BALANCING STANDARDIZATION AND PERSONALIZATION IN COMPLEX AF CARE PATHWAYS THROUGH PROCESS MINING

FINDING THE RIGHT BEAT

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Preface

Dear reader,

Before you lies my master thesis "Balancing standardization and personalization in complex AF care pathways through process mining", which marks the completion of my master's Industrial Engineering and Management.

This thesis also marks the end of my student life. I enjoyed actively engaging in various extracurricular activities, where I had the chance to develop both academically and personally. Therefore, I would like to thank my friends and family for making this a wonderful period of my life.

At Isala, I was warmly welcomed from the very beginning, and I am grateful for all the support I received. I was introduced to everyone who could make a valuable contribution to the research, had the opportunity to observe various departments, and gained a great deal of knowledge about the entire cardiac care process. In particular, I would like to thank Hans Lotgerink and Henrieke van der Lugt for all the opportunities they offered me during this period. I am grateful for their support and trust in my ideas throughout the thesis.

I would also like to thank the participants of my validation panel for answering all my questions and for their involvement in my model. In particular, I want to thank Sébastien Krul, Peter Kievit, and Tianne Numan for this. Their valuable feedback enabled me to shape my method in a way that aligns with Isala's vision, and made my research relevant.

Finally, I would like to thank my supervisors from the University of Twente, Gréanne Leeftink and Jedidja Lok-Visser, for their guidance throughout the entire thesis. I am grateful for their constructive feedback whenever I needed it. I always felt that I could turn to them with any question, which helped raise the level of my thesis after every conversation.

I hope you enjoy reading this thesis!

Charlotte Smit
Enschede, April 2025

Management Summary

The increasing pressure on healthcare necessitates structural changes to enhance efficiency (Wetenschappelijke Raad voor het Regeringsbeleid, 2021). Efficiently organizing care pathways - the paths that patients follow from diagnosis to treatment for a disease - has been proven to contribute to this efficiency (Samarasinghe et al., 2024). Standardizing care pathways helps to reduce waste, to minimize errors, and to improve patient outcomes (Gartner et al., 2022; Schrijvers et al., 2012). However, standardizing care pathways is not feasible for all conditions. Complex diseases require more personalization because comorbidities play a role (Bujold et al., 2022). For these conditions, it is essential to find a balance between standardization and personalization of care pathways to ensure both efficiency and increased patient outcomes.

Atrial fibrillation (AF), a heart rhythm disorder, is such a complex disease. In Isala, care providers use the AF-CARE framework designed by Gelder et al. (2024) to treat AF. This framework proposes a strategy and set of treatment options per AF classification, but each patient's care pathway is established through shared decision-making. Although AF-CARE supports standardization, patient preferences and physician interpretations lead to variation in care pathways. This results in differences in sequences of care activities and follow-up periods. There is a challenge to design the AF care pathways such that standardization is incorporated to enhance efficiency, while maintaining personalization due to the complexity of AF. Therefore, the objective of this study was to identify improvement opportunities to effectively balance standardization and personalization for AF care pathways. In this study, we focused on one classification of AF: paroxysmal. Given this objective, the research question of this research was: *"What processes indicate an imbalance between standardization and personalization in the care pathways of AF patients at Isala Heartcenter?"*

After a literature review, we selected Process Mining (PM) as a suitable technique to identify areas for improvement. PM translates real-world data (RWD) of care activities into a process model, allowing us to visualize and analyze patient care pathways (Gonzalez-Garcia et al., 2020). Therefore, this technique is well-suited for discovering unknown and unstructured processes, such as AF management (Yang et al., 2023). In this study, we used RWD from HiX as input for PM and, by incorporating relevant Key Performance Indicators (KPIs), were able to develop concrete improvement plans for balancing standardization and personalization for AF care pathways. Figure 1 illustrates the data we extracted from HiX.

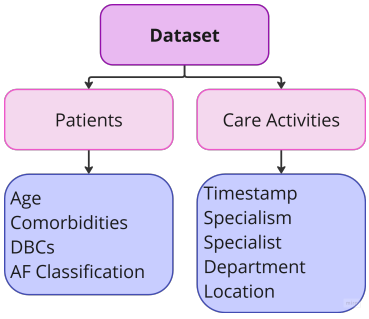

Figure 1: Datapoint Extracted from HiX

We used the data to obtain a comprehensive overview of the influences of care providers, departments, and/or locations on a patient's care pathway. We designed four experiments, each contributing to the objective of this study.

- **Experiment 1:** The Base Case, where we analyzed the whole patient cohort of patients

with paroxysmal AF. The goal was to compare the AF management at Isala with the AF-CARE framework.

- **Experiment 2:** We compared patients who started at the outpatient clinic (OC) with patients who started at the First Heart-Lung Aid (FHLA). The goal was to analyze the influence of different start points on the subsequent care pathway.
- **Experiment 3:** We compared patients who started at the OC with patients who started at the specialized OC for AF (AF-OC), which is run by Physician Assistants (PAs). We aimed to analyze the impact of the care provider on the care pathway.
- **Experiment 4:** We compared patients who had an ECV with patients who did not have an ECV, as ECVs are not recommended in AF-CARE. The goal was to analyze whether there were specific care pathways that included ECVs.

For each experiment, we adjusted the care activities to the necessary level of detail. For example, in the Base Case, only the care activity types are necessary to compare to AF-CARE. However, for experiment 2, we distinguished between department, and in experiment 3, we distinguished the care providers. To provide a complete picture of the AF care pathways, we executed a dataset analysis and process analysis for each experiment. We used the dataset- and process analyses to capture KPIs, allowing us to identify processes that indicate imbalance between personalization and standardization. Additionally, in Experiments 2, 3, and 4, we conducted a statistical analysis to validate our findings. The process of executing each experiment and KPIs resulting from the dataset- and process analyses are illustrated in Figure 2.

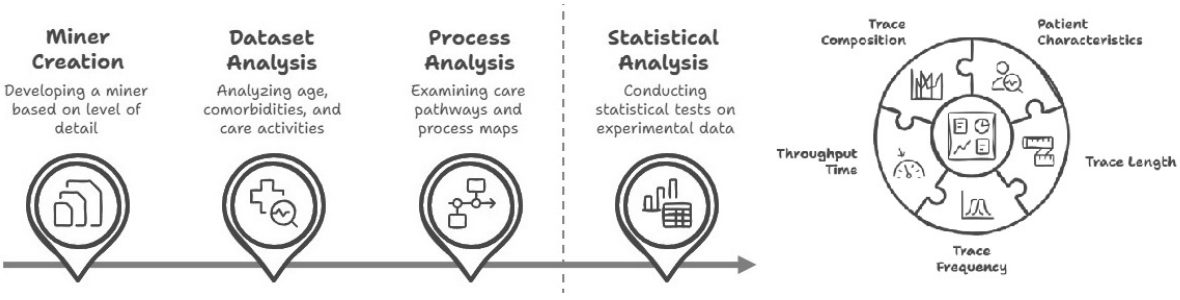

Figure 2: Process of Experiment Execution and Resulting KPIs

The experiments provided a comprehensive overview of AF management in Isala. If we compare the care pathways at Isala with the proposed care pathways of AF-CARE, we see that electrocardioversions (ECVs), a type of treatment, occurred in 45 care pathways (54 patients), whereas an ECV is not recommended in the AF-CARE framework. Additionally, the AF-CARE framework suggested a follow-up every 6 months. Therefore, we expected to see 2-5 consultations per patient in this study, keeping varying complexity of patients in mind. However, at Isala, we saw that patients had up to 10 consultations. This proved that, although AF-CARE takes a step towards standardization, the care pathways are still highly personalized. The processes that contributed to an imbalance between standardization and personalization in Isala are inconsistency of care providers and inconsistent use of ECVs and pulmonary vein isolation (PVIs), another type of treatment. Patients who had switched from physician to PA (or vice versa) had significantly longer care pathways. We expect that these patients were less well-monitored and, therefore, required more care activities. The inconsistent use of ECVs and PVIs is reflected in the care pathways involving these activities. The care activities preceding a PVI varied a lot, included several consultations and/or ECVs, while AF-CARE proposes a PVI as an effective treatment strategy. These results were discussed with a validation panel, consisting of cardiologists, a data analyst, and staff of the continuous improvement team. Together, we established three improvement plans for Isala Heartcenter, improving the balance between standardization and personalization for AF management.

1. **Increase continuity in care providers** - Ensure that patients remain under the care of a designated provider who has a comprehensive understanding of the patient. This allows for more timely and proper interventions, potentially via e-consultations or phone calls.
2. **Improve the use of the AF-OC** - By shifting more care to the PA, physicians have more capacity for complex patients. The PA has a better overview of the "standard" AF patients and can provide suitable care. Patients who fit this "standard" profile should be referred to the AF-OC instead of being scheduled with a physician.
3. **Establish stricter agreements on treatment strategies** - By setting clear criteria for when an ECV and/or PVI should be performed, care providers will have a reliable guideline. This enhances uniformity and reduces variability between care providers. Additionally, by recommending PVIs earlier - after 3 consultations or after 1 ECV, for instance - we expect that patient outcomes will improve, minimizing the follow-up care. Moreover, implementing a standard follow-up period after a PVI or between consultations, such as six months, enhances uniformity of the care pathways.

Based on these improvement plans, the Heartcenter can create several standardized pathways for AF patients, providing a reliable framework for care providers. Moreover, these structured pathways offer clear guidance on when a patient may deviate from them. As a result, we expect that more patients follow the standardized pathways, while the unique pathways will become explainable based on patient characteristics.

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List of Abbreviations

ADD	Antiarrhythmic Drug
AF	Atrial Fibrillation
AF-OC	Atrial Fibrillation Outpatient Clinic
BPMN	Business Process Model and Notation
DBC	Diagnose Behandel Combinatie [EN: Diagnosis Treatment Combination]
DES	Discrete Event Simulation
ECV	Electrical Cardioversion
EHLH	Eerste Hart Long Hulp [EN: FHLA]
ESC	European Society of Cardiology
FHA	First Heart Aid
FHLA	First Heart Lung Aid
FTE	Full Time Equivalent
GP	General Practitioner
HC	Herhaalconsult [EN: follow-up consultation]
HIS	Hospital Information Systems
IOM	Institute of Medicine of America
KPI	Key Performance Indicator
NP	New Patient
OC	Outpatient Clinic
OR	Operations Research
PA	Physician Assistant
PM	Process Mining
PVI	Pulmonary Vein Isolation
RA	Readmission
RWD	Real-World Data
SD	Standard Deviation
SDM	Shared Decision-Making
WHO	World Health Organization

1. Introduction

The pressure on the healthcare system is rising. As the population ages and previously lethal illnesses become chronic, diseases now also emerge simultaneously more often. This results in highly intensive and complex care (Ministerie van Volksgezondheid, Welzijn en Sport, 2022, 2024). The report by the Wetenschappelijke Raad voor het Regeringsbeleid (2021) states that, if this trend continues, in 2060 one in three individuals in the Netherlands will need to work in the healthcare sector. Currently, this is one in seven individuals (Wetenschappelijke Raad voor het Regeringsbeleid, 2021). Meanwhile, there is a growing staff shortage of healthcare professionals, such as nurses, general practitioners (GPs), and medical specialists (Ministerie van Volksgezondheid, Welzijn en Sport, 2022). If no changes are made, not everyone can receive proper care in the future. Hence, structural changes in the healthcare system are essential to meet the growing demand (Rijksoverheid, n.d.).

To implement these structural changes, the organization of care processes must be adjusted to a more effective structure. Therefore, healthcare providers need to agree on specific work agreements regarding these processes. A care process at the level of a specific disease is called a care pathway. A care pathway includes all relevant care activities, from diagnosis to treatment, that are important for that specific condition (Netwerk Klinische Paden, n.d.). Previously, healthcare professionals were largely responsible for designing care pathways themselves, which led to significant variations in procedures. As a result, patients do not follow a universal pathway, which can lead to them receiving either too much or too little care. With the increasing pressure on healthcare and the need for more efficient care processes, there is now more focus on standardization and uniform work agreements (Samarasinghe et al., 2024). Standardized care pathways have been shown to enhance the quality of care by improving efficiency, reducing variability, and minimizing the risk of errors (Gartner et al., 2022; Schrijvers et al., 2012). A well-structured care pathway allows for a faster diagnosis and treatment process, ensuring that patients receive appropriate care more quickly (Neame et al., 2019). Additionally, by continuously monitoring and adjusting care pathways, variations in care can be identified and improvements can be implemented over time (Netwerk Klinische Paden, n.d.).

For many conditions, standardized care pathways are effective, as they serve as clear and evidence-based guidelines for care providers. However, not all diseases are suitable for a uniform care pathway. Complex conditions, particularly those associated with comorbidities or those without an effective treatment, often require a more personalized approach. A single standardized care pathway will not yield the best outcomes for those patients. As a result, for each patient a unique care pathway is constructed by the physician and patient, resulting in high levels of variability. This counteracts the advantages of standardized care pathways, such as efficiency and reduced errors (Samarasinghe et al., 2024). In literature and practice, there is little research on how the advantages of standardized care pathways can be integrated in care processes of patients with complex diseases. For these patients, a balance between personalization and standardization is required to improve efficiency, reduce errors, and enhance patient outcomes.

This thesis presents a study in Isala Hospital, focusing on the balance between standardization and personalization of the treatment of complex diseases. This balance leads to improvement opportunities for care pathways, to obtain the benefits of care pathways while providing appropriate care. This study takes place at the Isala Heartcenter, which is specialized in cardiovascular diseases. As the prevalence of cardiovascular conditions increases with age, and our population is aging (Rodgers et al., 2019), the emphasis of this study is on the care pathways in the cardiovascular domain, more specifically, on atrial fibrillation (AF), a cardiac arrhythmia.

2. Background

This chapter discusses relevant theoretical and practical background information for this research. First, Section 2.1 describes the theoretical background. Next, Section 2.2 elaborates on the current practice at Isala Heartcenter. Section 2.3 discusses the objective of the research. The link between the theoretical and practical background forms the basis for this research.

2.1 Theoretical Background

The theoretical background connects theory on care pathways with European guidelines for AF management. Section 2.1.1 provides information about the definition of care pathways, their advantages and drawbacks, and their development. Section 2.1.2 explains what AF is and discusses guidelines for AF management and its complexity. Subsequently, Section 2.1.3 highlights the differences between standardized care pathways and AF management, as well as the challenges of their integration.

2.1.1 Care Pathways

In literature, there is no consensus about the definition of a care pathway. The terms "care pathway", "clinical pathway" and "critical pathway" are used interchangeably, while these pathways encompass different steps in patient's journey. A care pathway includes activities outside of the hospital as well as activities inside the hospital (Schrijvers et al., 2012). The clinical pathway only describes in-house activities in a clinic (Schrijvers et al., 2012). Critical pathways are organized care plans that contain specific steps for patients with a specific clinical condition (Dy et al., 2005). Numerous studies have investigated the precise definition of these pathways, often including all three types of care pathways.

The most frequently referred to definitions are:

> *"A multidisciplinary plan for delivering health and social care to patients with a specific condition or set of symptoms. Such plans are often used for the management of common conditions and are intended to improve patient care by reducing unnecessary deviation from the best practice" (Gartner et al., 2022)*

and

> *"A care pathway is a structured, multi-disciplinary plan of care where (meets at least three of the following criteria)*
>
> 1. *the intervention is used to channel the translation of guidelines or evidence into local structures, and/or;*
> 2. *the intervention details steps in a course of treatment or care in a plan, pathway, algorithm, guideline, protocol or any other inventory of actions, and/or;*
> 3. *the intervention had time-frames of criteria-based progressions (i.e., steps were taken if designated criteria were met, and/or;*
> 4. *the intervention aimed to standardize care for a specific clinical problem, procedure or episode of care in a specific population." (Neame et al., 2019).*

Manktelow et al. (2022) and Schrijvers et al. (2012) highlight the importance of a "well-defined patient group", "well-defined period of time", and "working in a multi-disciplinary team to

deliver care in a specific context". Other attributes of an effective care pathway include (1) patient and caregiver centricity, (2) roles of care professionals, (3) operational management, (4) coordination structures, (5) organizational and systemic context, (6) information systems and data management, and (7) the development of a learning system (Gartner et al., 2022). The aim of care pathways is to improve quality of care by enhancing risk-adjusted outcomes, ensuring patient safety, increasing patient satisfaction, and optimizing resource use (Aspland et al., 2021; Gartner et al., 2022; Schrijvers et al., 2012).

Moving forward, the definition of Gartner et al. (2022) will be used to refer to a care pathway. This definition is the most suitable for complex diseases, such as AF, since a patient group can also be seen as patients with a certain set of symptoms instead of all patients with a specific disease.

Care pathways play a significant role in:

- Reducing the duration of care processes through faster diagnosis, which in turn shortens throughput time and improves patient outcomes (Neame et al., 2019; Schrijvers et al., 2012).
- Increasing the fluidity of the process, reducing the risk of errors and variances (Gartner et al., 2022; Neame et al., 2019).
- Reducing production costs by standardization and efficient resource usage (Gartner et al., 2022; Neame et al., 2019; Schrijvers et al., 2012).
- Increasing job satisfaction for healthcare professionals since responsibilities become clearer. Moreover, clear guidelines and coordination can increase autonomy because professionals are allowed to start working independently (Schrijvers et al., 2012).

Standardized care pathways are designed considering these advantages. However, there are several drawbacks associated with standardized care pathways, as they can limit the personalization of care (Schrijvers et al., 2012). Additionally, complex patients do not fit into a standardized care pathway (Gartner et al., 2022). As complex diseases comprise comorbidities and multidisciplinary care, standardization is not feasible (Perron et al., 2024). Moreover, standardization affects both job and patient satisfaction (Schrijvers et al., 2012). Shared decision-making (SDM) is an approach to alleviate these drawbacks by incorporating patient preferences into the care pathway (Montori et al., 2023). An SDM approach is proven to enhance treatment adherence and improve patient outcomes (Fiorillo et al., 2020). Several studies concluded that SDM is also appropriate for complex patients, such as patients with cancer or AF (Andersen-Hollekim et al., 2021; Perron et al., 2024). However, this does not outweigh the challenges faced by comorbidities and multidisciplinary care (Bujold et al., 2022).

Theories such as Lean Six Sigma and Value-Based Care incorporate care pathways to reduce waste and improve quality of care (Cossio-Gil et al., 2022; Manktelow et al., 2022). This leads to enhanced coordination and, therefore, to seamless care delivery. New process innovations in healthcare, e.g, specialized outpatient clinics and telecare, depend on enhanced coordination to be implemented (Schrijvers et al., 2012). Well-defined indicators, care activities, and follow-up are important attributes of this coordination, emphasizing the need for care pathways (Schrijvers et al., 2012). These comprehensive care pathways serve as decision support tools for both physicians and patients (Aspland et al., 2021).

Over the past two decades, institutions such as the Institute of Medicine of America (IOM) and World Health Organization (WHO) have called for the improvement of quality and performance of healthcare services (Gartner et al., 2022). While the six traditional domains - safety, effectiveness, patient-centeredness, timeliness, efficiency, and equity - remain crucial, models should be developed to assess them more concretely. These models should also help organize healthcare and services to improve effectiveness and efficiency (Gartner et al., 2022). Both data for hospital information systems (HIS), for factual steps, and collaboration with professionals,

to understand decisions and variances, should be used to develop a validated model (Aspland et al., 2021). Studies suggest that incorporating Operations Research (OR) techniques, data simulation, and data analysis contributes to effective care processes and can aid decision-making processes (Aspland et al., 2021; Gartner et al., 2022).

2.1.2 Atrial Fibrillation Guidelines

This research focuses on atrial fibrillation (AF), a heart condition. This section elaborates on this condition and the current guidelines for managing AF.

The heart consists of four cavities: two atria and two ventricles. Blood enters the heart through the atria, the atria pump the blood into the ventricles and the ventricles pump the blood back into the body. This process is activated by an electrical circuit that starts in a clump of cells in the right atrium, which regulates the heartbeat. This regular heartbeat is called a sinus rhythm. When multiple circuits emerge in the atria, this process is no longer regulated properly, resulting in a high and irregular heartbeat. This is called atrial fibrillation (AF) (Hartstichting, n.d.). Although AF itself is not a life-threatening condition, AF can be the cause of several cardiovascular diseases. Inefficient pumping can cause damage to the heart, with heart failure or infarction as possible results (Gelder et al., 2024).

The prevalence of AF in the Netherlands is expected to increase from 1.6% in 2010 to 3.2% in 2060 (Kornej et al., 2020). The aging population and increased comorbidities are contributing factors, as are improved awareness and better detection technologies. Because AF manifests and progresses differently among patients, a uniform care pathway for all AF patients is not feasible. The task force for the management of AF of the European Society of Cardiology (ESC) has created a framework, AF-CARE, that serves as a guideline that can be individualized per patient. This framework takes into account a patient-centered, shared decision-making approach to tailor treatment strategies to individual needs. In addition, the framework emphasizes prevention, since evidence shows that early management reduces the progression and recurrence of AF (Gelder et al., 2024).

The AF-CARE framework organizes the management of AF into four components (Gelder et al., 2024):

C Comorbidity and risk factor management
Comorbidities and risk factors, such as hypertension, diabetes, and obesity are typical drivers of AF onset and progression. Evidence shows that addressing these factors improves outcomes and recurrence of AF (Shantsila et al., 2024). Therefore, assessment and management of these comorbidities and risk factors are the first step in the care pathway.

A Avoid stroke and thromboembolism
The next step in the care pathway is to treat the risk of stroke and thromboembolism, the major risks of AF, by appropriately using anticoagulants, a type of medication that prevents blood clots. (Gelder et al., 2024).

R Reduce symptoms
Rate and rhythm control strategies are employed to return to sinus rhythm, alleviate symptoms, and improve quality of life. Rate control includes medication that regulates the frequency of the heart rate. Rhythm control consists of strategies that restore and maintain sinus rhythm. Rhythm control includes rhythm-controlling drugs (AADs), electrical cardioversion (ECV), pulmonary vein isolation (PVI), and, in severe cases, hisbundle-ablation (Krul et al., 2013). Often, a combination of rate and rhythm control is required for optimal outcomes.

E Evaluation and dynamic reassessment

AF, and the related comorbidities and risk factors, can change over time. Therefore, all patients require timely (re-)evaluation. In this framework, Gelder et al. (2024) suggest re-evaluating the patient six months after the first presentation of AF, followed by annual re-evaluation or re-evaluation based on clinical needs.

The AF-CARE fundamentals are applied to the pathways of the different AF classifications; first-diagnosed, paroxysmal, persistent, and permanent. The main difference between these pathways is the choice of rhythm control strategy, which is related to the severity of symptoms. For first-diagnosed patients, it is common to initialize rate control and consider an ECV if AF becomes persistent. In case of paroxysmal AF, AADs or ablation are advised. If AF becomes persistent, rhythm control strategies such as AADs, ECV, ablation, or a combination of them are suitable. For paroxysmal and persistent AF, only the origin of the electrical circuit causing AF is ablated. Last, a more invasive type of ablation may be considered for permanent AF. Here, the atrioventricular node, the natural pacemaker of the heart, is ablated and a pacemaker is inserted. Figure 2.1 illustrates a simplified version of the care pathway for paroxysmal AF designed by Gelder et al., 2024. Simplified versions of pathways for the other classifications can be found in Appendix A.1.

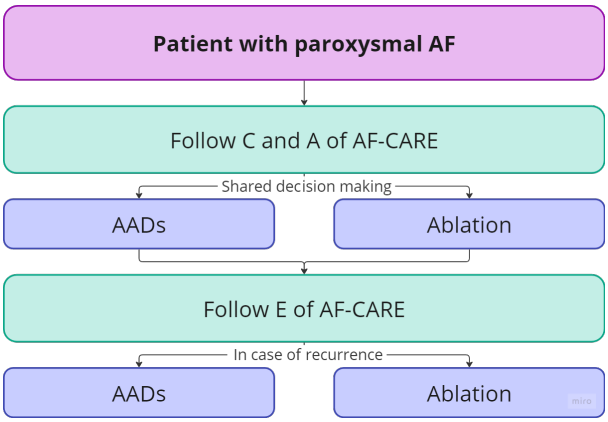


Figure 2.1: Simplified care pathway of patients with paroxysmal AF (Gelder et al., 2024)

ECVs can only be performed if certain requirements are met. This makes the choice for an ECV more complicated than, for example, AADs or an ablation. A simplified flowchart of eligibility for cardioversion can be found in Appendix A.2. First, there is a distinction between immediate and elective ECV. An immediate ECV is recommended when a patient has a worsening haemodynamic instability caused by AF, otherwise a wait-and-see approach is recommended. Studies show that there is no significant difference in the outcomes between these approaches for patients with recent onset AF without haemodynamic compromise. Moreover, if the onset is more than 24 hours, the risk of stroke or thromboembolism increases, and an ECV should only be performed if the patient has received at least three weeks of anticoagulants (Gelder et al., 2024).

The patient-centered nature of AF-CARE increases the likelihood of treatment adherence. This largely contributes to the outcomes and recurrence of AF. The framework comprises symptom control, lifestyle recommendations, comorbidity management and medical treatment. Hence, it integrates all aspects necessary for AF management. Moreover, the SDM approach is known to increase treatment engagement for complex patients, such as patients with AF (Perron et al., 2024).

While this framework incorporates patient preferences through SDM, it does not provide information on how to cope with certain comorbidities or symptoms. Strategies such as rhythm

and/or rate control are discussed, however, the choice and follow-up are up to the patient (Gelder et al., 2024). As a result, treatment approaches can vary per patients and per care provider. This leads to inconsistencies in care pathways for patients with AF.

2.1.3 Challenges in Integrating Care Pathways in AF Management

Care pathways, as described in literature, emphasize standardized, evidence-based, and multidisciplinary care. The care pathways rely on a clear patient population, predictable disease progression, clear time frames, and assume adherence to the pathway (Gartner et al., 2022; Manktelow et al., 2022; Schrijvers et al., 2012). However, due to comorbidities and risk factors associated with AF, AF is not a predictable condition. AF manifests differently in each patient. Its progression can only be partly managed by addressing comorbidities and risk factors (Vlachos et al., 2016). Currently, the AF-CARE framework distinguishes the treatment strategies solely on the classification of AF. This classification indicates the occurrence of AF: first-diagnosed, paroxysmal, persistent or permanent (Gelder et al., 2024). Since the classification and treatments are symptom-driven, the AF-CARE framework established by Gelder et al. (2024) serves to systematically treat AF patients, while tailoring the strategy to patients' preferences. This SDM approach is likely to enhance adherence, but does not take evidence-based treatments for sets of symptoms into account (Perron et al., 2024). Especially for lifestyle changes and medication, as parts of AF management, adherence is important. Moreover, treatment options such as AADs, ECV, and ablation are not always durable and AF might return (Xu et al., 2016). This may require changes in treatment strategy and thus flexible pathways. To summarize, the complexity, variability, and recurrence of AF create a challenge to integrate standardized care pathways into the personalized management of AF. Although AF-CARE provides a framework for AF management, there is room for interpretation per physician and patient. If we compare it with the definition of care pathways by Gartner et al. (2022), the AF-CARE framework does not fit the definition, since the treatment strategy is not adaptable per set of symptoms or disease, but per an individual patient's preferences. This leads to personalization per individual patient and, therefore, variation.

2.2 Operational Background

The operational background discusses the in-house problems regarding efficient AF care at Isala Heartcenter. First, Section 2.2.1 elaborates on several inefficiencies that were discovered along the AF care pathway. Additionally, Section 2.2.2 addresses the core problem at Isala by connecting the practical problems with the theoretical challenges.

2.2.1 Problem Identification

Isala is a regional hospital with five locations: Zwolle, Meppel, Steenwijk, Kampen and Heerde. With 7000 employees, 690,000 patients and 942 beds, it plays a vital role in providing healthcare across the region. The location in Zwolle offers top-clinical, complex care such as heart- and neurosurgery, neonatology, stem cell transplantations. Additionally, Isala Zwolle serves as the trauma center for Zwolle and surroundings. At the location in Meppel, basic care is offered next to various diagnostic opportunities (Isala, n.d.).

Isala Heartcenter delivers cardiac care to thousands of patients on a yearly basis. In the center, cardiologists, cardiothoracic surgeons, and thoracic anesthesiologists cooperate intensively to provide high-quality care. Due to this cooperative approach, a wide range of treatments can be offered (Isala, n.d.). The center aims to deliver appropriate care. This includes fast diagnosis, personalized treatment, and follow-up at Isala Harthuis or at home. Isala makes use of tele-monitoring to accommodate care at home. Tele-monitoring allows healthcare professionals to monitor patients remotely by using information technology. Other heart facilities in Isala are the first heart-lung-aid (FHLA) in Zwolle and the first heart-aid (FHA) in Meppel. These

are both emergency facilities where patients are brought in when there is an indication for cardiovascular disease (Isala, n.d.).

At Isala Heartcenter, all locations visited by AF patients were assessed to gain a comprehensive overview of the processes involved in AF care. These locations included the outpatient clinic, the AF-clinic, the FHLA, ECV-street in Meppel and Shortstay in Zwolle. The care providers at Isala Heartcenter utilize the AF-CARE framework. However, conversations with staff members involved in AF care unveiled several challenges impacting the efficiency of the care pathway. These challenges are presented in the problem cluster in Figure 2.2.

