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SAEID AMOUZAD MAHDIRAJI

# ON THE USE OF SIMULATION AND OPTIMIZATION FOR THE ANALYSIS AND PLANNING OF PREHOSPITAL STROKE CARE

MALMÖ UNIVERSITY

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*To my wife and parents*

# CONTENT

# ABSTRACT

Immediate treatment is of extreme importance for stroke patients. However, providing fast enough treatment for stroke patients is far from trivial, mainly due to logistical challenges and difficulties in diagnosing the correct stroke type. One way to reduce the time to treatment is to use so-called Mobile Stroke Units (MSUs), which allows to diagnose and provide treatment for stroke patients already at the patient scene. A well-designed stroke transport policy is vital to improve the access to treatment for stroke patients. Simulation and mathematical optimization are useful approaches for assessing and optimizing stroke transport policies, without endangering the health of the patients.

The main purpose of this thesis is to contribute to improving the situation for stroke patients and to reducing the social impacts of stroke. The aim is to study how to use simulation and optimization to achieve improved analysis and planning of prehospital stroke care. In particular, we focus on assessing the potential use of MSUs in a geographic area. In this thesis, optimization is used to identify the optimal locations of MSUs, and simulation is used to assess different stroke transport policies, including MSU locations. The results of this thesis aim to support public health authorities when making decisions in the prehospital stroke care domain.

In order to fulfill the aim of this thesis, we develop and analyze a number of different simulation and optimization models. First, we propose a macro-level simulation model, an average time to treatment estimation model, used to estimate the expected time to treatment for different parts of a geographic region. Using the proposed model, we generate two different MSU scenarios to explore the potential benefits of employing MSUs in Sweden's southern healthcare region (SHR).

Second, we present an optimization model to identify the best placement of MSUs while making a trade-off between the efficiency and equity perspectives, providing maximum population coverage and equal service for all patients, respectively. The trade-off function used in the model makes use of the concepts of weighted average time to treatment to model efficiency and the time difference between the expected time to treatment

for different geographical areas to model equity. In a scenario study applied in the SHR, we evaluate our optimization model by comparing the current situation with three MSU scenarios, including 1, 2, and 3 MSUs.

Third, we present a micro-level discrete event simulation model to assess stroke transport policies, including MSUs, allowing us to model the behaviors of the individual entities, such as patients and emergency vehicles, over time. We generate a synthetic set of stroke patients using a Poisson distribution, used as input in a scenario study.

Finally, we present a modeling framework with reusable components, which aims to facilitate the construction of discrete event simulation models in the emergency medical services domain. The framework consists of a number of generic activities, which can be used to represent healthcare chains modeled in the form of flowcharts. As the framework includes activities and policies modeled on the general level, the framework can be used to create models only by providing input data and a care chain specification. We evaluate the framework by using it to build a model for simulating EMS activities related to the complex case of acute stroke.

**Keywords:** Stroke Transport Policies, EMS, Mobile Stroke Unit, MSU, Simulation, Optimization, Modeling Framework.

# LIST OF PUBLICATIONS

## Included Papers:

Paper I. S. Amouzad Mahdiraji, O. Dahllöf, F. Hofwimmer, J. Holmgren, R.-C. Mihailescu, and J. Petersson, "Mobile stroke units for acute stroke care in the south of Sweden," *Cogent Engineering*, vol. 8, no. 1, 2021, doi: https://doi.org/10.1080/23311916.2021.1874084.

Paper II. S. Amouzad Mahdiraji, J. Holmgren, R.-C. Mihailescu, and J. Petersson, "An Optimization Model for the Trade-off Between Efficiency and Equity for Mobile Stroke Unit Placement," in *9th KES International Conference on Innovation in Medicine and Healthcare (KES-InMed-21)*, pp. 183-193. Springer, Singapore, 2021, doi: https://doi.org/10.1007/978-981-16-3013-2_15.

Paper III. S. Amouzad Mahdiraji, J. Holmgren, R.-C. Mihailescu, and J. Petersson, "A Micro-Level Simulation Model for Analyzing the Use of MSUs in Southern Sweden," in *Proceedings of the 11th International Conference on Current and Future Trends of Information and Communication Technologies in Healthcare (ICTH 2021)*, vol. 198, pp. 132-139, 2022, doi: https://doi.org/10.1016/j.procs.2021.12.220.

Paper IV. S. Amouzad Mahdiraji, J. Holmgren, A. Alshaban, R.-C. Mihailescu, J. Petersson, and J. Al Fatah, "A Framework for Constructing Discrete Event Simulation Models for Emergency Medical Service Policy Analysis," accepted for publication in *proceedings of International Conference on Computational Science*, 2022.

## Personal Contribution

For Paper I, the author of this thesis contributed to the planning, execution, and writing of the research. For Paper II & III, the author of this thesis was the main contributor with regard to the planning, execution, and writing of the research. For Paper IV, the author of this thesis contributed to the planning and execution of the research, and was the main contributor regarding the writing of the research.

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# List of Acronyms

| | |
|---|---|
| **MSU** | Mobile Stroke Unit |
| **CT** | Computed Tomography |
| **SHR** | Southern Healthcare Region |
| **DES** | Discrete Event Simulation |
| **EMS** | Emergency Medical Services |
| **TIA** | Transient Ischemic Attack |
| **tPA** | tissue Plasminogen Activator |
| **MRI** | Magnetic Resonance Imaging |
| **EV** | Emergency Vehicle |

# PART I: COMPREHENSIVE SUMMARY

# 1. INTRODUCTION

Stroke, also referred to as brain attack, is a major cause of death and disability around the world. It is widely known that immediate treatment is vital for a stroke patient in order to increase the chance of satisfactory recovery as well as to reduce the financial costs for society. Every minute passing from when a stroke occurs until the patient receives treatment is crucial for their recovery. One way to reduce the time to treatment is to apply well-established stroke transport policies. For example, improved service to stroke patients can be provided by the use of so-called Mobile Stroke Units (MSUs) in addition to regular ambulances for prehospital stroke care. An MSU is a specialized stroke ambulance equipped with computed tomography (CT) scan and trained staff that can provide initial diagnosis and treatment of stroke patients already at the patient scene, hence, enabling to cut down the time to treatment.

The prehospital stroke care chain is rather complex compared to typical emergency medical services (EMS) care chains for other diagnoses. One important reason for this is that the use of MSUs introduces multiple decisions that need to be taken, as there might be different types of emergency vehicles (EVs) available to provide service to the patient. In addition, decisions often need to be taken with incomplete information. For example, since it is not possible to diagnose the patient without conducting a CT scan, it is challenging to decide where to transport the stroke patient, that is, the closest hospital or special clinic. Hence, in order to avoid implementing stroke transport policies that lead to undesired effects, it is essential to evaluate different stroke transport policies before being applied in real-world situations. Due to the difficulties of evaluating decision policies using real patients, the use of computer simulation is a preferable solution. Simulation models are cost-effective and time-saving decision support systems, enabling to assess a large number of policies under different configurations and to avoid further posing danger to the health of the patients who are already in a vulnerable condition. In addition, the advantages of using MSUs and their impact on reducing the time to treatment depend on where and how they are located. Optimization can be utilized to identify optimal locations for MSUs depending on the chosen perspective. However, optimization can typically not take into account all aspects.

