Design and analysis of a UAV assisted medical emergency delivery system

Master of Science Thesis

Jelle Gerard van Haasteren

Technische Universiteit Delft
Student number: 4446127
Supervisor: Dr. O.A. Sharpanskykh

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Jelle Gerard van Haasteren

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Thesis committee:	Dr. B.F. Lopes Dos Santos TU Delft, Chaiman
	Dr. O. A. Sharpanskyk TU Delft, Supervisor
	Dr. A. Jamshidnejad TU Delft, Examiner
	ir. M. Dogterom Post NL, Examiner

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Preface

"My thesis is about medical drones, I have chosen this subject because it combines my interests in drones and social welfare." This is how I would have introduced my thesis about 15 years ago when we had to give our first presentations in class. My academic career coming to an end, I think it is only fitting to reflect on how it all started. I certainly have grown a lot since then, physically maybe not as much, but all the more as a student and as a person more generally. However, what has not changed is how or why I choose a subject for a presentation, topic of research, or this thesis. This has always been driven by intrinsic curiosity, a character trait that I value highly and believe to be at the core of science. Being in the car with my mom at a young age I would never stop asking questions about the world around me, she deserves a lot of credit for persevering this interrogation and nourishing my curiosity. Throughout my career, I was lucky enough to have a myriad of people who supported me in developing myself into the person I am today, to whom I can only be grateful.

Recently my supervisor, dr. Alexei Sharpanskykh contributed significantly to not only this thesis but also my personal well-being. Although this may sound a bit sentimental, his providing me with the time and trust he gave me during my concussion, will certainly not have hampered my recovery. Aside from the physical misfortunes, I think I enjoyed writing my thesis as much as I could enjoy writing a thesis. This is mainly due to the fact that I was given the freedom to pursue personal curiosity and formulate my own research accordingly. Undoubtedly this has led to a thesis that lacks academic depth, which was rightly pointed out to me on several occasions by Alexei. However, my personality being both generalist and stubborn, I often continued expanding laterally instead of narrowing down. Thus all the more reason for me to be very appreciative of the support, feedback, and most of all freedom he has given me throughout the entire process.

Next to my supervisor, I want to thank all members of the MDS team, friends, family, and others who have supported me throughout the process. Particularly everybody who challenged my thinking: Jorick Kamphof on the content of my research, my parents on what I value, and all the authors to whom I listened whilst taking a walk during the pandemic. Questioning common beliefs has been a big part of both how I wrote, and, the content of, this thesis. And although this past year has confirmed that I do not want to continue my academic career after obtaining my Master degree, it did change my mind on the value of scientific thinking. Next month I hope to renounce my official status as a student, but even more so hope to preserve my curiosity and keep on learning. Or in the words of Adam Grant, of whom I consumed several of audio-books during my walking study breaks: "Confident humility is knowing how little you know and how much you're capable of learning."

Jelle van Haasteren
Delft, May 2022

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List of Abbreviations

ABS	Agent-Based Simulation
AIS	Abbreviated Injury Scale
ASO	Alternate Simulation—Optimization
BSC	Blood Supply Chain
CBS	Central Bureau of Statistics
CCP	Chance Constrained Programming
DDP	Drone Delivery problems
DES	Discrete-Event Simulation
EF	Evaluation function
EMA	Analytical Model Enhancement
HTOL	Horizontal Takeoff and Landing
IFV	Insituut Fysieke Veiligheid
IRTAD	International Traffic Safety Data and Analysis Group
JIT	Just-In-Time
L&S	Lights and Sirens
LNS	Large Neighbourhood Search
LP	Linear Programming
MAIS	Maximum Abbreviated Injury Scale
MDP	Markov Decision Process
MDS	Medical Drone Service
MH	Meta-heuristic
MILP	Mixed Integer Linear Programming
MINLP	Mixed Integer Nonlinear Programming
MSSP	Multi-Stage Stochastic Programming
OSI	Optimization With Simulation-Based Iteration
PRBC	Packed Red Blood Cellconcentrate
QM	Queuing Models
RO	Robust Optimization
RPAS	Remotely Piloted Aircraft Systems
S-O	Simulation-Optimization

SA	Simulated Annealing
SG	Solution Generation
SMC	Surrogate Model Construction
SOI	Simulation with Optimization-based Iterations
SP	Stochastic Programming
SSM	Statistical Selection Methods
SSO	Sequential Simulation—Optimization
TNO	The Netherlands Organisation for applied scientific research
TSP	Traveling Salesman Problems
TSSP	Two-Stage Stochastic Programming
UA	Unmanned Aircraft’
UAS	Unmanned Aircraft System
UAV	Unmanned Aircraft Vehicle
UG	Uncontrolled Glide
VMI	Vendor Managed Inventory
VRP	Vehicle Routing Problems
VTOL	Vertical Takeoff and Landing
WB	Whole Blood

Introduction

Drone-assisted delivery of medical goods has gained popularity in the last decade. The Covid-19 pandemic boosted the interest in drones delivering vaccines and has also shown the importance of having reliable (medical) supply chains. Zipline, a Californian company, is already delivering blood products using drones daily in several sub-Saharan countries like Rwanda[145]. Not yet operational, but closer to home, the "Medical Drone Service" (MDS) project has been created by a group of Dutch stakeholders ranging from logistics companies to hospitals[146]. The MDS project is currently in the ironically named pilot phase, performing test flights in a controlled environment. MDS stakeholders, both governmental and commercial, are faced with the challenge of deciding whether or how drones for medical delivery purposes could be implemented at scale. However, many unknowns on the performance of a large-scale medical emergency Unmanned Aircraft System (UAS) still exist. Based on, and in cooperation with, the MDS project, this research aims at creating a better and quantitative understanding of the performance that can be expected from the proposed system.

The benefits and risks of a UAS for the delivery of medical goods in developed healthcare systems have been qualitatively studied [141][215][208][131][194][113]. Faster delivery and emission reduction are often named as expected benefits, whilst system delivery reliability and risks posed to outsiders are examples of potential negative consequences. The few quantitative studies that have been conducted mostly confirm expectations around faster delivery and CO2 reductions, but also emphasize the dependence on results on the modeled concept of operations[168] [161] [68] [114]. Additionally, most studies have a narrow focus on optimizing one design criteria based on a single KPI.

We propose an agent-based simulation model based on the MDS concept of operation to quantify several performance indicators. We incorporate multiple theoretical and statistical models on TPR and expected speed of delivery, enabling direct comparison between using cars or drones, which until now was never possible. Using this unique model we address important system design decisions, hopefully enabling policy- and decision-makers to be better informed when faced with these decisions.

This report contains multiple parts of the thesis, starting with the scientific paper in Part I. The extended version of the Literature Study is presented in Part II. Finally, Part III contains supplementary material. The route finding module and its results are elaborated upon in Appendix A, the statistical substantiation is described in Appendix B and finally, Appendix C contains additional results and analyses.

I

Scientific Paper

Design and analysis of a UAV assisted medical emergency delivery system

Jelle Gerard van Haasteren*

Delft University of Technology, Delft, The Netherlands

Abstract

The healthcare systems of developed countries are getting more centralized and specialized. In order for this trend to continue one requires a reliable medical emergency delivery system. Both governments and private companies recognize that drones might be a good fit for this job. Previous qualitative studies suggest benefits of an Unmanned Aircraft System (UAS) to be: less vulnerability to congestion, fewer emissions, and cost savings because it enables further healthcare centralization. However, unknown reliability and physical risks that drones pose to civilians, often referred to as third-party-risk (TPR), have prevented systematic adoption so far. Because little holistic and quantitative understanding of these risks and benefits exists, policy- and other decision-makers are unable to value them and compare options. We propose an agent-based simulation model that reflects a multi-use-case medical emergency delivery system sustained by drones, cars, or a heterogeneous vehicle fleet. A case study of the Dutch Medical Drone Service project is performed, incorporating road-risk statistics and hourly congestion predictions. Three system design decisions are covered: testing different modes of operation, vehicle fleets, and healthcare facility allocations. We show that flying/driving safely when possible and fast only when necessary reduces TPR while maintaining reliability. Additionally, not being forced to return to the departure hub after delivery is shown to increase system performance on all indicators. Case-study results suggest that drones are superior in terms of reliability, speed of delivery, and emissions compared to cars. Additionally, we find that commonly accepted road transport TPR is at least as big as UAS-induced risk. Total UAS costs are small compared to the potential healthcare centralization cost savings enabled by such a delivery system. Our results suggest that a system in which healthcare facilities are concentrated at a few easily accessible locations, supported by a UAS, is compelling.

1 Introduction

Drone-assisted delivery of medical goods has gained popularity in the last decade. The Covid-19 pandemic boosted the interest in drones delivering vaccines and has also shown the importance of having reliable (medical) supply chains. As healthcare systems are becoming more centralized and specialized, they become more dependent on the ability to deliver medical products quickly from one location to another. Currently, these are often transported by road, blood products in the Netherlands for instance, are distributed by Sanquin who perform over a thousand emergency deliveries per year[1]. Sanquin is legally obliged to deliver blood to any Dutch hospital within a single hour to guarantee patient safety. The urgent, high value, and low weight characteristics of these products make them particularly well fitted for drone delivery. An analysis of the current state of medically oriented drone delivery shows that developing African nations are leading in the adoption of such systems [2]. Zipline, a Californian company, is already delivering blood products using drones daily in several sub-Saharan countries like Rwanda[3]. Recently, Zipline has started its first projects in the United States, which is a big driver behind its rapidly growing economic evaluation but also an indicator that drone-assisted delivery of medical goods is not only suitable for developing countries[4].

In other developed countries, several pilot projects have been initiated aimed at investigating the feasibility of such still futuristic systems. In these projects, different medical goods have been considered ranging from vaccines to organs. Initiated by a group of Dutch stakeholders ranging from logistics companies to hospitals, the "Medical Drone Service" (MDS) project is aimed at delivering blood products, laboratory samples, and medicines by drone in the Netherlands[5]. The MDS project is currently in the ironically named pilot phase, performing test flights in a controlled environment. MDS stakeholders, both governmental and commercial, are faced with the challenge of deciding whether or how drones for medical delivery purposes could be implemented at scale. However, many unknowns on the performance and impact of a large-scale Unmanned Aircraft Vehicle (UAV) assisted delivery system still exist, such as the costs, reliability, and TPR. Since the distribution of goods on which lives may be dependent is considered, it is important to have a good understanding of the performance

*Msc Student, Air Transport and Operations, Faculty of Aerospace Engineering, Delft University of Technology on such wide-ranging indicators before making any long-term strategic decisions. Policy- and decision-makers lack the possibility to make informed assessments, quantitatively weighing costs and benefits that would result from high upfront investments in a large-scale medical delivery UAS.

Several qualitative studies have listed the main expected pros and cons of large-scale UAV-assisted medical delivery systems [6, 7, 8, 9, 10, 11]. These studies support stakeholders by providing guidance on which pros and cons might be expected but do not enable fully informed decision-making since a quantitative understanding of the order of magnitude of the listed pros and cons is lacking. This research aims at broadening the quantitative understanding of these pros and cons, extending on what has been found in earlier works and what has been suggested as interesting for future research[12, 13, 14, 15].

Formally put the goal of this research is to: **Create a quantitative understanding of the expected performance in terms of costs, reliability, emissions, risks, and speed of delivery, of large scale implementation of a UAV assisted medical distribution system.** To create this knowledge a modular simulation model was developed that can simulate the daily operations of a medical delivery UAS, reflecting the system complexity and operating uncertainties. Novel simulation models can better reflect the complexity of the (future) system as well as take into account uncertainty and the resulting reliability of these distribution systems, when compared to more traditional purely optimization models. Using this bottom-up simulation approach, we cover three main system design considerations, ascending in the size of decision consequences. This is done so big strategic decisions require fewer assumptions on other operational design considerations. First, we cover how a large-scale medical emergency delivery system can operate most efficiently. Currently, emergency vehicles reduce travel time by using preemption methods, however, this comes at the cost of increased TPR. Additionally, studies on for instance ride-hailing systems show benefits in pro-actively repositioning vehicles to locations where they are better able to serve new requests. We compare different modes of operation that include active repositioning after delivery, as well as flying/driving safe and slow or fast and with more risk. Having established our preferred mode of operation, we then want to know which type of vehicles are best suited to operate in our proposed emergency medical delivery system. Different fleet compositions are compared, analyzing the differences between drones, cars, and heterogeneous fleets. Lastly, based on the derived delivery capabilities, we turn our attention to designing a more centralized healthcare system. We assess if the costs of our proposed delivery system can be compensated by reducing the number of healthcare facilities and how these facilities should be distributed among hospitals.