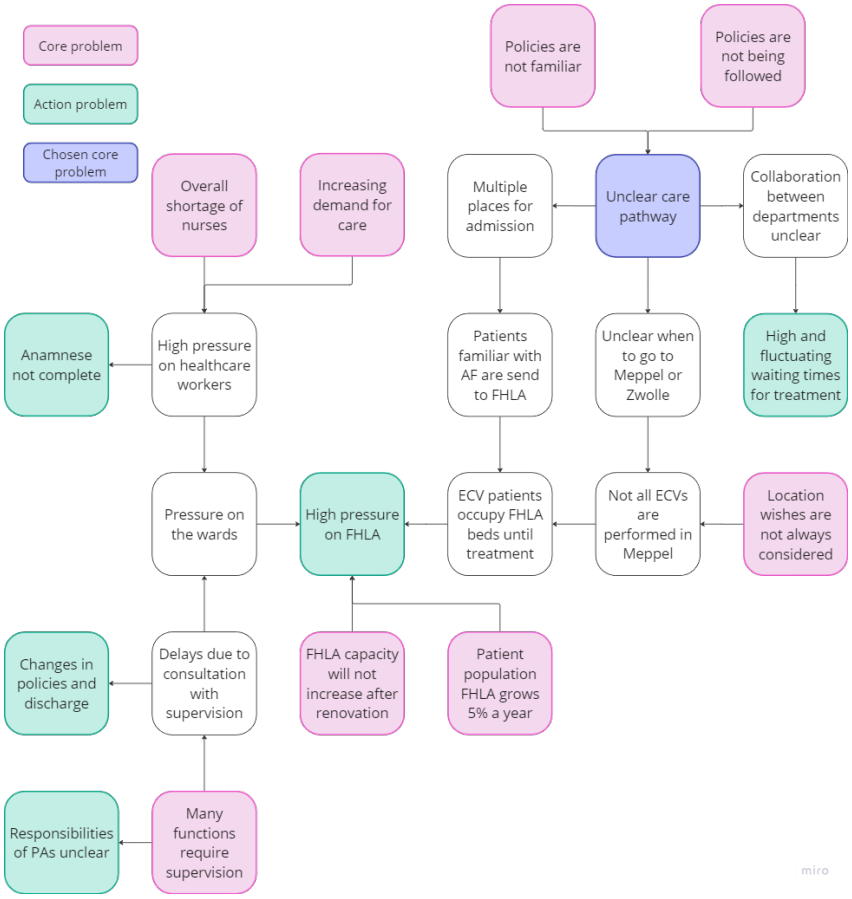


Figure 2.2: Problem cluster of operational problems at Isala Heartcenter

One of the challenges is the increased workload due to staff shortages and the growing AF patient population. As the prevalence of AF increases, the demand for care and pressure on healthcare professionals is expected to increase. Furthermore, the admission process lacks uniformity. Patients who experience AF symptoms can be referred to the outpatient clinic, the AF-clinic, the FHLA, the ECV-street in Meppel or a wait-and-see approach is suggested. However, no clear criteria exist to determine which strategy should be chosen when a patient calls with symptoms. Another area where clarity is lacking is in the criteria for determining when an acute or elective strategy should be applied. This is a part of the treatment strategy and thus largely influences the care pathway. These problems result from unclear care pathways. Currently, there is no desired care pathway, i.e., norm, designed by Isala, in addition to AF-CARE. Due to the highly personalized nature of AF-CARE, the care pathways are determined either inconsistently or dependent on the healthcare professional responsible at the time. As a result, there are high and fluctuating waiting times for certain treatments and resources are either under high pressure or underutilized.

2.2.2 Core Problem

Integrating standardized care pathways in AF management is difficult, as reflected in practice at Isala Heartcenter. Unstandardized and highly deviated pathways resulted in fluctuating waiting times and waste of resources. Theory on standardized care pathways states that these indicators, throughput and resource usage, are directly related to the efficiency of a care pathway (Gartner et al., 2022; Neame et al., 2019; Schrijvers et al., 2012). The many symptoms and comorbidities laid the ground for a variety of treatment strategies. As a result, the AF management at Isala has a personalized approach, lacking standardization.

2.3 Research Design

This section provides the research design. Section 2.3.1 states the research objective and related (sub)questions. Subsequently, Section 2.3.2 defines the scope of this research.

2.3.1 Research Objective

The increasing prevalence of AF calls for structuring AF care and, where possible, standardizing care pathways to alleviate pressure on healthcare professionals while providing appropriate care for AF patients. Additionally, innovations in healthcare require more streamlined processes, clear indicators, and comprehensive pathways. The incorporation of HIS and data analysis techniques can contribute to these comprehensive pathways by identifying variations and measuring relevant key performance indicators (KPIs). This knowledge forms the foundation for process improvement. In this context, care processes can be improved by standardizing complex care where feasible, while maintaining personalized care when necessary. Therefore, the objective of this research is to identify improvement opportunities to effectively balance standardization and personalization for the care pathways of AF patients at Isala Heartcenter.

Given the objective, the research question was formulated as follows:

> *"What processes indicate an imbalance between standardization and personalization in the care pathways of AF patients at Isala Heartcenter?"*

Answering this question requires several steps and related sub-questions. First, we needed to select the most suitable technique to visualize care pathways and make profound analyses. Therefore, we answered the question *"What modeling techniques are suitable for representing the care pathway of patients with atrial fibrillation?"* Chapter 3 provides the answer to this question through a literature review. Here, we evaluated the advantages and drawbacks of relevant techniques. Additionally, we determined what KPIs were relevant for this thesis based on literature and experts' opinions. We concluded the chapter by stating the technique and KPIs we used for this research.

Subsequently, we developed the model by designing the relevant care pathway and obtaining the required data. The questions related to this step were:

- *"What activities are important to include in the model, and which activities can be incorporated in sub-processes?"*
- *"What input data is required for the model and how can it be obtained?"*

Chapter 4 discusses all relevant input for the model. It also provides clear steps for processing the data and creating the model.

Once the model was created, we evaluated the visualized care pathways and other KPIs. We did this according to the question: *"What do the current care pathways of patients with AF look like?"* Chapter 5 states all outcomes and discusses the relevant results according to predetermined KPIs. We discussed the care processes with several stakeholders, to ensure reliable analyses.

Chapter 6 provides the conclusion, i.e., an overview of the processes that indicate an imbalance between standardization and personalization in the care pathways.

Last, Chapter 7 discusses the results and conclusion, and provides specific improvement plans. Moreover, Chapter 7 elaborates on the practical and scientific contribution of this research, the limitations, and provides recommendations for future research.

2.3.2 Scope

This study, conducted by Isala Heart Center, focused on the balance between standardization and personalization of care pathways for patients with paroxysmal AF (one of the four classifications). The focus was on the process level, including the sequence of care activities, the time intervals between these activities, and other relevant organizational factors that influenced them. The medical correctness of these choices was not assessed; where medical knowledge was required, input was obtained from cardiologists to provide a comprehensive overview. This study was limited to organizational aspects and aims to provide insights into how standardization and personalization interact within care pathways.

3. Literature Review

This chapter describes the literature review of this thesis. Section 3.1 describes the literature search strategy and the inclusion process. Section 3.2 summarizes and discusses the findings of the literature review. Subsequently, Section 3.3 summarized the literature on modeling techniques and concludes with the most suitable technique. Section 3.4 defines the KPIs relevant for this research, tailored to the chosen modeling technique.

3.1 Literature Search Methodology

The first research question was *"What modeling techniques are suitable for representing the care pathway of atrial fibrillation patients?"*. Literature on modeling techniques for care pathways were collected via Scopus. Various search terms were used to gain sufficient data. The search terms were as follows:

((“Care pathway” OR “Clinical pathway” OR “Critical pathway’ OR “Patient process”) AND “modeling” AND (“techn*” OR “approach”))

The pathway terms were chosen since they were often used interchangeable in literature. Both “modeling” and “modelling” yielded the same results. The search terms “techn*” and “approach” were included to specifically capture studies where “modeling” was described as a technique, technology, or approach.

The found records were assessed based on criteria to ensure relevance and quality. The inclusion criteria were:

- The record is an article, book chapter or review.
- The record is written in English or Dutch.
- The record is published after 2005 to provide state-of-the art techniques.
- The full text of the record is available to ensure a complete assessment.
- Full text screening ensures that the record provides significant insight in pathway modeling for this thesis.

The exclusion criteria during full screening were:

- Studies that model care pathways based solely on flowcharts, without quantitative data or operations research techniques are excluded. We aim to integrate HIS, as it is stimulated by the WHO due to its objectivity (Aspland et al., 2021; Gartner et al., 2022).
- Studies that do not align with the scope of this thesis are excluded. An example is when a study focuses on medicinal choices instead of patient process instances, such as arrival, appointments or treatments.
- Studies that model a department within a hospital rather than the pathway of a patient group are excluded. A department can treat several patient groups, while a patient group can visit various departments. The AF care pathway consists of one patient group who visits several departments.
- Studies should primarily aim to provide insight into the care pathway and may analyze performance indicators, such as utilization rates and waiting times (Gartner et al., 2022; Schrijvers et al., 2012). Studies that aim to predict disease progression based on patient characteristics are excluded, since this is not applicable for AF patients (Vlachos et al., 2016).

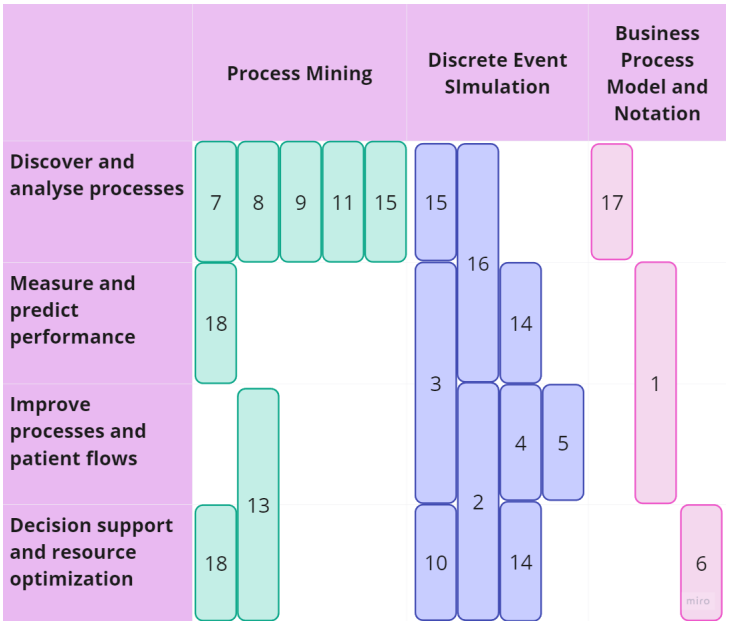
The Scopus search resulted in 529 records of which 19 records were included. Via snowballing, another 11 records were found and 6 of them were included. The inclusion process is displayed

according to PRISMA guidelines (Page et al., 2021) in Appendix B.1. In total, 25 studies were included in this literature review.

3.2 Suitability of Modeling Techniques

The literature review provided a representable overview of the literature on modeling care pathways. This literature was identified through the search string as described in 3.1. All commonly used techniques were therefore assumed to be in this review. An overview of all articles and the techniques used in these articles are integrated in the concept matrix in Table B.1 in Appendix B.2. The concept matrix shows that Process Mining (PM) and Discrete Event Simulation (DES) are the most frequently used techniques for modeling care pathways. The third most common technique is Business Process Model and Notation (BPMN). Although BPMN was not always explicitly applied, many articles did mention this technique. Therefore, the rest of the literature review focused on the articles that use PM, DES, and/or BPMN.

The articles that used PM, DES, and/or BPMN were integrated into a 'Research Goals-Approach' - matrix. The purpose of this matrix was to provide an overview of the research goals for which the techniques are used. Subsequently, conclusions were drawn about the most suitable technique for the goal of this thesis. Figure 3.1 contains the 'Research Goals-Approach' - matrix, and a list is provided to refer to the corresponding studies.



Studies:

1. Ajmi et al., 2015
2. Babashov et al., 2017
3. Bahou et al., 2018
4. Cardoen and Demeulemeester, 2008
5. Chemweno et al., 2014
6. Combi et al., 2017
7. Oliveira et al., 2020
8. Erdogan and Tarhan, 2018
9. Gonzalez-Garcia et al., 2020
10. Lahr et al., 2020
11. Mans et al., 2008
12. Ozcan et al., 2017
13. Peng et al., 2024
14. Pilgrim et al., 2009
15. Rejeb et al., 2018
16. Wood et al., 2022
17. Yan et al., 2018
18. Yang et al., 2023

Figure 3.1: 'Research Goals-Approach'- Matrix of the Literature Review

Horizontally, the matrix shows the three modeling techniques. Vertically, general descriptions of the research goals are listed. The research goals were divided into four categories, ascending in terms of optimization and implementation progression. The first goal, *discover and analyze processes*, primarily focused on visualizing and understanding processes. Based on data, a realistic depiction of the process was created, and conformance analysis was executed. While quantitative analyses were employed, they were primarily used to assess deviations and inconsistencies rather than focusing on performance metrics. These were more central in the second goal, *measure and predict performance*. This goal measured KPIs, such as waiting times and utilization, to analyze the quantitative performance of a process. Predictions regarding

process progression were also made on this data. The first two goals aimed to identify areas for improvement, both qualitatively and quantitatively. However, the actual search for solutions fell under the third and fourth goal. The third goal, *improve processes and patient flows*, focused on finding and testing solutions for process improvement. The aim was to streamline processes and align care pathways. Various solutions were often tested to examine the impact of the solutions. Lastly, the fourth goal, *decision support and resource optimization*, was defined as the final step in process optimization and implementation. Research in this area aimed to develop tools that served as decision-support systems to optimize resource usage. The main difference between the third and fourth goal was that in the third, solutions were tested to enable further analyses, while in the fourth, solutions served to make well-informed decisions.

All research goals of the reviewed studies fell into one of these four categories. Since these studies provided a comprehensive basis for research on care pathways and were relevant to this thesis, it could be assumed that the research goals in this theoretical framework were comprehensive as well.

3.2.1 Process Mining

PM is a suitable technique for discovering care processes. Erdogan and Tarhan (2018) stated that this is the primary goal of PM, namely process discovery. Oliveira et al. (2020), Gonzalez-Garcia et al. (2020), and Mans et al. (2008) aimed to demonstrate that PM is a suitable technique for visualizing care pathways. Gonzalez-Garcia et al. (2020) also highlighted the advantage of using Real-World Data (RWD) sets, enabling the mapping of empirical care pathways. The first step in PM involves collecting these RWD sets and extracting usable event logs from them (Gonzalez-Garcia et al., 2020). Based on this data, the care process can be discovered. If available, additional data can be incorporated to provide deeper insights (Gonzalez-Garcia et al., 2020). Thus, PM has the ability to provide data-driven insights into care processes.

Additionally to process discovery, PM is widely used for conformance checking. Mans et al. (2008) pointed out that, in practice, there is often a gap between the desired care pathways and the actual executed pathways. "Owners", such as managers, of the process are often unaware of this gap. The process model resulting from discovery can be used to identify deviations from the desired model (Erdogan & Tarhan, 2018). Rejeb et al. (2018) added that PM can create an interface that enhances communication between professionals and engineers. By detecting deviations and inconsistencies, PM provides opportunities to refine processes to enhance adherence to guidelines.

Beyond process discovery and conformance checking, PM is increasingly used for care pathway improvement. The 'Research Goals-Approach' - matrix (Figure 3.1) showed that PM is not a technique that is generally used for this purpose. However, Yang et al. (2023), Peng et al. (2024), and Rejeb et al. (2018) expanded the application of PM. Yang et al. (2023) developed a new approach that incorporates medical details into the model using statistical methods. This dynamic programming allows for the simulation of experimental outcomes over the long term. Peng et al. (2024) also implemented dynamic programming but adapts patient-specific care pathways based on medical events. This approach adjusted the care pathway according to the patient's health status, streamlining the process. These two studies integrated multiple techniques, including measuring and analyzing KPIs. Similarly, Rejeb et al. (2018) combined PM with DES to implement scenario analysis and randomness. This approach first established a foundation for the current process, and then used DES to improve the model's reliability. These studies illustrated opportunities to extent the application of PM.

3.2.2 Discrete Event Simulation

DES is a widely used modeling technique for analyzing and optimizing healthcare processes. In contrast to PM, DES is more frequently used for the second till fourth objective. DES was used in only two studies for process discovery but was more commonly applied to measure and improve process performance. DES can visualize processes, making it accessible for everyone to better understand the process. Lahr et al. (2020) outlined the three steps of simulation: model building, validation, and experimentation. The model must be built using empirical data from RWD sets to create a reliable model. This was the goal of Rejeb et al. (2018), who used DES to enhance the reliability of a previously built model. In this case, processes were not necessarily improved, but the reliability of the process model was. As such, DES is particularly valuable as a quantitative approach to analyze healthcare processes.

In addition to visualizing care pathways, DES distinguishes itself from PM since it allows for performance measurement. Wood et al. (2022)'s primary goal was to use simulation to visualize a care pathway while also aiming to calculate and statistically evaluate KPIs to assess performance. Another feature of DES is its capability for mathematical analysis, enabling statistically significant conclusions based on different scenarios (Bahou et al., 2018; Pilgrim et al., 2009). Pilgrim et al. (2009) used this feature to perform a cost-effectiveness analysis to determine under which conditions a specific test was cost-effective. Bahou et al. (2018) used the mathematical analysis feature, in combination with DES's next-event technique, to track patients in a simulation under various conditions to improve patient flow. Thus, DES provides a reliable approach to evaluate and improve the efficiency of healthcare processes, resulting in data-driven decision-making.

Another feature of DES to evaluate care pathways is the incorporation of a time-horizon (Cardoen & Demeulemeester, 2008). Patients may remain in a system for a long time due to lengthy treatments. Moreover, short-term indicators, such as waiting times, can be important for operational performance. Cardoen and Demeulemeester (2008) used this time-horizon feature in their study, analyzing flow probabilities, durations, and timings to evaluate and improve a care pathway. Babashov et al. (2017) and Chemweno et al. (2014) highlighted DES' ability to implement stochasticity and 'what-if'-scenarios. Chemweno et al. (2014) used scenario analysis to measure the impact of potential changes to the system. Babashov et al. (2017) expanded on this by using scenario analysis to decide the optimal allocation of resources to reduce, for example, waiting times. Lastly, Lahr et al. (2020) followed all modeling steps to quantify pathway logistics and performed cost-effectiveness analyses for activities and treatments, ultimately determining resource strategies based on these insights. These studies illustrated that DES is a powerful tool for both short-term and long-term process improvements and decision-making, which is an essential tool in resource management.

3.2.3 Business Process Model and Notation

BPMN is a standardized graphical language technique for modeling business processes, including healthcare workflows. Compared to PM and DES, BPMN was mentioned less frequently in literature. Its primary advantage lies in its ability to simplify complex processes by incorporating subprocesses, activities, and relevant data into a structured model (Ajmi et al., 2015; Combi et al., 2017; Yan et al., 2018). Yan et al. (2018) utilized this by focusing on identifying deviations in care pathways. In their study, event logs were linked to a BPMN model to detect variations. Ajmi et al. (2015) added that, under its simplified representation, BPMN takes subprocesses, activities, and other data into account. This makes it possible to make complex systems more transparent. Furthermore, other techniques, such as simulations, can be integrated for process optimization (Ajmi et al., 2015; Combi et al., 2017). Ajmi et al. (2015) combined BPMN with simulation to quantify bottlenecks and subsequently optimize processes. Combi et al. (2017) also applied this combination approach. They pointed out that BPMN's extensibility makes

the technique well-suited for healthcare. Combi et al. (2017) demonstrated in their study how BPMN can be integrated with other methods to visualize care pathways in a more standardized way. All three articles used a conceptual care pathway for the BPMN model. Despite its benefits, BPMN is primarily a visualization tool and is less suited for process discovery.

3.3 Conclusion Modeling Technique

The goal of this chapter was to identify the most suitable technique for modeling the AF care pathway at Isala Heartcenter. These care pathways need to be mapped to evaluate the current situation. As stated in Chapter 2, AF care at Isala involves numerous pathways without a clear explanation. Currently, there is no concept for the desired care pathways. More structure starts by gaining insight into the current AF care delivery at Isala Heartcenter. The literature search on modeling techniques for care pathways primarily highlighted the use of PM, DES, and BPMN. Each of these techniques has its own advantages, drawbacks, and suitability for different purposes.

BPMN is primarily used for visualization of complex processes. The studies that referenced it indicated that it builds upon a conceptual model which is already available. Since this is not the case for this thesis, and the process must be derived from HIS data, BPMN is not the most suitable technique for this research.

DES is mainly used to simulate processes and test optimization strategies. Like BPMN, DES requires a conceptual model as a basis for simulation. However, DES has the advantage over BPMN of incorporating stochasticity, making it more reliable for simulating processes. The DES model requires input data and probability distribution to simulate an accurate care pathway. Since neither the conceptual model nor the necessary input data are currently available, DES is not suitable for the main purpose of this thesis.

PM is primarily suitable for process discovery and the analysis of deviations according to literature. Event logs from RWD sets form an actual process, allowing patient pathways to be visualized. In this thesis, event logs of patients with AF could be used to construct a model that reveals their pathways. This model could identify areas for improvement and extensions could be developed for further process optimization.

As demonstrated in the 'Research Goals Approach' - matrix (Figure 3.1) and the analysis above, PM is the most suitable technique for this thesis. Isala has a database containing RWD for event logs, which can be used to model the actual pathways of AF patients, providing insight into processes at the Heartcenter.

3.4 Key Performance Indicators

After we established PM as the most suitable modeling technique, we determined the KPIs. The KPIs were essential for evaluating the balance between standardization and personalization of the AF care pathways. They were derived from literature on PM, care pathways, and through conversations with stakeholders. Figure 3.2 illustrates the five KPIs we established for this research.

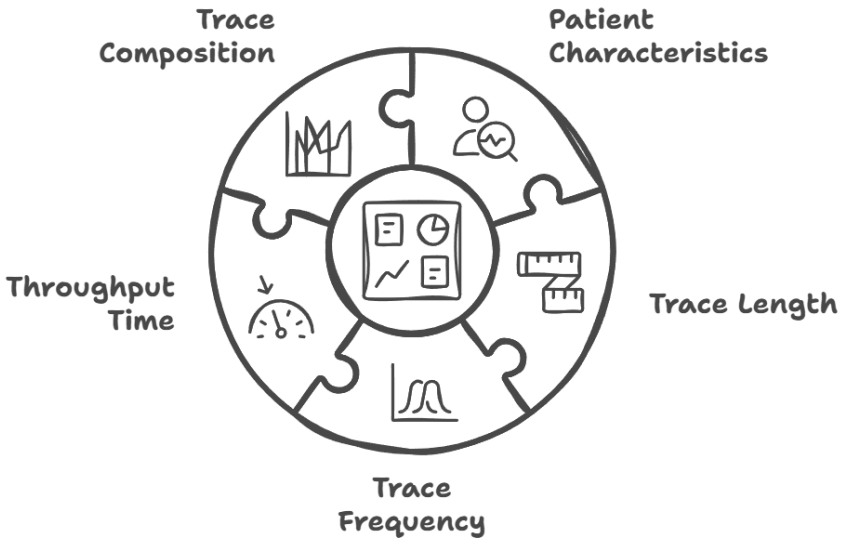


Figure 3.2: Key Performance Indicators for Process Mining

Since progression and occurrence of AF are correlated with **Patient Characteristics**, it is important to have a comprehensive overview of the patientgroup. Although it does not measure performance, the patient characteristics need to be kept in mind when evaluating the other KPIs. Therefore, we include the patient characteristics in this KPI-framework. For AF, these characteristics are commonly reflected in a CHADS2-score, as this score serves as an indicator for complications (Letsas et al., 2013). In this research, we stratify the CHADS2-score to age and comorbidities, as they should be treated for effective AF management. Hence, we expect that higher age and/or more comorbidities are reflected in the care pathways of those patients.

Additionally, we established **Trace Length** as a KPI. The trace length indicates how many care activities a patient had during their care pathway. Gonzalez-Garcia et al. (2020) also used this KPI, which they reflected in a trace explorer. We decided to use trace explorers as well, since they visualize both trace length and trace composition. This KPI provides information about how activity-dense the care pathway of a patient is. Therefore, we can connect the number of care activities and the type of care activities.

Trace Composition was our third KPI and comprises (1) the percentage of patients with a type of care activity, (2) the average number of a care activity per patient, (3) the combinations of care activities per trace, and (4) the sequences of care activities per trace. This KPI is also used by Yang et al. (2023), Peng et al. (2024), and Gonzalez-Garcia et al. (2020). They measured how many patients had a certain type of care activity and in what order the care activities took place. These compositions provided insight into the care pathways and the standardization of the sequences. Moreover, the composition of the care pathways that occurred less frequent became insightful.

The fourth KPI was **Trace Frequency**, which indicated how many patients follow a specific trace. Gonzalez-Garcia et al. (2020) used this indicator to discover whether patients follow the expected path. Therefore, the trace frequency was an indicator for the level of standardization of a care pathway. If a trace's frequency was high, the care pathway occurred frequently and was, therefore, considered standardized. Since Mans et al. (2008) and Erdogan and Tarhan (2018) emphasized the added value of visualizing care pathways, we reflected the trace frequencies in process models and trace explorers.

The last KPI was the **Throughput Time**, i.e., the time a patient spent in the system since their first appointment in weeks. This KPI was also used by Rejeb et al. (2018), Mans et al. (2008), and Gonzalez-Garcia et al. (2020). We calculated the throughput time as an average

in weeks for the patient cohort, as well as the time between two care activities in weeks. We reflected the latter in process maps as done by Gonzalez-Garcia et al. (2020). This indicated which patients required more time, when combined with the other KPIs, we were able to explain why.

By combining these KPIs, we gained a comprehensive overview of the care pathways, allowing us to detect both expected and undesirable variations. This enabled us to identify areas for improvement in how to balance standardization and personalization of the AF care pathways.

4. Process Mining Model

This chapter discusses the input data and design of the PM model. First, Section 4.1 elaborates on how the data was collected and which assumptions were made. Subsequently, Section 4.2 discusses the steps how the data was processed. Section 4.3 discusses the model design. This includes the software, a formulation of the model, and the assessment of the KPIs. Additionally, Section 4.4 explains how the dataset and model were validated and verified. Last, Section 4.5 outlines the design of the experiments.

4.1 Data Collection

This section describes the data collection process via CTcue, an AI tool that retrospectively searches electronic patient records from HiX, the HIS of Isala.

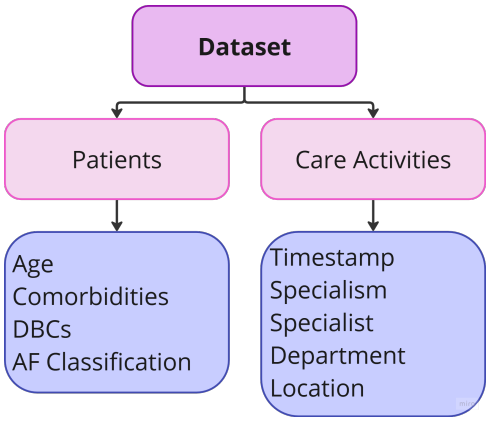


Figure 4.1: Overview Dataset Collected via CTcue

Figure 4.1 provides a general overview of the required data. This data was collected over a period of 18 months since the start date of each patient. Medical experts assumed this period sufficient to derive a reliable treatment strategy. The start date was defined by the date the first Diagnosis Treatment Combination (DBC [NL:Diagnose Behandel Combinatie]) - a code that bundles the care activities related to a diagnosis per period of three months - for AF was opened. The search queries in CTcue were designed such that all care activities during the 18 months succeeding that start date were retrieved. If a search term covered a different time period, this is explicitly noted and motivated in the next section. The data was collected in January 2025, thus, the latest date that patients could have started their care pathway was 01-07-2023. To create a substantial patient cohort, we included patients who started their AF care pathway at Isala between 01-01-2023 and 01-07-2023.

Section 4.1.1 provides a detailed explanation of these data points and the rationale behind their inclusion. Section 4.1.2 states the assumptions that were taken into account while collecting the data.

4.1.1 Dataset

This section details the components of the dataset, explaining their relevance. A detailed explanation of the inclusion and exclusion criteria can be found in Appendix C.1, including the specific search queries in CTcue.

Patient Characteristics
For each patient, we collected the patientID, age, and comorbidities at the start of their care

pathway. The patientID was used to retrieve data directly from HiX if data was not found with the CTcue search query. For example, the care provider who executed a certain care activity. Age and comorbidities were included to gain a comprehensive overview of the patient cohort. Age was measured at the time of the first care activity in the care pathway to establish a uniform reference point for all patients.

The comorbidities diabetes, obesity, and hypertension were included in the dataset. We chose these comorbidities based on the ESC guidelines, as they might have influenced recurrence, readmissions, and complications. Moreover, these comorbidities were quantifiable and were expected to be stable during the 18 month-period. Comorbidities such as physical activity and alcohol consumption were not included in the dataset due to measurement difficulties and variability over 18 months. The presence of the comorbidities was obtained at the start of the care pathway, as managing these risk factors should have been the first step in any care pathway. Their presence should therefore have influenced the subsequent trajectory.

DBC

Patients were included in the dataset if their first DBC for AF was opened between 01-01-2023 and 01-07-2023. A first DBC can be identified by code 11, while subsequent DBCs have code 21. Patients with any AF-DBC before 01-01-2023 were excluded.

All DBCs related to a specific diagnosis were grouped under a shared *Episode of Care ID* [NL: zorgtrajectnummer]. This overarching identifier remains the same for all DBCs associated with one disease. Since each care activity contained the DBC code, and all DBCs for the same disease contained the same Episode of Care ID, this ID connected all care activities related to a specific disease.

In addition to the initial AF-DBC, all subsequent cardiological, cardiothoracic, and anesthesiological DBCs were retrieved. Given the complexity of AF, patients might have visited the hospital for a variety of cardiac conditions. Since the hospital does not open multiple DBCs simultaneously, care activities related to AF might have been assigned to a DBC for a different cardiac condition. Additionally, patients might have visited the outpatient clinic to discuss multiple conditions. To ensure all relevant care activities were captured, the Episode of Care IDs of these subsequent DBCs were obtained to validate relevance for the AF care pathway.

In summary, the Episode of Care ID served as the key identifier that connected all disease-related care activities in a patient's pathway. By retrieving only the Episode of Care IDs for AF and related diseases, we ensured that all included care activities were connected to the AF care pathway.

Initial Classification

The ESC guidelines described different care pathways for various classifications. Thus, the classification determines which care activities should or should not appear in the care pathway. Therefore, the classification is essential for performing conformance checking against the ESC guidelines.

For each patient, the initial AF-classification was retrieved from their medical records. In HiX, the classification field was not often used, therefore, we searched in the text of reports via CTcue. Patients might have either begun their pathway at the hospital or were referred by their GP. Since the classification might have been documented in a referral letter, medical records were obtained starting two months before the opening of the first DBC to ensure all relevant information was gathered.

Care activities

Care activities define a patient's care pathway. These activities encompass all (outpatient) clinical appointments, day admissions, clinical treatments, readmissions, etc. Tracking these activities provided a comprehensive overview of all activities from the initial visit till 18 months

later.

We did not filter the query for care activities to the cardiology department, since we wanted to retrieve as many care activities as possible. The care activities were linked to the AF care pathway later on, as described in 4.2.