The purpose of this thesis is to contribute to the well-being of stroke patients and reducing the impacts of stroke on society. The main aim is to develop simulation and optimization models in order to achieve improved analysis and planning of prehospital stroke care. In order to fulfill the aim of this thesis, we explored three objectives:

- Identifying optimal MSU placements that can provide equal and efficient access to stroke treatment for all inhabitants of a region.
- Assessing stroke transport policies, including MSUs, using simulation.
- Contributing a modeling framework to construct simulation models for the analysis of EMS policies.

The findings of this thesis aim to help public health practitioners improve the current stroke transport policies.

For the rest of this chapter, we provide a brief background of stroke and stroke transport policy-making. In addition, we present an overview of the use of simulation and optimization modeling in the healthcare transport domain. Then, we present the problem statement and the research questions used throughout the thesis. We conclude this chapter by providing an overview of the current thesis.

## 1.1. Background

In this Section, the core concepts used in this thesis are described.

### 1.1.1. Stroke

Stroke is known as the second leading cause of death worldwide [1], and according to the World Stroke Organization [1], one out of four people is expected to suffer a stroke in their lifetime. Every year, 14 million persons suffer a stroke, and 5.8 million die [1]. According to the Swedish Stroke Register [2], each year over 21,000 individuals suffer a stroke in Sweden, and in Sweden's southern healthcare region (SHR), the number is approximately 3,900. The number of stroke patients is expected to increase as the population ages, and it is estimated that the yearly number of stroke incidents will increase by about 22% until 2030 [3, 4]. Also, stroke is one of the main causes of permanent physical and cognitive disability, leaving individuals paralyzed and unable to perform their daily activities [1].

Stroke is a disease occurring when a blood clot or a hemorrhage in the brain either cuts off or reduces the supply of blood to a part of the brain. Hence, a stroke leads to a lack of oxygen in the brain, which causes the patient to suddenly lose various functions, such as speech, movements, feeling, and sight. When a stroke interrupts the blood flow in the vessels inside the brain, it has been estimated that two million brain cells die every minute [5]. Hence, access to immediate treatment is essential for stroke patients to increase the chance of recovery.

There are three main types of stroke: ischemic, hemorrhagic, and transient ischemic attack (TIA). Although different stroke types typically have the same symptoms, each type requires specific treatment. An ischemic stroke refers to when one or several clots reduce the blood flow inside the brain, and the patient should receive thrombolysis and sometimes thrombectomy if the clot is large. In thrombolysis, the patient receives intravenous treatment using the tissue plasminogen activator (tPA) enzyme to dissolve the blood clot and restore the normal blood flow. In thrombectomy, the blood clot is removed with an intravascular device at a special clinic [5]. A hemorrhagic stroke occurs when a blood vessel in the brain ruptures and bleeds into the surrounding tissues. The treatment that can be immediately provided is to start blood pressure lowering therapy. A TIA, a mini stroke, occurs when the blood flow is temporarily blocked by a blood clot, allowing the brain functions to recover fully. Treatments for TIA attacks involve taking medications that will help prevent future strokes.

Ischemic stroke (including TIA) and hemorrhagic stroke make up about 87 % and 13% of all stroke cases, respectively. As a result, the majority of stroke research in the literature focus on developing effective treatment strategies for ischemic stroke. The type of stroke is typically determined by performing a CT scan or magnetic resonance imaging (MRI) on the patient's brain; techniques which are generally only available at hospitals. It should be underlined that performing treatment after misdiagnosis, mainly due to a failure to determine the type of stroke, would significantly endanger the health of the patient. For example, hemorrhagic stroke patients should never be given thrombolysis, as this could lead to severe complications for the patient.

The most effective solution for minimizing the consequences of stroke, in terms of permanent disability and death, is to provide quick treatment based on the correct diagnosis for stroke patients. In particular, the term *golden hour* has been proposed for ischemic stroke, implying that those patients who receive treatment within an hour of the symptom onset have much higher chances for satisfactory recovery than those patients whose treatment is initiated later [6]. However, providing immediate treatment for stroke patients is not always possible, mainly due to logistical challenges and failure to diagnose the correct type of stroke. Logistical challenges can be mainly caused by the inadequate number of ambulances in the region and the driving time to the hospital [7]. In addition, as CT scanners are generally only available at hospitals, it is not possible to start treatment until after the patient has been transported to and diagnosed at an acute hospital.

It is important to point out that the expected benefits of thrombectomy are higher than those for thrombolysis for ischemic stroke patients, particularly when the blood clot is large [6]. However, in reality, only a few regional hospitals can provide thrombectomy treatment due to the lack of expertise and resources. Thus, it takes longer time for patients who live far from the special clinic to receive thrombectomy treatment than for those living nearby. For example, the SHR is a vast region including four counties and 49 municipalities, and which has a population of about 1,687,000 (as of 2018). As presented in Figure 1, there are 13 acute hospitals equipped with a CT scanner and 39 active ambulance sites in the SHR. However, Lund SUS, illustrated by a yellow diamond in Figure 1, is the only hospital in the SHR providing thrombectomy treatment.

### 1.1.2. Stroke Transport Policy-making

A policy is a principle of action, in the form of guidelines, which can be used to make important decisions, including identifying different alternatives and choosing among them based on their impacts in a particular domain. Policy assessment is about evaluating and predicting the potential impacts of planned policies on the target group, and its social and economic outcomes will be provided to support decision-makers. Policy assessment in the healthcare domain leads to an improved level of patients' health and healthcare services.

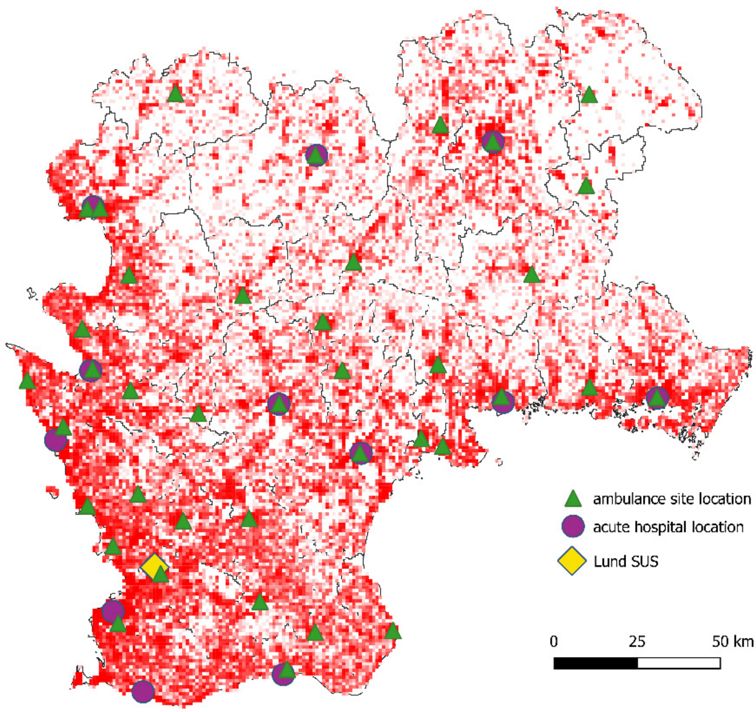


**Figure 1**. An overview of the SHR. The green triangles and purple circles represent the locations of ambulance sites and acute hospitals, respectively. The only special clinic for thrombectomy treatment in the SHR is Lund SUS, illustrated by a yellow diamond. The color of each square represents its population density, where the lighter squares have a lower density.

