

		N = 74	
No.	**Innovation**	**M**	**SD**
1.	Procedural clarity of the use of the ECG-based screening device	4.12	1.05
2.	Correctness based on factual knowledge	3.85	0.84
3.	Completeness of supplied information	4.03	0.95
4.	Complexity of use[a]	4.58	0.68
5.	Congruence with GP practice policy	3.91	0.92
6.	Visibility of outcomes	3.19	1.12
7.	Relevance for the patient	4.09	0.85
	User		
8A.	Personal benefit of using the ECG-based screening device	3.68	0.98
8B.	Personal drawbacks of using the ECG-based screening device[b]	3.20	1.10
9A.	Outcome expectation: Importance on possible detection of AF	3.68	1.04
9B.	Outcome expectation: Likelihood of possible detection of AF	3.73	0.67
10.	Job Perception	3.68	0.81
11.	Patient satisfaction of using the ECG-based screening device	4.22	0.65
12.	Client (Patients Cooperation in using ECG-based screening device)	4.45	0.58
13.	Social support (sufficient help from my colleagues)	4.08	0.64
14.	Descriptive norm[c]	1.86	0.87
15A.	Subjective norm: Normative beliefs (expectations from colleagues on the use of ECG-based screening device in the GP practice)	3.58	0.70
15B.	Subjective norm: Motivation to comply (caring about the opinion of others)	3.31	0.72
16.	Self-efficacy expectation about the ability to use the ECG-based screening device to possibly detect AF	3.81	0.84
17.	Sufficient knowledge about how to use the ECG-based screening device	4.28	0.61
18.	Awareness of content of innovation	3.65	0.58
	Organisation		
19.	Formal ratification by management[e]	32%	0.47
20.	Replacement when staff leave	2.70	0.98
21.	Staff capacity	3.55	0.94
22.	Financial resources	3.47	0.69
23.	Time available to explore the innovation	3.68	0.83
24.	Availability of material resources and facilities	3.93	0.69
25.	Coordinator[e]	46%	0.50
26.	Unrest in the organisation[e]	58%	0.50
27.	Information available about use of innovation	3.91	0.62
28.	Feedback to user about innovation process	2.15	0.89
	Socio-political context		
29.	Legislation and regulations	3.76	0.57

A higher mean score indicates that a healthcare professional perceives this determinant less as a barrier to implementing (ranging from 1 to 5).

a Determinant 4 is scored inversely for readability (low score is an indicator of high complexity).

b Determinant 8B is scored inversely for readability (low score is an indicator of little perceived disadvantage).

c Determinant 14 has 3 answer options: (1) Hardly any colleague; (2) Half; (3) Almost all colleagues.

d Determinant 18 has 4 answer options: (1) I do not know the MyDiagnostick; (2) I know the MyDiagnostick but have not received any instruction yet; (3) I know the MyDiagnostick and have read the instruction superficially; (4) I am familiar with the MyDiagnostick and have read the instruction completely and thoroughly.

e Determinant 19, 25 and 26 are yes/no questions. The percentage with the answer 'Yes' is displayed.

Discussion

Despite a well-organised screening programme and relatively high satisfaction, the number of people screened was low in this real-world study in a typical primary care environment. According to healthcare providers, factors, such as the usability of the ECG-based device, sufficient time to explore the intervention, receiving regular feedback, and a clear project leader, should be included in implementing such screening programmes.

According to the practice nurses, several inhibiting factors for implementation were related to the organisation of the GP practice. Firstly, the amount of time to explore the intervention during their workday was not sufficient to integrate the intervention into their daily work routines, which is, according to a prior study (31), essential for a successful screening programme. Secondly, similar to what was found in a prior study (32), there was no replacement in case of the absence of a practice nurse, which resulted in a significantly lower percentage of people screened than initially planned.

Other inhibiting factors reported include a lack of feedback regarding the screening programme and a lack of a clear project lead to report to or address for questions. A clear leader who coordinates the screening process prompts higher levels of engagement and successful implementation (5) and can motivate the practice nurses and GPs by using persuasive technologies, which are tools for motivating behaviour change such as competition, comparison, and cooperation (33). Another factor that inhibited the screening was that leadership in the GP practices was lacking. Most practice nurses indicated that they feel unsupported by the GP and rarely had staff meetings. Thus, the lack of leadership in the GP practice calls for the GP to take over the coordination of future screening programmes. In addition, practice nurses had different expectations due to the lack of information provided to them and lack of consequences in case they did not follow the intervention guidelines. The GP did not replace personnel in case of absence, which stagnated the intervention in case of absence. Future screening programmes should therefore adapt internal procedures in case of absent personnel.

Another factor that may have negatively influenced implementation is the users' expectation. In general, the expectation of the practice nurses about the amount of newfound AF did not match with the actual amount of detected AF, resulting in disappointment (cognitive dissonance). Practice nurses should have been better informed, as this could have minimised the gap between their expectations and reality, as suggested in a different study (34) on the expectation-confirmation model (ECM). The ECM is considered one of the notable theories that explain users' post-adoption behaviour. It is based on the expectation-confirmation theory, which reflects the academic validity of relationships among users' intention to repurchase, satisfaction, perceived performance, and expectations (34). Thus, the EMC should be incorporated in the implementation strategy. An additional strategy that may be applied to increase motivation levels, performance goals, and perceived abilities is the integration of motivational elements

such as peer competition within the GP practice (35). Findings from a prior study (20) indicated that motivation is an essential facilitator for successfully implementing a screening programme in primary care. The competition gives a sense of accomplishment, comparison allows for subtle and empowering peer pressure, and cooperation provides opportunities for mutual support, group encouragement, and reinforcement and offers opportunities to collaborate, make and interact with friends (33). However, as intrinsic motivation is not always self-evident, it is often necessary to receive encouragement from others (20). The GPs within each GP practice should have motivated the practice nurses (to increase the feeling of involvement). In addition, an essential element of motivating people to join and care about a project or intervention is to include them in the process and disclose and discuss a clear target goal with them (36). Throughout the screening programme, practice nurses indicated that they did not to understand or know the overall goal, did not prioritise the intervention and did not see the value of using the innovation over regular pulse palpation, which suggests a need for increasing their involvement (36). Therefore, it is advisable to include practice nurses in disclosing and discussing the intervention purpose.

Limitations

This study suffered from some limitations. First, this study may have been subject to selection bias since practice nurses who participated in the semi-structured in-depth interviews (N = 14) could be considered early adopters. Early adopters often have favourable perceptions of a new intervention (37). Additionally, the in-depth interviews may contain socially desirable answers due to participants' reluctance to criticise the intervention. However, this limitation is not expected to have a significant impact due to the anonymisation of the results. In fact, the anonymisation may even have resulted in a more negative attitude (38). Secondly, our study found that most GP practices had only one practice nurse trained. However, we did not have information on whether these practices had only one practice nurse available, or whether one nurse among multiple nurses was trained to use the single-lead ECG device. Resultingly, we could not distinguish the differences in facilitators and barriers between practices with only one and practices with multiple nurses. Thirdly, during the study, some of the screened patients visited the GP practice multiple times and were, therefore, screened for AF multiple times. As a result, we are not able to determine exactly how many patients were screened. Therefore, only the amount of times the ECG-based screening device was held can be confirmed. As the primary focus of this study was the evaluation of the implementation of the screening programme, we believe this will not have impacted the results. Finally, the time between the screening programme and the evaluation interviews was one year due to COVID-19 (patients were not allowed to come to the GP office), which could have caused participants to forget details when answering the online questionnaire (25).

Conclusion

Future screening programmes may be more successful if more time is provided for them during the workday and if the organisational policy is adapted to fit the intervention. Furthermore, implementation may benefit from appointing a clear project lead who can provide regular feedback about the screening programme, monitor the screening process and motivate the practice nurses and GPs. In addition, GP leadership in GP practices is essential to support practice nurses by having staff meetings, providing time to explore and implement the intervention and replacing absent personnel.