For each care activity, the Episode of care ID, care activity code, description, department, location, performing care provider position, and start date were collected. These were the data points we required to perform PM, detect pathway variations, and identify areas for improvement to balance standardization and personalization of the AF care pathways.

4.1.2 Assumptions

Several assumptions were made during data collection and processing. Despite these assumptions, we aimed for a model that represented real-world processes, ensuring reliable conclusions. We established the assumptions with medical experts, DBC experts, and data analysts. Moreover, these experts helped implement these assumptions in the search queries and the model.

- All patients had a DBC code indicating their initial diagnosis of AF rather than another underlying condition at the start of their care pathway. Thus, we assumed the patient population comprised individuals whose care pathways started with the same overarching condition, AF. For example, patients with a DBC for heart failure at the start of the care pathway were excluded. We consulted medical and DBC experts to create the queries such that this assumption could be implemented.
- The first registration at Isala was assumed to be a good indicator of the start of the care pathway. Patients who underwent treatment at another hospital and were subsequently referred to Isala were also included. This was the first time physicians of Isala had an influence on the care plan. Cardiologists agreed with this assumption, as they are responsible for the treatment strategy.
- Based on an expert's opinion (a cardiologist), we decided upon a follow-up period of 18 months. This period should be sufficient to make valid statements about the treatment strategy. Since a patient should be in the system for at least 18 months, the patient must be diagnosed at last on 01-07-2023. We decided to include patients who are diagnosed between 01-01-2023 and 01-07-2023 to ensure a large enough patient cohort, while ensuring that their treatment strategy represents the current work processes.
- By following all patients for the same period of time, we assumed that their care pathways were allowed to be compared. This ensured that observed variations in treatment and follow-up were due to differences in care delivery policies. The data analysts of Isala agreed with this statement.
- The first registered classification with which the patient presented was assumed to determine the care pathway, in accordance with the ESC guidelines. If a classification was recorded later in the trajectory, it was assumed to apply to the preceding care pathway.
- In accordance with a DBC registration officer, the period of two months before the opening of a new DBC was assumed to be sufficient to detect a referral.
- We assumed that BMI and blood pressure measurements taken within one month of opening the DBC accurately reflected the patient's condition at the start of the care pathway. This assumption was validated by a cardiologist.
- We assumed that data in the HiX electronic patient record was accurately and promptly registered. This included DBC codes, medical records, appointments, procedures, timestamps, and comorbidities. Healthcare providers are legally required to document this information accurately for billing and care quality purposes. However, if inconsistencies or missing values were found, manual validation was executed in collaboration with experts when possible.

- If a specific search query yielded no results, we assumed it was not applicable to the patient in question. For example:
  - All activities that we found with the queries were all the activities that took place. Since the care activities for the search queries were established in collaboration with a DBC registration officer, we validated this assumption.
  - Undocumented comorbidities were interpreted as absent, in accordance with a cardiologist.

4.2 Processing

After all search queries were executed, the data was assessed and labeled in CTcue, after which we processed it in RStudio. After the processing, the dataset was suitable for an event log, which served as the input for PM. The steps that involved this process of assessing, labeling and processing, are detailed below. Figure 4.2 contains an overview of these steps.

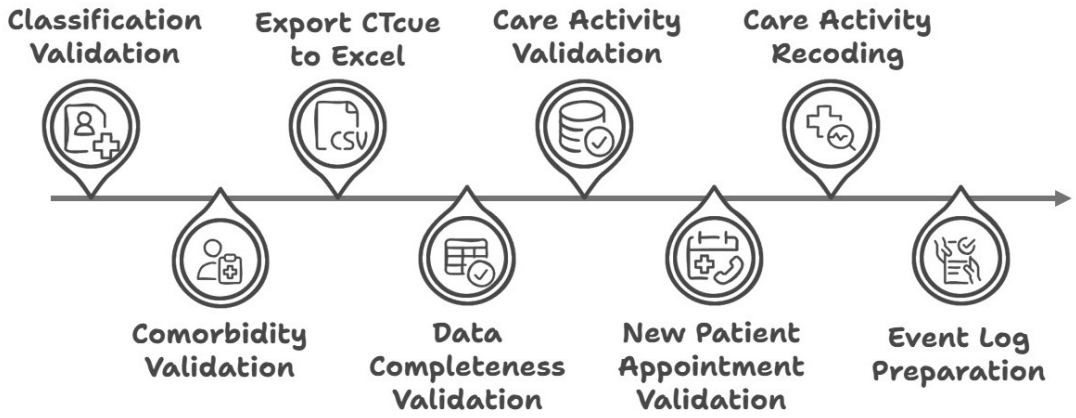


Figure 4.2: Data Processing Steps

Step 1: Classification Validation
For each included patient, we checked if there were medical records that stated the AF classification. At first, the snippets of the report that were shown in the "Data validation > Classification > Content" plane of CTcue were examined, and the classification was labeled according to the classification shown in the snippet. The labels were *Paroxysmaal* [EN: paroxysmal], *Persisterend* [EN: persistent], and *Permanent*.

Paroxysmaal appeared in the text as "paroxysmaal" and "paroxismaal", *Persisterend* as "persisterend", and *Permanent* as "permanent" or "chronisch". The classifications of patients without a report were labeled *Onbekend* [EN: unknown].

Subsequently, we validated the labels of all included patients to check if the patient was not familiar with AF before 01-01-2023. Despite the thorough search queries, it was possible that some patients incorrectly ended up in the dataset. Therefore, the reports of the included patients with a classification label *Paroxysmaal*, *Persisterend*, or *Permanent* were screened to exclude pre-existing AF. The classification labels for patients already diagnosed with AF were changed to *Recidief* [EN: recurrence].

Step 2: Comorbidity Validation
In this step, we labeled the comorbidities as *Aanwezig* [EN: present] or *Afwezig* [EN: absent]. All labels were initialized as *Onbekend*. The search queries were designed such that a result indicated the presence of a comorbidity. Therefore, per comorbidity, we first filtered on "results", and labeled all data points as *Aanwezig*. Then we filtered on "no results", and labeled all datapoints

as *Afwezig*. We repeated this for all three comorbidities. If executed correctly, there should be no *Onbekend* labels anymore.

Since we strived for 100% data completeness regarding the comorbidities, we checked if each included patient had a label for each comorbidity. We did this by filtering on the label *Onbekend* in the "Data validation > Comorbidity > Validation" plane in CTcue. If there were no results, all patients had the comorbidity labeled as either present or absent. Subsequently, we screened the labels to check for unusual data, e.g., outliers, to verify whether the labels were correct. Additionally, we examined the medical records of each patient to validate the correctness of the labels.

Step 3: Export CTcue to Excel
At this step, the dataset was labeled as much as necessary in CTcue and was ready to be exported. The last step in CTcue was to select the correct columns for export. We selected these columns in the "Data validation > Question > Customize column" plane. Table C.8 in Appendix C.2 contains all selected columns. After this, the data was ready to be exported to an Excel file and loaded into RStudio.

Step 4: Data Completeness Validation
After the data was exported to an excel file, we screened the file to evaluate the completeness of the data. For this thesis, we only screened the patients with a classification label *Paroxysmaal*, since this was the target group in the model. For all these patients, we checked:

- Did all patients have a registered age at the first appointment (care activity code 190060 or 1900164)?
- Did all patients have a first DBC and is the associated diagnosis AF?
- Did all patients have at least one care activity?
- Did all DBCs have an episode of care ID?
- Did all care activities have a start date and timestamp?
- Did all care activities have a care activity code?

These checks ensured that the data was sufficient and correct to serve as input for PM. If a patient did not have at least one care activity, the patient was excluded from the dataset, since we could not evaluate their pathway. Though, we looked into their medical records to find out why this patient appeared in the dataset. If data on the patient's age at their first appointment, the Episode of Care ID associated with AF, as well as any missing care activity codes and time stamps was missing, we used the patientID to open the patient's medical record in HiX to retrieve this data.

Step 5: Care Activity Validation
After the missing data was solved and the patient group was adjusted accordingly, we made the last few adjustments to the dataset in RStudio. First, all care activities should have been either requested or executed by the cardiology specialism. The search queries were designed such that appointments requested by cardiology but executed by, e.g., an anesthesiologist or appointment requested by, e.g, a neurologist but executed by a cardiologist were all included in the dataset. There might have been care activities that incorrectly appeared in this dataset. By this check, all care activities not related to the cardiology department were removed from the dataset. The care activities requested or executed by cardiothoracic surgery needed to be validated to ensure that the care activity was related to AF. We did this by evaluating the DBC corresponding to the Episode of Care ID. If the DBC was not related to AF, or a result of AF, the care activity was removed from the dataset.

Step 6: New Patient Appointment Validation
The dataset resulting from Step 3 contained all patients whose care pathways we were going to visualize. Since we no longer needed to look up additional data, we made the patientIDs

anonymous. We did this by recoding each patientID to a random number and kept the key file in a secured environment.

It is important that the patients' care pathways were correctly documented, to ensure representative pathways. Patients should only have had one appointment as a new patient. If we saw that a patient had multiple registered new patients appointments, we only kept the earliest registered new patient appointment and recoded the succeeding appointments as "follow-up".

There might have been patients who did not have a registered first appointment, but started their care pathway otherwise. For these patients, we looked into their data to obtain additional information about their starting point.

Step 7: Care Activity Recoding
Now that the dataset was essentially complete, it was prepared for an event log. The data points had many and/or long descriptions in the dataset. For example, there were twelve descriptions of a physician. Moreover, an outpatient clinical appointments was described as "190060 First outpatient clinical appointment". We wanted the process model resulting from the event log to be directly interpretable. Therefore, we encoded the data points such that the starting point of the care pathway, the follow-up appointments, readmissions, day admissions and clinical treatments were clear. Each care activity could have taken place at different locations and executed by different care providers. Therefore, per activity in the care pathway, we distinguished the care activity type, locations and/or care providers. Table C.9 in Appendix C.2 provides an overview of the exact locations, departments, and care providers and the corresponding activity descriptions.

Distinguishing between a first appointment and follow-up consultations do not influence a treatment strategy, hence, we did not incorporate this in the activity description. All consultations where defined as "consult". Consultations took place at the outpatient clinic (OC). This was the overarching term for the location of all consultations. At the OC, the care provider, usually a physician or resident, saw patients with a variety of conditions. The AF-OC is a subset of the OC, where all patients were suspected to have AF and is led by physician assistants (PAs). A consultation might have also been at the FHLA, either in Zwolle or Meppel. We assumed there is no difference between policies in Zwolle and Meppel. Therefore, the appointment description provided information about the department (OC/FHLA) and, if relevant, the care provider (Physician/PA).

Furthermore, we wanted to include the ECVs, PVIs and hisbundle-ablations into the event log. The ECVs were divided into elective ECVs, in Meppel, and immediate ECVs, in Zwolle. Hence, the location of the ECV care activity was key to make this distinction. The activity description included this location, by adding ZWO or MEP. For PVIs and hisbundle-ablations, the locations or care providers were not important, since they were all executed in Zwolle by a specialist. Their activity descriptions only contained PVI or, for the hisbundle-abaltion, HIS.

Step 8: Event Log Preparation
The last mutation to the dataset involved adding an index and a status, as they are required for an event log. The index was used as the activity_instance_ID and created by numbering each row in the dataset. This index classifies a specific event of a specific patient. The status indicates the status of an activity instance, usually *start, schedule, complete, etc.* Since we did not investigate the event durations, this variable was not relevant to the model. Therefore, we identified each status as "complete".

After these eight steps, the dataset was ready for PM and the experiments.

4.3 Model Design

After the literature review, we selected PM as the most suitable technique for the objective of this thesis. We chose RStudio in combination with the *bupaR*-package for the implementation of PM. This software is capable of building statistical models tailored to the complex and unstructured nature of AF care pathways at Isala. The clinical data team at Isala was already familiar with RStudio, which ensured that the tools and methodologies used in this thesis are accessible and applicable for continued use.

BupaR offers specific functionalities, such as the ability to discover and analyze care pathways based on their frequency. The package is able to focus on the most common paths, the rarest, or everything in between. These capabilities are crucial for revealing inefficiencies in the highly variable care processes of AF patients. Furthermore, the integration of RStudio enables a data-driven, Isala-specific approach, using real-world data from the hospital to create the event logs.

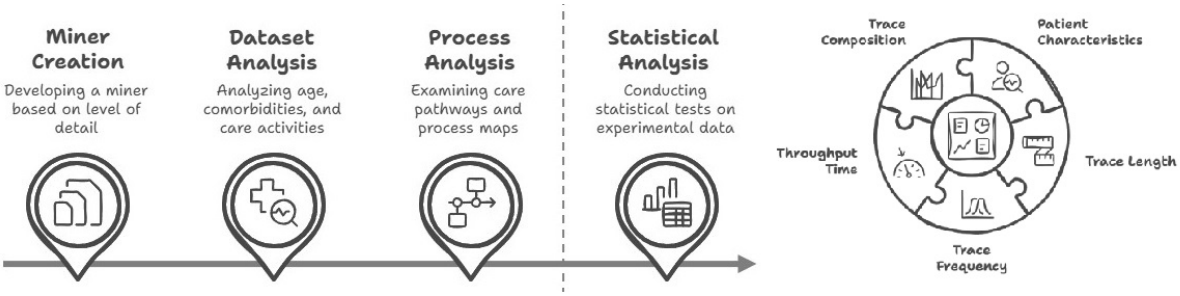


Figure 4.3: Process of Model Creation, Analyses and KPIs

Figure 4.3 illustrates the process of creating the model, performing the analyses, and KPIs we used for the identification of areas of improvement. First, we developed the model in RStudio. Subequently, we performed two main analyses; dataset analysis and process analysis.

4.3.1 Model Creation

The dataset consisted of many different data points, due to the various care activities, providers, and locations. In Step 7, we described how we categorized these data points. During the Model Creation, we utilized these categories to create activity descriptions. The aim of these activity descriptions was to simulate a Fuzzy Miner. This type of Miner allowed for zooming in and out on the details of processes on the level of detail (Yang et al., 2023). The Fuzzy Miner incorporates less frequent activities into overarching activities while zooming out. Therefore, all activities are still present in the model (van der Aalst, 2012). We simulated the Fuzzy Miner by creating three levels of detail. The first level, Basic, solely described the type of care activity. This level was used to compare the care pathway with the ESC guidelines, as they used the same level of detail. The second level, Medium, distinguished the care activities based on ECV location. The last level, Detail, divided the care activities further on care provider. This level provides a comprehensive overview of the care pathway and, therefore, detection of treatment strategy variations due to the department or care provider.

The activity descriptions were incrementally assigned to the dataset in three columns with corresponding levels of detail. They were called “Basic”, “Medium”, and “Detail”. The columns were initialized as “Unknown”. Table 4.1 provides how the columns reflected the care activities:

Basic	Medium	Detail
Consult	Consult	Consult_Arts
FHLA	FHLA	Consult_PA
ECV	ECV_MEP	FHLA
PVI	ECV_ZWO	ECV_MEP
HIS	PVI	ECV_ZWO
	HIS	PVI
		HIS

Table 4.1: Care Activities at Three Levels of Detail

In case an activity description could not be assigned to a level, we retained the description from the preceding level. Next, we validated the columns by retrieving the descriptions present in each column and checked whether they aligned with the expected descriptions. If any descriptions appeared in an incorrect column, e.g., Consult in the third column, additional information about the activity, such as the location and care provider, was retrieved from HiX. The additional information was then incorporated in the dataset to complete the dataset.

4.3.2 Dataset Analysis

The dataset analysis provided a comprehensive overview of the patient cohort by describing the age and comorbidities. This is represented as the KPI "Patient Characteristics". Moreover, we examined the care activities that occurred in the dataset, to gather information about their occurrence. This analysis did not provide insight in the specific traces or their standardization. First, we plotted the age in a distribution graph and provided the descriptive statistics to give a complete overview. Furthermore, we illustrated the presence of comorbidities by an Euler diagram. Additionally, we analyzed the occurrence of care activities at the Medium level, as it provides sufficient information to check conformance with AF-CARE, while distinguishing between elective and immediate ECV to incorporate Isala specific activities. This analysis provides the first insight into the trace composition. The occurrence of care activities was shown and evaluated in three ways:

1. A distribution graph of the total number of care activities per patient, in percentage of the total patient population. This graph provided data on how many care activities patients had during their 18-month care pathway. It did not show what the type of care activities were or in what order. However, it informed us whether certain subpopulations might have required more or less activities than others.

2. An Euler diagram of how many patients had what combination of care activity types. This Euler diagram did not show the order or occurrence rate of care activities per care pathway, but provided information about common types of combinations of care activities.

3. A table in which we calculated how many times a care activity took place, how many patients had this type of care activity, what proportion of the total patient population had the care activity, the mean number of times a patient, who had this care activity, had it, and the standard deviation of the mean. This table allowed us to evaluate differences between the occurrence of care activities within or between patient populations.

4.3.3 Process Analysis

After the data analysis, we continued with the process analysis. During this analysis we gathered information about the specific traces, i.e., care pathways, and their standardization. The level of standardization relied on a process map, trace explorer, the throughput time of patients, and

the trace frequencies. Therefore, we created an event log using the *eventlog* function. Algorithm 1 shows the pseudocode for the event log function.

Algorithm 1 Create an Event Log

```
Create a new eventlog
    Eventlog.name ← eventlog(
      case_id = "dataset[patient_id]",
      activity_id = "dataset[care activity]",
      activity_instance_id = "dataset[index]",
      timestamp = "dataset[start date]",
      lifecycle_id = "dataset[status]",
      resource_id = "dataset[care provider]" )
```

Based on this event log, we created a process map using the *process_map* function. The process map visualized the flow of patients using nodes and edges, i.e., the trace composition. Nodes represented care activity, with each node displaying the number of times the activity occurred. Edges illustrated the transition between activities, with their thickness proportional to the frequency the path is taken. Next to each edge, there was a number that indicated how often the path was followed and the average number of weeks patients took to move from one node to the next. Algorithm 2 contains the pseudocode for the process map function.

Algorithm 2 Create a Process Map

```
Create a new Process Map
    Process.Map.Name ← process_map(Eventlog.Name,
      type_nodes = frequency("absolute"),
      type_edges = frequency("absolute"),
      sec_edges = performance(mean, "weeks"),
      render = TRUE )
```

Subsequently, we retrieved the distinct traces that occurred in each dataset. In those traces, we saw the activities, care providers, and locations, providing a complete overview of the paths. Next to the traces, we obtained information about the absolute trace frequency, i.e., how many patients followed that same trace. We obtained this information with the *trace_explorer* function. Algorithm 3 shows the pseudocode for the trace explorer function.

Algorithm 3 Obtain distinct traces

```
Obtain the distinct traces in a dataset
    Eventlog.Name % > % trace_explorer(coverage = .xx,
      coverage_labels = c("absolute","cumulative"),
      show_labels = FALSE )
```

Finally, we calculated the throughput time and the trace frequency. These KPIs provided a general idea of the throughput time and trace frequency of a specific patient cohort. The throughput time was the time period during which patients had care activities, from the first care activity to the last care activity in an 18-month period. We retrieved this using the *throughput_time* function. The trace frequency indicated how many time a certain trace, i.e., care pathway, occurred in a dataset. We obtained this frequency with the *traces* function. This KPI provided information about the standardization of care pathways. If there was a high trace

frequency, the care pathway was highly standardized, and the other way around. We evaluated the trace frequency by the descriptive statistics.

Algorithm 4 contains the pseudocode for the throughput time function.

Algorithm 4 Obtain throughput time

Calculate the throughput time of the patients

```
tt.Eventlog.name ← Eventlog.Name %>%
      througput_time(level = "log", units = "weeks")
```

Algorithm 5 shows the pseudocode for the traces function.

Algorithm 5 Obtain trace frequency

Calculate the trace frequency of the event log

```
tr.Eventlog.name ← as.data.frame(traces(Eventlog.name))
```

4.3.4 Statistical Analysis

We initially conducted these analyses for the entire dataset to gain a comprehensive overview of the whole care process, as described in 4.5.1. Subsequently, we conducted three experiments to compare specific processes and patient groups. These focused on comparing patients' starting points and treatment strategies, ultimately identifying the processes that indicated imbalance of standardization and personalization. In Sections 4.5.2 - 4.5.4, we provide a more detailed explanation of these experiments. During the experiments, the data and process analyses were performed again, but supported by statistical tests to make well-founded statements about the differences. For both sets, the ages, the averages [± Standard Deviation] of care activities, combinations of care activities, and throughput time, we first executed the Shapiro-Wilk test to determine whether the data was normally distributed. The Shapiro-Wilk test is suitable for small sample sizes ($n < 50$) as well as for larger samples (Mishra et al., 2019). We chose a p-value below 0.05 to indicate a normal distribution. Subsequently, if both datasets were normally distributed, we performed Levene's Test for Homogeneity of Variances, determining whether the variances were statistically significant different ($p < 0.05$). There were three tests that could have followed:

1. If both datasets were normally distributed and their variances were not proven statistically significant different: we performed the Two Sample t-test.
2. If both datasets were normally distributed and their variances were statistically significant different: we performed the Welch Two Sample t-test.
3. If one or both datasets were not proven to be normally distributed: we performed the Mann-Whitney U test.

For all three tests, we chose a p-value below 0.05 to indicate a statistically significant difference between the two compared variables, such as age or mean HCs per patient.

The comorbidities and proportion of patients with a type of care activity were denoted as frequencies. To compare the frequencies, we performed Fisher's Exact Test for Count Data. This test is suitable for small numbers (Hae-Young, 2016), and we expected that many frequencies were less than 5, as we expected unstandardized care. Again, we decided that a p-value below 0.05 indicated a statistically significant difference.

4.4 Verification and Validation

Verification and validation during the development of the model were important steps to ensure the correctness and accuracy of the model. These steps align with the theory of Aspland et al. (2021), that combined data and collaboration with professionals.

The verification of the model involved carefully reviewing all steps in data processing and modeling process, ensuring that all functions were executed correctly. To keep the verification manageable, the model was initially tested with a smaller, simplified dataset. This allowed for a step-by-step check of whether all components functioned correctly before loading the complete dataset. During the verification, special attention was paid to preventing data loss when converting the original dataset into the event log.

Additionally, the code utilized the pre-programmed functions of the *bupaR*-package in RStudio. Assuming that the event log was correctly structured, and the *bupaR*-package is verified, we expected that the process model accurately reflected reality.

The validation of the model took place throughout the entire process in collaboration with stakeholders from various disciplines. From the creation of the dataset to the discussion of the experimental outcomes, regular conversations with relevant experts took place, making the validation a continuous process. The dataset was reviewed in consultation with medical specialists to ensure the data was both representative and relevant to the research question. In these discussions, the relevance as well as the impact of various variables were examined. Before creating the model, expectations were set regarding the influence certain variables might have on the process. After the model was developed, the predetermined expectations and other influences were revisited to verify the model's validity. We asked the questions:

- "What are the current care pathways for patients with AF at Isala?"
- "To what extent is AF-care standardized in the Heart Center?"
- "What patterns can be detected in the care pathways of AF patients?"
- "How can we explain the processes that result from the model?"
- "What processes do we want to improve?"

These questions were tailored to specific experiments, but served to obtain a comprehensive overview of the current practice.

In addition to medical experts, data experts were involved to ensure that the data was correctly represented within the model. The availability, structure, and interpretation of the data were thoroughly discussed. The model's usability for further research or possible expansion to other care pathways was also assessed. Furthermore, the model was reviewed with the innovation team experts within the hospital, focusing on its practical applicability, such as identifying relevant areas for process improvement.

By incrementally building and testing the model with smaller datasets and involving experts throughout the process, the validity and reliability of the model, its outcomes, the conclusions, and recommendations were ensured.

4.5 Experimental Design

In this section, we describe the experiments we executed. First, we created the base case (experiment 1), where we performed the dataset and process analyses for the complete dataset. For the second experiment, we evaluated the care pathways of patients who started at the OC vs at the FHLA. Then, the third experiment served to compare the care pathways of patients who started at the OC with a physician and patients who started at the AF-OC. The last experiment compared the care pathways of patients with and without an ECV. All these subsets were areas of interest to identify the balance between standardization and personalization, by

comparing different starting points and treatment strategies. These experiments were designed in collaboration with stakeholders.

The event logs, process maps, statistics, and other visualizations were created for all (sub)datasets used for the experiments. Based on the KPIs described in 3.4, we identified processes that indicated an imbalance between standardization and personalization. Subsequently, we compared the subsets of the second to fourth experiment to see if there were differences in the care pathways. For example, differences in how long patients were in the system or how many care activities were involved in care pathways. The differences were supported by a statistical analysis, to validate whether they were statistically significant.

4.5.1 Experiment 1: Base Case

This experiment served as the Base Case, as it performs the dataset analysis and process analysis for the complete dataset. These analyses provided a comprehensive overview of the patient cohort collected via CTcue. Through this experiment, we obtained information about the age of the group, the comorbidities, and the occurrence of activities. We expected the process maps and trace explorers resulting from the process analysis to be comparable to the care pathways designed in AF-CARE (Figure 2.1), as all patients with paroxysmal AF should fit this framework. Therefore, we expected the process map and trace explorers to show outpatient clinic appointments and PVIs.

Since the Base Case served to check conformance to AF-CARE, we executed the process analysis, as described in 4.3.3, on the Basic level. The process map and trace explorer only showed types of care activities, allowing us to compare the care pathway to AF-CARE.

4.5.2 Experiment 2: Starting at the OC vs FHLA

During this experiment, we compared the care pathways of patients who started at the outpatient clinic and of those who started at the FHLA. Therefore, we created two subsets based on the care activity types on level Basic. We suspected that patients who started at the outpatient clinic had fewer care activities and a lower throughput time. This was due to the fact that patients were already expected to have AF when they were referred to the outpatient clinic. When starting at the FHLA, we expected a more conservative approach, since the physician does not know the severity of the symptoms or the classification of AF yet. Hence, it took more time to create a suitable treatment plan. Furthermore, we expected the patients who started at the FHLA to be older than the patients who started at the outpatient clinic and/or the patients showed more comorbidities, since they should only be referred to the FHLA if they had a higher risk of stroke. That risk should be determined by the CHADS2 score, increasing with age and/or comorbidities. We only considered patients who started at the outpatient clinic or the FHLA. Therefore, we did not include patients who had a different (registered) starting point in the subsets of the data.

Since we were were interested in the care activity types following the OC and the FHLA, we executed the process analysis on the Medium level. This allowed us to distinguish all care activity types, including immediate and elective ECVs. With this experiment we aim to evaluate the influence of location and not care provider, therefore, the distinction in care provider is not necessary.

4.5.3 Experiment 3: Starting at the OC vs AF-OC

The third experiment was designed to evaluate the treatment plans created by physicians and PAs. The physicians hold outpatient clinic appointments for all cardiological patients, while the PA has different outpatient clinics for different conditions, in this case, the AF-OC. Additionally, physicians have less time per patient than a PA during a consultation. These factors may have led to different treatment plans. We suspected that treatment plans designed

by a PA corresponded closer to the guidelines and were more tailored to the patient, as the PA is specialized in AF and had more time to properly assess the patient and create the plan. Therefore, we expected to see a lower throughput time, fewer appointments, and less consultations between the first appointment and a PVI compared to patients who were seen by a physician. We did not have any hypotheses regarding patient characteristics.

During this experiment, we created the subsets based on the starting point of the patients, as we aimed to evaluate the subsequent care pathway. Since we distinguished between care providers, we created the subsets on level Detail. If patients switched between consultation with a PA and physician, this was shown in the process map and traces. Moreover, we only considered patients who started at the outpatient clinic. This means that patients who started at the FHLA, or elsewhere, and then went to a physician or PA were not included in the dataset.

4.5.4 Experiment 4: Patients with and without an ECV

In this experiment, we aimed to evaluate the care pathways that included ECVs. Since ECVs are not recommended for paroxysmal AF, we expected to see few to none ECVs. However, we distinguished between elective and immediate ECVs in Meppel and Zwolle, respectively. To analyze these differences, we created four subsets; (1) patients with any ECV, (2) ECVs in Meppel, (3) ECVs in Zwolle, and (4) no ECVs during the care pathway. The process analysis for the comparison of ECVs in Meppel and Zwolle are executed on level Detail, as that level incorporates most detail to make profound statements. Subsequently, the process analysis for comparing ECVs with no ECVs is on the Basic level. All ECVs are considered as one treatment strategy, therefore, we only needed to obtain the care activities preceding and following the ECV.

To ensure meaningful comparisons, we first analyzed whether there were significant differences between patients who received an ECV in Meppel versus Zwolle. If differences between these two groups were statistically significant, then combining all ECV patients into a single group, i.e., any ECV, would not be reliable for comparison against the group without an ECV (Bonovas & Piovani, 2023). For example, the trace composition could have depended on the location or the patient characteristics.

We expected ECVs to occur at the start of the care pathway, since the patient might not have been diagnosed properly yet, and symptoms were relieved with the ECV. Furthermore, we expected that ECVs performed in Zwolle were often linked to admissions to the FHLA, as an immediate ECV could have been requested at the FLHA. Since patients are not often sent to Meppel after a visit to the FHLA, we assumed that an FHLA activity succeeded by an ECV in Meppel were not related activities.

5. Results

This chapter presents the results of the data processing and experiments. Section 5.1 discusses the results of the data processing steps, discussed in 4.2. Then, Sections 5.2 to 5.5 provide the results of the Model Design steps from 4.3 for the experiments. Appendix D.2 contains all outcomes of the statistical tests.