In this thesis, we aim to evaluate *EMS* and *stroke transport policies* using the proposed models. In Figure 2, we provide an illustration of how these types of policies are related to the larger sets of *stroke policies*, *healthcare policies,* and *transport policies*. Healthcare policies are those policies that are applied within the healthcare domain. EMS polices and stroke policies are subsets of healthcare policies. EMS policies deal with providing emergency medical services for the prehospital stabilization, treatment, and

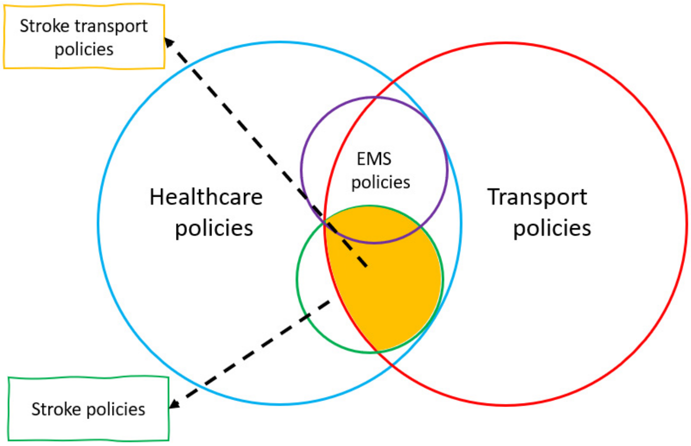


**Figure 2**. Illustration of how stroke transport policies are related to healthcare, EMS, stroke, and transport policies. The stroke transport policies, colored in orange, are subsets of the mentioned policies.

transport of severely injured and sick patients. A stroke policy is a type of healthcare policy applied within the stroke care domain. Transport policies are the set of policies that concerns the transport of goods and people. A stroke transport policy is a type of stroke policy applied to the transport of stroke patients, aiming to improve prehospital stroke care for stroke patients mainly by reducing the time to treatment. As presented in Figure 2, stroke transport policies are subsets of transport, EMS, and stroke policies.

In order to improve the care provided to stroke patients, all activities included in the stroke care chain should be performed precisely. For example, activities related to traveling time to the hospital, diagnosing the type of stroke, and monitoring the availability of resources. An optimal stroke transport policy for stroke patients is expected to lead to improved stroke treatment and allows many patients to receive the correct treatment as early as possible. However, it might not be possible to provide the same level of service to all patients, for example, due to geographical reasons.

An example of an effective stroke transport policy is to involve MSUs for prehospital stroke care. Nowadays, an MSU, in addition to regular ambulances and helicopter ambulances, has become an alternative for prehospital stroke care [7]. As mentioned above, an MSU is an ambulance equipped with a CT scanner and trained personnel, who can diagnose stroke patients and provide intravenous treatment at the patient scene. Hence, the use of MSUs allows to reduce the time to treatment with at least the time required to transport and diagnose the patient at the hospital. Studies on the operation of MSUs in Berlin [7], Cleveland [8], and Melbourne [9, 10] indicate that the use of MSUs in comparison with the situation where only regular ambulances are assigned for stroke patient transport has led to both a substantial reduction in the time to treatment [7, 8, 10] and long-term financial savings for society [9].

Below, we present the main flow of prehospital stroke care chain activities for an ischemic stroke patient from symptoms onset until the patient receives thrombolysis. We assume that both regular ambulances and MSUs are available to provide service to the patients.

- A stroke occurs, and the emergency center receives an emergency call.
- Based on the available EVs, ambulances or MSUs, and predefined decision policies, an EV is assigned for the patient.
- *If an MSU is assigned for the operation:*
    - The MSU is dispatched to the patient location.
    - The MSU arrives at the patient scene. The paramedics examine the patient, transfer the patient to the MSU, and diagnose the patient inside the MSU by performing a CT scan on the brain of the patient.
    - The paramedics prepare and secure the patient for transportation and thrombolysis.
    - The thrombolysis is initiated inside the MSU.
    - Once the thrombolysis is started, the paramedics decide to which hospital the patient should be transported based on the diagnosis and predefined policies.
    - The MSU departs for the destination hospital.
    - The MSU arrives at the hospital, and the patient is unloaded.
    - After unloading the patient, the MSU returns to its station to become available for the next operation.
- *If a regular ambulance is assigned for the operation:*
    - The chosen, regular, ambulance is dispatched to the patient location.
    - The ambulance arrives at the patient scene. The paramedics examine and transfer the patient to the ambulance.

- Depending on the hospital choice policy, a destination hospital will be chosen for the patient.
- The ambulance departs for the selected hospital.
- The ambulance arrives at the hospital, and the patient is unloaded.
- The patient is diagnosed at the hospital.
- The thrombolysis will be initiated at the hospital.
- After unloading the patient, the ambulance returns to its station to become available for the next operation.

As presented above, in general, a regular ambulance needs to travel to two distinct destinations (the patient location and a hospital) before an ischemic stroke patient can receive thrombolysis: 1) driving from the ambulance current location to the patient location; 2) driving from the patient location to the selected hospital. However, when an MSU is assigned to an ischemic stroke patient, the patient can receive thrombolysis already at their current location. In addition, the MSU can also be helpful for hemorrhagic stroke patients, at least in reducing the time required for diagnosis at the hospital.

When both regular ambulances and MSUs are available to be dispatched, a decision should be made regarding which type of ambulance should be assigned to provide service to a stroke patient. This decision can be made by analyzing the approximate time either to 1) get an ambulance to the patient site, 2) diagnose the patient, or 3) initiate treatment of the patient, as presented in detail in Paper IV. Another typical decision in the stroke care chain is choosing a hospital to where the patient should be transported. This decision can be made by identifying the closest hospital to the patient location or identifying the closest hospital to the patient location located in the direction of a special clinic.

As an example of studying stroke transport policies using only regular ambulances, Al Fatah et al. [11] develop an agent-based simulation model to evaluate two stroke transport policies concerning where to transport potential stroke patients for diagnosis, that is, the *nearest hospital policy* and the *nearest hospital towards the stroke center policy*, which respectively analyze whether patients should be transported to the closest hospital or to the closest hospital in the direction of a special clinic. The simulation results show that the patients requiring special treatment, that is, thrombectomy, benefit from being transported to the closest hospital in the direction of a special clinic, while the patients who do not need special treatment favor from being transported to the closest hospital. In addition, the authors conclude that since the time required to transport the patient to the hospital for diagnosis is higher for the *nearest hospital towards the stroke center* policy, the *nearest hospital* is most likely a better policy to be implemented in the SHR.

It should be further emphasized that when an EV delivers a stroke patient to the acute hospital, the ambulance paramedics typically do not remain at the patient's bedside, and the EV leaves the hospital. Glober et al. [12] contribute a clinical-based study to examine the use of a new EMS policy, asserting that after delivering a patient with a suspected stroke to an acute hospital, the paramedics should remain at the patient's bedside until clinical assessment and diagnosis are completed, and they get the permission to leave the hospital. In case the patient is in need of special treatment, the ambulance paramedics at the bedside transfer the patient using the same ambulance to the closest special clinic. The results demonstrate that the proposed policy reduces the time required to transfer patients in need of thrombectomy to a special clinic. However, the authors do not take into account the availability of the regular ambulance and its paramedics remaining at the hospital for other patients who may need the same regular ambulance simultaneously.