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Chapter 10

Epilogue

Epilogue

Many healthcare providers in the Netherlands, as well as in the rest of the Western world, are striving to improve outcomes and lower healthcare costs, to reduce healthcare quality variations and to keep healthcare accessible for everyone (1). Value Based Health Care (VBHC) is increasingly being used to achieve these goals by improving patient value, which is defined as outcomes that matter most to patients divided by costs of healthcare delivery (2). In VBHC, several principles have been defined to improve appropriate treatment and coordinate care more effectively, including measuring and improving outcomes while reducing costs, and integrating care(3). However, insights on how to implement these principles in practice are lacking.

Part 1 of this dissertation reveals that implementing VBHC principles in the full cycle of care for cardiac patients is feasible in a multi-provider network by using the Netherlands Heart Network (NHN) as a unique and leading example in the Netherlands (4). The NHN methodology provides valuable insights into barriers and facilitators for continuous process optimization and improvement of outcomes that matter most to patients with atrial fibrillation (AF). The NHN received the prestigious international VBHC prize in 2018 from Prof. Dr. M.E. Porter, and the Dutch association for cardiology (NVVC Connect) has proclaimed the NHN to be the best practice for cardiac network care in the Netherlands.

In **part 2**, the first results of the AF NET study are presented. They show that the quality of AF care can be improved in smaller and non-academic hospitals when collaboration between hospitals is reinforced by uniform standards, nurse-led outpatient AF clinics, and education of AF patients. Besides the use of outcomes like quality of life (QoL) to evaluate patient value, part 2 emphasizes that QoL can also be used as a prognostic indicator of the expected disease course. In fact, AF patients with a lower QoL at diagnosis more often develop major adverse cardiovascular events (MACE), more often improve on their symptoms, and incur higher healthcare costs compared to AF patients with a higher QoL.

The integration of e-health into future healthcare systems improves patient value even further (5). To increase the likelihood of successful implementations of e-health interventions in care networks, we developed an e-health implementation guideline, which is presented in **part 3**. In addition, we evaluated the process of implementation of a large-scale screening program for AF. Despite general awareness that large-scale screening for AF is technically possible and could reduce health hazards, implementation of such screening programs lags behind these technological developments (6,7). To close this gap and to make future AF screening programs more successful, barriers and facilitators experienced by healthcare providers are presented.

In this final chapter, a reflection on the main findings and the strengths and limitations of the research, are presented. Implications of these findings for practice, regional and national partnerships and future research will be discussed.

Part 1. Development and organization of an AF network according to VBHC principles

Although an integrated chronic care model (ICCM) for AF and the implementation of VBHC principles in daily practice are advised by the European Society of Cardiology (ESC) to enhance appropriate treatment and to coordinate care delivery more effectively (8), practical guidelines on large-scale implementation of ICCM are currently not available. This part of the dissertation focuses on what is needed to build a multi-provider network in the full cycle of care for cardiac patients. It therefore addresses the first research question:

Is it feasible to put VBHC principles into practice for AF patients in a multi-provider network?

In **chapter 2** the first research question is addressed by describing the development and organization of the NHN initiative. The initial focus was on measuring outcomes and integrating care delivery across separate facilities, elements two and four of the Value Agenda, respectively (9,10). To stimulate the integration of care, connectedness between healthcare providers is crucial (3). This was a major challenge since healthcare is organized in silos. Due to the introduction of competition in healthcare, mutual appreciation and connectedness among healthcare professionals in the Southeast Brabant region was low at the onset of the NHN initiative, as in other regions in the Netherlands. To improve provider connectedness – described by Price et al. 2013 (11) as the sense of knowing and trust between providers who share care of a patient – good communication patterns used to support continuity across the circle of care are essential. Previous projects, in which attention was primarily paid to financial triggers, had failed (i.e., Slimmer met Zorg). Provided care and cure for patients were considered adequate; however, physicians lacked structural insights into the outcomes that matter most to patients, and quality systems were only organized on institutional levels. For these reasons, the NHN started as a doctor-driven initiative that aimed at generating more in-depth insights for physicians. This primary focus on improving outcomes, and not on healthcare costs, created companionship and trust between healthcare providers and strongly motivated them to make the NHN initiative successful.

The healthcare providers realized that they needed a regional quality system for continuous outcome improvement. To accomplish this, the NHN developed a practical stepwise methodology, to implement and continuously increase patient value in the full cycle of care (primary, second-line and third-line care). In this phase, directors of the involved healthcare organizations were informed but had no formal role in the NHN. The NHN started on a small scale with one cardiac condition (AF), presented in **chapter 3**, incorporating Porters' VBHC principles for moving to a high-value healthcare delivery system and Wagner's key principles of creating an integrated chronic care model (ICCM) (10,12,13). Conditions that potentially result in improved healthcare quality in the total care delivery value chain (i.e., transmural agreements, registration of main patient-relevant outcomes, adherence to guidelines, following a PDSA cycle) are included in the presented

stepwise methodology (14). The results presented in this dissertation, obtained using the NHN's stepwise methodology for AF, demonstrate that it is feasible to implement VBHC principles in a real-world network organization. Subsequently, the NHN included three other prevalent medical conditions (i.e., coronary disease, hearth failure and aortic valve disease), taking previous experiences into account. The annual PDSA cycle for all four cardiac conditions mentioned above makes it possible to evaluate improvement projects on patient-relevant outcomes and changes in healthcare costs (15). Previous studies have already shown that the application of a PDSA cycle management model in nursing quality management can greatly improve nursing quality and patient satisfaction (16). The PDSA cycle method has, for example, also proven its worth in the treatment of patients in the intensive care unit and in the treatment of patients with an acute myocardial infarction by means of percutaneous coronary intervention (17,18). However, PDSA is not a 'set-it-and-forget-it' proposition. Team members often need coaching and must experience some small wins before they trust the reward is worth the effort. It is a continuous, often repeated process that requires commitment and acceptance from the top down. Effective leadership can help overcome these challenges by providing feedback, listening to team members' concerns, and recognizing every success, no matter how small. Future research should focus on identifying barriers and facilitators besides effective leadership for implementing and maintaining an effective PDSA cycle in a multidisciplinary network of healthcare providers (19).

Part 2. Real life data from this AF network

The second part of this dissertation describes the evaluation of the AF network and addresses the second research question:

How can real-life data from such an AF network create relevant insights for improving patient value?

The preliminary prospective data from the AF-NET study (**chapter 4**) show that the joint implementation of the regional care standard for the outpatient AF clinic was associated with significant improvements in European Heart Rhythm Association (EHRA) score, hypertension treatment, and the percentage of persistent AF patients (4). Furthermore, high registration completeness of patient-relevant outcomes and high adherence to prevailing guidelines (i.e., process and structure indicators) were observed. These findings are in accordance with the results presented in a study by Hendriks et al. 2012 (20) in which adherence to guidelines, by introducing a protocol-driven outpatient AF clinic, resulted in improved patient-relevant outcomes and reduced healthcare costs. The preliminary data of the AF-NET study indicate that the findings are in line with prior research, and add that outpatient AF clinics in collaborating general hospitals may be as effective as those in academic settings. This is an important finding, as most AF care in the Netherlands is provided in 98 general hospitals and a much smaller proportion in 8 academic hospitals.

Besides a positive trend of the outcome measures, the high registration density can result in better decision-making support for medical specialists. This underlines the notion that outpatient AF clinics employed by AF-nurses is both an effective as well as an applicable setting in non-academic hospitals (4).