5.1 Data processing

5.1.1 Processing patients

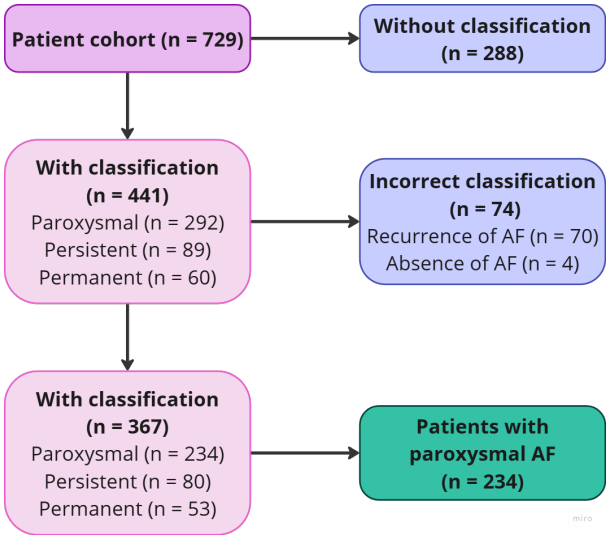


Figure 5.1: Inclusion Process of Patients in Cohort

Figure 5.1 illustrates the assembling process of the patient cohort, based on the availability of data. The patient cohort collected in CTcue consisted of 729 patiënts, diagnosed with AF between 01-01-2023 and 01-07-2023. Classification results were available for 441 [60.49%] patients. 292, 89, and 60 patients were labeled *Paroxysmaal, Persisterend, Permanent*, respectively. After validation, 55 *Paroxysmaal* labels, 8 *Persisterend* labels, and 7 *Permanent* labels were adjusted to *Recidief*. Moreover, 3 *Paroxysmaal* labels and 1 *Persisterend* label were deemed as *Afwezig*, since the report showed no occurrence of AF. Overall, the error margin of mislabeled classifications was 16.78% (74 of the 441 patients). The error margins per classification were 16.8% for paroxysmal, 19.86% for persistent, and 11.7% for permanent. In the final dataset, we classified 234 patients with paroxysmal AF, 80 with persistent AF, and 53 with permanent AF.

From this point, we only considered patients with paroxysmal AF. All comorbidities were labeled as *Aanwezig* or *Afwezig*. During the validations of the labels, 1 [0.43%] of the 234 patients had a registered BMI of 280.27 kg/m^2, which is exceptionally high. The medical record showed a BMI of 27.68 kg/m^2, indicating a mislabeling of the comorbidity. Moreover, 6 patients [2.18%] had an incorrect label for hypertension, 7 patients [2.99%] for obesity, and 2 patients [0.73%] for diabetes. This wrong label could be either *Aanwezig* when it should be *Afwezig*, or vice versa. In this dataset, we did not adjust the labels due to the small error margins.

All data points checked during Step 4, showed 100% completeness. In other words, all patients had a registered age during the first care activity, a first DBC associated with AF, and at least

one care activity. All DBCs had a Episode of Care ID, all care activities had a timestamp and a care activity code.

5.1.2 Processing care activities

The exported dataset contained 2,155 care activities. These were all the activities of the 234 patients at Isala between their AF diagnosis and the 18 subsequent months, whether AF-related or not. Of these, 909 care activities were requested by the Cardiology department and 17 by the Cardiothoracic Surgery department, while 986 were performed by Cardiology and 12 by Cardiothoracic Surgery. All care activities that were neither requested nor performed by Cardiology or Cardiothoracic Surgery were removed from the dataset. This resulted in 1,230 remaining care activities, i.e., 925 care activities were removed since they did not involve a Cardiology-related department. Among the 1,230 remaining care activities, 18 care activities were either requested or performed by Cardiothoracic Surgery. The DBCs associated with these 18 procedures were not relevant to the AF care pathway. For example, a care activity belonged to a DBC for valve replacement. There were also 220 activities that were neither requested or executed by the Cardiology department, and their DBCs did not relate to a relevant Episode of Care ID. Therefore, we retained only the activities that were requested and/or performed by the Cardiology department and were assigned to a relevant DBC, resulting in 992 care activities. These care activities belonged to 232 patients. During this process of excluding certain care activities, two patients were removed, as they had no relevant recorded care activities.

In total, 42 patients had duplicate NP appointments. For each of them, the first NP registration was retained, and the rest were converted to HC. In total, 76.29% (177 of 232) of the patients had an NP appointment, the other 23.70% (55 of 232) of the patients did not.

For 18 patients, CTcue did not obtain the specialist executing an NP. A deep dive in HiX revealed that all these NP appointments were executed by a cardiologist. For 48 patients, CTcue did not find the specialist executing an HC, and again, HiX confirmed that all HCs were performed by a cardiologist.

5.2 Experiment 1: Base Case

Experiment 1 served as the Base Case. The analyses described in Section 4.3 were executed for the whole dataset of patients with paroxysmal AF. The aim of this experiment was to compare the care pathways of these patients to the AF-CARE framework.

5.2.1 Data analysis

The average age of patients with paroxysmal AF was 70.5[$\pm$12.8] years, with a range from 25 to 94. Figure 5.2 displays the distribution of age among the patient group. The graph is left-skewed, indicating that the patients tend to be elder. Furthermore, 206 patients presented hypertension, 40 obesity, and 29 diabetes. Figure 5.3 shows the overlap in comorbidities in a Euler Diagram. There were 6 patients who had all three comorbidities. 26 patients had both hypertension and diabetes, 35 patients had hypertension and obesity, and 7 patients had a combination of diabetes and obesity.

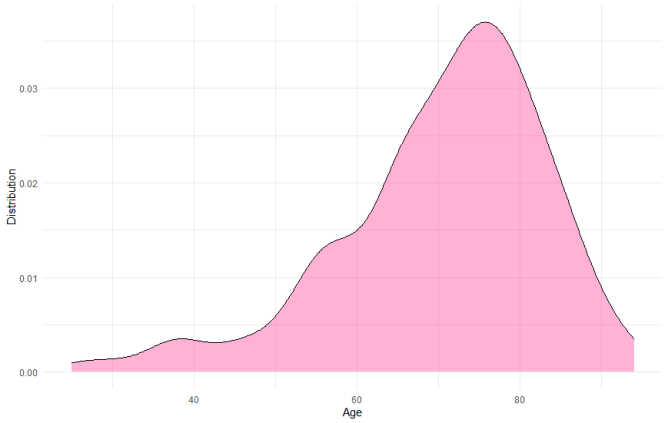


Figure 5.2: Distribution of Age of Patients with Paroxysmal AF in Experiment 1

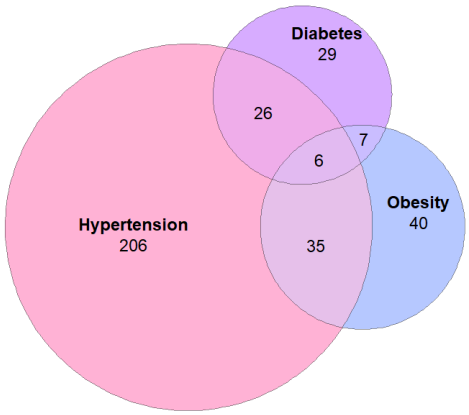


Figure 5.3: Comorbidities of Patients with Paroxysmal AF in Experiment 1

Figure 5.4 shows the distribution of the number of care activities per patient. Figure 5.5 illustrates the combinations of care activities.

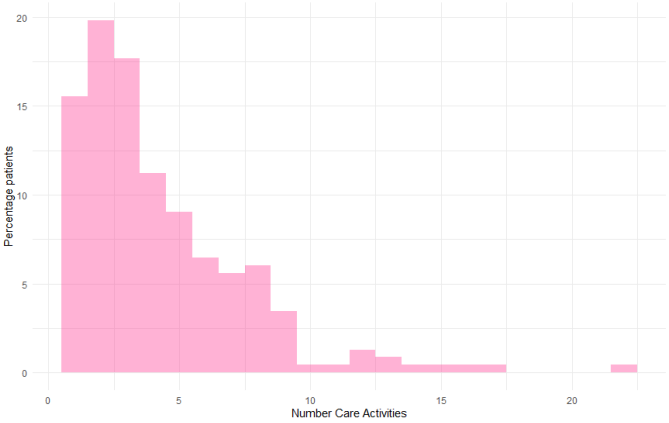


Figure 5.4: Number of Care Activities per Patient (%) in Experiment 1

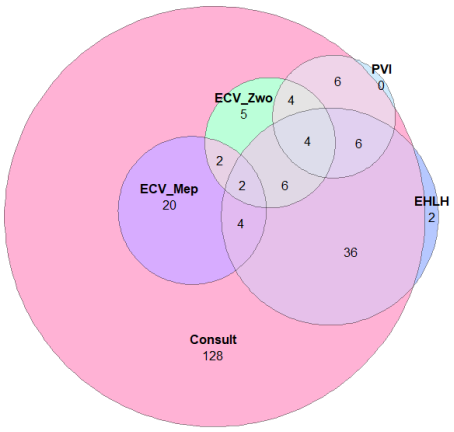


Figure 5.5: Intersection of Appointment Types per Patient in Experiment 1

Figure 5.4 shows a right-skewed distribution, indicating that most patients had 1 to 5 care activities during their 18-month care pathway. These care activities could include outpatient clinic appointments, visits to the FHLA, ECVs, PVIs or hisbundle-ablations. Furthermore, Figure 5.5 shows that almost all patients had consultations in combination with an ECV, PVI, or readmission. There were two patients who only visited the FHLA. We see that there were no care pathways that contained both an elective ECV and PVI. Moreover, immediate ECVs were often combined, eight times with a PVI and four times with an elective ECV. PVIs often occurred in the same care pathways as visits to the FHLA (10 times) or immediate ECV (8 times).

In total 229 (98.7%) patients had a combined total of 802 consultations. Table 5.1 shows the number of appointments and averages per patient. The 229 patients with consultations had on average 3.50[±2.52] outpatient clinic appointments. Furthermore, the table shows that 28.4% of all 232 patients were admitted to the FHLA at least once.

Type	Total Activities	Unique Patients (n (% of total))	Mean [$\pm SD$]
Consult	802	229 (98.7)	3.50 [2.52]
EHLH	78	66 (28.4)	1.18 [0.493]
ECV MEP	46	34 (14.7)	1.35 [0.646]
ECV ZWO	37	28 (12.1)	1.32 [0.612]
PVI	28	26 (11.2)	1.08 [0.272]

Table 5.1: Statistics Care Activities per Patient, level Medium, Experiment 1

5.2.2 Process Mining Analysis

An event log was created for all three levels of detail. Table 5.2 gives an overview of the number of distinct traces in each event log. With each decreasing level of abstraction, i.e., more detail in the care activities, the number of distinct traces increased.

	Traces
Basic	85
Medium	87
Detail	104

Table 5.2: Traces per Event Log in Experiment 1

The increase in distinct traces for the same number of patients resulted in increasingly complex process maps from Medium to Detail level. Since we aimed to check conformance to AF-CARE, we analyzed the process, as described in 4.3.3, on the Basic level. Figure 5.6 shows the process map for all traces.

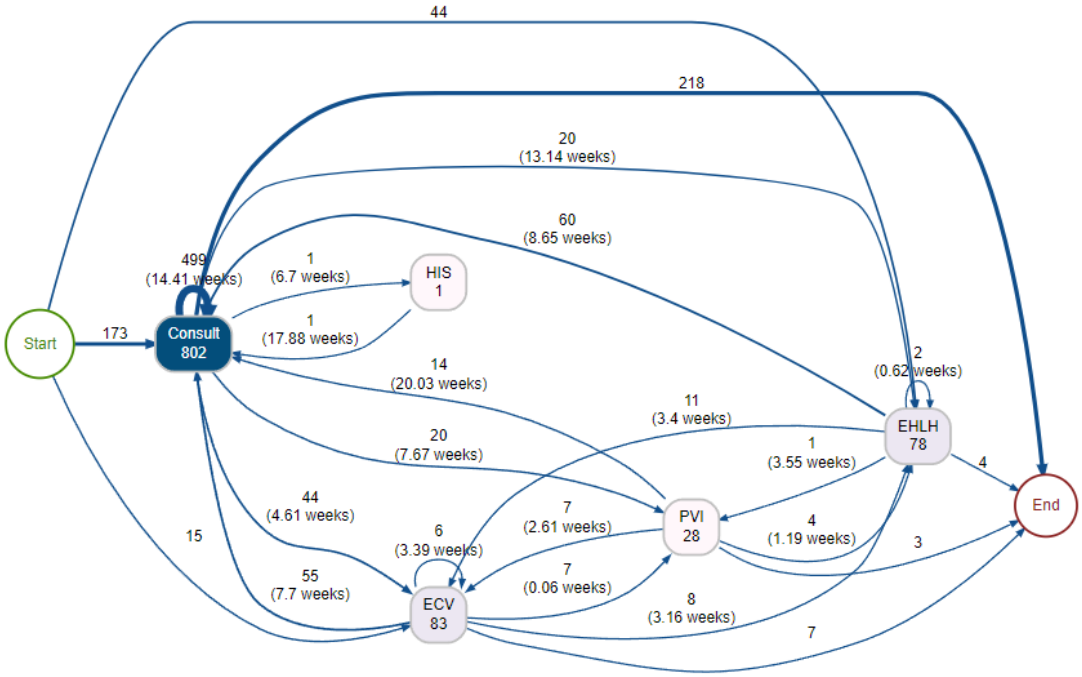


Figure 5.6: Process Map Base Case on Level Basic

We see that 173 patients started their care pathway with an outpatient clinical appointment.

Additionally, 44 patients started at the FHLA [NL: EHLH], and 15 patients started with an ECV. After an ECV, as either a start point or succeeding a Consult, 55 patients had a follow-up consultation, 8 patients were readmitted to the FHLA, 7 patients had a PVI, and for 7 patients, their pathway ended. There were 20 patients who had a PVI succeeding a Consult after, on average, 7-8 weeks. Of the 78 instances of a visit to the FHLA, 60 had a follow-up consultation, 1 had a PVI, 2 were readmitted, 11 had an ECV, and for 4 patients, their pathway ended. Overall, we see that most patient's pathway consisted of outpatient clinical appointments and/or visits to the FHLA. PVIs occurred less than ECVs, and a hisbundle-ablation only occurred once.

Figure 5.7 shows the traces of all patients from the complete dataset, of which 22 traces occurred more than once in the event log.

Figure 5.7: Traces of Base Case on Level Basic

Figure 5.7 shows that most traces included outpatient clinical appointments. The traces with an absolute frequency above one almost solely consisted of consultations, either at the OC or the FHLA. The number of consultations on these traces ranged from 1 to 9. Of the 7 traces (27 patients) where the patient started at the FHLA, 6 traces (25 patients) only had succeeding

consultations. The other trace (2 patients) had an ECV after the visit to the FHLA, and then follow-up consultations. There were 6 traces (15 patients) who had an ECV in the traces that occurred more than once. These ECVs were all either the first or second care activity, followed by follow-up consultations. Last, in these traces, there was 1 trace (2 patients) with a PVI.

The traces that occurred once, i.e., unique traces, in Figure 5.7 were, on average, longer than the traces that occurred more than once. The unique traces comprised mostly outpatient clinical appointments, but also ECVs, PVIs, and visits to the FHLA. In these traces, patients were also readmitted to the FHLA. This happened at different places on the traces, followed by and succeeding various care activities. There were 24 traces/patients that had at least one PVI. These PVIs were preceded by one or more ECVs, readmissions to the FHLA, or several consultations. In total, there were 8 traces where a PVI succeeded multiple ECVs and/or readmissions to the FHLA. Additionally, there were 7 traces where more than three consultations took place before the PVI was executed.

Throughput Time

The throughput time of all three event logs per level of detail was the same, since they all included the same set of patients. The patients stayed in the system between 0 - 78.42 (18 months) weeks, with a mean of 39.51[$\pm$27.2] weeks. The median was 45.8 weeks.

Trace Frequency

Table 5.3 contains information about the trace frequencies of the three event logs. They all had 232 traces, as each patient had a trace. The table shows the average [$\pm SD$], minimum, and maximum of patients following the same trace. The median for each event log was 1.

Eventlog	**Mean** [$\pm SD$]	**[Min, Max]**
Basic	2.73 [6.04]	[1, 38]
Medium	2.67 [5.98]	[1, 38]
Detail	2.23 [4.46]	[1, 34]

Table 5.3: Trace Frequencies of the Base Case

5.2.3 Discussion of Outcomes

This experiment served to compare the complete patient cohort with paroxysmal AF collected through CTcue to the AF-CARE guidelines. We expected the traces to include consultations, PVIs, and, perhaps, visits to the FHLA. ECVs should not occur in the traces, as it is not recommended in AF-CARE (Figure 2.1). We compared the results with the hypotheses with a validation panel, as elaborated below.

About 75% of the patients had 1 to 5 care activities during their care pathway. Most of these activities were consultations, some included an ECV, PVI, or readmission. ECVs in Meppel rarely occurred in combination with other healthcare activities besides consultations, whereas ECVs in Zwolle were more often combined with visits to the FHLA (12 times) or PVIs (8 times). Since an immediate ECV might be requested at the FHLA, the combination of an ECV in Zwolle and a readmission is logical. Figure 5.6 shows the edge from FHLA to ECV with a mean of 3.4 weeks in between. The cardiologists we consulted stated that they expect that these patients are referred to the ECV in Zwolle via phone, and therefore, the activity is not registered as readmission. The cardiologists added that these patients are probably more symptomatic, as they visited the FHLA.

Most patients had care activities over a span of 46 weeks, while the observation period lasts 78 weeks. This means that most patients do not have care activities throughout the entire 18 months. The cardiologists stated that patients start with one or more tests and consultations, after which a policy is created, and follow-up might be later than the 18 months we collected. Moreover, once a patient is no longer symptomatic or decided to settle for the symptoms, the patients did not necessarily require follow-up.

The trace frequencies in Table 5.3 showed that traces occurred on average only 2-3 times, with a maximum of 34-38. If we verify this in the trace explorer in Figure 5.7, we see that the most frequent pathways mainly consisted of consultations. Complex and/or symptomatic patients - who required a more personalized approach - are expected to have had a greater need for follow-up, readmissions, and/or other treatment strategies. However, the validation panel also contributed the high number of consultations to a lack of continuity in the care provider. Patients might have seen different care providers along the care pathway, all with different policies regarding follow-up. Additionally, if a patient saw different care providers, the care provider did not know the patient as well as when the patient had seen the same care provider each consultation. The cardiologists explained that this might have led to an excess of follow-up consultations.

Furthermore, the absolute frequency decreased when other types of care activities were introduced in the trace. According to the ESC guidelines, ECVs should not occur, yet they appeared in 45 traces. They appeared mostly at the beginning of the care pathway, which might be due to the absence of a final diagnosis at that time. However, since we saw that this type of activity appeared in less standardized pathways, it could be an indication that there were no clear agreements regarding ECVs. We expected PVIs to show up in more traces, since a PVI is a more sustainable treatment than an ECV for patients with paroxysmal AF. The PVIs often appeared late in the pathway, succeeding multiple consultations and sometimes ECVs. It could be that there were few agreements on when an ECV/PVI should be performed and what the follow-up should look like. The cardiologists agreed with this statement, as there was a different mindset between the physicians in Meppel and in Zwolle in the past. Physicians in Meppel often opted for an ECV, while physicians in Zwolle were more 'PVI-minded'. Currently, they expect the physicians to be more PVI-minded due to a shift in the staff.

5.3 Experiment 2: Starting at the OC vs FHLA

Experiment 2 aimed to compare the care pathways of patients who started at the OC with the care pathways of patients who started at the FHLA. This experiment provided insight into treatment strategies following from different start departments.

5.3.1 Data analysis

The dataset was split into two subsets, one containing all patients who started with a consultation and one with all patients who started at the FHLA. The first group consisted of 173 patients and the second of 44.

Appendix D.1 contains the graphs that illustrate the age, comorbidities, and occurrence of comorbidities. The differences between the ages of the groups ($p = 0.2315$) and combinations of comorbidities ($p = 0.5114$) were not proven to be statistically significant. However, the number of care activities and combinations of care activities both had a p-value < 0.05, thus were significantly different, i.e., patients who started at the FHLA had significantly more care activities than patients who started at the outpatient clinic. Table D.1 in Appendix D.1 contains the data of the specific care activity types. In this table, we see that the percentage of patients who had a consultation is significantly higher ($p = 0.04$) for patients who started at the OC. Additionally, the percentage of patients who visited the FHLA is significantly higher ($p <$

2.2e-16) for patients who started at the FHLA.

5.3.2 Process Mining Analysis

Table 5.4 gives an overview of the number of traces per event log.

	Consult	**FHLA**
Basic	49	24
Medium	49	24
Detail	65	25

Table 5.4: Traces Per Eventlog of Experiment 2

We see that the number of traces increased when more detail was incorporated in the event log. The increase was slightly higher for the event logs of patients who started with a consultation, since that event log contained more care activity types.

Figure 5.8 contains the process map of patients who started at the OC and Figure 5.9 of the patients who started at the FHLA, both on level Medium.

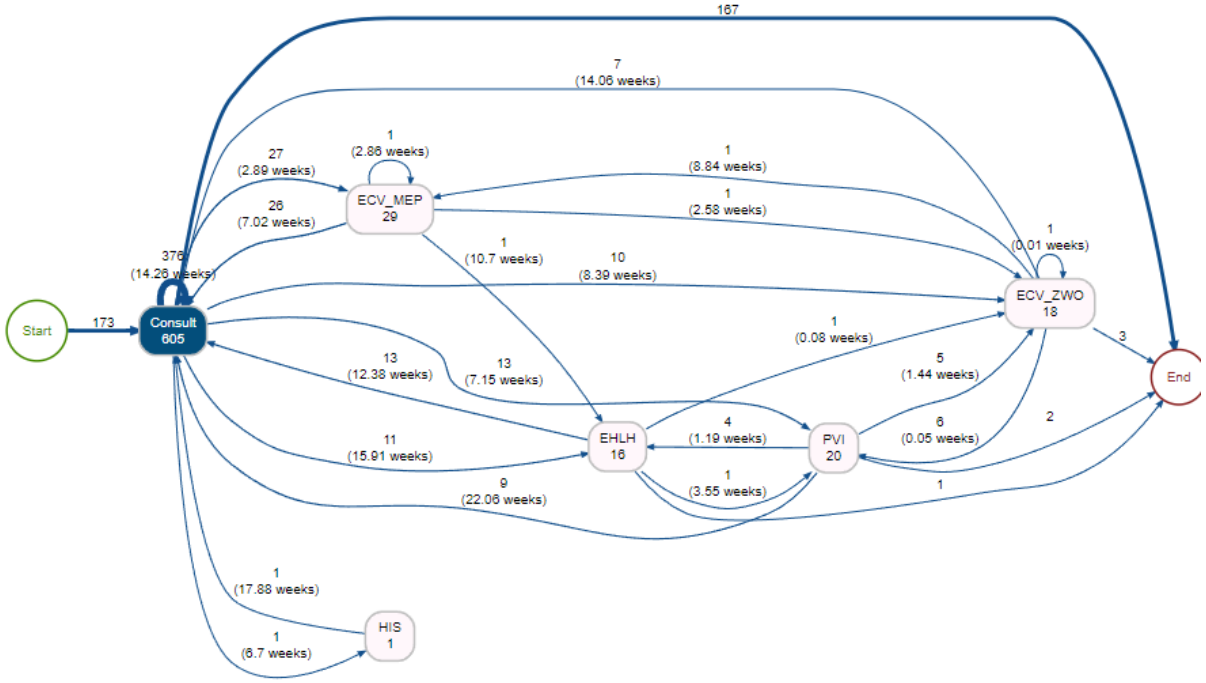


Figure 5.8: Process Map Patients Who Started at the OC, level Medium

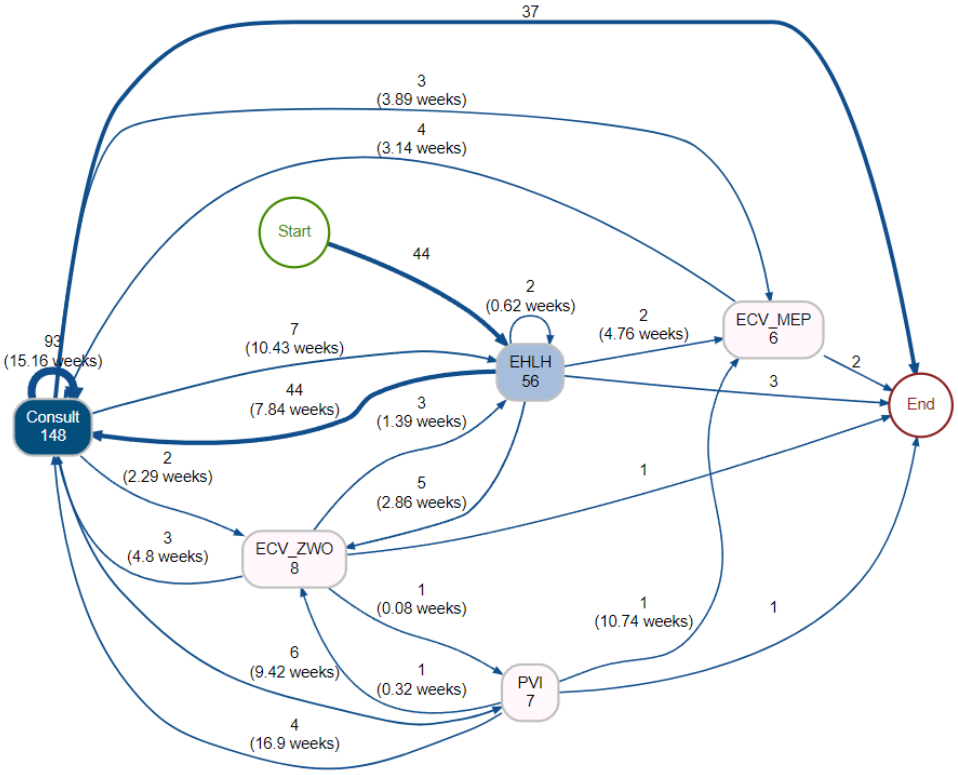


Figure 5.9: Process Map Patients Who Started at the FHLA, level Medium

We see that patient who started at at the OC, most often proceeded with a follow-up consultation (376 instances). If a consultation was followed by an ECV, 27 times this was elective and 10 times it was immediate. The time between a consultation and immediate ECV was, on average, 8-9 weeks. There were 13 instances where a patients had a PVI after a consultation, and 11 patients were readmitted to the FHLA.

For the patients who started at the FHLA, the most frequent follow-up path was to the OC, as this was the thickest edge. The other paths were an elective ECV (2 instances), immediate ECV (5 instances), readmission (2 instances), or the pathway ended for 3 patients. There were 7 instances where a patient was readmitted after a consultation and 3 after an immediate ECV. The average time between a visit to the FHLA and an immediate ECV was around 2 weeks, which indicated that there was not a direct referral between the FHLA visit and the ECV.

The main difference between these two process maps is not the sequences or occurrence of care activities, but the time between the care activities. The average time between a consultation and elective ECV was around 3 weeks for both groups, but the follow-up after the elective ECV was 7 weeks for patients who started at the OC and 3 weeks for patients who started at the FHLA. Moreover, patients who started at the OC had 10 weeks to go from the OC to an immediate ECV, while patients who started at the FHLA had their immediate ECV after 2-3 weeks. The time between the immediate ECV and consultations was 14 weeks for the first group and 5 weeks for the latter.

Figure 5.10 shows the traces of patients who started at the OC at the Medium level.

Figure 5.10: Traces of Patients Who Started at the Outpatient Clinic, level Medium

We see that 13 traces occurred more than once, of which 1 trace (2 patients) had a PVI and 3 traces (8 patients) had an elective ECV. The rest of these traces solely comprised outpatient clinic appointments, ranging from 1 to 9 consultations. Additionally, the PVI and ECVs all occurred after one consultation in these traces. Subsequently, the traces that occurred once, i.e., unique traces, had more care activities on them, ranging from 3 - 17 care activities. Of these unique traces, 17 traces contained at least one PVI, of which 13 traces had multiple consultations, ECVs, and/or readmissions to the FHLA before the PVI. Moreover, there were 13 traces that included at least one immediate ECV, of which 9 directly proceeded or succeeded a PVI. Finally, there were 15 traces that included a readmission to the FHLA. Of these, 4 readmissions followed the first OC appointment, the readmissions of the other 14 traces succeeded multiple consultations, ECVs, and/or PVIs.

Figure 5.11 provides the traces of patients who started at the FHLA at Medium level.

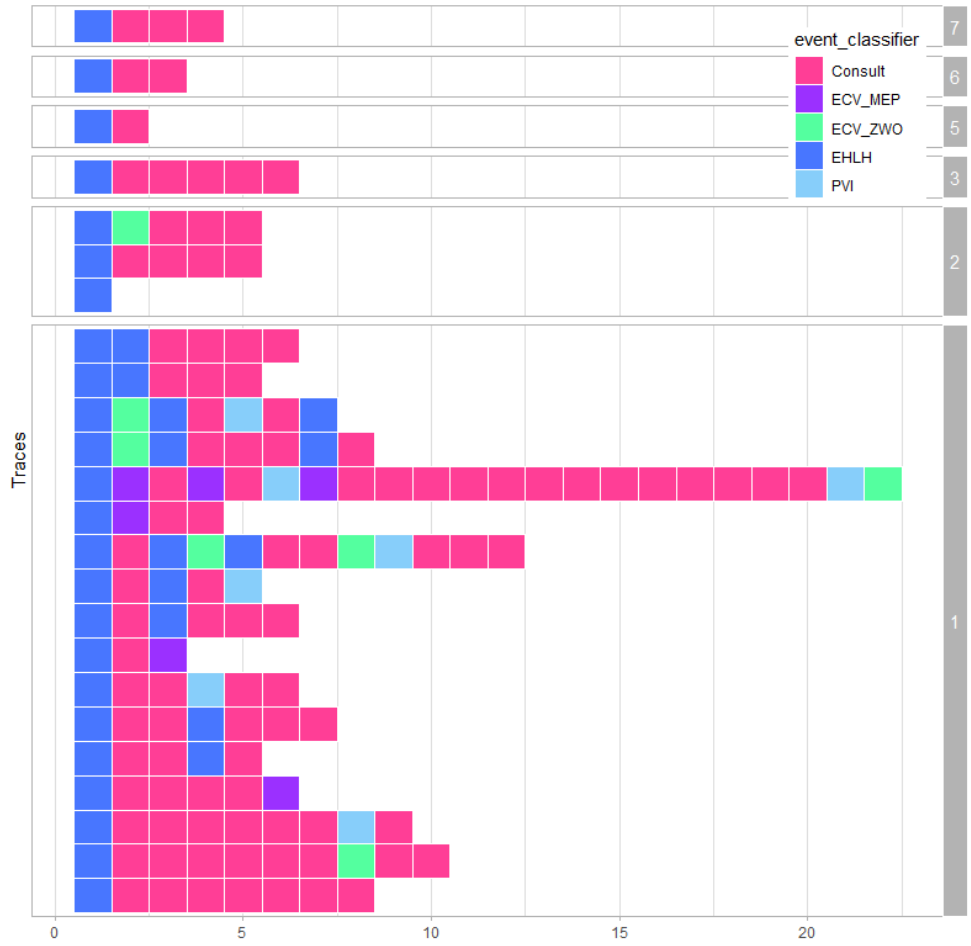


Figure 5.11: Traces of Patients Who Started at the FHLA, level Medium Experiment 2

Figure 5.11 shows that the traces that there were 7 traces that occurred more than once. Of these traces, 1 (2 patients) included an immediate ECV succeeding the visit to the FHLA and 1 trace (2 patients) did not have any appointments after the visit to the FHLA. The other 5 traces (23 patients) had consultations after the start at the FHLA, ranging from 1 to 5 appointments. The traces that occurred once, i.e., unique traces, included PVIs, elective ECVs, and readmissions to the FHLA as well. There were two patients who were readmitted to the FHLA immediately after the first visit. Additionally, there were 7 patients readmitted later along the care pathway. There were 6 patients with a PVI, all succeeding multiple OC appointments, readmissions, and/or ECVs.