When introducing EVs in a geographic region, it is essential to consider the effects of the locations of the EVs, so that they can provide maximum benefit for all inhabitants regardless of where they live. Previous studies in the EMS domain propose two perspectives for how to locate EVs in a region: efficiency and equity [13, 14]. Efficiency refers to placing EVs in an optimal way to cover as many patients as possible to receive treatment in a shorter window of time. Equity focuses on placing EVs in a region in a way that they contribute to equal care for all patients, no matter where they live. EVs are typically placed in either urban or rural areas to address efficiency or equity, respectively. Dahllöf et al. [15] study the effects of an MSU placement in the Skåne county of Sweden in light of the efficiency and equity perspectives.

The assessing of policies contributes to establishing a practical strategy to, for example, expedite the quick response to stroke incidents and reduce the time frame from when stroke symptoms have appeared in the patient until the patient receives treatment. It is generally complicated to assess policies manually, for example, due to the large number of different cases that might occur. Complex policies can instead be analyzed through computer-aided modeling, which enables to model and predict the behavior of real systems on different levels, for example, micro-level or macro-level, without putting the health of the people at further risk. The use of modeling, in the form of optimization and simulation, can be used to assist policymakers to build more helpful policies on the basis of the strengths and weaknesses of the model results. For example, assessing policies related to prehospital stroke care leads to achieving an optimal stroke transport policy for stroke patients.

### 1.1.3. Modeling

Modeling is the process of constructing a model of a real system, where the model is a representation, typically an abstraction, of the key characteristics or behaviors of the system. A model of the system can be used, for example, for simulation or optimization, and it typically contains data and components that are linked in a certain way. The model should be typically simple but a sufficiently accurate approximation of the system it aims to represent. It can become a tool to support authorities in the decision-making process.

The use of modeling is increasing in the healthcare domain mainly due to the availability of data, availability of fast computers, and awareness in the medical field that modeling can be useful. EMS models are mainly constructed using simulation and optimization approaches. Simulation models are typically useful for studying a healthcare system over time and analyzing different scenarios and policies. Optimization models aim to identify the optimal solutions for given problems without violating the defined constraints.

### 1.1.4. Healthcare Transport Simulation

Simulation can be described as the imitation of the operation of a real or fictive system, which is often done over time. Simulation modeling is to study a model numerically to predict its performance in real-world situations and to retrieve useful output from it [16]. In general, the main components of simulation models are system entities, input parameters, performance measures, and functional relationships. During the simulation, a set of entities are modeled, and the actions and connections between these entities are studied, sometimes over a specific period of time. The use of simulation allows to model the complicated relations between different entities, whereas it might be difficult to model these relationships in a mathematical model. In addition, using simulation, it is possible to evaluate the performance of a system under different setups over long periods of time, and assess decision policies before being implemented in the real system. Thus, simulation enables to avoid performing costly and time-consuming experiments on real systems.

The type of simulation models can be categorized into deterministic and stochastic. A deterministic model contains no random variables, and it will generate the same results if it is executed multiple times for a particular set of inputs. On the other hand, a stochastic model is inherently random and has one or more random variables as input. Simulation models are generally stochastic, meaning that at least one of the input or output variables is defined by probability distributions [16].

Simulation models can be classified into microscopic, macroscopic, and mesoscopic. A microscopic simulation model is able to model entities and their interactions on the individual level. Macroscopic models make use of aggregate data representing the individual entities, for example, on the regional level, and do not study the behaviors of individual entities. Macro-level model typically does not simulate over time. Mesoscopic models bridge the gap between microscopic and macroscopic models. Mesoscopic models describe the entities at a high level of detail; however, their behavior and interactions are modeled at a lower level of detail. Macroscopic and mesoscopic models are typically not as computationally expensive as microscopic models; hence, they are more appropriate for studying systems on a large scale.

A wide range of simulation models are used in the healthcare domain, mainly due to the capability of these simulation models in analyzing complex healthcare systems. Simulation models in the healthcare domain mainly focus on staff scheduling, allocation of human resources, patient flow management inside emergency rooms, hospital bed utilization, and prehospital healthcare service management [17]. In particular, Keshtkaran et al. [18] classify the potential simulation modeling approaches in the stroke care systems into simulation modeling for stroke care operations improvement, economic analysis, public policy, and clinical applications.

Discrete Event Simulation (DES) and agent-based simulation are the most popular simulation modeling approaches that are used in the EMS domain, including stroke transport [11, 19]. DES is a simulation modeling paradigm used to model the behavior of a system as a sequence of discrete events that occur over time. It only models the points of time where events occur and where the system's state can change. In contrast, in the fixed-increment time approach, the simulation is advanced using fixed length time steps, where each time step is explicitly simulated. DES is a form of micro-simulation model, where the behaviors of individual entities and their interactions are explicitly modeled over time, typically allowing more realistic modeling. For example, in an EMS model, the DES model enables to study the behavior of individual patients and EVs. Whilst the macro-level simulation paradigm models the average of the characteristics for the whole population; hence, it is impossible to consider the effects of unexpected and simultaneous events using the macro-level paradigm.

An agent-based model is a modeling approach with a collection of agents used to simulate the activities and interactions of individual entities in order to analyze the behavior of a system. Each agent is a program entity with a high level of autonomousity, which is capable of, for example, making autonomous actions and decisions.

In this thesis, we followed the process of simulation presented in Figure 3 [16]. The first phase of the modeling process is identifying and formulating a real-world problem, followed by the acquisition and processing of real data in the observation phase. Then, in the third phase, the collected data are used to develop a simulation model, consisting of variables, assumptions, and statements related to the problem. The model is implemented as a computer program and verified using different techniques. In the evaluation phase, the output of the simulation model is assessed and analyzed under various conditions to observe whether the model functions as expected and addresses the formulated problem. If an improvement is needed, the model is refined to improve the output. Eventually, after choosing the model configurations and applying them, the analysis of the model output yields the simulation results that can be used for decision-making [16].

A modeling framework is a tool with reusable components that typically provides a general structure to build models of a real system. In the healthcare domain, modeling frameworks are used, for example, to build models for home healthcare service delivery decisions of the aging society [20] and resource allocation [21]. Modeling frameworks generally provide a graphical user interface to facilitate the construction of models, for example, using an activity diagram. An activity diagram or workflow

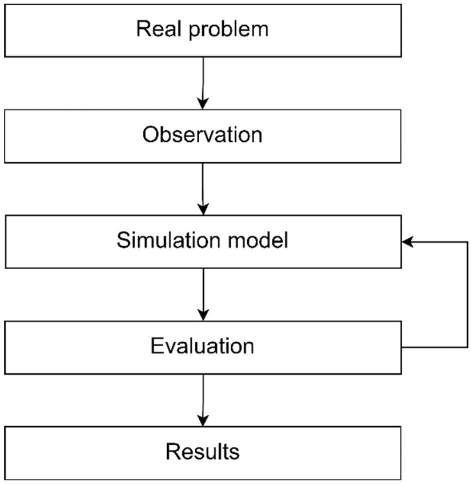


**Figure 3**. An outline of the simulation process [16].

diagram is a behavioral diagram that describes the workflow of activities from a starting point to an ending point, typically with the help of decisions. As activities and policies are modeled on the general level in the framework, the framework can be used to build specific models only by specifying the input data and a care chain specification.