Another insight derived from part 2 of this dissertation is that QoL, commonly used as an outcome in patient value, can also be used as a prognostic indicator for patient value in AF patients. Patients with a lower QoL at diagnosis more often develop MACE, are more often hospitalized, and more often improve on their symptoms, compared to AF patients with a higher QoL (**chapter 5**). We also focused on identifying subgroups. As age is a prominent factor in both the experienced symptoms at the onset of AF and the disease course, we first studied which age group experienced the most improvement in EHRA score at 12 months of follow-up. In analyses stratified by age categories, patients above the age of 65 and below the age of 75 with lower QoL at baseline were most likely to improve their EHRA score between baseline and 12 months of follow-up (**chapter 6**) (21). This highlights the importance of accounting for both the patients' perception of their general state of health and patient characteristics, such as age, at the moment of diagnosis to predict symptom improvement in the year post-diagnosis. Future research should focus on other patient characteristics, such as gender or other CHA_2DS_2-VASc risk factors (Congestive heart failure, Hypertension, Age ≥ 75 years (doubled), Diabetes mellitus, Stroke (doubled), Vascular disease, Age 65 to 74 Years, and Sex category) besides age. To our knowledge, no studies have been published regarding the association between QoL at diagnosis and the subsequent development of major adverse cardiovascular events (MACE) during follow-up in a broad spectrum of AF patients. Hospitalization was not included in our definition of MACE. In line with findings from this dissertation, Schron et al. 2014 (22) also reported that patients' QoL is a predictor for hospitalization (23). The use of QoL as a prognostic indicator for patient value in AF patients may also be valuable in managing healthcare costs.

Whereas treatment decisions in AF patients are typically made based on symptoms in combination with the expected benefits and risks for the patient, physicians may benefit from more resources, like QoL, to help them decide on a course of action (24,25). Focus groups within the RATE-AF trial (26) have already indicated that improvement of QoL, ahead of mortality and hospitalizations, is of paramount importance for AF patients, while patients perceive that healthcare professionals tend to base their decisions on other factors which are more important to them (27). Therefore, our findings could help with shifting the focus from symptoms and treatment options to a more patient-centered perspective in clinical care and contribute to shared-decision making in the treatment of AF. Disease course prediction, by defining traditional risk groups or by artificial intelligence incorporating both traditional patient characteristics and symptoms, may help professionals make well-informed decisions on the preferred treatment regimens,

identify areas of improvement, and avoid treatment that is unlikely to benefit the individual patient (28). This will lead to more patient-specific care pathways.

Besides outcomes like QoL, patient reported experience measures (PREMs) are often used to indicate elements for quality improvement. PREMs have gained international recognition as an indicator of healthcare quality. This is largely because they enable patients to comprehensively reflect on the interpersonal aspects of their care experience. PREMs can also be utilized as a common measure for public reporting and benchmarking of institutions/centers and healthcare plans. Moreover, they can provide patient-level information that is useful in driving service quality improvement strategies. While there is clear merit behind the use of PREMs in healthcare quality assessments, some doubt remains about their use. Manary et al. 2015 (29) identified three main limitations. First, patient-reported experience is largely seen as congruent with terms such as "patient satisfaction" and "patient expectation," which are both subjective terms that may reflect judgements of health adequacy and not quality. Second, PREMs can be confused by factors not directly related to the quality of health care perceived by the patient, such as health outcomes. Finally, PREMs may reflect the preconceived healthcare "ideals" of patient's expectations and not their actual care experience. These limitations are indicative of a blurring of concept boundaries and inappropriate interchanging of concepts. Moreover, in AF care it is not well established whether AF patients' experiences fully represent the quality of care provided by health professionals. In **chapter 7** the Consumer Quality Index (CQI) is used to assess the patient's experiences concerning the quality of AF care. The results presented in this dissertation show an inconsistent correlation between PREMs of AF patients and improvements of AF patients' relevant outcomes. In accordance with previous research, we observed a significant correlation between the information provided by and the communication with the doctor or other healthcare providers (i.e., AF nurse) at baseline and the patient's health outcomes (30,31). As reported by Stewart, providing patients with more in-depth and tailored information is likely to result in improved healthcare outcomes for patients (32). However, our results show converse associations between communication by the doctor and information by AF nurses after three and six months of follow-up. Manary et al. 2015 (33) also found that when focused on a specific hospital visit PREMs are consistently correlated with accepted outcome measures, such as mortality and readmissions rates. In contrast, the use of PREMS in healthcare trajectories tends to produce null to opposite results. These findings are consistent with our findings. One reason may be that healthcare trajectories tend to assess all care provided over a longer period of time, leaving patients to determine which interactions should play a role in evaluations. Based on previous findings and our results, showing that experience measures are strongly related to patients' first impression and do not hold over time, it may be suggested that clinical outcome monitoring is currently a more valid and reliable representation of healthcare quality over time (34).

Part 3. Successful e-health implementation in AF care

The application of VBHC and a PDSA cycle in the NHN methodology for continuous improvement of outcomes has been shown to be a promising strategy. However, to gain even more depth in this, it is important to investigate how the care process can be further optimized, considering the patient's perspective. As the integration of e-health into future healthcare systems can improve patient value even further, it is crucial that e-health interventions are implemented successfully in cardiac networks (3). This part of the dissertation focuses on the third research question:

What conditions in AF care are needed for the successful implementation of e-health interventions in such a network?

The implementation of e-health into traditional healthcare often requires complex organizational and behavioral changes for both healthcare professionals and patients and thereby has a major impact on healthcare organizations (35,36). At present few e-health programs have shown the desired effects on patient-relevant outcomes after implementation in practice (35). This may be due to the lack of successful implementation strategies and/or the inefficacy of the instruments (37,38). With different definitions of e-health available in literature and unclear barriers and facilitators in e-health implementation, there is a need for further research on how to successfully implement e-health into healthcare. In **chapter 8** a unique e-health implementation guideline is presented that provides a concrete checklist to guide e-health interventions (39). This guideline was based on a literature review followed by a two-round Delphi study by an international panel of experts to identify key determinants in a total of five domains (technology, acceptance, financing, organizational, legislation and policy), promoting e-health implementation (40,41). In contrast with previous studies, which have developed an instrument to assess the implementation process after the implementation (42–45), we developed a framework to guide the implementation of an e-health intervention from the start, to increase the likelihood of a successful implementation. As outlined by Verweij et al. 2022 (52), a next step could be to further develop this generic guideline by differentiating between simple forms of e-health and more advanced multi-component innovations. Prospective research is needed to demonstrate that the presented guideline leads to better implementation results.

e-Health offers many opportunities, but there are certainly challenges. In the literature there is an overall awareness that AF is a disease with a high medical and societal impact, and there is a need for technology-assisted AF screening (46). In contrast to other healthcare promotion efforts, risk-based AF screening programs at a comprehensive national healthcare level do not currently exist in any of the European countries nor in the US (46). Although opportunistic screening for AF is recommended by the ESC, clear guidance on large-scale implementation of technology-assisted AF screening programs is lacking (47). Whereas the European Heart Rhythm Association (EHRA) provided practical

guidelines on using digital devices to detect and manage arrhythmias, advice on how to implement the most appropriate screening strategy was not provided (48). With the growing number of technological solutions, AF screening is expected to be easier and more widely available in the near future (49). In **chapter 9** we try to close the gap between guideline recommendations and implementation of AF screening in practice by determining the facilitating and inhibiting factors experienced by healthcare providers directly involved in a large-scale opportunistic AF screening program in a unique real-world primary care setting. In particular, we focused on the healthcare provider's perspective, as the healthcare professionals' opinion (e.g., knowledge, attitude, and time) is critical to identify barriers and facilitators for implementation. Incorporating what was previously assumed, we have now demonstrated for the first time in a transmural real-life setting that future screening programs may be more successful if more time is provided for the screening during the workday and that the organizational policy should be adapted to fit the intervention (50,51). Furthermore, the implementation may benefit from appointing a clear project lead who can provide regular feedback about the screening program, monitor the screening process, and motivate the practice nurses and general practitioners (GPs). In addition, GP leadership in GP practices is essential to support practice nurses by having staff meetings, providing time to explore and implement the intervention and replacing absent personnel. These factors should also be incorporated into the presented e-health implementation guideline (39).