To measure system performance on all three design considerations we have defined five KPIs based on what is indicated by stakeholders and academics to be most relevant and interesting. **Costs** take into account fixed and variable costs of both the logistical UAS and medical facilities. **Reliability** is assessed by looking at the share of medical requests that are not processed within the required hour. **Emissions** are defined as the amount of CO2 emitted when driving a regular car or when producing the energy needed to fly the electric drone. Third-party-risk is estimated by integrating state-of-the-art TPR models for drones and using emergency vehicle statistics for cars. These **risks** are expressed as an expected number of casualties as a consequence of the delivery system. In this research, a casualty is defined as somebody with a severe injury or worse, including deadly. Severe injuries being a rating of 2 or more on the Maximum Abbreviated Injury Scale (MAIS2+). Finally, the **speed of delivery** is measured as the time between a request for delivery being made and the completion of this request.

The contribution of our work is threefold: first, we developed a bottom-up simulation model that reflects the operational complexity and uncertainty of the proposed concept of operation, enabling more robust system reliability testing. Secondly, we incorporate multiple theoretical and statistical models that enable direct comparison between cars and drones in terms of TPR and expected speed of delivery. Lastly, we provide a quantitative assessment of the expected performance of a UAV-assisted medical emergency delivery system on multiple KPIs.

The structure of the paper can be summarized as follows. In section 2 previous academic findings and methods, on top of which this research builds, are discussed. section 3 elaborates on the MDS case study. Next section 4 describes in further detail the proposed concept of operations and how this is translated into the simulation model, as well as the overall structure and validation of the model. The 3 main system design questions, corresponding hypothesis, experiments, and results are presented in section 5. further implications of these results and research limitations are discussed in section 6. Finally section 7 contains the conclusions and future work recommendations.

2 Related work

This section provides an overview of what is already known about the different topics and techniques on top of which this study builds. First, the context of medical goods logistics is presented in section 2.1. Next, in section 2.2, both qualitative and quantitative findings on medical drone delivery systems are discussed. In section 2.3 the theoretical background quantifying third-party drone risks is evaluated. Finally, findings on both risks and potential time saving of driving with pre-emption methods are discussed in section 2.4.

2.1 Healthcare logistics

The cost of Dutch healthcare, often regarded as one of the best functioning systems worldwide, is expected to double to €174 billion by 2040 [16]. Material and its logistics pose the second highest source of costs, after labor, within the healthcare industry[17]. Not surprisingly logistics problems have gained attention within the healthcare industry, with a high potential for improved efficiency[18]. In the well-studied context of Blood Supply Chain (BSC) design, Shokouifar et al. showed that lateral transshipments between hospitals can decrease shortage costs by 38.1% and wastage costs by 35.9% when having uncertain demand[19]. To achieve the benefits in terms of costs and efficiency hospitals will need to collaborate more effectively, for instance when the inventory of blood products is being shared [20, 21]. Just-in-time delivery (JIT), although applied successfully in other supply chains, has not yet been adopted in healthcare, most likely due to the fear and severe consequences of stock-out situations[22]. Pakdil et al. argue that healthcare delivery systems naturally run based on “pull” principles, a term commonly associated with JIT and lean supply chain policies to state that demand "pulls" production levels[23]. Improved performance is shown to be directly related to the number of hospitals in collaboration. Real-world implementation and realization of such benefits are dependent on challenges related to among others transportation reliability [24]. Thus it is interesting to investigate whether a UAS could remove some of these transportation-related barriers for a more efficient healthcare system.

Medical goods	Size	Weight	Economic value	On-demand deliveries	Transport requirements	Replaceability
Medical devices	Small to large	Low to high	Low to high	Rarely	-	Yes
Pharmaceuticals	Small to large	Low to high	Low to high	Sometimes	Traceability Temperature Humidity Stability Security	Yes
Sterile goods	Small to medium	Low to medium	Low to medium	Rarely	Three layer packaging	Yes
Laboratory samples	Small	Low to medium	Low	Daily	Traceability Temperature Stability	No
Blood products	Small	Low	Medium	Sometimes	Traceability Temperature	Yes

Table 1: Medical goods characteristics. Source: [6]

2.2 UAS medical delivery

The potential benefits of inventory and facility sharing discussed in the previous section, the small size, low weight, and high economic and societal value, make medical goods particularly interesting for drone distribution. Thiels et al. were one of the first to explicitly explore demand, feasibility, and risks associated with UAV-based medical delivery back in 2015[7]. They concluded that UAVs could be a particularly viable option for medical transport in situations of critical shortages. To assess which medical goods within healthcare logistics are most suited for drone delivery Magnusson & Hagerfors used literature, secondary data, and expert interviews, to obtain a better understanding of the specific characteristics and needs of the different products[6]. Their findings are summarized in Table 1, merging their defined subgroups into the 5 main categories of medical goods. Studies on the economic viability of UAS transport of medical goods have generated different results dependent on the context. A case study on the London blood supply chain suggested that operational costs of current transport means are up to three times higher compared to a drone-based hospital delivery network [12]. Fuel-specific costs could be reduced by almost 90% according to this study, additionally, this translated into fewer emissions. The authors suggest that additional benefits may come from considering a heterogeneous fleet, and an increase in overall demand levels. The dependency of economic viability on the scale is confirmed by Wright et al. [25]. They state that combining different use cases into a single system can increase cost-effectiveness. Analysis of the results from Otero Arenzana et al. on the London case study showed that with a big hub capacity, the model preferred placing hubs at hospitals over blood banks[12]. This suggests that indeed a horizontal on-demand delivery system of blood products supported by drones could save transportation costs in the end. A model representing a full-scale drone logistics system, for the centralization of a large Laboratory within Oslo University Hospital was created by Johannessen, Comtet & Fosse[15]. They stress the potential benefit of merging laboratories with duplicate facilities enabled by drone delivery. Although no estimation of the costs of the UAS was provided, it did suggest cost savings between 10 and 20 Million euros annually by reducing duplicate facilities. Their model also showed the reliability of drone delivery times for sample transportation, all occurrences where the maximum total time in the system was exceeded were due to delays in the laboratory or other in-hospital processes. A simulation study by Haidari et al. suggests that vaccine distribution using drones reduces costs and increases vaccine availability, compared to land transport systems [26]. The authors state that the simplification of their model is one of the main limitations of their study.

2.3 Drone risk models

A literature review on commercial drone usage states that safety was mentioned most often as the biggest concern around drone usage [27]. Safety is a broad term, so we focus here on the physical risk for third parties. As civilian drone usage is expected to grow around the world, the risk of physical accidents is destined to multiply [28]. Hirling and Holzapfel identify a lack of historic data regarding UAS incidents, to generate reliable statistics on drone safety[29]. They state that cross-industry comparison of such risks is thus impossible, which makes it difficult to put safety numbers like fatalities per operating hour into perspective. Since data does not offer a viable solution when estimating physical drone risks, theoretical models have been developed aimed at quantifying risks posed by drones. In order to tackle this problem systematically, most researchers have tried to compute the probability of fatality or heavy injury for people on the ground in a way that is widely applicable. Melnyk et al. presented compelling reasons for expressing risk as fatality rate instead of for instance economic impact[30]. Although the exact implementation of the equation differs, most studies use something similar to Equation 1 to compute the risk and subdivide the problem. Here the simple and clear formulation found in a study aimed at quantifying small UAV risk is provided [31]. The latest literature has considered different failure types when evaluating the probability of a failure event[32, 31, 33]. These heterogeneous failures subsequently lead to different ways in which the UAV descents to the ground, which is the current state of the art and is believed to be the most reliable method for estimating UAV TPR.

$$p_{\text{fatality}} = p_{\text{event}} \cdot p_{\text{impact person}} \cdot p_{\text{fatal impact}} \tag{1}$$

2.4 Road transport

In order to be able to compare drones and cars on the topics of TPR, speed of delivery, and reliability, knowledge was derived from past research and statistics on emergency vehicles. Different studies analyzing response times of ambulances and quantifying the effectiveness of pre-emption methods have suggested various time-saving percentages[34, 35, 36, 37, 38, 39]. The most elaborate study by Poulton et al., relying on the biggest dataset, from the London ambulance service, in an environment that can be considered similar to the road system of the Netherlands found an almost consistent 33% reduction in travel time[40]. They compared recorded trips from the data set with estimates retrieved from the Google Maps Distance Matrix API.
Although travel time is reduced this comes with a significant increase in risks created by emergency vehicles. In the Netherlands, the "Instituut Fysieke Veiligheid" (IFV), has studied accidents involving emergency vehicles over the last decade. Their most elaborate study from 2014 analyzed emergency vehicle accident data from the period between 2010 and 2013 [41]. Total hours driven, along with the number of fatalities and seriously injured, suggested 9 and 59 accidents per million hours driven leading to a fatality or heavy injury respectively. Recent statistics provide similar results[42, 43]. The latest report also confirmed the hypothesis that emergency vehicle risks also apply to emergency transport of medical goods. As two drivers of Sanquin, the blood bank in the Netherlands, were involved in a recorded accident[43]. Note that these statistics only include accidents with an emergency vehicle, some research from the U.S. suggests that the amount of accidents that occur because of other vehicles getting out of the way is significantly higher[44].

3 Description of the Case Studies

The majority of literature on medical drone delivery, and this paper is no exception, has been written with a certain project in mind. As such models resemble the envisioned systems concept of operation of the related project. "Medical Drone Service" is a project initiated by a group of Dutch stakeholders ranging from logistics companies to hospitals aimed at delivering blood products, laboratory samples, and medicines by drone in the Netherlands [5]. The focus of this research is on emergency requests that need to be processed within an hour of arising. Regarding requests for blood products or medicines, this means that the object should be delivered to the hospital that needs it within 60 minutes. Alternatively, laboratory samples require a pick-up from the requesting hospital and should be delivered to another hospital that can perform the required diagnosis on the sample, all within the same temporal deadline. It should be noted that this combination of different use-cases, that require different processing procedures, has not been modeled or simulated in previous works and adds significant system complexity which is hard to translate in traditional optimization models.
The proposed concept of operation is most similar to the systems described by, Otero Arenzana et al. and Dhote & Limbourg. The first designed a UAV hospital delivery network for blood products in London[14]. The latter investigated the logistical issues around a UAS for biomedical material transportation called Drone4Care in Belgium[12]. A detailed description of our model, and the assumed concept of operation it reflects, is presented in section 4.
For this study, an area that covers a majority of the Dutch province of South Holland was taken as a case study. Within this area 19 hospitals operate, ranging from large academic to smaller sister hospitals. Next to the

variety of hospital sizes, this area contains both urban areas, where population density is high and congestion is generally a big problem, and rural areas.

4 Methodology

The framework presented in this paper aims to quantify the delivery performance and external effects like TPR, of a drone-assisted emergency medical delivery system. This section discusses the concept of operation used in this study in more detail and in parallel how this is reflected in the simulation model simultaneously. Given a set of hospitals, assumed to be in full cooperation, a system is designed and evaluated that processes all incoming demand for healthcare. Our modeling approach consists of two main processes. First, in the pre-processing phase routes and associated risks are determined for all hospital origin and destination pairs and both drones and cars, which is described in section 4.1. Subsequently, in section 4.2 the agent-based simulation model is discussed. Lastly in section 4.3 we discuss how a visualization dashboard was used to validate the functioning of the model and enable (local) behavior analysis.