Throughput Time

The throughput time in weeks of the patients were assembled in Table 5.5. The Welch Two Sample t-test gave a p-value of 0.0398, indicating the throughput time of patients who started at the FHLA is statistically significantly longer.

	Mean	**SD**	**Median**	**Min**	**Max**
Consult	36.7	29	38.1	0	77.3
FHLA	46.3	24.6	53.1	0	78.17

Table 5.5: Throughput Time for Patients Starting at the Outpatient Clinic and FHLA (Experiment 2)

Trace Frequency

Table 5.6 shows the average frequency [$\pm SD$] a trace occurred in the dataset, the minimum frequency, and maximum frequency. The median frequency for all event logs was 1.

Eventlog	**Mean** [$\pm SD$]	**[Min, Max]**
Consult	3.53 [7.80]	[1, 38]
FHLA	1.83 [1.71]	[1, 7]
p-value		*0.9226*
Consult	3.53 [7.80]	[1, 38]
FHLA	1.83 [1.71]	[1, 7]
p-value		*0.9226*
Consult	2.66 [5.51]	[1, 34]
FHLA	1.76 [1.61]	[1, 7]
p-value		*0.8003*

Table 5.6: Summary Trace Frequencies Experiment 2

5.3.3 Discussion of Outcomes

In this experiment, we investigated whether there were differences in the care pathway of patients who started at the OC (n = 173) and those who started at the FHLA (n = 44). We expected that patients who started at the FHLA would have been older and/or had more comorbidities than those who started at the OC, as referrals to the FHLA should be based on the CHADS2 score. However, we did not find a significant difference. It is possible that patients who started at the FHLA were admitted due to the severity of symptoms rather than other CHADV2-variables. The cardiologists confirmed this during the validation meeting, as patients who visit the FHLA tend to be more symptomatic or are more complex than patients who start at the OC.

Additionally, we thought that patients who started at the FHLA would have fewer care activities and a shorter throughput time than those who started at the FHLA. In the latter group, there is no differential diagnosis yet, making it harder to prepare in advance. As a result, we expected that it would have taken longer for these patients to have had a proper medication plan. The difference in the number of care activities per patient was significantly higher for patients who started at the FHLA. There was also a significant differences in the combinations in which these activities occurred. Subsequently, the throughput time of patients who started at the FHLA was significantly higher than the throughput time of patients who started at the OC.

Regarding the frequency of care pathways, no statistically significant differences were found between the two groups. This means that starting at the OC versus the FHLA did not lead to a more or less standardized care pathway. The average frequency of the care pathways for both groups was between 1 and 3, suggesting that, in general, there was little standardization in either group.

When looking at the individual care activities, we saw that patients in one group did not have a certain care activity more frequently than those in the other group. However, Table D.1 does show a significant difference in the percentages of patients in each group who had a consultation or visit to the FHLA. However, since we split the datasets on a visit to either department, these results might be skewed. Though, the difference in visits to the FHLA for both groups is quite big, as only 9.25% of the patients who started at the OC visited the FHLA. Cardiologist did point out that visits to the FHLA might have been related to the absence of a final diagnosis during the first visit to the FHLA. Since heart-related complaints require a cautious approach, patients might have been referred to the FHLA sooner in case of recurring or worsening symptoms, rather than being referred to the OC. The pathways that included

readmission often included switches between the care providers. Therefore, they added the expectation that care provider continuity might have contributed to the readmissions as well.

5.4 Experiment 3: Starting at the OC vs AF-OC

This experiment served to compare the care pathways of patients that started with a physician to those who started with a PA. The aim was to compare the influence of a care provider on the succeeding care pathway.

5.4.1 Data Analysis

We created two datasets, the first only with patients who started with a consultation with a physician. We refer to this dataset as "patients who started at the OC". There were 146 patients who had Consult_Arts as first appointment and were included in this dataset. The other dataset consisted of 27 patients who started with a consultation with a PA, i.e., Consult_PA. We refer to these patients as "started at the AF-OC".

Appendix D.2 contains the graphs that illustrate the age, comorbidities, and occurrence of care activities. There were no statistically significant differences between the groups regarding age ($p = 0.4232$) and comorbidities ($p = 0.6936$). The number of care activities was significantly higher for patients who started at the OC ($p < 0.05$). Additionally, Table D.10 in Appendix D.2 contains the information about the specific care activity types. Due to the low number of datapoints, several statistical tests to compare the means could not be executed.

5.4.2 Process Mining Analysis

Table 5.7 provides an overview of the number of traces per event log.

	OC	**AF-OC**
Basic	46	10
Medium	46	10
Detail	53	12

Table 5.7: Traces Per Eventlog of Experiment 3

As the level of detail increased, the number of distinct traces increased as well. The increase is larger for the event logs of patients who started at the OC than patients who started at the AF-OC. This was expected, since there were less different types of care activities for the latter.

Figure 5.12 contains the process map of the traces of patients who started at the OC. Figure 5.13 shows the traces of patients who started at the AF-OC.

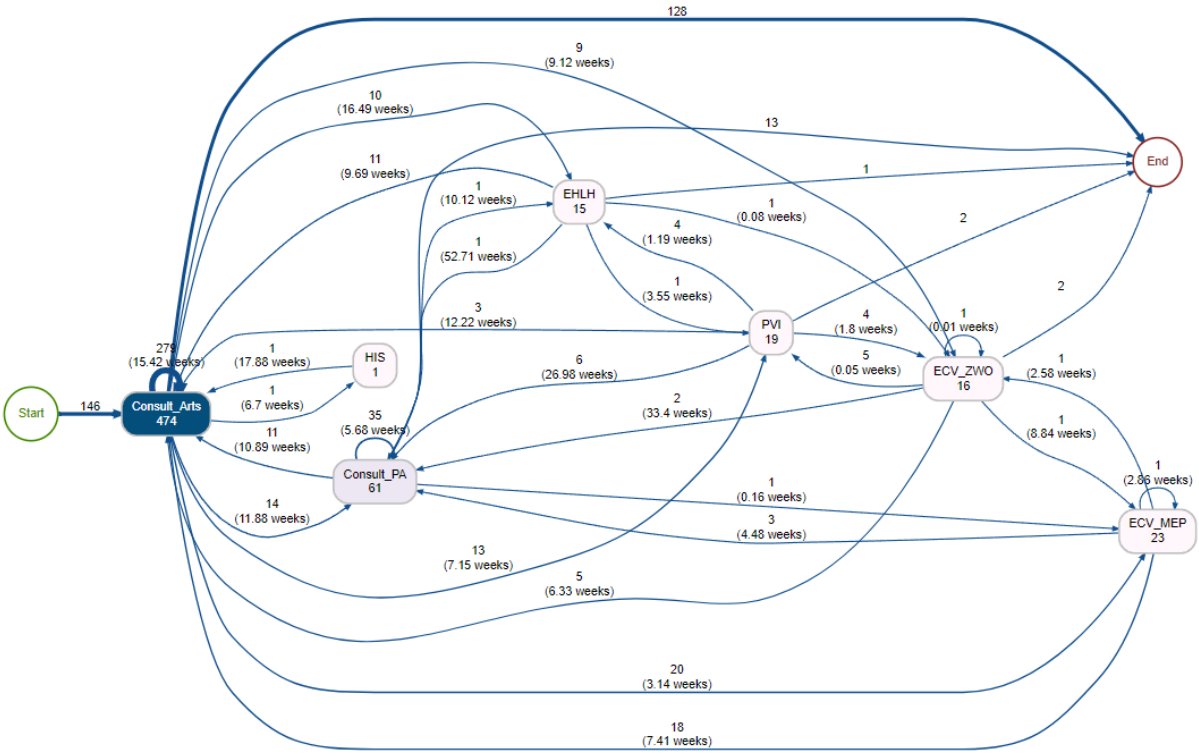


Figure 5.12: Process Map Patients Who Start at the OC, level Detail

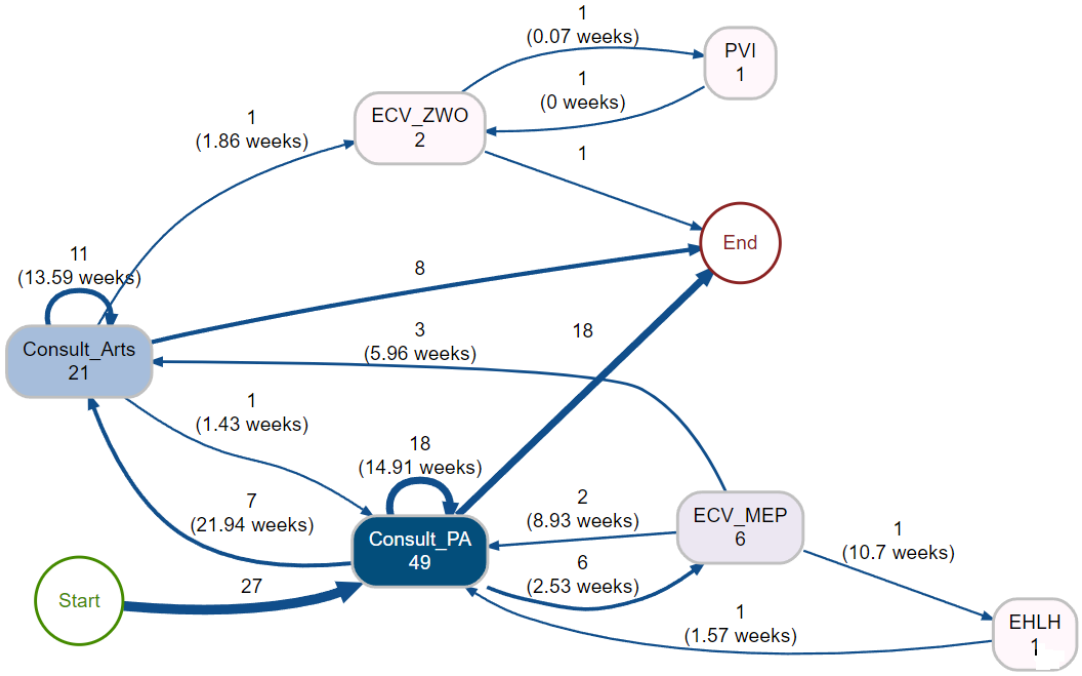


Figure 5.13: Process Map Patients Who Start at the AF-OC, level Detail

Figure 5.12 shows many traces, representing the care pathways of 146 patients. It looks similar to the process map of patients who started at the OC in Experiment 3 (Figure 5.8, therefore we do not discuss the process map again. However, the patients who started at the AF-OC are excluded and shown in Figure 5.13. This process map shows that patients who started at the AF-OC most often have follow-up consultations at the AF-OC and/or end their care pathway.

There were 7 instances where a patient transferred to the OC of a physician. Additionally, there were 6 instances where a patient had an elective ECV. Of those 6 patients, 2 went back to the AF-OC, 3 went to the OC, and one was readmitted after which the patient went to the AF-OC. An immediate ECV only occurred succeeding consultation with a physician, hence, the PVI also followed from consultation with a physician. The time between the PVI and immediate ECV indicate that those activities happened during the same visit to the hospital.

The difference in complexity of the process maps resulted from the number of patients represented in those maps. There were 119 more patients who started at the OC than at the AF-OC, therefore, Figure 5.12 illustrates the traces of 119 more patients, resulting in higher complexity.

Figure 5.14 illustrates the traces from the process map of patients who started at the OC.

Figure 5.14: Traces of Patients Starting at the OC, level Detail

Figure 5.14 contains 12 traces that occurred more than once, representing the traces of 105 patients. Of these 12 traces, 3 traces (7 patients) included an elective ECV as second care activity and 1 trace (2 patients) had a PVI, after which they went to the PA. The other 8 traces (96 patients) included solely outpatient clinic appointments with a physician, ranging from 1 to 9 appointments. The other 41 traces occurred once and ranged from 2 to 17 care activities. These traces included all care activity types, i.e., readmissions, elective and immediate ECVs,

PVIs, and a hisbundle-ablation. Since the traces were comparable to the traces in Figure 5.10, we only discuss the added value of increasing the level of detail. In Figure 5.14 we see which consultations took place with a physician and which with a PA. There were 7 traces where a patients went to the PA after a PVI. Moreover, there were 10 traces where a patient switched between a physician and PA, whereas there were 9 traces where the patient changes from consultations with a physician to a PA. There were 6 patients that went to the PA directly after the first consultation with a physician, of which 4 patients went back to the physician.

Figure 5.15 shows the traces that occurred in the event log of patients who started at the AF-OC at the most detailed level.

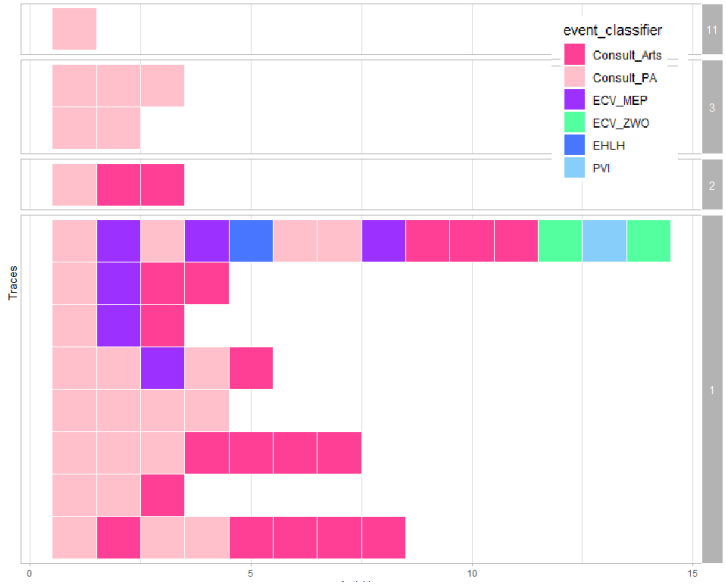


Figure 5.15: Traces of Patients Starting at the AF-OC, level Detail

The trace that solely consisted of an initial consultation with a PA occurred the most, namely for 11 patients. The second most frequent traces also contained one or two follow-up consultations with a PA (6 patients). Subsequently, two patients went to the physician after the first consultation at the AF-OC. The remaining 8 traces comprised 3 to 14 care activities. Of these 8 traces, 4 included solely outpatient clinic appointments with a PA or they switched to the physician. There were 3 traces that also included one elective ECV, after which these patients went to the physician. There was one trace with 14 care activities, including elective and immediate ECVs, a readmission, and a PVI. This patient saw both the PA as the physician.

The main difference between the traces of these two groups is the trace composition. Where the traces of patients who started at the OC included all types of care activities in multiple traces, the traces of patients who started at the AF-OC mostly consisted of consultations, some included an elective ECV, but only one trace also included a readmission, immediate ECV, and readmission. The readmissions in the traces op patients who started at the OC, were significantly more in the traces that included solely appointments with a physician. Figure 5.14 shows that of the 22 traces that included an appointment with a PA, 5 traces also included a readmission to the FHLA.

Throughput Time

Table 5.8 gives the descriptive statistics of the throughput time of both groups. The p-value of the Welch Two Sample t-test was 0.005. Thus, there the throughput time of patients who

started at the AF-OC was significantly lower than for patients who started at the OC.

	Mean	**SD**	**Median**	**Min**	**Max**
OC	40.1	27.6	45.5	0	78.42
AF-OC	23.6	26.3	8.4	0	73.5

Table 5.8: Throughput Time for Patients Starting at the OC and AF-OC (Experiment 3)

Trace Frequency

Table 5.9 provides an overview of the average [$\pm SD$] absolute frequency, minimum frequency, and the maximum times a trace in the event log was followed. The median for each trace was 1.

Event log	**Mean** [$\pm SD$]	**[Min, Max]**
OC	3.17 [6.50]	[1, 35]
AF-OC	2.7 [3.34]	[1, 11]
p-value		*0.8195*
OC	3.17 [6.50]	[1, 35]
AF-OC	2.7 [3.34]	[1, 11]
p-value		*0.8195*
OC	2.75 [5.97]	[1, 34]
AF-OC	2.25 [2.86]	[1, 11]
p-value		*0.4466*

Table 5.9: Summary Trace Frequencies Experiment 3

5.4.3 Discussion of Outcomes

This experiment aimed to identify differences in care pathways between patients who started at the OC (n = 146) and those who started at the AF-OC (n = 27). Due to the low number of patients who started at the AF-OC, various statistical tests could not be performed. This made it difficult to draw well-founded conclusions. However, we were able to identify certain patterns, that provided areas for further exploration. We expected patients who started at the AF-OC to have had a lower throughput time, which is confirmed, fewer appointments, which is confirmed, and less consultations between a consultation and PVI, which we were not able to confirm. The PA likely had more standardized plans prepared in advance of the appointment. Additionally, the PA had more time during the consultation than a physician. Together, this allowed for creating a personalized plan, which might have been more effective, and therefore, reduced the need for a consultation. The cardiologists expected that PAs work more according to guidelines, however, also the traces controlled by PAs included ECVs.

It was evident that patients who started at the AF-OC mostly only had consultations. There were few patients that also had an ECV and/or PVI, which could indicate that they were less complex patients. Fewer clinical treatments also directly lead to fewer follow-ups, and therefore, fewer activities. Although no statistical differences in age or comorbidities were found, there might have been other factors related to their complexity. These assumptions were confirmed by the cardiologists. They stated that the patient population who goes to the PA is a selection of patients who require low-complex care. However, the low volume of patients who went to the PA is likely due to the planning method. The validation panel explained that if there was not an explicit request for a PA, the consultation was planned with a physician. If a patient had two consecutive consultations with a PA, this request was explicitly for the PA, but if the

patient had an ECV and then a follow-up, the specific PA request probably disappeared.

We observed that PVIs in physician-led traces typically occurred late in the process, often following several consultations and/or ECVs. This was not our expectation, as a PVI is the most durable solution for paroxysmal AF apart from medication. If medication has not been properly adjusted after three consultations, it raises the question of what additional consultations would contribute. The cardiologists were surprised as well by this observation. They explained that the current policy is to refer patients, when eligible, to a PVI soon during the care pathway, as a PVI is proven more durable. However, they stated that this policy and mindset is relatively new, which could explain why it is not yet visible in this dataset.

The process map in Figure 5.13 shows that patients who started with a PA could proceed to an ECV after an average of 2.5 weeks, which means they already used anticoagulants. Therefore, these patients' conditions were well-known, which is likely why they were referred to the AF-OC. The cardiologists confirmed this, as the referral to the AF-OC is usually through the GP, and the GP already started anticoagulants. They added that the referral time between the GP and AF-OC was not included in the model, which could also influence the throughput time of this group.

Another difference between pathways that occurred once or more was the continuity of the care provider. In pathways that occurred more than once, there was no switch between physicians and PAs, whereas in unique pathways this switch did happen in 12 traces. A one-time switch could have been due to an increased complexity of the patient, when a patient developed, for example, heart failure and the physician took over. There were also traces where a PA took over, this happened after a PVI, when a patient might have only required one follow-up appointment. These statements were confirmed by the cardiologists. There were also 27 traces where there was a back and forth switch between physicians and PAs. The validation panel contributed these switches to a gap in the planning methods. If there was no specific request for the AF-OC, the patient was planned for a consultation with a physician.

5.5 Experiment 4: Patients with and without an ECV

Experiment 4 compared the care pathway of patients with and without an ECV, as ECVs should not occur during the care pathway according to ESC guidelines (Figure 2.1). The aim of this experiment was to assess the care activities preceding and succeeding an ECV as well as the sequence of care activities of patients without an ECV.

5.5.1 Data Analysis

For this experiment, we created four datasets; (1) patients who had any type of ECV, (2) patients who had an ECV in Meppel, (3) patients who had an ECV in Zwolle, and (4) patients who had no ECV. The second and fourth dataset also included patients who had ECVs in both Zwolle and Meppel, who appeared in both subsets. In total, there were 54 patients who had an ECV, 34 patients had an ECV in Meppel, 28 in Zwolle, and 178 patients did not have an ECV.

Appendix D.3 contains the graphs of the age, comorbidities, and occurrence of care activities for all four groups. The statistical tests pointed out that there were no statistically significant differences between the ages ($p = 0.4$), comorbidities ($p = 0.9$), and number of care activities ($p = 0.2$) of the group with an ECV in Meppel and the group with an ECV in Zwolle. Between the patients with and without an ECV, there was no statistically significant difference between the age ($p = 0.09$) and comorbidities ($p = 0.08$). However, the p-value of 3.7e-13 showed that patients without an ECV have statistically significant less care activities than patients with an ECV. Moreover, the p-value of 2.2e-16 shows that there is a statistically significant difference in the combinations of care activities.

Table D.12 in Appendix D.3 shows data of the specific type of care activities of patients with an ECV in Meppel and patients with an ECV in Zwolle. Table D.13 provides data of the specific care activity types for patients with and without an ECV. The proportion patients with a readmission or PVI is significantly higher for patients with an ECV ($p = 0.03$ and $p = 0.0003$, respectively). Additionally, patients with an ECV have a statistically significant higher ($p =$ 1.9e-06) mean number of consultations per patient.

5.5.2 Process Mining Analysis

In total, we created twelve event logs, on for each level of detail for each dataset. Table 5.10 provides an overview of the number of distinct traces in each event log.

	Basic	**Medium**	**Detail**
ECV MEP	28	28	29
ECV ZWO	27	27	27
ECV	45	47	48
No ECV	40	40	56

Table 5.10: Traces Per Eventlog of Experiment 4

The number of traces did not increase much as we increased the level of detail.

Since we already established that there were no significantly important differences between the processes of patients with an ECV in Meppel and Zwolle, we were able to compare the patients with and without an ECV. This was the area of interest, therefore, we created the process maps for the latter groups. Figure 5.16 illustrates the process map patients with an ECV and Figure 5.17 the process map of patients without an ECV.

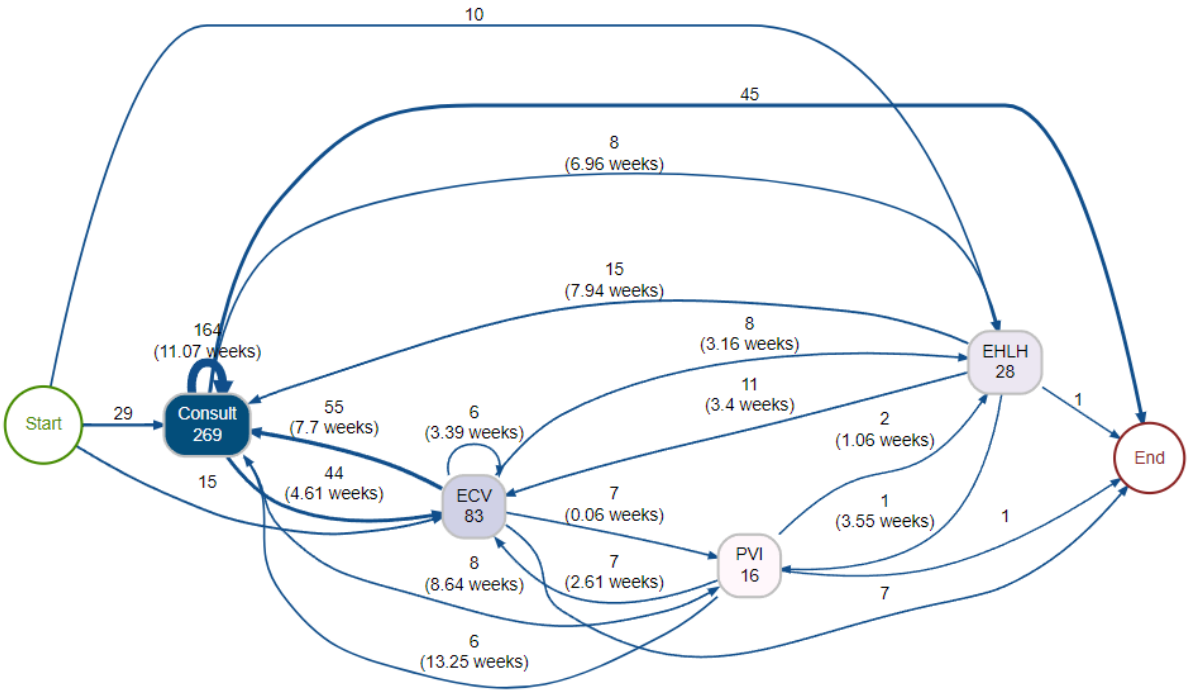


Figure 5.16: Process Map Patients With an ECV, level Basic

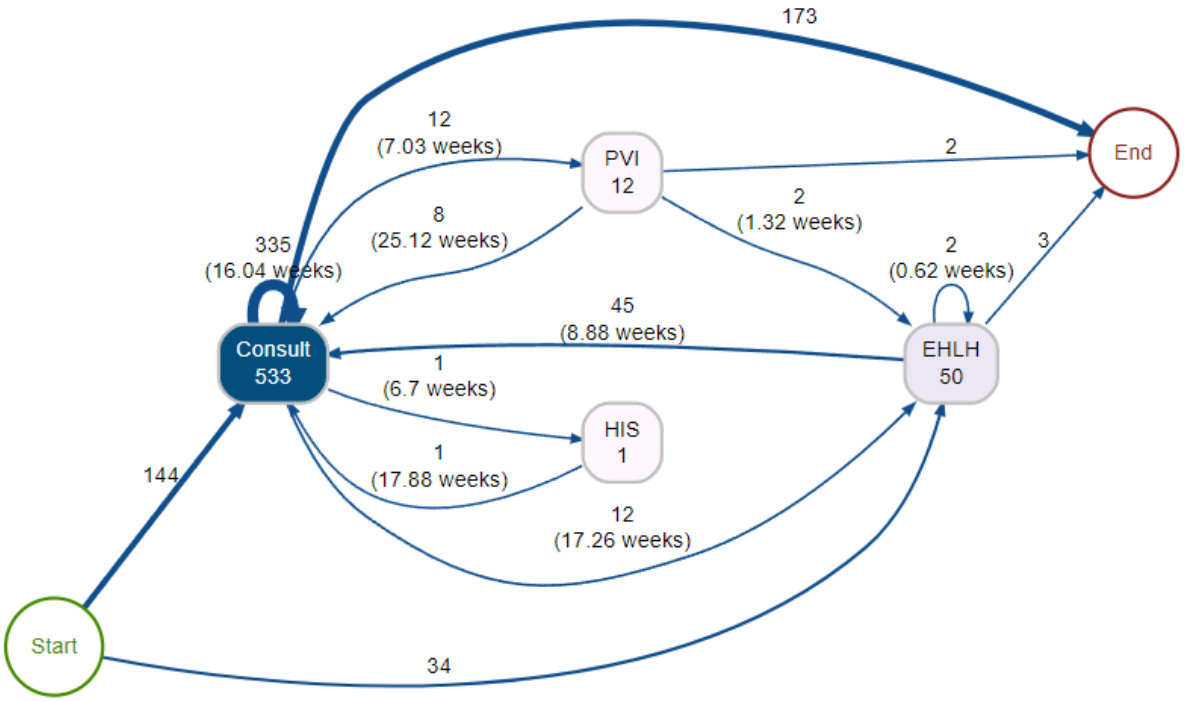


Figure 5.17: Process Map Patients Without an ECV, level Basic

Figure 5.16 is more complex, due to the inclusion of an ECV. Patients with an ECV had three starting points; a consultation, ECV, or visit to the FHLA. The thickness of the edges indicates that most patients have a consultation, follow-up consultations, and an ECV. We see that patients have a follow-up consultations after, on average, 7-8 weeks. An ECV was repeated 6 times without another care activity in between. The average time of 3-4 weeks between the ECVs indicates that these ECVs were not during the same visit to the hospital. The ECVs followed from a consultation, visit to the FHLA, or a PVI. All these ECVs were not on the same day as the preceding activity, as the period on the edges were at least 2 weeks. After an ECV, patients went back to the OC, had a PVI (on the same day), were readmitted to the FHLA, or their pathway ended. Figure 5.17 shows that the patients without an ECV started at the OC or the FHLA. The most common path, i.e., the thickest edges, were from the OC, to a follow-up consultation and/or their pathway ended. Moreover, patients who visited the FHLA most often (45 times) went to the OC, 2 times a patient was readmitted to the FHLA within the same week, and 3 patients ended their pathway after a visit to the FHLA. The average time between two consecutive OC appointments was 16 weeks, which is one month more than for patients who had an ECV. After a consultation, patients either went to the FHLA after 17-18 weeks, had a PVI after 7 weeks, or their pathway ended. After a PVI, these patients went back to the OC after, on average 25 weeks, ended their pathway, or two patients went to the FHLA after 1-2 weeks. The hisbundle-ablation only occurred once, therefore, we cannot make significant statements about that care activity.

We only compared the traces of patients who did and did not have an ECV. Figure 5.18 shows the traces of patients with an ECV.