Unfortunately, we were unable to use the guideline in the screening program for AF because this program was an ongoing screening and not a pre-designed trial. Furthermore, the development of the implementation guideline and the evaluation of the implementation of the AF screening were both conducted simultaneously. Our results are in line with the recently published systematic literature review of Tossaint-Schoenmakers et al. (35). The above-mentioned findings clearly demonstrate the importance of collaboration in innovation with all stakeholders from the very beginning. We need to be vigilant regarding the many pitfalls if we want to implement new technology on a large scale. Within the NHN, lessons are learned from previous implementations and taken into account in new projects. Our results will be applied to a new and larger trajectory, Check@ Home, which aims to screen 40,000 people for both AF and hearth failure (HF) in the NHN region. This should ultimately lead to a national screening program for both diseases. In this way, a significant impact can be made nationwide on both outcomes and healthcare costs.

Strengths and Limitations

This dissertation has several strengths. **First**, physicians in the NHN have taken the lead in developing a unique value-driven ICCM for AF. This is of great importance as physicians have the knowledge to combine outcomes from real-world data with clinical insights, which can lead to process optimalisation and improvement of outcomes. Using real-

world data and applying a PDSA cycle has created a continuous improvement cycle that potentially generates infinite improvement in patient outcomes and provides more care per euro spent. A **second** strength is that the NHN methodology presented in this dissertation encourages patient-centeredness and creates a continuum of care by breaking down the silos in current healthcare and fostering the connection between healthcare professionals. **Third**, this dissertation is unique because it describes for the first time the development, implementation and the evaluation of a value-driven AF ICCM for cardiac patients, involving the full circle of care. This was done in a region of +/- 800,000 inhabitants, not only at the care process level, but also through cross-sectional innovations. A **fourth** strength of this dissertation is that the NHN's stepwise methodology for creating a ICCM for cardiac patients is independent of the healthcare system and/or medical condition and is described from start to the current situation in detail, which makes it easy for other initiatives to use. As a result, the presented methodology in this dissertation can have an impact on patient value in other diseases unrelated to cardiology. A **fifth** strength of the dissertation is that, in addition to clinical outcomes (hospitalizations, mortality, MACE, etc.), patient experience measures such as QoL and CQI have also been included. As a result, this dissertation goes beyond the impact on clinical outcomes and includes the patient's perspective, which is a crucial element for diagnosing and treating patients correctly. A **final** strength of this dissertation is that the presented e-health implementation guideline and evaluation of barriers and facilitators for e-health interventions can be used to increase the effectiveness of implementation of e-health interventions in practice, which is of great importance for large-scale implementation of e-health within and beyond cardiology in the future.

This dissertation also had some limitations. **First**, although the first results of the implementation of the NHN methodology in AF patients are positive, the real impact on patient value has yet to be demonstrated. For example, cost data are still missing and results in other diagnosis groups are still being evaluated. **Secondly**, it remains to be demonstrated whether and how the PDSA cycles for impactful innovations function. For example, some innovation projects have been started, such as setting op telemonitoring for heart failure patients or more effective medical cardioversions for AF patients, but the PDSA cycles have not yet been completed. **Thirdly,** data used in this dissertation are mainly secondary care and tertiary care data. A link has recently been made between the primary, secondary and tertiary data via the Netherlands Heart Registration (NHR), making Southeast Brabant, the region where the NHN is active, the first region in the Netherlands to provide cardiac data to the NHR for the full care cycle. A **final** limitation is that, although the use of QoL to predict the cardiovascular disease course is unique, the data presented in this dissertation underlining this finding are still limited. As hospitals and GP's computer systems are not connected to the NHR, data is still supplied manually, not automatically.

This delivery process has been optimized, resulting in additional datasets that can be used to strengthen the conclusions found.

Future perspectives for research

First, for the further development of the presented physician-driven and patient-centered multi-provider regional ICCM for AF patients, more research is needed to gain insight into the impact of the presented methodology on patient value. Future studies could investigate in a controlled setting which process elements generate differences in outcome. At present, approximately 30% of the NHR AF data database was provided by the NHN. By comparing retro- and prospective datasets, many insights can be generated. At present it is not possible to benchmark these data with other regions because in other regions data collection is limited or has not yet started. Benchmarking different regions is, however, crucial in this perspective, as it creates the opportunity to share information and improve patient value even further by developing predictive models and comparative effectiveness research using real-life data. For example, a region with standard care can be compared with a region in which the NHN methodology is applied. A precondition is, however, that each region measures the same outcomes, in order to avoid misinterpretations of trend effects. Because the Federation of Medical Specialists (FMS) and the Dutch Society of Cardiology (NVVC) want to embed VBHC in cardiovascular care in the Netherlands, data registration will also have to be introduced in other regions. Currently NHN data are being benchmarked with the remaining NHR data; the results of these studies are expected in the near future. **Second**, outcomes are most relevant for patients and highly interesting for healthcare providers. However, to calculate patient value, costs should be linked one-on-one with outcomes. Due to current legislation, it is still very complex to link costs to outcomes and it is a challenge for future research to develop workable routes. A possibility could be to link outcomes to Dutch Hospital Data (DHD). DHD collects, manages, and processes data from hospitals and university medical centers. Another option is to link outcomes to health insurance data (Vektis data), or to link outcomes to healthcare consumption data from the relevant healthcare institutions. **Third**, the predictive value of QoL at diagnosis needs further validation in future large-scale studies. Validation of these results will enable future research to further define patient subgroups for which symptom improvements or other cardiovascular outcomes can be predicted using patient-reported outcome measures like QoL. For future research it may be interesting to merge large existing registries to develop predictive models with sufficient statistical power in different subgroups. These models could prospectively be compared with treatment/monitoring/education strategies tailored to specific characteristics such QoL and age. **Fourth**, future research is required to determine the effectiveness of the implementation guideline for the implementation of new e-health interventions and to discover the validity of this implementation guideline in different disease trajectories. The guideline needs to be validated and periodically recalibrated to increase the potential

to improve e-health implementation strategies. Lessons learned, such as the determined facilitating and inhibiting factors experienced by healthcare providers directly involved in a screening process, should be incorporated into the guideline. **Finally**, due to the continuous increase in the care that the GP's must provide and the higher expectations that patients have of the care provided, successful innovations in general practitioner care are necessary to be able to continue to provide care in the future. It should be investigated whether the determined facilitating and inhibiting factors experienced by healthcare providers can be used to support practice-wide motivation/engagement to implement various programs and innovations in general practice.

Future perspectives for practice

The main findings presented in the previous sections have several important implications for practice. **First**, the results of the presented regional ICCM for AF patients are promising. However, to gain more insight into causality, it is important to benchmark with other regions in the Netherlands or with all of the Netherlands. A first national registry of patients with recently diagnosed AF, Dutch-AF, was started in 2018, in close collaboration with Dutch hospitals, thrombosis services and general practitioners. A major concern is, however, that only a few regions in the Netherlands have started with registering patient outcomes and providing transparency via the NHR. To empower benchmarking between regions, the introduction of ICCM for AF patients should be taken to a national level. Medical professional associations, including the Dutch Society of Cardiology (NVVC), will have to convince and facilitate their members to register the most important national data sets. In this manner, the NHN's methodology can be evaluated properly, and successful elements can be expanded to other regions and to other medical conditions, making it possible to work towards a quality system at the national level. **Second**, developing other organizational structures can lead to more optimal exchange of data and knowledge. One of the main purposes of developing a ICCM is creating a continuum of care without fragmentation between primary, secondary, and tertiary care. Currently the vast majority of cardiac patients referred back to primary care for regular CVRM check-ups are treated by practice nurses. These practice nurses are supervised by GPs and most of them are not specialized in cardiology. Changing this organizational structure, either by having cardiologists supervise practice nurses or having specialized cardiology nurses, could improve cardiac care in primary care. Future research should focus on examining whether this new organizational structure leads to enhanced patient value. **Third**, widespread adoption of technology-enabled care and emerging technologies is expected to transform healthcare. A digital data infrastructure is the foundation for developing new digital technologies and creating the connected health ecosystem of tomorrow. The NHN is developing a digital data infrastructure, starting with a digital healthcare platform for remote patient monitoring which will be implemented in the NHN region next year. The presented e-health implementation guideline and the facilitating and inhibiting