A micro-level simulation model for prehospital stroke care analysis is driven forward by a population of patients, where each patient appears at different times and locations in a considered geographic region. Each patient can be specified using a number of attributes such as stroke time, patient location (coordinates), age, sex, and diagnosis. The population of patients can be either real (representing actual historic patients) or synthetic (where synthetic patients are created using available statistics). From a modeling perspective, it is not important whether the population is real or synthetic; however, a synthetic population is preferable from a privacy perspective as there is usually no access to individual patient data. A synthetic population generation model allows the creation of various populations of synthetic patients, where each set includes patients with different attributes. The use of a synthetic population can also be beneficial when the number of instances in the real data set is insufficient to run the simulation model. Related studies in the stroke care domain mainly use Monto Carlo simulation [11, 22] or Poisson distributions [23-25] to create a synthetic stroke population. Al Fatah et al. [11] generate a synthetic stroke population using aggregate stroke patients' data, and they use Monte Carlo simulation for sampling the patients' attributes such as patient's age, address, incident time, and the type of stroke. Wang et al. [25] and Aked et al. [24] investigate age and disparities in stroke incidences and case-fatality over time by creating a synthetic population, assumed to be Poisson distributed, attributed by age, ethnicity, and sex. Alassadi et al. [23] create a synthetic population using the socio-demographic census data, real stroke patients data, and travel data to study the travel patterns of the suspected stroke patients. For each generated patient in the synthetic data, they sample patient's age group, municipality, and stroke incident time using a non-homogeneous Poisson distribution.

### 1.1.5. Healthcare Transport Optimization

Mathematical optimization is the use of mathematical models and methods to identify the best possible solution for a decision problem under consideration. An optimization model consists of a number of decision variables that are used to minimize or maximize the value of an objective function, and a number of constraints that restrict the values of the decision variables. The objective of an optimization model is to find the values of the decision variables that yield the best value of the objective function while fulfilling the constraints defined on those variables [26]. The purpose of an optimization model in the EMS domain can be, for example, to identify the optimal placement of EVs in the region under study.

A few articles in the literature contribute to addressing the optimal placement of MSUs, where the main focus is on the benefits for residents in urban areas (efficiency perspective) [27, 28] or rural areas (equity perspective) [29]. The major focus of the prior studies lies in reaching maximum population coverage by considering efficiency, that is, placing an MSU in order to cover as many inhabitants as possible. Equity, which is covered in a few studies, seeks to place an MSU in order to provide equal service for all inhabitants, regardless of where they live.

It should be underlined that each of the above perspectives is biased towards a group of inhabitants, that is, residents of densely populated or rural areas, respectively. The main focus of some recent studies in the EMS domain is the trade-off between efficiency and equity for the optimal placement of regular ambulances in a region [30-32].

In this thesis, we followed the process of optimization [26], as presented in Figure 4, which indicates how a decision problem can be solved using optimization modeling, allowing to apply the creation and evaluation to an overarching process. The optimization process starts with the identification and simplification of a real-world problem. Next, the simplified problem is formulated mathematically as an optimization model. After that, an appropriate optimization method is applied to find a solution to the optimization model for the considered input. Then, the generated solution is evaluated by verifying its correctness using the formulated optimization model and validating whether the model describes the problem accurately enough. This is rather a continuous process, which is represented by the verification and validation arrows in Figure 4. The outputs obtained after the evaluation are the results of the optimization process.

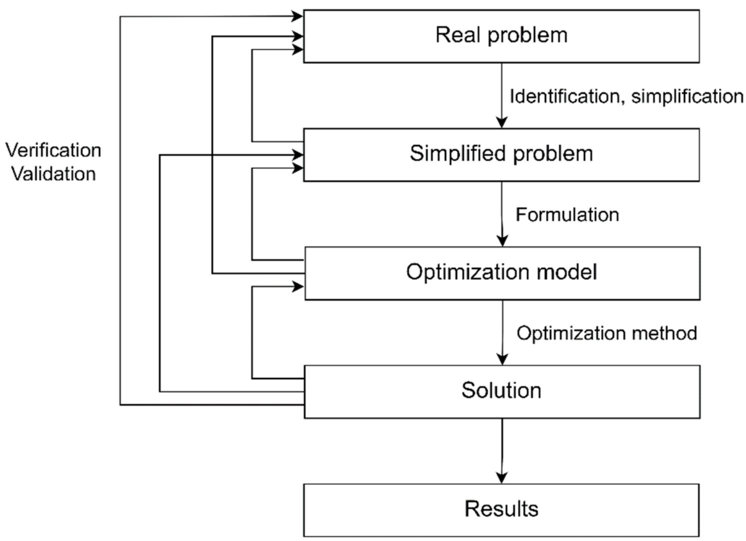


**Figure 4**. An illustration of different steps in the optimization process [26].

## 1.2. Problem Description

As mentioned earlier, recent studies both at the clinical- and computer-based levels indicate that the use of MSU, which is an example of a stroke transport policy, has the potential to reduce the time to treatment for stroke patients. The aim of this thesis is to study how simulation and mathematical optimization can be utilized to obtain improved analysis and planning of prehospital stroke care. As discussed earlier, simulation and optimization are valuable approaches that enable to study prehospital stroke care. Simulation can be used to assess different policies related to prehospital stroke care before being applied in real-world situations. Mathematical optimization can be used to identify the optimal location for MSUs in a region depending on the intended perspectives and constraints.

Some recent works study the optimal placement of an MSU in a geographic region, where the main focus is on investigating the impact of optimal placing an MSU for inhabitants of urban (efficiency perspective) or rural areas (equity perspective). However, none of the prior works concentrate on the optimal placing of MSUs in a larger region considering both of the mentioned perspectives. In addition, some studies in the EMS domain use optimization modeling to make a trade-off between efficiency and equity for the regular ambulance placement problem. Hence, we have identified the need to propose an optimization model that makes a trade-off between efficiency and equity for optimal MSU placements in a region so that all inhabitants have equal and efficient access to stroke treatment no matter where they live.

The use of simulation enables to assess different stroke transport policies on different levels, for example, micro-level or macro-level. Prior studies mainly use simulation to analyze the advantages of deploying an MSU in densely populated areas. However, we have identified the need to present a macro-level simulation model to analyze the potential benefits of using MSUs in a larger area, including both urban and rural areas, for example, in the SHR. The use of a macro-level simulation model enables to obtain the average time to treatment for different parts of a region.

It is also relevant to use a micro-level simulation model to assess stroke transport policies, enabling to study the behavior of individual entities. A number of research studies propose micro-level simulation models to assess stroke transport policies, including only regular ambulances. Despite the advantages of simulation modeling, no prior study employs simulation models, particularly a DES model, to assess stroke transport policies, including MSUs, for stroke patients. In addition, a micro-level simulation model needs to be fed by a population of stroke patients. Using a synthetic stroke population, compared to the real stroke patients' data, as input for the simulation model enables to generate various sets of synthetic stroke patients with different attributes.

Constructing simulation models can be a complex and time-consuming task. A modeling framework can be useful in simplifying the generation of DES models in the EMS domain; hence, it reduces the complexity of the model construction activities. Considering the advantages of using a modeling framework, no existing framework in the EMS domain focuses on developing a general structure for constructing simulation models.

## 1.3. Research Questions

The main aim of this thesis is to improve the analysis and planning of prehospital stroke care by means of simulation and optimization. The focus is on assessing stroke transport policies related to MSUs. The result of this thesis aims to support practitioners of the healthcare domain to improve the existing stroke transport policies in a geographic region. In order to fulfill the aim of the thesis, the main research question is formulated as follows:

### **RQ.** How can optimization and simulation modeling be used for improved analysis and planning of prehospital stroke care?