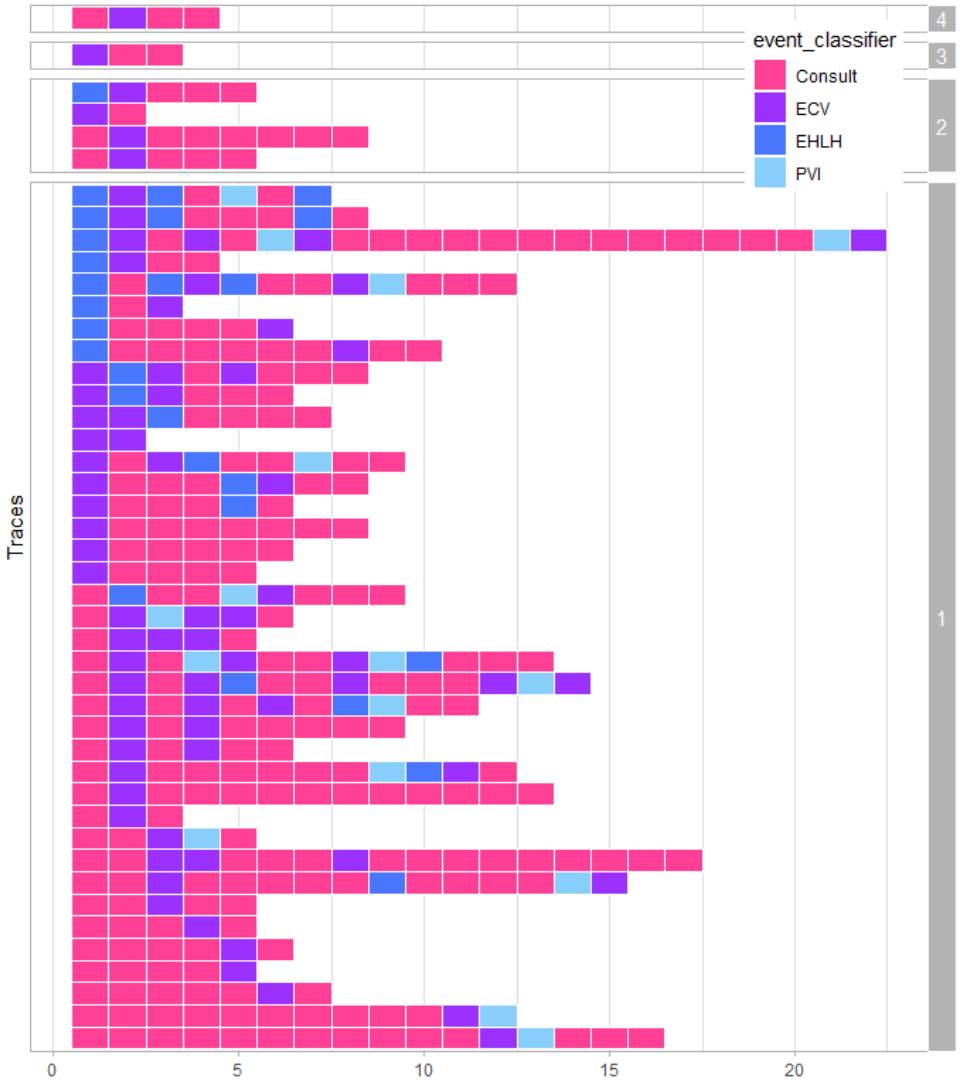


Figure 5.18: Traces of Patients with an ECV, level Basic

Figure 5.18 shows there were 6 traces that occurred more than once. They all included one ECV as either the start point or second care activity. One trace (2 patients) started at the FHLA, after which the first activity was an ECV. The 5 traces only included consultations next to the ECV, ranging from 1 to 7 consultation. The other 39 traces occurred once. Of these, 8 traces started at the FHLA, of which half had a consecutive ECV. Of the 8 traces that started at the FHLA, 4 traces included a PVI, all after multiple ECVs, readmissions, and/or consultations. There were 20 traces where the ECV was either the starting point or second care activity of the trace. Of these, 12 traces included multiple ECVs and/or readmissions to the FHLA. PVIs occurred in 14 traces, of which 11 included several ECVs and/or readmissions. The other PVIs occurred after multiple 10 or 11 consultations. Last, there were 10 traces that occurred once and included one ECV and multiple consultations, ranging from 2 to 13 consultations.

Figure 5.19 illustrates the traces of patients without an ECV.

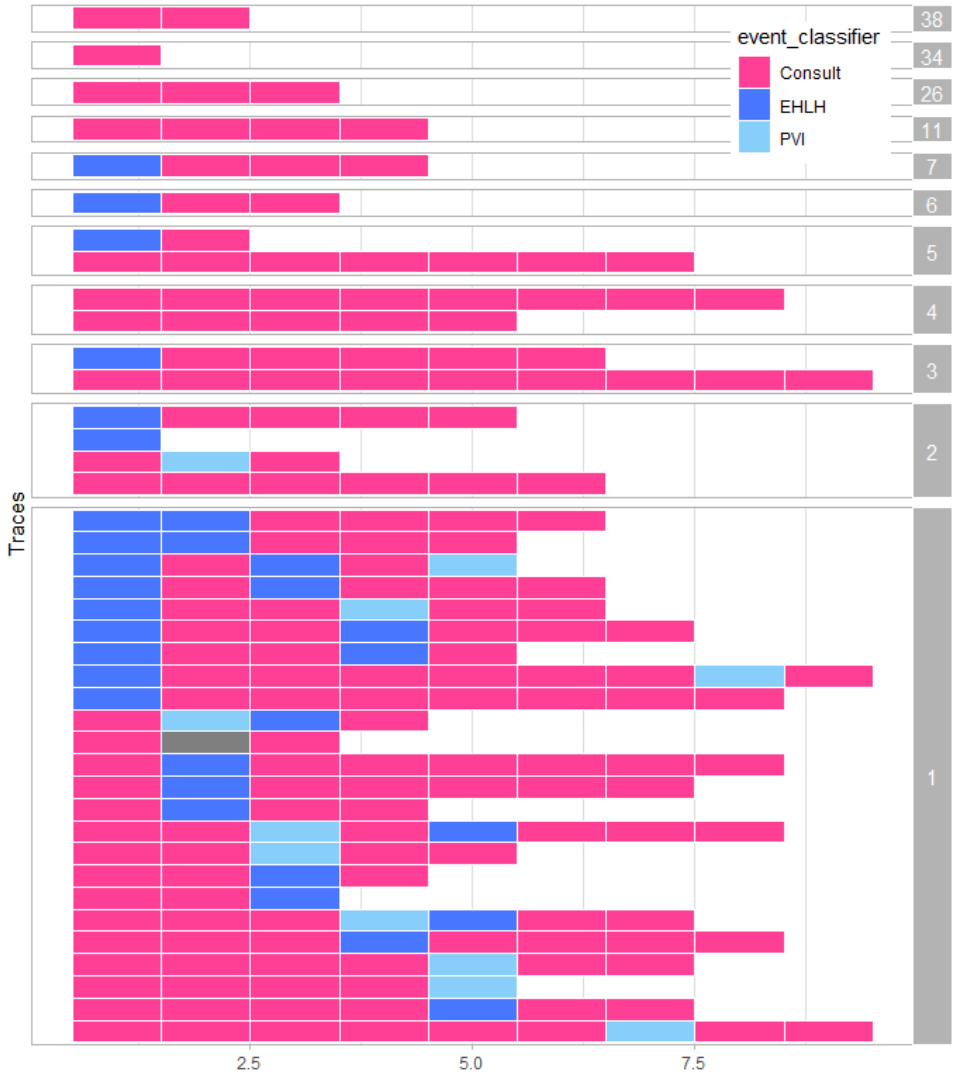


Figure 5.19: Traces of Patients without an ECV, level Basic

Figure 5.19 illustrates 16 traces that occurred more than once, representing the traces of 154 patients. Of these, there was one trace (2 patients) that included a PVI. Moreover, there were 6 traces (25 patients) that started at the FHLA, after which 1 trace (2 patients) did not come back and the other 5 traces had consultations. The other 9 traces all comprised solely consultations, ranging from 1 to 9 appointments. The other 24 traces also included readmissions (16 traces), PVIs (10 traces), and one hisbundle-ablation. The number of consultations ranged from 2 to 9. The PVIs occurred after more than three consultations or a readmission in 7 traces. The other 3 PVIs took place after one or two consultations. Overall, the traces of patients without an ECV mostly contained consultations and some included one readmission and/or one PVI.

Throughput Time

Table 5.11 provides an overview of the throughput times in weeks of patients with an ECV and without an ECV. The p-value of the Welch Two Sample t-test for the difference between throughput time of patients with and without an ECV is 4.045e-06, thus the patients with an ECV have a statistically significant longer throughput time.

	Mean	**SD**	**Median**	**Min**	**Max**
ECV	53.2	22.3	61.8	9.9e-05	78.4
No ECV	35.4	27.3	38.9	0	78.2

Table 5.11: Throughput Time for Patients with an ECV and without an ECV (Experiment 4)

Trace Frequency

Since there were no differences between patients who had an ECV in Meppel and Zwolle, we only compared the trace frequencies of the group with and without an ECV. Table 5.12 contains the average frequency [$\pm SD$] a trace occurred in each dataset, the minimum frequency, and the maximum frequency. The Mann-Whitney U Test provided p-values below 0.05 for all event logs. Hence, the trace frequency is statistically significant lower for the event log of patients with an ECV.

Event log	**Mean** [$\pm SD$]	**[Min, Max]**
ECV	1.2 [0.59]	[1, 4]
No ECV	4.5 [8.52]	[1, 38]
p-value	*0.002205**	
ECV	1.1 [0.51]	[1, 4]
No ECV	4.5 [8.52]	[1, 38]
p-value	*0.000645**	
ECV	1.1 [0.39]	[1, 3]
No ECV	3.2 [5.92]	[1, 34]
p-value	*0.002458**	

Table 5.12: Summary Trace Frequencies Experiment 3

5.5.3 Discussion of Outcomes

During this experiment, we aimed to compare the pathways with (n = 54) and without ECVs (n = 178). Theoretically, ECVs should not occur due to the episodic nature of paroxysmal AF. ECVs in Zwolle would be more logical, as they are performed in cases of severe symptoms. ECVs in Meppel should, in principle, not occur, except at the beginning of a care pathway due to an unclear diagnosis.

First, we examined the differences between patients with an ECV in Meppel and Zwolle. No relevant statistically significant differences were found, except that a higher percentage of patients with an ECV in Zwolle was readmitted or had a PVI. The link between the ECV in Zwolle and the PVI is explained by the cardiologists. They stated that patients who had this type of treatment are more likely to be referred to Zwolle, as the patients underwent an invasive procedure.

For the comparisons between the groups with and without ECVs, some differences emerged. First, we observed that patients with an ECV have a significantly longer throughput time than patients without an ECV. Additionally, the patients with an ECV had significantly more care activities during their care pathway than patients without an ECV. For the group without an ECV, this likely means that their pathway consisted of creating a medication plan and, in case of severe symptoms, a PVI is recommended. Therefore, the strategy to start with consultations and recommending a PVI by persisting symptoms seems to reduce the number of care activities and the throughput times. The cardiologists support that observation, as a PVI is a suitable treatment for paroxysmal AF. If the strategy included ECVs, the outcomes were less durable and the cardiologists expect that it increases the number of care activities and throughput time.

The care pathway frequency was significantly higher for patients without an ECV than for those with an ECV. This indicates that patients without an ECV followed more standardized pathways than those with an ECV. In Figure 5.19, we see that most of these traces consisted solely of consultations. For patients with an ECV, almost all pathways were unique, with a maximum trace frequency of 4. This could indicate that as soon as activities other than consultations were included in the pathway, the structure was lost. One possible explanation is that each patient is unique and, therefore, follows their own path. However, there could be more standardization regarding the number of consultations in a care pathway or before and after an ECV or PVI. Furthermore, we, the researcher and the validation panel, expect that patients with an ECV had more variation in care providers. These variations may have contributed to less standardization, as the care provider was less familiar with the patient and policies varied between specialists.

6. Conclusion

In this chapter, we answer the research question: *"What processes indicate an imbalance between standardization and personalization in the care pathways of AF patients at Isala Heartcenter?"* The answer is based on the results of the experiments and supported by the validation panel.

In experiment 1, 10.6% of all traces solely included consultations. These traces belonged to 55% of all patients. If we include a visit to the FHLA, where a patient has a consult with a physician as well, this is 15% of the traces and 73% of the patients. Therefore, Isala made a step towards standardization: if possible, install the patient on medication during consultations and check with follow-up consultations if the medication is correct. However, the number of consultations ranges from 1 to 9 appointments over a period of at most 18 months in the traces that included solely consultations. Hence, the number of follow-up consultations is highly personalized. The other traces also included ECVs and/or PVIs. However, the trace composition, both the type and number of care activities preceding or succeeding ECVs and/or PVIs, were significantly variable. This means that ECVs and PVIs are more often the exception than the norm. Moreover, the variability of traces that included ECVs and PVIs indicates little standardization on when to incorporate those treatments in the care pathway.

The type of care provider also contributed to an imbalance between standardization and personalization. There was a distinction between traces where a patient switched once from PA to physician (or vice versa) and traces where the switch was reversed again. Patients who go to a PA are expected to be less complex and have already been assessed by their GP, allowing the PA to create an appropriate treatment plan. A reason for switching from PA to physician is that the patient's condition has become more complex. However, we also saw that in three out of four traces where a patient had an ECV after consultation with a PA, the patient had a follow-up with a physician. The reason for this is that a patient was only referred to a PA if this was explicitly stated in the referral; otherwise, they were scheduled with a physician.

The scheduling of patients also affected by the utilization of the AF-OC and OC. If a patient called with symptoms, they were scheduled at the first available slot, which was at an arbitrary cardiologist. This was not visible in the trace explorers, but was noted by the validation panel. As a result, patients often saw multiple physicians and, therefore, there was no physician with a complete picture of the patient. These patients thus required more time to be properly installed on medication, and other treatment options were discussed later, i.e., the care pathway was more personalized.

Different physicians also followed different policies regarding consultations, ECVs, and PVIs. In the pathways that included ECVs and/or PVIs, we saw not only more consultations, but also more variability in the number, timing, and placement of ECVs and/or PVIs during the care pathway. The fact that the traces involving a PVI had only one consultation with a PA after the PVI confirmed that a PVI is an appropriate treatment for paroxysmal AF. However, the traces preceding the PVI were highly variable. There were 25 traces (26 patients) with at least one PVI, of which 36 % traces (38.5% of the patients) had at most three care activities beforehand, either consultations and/or ECVs. For patients who started at the FHLA, which indicates severe symptoms, the PVI occurred in one of nine traces after at most three care activities. This indicates a cautious approach towards early PVIs, whereas earlier interventions might reduce the overall pressure on the healthcare.

In summary, the imbalance between standardization and personalization results from variability in follow-up consultations, inconsistent in the use of ECVs and PVIs, variation in policy per care provider, and scheduling constraints.

7. Discussion

In this chapter, we discuss the recommendations, relevance and limitations of this thesis. Moreover, we provide recommendations on how to expand this research. First, Section 7.1 elaborates on the recommendations for Isala based on the results of this thesis. Section 7.2 discusses the scientific contribution of this research. Section 7.3 elaborates on the practical contribution, i.e., what Isala can do with this research. Additionally, Section 7.4 lists the limitations of this thesis. This regards the methodology, model, data, and other relevant factors. Last, 7.5 provides recommendations to extend this study as well as for other additional studies.

7.1 Recommendations

The conclusion, stated in Chapter 6, contains the processes that indicated an imbalance between personalization and standardization of the care pathways of patients with paroxysmal AF. The research goal was to provide improvements plans to effectively balance standardization and personalization, i.e., how to improve the processes pointed out in Chapter 6. Therefore, we discussed the results with the validation panel, consisting of medical experts and staff of the continuous improvement team. Together, we established three pillars, all representing a different process that can be improved. These three pillars and related improvement plans are (1) increasing continuity in care providers, (2) more efficient use of the AF-OC, and (3) stricter agreements on treatment strategies.

Increasing Continuity in Care Providers
Based on our analysis, we expect that patients who had more care activities and a more unique care pathway, saw multiple care providers during their care pathway. Here, we do not only distinguish between PA and physician, but also the specific PA and/or physician. We were not able to validate this statement with data, but we confirmed this with the validation panel. By creating more continuity - a patients sees the same care provider during their care pathway - we expect to bring more consistency in the care pathways. When a patient is under the supervision of a specific care provider, this ensures that the patient is monitored better. As a result, the provider is more familiar with the patient and, if necessary, can offer appropriate advice remotely through e-consultations or telephone consultations. This reduces the need for appointments at the OC, and therefore, creates capacity for more complex patients.

More Efficient Use of the AF-OC
Shifting care from the OC to the AF-OC offers two major advantages. First, it reduces the workload for cardiologists, allowing them to focus more on complex patients. Second, by assigning responsibility for AF patients to the PA, this patient group will be monitored better, ensuring timely and appropriate interventions. Currently, the AF-OC is not optimally utilized. This is partly due to capacity shortage, since there is 0.5 Full Time Equivalent (FTE) - a unit of measurement that represents the total working hours of a full-time employee - currently available for the AF-OC. Though, the suboptimal use can also be contributed to patients that not being referred to the AF-OC. We propose informing the scheduling staff about planning patients at the AF-OC based on specific patient criteria; patients who are less complex can be referred to the AF-OC either directly from their GP or after an initial consultation with a cardiologist. By shifting this care, less complex patients will receive more appropriate care, as they are monitored by the PA. Additionally, complex patients will be able to see cardiologists more quickly due to the freed-up capacity, improving the quality of care.

Stricter Agreements on Treatment Strategies
Our analysis showed that care pathways involving ECVs and PVIs have more variation compared

to those with solely consultations. This is due to the varied number of consultations preceding a PVI. We recommend introducing PVIs earlier in the care pathway for patients for whom medication is insufficient (more than three consecutive consultations) and for those for whom an ECV does not provide durable results (multiple ECVs). By setting a clear threshold - such as three consultations or one ECV - the treatment strategy can be standardized. Offering PVIs earlier will reduce the number of follow-up consultations per patient, as the standardized approach will require fewer preceding consultations, and the follow-up care for PVIs involves minimal consultations. By categorizing patient characteristics and symptoms into structured frameworks, standardized care pathways can be established, providing care providers clear strategies. Meanwhile, flexibility to personalize pathways for more complex patients remains.

Additionally, if a patient does not require an ECV or PVI, or the patient is in the follow-up phase after an ECV or PVI, clearer agreements of the time period between consecutive consultations could enhance uniformity of the care pathways. According to AF-CARE, a period of six months is appropriate for follow-up. In this model, that would mean that per patient, on average, three to four consultations would occur. This follow-up could be at the OC, AF-OC, via telephone, or perhaps in the future, based on telemonitoring. Ultimately, a number around 3 consultations (2-5) per patient in this model, would indicate standardization of the follow-up period.

By implementing these improvements, we expect an increase in the frequency of standardized pathways and a reduction in the number of consultations. Structuring care pathways based on patient characteristics and symptom severity will provide care providers with clear guidelines on the most suitable path for each (low complex) patient. This approach integrates the benefits of standardized care pathways while incorporating personalization due to the complex nature of AF. In the PM analysis, standardized patients will apply to less complex patients, whereas we should be able to explain the unique pathways by the complexity of the patient.

7.2 Scientific Contribution

The scientific contribution entails the added value of the technological contribution, such as data collection and the design of the PM model.

The implementation of HIS for analyzing and improving care pathways is encouraged by the WHO (Gartner et al., 2022). While care pathways offer advantages in terms of efficiency and quality, the unpredictable nature of conditions such as AF makes standardization of care pathways challenging. This study contributed to bridging this gap by demonstrating that standardization and personalization of care do not have to be contradictory, but can complement each other. Specifically, we provided a structured framework for care providers, allowing for standardized procedures while enabling necessary deviations without compromising overall consistency.

This study extends the primary goal of process discovery and process analysis by incorporating performance measurement, such as trace frequencies, and identifying areas for improvement. Similar to Peng et al. (2024) and Yang et al. (2023), we aimed to extend PM beyond its basic features. In this research, we used the fundamentals of PM—event logs—and modified them to mimic a Fuzzy Miner. This novel approach allowed for control over the level of detail presented in the analysis, ensuring a more targeted and meaningful evaluation. To our knowledge, this is the first study to apply this method. By adjusting the granularity of the displayed details, we went beyond the process analyses performed by prior studies included in the Research Goals-Approach matrix (Figure 3.1). Furthermore, we integrated KPIs in a manner that not only measured overall performance (including throughput times and resource utilization) but also highlighted process variations based on strategic decisions. This approach enabled us to detect not only deviations but also their underlying causes, thereby identifying areas for targeted improvements.

This research aligns with the first three rows of the Research Goals-Approach matrix (Figure 3.1), covering process discovery, process analysis, performance measurement, and process improvement. Unlike existing studies, no prior research integrates a single technique to fulfill all three purposes without relying on a conceptual care pathway. Measurement and improvement are typically executed using DES based on conceptual care pathways. For example, (Rejeb et al., 2018) first applied PM to obtain a conceptual model, followed by DES for further analysis of the care pathway. Our research differs from Rejeb et al. (2018) by remaining within the PM framework rather than transitioning to DES. Instead, through an effective combination of KPIs, we achieved a comprehensive and actionable analysis of care pathways.

Furthermore, (Yang et al., 2023) and (Peng et al., 2024) initially applied PM but incorporated additional techniques to simulate hypothetical experiments. Since we have not yet executed experiments based on the improvement plans, we did not require the extensions proposed by Yang et al. (2023) and Peng et al. (2024). However, our method establishes a strong foundation for future experimental validation. Our approach could be extended to align with their methods to measure the impact of our proposed improvements, or the data extracted from our analysis could serve as input for DES, following the methodology of Rejeb et al. (2018).

By demonstrating that PM can be effectively used for discovery, analysis, and improvement, without requiring other modeling techniques, this study advances the field of healthcare process optimization. The integration of relevant visualizations and KPIs provides a novel methodology that enhances PM's applicability in healthcare. This method can, after several improvements, be used for other diseases or other hospitals as well through small adjustments. Therefore, this method does not only serve to detect imbalance between standardization and personalization of AF care pathway, but also for other (complex) diseases. This makes this research a novel approach to analyze current care processes, identifying areas of improvement, and re-evaluating the processes after implementation of the improvement plans.

7.3 Practical Contribution

The practical contribution encompasses the usefulness of this research for Isala and the overall healthcare sector.

This study contributes to the integration of standardized care pathways in the treatment of complex conditions. As discussed in Chapter 1, standardized care pathways play a crucial role in improving the quality of care by increasing efficiency and reducing errors (Gartner et al., 2022; Schrijvers et al., 2012). In the current healthcare system, there is growing attention to organizing care processes more efficiently through the implementation of care pathways (Samarasinghe et al., 2024)). While the effectiveness of this transformation has been demonstrated for low-complexity conditions (Montori et al., 2023), there is still limited research on its application to complex conditions, such as AF (Perron et al., 2024). This study contributes to the shift in healthcare structure by demonstrating how a balance can be found between standardization and personalization. By integrating standardized care pathways with sufficient flexibility for individual adjustments, both efficiency and quality of care can be ensured.

The problem cluster (Figure 2.2) illustrates this challenge of integrating care pathways with management of AF at Isala. The core problem, identified as "unclear care pathways", led to unclear responsibilities, fluctuating waiting times, etc. This proves the statement that unclear care pathways counteract the advantages of standardized care pathways (Bujold et al., 2022; Samarasinghe et al., 2024). We expected that the unclear care pathways were influenced by either unfamiliarity with policies or that policies were not being followed. This research highlighted that both influences contributed to the unclear care pathways at Isala. First, the policy, AF-CARE, is open to interpretation, reducing the uniformity of this policy. Hereby, the policy was not always followed, since we saw ECVs along the care pathways and variability in

the follow-up periods. This study obtained the current care processes at Isala, and together with the questions we asked the validation panel (Section 4.4), we were able to gain knowledge about when and why AF-CARE was not being followed. Returning to the problem cluster (Figure 2.2), this research aimed to clarify care pathways by incorporating standardization where possible. Through the improvement plans resulting from this study, the multiple places for admission still exist, but do not form a bottleneck, as they are established in Isala's policy for AF care. Hence, the problems resulting from the multiple places of admission will be reduced. Moreover, the collaboration between departments will be increased, as we standardize which patients should go to the OC, AF-OC, and FHLA, reducing the fluctuating waiting times. These improvements contribute to a more structured and efficient AF care pathway at Isala, ultimately enhancing patient outcomes and resource utilization.

While this study focuses on improving care pathways for AF within Isala, it can be extended to other hospitals as well. The methodology developed in this study provides a structured approach that can be adapted to other hospitals. The dataset was retrieved via CTcue, which searches in HiX, a HIS that was used by 72% of Dutch hospitals on 01-01-2024 (de Bruyn et al., 2024). Moreover, the search terms in CTcue are easily adaptable to a hospitals' own structure, as they included department names, Dutch DBC codes, Dutch care activity codes, and the universal names for AF classifications. Moreover, the RStudio scripts are generalizable, as long as the right terms are assigned to the correct activity descriptions. Checking the conformance with AF-CARE can be executed with solely the Dutch care activity codes, making Experiment 1 (Section 4.5.1) generalizable to other hospitals. Simulating the Fuzzy Miner can be adapted to each hospital's individual wishes, as the details are based on the hospital's structure. Therefore, each hospital can decide what they want to reflect in the dataset- and process analyses (Section 4.3). For example, in this study we distinguished the OC and AF-OC, as this is an important reflection of Isala's structure, while another hospital might have another structure they want to reflect.

The combination of analyses and visualizations not only provides a comprehensive view of care processes within Isala, but can be implemented in other hospitals as well. By offering insights into hospital-specific decisions and the organizational impact of different strategies, this study makes a valuable contribution to improving care pathways for complex conditions. The results demonstrate that it is possible to obtain the benefits of standardization while maintaining room for patient-specific adjustments. Ultimalty, this methodology can be used to convert RWD into concrete improvement plans that balance standardization and personalization in the care pathways of complex conditions.

7.4 Quality and Reliability

We collected patients based on AF-DBCs, including patients who had a new AF-DBC between 01-01-2023 and 01-07-2023 without a prior cardiological history. With this inclusion period, we included 232 patients in the dataset of patients with paroxysmal AF. This period was long enough to gather a sufficiently large dataset. Despite the extensive queries in CTcue, it is possible that we included patients who did have a prior cardiological history, whether or not in Isala. This is evident in a patient undergoing a hisbundle ablation, whose trace appears as 'consult-hisbundle ablation-consult.' This path does not correspond to a new paroxysmal AF patient but rather to a patient already undergoing treatment for a different AF classification, such as permanent AF. If this happened for one patient, it is likely that it happened more frequently.

We assumed that the first appointment in Isala for AF represented a valid starting point for each patient's care pathway. However, this assumption also included patients who may have already started their care pathway at another hospital. These patients could not be filtered out

based on our queries, but their traces may have been affected, potentially appearing shorter due to prior care activities elsewhere. Had we excluded these patients, the pathways might have been longer on average. However, doing so would have removed many relevant patients from the dataset, requiring a longer inclusion period to gather the same number of patients.

We retrieved comorbidities for all patients using CTcue, specifically diabetes, obesity, and hypertension. Diabetes could be accurately identified via the DBC, but obesity was only included if explicitly recorded. This means that obesity for patients with obesity but their BMI was not registered was incorrectly classified as absent in the dataset. For hypertension, there is a risk of overestimation due to 'white coat hypertension,' which can influence blood pressure measurements. Cardiologists mentioned that the blood pressure can be up to 30mmHg higher in the hospital than at home.

We obtained AF classification from the medical records, specifically from reports. Classification was known for only 60% of patients, which could be due to two reasons. The first is that our queries were not comprehensive. Because we searched in plain text, we may have missed certain typos or abbreviations, resulting in missing classifications. The second reason is that classification may not have been recorded for some patients, indicating complexity or an inability to determine a classification. For these patients, standardized care pathways may not be available, as the patients do not fall within an AF-CARE care pathway. If this is the case, we may have overestimated the standardization of AF care pathways in this study. For the 60% of patients with a classification, we had to manually relabel a significant portion. Although there is a field in HiX where classification can be recorded, it is not currently used. If this were implemented, the query would be more thorough, and the data would be more reliable. We also found that relabeling was often necessary due to recurrent AF. This indicates that our queries should be refined to better exclude previous AF cases.

The first classification was not always recorded at the beginning of the pathway, making it debatable whether the classification was correct or whether the pathway matched the classification. Some patients had complex pathways involving various care activities, which could indicate comorbidities or classification changes. If a patient, for instance, switches from PA to physician, classification changes or increasing complexity could be factors. Additionally, we did not retrieve data on reclassifications. Since identifying the initial classification was already challenging, retrieving reclassifications would require even more manual validation, reducing reliability. However, incorporating reliable reclassification data could improve data quality by providing more insight into deviations from standardization or specific treatment decisions. Finally, the two-month period before the first DBC proved to be a sufficient period for retrieving classification data. Different timeframes showed that a two-month period before the DBC yielded the most complete results. A shorter period led to data loss, while a longer period added little extra information.

We collected care activities over a period of 18 months per patient. The data revealed that most patients had care activities for about 46 weeks within the 18-month period. This suggests that after these 46 weeks, patients had longer intervals between appointments, likely for follow-ups. Our traces also showed all types of care activities, including consultations, ECVs, and PVIs. Follow-up consultations after these treatments were also observed, as well as repeat ECVs and repeat PVIs in some cases. Overall, the 18-month period was sufficient to provide insight into treatment strategies and follow-up decisions. Extending this period would likely result in more follow-up consultations and potentially more repeat PVIs, increasing variability in care pathways and making the data more complex. Since we followed all patients for the same duration, we were able to make strong conclusions regarding strategies, the occurrence of care activities, and follow-up intervals. We found significant variability in follow-up intervals within the same period, making this assumption valuable for the study.

We retrieved care activities using care activity codes, ensuring reliability. These codes are standardized across the hospital, preventing missed appointments due to keyword-based queries. However, there is a high likelihood that some appointments were missed because activities were only included if they were linked to a relevant DBC. The complex nature of AF means that it often coexists with other cardiological conditions. While the DBC provides structured registration, there remains a risk that not all relevant consultations were included, particularly when multiple cardiological conditions were discussed during a consultation.

The experiments added depth to our results, conclusions, and recommendations. By splitting the data down into subprocesses, we were able to support our findings better and gain more insight into when and why deviations from standardization occurred. However, for experiment 3 (OC vs. AF-OC), the dataset of patients starting at the AF-OC was too small to perform some statistical tests. If the improvement plans are implemented, i.e., leading to more patients starting at the AF-OC or being referred there, this issue could be resolved. Additionally, instead of splitting patients based on their starting location, we could consider grouping them based on whether they had appointments at the AF-OC. This approach would capture more patients in the AF-OC group, including those deemed suitable for the AF-OC after an initial consultation.