factors experienced by healthcare providers directly involved in a screening process will be applied in the implementation process. Lessons learned can also be used in other trajectories such as the nationwide implementation of Check@Home. **Fourth**, currently, transparency and/or quality improvements can lead to financial losses for healthcare institutions, GPs, and/or cardiologists. Therefore, a radical change of course is needed. Transparency, improvement of outcomes and diminishing costs should be rewarded. Within the NHN, first steps have been taken in the form of a shared agreement regarding the implementation of innovations. Part of this agreement contains the sustainability of the project organization of the NHN. Moreover, the health insurance companies have agreed to compensate healthcare institutions if implementing impactful innovations results in financial losses. However, for the future, fundamentally different choices must be made to arrange sustainable funding for network organizations that are valuable to patients. Although it is not yet clear how this can be organized within a network approach, a multi-provider investment seems to be a precondition. Future research should elaborate on whether this approach indeed leads to a better model that results in higher outcomes and lower costs. **Finally**, healthcare providers in the Netherlands are currently financed individually and paid for volume of healthcare delivery. Introducing bundled payment models might encourage the current collaboration and facilitate the shift from a 'volume focus' towards a 'value focus'. The design of outcome-based bundled payment models needs to be further developed. The aim of these models is to increase quality and care coordination at a lower cost. According to Porter, these bundles should 1) cover all care for the treatment of a medical condition, 2) include care guarantees that hold the provider responsible for avoidable complications, 3) measure good condition-specific outcomes, 4) have a defined patient population and/or adjusted for risk, 5) have clearly defined responsibilities, and 6) have a price that leaves a reasonable margin for healthcare providers that deliver efficient and effective care (3). The shift from 'volume focus' towards a 'value focus' requires a system change from fragmented care towards integrated care, but maybe even more important is the change to the joint responsibility of care providers, health insurers, government, and industry. One of the first steps for a successful transition to a 'value focus' should be to establish more trust between these parties.

Future perspectives on regional and national partnership

The NHN's vision is that optimal patient value can be achieved if all relevant healthcare providers in primary, secondary and tertiary cardiac care join forces, prioritize improving patient value as their shared goal, and use data from daily practice to continuously measure and improve the added value of healthcare delivery. This vision can be realized through good cooperation between healthcare professionals and their institutions, but because of NHN's unique collaboration with Eindhoven University of Technology (TU/e) and Eindhoven MedTech Innovation Center (e/MTIC) unprecedented opportunities are created precisely at the intersection of network care, measurement of outcomes/costs,

PDSA optimalisation and implementation of new techniques. The NHN and e/MTIC complement each other in their shared mission: to drive VBHC by growing an ecosystem that creates a fast track in research, development, and implementation of sustainable innovations in clinical practice by strengthening the institutionalized collaboration between regional partners focusing on research and innovation in pre-defined clinical domains. The NHN's collaboration with TU/e and e/MTIC ensures unique ingredients that are lacking in other regions and fits perfectly into the Dutch CardioVascular Alliance (DCVA) agenda. The ecosystem created by this collaboration can help the DCVA to realize their ambition to lower the cardiovascular disease burden by 25% by 2030 in the Southeast Brabant and North Limburg regions. First trajectories like Check@Home have already started. By stimulating integrated care and introducing VBHC via the NHN methodology in the rest of the Netherlands, the DCVA creates a starting position that makes it possible to realize their ambition throughout the Netherlands in the short time they have set for themselves.

General conclusions

The findings of this dissertation indicate that it is feasible to put VBHC principles into practice for AF patients, by building a physician-driven and patient-centered multi-provider regional ICCM for AF patients, in a region with non-academic hospitals and large GP organizations. Building a continuum of care is indispensable because it contributes to optimizing substantive coordination between primary, secondary, and tertiary care. The NHN's methodology used to implement VBHC principles contributes to insight and improvements of outcomes that matter most to patients and costs. The implemented methodology resulted in a high registration density of patient outcomes, good adherence to the regional transmural standard, and was associated with improvements in EHRA score, hypertension, and type of AF.

Besides the use of outcomes like QoL to improve patient value, this dissertation highlights that the integration of QoL can be used as a prognostic indicator of the expected disease course for AF-patients. This could help with shifting the focus from symptoms and treatment options to a more patient-centered perspective in clinical care and could contribute to shared-decision making about how to treat AF, resulting in more tailored AF care.

To improve patient value even further, it is crucial that e-health interventions be implemented successfully in cardiac networks. The developed e-health implementation guideline is expected to contribute to the effectiveness of implementing e-health interventions in practice. The identified facilitating and inhibiting factors in AF screening, described in this dissertation, can narrow the gap between guideline recommendations for AF screening and successful implementation, resulting in a greater impact on patient outcomes and costs.

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Appendix

Summary

Implementing a value-driven care model for atrial fibrillation

As in many countries worldwide, healthcare providers in the Netherlands strive for better outcomes and lower healthcare costs, with the aim to keep healthcare accessible to everyone and to reduce quality differences between the various healthcare providers. To achieve these goals, value-based healthcare (VBHC) is increasingly being used. VBHC strives to improve patient value, which is defined as outcomes that matter most to patients divided by costs of healthcare delivery. In VBHC, several principles have been defined to improve outcomes while reducing costs and integrating care, such as organizing care around clearly defined patient groups, measuring outcomes and costs per patient, bundling payment for care cycles, integrating care delivery across separate facilities and geographical expansion of best practices. In addition to optimizing healthcare processes, outcomes can also improve, and healthcare costs can be reduced by applying supporting technological innovations such as e-health. However, there are currently no practical guidelines for implementing these principles in practice.

This dissertation aims to increase the current knowledge on developing, implementing, and evaluating an integrated chronic care model (ICCM) for patients with atrial fibrillation (AF) by using VBHC principles. The knowledge gained can be used as a blueprint for the implementation of VBHC principles in other medical conditions. Because patient value can be further improved by implementing e-health interventions more effectively, we also aim to provide practical recommendations for better implementation of e-health interventions in AF care.

To achieve these objectives, the following research questions have been formulated.

1. Is it feasible to put VBHC principles into practice for AF patients in a multi-provider network?
2. How can real-life data from such an AF network create relevant insights for improving patient value?
3. What conditions in AF care are needed for the successful implementation of e-health interventions in such a network?

This dissertation consists of three parts. Each part and its corresponding chapters address a research question. The remainder of this chapter provides a summary of chapters 1 through 10.

Chapter 1, **introduction**, describes the health problems caused by AF. Due to its complications, AF can have major consequences for patients and for the Dutch healthcare system. The number of patients with AF and the complications caused by AF are increasing

sharply because of the rapid aging of the population. This has major consequences for Dutch healthcare, including increasing pressure on healthcare use and rising healthcare costs. Quality improvement in AF care is needed to overcome these challenges. The following is a description to how Dutch AF care is currently organized and how it should be transformed into integrated chronic AF care. Subsequent, an explanation is given about the principles of VBHC as well as what an integrated care model should look like according to these principles. Next, the Netherlands Heart Network (NHN) is presented as an organization that facilitates the integration of healthcare delivery facilities and aims to contribute to the continuous increase of patient value for heart patients. Finally, e-health is introduced as a potential method to further improve patient value. The fact that the implementation of e-health innovations lags behind the technical possibilities is also addressed.