To address the main research question, three sub-research questions are formulated, as presented in the following. It should be pointed out that each sub-research question corresponds to a distinct objective, and the aim of this thesis will be reached by fulfilling the objectives.

### **RQ1.** How can optimization be used to determine the optimal placement of MSUs in order to provide equal and efficient access to stroke treatment for all inhabitants in a region?

In prehospital stroke care, mathematical optimization can be helpful in identifying the best MSU locations with regard to constraints and perspectives, that is, efficiency and equity. RQ1 focuses on developing an optimization model to take into account the trade-off concept, between efficiency and equity, for the optimal placement of MSU(s) in a region. In particular, the interest lies in observing the benefits of placing MSU(s) for all inhabitants of the region under study concerning each of the mentioned perspectives as well as the trade-off perspective. As mentioned earlier, each of the efficiency and equity perspectives has a bias towards a group of inhabitants, that is, inhabitants of densely populated or rural areas. When it comes to studying the benefits of different MSU placements, it is important to consider the trade-off between efficiency and equity for the optimal placement of MSUs, allowing to provide equal and efficient access to stroke treatment for all inhabitants of a region. To partially answer RQ1, in Paper I, we present a macro-level simulation model in order to analyze the potential benefits of placing MSUs in the SHR using two different MSU allocations. These two scenarios allowed us to study the impacts of different MSU placements in the SHR. To address RQ1, in Paper II, we contribute an optimization model for the optimal placement of MSUs in the SHR, designed to make a trade-off between efficiency and equity in the optimization process.

### **RQ2.** How can simulation be used for stroke transport policy assessment?

The use of computer simulation in the healthcare domain is growing, as simulation can be used as a tool to support decision-makers in healthcare. For example, a macro-simulation model can be helpful to achieve the average time to treatment for the population of a geographic region. In addition, a micro-level simulation model, for example, based on the DES paradigm, can be used to assess stroke transport policies in a geographic region. This research question mainly explores the use of simulation to study and assess different stroke transport policies, in particular, the policies related to the use of MSUs. RQ2 is partially addressed in Paper I, where a simulation model was contributed through an average time to treatment estimation model that can be used to analyze the potential benefits of placing MSUs on the macro level. In addition, RQ2 is mainly answered in Paper III, where we contributed a micro-level DES model to study the advantages of using MSUs in the SHR by assessing different stroke transport policies.

### **RQ3.** What is an appropriate modeling framework for constructing DES models for the analysis of EMS policies?

Building simulation models can be a complicated and time-consuming task, particularly if a general-purpose simulation modeling is intended. The objective of RQ3 is to create a modeling framework for constructing DES models for the analysis of EMS policies. To address RQ3, we present a modeling framework in Paper IV, which is a tool with reusable components that can be used to simplify the process of building DES models for EMS policy analysis. The proposed framework can be utilized to construct various EMS simulation models for different medical conditions, including stroke.

## 1.4. Thesis Outline

The current thesis is split into two parts: the first part presents a comprehensive introduction, and the second part consists of the four publications that constitute the basis of this thesis.

The remainder of the first chapter of the thesis is organized as follows. Chapter 2 presents the research method that has been employed to address the research questions. Chapter 3 describes the core contributions of the research and how they are linked to the research questions. Finally, Chapter 4 draws the main conclusions and proposes some directions for future work.

# 2. RESEARCH METHOD

This chapter describes the applied research method and how it was followed throughout this thesis. Using design science, we created four artifacts to fulfill the objectives of the thesis: a macro-simulation model (Paper I), an optimization model (Paper II), a micro-simulation model (Paper III), and a modeling framework (Paper IV).

Design science attempts to create innovative artifacts to extend human knowledge and evaluate those artifacts to solve and address identified problems and research questions. An artifact is an object made by humans to solve real-world problems that people encounter in practice [33].

We applied design science to build an optimization model (RQ1) to determine the optimal placement of MSUs so that all inhabitants of a region have equal and efficient access to stroke treatment. In addition, we created two artifacts in the form of macro- and micro-level simulation models (RQ2) to study the potential benefits of using MSUs and to assess stroke transport policies. We also built a modeling framework (RQ3) used to construct DES models to analyze EMS policies.

According to March and Smith [34], information technology artifacts created through design science can be classified into four categories: constructs, models, methods, and instantiations. Constructs are symbols and concepts used to formulate problems and possible solutions. Models are representations of practical problems and possible solutions that are built up from constructs. Methods are the processes that are performed to solve problems. An instantiation is the representation of an artifact in its context. Instantiations make use of constructs, models, and methods to demonstrate the feasibility and effectiveness of the design process and built artifacts [34]. The construction of the four artifacts presented in this thesis lies under the model category. Performing different experiments to analyze and evaluate the effectiveness of different MSU placements and stroke transport policies for their intended use belongs to the instantiation category.

In design science, the research process is typically divided into five main activities: problem explication, requirements definition, artifact design and development, artifact demonstration, and artifact evaluation [35]. In the following, we briefly represent how these five activities were applied within this thesis.

**Activity 1: problem explication**. In the first activity, we investigated and analyzed different aspects of the problem through related work, group discussions, and discussions with domain experts. The output and knowledge acquired from addressing the research questions led to the problem formulation. Moreover, we identified the existing gaps in the research area, as presented in Section 1.2, which this research should address.

**Activity 2: requirements definition**. In the second activity, we identified and defined the requirements and main components needed to design and develop the research and outlined the possible solutions for the problem in the form of artifacts. We also reviewed simulation and optimization models developed in the EMS and prehospital stroke care domains.

**Activity 3: artifact design and development**. In order to fulfill this activity, in Paper I, we present a macro-level simulation model using an average time to treatment estimation model to explore the advantages of using MSU-related transport policies and different MSU placements for prehospital stroke care in a region. In Paper II, we contribute an optimization model to tune the trade-off between the efficiency and equity perspectives for placing MSUs in a region. In Paper III, we propose a DES model that can be used to analyze different stroke transport policies, including MSUs. Finally, in Paper IV, we present a modeling framework to simplify the construction of DES models in the EMS domain.

**Activity 4: artifact demonstration**. The artifact demonstration activity can be viewed as the preceding step for the evaluation activity, where each artifact is used to solve an instance of a real-life problem as proof of concept to demonstrate the feasibility of the artifact. Hence, it is associated with the evaluation activity. In this activity, the performance and effectiveness of each artifact were studied using scenarios in the SHR.

**Activity 5: artifact evaluation**. In the evaluation artifact activity, the goal is to determine how well the proposed artifact can solve the problem that motivated the research. As mentioned above, it is related to the artifact demonstration activity. In Paper I-IV, all created artifacts were evaluated and analyzed through an experimental study conducted in the SHR based on the considered policies or perspectives. In Paper I, in a case study, we evaluated the proposed macro simulation model using two generated MSU scenarios and compared the corresponding experimental results with a baseline scenario. In Paper II, we conducted a case study in the SHR, where we analyzed the performance of the presented optimization model by generating three MSU scenarios, including 1-3 MSUs. In Paper III, in a scenario study, we studied and analyzed the outcome of the different stroke transport policies and their effectiveness. In addition, we performed a sensitivity analysis to evaluate the performance of the proposed DES model. In Paper IV, we evaluated the framework in a case study by using it to construct a DES model to simulate the EMS activities related to acute stroke. The experimental results showed the ability of all proposed artifacts for, for example, identifying the optimal MSU locations to provide equal and efficient access to stroke treatment, assessing different stroke transport policies and MSU allocations, and simplifying the construction of DES models for the analysis of EMS policies. The experiment results are described further in the following chapters.