RStudio proved to be a user-friendly environment with many capabilities, offering flexibility. Since RStudio did not specify what type of miner it uses, we simulated a Fuzzy Miner manually, which was labor-intensive. While RStudio allows for frequency scaling, this approach removes entire pathways, potentially losing critical data. Creating levels of detail was highly useful for analyzing processes based on the desired level of granularity. However, manually creating these details meant that we were constrained by the dataset's structure. If alternative details needed comparison, a new column had to be created. Perhaps an interface in Shiny could allow for more dynamic detail selection, though this would require further research.

A key strength of this study was the validation of results by experts. Their contributions provided a better understanding of care pathways and insights into why certain traces deviated from expectations. Experts could, for example, assess why some traces required multiple treatments or were unusually long or short.

By combining process maps, trace explorers, Euler diagrams, and statistical tests, we were able to analyze results from multiple angles. This increased the reliability of our conclusions, as different analytical methods reinforced each other. For example, care activities from the table could be found in the process map. Subsequently, frequent traces from the process map could be looked up in the trace explorer. However, to obtain meaningful insights, we had to integrate the outcomes of the KPIs effectively, leaving room for interpretation and potential errors.

7.5 Future Research

Our research was a good first step in analyzing AF care pathways and developing improvement plans. However, the model can be extended in various ways to conduct more in-depth analyses to improve the quality of the improvement plans. These extensions depend on (improved) healthcare registration and new data collections.

Before we discuss the extensions, we recommend a few adjustments to the data processing method. During this study, we manually validated all datapoints, which required significant effort. The classifications had an error margin of 16.78%, which is quite high, meaning this step would need to be repeated in any future iteration of this research. However, since the classification can be registered in HiX, we recommend registering it properly to make the data more reliable, eliminating the need for this manual step. Additionally, we validated the comorbidity labels, which had error margins between 0.73% and 2.99%. These errors were either falsely present or falsely absent, meaning they canceled each other out. As a result,

this step does not need to be repeated in a future iteration. Subsequently, a significant amount of time was spent validating the care activities. It turned out that the remaining activities were either performed and/or requested by the Cardiology department and linked to a cardiological DBC. In the future, the care activities can be retrieved directly from CTcue with these restrictions, eliminating the manual validation. Lastly, there were issues with the registration of appointments and care providers, as this information was not always present or correct. We recommend paying close attention to this registration to reduce the need for corrections in future iterations, to improve data reliability.

The first extension of the model involves incorporating specific healthcare providers. This study suggested that, if there were many consultation, they likely took place with different care providers. By retrieving the specific care providers from CTcue, we can validate this assumption. Adding this data would support the conclusions drawn from this study and make the improvement plans more concrete. Additionally, it would allow us to identify which providers follow which policies and determine whether they adhere to the improvement plans.

Second, we recommend gathering more information about the patient group. By conducting a detailed patient analysis of those with unique care pathways, we can better validate these variations. These analyses can confirm whether the variations are logical or highlight random variations. Factors that could be included in this analysis are other comorbidities, worsening symptoms, and the development of heart failure. All these factors can influence a patient's care pathway. The more these factors can be quantified, the better we can determine which pathways are standardized and which are personalized. Additionally, a patient analysis of those starting at the FHLA would support the analysis of their care pathways. If we can categorize these patients, we can also determine which subsequent pathway suits their profile, and validate them using the method of this study.

Another recommendation is to incorporate the reclassification of AF, once the classification is consistently registered in HiX. Since a patient's classification often changes over time, the corresponding care pathway also changes. These changes could explain certain deviations from the initial care pathway. To accurately identify these variations, classifications must be correctly recorded to be included in the analysis.

By incorporating the above mentioned recommendations - specific care providers, a more detailed patient analysis, and reclassification - into the model, the research can be meaningfully repeated over time. This allows us to measure whether patients indeed follow the standardized pathways suited to their profile and whether unique pathways arise due to care providers or other patients' characteristics. Additionally, other improvement plans, such as increasing the role of PAs and promoting earlier PVIs, can be assessed. Expanding the analysis will also help determine why a particular improvement plan was successful or not.

Once these changes are implemented, the data generated from this method can be used to extract distributions for a DES model. The AF care process, including patient flow and care activities, can be simulated based on how patients move through the process map. This DES model can be used to analyze specific policy changes and be updated accordingly. For example, it could be applied to telemonitoring, where patients complete a questionnaire before a consultation, and a physician determines whether they need to come to the OC based on several factors. Costs can be linked to this process, as well as patient utilities. These factors can be calculated in the DES model to evaluate the impact of specific policy changes. Moreover, the DES model could be used to test different resource allocation policies, such as the use of the AF-OC.

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Yan, H., Gorp, P. V., Kaymak, U., Lu, X., Ji, L., Chiau, C. C., Korsten, H. H. M., & Duan, H. (2018). Aligning event logs to task-time matrix clinical pathways in bpmn for variance analysis. *IEEE Journal of Biomedical and Health Informatics*, *22*, 311–317. https://doi.org/10.1109/JBHI.2017.2753827

Yang, X., Huang, W., Zhao, W., Zhou, X., Shi, N., & Xia, Q. (2023). Exploring acute pancreatitis clinical pathways using a novel process mining method. *Healthcare*, *11*, 2529. https://doi.org/10.3390/healthcare11182529

A. Background

A.1 Care pathways for AF patients

The ESG Guidelines developed by Gelder et al., 2024 include several flowcharts representing the care pathway for AF-patients. These pathways are categorized into four types of AF: first-diagnosed, paroxysmal, persistent and permanent. The pathways from the guidelines are simplified to enhance understandability. Most medical terms and checks are removed, emphasizing treatment decisions and differences in the pathways.

A.1.1 First-diagnosed AF

Figure A.1 illustrates the care pathway for patients with first-diagnosed AF.

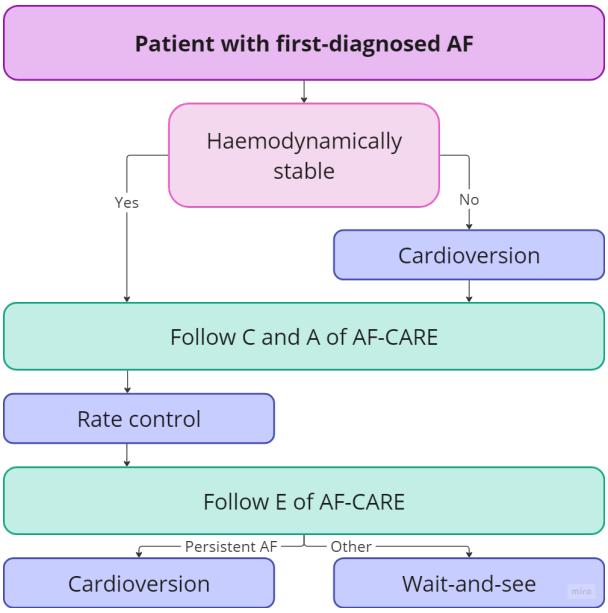

Figure A.1: Simplified care pathway of patients with first-diagnosed AF (Gelder et al., 2024)

This patient group's treatment strategy focusses mostly on rate control to reduce symptoms. Evaluation and re-assessment serve to monitor these symptoms' progression. If AF recurs, patients may move to the paroxysmal, persistent or permanent group. For persistent AF, cardioversion is recommended; otherwise, a wait-and-see approach is advised. From this stage onwards, rate control is always induced for AF-patients.

A.1.2 Persistent AF

Figure A.2 contains the care pathway for persistent AF.

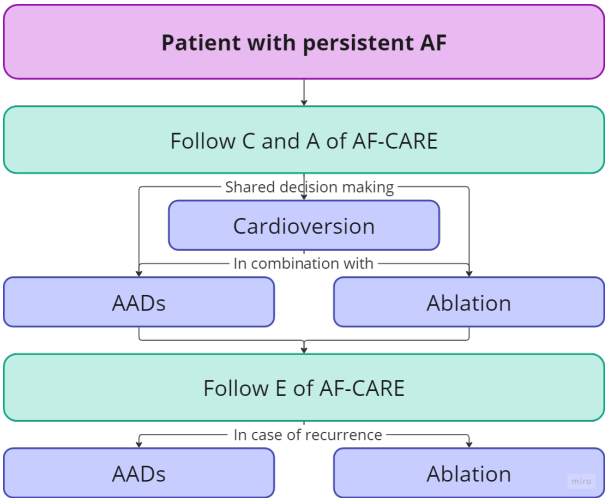

Figure A.2: Simplified care pathway of patients with persistent AF (Gelder et al., 2024)

Persistent AF can be treated by several strategies, all decided upon shared decision-making. The first step may be to perform a cardioversion to reduce symptoms. Additionally, patients may choose between AADs and ablation, either following cardioversion or als a standalone approach. Follow-up should point out recurrences, after which adjustment of AADs therapy or a new ablation can be chosen.

A.1.3 Permanent AF

Figure A.3 shows the care pathway of patients with permanent AF.

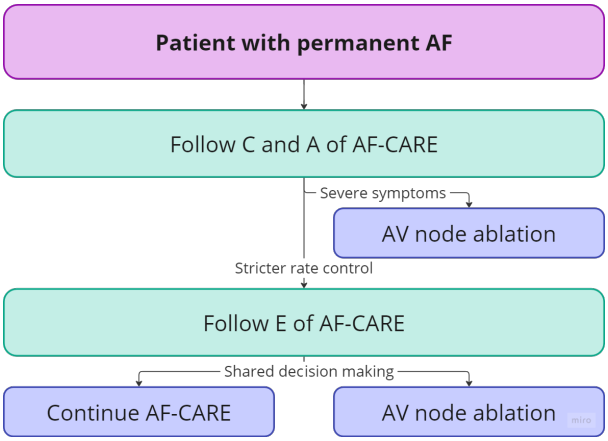

Figure A.3: Simplified care pathway of patients with permanent AF (Gelder et al., 2024)

Permanent AF cannot be treated by a normal ablation or cardioversion. This strategy mostly encompasses continuous AF-CARE and evaluation of symptoms. If symptoms are severe, an AV node ablation can be considered.

A.2 Cardioversion

The ESC guideline by Gelder et al., 2024 contains a flowchart that shows when cardioversion may be performed. The flowchart from the guidelines is simplified, highlighting only the parts that are interesting for this thesis. Figure A.4 shows the simplified cardioversion guideline.

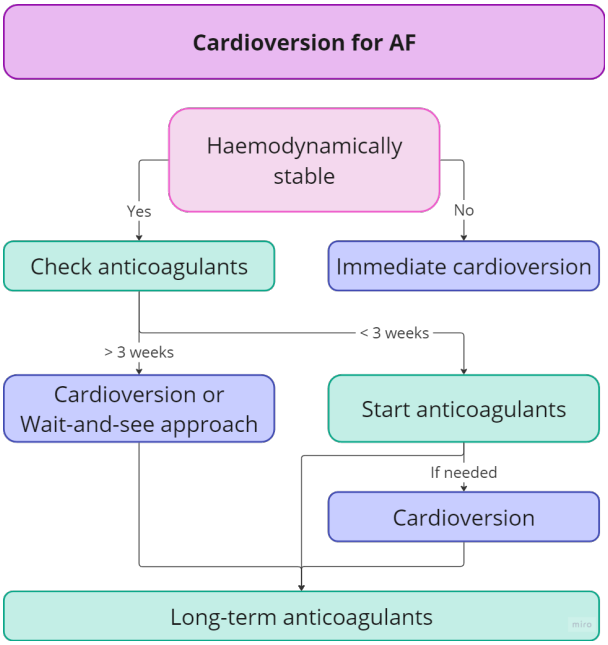

Figure A.4: Simplified guideline for cardioversion (Gelder et al., 2024)

Immediate cardioversion is performed only if a patient is haemodynamically unstable. For stable patients, the use of anticoagulants is checked. Anticoagulants must be used for at least three weeks before cardioversion, decreasing the risk of stroke or thromboembolus. Alternatively, a wait-and-see approach may be considered to allow for spontaneous cardioversion. If the patient is not eligible for cardioversion, anticoagulants should be started. After three weeks, elective cardioversion can be planned if necessary, during which spontaneous cardioversion might occur. Long-term anticoagulants are recommended for all patients to minimize the risk of stroke and thromboembolism.

B. Literature Review

B.1 Systematic Literature Review

The inclusion process of the systematic literature review is visualized in a flowchart in Figure B.1. The flowchart distinguishes the identification, screening and inclusion process, and the identification via Scopus and snowballing. For the identification via the database, Scopus, the identification consisted of using the search strings and removing all records that were not an article, book chapter or review, were not written in English or Dutch, and/or were published before 2005. Subsequently, the titles and abstracts of the remaining articles were screened to assess the eligibility of the studies. Next, duplicates of the remaining studies were removed. Furthermore, the full texts of the records were sought and screened. If there was no full text, or the study did not meet the exclusion criteria, the study was removed. This resulted in 19 studies.

The reference lists of these 19 studies were checked for relevant sources. This resulted in 11 records, which were assessed the same way as the database records. 6 of these studies met the criteria and were included in the study. In total, 25 studies were included in this systematic literature review.

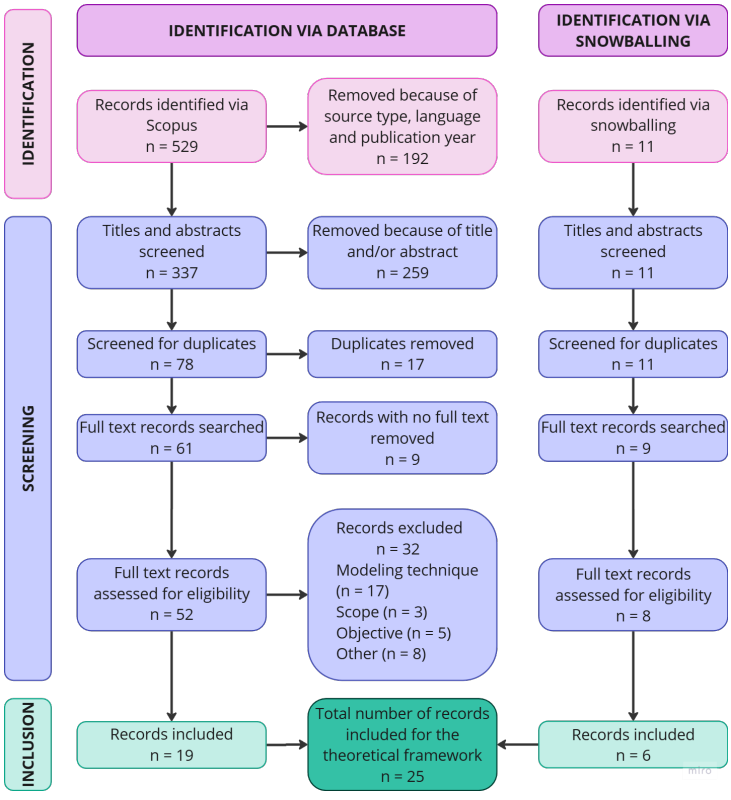

Figure B.1: PRISMA flowchart of the systematic literature review process on modeling techniques

B.2 Concept Matrix

The studies included in the literature review all modeled care pathways, using different types of modeling techniques. The concept matrix in Table B.1 displays what type of modeling technique was used in which study. The concepts are displayed as acronyms for the following modeling

techniques:

- **GLMM**: Generalized Linear Mixed Model
- **MLM**: Multinomial Logit Model
- **DES**: Discrete Event Simulation
- **BPMN**: Business Process Modeling Notation
- **DMN**: Decision Model and Notation
- **PM**: Process Mining
- **GA**: Genetic Algorithm
- **LDA**: Latent Dirichlet Allocation
- **PVA**: Pathway Variance Analysis

From Table B.1 we can see that the most frequently used modeling techniques were DES, PM and BPMN. An important note is that BPMN was commonly used in combination with another technique, such as DMN or PVA.

Table B.1: Concept Matrix Theoretical Framework

Article	Concept										
	Cox	**GLMM**	**Markov**	**MLM**	**DES**	**BPMN**	**DMN**	**PM**	**GA**	**LDA**	**PVA**
Adeyemi and Demir, 2020	X	X									
Adeyemi et al., 2013			X	X							
Ajmi et al., 2015						X					
Babashov et al., 2017					X						
Bahou et al., 2018					X						
Cardoen and Demeulemeester, 2008					X						
Chemweno et al., 2014					X						
Combi et al., 2017						X	X				
Oliveira et al., 2020								X			
Erdogan and Tarhan, 2018								X			
Funkner et al., 2022									X		
Gonzalez-Garcia et al., 2020								X			
Huang et al., 2013										X	
Huang et al., 2014										X	
Lahr et al., 2020					X						
Lanzarone et al., 2010			X								
Mans et al., 2008								X			
Ozcan et al., 2017					X						
Peng et al., 2024								X			
Pilgrim et al., 2009					X						
Rejeb et al., 2018					X			X			
Shukla et al., 2015											X
Wood et al., 2022					X						
Yan et al., 2018						X					X
Yang et al., 2023								X			
Frequency	1	1	2	1	9	3	1	7	1	2	2

C. Process Mining Model

C.1 CTcue Search

The search terms used in CTcue to collect the dataset are stated in the tables below. First, the patient cohort was assembled based on the following in- and exclusion criteria:

The inclusion criteria for the patient cohort consisted of patients who started at the outpatient clinic and patients who started at the FHLA. Therefore, the search queries were as follows:

Source	*Startdate*	*Enddate*	*Code*	*Status*	
DBC	01-01-2023	01-07-2023	0320 11 401	Gefactureerd, Gesloten	
OR					
DBC	DBCstart		0320 401		
Source	*Startdate*	*Enddate*	*Specialism*	*Department*	*Care activity code*
Care activities	01-01-2023	01-07-2023	Cardiologie	VPL.30A2 Spoed EHLH V3.0 SEH-M SEH Meppel VPL.M0J Acute zorgafdeling	190060 Eerste polikliniekbezoek 190021 Klinische opname

Table C.1: Inclusion Criteria of Patient Cohort

The startdate of the DBC on which patients were included, was defined as DBCstart. The exclusion criteria were patients who have had a DBC for AF before 01-01-2023, a DBC for heart failure before their an AF-DBC, and/or had not given permission for scientific research.

Source	*Startdate*	*Enddate*	*Code*	*Status*
DBC		31-12-2022	0320 401	Gefactureerd, Gesloten
DBC		DBCstart	0320 301 0320 302	Gefactureerd, Gesloten
	Policy			*Permission*
Consents	Wetenschap, Wetenschap en scholing			N

Table C.2: Exclusion Criteria of Patient Cohort

After the patient cohort was obtained, the data of these patients was collected. The search terms for all this data collection are described below.

The first AF related DBC was retrieved to obtain the episode of care ID. The query was:

Source	*Startdate*	*Enddate*	*Code*	*Status*
DBC	01-01-2023	01-07-2023	0320 11 401	Gefactureerd, Gesloten

Table C.3: Search Query first DBC

Then, all subsequent cardiological, cardiothoracic, and anesthesiological DBCs are obtained by:

Source	*Startdate*	*Enddate*	*Code*	*Status*
DBC	DBCstart	DBCstart + 18 months	0320 0328 0389	Gefactureerd, Gesloten

Table C.4: Search Query Preceding DBCs

The classification was retrieved using the following search queries:

Source	*Startdate*	*Enddate*	*Content*	*Specialism*
Reports	DBCstart - 2 months	DBCstart + 18 months	INCLUDE Diagnose/Conclusie/Samenvatting + Paroxysmaal/Paroxismaal/Persisterend/ Permanent/Chronisch, Paroxysmaal/Paroxismaal/Persisterend/ Permanent/Chronisch + Atriumfibrilleren/Atr/AF/Boezemfibrilleren/ Boezem EXCLUDE Atriumflutter/Flutter/Afl	Spoedeisende hulp, Cardiologie

Table C.5: Search Query Classification

The care activities were obtained by this query:

Source	*Startdate*	*Enddate*	*Care activity code*
Care activity	DBCstart	DBCstart + 18 months	190060 Eerste polikliniekbezoek 190013 Herhaal-polikliniekbezoek 190162 Belconsult ter vervanging van een herhaal-polikliniekbezoek 190164 Belconsult ter vervanging van een eerste polikliniekbezoek 033290 Behandeling met de cardioverter 032940 Hisbundel-katheterablatie 032941 Katheterablatie rechter atrium 032942 Katheterablatie accessoire bundel 032946 Katheterablatie linker atrium

Table C.6: Search Query Care Activities

The comorbidities were obtained by queries based on the following information:

Diabetes was identified through DBC diagnosis, HbA1c blood levels, and/or DBCs for diabetes. These values were checked before the AF-DBC opened, as we want to know if the patient had a history of diabetes. If multiple measurements were available, the most recent result was selected. An HbA1c value above 53 mmol/mol indicated diabetes.

BMI and blood pressure were derived from vital signs. The values were sought between the opening of the DBC and one month afterward. A BMI above 31 kg/m^2 was classified as obesity. Hypertension was defined as a systolic blood pressure above 140 mmHg. Only the first recorded blood pressure was included in the dataset to confirm or exclude hypertension at the start of the care pathway.

Comorbidity	*Source*	*Startdate*	*Enddate*	*Description/Name*
Diabetes	Diagnoses		DBCstart	Suikerziekte, DM, Diabetes, Diabetes Mellitus
	Measurements		DBCstart	Hb1Ac > 53 mmol/mol
	DBC		DBCstart	0313 221 0313 222 0313 223
Obesitas	Vital signs	DBCstart	DBCstart + 1 month	BMI > 31 kg/m^2
Hypertension	Vital signs	DBCstart	DBCstart + 1 month	Bloeddruk, Bloeddruk bovendruk > 140 mmHg

Table C.7: Search Query Comorbidities

C.2 Processing Dataset

To export the correct data from CTcue to Excel, certain data points needed to be checked. Per variable, we checked the following data points:

Patient	**DBC**	**DBC all**	**Classification**	**Care activities**	**Comorbidities**
PseudoID PatientID Age	Episode of care ID Specialty label Diagnosis code Diagnosis label Start date	Episode of care ID Specialty label Diagnosis code Diagnosis label Start date End date	Validation (Absent/Present labels)	Episode of care ID Description Care activity code Age at time of event Type Department Location Performing care provider position Performing care provider specialism Requesting care provider position Requesting care provider specialism Start date	Validation (Absent/Present labels)

Table C.8: Customized Columns for Export CTcue

The information that was relevant for the care activities needs to be uniformly coded. Therefore, we standardized certain care professionals, departments, and locations. Table C.9 provides an overview of what how the descriptions from CTCue were recoded, according to Step 7 in Section 4.2.

Category	*New description*	*Old description*
Care Professional	Arts [EN: Doctor]	AIOS Cardiologie AIOS Interne Geneeskunde ANIOS Cardiologie ANIOS IC Arts Assistent Cardiologie Arts-assistent Cardioloog cardioloog Chef de clinique chef de clinique cardiologie Sportarts Thoraxchirurg
	PA	Physician Assistant Physician assistant Cardiologie Physician assistant Cardiologie i.o. Verpleegkundige in opleiding tot specialist Verpleegkundig specialist Cardiologie Verpleegkundig specialist cardiologie
Department	Consult [EN: Consultation]	CAR - Cardiologie CONS - Consulten
	Spoed [EN: Emergency]	VPL.30A2 - Spoed EHLH V3.0 VPL.M0J - Acute zorgafdeling
Locations	Zwolle	Isala Hart Centrum Zwolle Isala Zwolle
	Meppel	Isala Diaconessenhuis Meppel Isala Meppel

Table C.9: Recoded Descriptions Care Activities

D. Results

D.1 Experiment 2: Starting at the OC vs FHLA

Figure D.1 illustrates the age distributions of both groups. The average age of the NP_Consult group was 70.1[±12.2] years, ranging from 28 - 94. For the NP_FHLA group, the average age was 67.8[±14.2] years, ranging from 31-94.

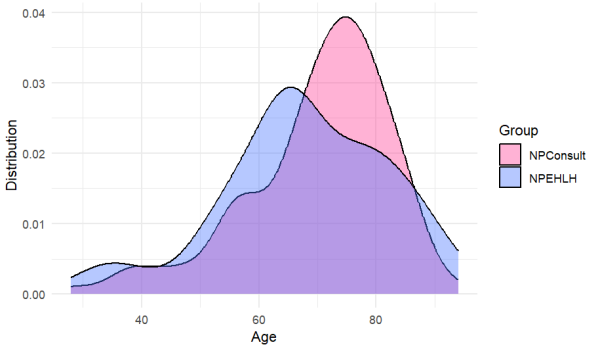

Figure D.1: Distribution of Age of Patients Starting at the OC or FHLA

According to the statistical tests, the age of the NP_Consult group was not proven to be normally distributed, but the age of the NP_FHLA group was. Hence, we performed a Mann-Whitney U Test, which gave a p-value of 0.2315, indicating no statistically significant difference between the age distributions between the groups.

Figures D.2 and D.3 provide information about the comorbidities of the patients in both subsets. The p-value of Fisher's Exact test (0.5114) indicates no statistically significant differences between the distributions of the comorbidities between the two groups.

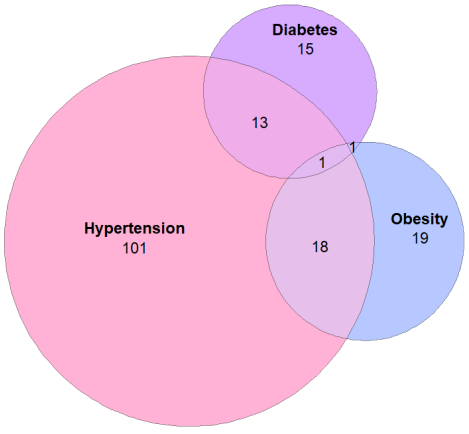

Figure D.2: Comorbidities of Patients with NP Consult

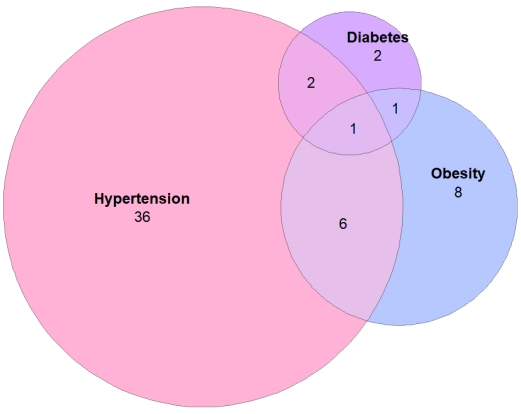

Figure D.3: Comorbidities of Patients with NP FHLA

Figure D.4 shows the percentage of patients who had a certain number of care activities during their care pathway for both groups. Figures D.5 and D.6 show the intersections of care activities. The patients who started with an NP_Consult had, in general, fewer care activities than patients who started at the FHLA. Figures D.5 and D.6 show that, when starting at the FHLA, more care activity types were included in the care pathway.

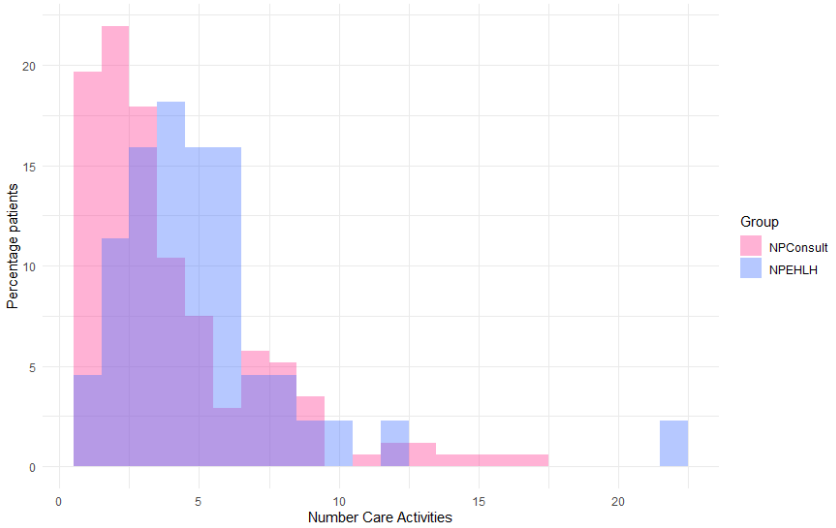

Figure D.4: Number of Care Activities per Patient Starting at the Consult or FHLA (%)

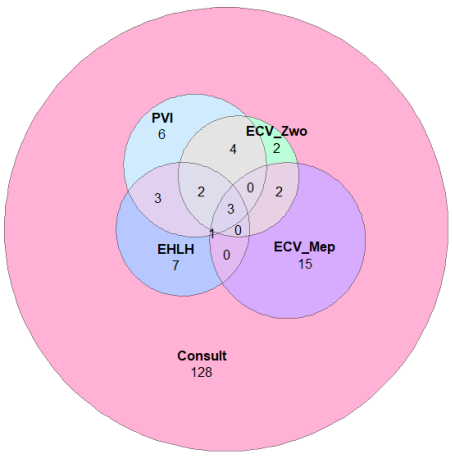

Figure D.5: Intersection of Care Activities of Patients with NP Consult

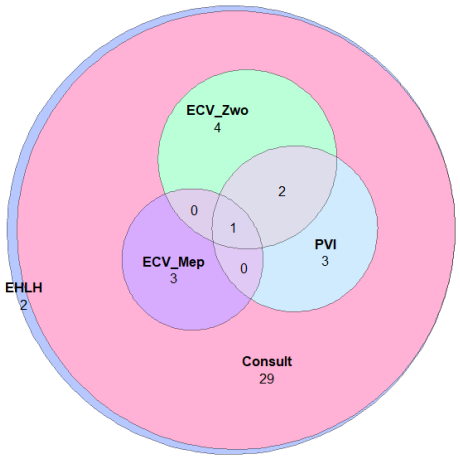

Figure D.6: Intersections of Car Activities of Patients with NP FHLA

The Shapiro-Wilk test for the groups gave a p-value below 0.05 for both groups. Hence a normal distribution was not proven. The Mann-Whitney U Test gave a p-value of 0.003, indicating the total number of care activities of patients who started at the FHLA was significantly more than for patients who started at the OC. Moreover, the Mann-Whitney U Test to assess the difference between combination of care activities per patient gave a p-value of 1.204e-15. Hence, there is a statistically significant difference.

Table D.1 provides more in-depth information about the occurrence of specific care activities.