Part 1 focusses on developing and organizing an AF network according to VBHC principles.
Chapter 2 describes the development, organization, and implementation of the NHN. The NHN is an organization with four Dutch hospitals, including a heart center, three referring hospitals, three large general practitioner (GP) organizations and various other healthcare providers. The NHN is an example of a physician-driven and patient-centered collaboration of healthcare providers in primary, secondary, and tertiary care based on VBHC philosophy, in which multidisciplinary networks are initiated for the most prevalent cardiac conditions, such as AF. Following a stepwise methodology, the physicians develop and maintain transmural care standards. With data from daily practice and by using a Plan-Do-Study-Act cycle (PDSA cycle), it has proven possible to continuously improve patient value. The primary focus of these multidisciplinary networks, in which the patient perspective is central, is to increase the patient value of cardiac patients.

Chapter 3 discusses the detailed step-by-step methodology developed by the NHN for defining, implementing, evaluating, and continuously improving patient-relevant outcomes and costs in the full care cycle. This method, which uses the main features of the VBHC strategy, is outlined in this chapter for AF as a proof of concept. The presented methodology has proven to be feasible in daily practice and includes the Plan-Do-Study-Act cycle to ensure continuous improvement of patient-relevant outcomes. The first results are also presented. The use of the step-by-step methodology results in adequate registration of patient-relevant outcomes and a structured evaluation of adherence to applicable guidelines. Based on the methodology followed, detailed improvements are defined to optimize patient-relevant outcomes.

Part 2 presents real-world data from the AF network described in Part 1.
Chapter 4 describes the first preliminary data from the AF-NET study, a prospective cohort study collecting baseline and six-month data from newly and recently diagnosed

AF patients from the four hospitals involved in the NHN. The primary aim of this study was to assess whether nurse-led care in a collaborating region of four non-academic hospitals of different sizes in the Netherlands is effective at improving patient-relevant outcomes. Based on the preliminary findings presented in this chapter, it can be concluded that the quality of care for AF can be improved in smaller and non-academic hospitals when interhospital collaboration is strengthened through uniform standards and intensive patient education. These findings are consistent with previous research, supporting the hypothesis that AF outpatient clinics in collaborative, smaller hospitals may be just as effective as those in (larger) academic institutions. Developing and implementing regional standards of care for specific heart conditions appears to be an effective approach to continuously increase patient value within a network of healthcare professionals.

In **chapter 5** a prospective cohort study is described in patients with newly diagnosed AF. The aim of this study was to assess the association between baseline AF-related Effect on QualiTy of life (AFEQT) and Major Adverse Cardiovascular Events (MACE), the association between baseline AFEQT and improvement in perceived symptoms, European Heart Rhythm Association (EHRA) score, and the association between baseline AFEQT and AF-related hospitalizations. The AF patients were followed up after 12 months to record patient characteristics, the occurrence of patient-relevant outcomes and to evaluate the initiated therapy. The results show that patients with an AFEQT below the median develop MACE more often than patients with a higher AFEQT. In addition, AF patients with a lower AFEQT at diagnosis are more likely to have improvement in AF-related symptoms (EHRA score) during follow-up compared to patients with a higher AFEQT. Finally, patients with a lower AFEQT were more likely to be hospitalized in the first 12 months after diagnosis, compared to patients with a higher AFEQT. Hospital admissions were used in this study as a proxy for health care costs. These findings suggest that patient-reported outcomes, such as quality of life, can be used as a prognostic indicator of the expected disease course of AF in daily clinical practice.

Chapter 6 describes a prospective cohort study investigating the relationship between AFEQT score at baseline and improvement in perceived symptoms and general health status, and EHRA score at 12 months follow-up. Another goal of this study was to identify patient subgroups that experienced the most improvement in EHRA score over this period. The results in this chapter show that AF patients with a lower AFEQT score at diagnosis were more likely to improve their EHRA score during follow-up, compared to patients with a higher AFEQT score at diagnosis. The age-stratified analyses showed that this effect was most pronounced in patients ≥65 years of age and patients <75 years of age, compared to patients <65 and ≥75 years, respectively. Future research should focus on further defining characteristics of these age-groups to enable the implementation of age-tailored treatment.

Chapter 7 reports on a prospective cohort study performed among outpatient AF patients. All patients were asked to complete the Consumer Quality Index (CQI) to assess their experiences with the outpatient AF clinic. Analyses were performed to assess the association between patients' experiences and clinical outcomes of AF patients (i.e., EHRA score) after three and six months of follow-up. In this chapter we aim to determine whether there is a correlation between patient experiences regarding the outpatient AF clinic and clinical outcomes of AF patients at both three and six months. At baseline, a significant association was found between clinical outcomes and information and communication received by a doctor or other healthcare professionals. However, follow-up results show inconsistent findings. This inconsistent correlation between AF patients' PREMs and AF patients' clinical outcomes suggests that clinical outcome monitoring is currently a more valid and reliable representation of medical care quality.

Part 3 focusses on how e-health interventions can successfully be implemented in AF care. E-health interventions have the potential to improve healthcare quality and reduce costs. However, to implement e-health interventions successfully, instruments are needed to facilitate this process.
Chapter 8 presents the results of a literature research as well as a two-round Delphi study including 13 international e-health experts in the field of healthcare, ICT & technology. A total of five domains (i.e., technology, acceptance, financing, organizational, and legislation & policy) with 24 corresponding determinants were assessed by the experts. After the second Delphi round, consensus was achieved on the five main domains and 23 determinants. Based on 23 determinants, an e-health implementation guideline was developed to implement e-health innovations in healthcare more effectively. While previous studies have developed ways to assess an e-health intervention after implementation, this guideline may assist healthcare providers/researchers in assessing the determinants of successful e-health intervention prior to implementation of the e-health program.

In **chapter 9** facilitating and inhibiting factors are identified for successful implementation of a screening program for AF, from the perspective of healthcare providers. This is of great importance as large-scale implementation of screening for AF lags behind technological developments. A mixed-methods approach was used to gather data among practice nurses in primary care to evaluate the implementation of an ongoing single-lead electrocardiogram (ECG)-based AF screening program. Potential facilitating and inhibiting factors were evaluated using online questionnaires and 14 semi-structured in-depth interviews. Facilitating factors included 'receiving clear instructions', 'easy use of the ECG-based device', and 'patient satisfaction'. Inhibiting factors were 'time availability', 'insufficient feedback to the practice nurse', 'absence of coordination', and the 'lack of

fitting policy'. Based on the perceived barriers by healthcare providers, future AF screening programs should create preconditions for integrating the intervention into daily practice by appointing an overall project lead and a GP as a coordinator within every GP practice.

Finally, **chapter 10 contains the epilogue** that reflects on the main findings in the three parts of this dissertation. This chapter also introduces suggestions for future research and perspectives for practice to further optimize cardiac care in the Netherlands. In addition, the extensive opportunities arising from the intensification of the NHN's collaboration with regional and national partners are discussed – all with the fundamental goal of maximizing patient value for cardiac patients.

Samenvatting

De implementatie van een waardegedreven zorgmodel voor atriumfibrilleren
Net als in veel landen wereldwijd, streven zorgaanbieders in Nederland naar betere uitkomsten van zorg en lagere zorgkosten, met als doel de zorg voor iedereen toegankelijk te houden en kwaliteitsverschillen tussen de verschillende zorgaanbieders te verkleinen. Om deze doelen te bereiken wordt steeds meer gebruik gemaakt van Value Based Healthcare (VBHC). VBHC streeft naar het verbeteren van patiëntwaarde. Deze wordt gedefinieerd als de uitkomsten die er voor de patiënt het meest toe doen, gedeeld door de kosten van de zorg. In VBHC zijn verschillende principes gedefinieerd om uitkomsten te verbeteren en tegelijkertijd kosten te verlagen en zorg te integreren, zoals het organiseren van zorg rond duidelijk gedefinieerde patiëntengroepen, het meten van uitkomsten en kosten per patiënt, integrale betaling voor zorgcycli, integratie van zorg over afzonderlijke faciliteiten en geografische uitbreiding van de beste praktijkvoorbeelden (best practices). Naast het optimaliseren van zorgprocessen, kunnen ook uitkomsten van zorg verbeteren en zorgkosten worden verlaagd door het toepassen van ondersteunende technologische innovaties zoals e-health. Er zijn momenteel echter geen praktische richtlijnen om deze principes in de praktijk te implementeren.