4.1 Pre-processing

In order to assess the differences between car and drone use in a medical delivery system, the routes both vehicles will take when delivering goods from one hospital to the other have been modeled. Since emergency deliveries are considered, and as such current emergency medical deliveries are often made using pre-emption signals, two types of routes have been modeled for both vehicles: a safe route, minimizing TPR, and a fast route, in which the main objective is to minimize travel time. Whilst the drone route model allows for finding more balanced routes, it is more difficult to model emergency vehicles driving 'a little faster'. To enable fair comparison we thus only modeled the two extreme options, and additionally, we considered a more balanced operational strategy later. Analysis of the travel times and TPR found for both vehicle types is presented in section 5.2.

4.1.1 Drone routes

The routes and associated risks of drones flying from one hospital to the other have been modeled using methods similar to the state-of-the-art on drone TPR[33]. A ground risk map is made up of a rectangular grid consisting of square cells each representing an area of 100 by 100 meters. Each cell contains a risk value that corresponds to the population density at that geographical location. The 4 different failure types, and their corresponding probability of event, impact area, and shelter factor, used in this study are presented in Table 2. These numbers have been derived from the work of la Cour-Harbo, because of similarities in assumed drone characteristics[31]. It is assumed that a drone will crash in the same cell as where a failure event occurs. The validity of this assumption is strengthened by the results of Primatesta et al. who show that assuming no wind and with the exception of parachute events, the majority of crash locations are within 50 meters of the failure location [33], which is thus still within the same grid cell.
Subsequently, using a modified A* algorithm in which one can move horizontal, vertical, and diagonally, routes between all hospitals are derived. The fast routes, for emergency deliveries, minimize distance which results in route lengths almost equal to the absolute distance between hospitals, the differences are a result of drones only being able to move in one of the three before-mentioned directions. When searching for the safest routes, the path-finding algorithm tries to minimize TPR, thus leading to routes avoiding highly populated areas. Next to the route distance, the associated TPR is stored in a matrix for all hospital combinations and for both the safe and fast routes.

	Ballistic	**UG**	**Parachute**	**Flyaway**
Probability of event [events/ hr]	1/125	1/150	1/100	1/200
Impact area [m^2/person]	0.3	0.6	0.3	0.6
Shelter factor [-]	0.3	0.3	0.6	0.3

Table 2: Drone risk model values [31]

To assess the emissions we used Equation 2 derived from the work by Otero et al.[12]. e_{dijm} stating the emissions in kg of CO2 resulting from a drone flying from location i to j in modus m. Similarly s_{dijm} indicates the distance between the two hospitals. σ_v states the emissions produced per kWh, mostly dependent on the energy mix provided by the national grid. m_v represents the mass of the vehicle, which was assumed to not change significantly when carrying a load. η and κ are the power transfer efficiency and lift to drag ratio respectively. Lastly, the power consumed by the onboard electronics is given by p and v states the speed of the drone.

$$e_{\text{dijm}} = s_{\text{dijm}} * \frac{\sigma_v}{1000}\left(\frac{m_v}{370\eta\kappa} + \frac{p}{v}\right) \tag{2}$$

4.1.2 Car routes

Unlike drones, cars are limited to existing infrastructure when it comes to finding a route from one hospital to the other. Additionally whilst we have assumed that the time it takes for a drone to fly a certain route is fairly constant and independent of the time or day, we know for a fact that this is not the case for cars. In fact, one of the main reasons for Sanquin, currently responsible for delivering blood products in case of emergency, to participate in the MDS project is because their delivery time reliability is negatively impacted by urban congestion. In order to include these congestions into the model, travel times for cars between hospitals are time and day dependent. Using the BING maps distance matrix API, the expected travel time and distance are determined for every hour within a week, so 7 * 24 values per hospital pair. These traveltime estimates are considered the safe option for cars. Emergency vehicles are expected to be able to reduce this time by 33% when using lights and sirens according to the extensive study by Poulton et al.[40]. In this study, they too compared actual travel times with estimates of normal route planners (they used the google matrix API). It is assumed that the route taken when driving with lights and sirens is of a similar length as the normal route.
To derive the third-party risk associated with the safe car routes, average dutch accidents statistics are used, since cars will act as normal cars when no sirens are used. Combining accident and total vehicle kilometers statistics it was derived that for every kilometer driven, the probability of a casualty (MAIS 2+ or worse) is 2.33 * 10^{-8}. The use of lights and sirens by emergency vehicles is measured in hours driven. Thus in combination with the accident statistics from IPV on emergency vehicle accidents, an accident rate (resulting in a MAIS 2+ or worse) is derived to be 0.00006 casualties per hour.
Similarly to drones, emissions are derived using the simple equation: $e_{\text{cijm}} = s_{\text{cijm}} * \mu$, with μ stating the car emissions produced per km, again using the same value as used in [12] who assumed a Ford Focus.

4.1.3 Medical facility distribution

The reason one might want to use cars or drones to transport medical goods from one hospital to the other is that not all hospitals possess the facilities to provide a particular type of healthcare. Different methods of distributing the facilities and the resulting effects on the systems are discussed in section 5.5. The resulting facility allocation acts as the input for the Agent-based simulation model.

4.2 Agent-based simulation model

Novel to the subject of quantitative medical drone delivery research, we use an Agent-Based simulation model to compare different scenarios. This 'bottom-up' modeling approach has the benefits that, it can reflect the complexity of the system, be built modular, and enable both system-wide and local behavior analysis. For our Python implementation, we modified an openly available library called Mesa [45]. First, a bird's-eye view of the model is presented in section 4.2.1, introducing the environment, different agents, and their interactions. Next in section 4.2.2 till section 4.2.5, these elements will be discussed individually in more detail. To see the entire model, we refer readers to the online available implementation on Github[46].

4.2.1 Model overview

Figure 1 provides an overview of the model proposed for this research. Both the pre-processing and agent-based modules of the simulation model are included in this overview to demonstrate their relation. Note that the overview is intended to make the written model specification more comprehensible, and some details and/or trivialities have been left out from the overview for this reason. Next, the model environment and agents will be discussed in more detail in a narrative style. In the remainder of this paper, we will distinguish two definitions. Firstly when a particular type of healthcare is requested in a hospital we talk about a *request*. Thus, a *request* has a parent hospital, a use-case, and a deadline. When a *request* requires transport, a particular planned transport is called a *schedule item*. A *schedule item* has a parent vehicle, a planned route, time and can deliver no, one, or multiple requests.

4.2.2 Environment

The environment is structured as a network, where nodes contain hospitals and have weighted links with every other node. The link weights indicate the time, risk, emission, and distance for both vehicle types and

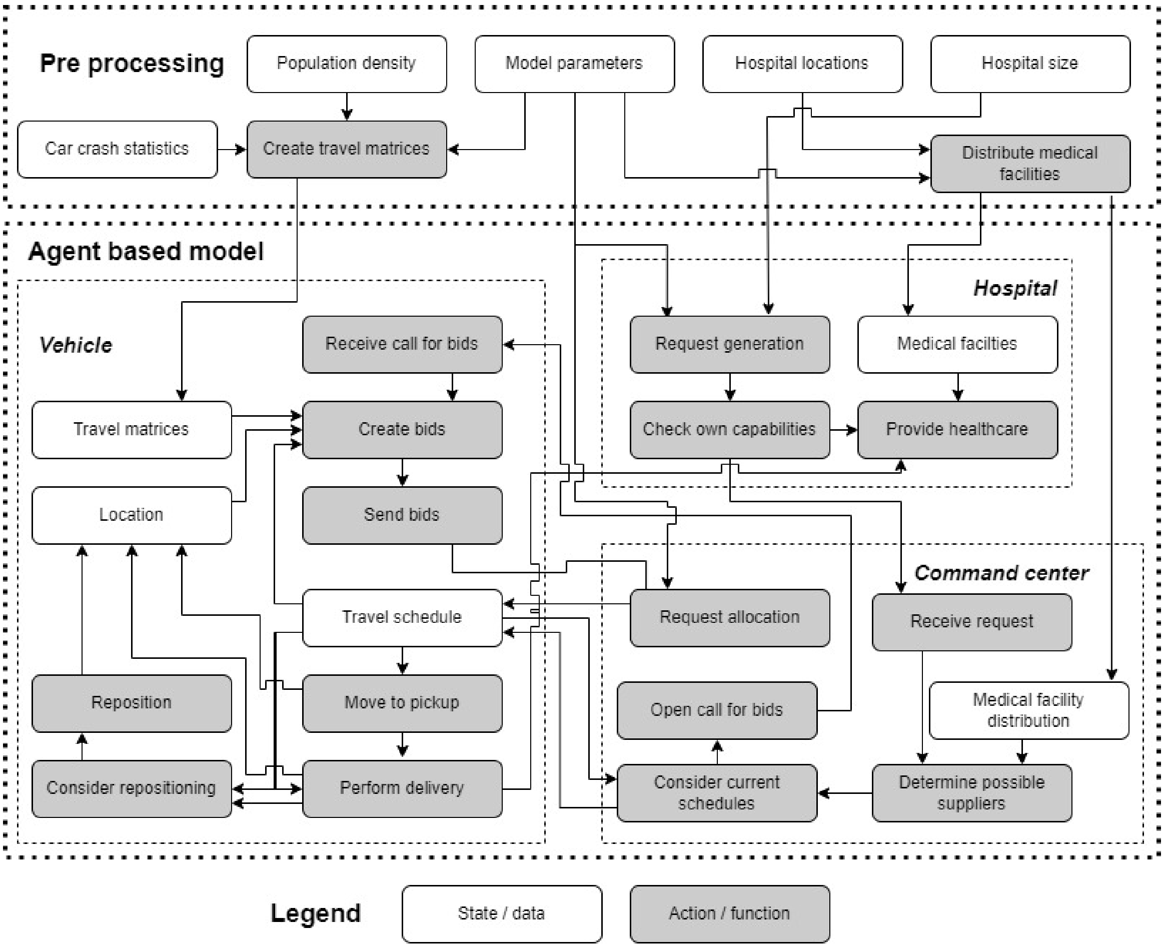


Figure 1: Model overview

urgency levels, which were computed in the pre-processing module. Thus these weighted links represent a more comprehensive environment, described in the previous section. Note that some link weights are, next to the vehicle and urgency-level, also time-dependent. Vehicle agents can access both links and nodes. A command center agent can access the state of the entire environment, including that of both all hospital and vehicle agents.

4.2.3 Hospital agent

The hospital aims to provide healthcare and functions as both the starting and end-point of the system. Thus its main actions are defined as the generation of new healthcare requests and the completion of such requests by providing healthcare. Whilst location and amount of beds are fixed, the amount and type of healthcare facilities it possesses are varied between different simulated scenarios and derived from the pre-processing module. Hospitals possessing facilities for the blood product or rare medicine use-case are considered hubs. The laboratory sample use-case requires pick-up actions and thus hospital agents possessing only these facilities are not considered hubs. Hospital agents are placed at nodes in the network.

Request generation: First each hospital determines for each use case the total amount of orders for that day depending on the size of the hospital, measured in the number of beds (b), and the input variable (λ) indicating the total demand level in the average number of requests per 1000 beds per day. The total daily demand for each use case is modeled as $Poisson(\lambda * \frac{b}{1000})$. The use of this function and a variable demand rate specifically is because of two reasons. Firstly no reliable healthcare data could be provided by healthcare partners. Secondly, the intensity with which hospitals would use the system, for all cases or for particular categories within a use-case, was indicated to be dependent on the distribution system quality, creating a chicken and egg problem. Next, each request is given a random time of generation, the time at which a doctor creates the request, by randomly picking a time from a uniform distribution. The proposed system and therefore the representative model focuses mainly on emergency requests, thus a uniform distribution was assumed. Note that the request schedule is created by each hospital at the beginning of a simulation run because of computational efficiency. However in reality one does not know, at the beginning of the day, when which type of emergency request will occur. Thus the hospital agent acts naively until the time the request item is officially created. Then the agent decides, based on the medical facilities the agent possesses, whether the request requires transportation. This action is referred to as *Check own capabilities* in Figure 1. If the agent has the needed medical facilities, it can directly perform the *provide healthcare* action. Alternatively, the request is passed on to the command center which will process it further.