We used quantitative data in the design science process to evaluate the proposed artifacts. We collected demographic data from Statistics Sweden [36] and age-based stroke data from Sweden's Southern Regional Healthcare Committee [37]. The demographic data includes the number of inhabitants for each age group and each considered sub-region. The collected stroke data specifies the hour-based statistics for the number of reported stroke cases for 21 age groups for each municipality in the SHR. These datasets were used as input for the proposed models in Paper I and Paper II. Moreover, we utilized the stroke data and demographic data in a synthetic population generation model to create a synthetic stroke population used as input for the DES models in Paper III and Paper IV.

One of the main goals of design science is to generate new knowledge that can assist the decision-makers of the discipline in designing a solution for the problem in the area of concern. Therefore, it is expected that the application of the presented artifacts can help the decision-makers in the domain to improve the prehospital stroke care and treatment of stroke patients, leading to reducing human suffering as well as reduced social costs of stroke.

# 3. CONTRIBUTIONS

This chapter outlines the research contributions of the publications included in this thesis in relation to the considered research questions. The contributions are organized and presented in a manner that corresponds to the research questions, beginning with RQ1. The connection between the research questions and publications is represented in Table 1.

**Table 1**. The relationship between the research questions and the papers included in this thesis.

| RQ | Papers |
|---|---|
| RQ1 | Paper I, II |
| RQ2 | Paper I, III |
| RQ3 | Paper IV |

## **RQ1.** How can optimization be used to determine the optimal placement of MSUs in order to provide equal and efficient access to stroke treatment for all inhabitants in a region?

Mathematical optimization can be used to identify the best MSU locations based on the defined constraints, that is, the number of available EVs and the choice of how to trade-off between efficiency and equity. The optimal placement of an MSU in terms of either efficiency or equity is the focus of related studies in the prehospital stroke care domain. However, no previous study proposes an optimization model to make a trade-off between efficiency and equity for the optimal placement of MSUs in a region.

To partially answer RQ1 and fill the gap in the literature, in Paper I, we presented a macro-level average time to treatment estimation model to examine the possible benefits of different MSU placements in the SHR using two MSU scenarios. In one of the MSU scenarios, MSUs are placed in a way to potentially improve the situation for a larger share of the population of SHR (efficiency perspective). In contrast, in the other MSU scenario, MSUs are placed to potentially improve the situation for a larger share of those patients who currently have the longest time to treatment (equity perspective). The experimental results indicated how different MSU locations influence inhabitants living in different parts of the SHR.

To further answer RQ1, in Paper II, we contribute an optimization model designed to make a trade-off between the efficiency and equity perspectives when allocating MSUs in a geographic region. The trade-off is based on the concepts of weighted average time to treatment (WATT) and range, defined as the time difference between the expected time to treatment for inhabitants at different geographical locations. In a scenario study, we evaluated the proposed model by comparing the current situation, including only regular ambulances, in the SHR with three generated MSU scenarios, each including 1, 2, and 3 MSUs. The computational results demonstrated that the suggested optimization model could make a balance between efficiency and equity for the MSU allocations by reducing both WATT and range. Furthermore, the proposed optimization model enabled not only a high degree of equal care, but also reduced time to treatment for the majority of residents in the region under consideration.

## **RQ2.** How can simulation be used for stroke transport policy assessment?

As mentioned earlier, simulation is one of the most common approaches to model and analyze healthcare systems. In the prehospital stroke care domain, the main focus of prior studies lies in developing simulation models to assess stroke transport policies, including only regular ambulances. No previous study explicitly uses mathematical modeling to study stroke transport policies related to MSUs as well as to study the effects of different MSU placements. RQ2 is addressed in Paper I and Paper III.

In Paper I, we extended the work of Dahllöf et al. [8], who study the potential benefits of using MSUs within the Skåne county of Sweden, which is a subregion of the SHR. We presented a macro-level simulation model using an average time to treatment estimation model in order to analyze the potential benefits of placing MSUs in the SHR. The proposed model was able to estimate the average time to treatment for the entire population of a region. The contribution of Paper I was twofold: i) a model for estimating the expected time to treatment for different parts of a geographic region and ii) the results of a case study where we applied the model within the SHR. In particular, we compared the current situation with two extended scenarios, where we added three MSUs in each.

The experimental results showed that the use of MSUs is expected to decrease the expected time to treatment for the whole region, for each municipality, and for each subregion covering SHR, and how the population is expected to benefit from MSUs. Another finding was that different placements of MSUs are anticipated to be beneficial for different parts of SHR.

The proposed approach in Paper I was a macro-level simulation model, which provided an overview of the problem and enabled us to analyze the outcomes on a large scale. However, the use of a micro-level simulation model can be beneficial when it comes to studying the behavior of individual patients and individual EVs over time. It also allows adding stochasticity to the model, such as the effects of simultaneous stroke incidents, for example, if an MSU is required at two places simultaneously.

In Paper III, we contributed a micro-level simulation model built according to the DES paradigm to evaluate the potential benefits of using stroke transport policies related to MSUs in the SHR. In the prehospital stroke care chain, almost all activities and events occur as a sequence of discrete events; hence, we consider DES to be a preferable choice to model such systems. This type of modeling allows simulating individual entities' activities over time, leading to more realistic modeling. In particular, it enables to incorporate stochasticity, including location and time of stroke incidents, into the model. Thus, the proposed model in Paper III is able to simulate the main activities and decisions involved in the logistical operations of stroke patients, and it takes as input a synthetic population of stroke patients. We compared the time to treatment, the number of MSU dispatches, and the average dispatching distance of MSUs for the different scenarios using the simulation outputs. We also conducted a sensitivity analysis to further evaluate the presented DES model, that is, varying the number of MSUs in each site and the number of patients in the synthetic population. The simulation results showed that the use of MSUs is expected to reduce the time to treatment in the considered case study, that is, in the SHR, and to help more stroke patients get treatment earlier. Also, with the use of MSUs, the share of patients who are expected to receive treatment within an hour was approximately tripled. Another finding was that when MSUs are located in or near densely populated areas, the number of MSU dispatches is expected to considerably increase as more patients can benefit from the MSUs. Finally, the results also indicated that the use of the DES paradigm provides a more realistic representation of reality than the macro-level modeling approach, based on a comparison of the results of this study with the results of our macro-level model (Paper I), supported by our sensitivity analysis.

It should be further mentioned that a DES model is an individual-based approach, which needs to be fed by a set of stroke patients as input to initiate the execution. Due to the limitations in accessing real patients' data, a synthetic stroke population generation model can be used to create a synthetic stroke population. The use of synthetic stroke data enables to generate different sets of stroke populations with attributes, such as varying age, location, sex, symptoms, and diagnosis. In Paper III, we present a synthetic population generation model, assuming the occurrence of stroke incidents to be Poisson distributed, to create stroke patients based on real aggregated stroke data [37] and demographic data [36]. These data sets contain the number of inhabitants in each sub-region and the statistical distributions of the time, location, and age of the stroke patients. The model is stochastic and generates a new set of patients with varying sizes, locations, and stroke times each time it is run.