Dit proefschrift heeft tot doel de huidige kennis over het ontwikkelen, implementeren en evalueren van een geïntegreerd chronisch zorgmodel (ICCM) voor patiënten met atriumfibrilleren (AF) te vergroten door gebruik te maken van VBHC-principes. De opgedane kennis kan worden gebruikt als blauwdruk voor de implementatie van VBHC-principes bij andere medische aandoeningen. Aangezien de patiëntwaarde verder kan worden verbeterd door e-health interventies effectiever te implementeren, willen we ook praktische aanbevelingen doen voor een betere implementatie van e-health interventies in de AF-zorg.

Om deze doelstellingen te bereiken zijn de volgende onderzoeksvragen geformuleerd.
1. Is het haalbaar om VBHC-principes praktisch te implementeren in een multi-provider netwerk voor AF-patiënten?
2. Hoe kunnen real-life data van zo'n AF-netwerk relevante inzichten creëren voor het verbeteren van de patiëntwaarde?
3. Welke voorwaarden in de AF-zorg zijn nodig voor de succesvolle implementatie van e-health interventies in een dergelijk netwerk?

Dit proefschrift bestaat uit drie delen. Elk deel en de bijbehorende hoofdstukken behandelen een onderzoeksvraag. Hieronder worden de hoofdstukken 1 tot en met 10 van het proefschrift beknopt samengevat.

Hoofdstuk 1, **inleiding**, beschrijft de gezondheidsproblemen die door het ziektebeeld AF worden veroorzaakt. AF kan niet alleen voor patiënten grote gevolgen hebben gezien de door AF veroorzaakte complicaties, maar ook voor de Nederlandse gezondheidzorg. Door de sterke vergrijzing neemt het aantal patiënten met AF en de complicaties veroorzaakt door AF sterk toe. Dit heeft significante consequenties voor de Nederlandse gezondheidzorg, waaronder toename van druk op het zorggebruik en de toename van zorgkosten. Om dit op te kunnen vangen, is er behoefte aan kwaliteitsverbetering in de AF-zorg. Hierna wordt beschreven hoe de Nederlandse AF-zorg momenteel is georganiseerd en hoe deze moet worden omgevormd tot een geïntegreerde chronische AF-zorg. De principes van VBHC worden uitgelegd en er wordt uitgelegd hoe een integraal zorgmodel er volgens deze principes uit zou moeten zien. Vervolgens wordt het Nederlands Hart Netwerk (NHN) gepresenteerd als een organisatie die de integratie van zorginstellingen faciliteert en wil bijdragen aan het continu verbeteren van de patiëntwaarde voor patiënten met een hartaandoening. Ten slotte wordt e-health geïntroduceerd als mogelijke methode om patiëntwaarde verder te verbeteren, maar er wordt ook ingegaan op het feit dat de implementatie van e-health innovaties achterloopt op de technische mogelijkheden.

Deel 1 richt zich op het ontwikkelen en inrichten van een AF-netwerk volgens de VBHC-principes. In **Hoofdstuk 2** wordt de ontwikkeling, organisatie en implementatie van het NHN beschreven. Een organisatie van 4 Nederlands ziekenhuizen in de regio Zuid-Oost Brabant, waaronder een hartcentrum, 3 verwijzende ziekenhuizen, 3 grote huisartsenorganisaties en enkele andere zorgaanbieders. Het NHN is een voorbeeld van een artsgedreven (op initiatief van artsen) en patiëntgerichte samenwerking van eerste-, tweede- en derdelijns zorgverleners vanuit de VBHC-filosofie. Er zijn multidisciplinaire netwerken geïnitieerd voor de meest voorkomende hartaandoeningen, zoals AF. Door een stapsgewijze methodiek te volgen, ontwikkelen en handhaven artsen transmurale zorgstandaarden. Met gegevens uit de dagelijkse praktijk en door gebruik te maken van een Plan-Do-Study-Act-cyclus (PDSA-cyclus) is het mogelijk gebleken de patiëntwaarde continu te verbeteren. De primaire focus van deze multidisciplinaire netwerken is het vergroten van de patiëntwaarde van hartpatiënten, waarbij het patiëntperspectief centraal staat.

Hoofdstuk 3 gaat in op de door het NHN ontwikkelde gedetailleerde stapsgewijze methodiek voor het definiëren, implementeren, evalueren en continu verbeteren van patiëntrelevante uitkomsten en kosten gedurende de volledige zorgcyclus. Deze methodiek, die gebruik maakt van de belangrijkste principes van de VBHC-strategie, wordt in dit hoofdstuk toegepast bij het ziektebeeld AF. De gepresenteerde methodiek is uitvoerbaar gebleken in de dagelijkse praktijk en omvat de PDSA-cyclus om continue verbetering van patiëntrelevante uitkomsten te waarborgen. Ook worden de eerste

uitkomsten gepresenteerd. Het gebruik van de stapsgewijze methodiek resulteert in een adequate registratie van patiëntrelevante uitkomsten en een gestructureerde evaluatie van het naleven van geldende richtlijnen. Op basis van de gevolgde methodiek worden gedetailleerde verbeteringen gedefinieerd om patiëntrelevante uitkomsten te optimaliseren.

In **deel 2** worden real life data van het in deel 1 beschreven AF-netwerk gepresenteerd.
In **hoofdstuk 4** worden de eerste voorlopige resultaten van de AF-NET-studie gepresenteerd. Dit is een prospectieve cohortstudie die basisgegevens en gegevens over een periode 6 maanden verzamelt van nieuw en recent gediagnosticeerde AF-patiënten van de 4 ziekenhuizen die betrokken zijn bij het NHN. Het primaire doel van deze studie is om te beoordelen of de verpleegkundige zorg in een samenwerkende regio van 4 niet-academische Nederlandse ziekenhuizen van verschillende omvang effectief is in het verbeteren van patiëntrelevante uitkomsten. Op basis van de in dit hoofdstuk gepresenteerde voorlopige bevindingen kan worden geconcludeerd dat de kwaliteit van de zorg voor AF kan worden verbeterd in kleinere en niet-academische ziekenhuizen, wanneer de samenwerking wordt versterkt tussen ziekenhuizen door gebruikt te maken van uniforme standaarden en intensieve educatie van AF-patiënten over het ziektebeeld en over de behandeling. Deze bevindingen komen overeen met eerder onderzoek dat de hypothese onderschrijft dat AF-poliklinieken in samenwerkende, kleinere ziekenhuizen net zo effectief kunnen zijn als die in (grotere) academische instellingen. Regionale zorgstandaarden voor specifieke hartaandoeningen ontwikkelen en implementeren, lijkt een effectieve aanpak voor het continu verbeteren van AF-zorg in een netwerk van zorgprofessionals.

In **hoofdstuk 5** wordt een prospectieve cohortstudie beschreven bij patiënten met nieuw gediagnosticeerd AF. Het doel van deze studie is te onderzoeken wat de associatie is tussen AF gerelateerd effect op de kwaliteit van leven, Atrial Fibrillation Effect on QualiTy-of-Life (AFEQT)-score bij start van het onderzoek (baseline) en het plaatsvinden van ernstige cardiovasculaire incidenten, Major Adverse Cardiovasculair Events (MACE). Hiernaast is de associatie onderzocht tussen AFEQT bij baseline en de verbetering van waargenomen symptomen en algemene gezondheidstoestand, European Heart Rhythm Association (EHRA)-score en de associatie tussen AFEQT bij baseline en AF-gerelateerde ziekenhuisopnames. De patiënten werden gedurende 12 maanden gevolgd om patiëntkenmerken, het optreden van patiëntrelevante uitkomsten en de gestarte therapie te evalueren. De resultaten laten zien dat patiënten met een AFEQT onder de mediaan vaker MACE ontwikkelen dan patiënten met een hogere AFEQT. AF patiënten met een lagere AFEQT bij diagnose verbeteren vaker op EHRA-score tijdens de follow-up in vergelijking met patiënten met een hogere AFEQT. Tenslotte hebben patiënten met een lagere AFEQT meer kans om in de eerste 12 maanden na diagnose in het

ziekenhuis te worden opgenomen, in vergelijking met patiënten met een hogere AFEQT. Ziekenhuisopnames worden in deze studie gelijkgesteld (proxy) aan de zorgkosten. Als zodanig benadrukt deze studie dat de door de patiënt gerapporteerde uitkomsten, zoals kwaliteit van leven, kunnen worden gebruikt als een prognostische indicator van het verwachte ziekteverloop van AF in de dagelijkse klinische praktijk.