Provide healthcare: Providing healthcare is the last stage of medical requests in this model. A hospital agent possessing the right facilities receives a request, which could originate from the same hospital, and completes it. The request is added to the list of completed items, recording if delivery was needed, which vehicle performed it, and the delivery-related KPIs.

4.2.4 Command center agent

The goal of the command center is to match incoming requests with hospitals that can provide the healthcare, and additionally assigns the subsequently needed delivery to a vehicle agent. As discussed in section 3 the use-case of a request determines whether it requires a delivery at the requesting hospital (blood product and medicines), or pick-up (laboratory samples).

Consider current schedules: Hospitals that are not able to process a request for healthcare themselves forward the request to the command center. Having *received the request* the command center agent subsequently checks which hospital agents do possess the needed facilities and as such *determines possible suppliers*. Knowing all the possible combinations of origin(s) and destination(s) as well as all the travel schedules of the vehicles, the command center tries to add the new request to existing schedule items. Next to the origin and destination of schedule items the command center takes into account the capacity of the vehicle and the expected time of arrival. If a compatible schedule item exists the command center assigns the new request to the already existing schedule item and the corresponding vehicle.

Task allocation: When the *consider current schedules* concludes that a new delivery should be planned, the command center *opens a call for bids*. Providing the request details, and the possible origins (blood product or medicine requests), or destinations (laboratory samples), it asks the vehicle agents to create a bid. Vehicles thus determine themselves how they could best perform the delivery. The vehicles each return their best bids to the command center agent who scores and ranks bids. The command center finally notifies the vehicle with the winning bid, who will add the schedule items comprising its bid to its schedule. Equation 3 shows how bids are scored, the bid with the lowest score wins the bid tender. $bid_{on-time}$ is a binary, having a value of 0 if the proposed delivery will complete the request within the hour deadline and 1 otherwise. Since the primary objective is to deliver all requests on time $\rho \gg \beta, \gamma, \delta, \omega$, so the total score, of a bid that will not arrive on time, will always be higher than bids that will finish within the hour. bid_{risk} states the number of casualties that can be expected when the bid and its corresponding schedule items are executed a million times. The amount of minutes between request generation and final delivery is defined as bid_{ETA}. $bid_{Emission}$ and bid_{costs} state the kg of CO2 emission and fuel costs of the bid respectively. β, γ, δ, and ω represent the weights that define the relative importance of the different indicators.

$$bid_{score} = \rho * bid_{on-time} + \beta * bid_{risk} + \gamma * bid_{ETA} + \delta * bid_{emission} + \omega * bid_{costs} \tag{3}$$

4.2.5 Vehicle agent

Vehicle agents aim to perform deliveries. They create schedules containing trips and in parallel execute these schedules. There are two types of vehicle agents, drones and cars. In this research it is assumed that a drone has a capacity of one request, meaning that it can carry only one product per flight. Cars however have a maximum capacity of 10 products, which can be of different use-cases, reflecting the fact that a car has a significantly bigger load volume. Other vehicle parameter values will be provided in section 5.1. Both agent types can execute movements in two modes, referenced in this paper as *safe* and *fast*. We define three modes of operation regarding which option to take, the *Safe* and *Fast* mode only use their respective route option. In the last mode, which we will refer to as *Combi*, vehicle agents create bids using both route options. Additionally, we introduce 4 repositioning strategies referred to as *Forced*, *None*, *Simple*, and *Closest hub*. More common in for instance ride-sharing research, we define repositioning as actively anticipating unknown future demand, by moving towards a location where a vehicle agent is more likely to serve upcoming requests. In our concept of operation, this translates into driving or flying to a hub hospital agent, where blood products and rare medicines are stored.

Create bid: Having received a request for bids by the command center agent, a vehicle agent then evaluates its options and returns the best as its bid. The start time and location, from which it starts creating a bid, are either the current location and time when it has an empty schedule or the end time and location from its current schedule. Using the travel matrices it evaluates the different routes it can take to perform the delivery/pick-up. The total bid can contain multiple schedule items, as it will always contain a flight/ride performing the actual delivery, but can also contain a prior movement towards the pick-up location. If the vehicle operates according to the *Forced* repositioning strategy, a schedule item in which a vehicle returns to its hub of departure is also always included. Depending on the mode of operation the vehicle will create bids using *safe*/*fast* routes or both. The expected time of delivery, TPR, emissions, and costs will together determine the ranking of the bid, similar to the command center as presented mathematically in Equation 3. Finally, the vehicle returns its best bid to the command center which will decide whether the vehicle gets allocated to perform the delivery.

Perform delivery: The travel schedule of a vehicle contains all the planned movements of the vehicle, the time of departure, arrival, and other flight/ride details. One might consider a schedule item a *move to pick-up* when it does not transport any medical goods during the movement but will pick-up at least one for delivery on the next movement. The subsequent performance of a schedule item, that carries one or more requests, is referred to as *perform delivery*. As a result of the delivery, the destination hospital is able to *provide healthcare*. Following the delivery, a vehicle may already have the next schedule item planned. Between two schedule items, it is assumed that some kind of turnaround actions are needed, depending on the vehicle type. For cars, the driver needs to park the car and potentially walk to/from the location in the hospital where it must deliver or pick-up the desired medical goods. Next to (de)loading of any medical goods, drones will need some additional supporting actions at the hospital too, for instance, switch batteries if needed and perform a basic checklist before the next flight. The assumed time these turnarounds take will be covered in section 5.1.

Consider repositioning: If a vehicle has an empty schedule after a delivery and adheres to the *None* repositioning strategy it will simply remain at its current location. The *Simple* strategy requires vehicles to return to their original departure hub. Note that contrary to the *Forced* strategy, an agent only does so if it has an empty schedule. Since up to this point its schedule ended after the delivery, it was more flexible in creating bids for new requests, starting from the end location and time of delivery. Similarly, vehicles adhering to the *Closest hub* strategy will only reposition when it has no future plans, but rather than always returning to their departure hub, they will go to the hub nearest to their drop-off location.

4.3 Verification and validation

In order to determine whether the presented model functioned as intended and was a good representation of the proposed delivery system, several validation steps were taken. By continuous verification of behavior, results, and intermediate values during the development phase, code verification was conducted in a constant and iterative process. Pre-processing results of the drone TPR model were compared with the absolute values found in previous studies [33] to validate that results did not differ by an order of magnitude on comparable routes and environments. Similarly, emissions, distances, and travel times of the routes found were both compared with previous works and validated with common online tools like Google maps.
The Agent-based simulation model has been fitted with a dashboard presented in Figure 2 partially because it enables thorough model analysis and validation, by observing whether agents behave as expected in different scenarios. As can be seen, when looking closely at the middle map, the dashboard is able to visualize all possible states and types of agents. Vehicle agents move around the environment and are represented by an icon of the vehicle type potentially carrying a package and with the addition of a stopwatch when taking the *fast* route. Hospitals show up at the corresponding physical location as the grey rectangles containing 3 squares each symbolizing one of the three medical use-cases. If a hospital possesses the facilities to provide healthcare the corresponding square is green otherwise the base color is white. When a hospital creates a request that requires a delivery the square turns red until a vehicle carrying a package arrives and the healthcare can be provided. Continuously updating values in the right column on some of the major KPIs and model parameter tuning in the left column enable additional validation and analysis. By testing extreme conditions and policies both model structure and behavior could be further validated.
Next to visual validation, quantitative simulation results were thoroughly analyzed on explainability and reproducibility. Additionally, sensitivity analyses were conducted, of which some will be discussed in more detail in section 5, which also contributed to model verification. Since the model represents a largely hypothetical system, no real data was available for comparison.

5 Experiments & Results

The presented simulation model has been developed in order to quantitatively assess the effects of different medical delivery system configurations. General model parameters and experimental setup used to compare different configurations are discussed in section 5.1. Next, the experiments, results, and analysis used to investigate

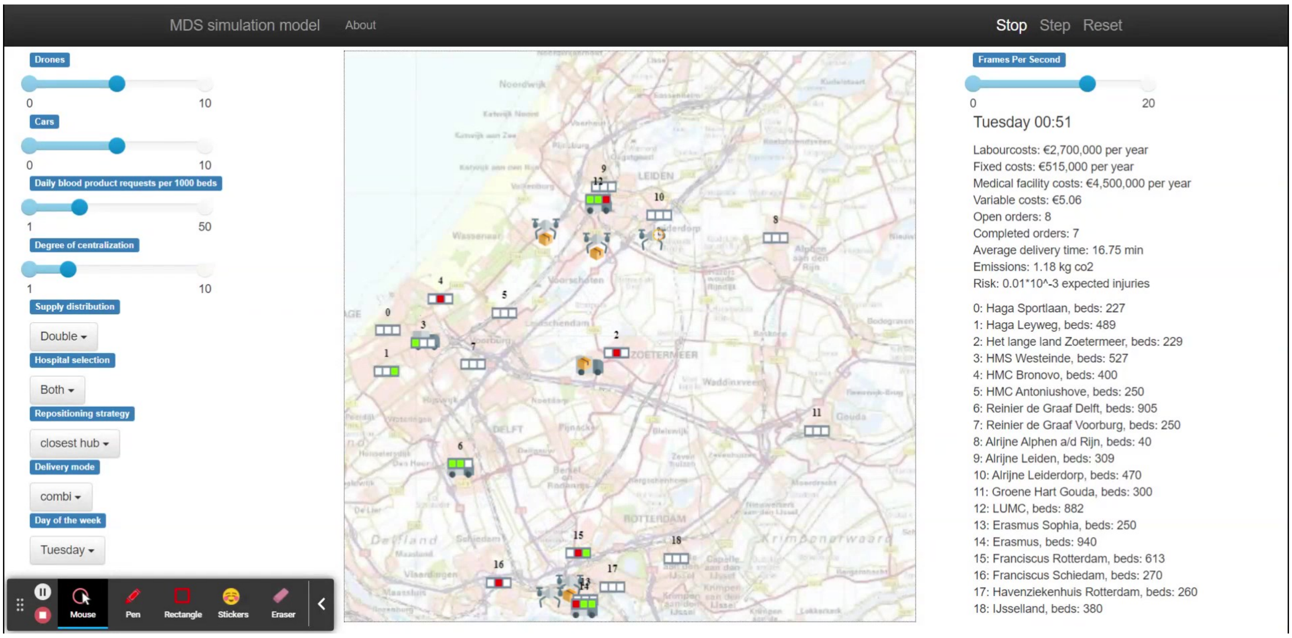


Figure 2: Model dashboard

the different system design considerations are discussed. First, an analysis of the drone and car routes derived from the pre-processing module is presented (A). Next, we study the effects of different modes of operation, combining different strategies for repositioning and whether to take the *Safe* or *Fast* route in one experiment (B). One of the main contributions of our work is the ability to compare the performance of different vehicle types, which is the focus of experiments C, D, and E. We first perform a global analysis of different fleet sizes and compositions (C). Subsequently, we analyze the differences between just using drones or cars more in-depth (D). Additionally, we test how much performance for both vehicle types changes when bidding weights are altered (E). In experiment F the most strategic problem is addressed, knowing the potential performance of the delivery system, we analyzed the effects of different healthcare facility allocation configurations. Finally, we test the sensitivity of our results to the assumption that all hospitals are in full collaboration, by looking at route usage patterns (G). Table 3 shows the goals and sections corresponding to the above-described experiments and analysis.

	Goal	Section
A	Comparison of drone and car routes	section 5.2
B	Determine prefered mode of operation	section 5.3
C	Study effects of different fleet sizes and compostitions	section 5.4.1
D	Analyse performance differences between cars and drones	section 5.4.2
E	Explore the effects of different bidding weights	section 5.4.3
F	Test different healthcare facility allocation configurations	section 5.5
G	Identify route usage patterns and their implications	section 5.5.1

Table 3: Overview of experiments and analysis

5.1 Experimental setup

In the introduction, the KPIs: *costs*, *reliability*, *emissions*, *risk*, and *speed of delivery* were introduced. The model parameters used as input, unless specified otherwise in the experiment, are presented in Table 4. Data on the hospitals and population density have been derived from the open sources ESRI[47] and CBS[48] respectively. Parameter values have been derived from previous studies, discussions with industry experts, and publicly available data. Drone TPR parameters have been left out from this table as they have been covered in more detail in Table 2.