Type	**Group**	**Total Activities**	**Unique Patients (n (% of total))**	**Mean** [$\pm SD$]
Consult	OC	605	173 (100)	3.50 [2.58]
	FHLA	148	42 (95.5)	3.52 [2.49]
p-values			*0.04037**	*0.5286*
FHLA	OC	16	16 (9.25)	1 [0]
	FHLA	56	44 (100)	1.27 [0.585]
p-values			*2.2e-16**	*0.05403*
ECV MEP	OC	29	21 (12.1)	1.38 [0.669]
	FHLA	6	4 (9.09)	1.5 [1]
p-values			*0.8186*	*1*
ECV ZWO	OC	18	13 (7.51)	1.38 [0.650]
	FHLA	8	7 (15.9)	1.14 [0.378]
p-values			*0.1917*	*0.4317*
PVI	OC	20	19 (11.0)	1.05 [0.229]
	FHLA	7	6 (13.6)	1.17 [0.408]
p-values			*0.4464*	*0.1949*

Table D.1: Summary Care Activities Experiment 2

Table D.2 contains all p-values resulting from the Shapiro-Wilk Normality Tests and Mann-Whitney U Tests for comparing the age and activities.

Age	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	3.087e-05*	0.2315
FHLA	0.3121	
Total Number Care Activities	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	1.26e-13*	0.002605*
FHLA	2.703e-07*	
Consult	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	3.547e-13*	0.5286
FHLA	6.574e-07*	
RA	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	NA	0.05403
FHLA	8.076e-11*	
ECV Meppel	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	2.966e-06*	1
FHLA	0.001241*	
ECV Zwolle	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	0.0001816*	0.4317
FHLA	4.136e-06*	
PVI	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	5.28e-09*	0.1949
FHLA	2.073e-05*	
Activity Combinations	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	2.2e-16*	1.204e-15*
FHLA	1.22e-07*	

Table D.2: Results from Shapiro-Wilk Normality Test and Mann-Whitney U Test for Comparisons of Age and Activities in Experiment 2

Table D.3 contains the p-values resulting from the Fisher's Exact Test for the patient proportions who had a certain type of care activity.

Patient proportion	**Consult**	**FHLA**	**ECV Meppel**	**ECV Zwolle**	**PVI**
Fisher's Exact Test	0.04037*	2.2e-16*	0.8186	0.1917	0.4464

Table D.3: Results of Fisher's Exact Test for Patient Proportions in Experiment 2

The throughput times of both datasets were examined with a Welch Two Sample t-test, calculated with the means and standard deviations of the datasets. Table D.4 contains the values that were used, resulting in the following p-value:

t-value	-2.085178
df	91.8071
p-value	0.03983*

Table D.4: Results of Welch Two Sample t-test for throughput times in Experiment 2

The trace frequencies were compared at each level of detail. The Shapiro-Wilk Test calculated whether the data was normally distributed and the Mann-Whitney U Test provided information about the difference between the two datasets. For example, if the Mann-Whitney U Test gave a p-value below 0.05, it indicates that the trace frequencies between the two datasets was statistically significant different. Table D.5 contains the p-values for these tests for all three levels of detail.

Basic	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	3.004e-13*	0.9226
FHLA	2.429e-07*	
Medium	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	3.004e-13*	0.9226
FHLA	2.429e-07*	
Detail	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
Consult	1.473e-15*	0.8003
FHLA	1.199e-07*	

Table D.5: Results from Shapiro-Wilk Normality Test and Mann-Whitney U Test for Comparisons of Trace Frequencies in Experiment 2

D.2 Experiment 3: Starting at the OC vs AF-OC

The average age of patients who started at the OC was 69.7[±12.2] years, ranging from 28-88. The patients who started at the AF-OC are, on average, 72.6[±12.5] years, ranging from 41-94. Figure D.7 shows the age distributions of both groups.

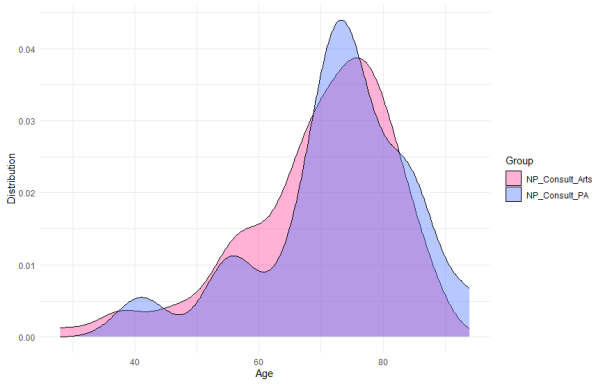

Figure D.7: Distribution of Age of Patients Starting at the OC or AF-OC

According to the Shapiro-Wilk test, the age of patients who started at the AF-OC is proven to be normally distributed, while the age of patients who started at the OC is not. The graph and descriptive statistics did not give the impression of a clear difference. Since not both datasets were proven normally distributed, we performed the Mann-Whitney U Test to test the difference. The p-value of 0.4232 did not prove that the difference of the ages of both groups was statistically significant.

Figures D.8 and D.9 illustrate the presence and overlap of comorbidities in both patient groups. Where diabetes was combined with hypertension for patients who started at the OC, the comorbidity did not intersect with other comorbidities for patients who started at the AF-OC. The Fisher's Exact test provided a p-value of 0.6936, indicating that there is no statistically significant difference between the distributions of the comorbidities in both groups.

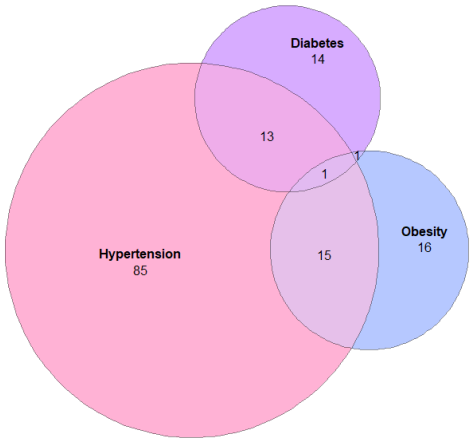

Figure D.8: Comorbidities of Patients Starting at the OC

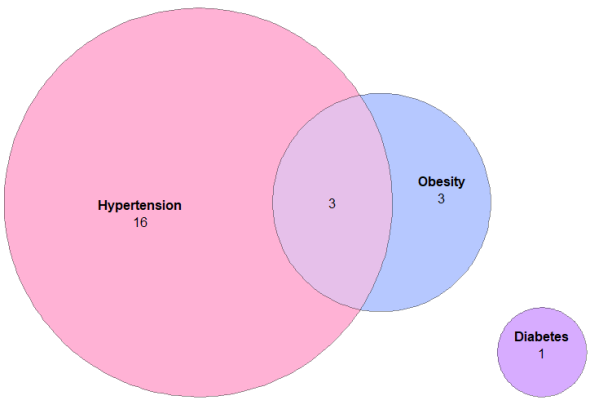

Figure D.9: Comorbidities of Patients Starting at the AF-OC

Figure D.10 illustrates how much percent of the patients had a certain number of care activities during their care pathway for both groups. Figures D.11 and D.12 show the proportions and intersections of the types of care activities that occurred for the patients. We see that patients who started at the OC had a variety of care activity types, while the patients who started at the AF-OC only had HCs and ECVs in Meppel. In these figures, there was no distinction between HC with a physician or with a PA.

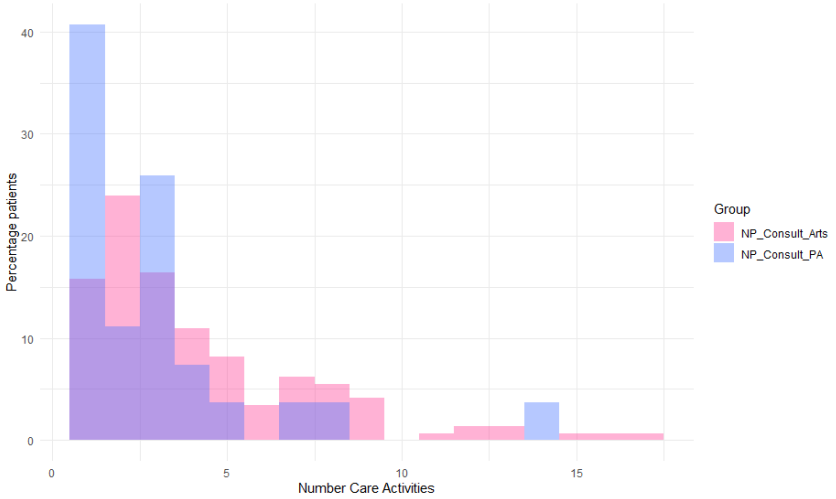

Figure D.10: Number of Care Activities per Patient Starting at the OC or AF-OC (%)

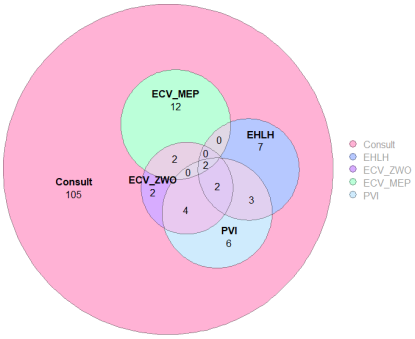

Figure D.11: Intersection of Care Activities of Patients Starting at the OC

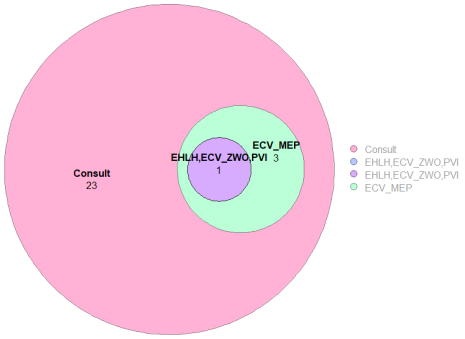

Figure D.12: Intersections of Car Activities of Patients Starting at the AF-OC

We concluded, from the Shapiro-Wilk test, that both distributions of total number of care activities were not proven to be normally distributed. Due to the distributions, we performed the Mann-Whitney U Test to see if there was a statistically significant difference between the distributions in Figure D.10. This test gave a p-value of 0.02, meaning patients who started at the OC had significantly more care activities. Additionally, the Mann-Whitney U Test to assess differences in care activity combinations gave a p-value of 0.1528. This indicates that there was no statistically significant difference between the combinations of care activities for both groups.

Table D.6 gives an overview of the specific care activities. The top row of each activity contains data of patients who started at the OC, the second row contains data of patients who started at the AF-OC.

Type	**Group**	**Total Activities**	**Unique Patients (n (% of total))**	**Mean** [$\pm SD$]
Consult	OC	535	146 (100)	3.66 [2.65]
	AF-OC	70	27 (100)	2.59 [1.99]
p-values			*1*	*0.02362**
FHLA	OC	15	15 (10.3)	1 [0]
	AF-OC	1	1 (3.7)	1 [*NA*]
p-values			*0.4722*	*NA*
ECV MEP	OC	23	17 (11.6)	1.35 [0.606]
	AF-OC	6	4 (14.8)	1.5 [1]
p-values			*0.4067*	*1*
ECV ZWO	OC	16	12 (8.22)	1.33 [0.651]
	AF-OC	2	1 (3.7)	2 [*NA*]
p-values			*0.7424*	*0.2493*
PVI	OC	19	18 (12.3)	1.06 [0.236]
	AF-OC	1	1 (3.7)	1 [*NA*]
p-values			*0.321*	*NA*

Table D.6: Summary Care Activities Experiment 3

Table D.7 contains all p-values resulting from the Shapiro-Wilk Normality Tests and Mann-Whitney U Tests for comparing the age and activities.

Age	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	3.914e-05*	0.4232
AF-OC	0.2564	
Total Number Care Activities	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	7.503e-12*	0.01804*
AF-OC	2.63e-06*	
Consult	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	1.002e-11*	0.02362*
AF-OC	3.991e-05*	
FHLA	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	NA	NA
AF-OC	NA	
ECV Meppel	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	2.083E-05*	1
AF-OC	0.001241*	
ECV Zwolle	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	9.189e-05*	0.2493
AF-OC	NA	
PVI	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	NA	NA
AF-OC	NA	
Activity Combinations	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	2.2e-16*	0.1528
AF-OC	8.926e-10*	

Table D.7: Results from Shapiro-Wilk Normality Test and Mann-Whitney U Test for Comparisons of Age and Activities in Experiment 3

Table D.8 contains the p-values resulting from the Fisher's Exact Test for the patient proportions who had a certain type of care activity.

Patient proportion	**Consult**	**FHLA**	**ECV Meppel**	**ECV Zwolle**	**PVI**
Fisher's Exact Test	1	0.4722	0.4067	0.7424	0.321

Table D.8: Results of Fisher's Exact Test for Patient Proportions in Experiment 3

The throughput times of both datasets were examined with a Welch Two Sample t-test, calculated with the means and standard deviations of the datasets. Table D.9 contains the values that were used, resulting in the following p-value:

t-value	2.97137
df	37.391
p-value	0.0052*

Table D.9: Results of Welch Two Sample t-test for throughput times in Experiment 3

The trace frequencies were compared at each level of detail. For example, if the Mann-Whitney U Test gave a p-value below 0.05, it indicated that the trace frequencies between the two datasets were statistically significant different. Table D.10 contains the p-values for these tests for all three levels of detail.

Basic	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	1.218e-12*	0.8195
AF-OC	7.172e-05*	
Medium	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	1.218e-12*	0.8195
AF-OC	7.172e-05*	
Detail	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
OC	3.737e-14*	0.4466
AF-OC	2.006e-05*	

Table D.10: Results from Shapiro-Wilk Normality Test and Mann-Whitney U Test for Comparisons of Trace Frequencies in Experiment 3

D.3 Experiment 4: Patients with and without an ECV

Table D.11 provides an overview of the ages in all datasets. Figure D.13 plots this information in a graph, visualizing the distributions.

	Mean	**SD**	**Median**	**Min**	**Max**
ECV	68.1	12.5	71	25	89
ECV_MEP	70.1	8.85	72	49	83
ECV_ZWO	66.5	14.4	68.5	25	89
No ECV	71.2	12.8	73	28	94

Table D.11: Age of Patients With or Without an ECV

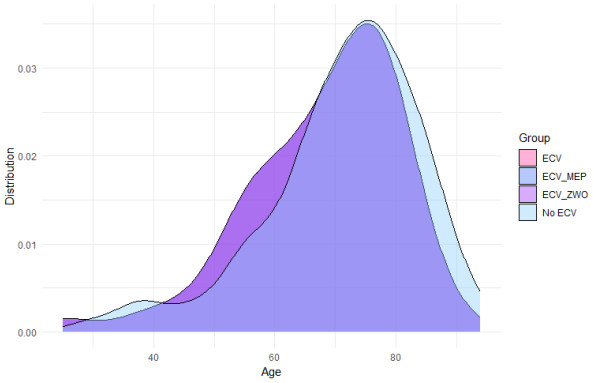

Figure D.13: Distribution of Age of Patients with or without an ECV

The ages of the groups with an ECV, with an ECV in Meppel, and without an ECV were normally distributed according to the Shapiro-Wilk test. Thus we performed a Mann-Whitney U Test to compare the ages between these groups. This gave a p-value of 0.3874, i.e., there is no statistically significant difference between the ages of the two groups. This means that we tested the age of the full ECV group against the age of patients without an ECV. The Two Sample t-test gave a p-value of 0.08775, thus the difference in age of patients having and not having an ECV was not statistically significant.

Figures D.14 and D.15 give the presence of comorbidities of the patients who had an ECV in Meppel or Zwolle, respectively. The presence and overlap of these comorbidities appeared to be similar. The Fisher's Exact test gave a p-value of 0.9585, supporting the expectation that there is no statistically significant difference between the presence and overlap in comorbidities between patients having an ECV in Meppel or Zwolle.

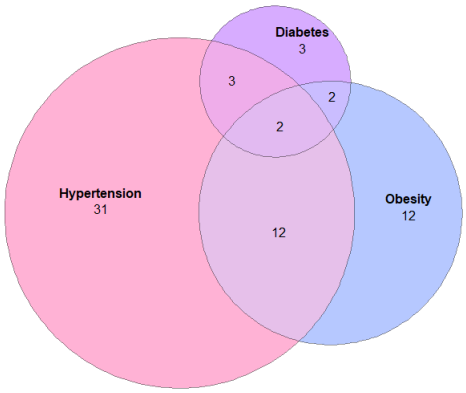

Figure D.14: Comorbidities of Patients with an ECV in Meppel

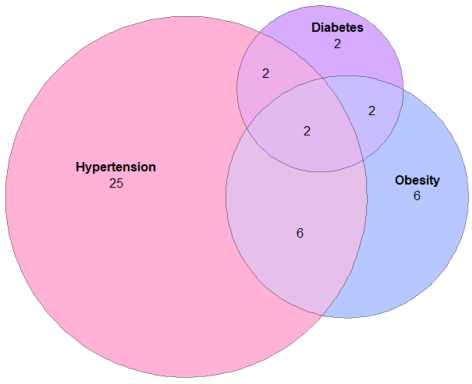

Figure D.15: Comorbidities of Patients with an ECV in Zwolle

Since there was no statistical difference between patients having an ECV in Meppel and Zwolle, we also compared the patients who had an ECV with patients who did not have an ECV. Figure D.16 and D.17 present the presence and overlap of the comorbidities of patients who had an ECV and did not have an ECV, respectively. The p-value of 0.07849 for the Fisher's Exact test indicates that the difference is not statistically significant.

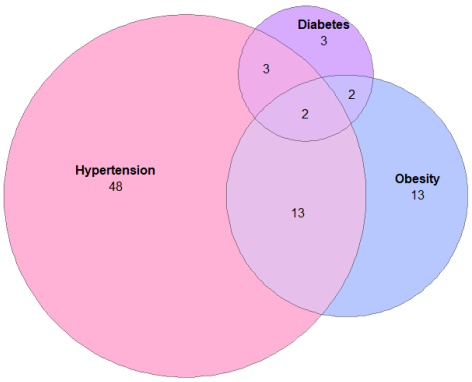

Figure D.16: Comorbidities of Patients with an ECV

Figure D.17: Comorbidities of Patients without an ECV

Figures D.18 and D.19 illustrate how much percent of the patients had a certain amount of care activities during their care pathway. Figure D.18 shows the distributions for patients with an ECV in Meppel and Zwolle, and Figure D.19 for patients with and without an ECV. Figures D.20, D.21, D.22, and D.23 give an overview of the combinations of care activities.

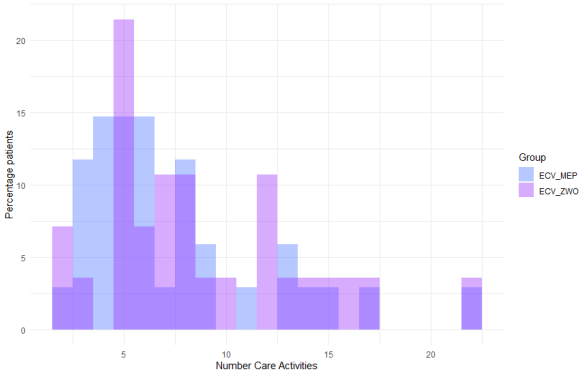

Figure D.18: Number of Care Activities per Patient with an ECV in Meppel or Zwolle

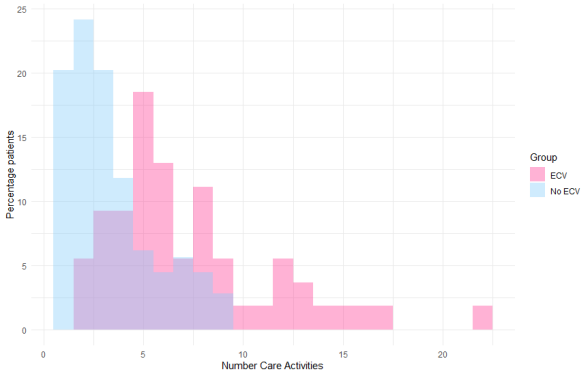

Figure D.19: Number of Care Activities per Patient with and without an ECV

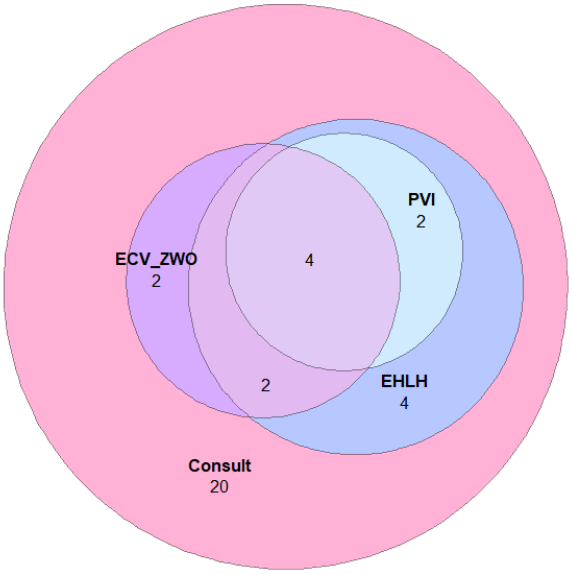

Figure D.20: Intersection of Care Activities of Patients with an ECV in Meppel

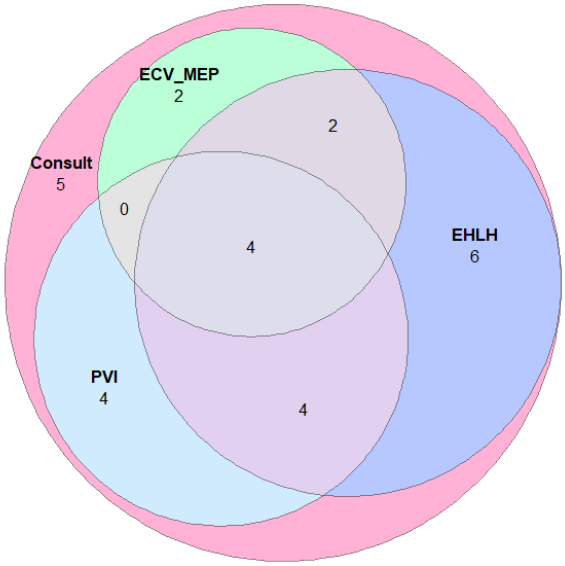

Figure D.21: Intersection of Care Activities of Patients with an ECV in Meppel

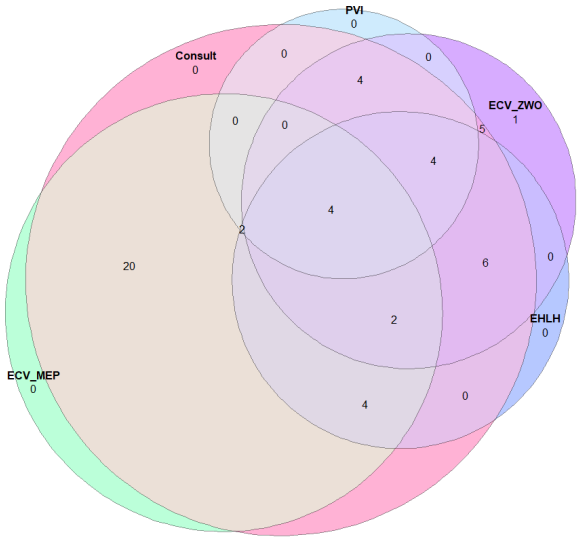

Figure D.22: Intersection of Care Activities of Patients with an ECV

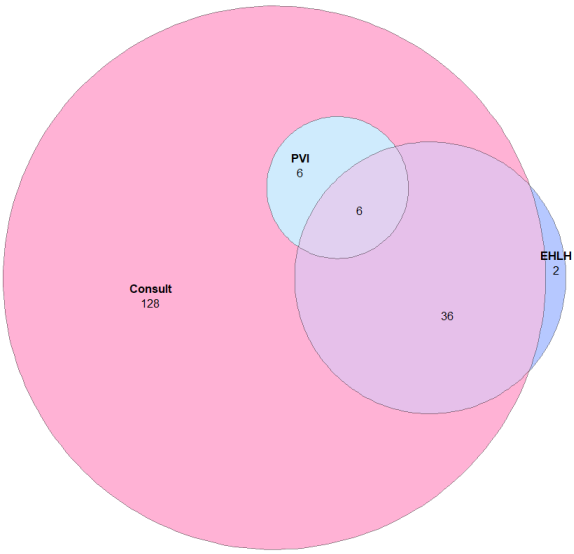

Figure D.23: Intersection of Care Activities of Patients without an ECV

The Shapiro-Wilk test pointed out that the distributions of total number of care activities of patients with an ECV in Meppel was not proven to be normally distributed. The subsequent Mann-Whitney U Test gave a p-value of 0.1814, indicating the number of care activities was not statistically significant different. Therefore, we were allowed to compare the group of patients with an ECV with the group without an ECV. Both distributions of number care activities were not proven to be normally distributed. The subsequent Mann-Whitney U Test gave a p-value below 0.05, indicating a statistically significant difference between the number of care activities of patients who have an ECV and do not have an ECV. The patients with an ECV have a larger total number of care activities during their care pathway.

Table D.12 provides an overview with more detail on the occurrence of specific care activity types. For each type of care activity, the top row gives data for patients with an ECV in Meppel

and the second row for patients with an ECV in Zwolle.

Type	**Group**	**Total Activities**	**Unique Patients (n (% of total))**	**Mean** [$\pm SD$]
Consult	ECV MEP	175	34 (100)	5.15 [3.46]
	ECV ZWO	159	27 (96.4)	5.89 [3.93]
p-values			*0.4516*	*0.5049*
FHLA	ECV MEP	12	12 (35.3)	1 [0]
	ECV ZWO	22	16 (57.1)	1.38 [0.806]
p-values			*0.1243*	*0.1296*
PVI	ECV MEP	8	6 (17.6)	1.33 [0.516]
	ECV ZWO	14	12 (42.9)	1.17 [0.389]
p-values			*0.04809**	*0.4751*

Table D.12: Summary Care Activities Experiment 4: Meppel vs Zwolle

This table contains one difference that was statistically significant; the proportion patients with a PVI. Hence, patients who had an ECV in Zwolle were more likely to have a PVI. Since there were no statistically significant differences between the averages and standard deviations, and the differences in proportions could be explained, we decided to execute the same comparisons for patients with and without an ECV. Table D.13 contains the results of these comparisons.

Type	**Group**	**Total Activities**	**Unique Patients (n (% of total))**	**Mean** [$\pm SD$]
Consult	ECV	269	53 (98.1)	5.08 [3.34]
	No ECV	533	176 (98.9)	3.03 [1.99]
p-values			*0.5501*	*1.876e-06**
FHLA	ECV	28	22 (40.7)	1.27 [0.703]
	No ECV	50	44 (24.7)	1.14 [0.347]
p-values			*0.026**	*0.8462*
PVI	ECV	16	14 (25.9)	1.14 [0.363]
	No ECV	12	12 (6.74)	1 [0]
p-values			*0.04809**	*0.2003*

Table D.13: Summary Care Activities Experiment 4: ECV vs No ECV

We see that the proportion patients who visit the FHLA and/or have a PVI is significantly more for patients with an ECV. Moreover, the average number of consultations is significantly more for patients with an ECV.

Table D.14 contains all p-values resulting from the Shapiro-Wilk Tests and Mann-Whitney U Tests for comparing the age and activities. First, we compared the patients with an ECV in Meppel and Zwolle, subsequently patients with and without an ECV. We have not compared the activities ECV in Meppel and Zwolle, since the datasets were split on this activity and therefore, their occurrence must have been different.

Age	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
ECV Mep	0.01833*	0.3874
ECV Zwo	0.08907	
ECV	0.002991*	0.08775
No ECV	1.69e-06*	
Total Number Care Activities	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
ECV Mep	0.0003334*	0.1814
ECV Zwo	0.05513	
ECV	0.000123*	3.742e-13*
No ECV	2.376e-11*	
Consult	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
ECV Mep	0.0002445*	0.5049
ECV Zwo	0.003843*	
ECV	1.331e-05*	1.876e-06*
No ECV	2.009-12*	
EHLH	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
ECV Mep	NA	0.1296
ECV Zwo	1.575e-06*	
ECV	2.154e-08*	0.8462
No ECV	4.197e-12*	
PVI	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
ECV Mep	0.001351*	0.4751
ECV Zwo	9.811e-06*	
ECV	1.712e-06*	0.2003
No ECV	NA	
Activity Combinations	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
ECV Mep	8.509e-07*	0.01283*
ECV Zwo	0.002729*	
ECV	2.368e-06*	2.2e-16*
No ECV	2.2e-16*	

Table D.14: Results from Shapiro-Wilk Normality Test and Mann-Whitney U Test for Comparisons of Age and Activities in Experiment 4

Table D.15 contains the p-values resulting from the Fisher's Exact Test for the patient proportions who had a certain type of care activity. For example, a p-value below 0.05 indicates that there was a statistically significant difference between the proportion patients who had an HC between the patients with an ECV in Meppel and patients with an ECV in Zwolle or patients with and without an ECV.

Patient proportion	**Consult**	**FHLA**	**PVI**
Meppel vs Zwolle	0.4516	0.1243	0.04809*
ECV vs No ECV	0.5501	0.026*	0.0003126*

Table D.15: Results of Fisher's Exact Test for Patient Proportions in Experiment 4

The throughput times of patients with and without an ECV were examined with a Welch Two Sample t-test, calculated with the means and standard deviations of the datasets. Table D.16 contains the values that were used, resulting in the following p-value:

t-value	4.863298
df	105.613005
p-value	4.045368e-06*

Table D.16: Results of Welch Two Sample t-test for throughput times in Experiment 4

The trace frequencies were compared at each level of detail for patients with and without an ECV. For example, if the Mann-Whitney U Test gave a p-value below 0.05, it indicated that the trace frequencies between the two datasets were statistically significant different. Table D.17 contains the p-values for these tests for all three levels of detail.

Activity 1	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
ECV	2.189e-12*	0.002205*
No ECV	5.543e-11*	
Activity 2	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
ECV	2.293e-13*	0.000645*
No ECV	5.543e-11*	
Activity 3	**Shapiro-Wilk Normality Test**	**Mann-Whitney U Test**
ECV	3.455e-13*	0.002458*
No ECV	1.637e-13*	

Table D.17: Results from Shapiro-Wilk Normality Test and Mann-Whitney U Test for Comparisons of Trace Frequencies in Experiment 4