### **RQ3.** What is an appropriate modeling framework for constructing DES models for the analysis of EMS policies?

A modeling framework is a useful tool for constructing simulation models. The key advantage of a modeling framework is its simplicity in generating specific models. However, no prior study explicitly contributes a modeling framework for constructing DES models for the analysis of EMS policies.

To address RQ3, we proposed a modeling framework, called the model construction framework, in Paper IV in order to construct DES models to analyze EMS policies, leading to simplifying the construction of DES models in the EMS domain. The suggested framework was established on the idea of modeling EMS care chains using standard flow charts consisting of connected activities and decisions. The main activities identified in most EMS care chains are included in the proposed framework, regardless of the diagnosis of the patient. As the framework includes activities and policies modeled on a general level, the framework can be used to build most EMS models only by specifying input, such as geographic region, patient population, hospital data, ambulance data, and the care chain.

In a case study, we utilized the framework to build a model for simulating EMS activities associated with acute stroke, which has a more complex care chain than the conventional EMS chain. One reason is that the use of MSUs in the prehospital stroke care chain allows to perform diagnosis and treatment already at the patient's scene, and incorporating these specifications into the prehospital stroke care chain makes it more complex. Another reason is that decision-making is to a larger extent based on incomplete information about the status of the patient, compared to many other diagnoses. The evaluation outcome revealed that the general care chain activities included in the framework are sufficient, at least for modeling the relatively complex case of acute stroke.

# 4. CONCLUSIONS AND FUTURE WORK

## 4.1. Conclusions

It is known from the literature that the use of MSUs enables to provide better care for stroke patients. In this thesis, we explored the application of MSU in prehospital stroke care using simulation and optimization. We showed that optimization can be useful in identifying the optimal MSU locations considering, for example, the number of available EVs and the choice of how to trade-off between efficiency and equity. Simulation can be employed to assess different stroke transport policies, including different MSU placements. The purpose of this thesis was to contribute to the well-being of stroke patients and reducing the social costs of stroke. The main aim was to improve the analysis and planning of prehospital stroke care using simulation and optimization. In particular, we attempted to answer the three research questions, each corresponding to a specific objective, that were formulated in this thesis.

The first objective (RQ1) was to build an optimization model that can be used to identify the best MSU locations, enabling to make a trade-off between the efficiency and equity perspectives of acute stroke care. Previous studies in the domain only seek to create an optimization model to place an MSU based on only one of the efficiency and equity perspectives. RQ1 is partially answered in Paper I, where we used the average time to treatment estimation model to study the advantages of different MSU placements in the SHR in two scenarios. By comparing the results for the two MSU scenarios, we concluded that different placements of MSUs are expected to lead to benefits for different parts of SHR. For example, in one MSU scenario, the expected time to treatment is improved for a higher share of the population, while in the other MSU scenario, the expected time to treatment is mostly improved for the patients who currently have the longest time to treatment.

To further address the first objective, in Paper II, we presented an optimization model for identifying the best MSU placements concerning the trade-off between efficiency and equity, enabling to provide equal and efficient access to stroke treatment for all inhabitants in the SHR. The experimental results showed that the proposed trade-off function had the potential to balance efficiency and equity for the MSU placement problem. We also came to the conclusion that adopting the proposed optimization approach for MSU placement could help ensure that most residents receive equal service and significantly increase the number of people who are expected to receive treatment earlier.

The second objective (RQ2) was to use simulation in order to assess stroke transport policies, particularly policies including MSU. None of the related research studies the MSU-related stroke transport policies using simulation. To partially achieve this objective, in Paper I, a macro-level simulation model, an average time to treatment estimation model, was constructed to investigate the potential benefits of employing MSUs in the SHR. Using two generated MSU scenarios, we assessed how much the expected time to treatment is estimated to decrease for the entire region and each subregion of SHR, as well as how the population is likely to benefit from the deployment of MSUs. In particular, from the results, we could observe that the share of the inhabitants that is expected to receive treatment within an hour was tripled.

In addition, in Paper III, we presented a DES model to assess stroke transport policies, including MSUs, in the SHR, which allowed us to model the behaviors of the individual entities, such as patients and EVs, over time. According to the simulation results, the use of MSUs in the SHR has the potential to lead to a shorter time to treatment, allowing more stroke patients to receive treatment earlier. Another finding was that by placing MSUs in or near highly populated regions, the number of MSU dispatches is expected to significantly increase, and MSUs can be dispatched to farther distances compared to the situation when MSUs are placed in rural regions. Based on our simulation results and conducted sensitivity analysis, we were able to conclude that the developed DES paradigm could provide more realistic results than the macro-level modeling approach for the same problem of studying MSU locations.

The third objective (RQ3) was to develop a framework that provides a general structure to build simulation models for the analysis of EMS policies. To address this objective, in Paper IV, we presented a modeling framework that can be used to simplify the creation of EMS simulation models and to represent different scenarios only by specifying the identified activities and decisions involved. We evaluated the proposed framework in a case study by applying it to build a model for analyzing EMS activities for stroke patients. We concluded, on the basis of our evaluation, that the predefined activities included in the framework are sufficient, at least for modeling the rather complex case of acute stroke.

## 4.2. Future work

In light of the findings reported in this thesis, there are a number of possible directions to follow, which are described below.

In this thesis, the proposed simulation and optimization models took into account the time to treatment for patients with ischemic stroke who needed thrombolysis. The reasoning behind this choice was that the majority of stroke patients suffer from ischemic stroke, and that thrombolysis is the standard treatment that can be initiated almost immediately after the diagnosis of ischemic stroke. However, the ischemic patients with larger clots often benefit from thrombectomy treatment, which is only available in special clinics, for example, Lund, in the southwest of SHR. The expected benefits of MSUs are significant in terms of reducing the time to thrombolysis. However, it should be highlighted that the expected benefits for thrombectomy patients are even greater as there would be, in this case, time savings equivalent to at least the driving time from the patient location to the acute hospital and from the acute hospital to the thrombectomy center plus the acute hospital layover time. An MSU can instead drive directly to the thrombectomy center. As a result, it is also relevant to enable to study thrombectomy using the proposed models.

Confirmation of the diagnosis of either ischemic or hemorrhagic stroke, including clinical assessment with a CT of the brain, is a key decision. If a hemorrhagic stroke is detected, urgent actions like early blood pressure control can be started immediately, and a decision about whether to transport the patient to a primary or secondary hospital can be made. This means that the use of MSUs can also be beneficial for hemorrhagic stroke cases. Future research will look towards incorporating different types of stroke, that is, both ischemic and hemorrhagic, in the simulation model.

We made a number of assumptions in the current DES model to make it simpler. For example, we did not include information related to the dynamic ambulance and MSU traveling times, the varying effects of traffic congestion during the day, travel patterns of EVs and patients, and the operating hours of ambulance services in the presented model. It should be further highlighted that the co-dispatching of an MSU with a regular ambulance was not considered in the presented model. As part of future work, we will use the simulation model to assess relevant cooperation policies involving MSUs and regular ambulances of ambulance resources. Another possible direction for future work is applying the proposed simulation model to different geographic regions to assess its performance further.

Furthermore, we aim to include the cost function of MSUs as part of our optimization model to study the cost-effectiveness of the use of MSUs versus stroke treatment costs using available health economic data for the use of MSUs over a region. A literature review will be conducted as a primary step to identify relative measures to quantify costs for patients and ambulances/MSUs.

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