Additionally, several input parameters are introduced that have been changed and tested throughout this research. Related to fleet composition N_{drone} and N_{car} state the amount of drone and car agents respectively, combined N_{total} refers to the total amount of vehicles in the system. The demand level is indicated by λ, introduced previously as the average daily number of requests per use-case per 1000 beds.

A single simulation covers an entire day of operation (1440 minutes) in which requests can occur. In the end, open requests are completed and subsequently, results are stored in a CSV file along with its input parameters. The demand uncertainty reflected in the model through the *request generation* action of the hospital agent required conducting Monte Carlo (MC) simulations of all tested configurations. Seeds were used so that different configurations were tested under the same randomly created demand scenario in each iteration of the MC. The number of simulation iterations needed for each configuration to obtain reliable results was determined by analyzing the coefficient of variation. Shapiro-Wilk tests were used on the different individual indicators to determine whether the results were normally distributed. If the found P-values for a single indicator in different scenarios were not consistently lower or higher than the assumed significance level of $\alpha = 0.05$, the corresponding QQ-plots were manually analyzed to decide on the normality of the result distribution. Subsequently, the statistical significance of the results was determined using an unpaired t- or Mann-Whitney test, for normally and non-normally distributed indicators respectively.

Drone		**Car**	
Parameter	Value	Parameter	Value
Capacity [requests]	1	Capacity [requests]	10
Turn around time [seconds]	300	Turn around time [seconds]	180
Speed [km/h]	60	Speedingfactor emergency [-]	1.5
Variable cost [€/km]	0.1	Variable cost [€/km]	0.25
Fixed yearly cost [€/yr]	50,000	Fixed yearly cost [€/yr]	5,000
Pilots needed [FTE/Fleet]*	13	Drivers needed [FTE/Car]	6
Pilot salary costs [€/yr]	60,000	Driver salary costs [€/yr]	50,000
Command center costs [€/yr]	90,000	Regular driving risk [casualties/km]	$2.33 * 10^8$
Takeofftime [seconds]	30	Emergency driving risk [casualties/hr]	$6 * 10^{-6}$
Landing time [seconds]	30	Emmissions [kgCo2/km]	0.12
Massa [kg]	15	**Medical**	
Power transfer efficiency [-]	0.5	Parameter	Value
Lift to drag ratio [-]	3	Blood product facility costs [€/yr]	800,000
Power consumed by electronics [kw]	0.1	Laboratory samples facility costs [€/yr]	350,000
Electricity emmissions [kgCo2e/kwh]	0.355	Rare medicine facility costs [€/yr]	350,000
electriciy price [€/kwh]	0.1	Drone handling costs [€/yr]	30,000
Bidding weights			
Risk weight - β	1	Delivery speed weight - γ	1
Emission weight - δ	0	Variable cost weight - ω	0

Table 4: Model parameters

5.2 Routes

The routes established in the pre-processing phase already provide interesting insights into the differences between cars and drones, as well as differences between *safe* and *fast* routes. We confirmed the issues around congestion for cars when analyzing the travel times during different times of the week. Morning and afternoon rush hours caused travel times to be up to 97% longer compared to the quiet night hours. During weekends a single, more spread out and lower peak could be observed around mid-day, Saturdays being slightly more congested than Sundays. These increases in travel time due to congestion were notably larger from and to hospitals located in city centers. When comparing these projected travel times by car with the routes found by the drone pathfinding algorithm, we see that drones are often faster than cars. When both cars and drones take the safe option, on 88% of the routes drones are faster than cars during the least congested time of the week. When cars use pre-emption methods this percentage drops to 24%, however when drones also take the direct route between hospitals they are faster in 55% of cases. At the most congested moment of the week, a drone taking the direct route is faster than a car using lights and sirens 99% of the routes.
When comparing TPR we see that for the *fast* option, direct routes for drones, and using lights and sirens for cars, drones are safer on all routes. Note that car TPR for fast routes depends on the travel time, for this analysis the most favorable moment during the week was used, during rush hour car TPR would be even bigger. However, for the safe option, we see that on 11% of the routes using a car is the safer option. This difference can be explained by looking at the increased risk of using the fast option. Whilst TPR increases on average by a factor of 24 when a drone uses the fast option over the safe option, this factor is 42 for cars.
Unsurprisingly drones emit significantly less CO2 moving from one hospital to another compared to cars. The magnitude of the difference in environmental impact will be discussed more elaborately later.

5.3 Modes of operation

The agent-based simulation model enables comparing different and more complex modes of operation, we focussed specifically on whether to take safe or fast routes and different options for active repositioning. This experiment aims to study the influence of different modes of operations on the overall performance of the system. In this section, we will first discuss the hypothesis. Next, the scenario on which these were tested is briefly described. Lastly, we compare the results and conclude which mode of operation was found best suited and used in the remainder of this study.
In section 4.2.5 we introduced the three modes of operation, always taking the fastest route (*Fast*), the safest route (*Safe*) or consider both (*Combi*). The hypothesis is that *Combi* performs best in reducing TPR whilst reliably delivering within the hour limit. In parallel, we introduced the four repositioning strategies referred to as *Forced*, *None*, *Simple* and *Closest hub*. It is hypothesized that in a more complex system, with multiple hubs and both pick-ups and deliveries, *Forced* strategy limits flexibility and thus system performance. Additionally, it is expected that active repositioning when possible benefits speed of delivery and reliability.
The results presented below, providing insights on the above-mentioned hypothesis, are generated using a scenario with 3 hub hospitals all possessing facilities for all use cases ($\chi = 3$). Fleets of $N_{total} = 12$ consisting of only drones, cars or a 50/50 mix. Shown values contain the averages of 3 different demand levels and fleet configurations since exact system demand is not fully known and will likely vary across different days and or seasons. These results are consistent with findings from other system configurations not included in this paper. Also, we are more interested in the relative performance over the exact numerical values of the different KPIs since optimal fleet and facility distribution is not yet known.

	Forced	None	Simple	Closest Hub
Safe	93%	92.1%	93.4%	93.9%
Fast	99.6%	99.9%	99.9%	99.9%
Combi	92.9%	99.7%	99.3%	99.5%

(a) Percentage of requests served within 60 min

	Forced	None	Simple	Closest Hub
Safe	85.1	52.5	48.1	47.8
Fast	22.3	25.4	21.4	20.7
Combi	41.5	32.6	29.5	28.3

(b) Average delivery time [min]

	Forced	None	Simple	Closest Hub
Safe	0.06	0.04	0.05	0.05
Fast	2.60	1.97	2.56	2.45
Combi	0.41	0.52	0.49	0.49

(c) Expected number of casualties per operating year

	Forced	None	Simple	Closest Hub
Safe	454	339	419	411
Fast	531	395	527	486
Combi	487	353	456	438

(d) Daily CO2 emissions [kg]

Table 5: Reliability, delivery speed, risk, and emissions of different modes of operations

Table 5 largely confirms the hypothesis around the 3 different safety modes. *Safe* operation reduces TPR by a factor of on average around 10 and 50 compared to *Combi* and *Fast* respectively. However, this comes at the cost of a significant decrease in delivery reliability where, except when repositioning is enforced, *Combi* is almost as reliable as always taking the fastest option. Increasing system capacity, which is costly and decreases system efficiency, positively impacts reliability and can thus mitigate this negative effect of the *Safe* operating mode. However, it should be noted that in such a system configuration *Combi* mode will strongly resemble *Safe* since it can pick the slower and safer option without compromising the delivery deadline more regularly. Always opting for the fastest option non-surprisingly reduces average delivery time whilst the increase in overall emissions is not consistent between different configurations. *Safe* mode performs worst on speed of delivery, whilst *Combi* numbers are most often closer to *Fast*. In short the flexibility of *Combi* mode, using increased urgency delivery only when truly needed, makes the system safe and reliable for both those directly dependent on it and third parties.
Focusing on repositioning strategies, the results support our initial beliefs on both the negative impact of *Forced* repositioning and the potential benefits of more deliberate strategies. Removing the constraint of having to return to your departure hub improves system performance on all KPIs, but most significantly impacts reliability and speed as seen in Table 5b and Table 5a. This implies that simulation-based system analysis and design, which are able to reflect more complex concepts of operation, are better able to capture operational benefits. Active (*Simple* and *Closest hub*) repositioning mainly benefits speed of delivery, since vehicles can directly perform the delivery instead of having to go to the pick-up location more often. Although differences are relatively small, the *Closest hub* strategy performs better or equal to the *Simple* strategy on all main KPIs. Visual simulation analysis revealed some emergent behavior that is (partially) responsible for these differences. When demand

around a certain hub exceeded local vehicle delivery capacities, vehicles from other hubs performed a delivery moving towards the high-demand region. Subsequent to the delivery a vehicle would then reposition to the hub which lacked vehicle capacity before since this hub is now closer than its original hub. *Closest hub* repositioning thus indirectly balances demand and delivery supply.
Finally, we analyzed the combinations and relations of different safety and repositioning strategies. Note that the results presented in Table 5 combine results of different scenario configurations, exact differences between individual configurations vary. Comparing different combinations more extensively under different demand and fleet configurations we concluded that the results described above are robust. Except for *Forced* combinations, general conclusions on differences in safety and repositioning strategies are consistent when comparing individual combinations. Although KPI prioritization is up for debate, we argue that the *Combi* safety strategy along with *Closest hub* repositioning performs best overall, and was thus picked as the default mode of operation in the remainder of this study. The differences between *Combi-Closest hub* and *Combi-Simple hub*, although sometimes small, were found to be statistically significant for all described fleet/demand configurations and KPIs shown in Table 5 except for the risk expressed in the expected number of casualties. Note that since a high number of statistical tests were performed the probability that one of these contains a type 1 error is increased, however, by manually checking the consistency of findings across different configurations the likelihood of making false overall claims is reduced.

5.4 Fleet composition

One of the novelties of this study is the ability to quantitatively compare drones and cars performing (emergency) medical deliveries, and also test heterogeneous fleets made up of both vehicle types. In this section, we present the experiments and results that aim to shed light on the differences in system performance of different fleet sizes and configurations. First, multiple fleet configurations will be compared in section 5.4.1, followed by a more extensive comparison of just using drones or cars in section 5.4.2. The experimental setup in terms of hospital facility allocation is kept the same compared to section 5.3 throughout all results presented in this section. It was hypothesized that a UAS is better suited for urgent deliveries than cars in terms of speed of delivery, reliability, and emissions at the cost of higher TPR, and more cost-efficient on a larger scale. Additionally, benefits of heterogeneous fleets are not expected.