Hoofdstuk 6 beschrijft een prospectieve cohortstudie waarin de relatie wordt onderzocht tussen de AFEQT-score bij baseline en EHRA-score na 12 maanden follow-up. Een ander doel van deze studie is om patiëntsubgroepen te identificeren die de meeste verbetering van de EHRA-score hebben ervaren gedurende deze periode. De resultaten in dit hoofdstuk laten zien dat AF-patiënten met een lagere AFEQT-score bij diagnose een grotere kans hebben op verbetering van hun EHRA-score tijdens de follow-up, vergeleken met patiënten met een hogere AFEQT-score bij diagnose. De naar leeftijdscategorieën gestratificeerde analyses tonen aan dat dit effect het meest uitgesproken is bij patiënten van ≥65 jaar en patiënten <75 jaar, in vergelijking met patiënten <65 en ≥75 jaar. Toekomstig onderzoek zou zich moeten richten op het verder definiëren van kenmerken van deze leeftijdsgroepen om de implementatie van een bij de leeftijd passende behandeling mogelijk te maken.

Ook **hoofdstuk 7** beschrijft een prospectieve cohortstudie uitgevoerd onder poliklinische AF-patiënten. Alle patiënten is gevraagd de Consumer Quality Index (CQI) in te vullen om hun ervaringen met de AF-polikliniek te beoordelen. Er zijn analyses uitgevoerd om het verband te onderzoeken tussen de ervaringen van deze patiënten met de poliklinische zorg en de klinische uitkomsten van deze AF patiënten (d.w.z. EHRA-score) na 3 en 6 maanden follow-up. Bij aanvang wordt een significant verband gevonden tussen klinische uitkomsten en informatie en communicatie verstrekt door een arts of andere beroepsbeoefenaren in de gezondheidszorg. Follow-up resultaten laten echter inconsistente bevindingen zien. Vanwege deze inconsistente correlatie tussen de Patient-Reported Experience Measures (PREM's) van AF-patiënten en de klinische uitkomsten van AF-patiënten, kan worden geconcludeerd dat klinische uitkomstmonitoring momenteel een meer valide en betrouwbaardere weergave is van de kwaliteit van medische zorg.

In **deel 3** wordt onderzocht hoe e-health interventies succesvoller kunnen worden geïmplementeerd in AF-zorg. E-health interventies hebben het potentieel om de kwaliteit van de gezondheidszorg te verbeteren en de kosten te verlagen. Om ze succesvol te implementeren zijn echter instrumenten nodig om dit proces te faciliteren.
In **hoofdstuk 8** worden de resultaten gepresenteerd van een literatuurstudie en een Delphi-studie in twee ronds met 13 internationale e-health experts op het gebied van gezondheidszorg, ICT & technologie. De experts hebben in totaal 5 domeinen (te weten technologie, acceptatie, financiering, organisatie en wetgeving & beleid) met 24

bijbehorende determinanten beoordeeld. Na de tweede Delphi-ronde is er consensus over de 5 hoofddomeinen en 23 determinanten. Op basis van deze 23 determinanten is een e-health implementatierichtlijn ontwikkeld om e-health innovaties in de zorg effectiever te implementeren. In tegenstelling tot eerdere studies, waarbij manieren zijn ontwikkeld voor beoordeling van een e-health interventie na implementatie, kan deze richtlijn zorgverleners/onderzoekers helpen bij het beoordelen van de determinanten van succesvolle e-health interventie voorafgaand aan de implementatie van het e-health-programma.

In **hoofdstuk 9** worden faciliterende en remmende factoren geïdentificeerd voor een succesvolle implementatie van een AF-screeningsprogramma, vanuit het perspectief van zorgverleners. Dit is van groot belang, omdat grootschalige implementatie van screening op AF achterblijft bij de technologische mogelijkheden. Een mixed-methods benadering is gebruikt om gegevens te verzamelen onder praktijkondersteuners in de eerste lijn om de implementatie van een lopend AF-screeningprogramma te evalueren. Met behulp van online vragenlijsten en 14 semigestructureerde diepte-interviews zijn mogelijke faciliterende en remmende factoren geëvalueerd. Faciliterende factoren zijn onder meer: 'duidelijke instructies ontvangen', 'gemakkelijk gebruik van het ecg-apparaat' en 'patiënttevredenheid'. Remmende factoren zijn 'onvoldoende beschikbare tijd voor het screeningsproces', 'onvoldoende terugkoppeling naar de praktijkondersteuner', 'ontbreken van coördinatie' en het 'gebrek aan passend beleid'. Op basis van de door zorgverleners ervaren barrières zullen toekomstige AF-screeningsprogramma's randvoorwaarden moeten scheppen om de interventie in te passen in de dagelijkse routine, door binnen elke huisartsenpraktijk een projectleider en een huisarts als coördinator aan te stellen.

Hoofdstuk 10 bevat de epiloog waarin een reflectie wordt gegeven op de belangrijkste bevindingen in de drie delen van dit proefschrift. In dit hoofdstuk worden ook perspectieven geïntroduceerd voor vervolgonderzoek en worden suggesties gedaan om te komen tot verdere optimalisatie van de cardiale zorg in Nederland. Tot slot wordt een beeld geschetst van de vele mogelijkheden die kunnen ontstaan bij intensivering van de samenwerking van het NHN met regionale en nationale partners met als belangrijkste doel: maximaliseren van patiëntwaarde voor patiënten met een hartaandoening.

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Curriculum vitae

Luc Theunissen was born in Heerlen, the Netherlands on the 29th of April 1972. After obtaining his VWO diploma at the Scholengemeenschap Groenewald in Stein, he studied medicine at Maastricht University between 1991 and 1998.

From 1998 until 2000, he worked as a resident in the cardiology departments of Maasland Hospital Sittard and the Academic Hospital Maastricht. In 2000 he started his training at the Academic Hospital Maastricht (now Maastricht UMC+) under the supervision of Dr. Miel Cheriex and department heads of cardiology prof.dr. Hein Wellens and later prof.dr. Harry Crijns.

In 2006 he completed cardiology training and started working as a cardiologist at the Máxima Medical Center in Veldhoven/Eindhoven. At the end of 2006, he obtained his Level 2 CMR certificate at the Royal Brompton Hospital in London. In 2007 he joined the Cardiology partnership of the Máxima Medical Center, of which he was chairman between 2013 and 2019. In this capacity, he became increasingly interested in optimizing healthcare in general and heart care in particular.

In 2014 Luc became chairman of the Stichting Cardiologenkring Zuid Oost Brabant. In 2016, he co-founded the Netherlands Heart Network – a joint effort of all relevant healthcare providers in Southeast Brabant who treat heart conditions in primary, secondary and tertiary care – of which he was also chairman from the start. In 2016 the first regional atrial fibrillation network was established, of which Luc was also chairman until 2020. In 2018 the Netherlands Heart Network received the prestigious Value Based HealthCare award from prof.dr. Michael Porter in recognition of the approach and impact of the initiative.

In April 2023, he started as head of Máxima Medical Center's IMPULS care group, which consists of the departments of cardiology, pulmonary medicine, neurology, pain medicine, rehabilitation medicine and sport medicine.

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