5.4.1 Mixed fleets

Differences in system performance as a result of different fleet sizes and compositions were tested under increasing demand levels. Larger fleets are, non-surprisingly, able to process a higher volume of deliveries, caused by larger values of λ. Thus we introduce a normalizing variable that scales demand to fleet size, using λ/N_{total} system efficiency and performance is argued to be better comparable. 3 fleet sizes and 5 fleet compositions were jointly tested creating a total of 15 fleets in the experiment. The fleet compositions tested are referred to as *Cars only*, *25% Drones*, *50% Drones*, *75% Drones*, and *Drones only*. In *25% Drones* $N_{drone} = 0.25 * N_{total}$ which implies $N_{cars} = 0.75 * N_{total}$. Fleet sizes ($N_{total}$) in this experiment were 4, 8 and 12. As a reference, for this case study and facility allocation containing 19 hospitals with a total of 7991 beds, $\lambda/N_{total} = 2$ leads on average to 135, 270, and 405 daily requests requiring delivery for the above-mentioned fleet sizes respectively.
For all fleets, we observe a sharp drop in reliability once demand per vehicle surpasses a certain cut-off value, as shown in Figure 3. A fleet of 12 vehicles can process twice as much demand per vehicle reliably compared to a 4-vehicle fleet. From these results, we derive that increased system utilization, requiring larger fleets, has a bigger impact on system vehicle operating efficiency than fleet composition. Additionally, we observe that having a higher share of drones within a fleet results in an increased system capacity. System behavioral analysis shows that within mixed fleets, drones are the preferred option when both vehicle types are available. In a fleet of 12 vehicles, operating at a demand level of $\lambda/N_{total} = 1$, 56%, 82% and 93% of deliveries are performed by drones in *25% Drones*, *50% Drones* and *75% Drones* fleets respectively. These percentages approach the Drone share within the fleet as demand levels rise to the operating limit. In this scenario, having a big fleet operating at increased demand levels, we observe that combined fleets can execute deliveries more reliably, as seen in the bottom right corner of Figure 3. This is due to the higher vehicle capacity of cars, which enables them to execute multiple deliveries at once. Due to the modeled concept of operation, directly performing a delivery when a vehicle is available, combining multiple requests in a single delivery only occurs when fleets are (almost) fully occupied. A request needs to be generated, that is compatible with another already planned delivery, in the time window of that delivery schedule item being created and departing. Next to vehicles needing to have a filled travel schedule, the probability of such a situation is bigger when total demand levels are higher. Thus we only observe a slight benefit of mixed fleets in terms of reliability at $\lambda/N_{total} > 3.5$, which translates to over 700 daily deliveries in the presented case study. The total car capacity is never fully utilized, as the average amount of requests fulfilled per car delivery never surpasses 1.5 if +95% reliability is desired.
To compare system performance in terms of speed of delivery, risk, emissions, and costs, we analyzed the fleet

when operating around its limit in terms of reliability. This operating limit defined by reliability between 98% and 99.5% was chosen so it reflects the fleet cut-off value in terms of demand as observed in Figure 3. This approach assumes that fleet size and composition will be determined on the basis of an expected demand level and a known facility allocation. The amount and type of vehicles needed to reliably run the anticipated delivery needs are likely to be optimized for minimal costs. Thus, a fleet performing at the limit of its capacity is most favorable. A delivery system operating far below its maximum capacity might be able to increase its performance on other KPIs, however, these potential gains were found to be limited. This is due to the bidding process, in which on-time delivery is prioritized. If delivery within the hour is possible for the vast majority of requests, indicated by the 98% to 99.5% reliability window but also true when operating beneath this maximum capacity, performance on other indicators is mostly dependent on the ratio of bid-scoring weights. Additionally, by applying this filter we included both positive and negative outliers from demand levels higher and lower than the average demand level that falls within the window. This resulted in more normally distributed results on the delivery time, TPR, and emissions parameters compared to results of a fixed demand level. It might be argued that we are more interested in comparing a typical day of operation, given a particular level of demand, instead of the average which might be more heavily influenced by a single day where operations got stuck.

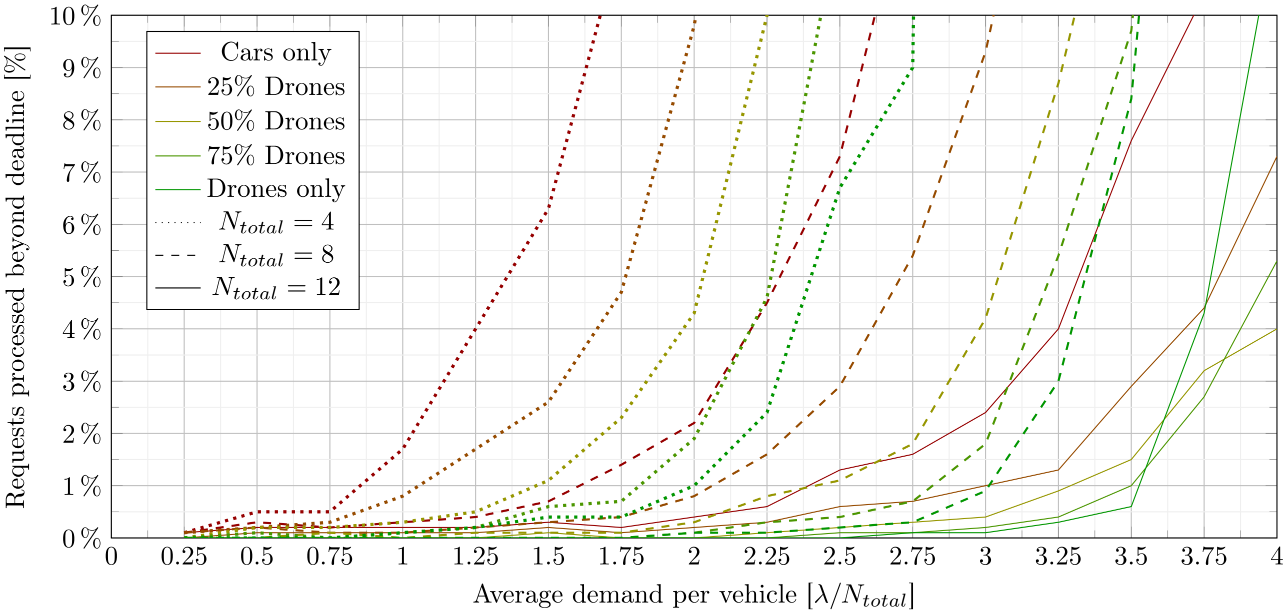


Figure 3: Fleet reliability under increasing demand

Both total yearly delivery-system costs and costs per delivery of the before mentioned 15 fleets operating at their operational limit are presented in Table 6. These results confirm the cost-effectiveness of a large-scale UAS. The use of drones within the system induces high initial investments related to pilots and infrastructure, which require sufficient system usage to be sensible. However, the marginal costs of increasing the number of drones in the system are relatively low since a control system is assumed where a single team of pilots is able to control up to 20 drones. By contrast costs of cars scale almost linearly with the number of cars, the decrease in costs per delivery is thus driven by an increased system efficiency resulting in a bigger capacity. From a financial perspective, mixed fleets are not beneficial, in the assumed concept of operations. Differences in terms of risk, speed, and emissions mostly scale with either the fleet's capacity and/or share of drones in the fleet. This largely confirms the hypothesis that heterogeneous fleets are not necessarily beneficial in improving the system performance, with the exception of increased capacity for large mixed fleets.

5.4.2 Drones versus Cars

This section presents a more in-depth analysis of system performance differences between cars and drones. *Cars only* and *drones only* fleets were tested with N_{drone} or N_{car} ranging from 1 to 14 in terms of fleet sizes. To compare different KPIs the operational limit of 98% $< Reliability <$ 99.5% described in section 5.4 was again used. In the assumed combination of case study, facility allocation, and mode of operation, a fleet of $N_{total} = 1$ was found incapable of reliable delivery for both vehicle types.

Performance of the different fleets in terms of system capacity, risk, speed of delivery, and CO2 emissions are presented in Figure 4. The results were found to be not consistently normally distributed, thus medians are shown along with the 10th and 90th percentiles indicating the spread. Again prioritizing comparison of typical days over averages. The spread of results of car-based fleets is often larger because of its dependence on the

Fleet composition	$N_{total} = 4$		$N_{total} = 8$		$N_{total} = 12$	
	Total yearly costs [€ mln]	Cost per delivery [€]	Total yearly costs [€ mln]	Cost per delivery [€]	Total yearly costs [€ mln]	Cost per delivery [€]
Cars only	1.36	54	2.77	44	4.26	32
25% Drones	2.52	84	3.66	49	4.88	26
50% Drones	2.25	64	3.14	29	4.07	16
75% Drones	1.99	49	2.62	18	3.23	12
Drones only	1.73	39	2.07	14	2.40	9

Table 6: Fleet costs at the operating limit

day of the week and the hour within the day. On a Sunday where the majority of requests occur early or late in the day, cars are able to perform a lot more deliveries reliably. This is reflected directly in Figure 4a. Additionally, when requests occur during a time with high congestion, cars are more often forced to use the fast and more risky option of using pre-empting signals. The increased system flexibility caused by the *Combi* mode of operations causes a higher spread of TPR when operating near the operating limit as seen in Figure 4b. Additionally, results from *Combi* MC simulations were found to be less often distributed normally.

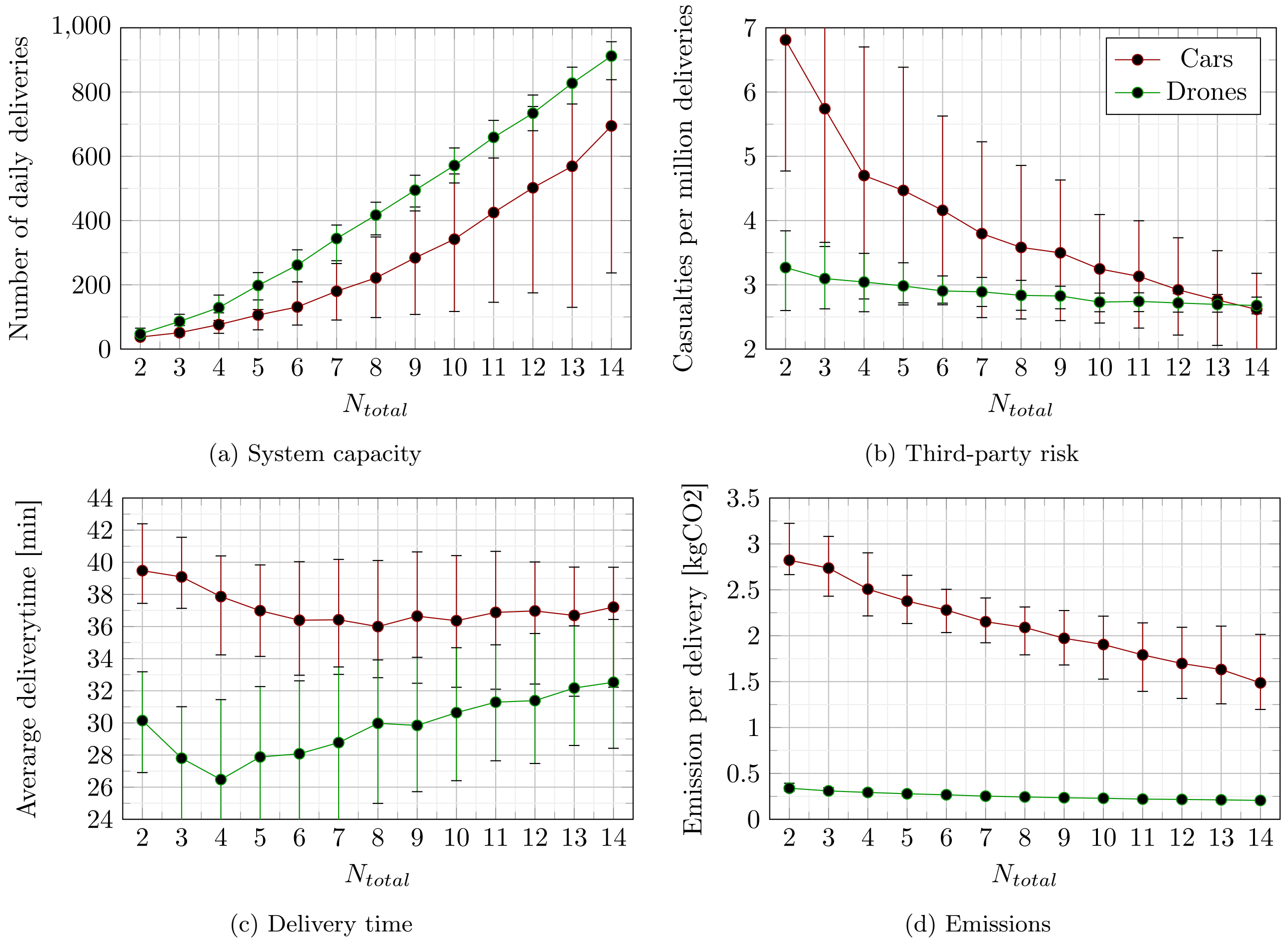
The results shown in Figure 4 confirm the positive expectations of a drone-based system in terms of speed of delivery, and emissions and indirectly prove that in fleets of comparable sizes and at similar demand rates drones are more reliable. Additionally, the initial hypothesis regarding TPR can be rejected on the basis of these results, since Drone TPR numbers are actually less than cars, as could already be expected from the route analysis from section 5.2.

The TPR and emissions shown are averages per delivery, defining a delivery as a request that requires transport. Thus combining deliveries into a single transport, which is only possible for cars, reduces these per delivery numbers significantly. The increased likelihood of deliveries that can be combined when demand levels are high, causes the observed downward trend for *Cars only* fleets since these numbers are derived from demand levels near the operating limit. When demand increases from $\lambda/N_{total} = 0.25$ to $\lambda/N_{total} = 3$ for a fleet of $N_{car} = 14$, we see that the percentage of requests that get a 'private' transport drops from 98% to 59%. As a result, TPR and emissions per delivery decreased by 37% and 32% respectively. Whilst for an equally sized *Drones only* fleet the same numbers only decrease by 19% and 10%. Total TPR and emission numbers will thus favor drones more when fleets are operating beneath their operational capability. The decrease in per delivery numbers for drones, which might be interpreted as increased efficiency, can be explained by a decrease in the number of active repositionings. At $\lambda/N_{total} = 0.25$, 63% of deliveries are followed by a repositioning flight whilst at $\lambda/N_{total} = 3$, which is still far beneath its operating limit, this happens after 44% of deliveries. These additional flights, which do lead to faster average deliveries at low demand levels, add to the total system TPR and emissions. Active repositioning, when an excess of vehicles exists, might thus not always be beneficial.

The financial benefits of scale of a drone-based system discussed at the end of section 5.4.1 leads to a crossing point in terms of costs when scaling the system. Total costs of a *Cars only* fleet with $N_{car} = 5$ are almost equal to that of a *Drones only* fleet of $N_{drone} = 4$ (€1.72 million and €1.73 million respectively). Since a *Drones only* fleet outperforms a *Cars only* fleet on all other KPIs presented in Figure 4 we argue that opting for the car-based system, in the assumed case study and concept of operation, can only be rational in a situation where a *Cars only* fleet with $N_{car} = 4$ is able to reliably run the system.

5.4.3 Bidding weights

The weights used to rank different bids determine how different KPIs are prioritized. In this study, it was assumed that marginal variable costs and emissions are not taken into account in bid prioritization, reflected in $\delta = \omega = 0$. To study the effects of different prioritization between TPR and speed of delivery a changing β/γ ratio was tested. The experiment presented was conducted for vehicle fleets of $N_{total} = 9$ and a demand level of $\lambda/N_{total} = 2.5$. Table 7 shows the change in TPR, delivery time, and the relative change compared to the base case of $\beta/\gamma = 1$. Additionally, we show the share of deliveries that are executed using the *safe* route. It was found that for $\beta/\gamma < 0.125$ and $\beta/\gamma > 8$ results would not change significantly, suggesting that beyond these ratios full priority is given to the speed of delivery or TPR minimization respectively. We observe that compared to the base case, changing the bidding weights can not decrease TPR much for a *Cars only* fleet. Differences in TPR, delivery time, and share of *safe deliveries* for *Cars only* between $\beta/\gamma = 1$ and $\beta/\gamma = 8$ were found to be non-significant. The null hypothesis being that the averages would be the same, p-values were 0.26, 0.60, and 0.46. By contrast, risk reduction and delivery time increase were significant if bidding weights prioritized TPR minimization for a *Drones only* fleet. It should be noted that the average delivery time for $\beta/\gamma = 1$ is significantly lower than the results shown in Figure 4 because of a demand level far beneath its



(a) System capacity

(b) Third-party risk

(c) Delivery time

(d) Emissions

Figure 4: System performance for *Cars only* and *Drones only* fleets of different sizes; Median, 10th and 90th percentiles

operating limit. Although exact differences between different bidding weight ratios differ for different demand levels. The conclusion was found to be robust that for cars $\beta/\gamma = 1$ risk minimization dominates the request allocation, changing the ratio can thus only improve delivery time at the expense of approximately quadrupling TPR. Changing β/γ for *Drones only* fleets can decrease both TPR and delivery time (one at the expense of the other) compared to the results shown in Figure 4.

	Third party risk [Casualties per million deliveries]		Delivery time [min]		Share of safe deliveries	
β/γ	*Cars only*	*Drones only*	*Cars only*	*Drones only*	*Cars only*	*Drones only*
0.125	16.2 (+333%)	4.6 (+61%)	27.5 (-32%)	19.9 (-9%)	1%	9%
1	3.8	2.8	40.8	21.8	85%	41%
8	3.6 (-5%)	0.6 (-80%)	40.5 (-1%)	31.4 (+44%)	86%	95%

Table 7: Effect of changing bidding weights on risk and speed of delivery

5.5 Healthcare facility allocation

An often named advantage in qualitative studies on the potential of drone-assisted medical distribution systems is that it can enable further centralization and specialization of healthcare. In this paper, we refer to centralization as the process of reducing the number of hospitals that are able to process healthcare of a certain use-case. This section covers experiments on the effects of this centralization of healthcare facilities and additionally differences in how these facilities are distributed among hospitals. We hypothesize that centralization can bring significant overall cost reductions and that medical facilities of different use-cases should be distributed among the biggest hospitals, so that share of requests that require transport is minimized despite the high degree of centralization. We define χ as the number of hospitals that, for each use case, possess the facilities to provide healthcare. In our case study, containing 19 hospitals, previous experiments assumed $\chi = 3$. Being a low number this reflects a fairly centralized system which emphasizes the effects of differences in delivery system performance. In a scenario with $\chi = 19$ no distribution system is required as all hospitals can provide all healthcare themselves. Next to the number of healthcare facilities, we tested how different methods of distributing these among hospitals affect system performance. Here we distinguish **hospital-selection** and **facility-distribution** as the two main levers. Location-prioritization regards which hospitals should be prioritized in allocating the limited amount of facilities. We define 2 hospital-selection methods to be:

- *Size*; The biggest hospitals, having the most beds and biggest demand levels, are prioritized.
- *Location*; Hospitals that minimize travel time to all other (non-priority) hospitals are prioritized.

Facility-distribution states how facilities of the different use-cases are distributed among the prioritized hospitals, for this lever two options were defined to be:

- *Concentrated*; Facilities of different use-cases are concentrated in a single hospital, a fewer amount of hospitals thus possess all facilities.
- *Scattered*; Hospitals can only process a single use-case, the same amount of facilities are scattered among a larger amount of hospitals.

In the presented model total fixed costs for a given χ are the same no matter the **hospital-selection** and **facility-distribution** method used to distribute supply. Visualization of different combinations is provided in Figure 5. Note that hospital-selection and facility-distribution was done manually for the base case.

(a) Base case ($\chi = 3$, *Concentrated*) (b) $\chi = 1$, *Location* and *Scattered* (c) $\chi = 5$, *Size* and *Concentrated*

Figure 5: Examples of different hospital-selection and facility-distribution methods

We tested the four combinations of **hospital-selection** and **facility-distribution** along with 5 centralization levels [1,2,3,6,9]. Three options were tested for fleet size and total demand (N_{Drone} and λ), both having values of 5,10 or 15.
Table 8 shows reliability, risks and average delivery time for the different facility distribution combinations for the three highest levels of centralization and $N_{Drone} = 10$ and $\lambda = 15$. With a less centralized configuration, it was found that performance differences among facility distribution methods are negligible. Partially contrary to our initial hypothesis, we conclude that when a limited amount of facilities need to be distributed, deliveries are fastest and most reliable when these are concentrated in a location well accessible by other hospitals. This could be explained by the fact that the drop in the share of requests that require transport is small in an already highly centralized system, thus favoring *location* over *size*. This conclusion implies that establishing a hub with all medical facilities which is not at a hospital, but at an optimized location might be even more beneficial. At higher demand levels we see that a *concentrated* facility distribution becomes more beneficial because vehicles being able to combine a delivery and a pick-up from and back to the main hub becomes more likely. Additionally, the (negative) impact of the system in terms of risk, emissions, and variable costs scale with the number of requests that require transport. However, we observe a conflicting rise in TPR for *Concentrated-Location* distribution when the amount of facilities grows from $\chi = 2$ to $\chi = 3$. This increase in risk with a 95% confidence interval of [0.019, 0.035] casualties per year, could be partially explained by the fact that locations are optimized for travel time and not the TPR of routes. Thus the opening of facilities at a new hub causes more flights to be conducted from a hospital with more risky approach routes.
In our case-study and reflecting model, we assumed the total costs of running one facility of all use cases to be €1.5 million. A drone distribution system containing 15 drones, capable of executing almost a thousand deliveries per day (depending on the exact facility distribution), yearly costs around €2.6 million. Thus the hypothesized financial attractiveness of closing medical facilities enabled by a drone-assisted distribution system

is confirmed by these results. Closing facilities at 16 of the 19 hospitals ($\chi = 3$) would potentially save €24 million in medical costs, almost tenfold of the costs of a drone distribution system that would be needed to accommodate the closures. Operating at maximum capacity a $N_{Drones} = 14$ fleet, around 900 deliveries per day, costs per delivery become less than €8 excluding medical facility closure savings.

Facility-distribution	Hospital-selection	Reliability [% of requests processed <60 min]			Delivery time [min]			TPR [# of casualties per year]		
		$\chi = 1$	$\chi = 2$	$\chi = 3$	$\chi = 1$	$\chi = 2$	$\chi = 3$	$\chi = 1$	$\chi = 2$	$\chi = 3$
Concentrated	*Size*	83%	99%	100%	47	29	21	0.26	0.23	0.15
	Location	98%	100%	100%	30	22	18	0.25	0.22	0.24
Scattered	*Size*	51%	96%	99%	76	39	31	0.30	0.29	0.22
	Location	35%	95%	99%	93	39	33	0.28	0.27	0.18

Table 8: System performance for different levels of centralization and facility allocation methods

5.5.1 Route usage patterns

In order for the hypothetical distribution to work in practice, full cooperation between hospitals is assumed. Intensive sharing of resources is already somewhat common on a local level between different locations of the same hospital. Our case study, for instance, includes 3 locations of the Alrijne hospital, which are not coincidentally near each other. Collaboration between these hospital locations could be regarded as much easier than in a regional or even national system, in which there are hospitals with different owners and operating structures. To gain insight into the fragility of the proposed system on this assumption of full collaboration between all hospitals we look at the emergent behavior in terms of drone movements. Given a centralized system ($\chi = 3$, *Location* and *Concentrated*) we analyzed to which extent flights and more specifically deliveries stay within the region. We define a region as a set of hospitals that share the same hub to be nearest. A *Drones only* fleet of 12 vehicles was tested under different demand levels. At $\lambda/N_{total} = 2.5$, 90% of flights are from or to the hub of a region, and 3% are between hospitals within the same region. The remaining 7% of flights are primarily from or to the hub of a different region, and less than one percent of flights are between non-hub hospitals of different regions. The share of flights that stay within the region is mostly dependent on the demand pressure on the delivery system. With great overcapacity, $\lambda/N_{total} = 1.25$, over 98.5% of flights stay within the region. When demand reaches or surpasses the operational capacity of the delivery system, we observe that 85% of flights remain in the region, and 12% of flights go to or from the hub of a different region. It should be noted that this behavior emerges naturally, we expect that additional constraints that enforce deliveries to be made within the region will have limited negative consequences on system performance. Thus we conclude that in order to take advantage of the benefits of scale linked to a drone delivery system, the total collaboration between hospitals in terms of sharing medical facilities is not crucial. Rather regions collaboratively participating in the proposed common delivery system makes it economically more feasible since for instance pilot costs can be shared. Additionally, increased reliability is achieved since spare drones can come to the rescue in regions that experience a spike in demand.

6 Discussion

In previous sections, the methodology, agent-based simulation model, and results or our research have been presented, which already included some implications on individual results specifically. This section will discuss the broader implications of and reflections on this research. The discussion is structured in 3 sections: our approach and overall methodology in section 6.1; the implications on the MDS project and beyond in section 6.2; and lastly section 6.3 contains a discussion on the agent-based simulation model.

6.1 Methodology

The holistic approach taken in this research is aimed at providing strategic decision-makers quantitative insights on the major risks and benefits when considering the described medical emergency UAS. However, the multitude of system design questions, KPIs, and covered topics, has come at the expense of the thoroughness of a single issue. We argue that this wide-ranging research is preferable in the current adaptation phase of UAV-assisted medical distribution systems. By covering multiple stages of the design process we had to make fewer assumptions which decreased the risk of in-depth results becoming less relevant because of faulty assumptions on other parts of the system. We argue that many covered topics can better be studied in-depth in more developed industries. Optimizing task allocation within distribution systems, for instance, might be better studied in the context of an Amazon delivery service. Studying active repositioning, by contrast, might be better more relevant in an Uber right hailing system. The novelty of this research is thus not in any of these topics specifically, but rather in combining knowledge from different industries in a new context. This idea is backed by the findings of Wang et al. who showed the potential impact of 'novel' papers combining different fields, but also recognize the bias by the scientific community against this type of higher-risk research[49].

An example of this cross-industry combination of knowledge is our approach on TPR. We recognize that both risk models, based on statistics for cars and the theoretical descent model for drones, might not give the most precise TPR estimations for either vehicle. However, it does enable cross comparing risks, dissolving the point made by Hirling et al. who argued that this is not feasible due to a lack of historical drone crash data[29]. We argue that drone TPR numbers are generally difficult to put into perspective without any benchmark. Additionally, we want to emphasize the risk we are already (unknowingly) taking by allowing vehicles to use pre-emption methods. This cross-comparison methodology, although arguably harsh and imprecise, can help prevent biases of overemphasizing risks of innovation by stakeholders.

The bottom-up and modular modeling approach enabled the iterative model design and continuous model improvements and expansion. However, the agent-based model and more specifically the way in which we used this tool did compromise on the search for optimal solutions. Scenarios, configurations, and strategies tested have been mostly manually defined. Comparing these gives some insights into which direction might be more beneficial, but the optimal solution remains unknown. In the future, more in-depth research on a single aspect of UAV-assisted medical delivery system design might opt for using novel simulation-optimization methods, like based on meta-heuristic optimization, to create more optimal solutions.

Lastly, our analysis methods, using the operational limit of $98\% < \textit{Reliability} < 99.5\%$ might be regarded as sub-optimal. This method was introduced to evaluate different system configurations fairly, at the top of their respective abilities. However *reliability* is a system output by itself, thus we found that using only results from within this output window sometimes created biases. At low demand levels, we noticed that results within the operational limit window contained relatively more positive outliers, which skewed the results somewhat and made them less normally distributed. At higher demand levels both negative and positive outliers would be caught in the defined operational limit window, whereby the described bias was found to be less of an issue. Preferably one knows or fixes variables like demand or fleet composition, which would allow for more direct input-output comparisons.

6.2 Case study and concept of operation

This research was conducted on a single case study. We argue that this benefits the real-life applicability of the research results. However, the transferability of conclusions to other environments is difficult to predict. In terms of the geographical location, project-specific results are dependent on among others, road infrastructure, physical distribution of hospitals, and population density. Even the level of representation of results on a project covering all provinces of the Netherlands is debatable. For instance, islands and more remote regions of the country were not included in this case study.

Although exact results are expected to differ project by project, general conclusions were found to be in line with earlier findings and/or expectations. Similar to the findings of Otero et al. on the Londen case study, novel transportation methods can be cheaper on a per delivery bases and can significantly reduce pollution[12]. Although the precise effects of combining different case studies have not been studied in-depth, we expect it to be partially responsible for potential efficiency gains, and can certainly increase system utilization. Which might contribute to the benefits of scale observed in this study and suggested by Wright et al.[25]. The delivery capacity of a *Drones only* fleet compared to land-based vehicles, is in line with the findings of Haidari et al. on vaccine distribution in low and middle-income countries[26]. Although causation might be different and more due to bad road conditions instead of congestion experienced in higher-income countries like the Netherlands. Total system cost savings, due to drone-enabled centralization of healthcare facilities, are largely indicative but similar in order of magnitude to what has been suggested by[15].

Capitalizing on what has been stated in this and the previous section, accuracy and applicability of results are limited by the quality of input data and assumptions. For instance, both the current use of emergency medical transportation means and the intended use of the proposed system was largely unknown. Thus different overall demand levels have been used throughout this study. Additionally, intra-day demand patterns have not been incorporated, although one might expect that during certain times of day more medical requests occur. Better knowledge of on-demand magnitude and patterns will improve the quality of the input data and thus modeling results.

Based on the results presented in this study we argue that the MDS project has the potential of being successful in creating a safe and reliable medical emergency delivery system. To further develop the project we formulate practical recommendations, that are synthesized from this research, for decision-makers:

- Quantify the demand for each use case at the different hospitals.
- Further formulate the business model in cooperation with all stakeholders, devising how earnings and cost-savings are passed on to both operator and hospitals.
- Execute end-to-end test flights, testing all proceedings from request occurrence to healthcare being provided, enhancing knowledge on the time needed to complete each step.
- Increase knowledge on and awareness of current TPR resulting from (emergency) road transport.
- Develop a decision-making framework that provides guidance in weighing delivery speed and TPR.
- Conduct extensive drone safety tests, enhancing accuracy and reliability on the failure modes, probability of these failures and subsequent descent models.
- List all (potential) hospital modifications and their associated cost (savings).

Other aspects left out of scope for this study that are known to be important in order for system implementation to happen are related to drone operation and airspace integration. Additionally, quality needs and preservation of medical goods during flight might add additional limitations.

6.3 Simulation model

The last part of our discussion contains reflections on the implementation of the proposed simulation model. Regarding the pre-processing route generation module, we recognize the simplifications made in the Drone TPR decent models with respect to previous works. It was found that adding a building layer, commonly used to better estimate the vulnerability of people on the ground, was computationally expensive on the scale of this case study. However, our more simplistic risk model produced TPR estimates similar to that of [33] comparable routes in terms of length and environment.

The pre-processing module distributing medical facilities used to assess the impact of centralization and different facility allocation strategies had limitations. The facility distributions created for the *scattered* options could be considered sub-optimal. Distances or covered beds were optimized on a system level, causing facilities of a single use case to be distributed less optimal. Additionally, the distribution of facilities with respect to hospital accessibility only took into account travel times. In a system that prioritizes risk minimization through task allocation, it would be more sensible to distribute facilities among hospitals with the same goal of TPR mitigation.

The agent-based simulation model, and specifically the task allocation bidding process, was implemented so it resembles how one might expect it to go in real life. Directly creating and sometimes departing a new schedule item might make sense in the context of medical emergencies, however, system efficiency and maybe even long-term reliability might gain from waiting for a while so to increase the likelihood of combining requests. This would especially benefit the performance of cars with a higher capacity. More sophisticated task allocation methods are expected to enable increased system performances by reallocating, bundling, and postponing requests.

Lastly, we highlight the effects of simulating a single day of operation per iteration on our results. Firstly we simulated no open requests at the start of the simulation and requests could be generated until the last minute of the day after which they were allowed to be completed after the day was officially over. This prevented the simulation to take into account the implications of having a 24/7 operational system, in which requests arising at the end of one day prevent vehicles from directly executing new requests at the beginning of the next. Secondly, the input of a single simulation iteration would depend on the week of day to be simulated for car travel times. Although an equal amount of each day of the week was included in each MC simulation, results were less normally distributed for each tested scenario.

7 Conclusions

This research has highlighted the benefits of using simulation, and more specifically agent-based, methods over conventional optimization models in designing a complex emergency medical delivery system. More holistic insights have been created on the performance decision-makers might expect when considering such a system. Three system design decisions have been studied specifically, creating the insights described below.

First, a flexible and tailored mode of operation enables significant system efficiency gains. Not forcing vehicles to return to their departure location can cause a system to operate reliably, delivering +99% of requests within an hour, which would otherwise not do so. Performance in terms of delivery time does improve when vehicles pro-actively reposition to a hub hospital when idle, with improvements being most significant when repositioning to the nearest hub instead of its hub of origin, because of naturally emerging vehicle supply and demand balancing. The *Combi* mode of operation, using the *Fast* delivery option only when needed to ensure in-time request processing, was shown to make the system reliable and safe for those directly involved and third parties. Secondly, we showed that overall system performance is more dependent on system utilization and thus scale than fleet composition. Heterogeneous fleets only create marginal capacity improvements on a large system scale but are not beneficial overall. *Drones only* vehicle fleets can process more deliveries per day, with a better speed of delivery, and emit at most 20% of the CO2 per delivery compared to cars. TPR as a result of road transport is found to be at least as big as that created by a UAS and unlike cars, drones are able to further decrease TPR by approximately 80% when task allocation prioritizes risk minimization over speed of delivery. The resulting increase in delivery time would reduce the advantage of drones to around 5 minutes on this KPI. Lastly, the centralization of healthcare facilities, enabled by a large-scale drone distribution system, is shown to reduce overall system costs of both the UAS and medical facilities significantly. Costs per delivery will be less than €10 when the proposed system is utilized at its operating capacity, not including medical facility closure cost savings. Concentrating facilities of different use-cases in a limited amount of hospitals optimized for accessibility is suggested to be most favorable.

Future work might explore either one of the three system design questions in more detail. Applying heuristic-based optimization methods on bottom-up simulation models is recognized as a promising approach that can reflect system complexity whilst still approaching solution optimality. Additionally applying these approaches to other case studies is suggested, so the robustness of these conclusions can be analyzed.

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II

Literature Study
previously graded under AE4020

1

Introduction

1.1. Drones delivering medical goods

Drone assisted delivery of medical goods has gained popularity in the last decade. The Covid-19 pandemic boosted the interest in drones delivering vaccines and has also shown the importance of having reliable (medical) supply chains. Currently, medical products are often transported by road, blood products in the Netherlands for instance, are distributed by Sanquin who perform over a thousand emergency deliveries per year[209]. Sanquin is legally obliged to deliver blood to any Dutch hospital within the hour to guarantee patient safety. The urgent, high value and low weight characteristics of these products makes them particularly well fitted for drone delivery. An analysis of the current state of medically oriented drone delivery shows that developing African nations are leading in the adoption of such systems [203]. Zipline, a Californian company, is already delivering blood products using drones daily in several sub-saharan countries like Rwanda[145]. Recently, Zipline has started its first projects in the United States, which is a big driver behind its rapidly growing economic evaluation but also an indicator that drone assisted delivery of medical goods is not only suitable for emergency delivery or developing countries[4].
In other developed countries several pilot projects have been initiated aimed at investigating the feasibility of such still futuristic systems. In these projects different medical goods have been tested ranging from vaccines to laboratory samples. One of these, initiated by a group of Dutch stakeholders ranging from logistics companies to hospitals, is the "Medical drone service" (MDS) project, which is aimed at delivering blood products, laboratory samples and medicines by drone in the Netherlands[146]. The MDS project is currently in the ironically named pilot phase, performing test flights in an controlled environment. MDS stakeholders, both governmental and commercial, are faced with the challenge of deciding whether or how drones for medical delivery purposes could be implemented at scale. However, many unknowns on the long term impact of a nationwide Unmanned Aircraft Vehicle (UAV) assisted delivery system still exist, for instance considering the cost, reliability and risks to outsiders. Since the distribution of goods on which lives may be dependent is considered, it is important to have a good understanding of these impacts before making any long term strategic decisions.

The benefits and risks of an Unmanned Aircraft System (UAS) for delivery and distribution of several medical goods in developed healthcare systems under regular operating conditions have been qualitatively studied [141][215][208][131][194][113]. Cost and emission reduction are often named expected benefits, whilst system delivery reliability and risks to outsiders are examples of potential negative consequences. Quantifying these risks and benefits requires compiling knowledge from many fields of research like healthcare logistics and UAS optimization. This work provides a holistic overview of what has been found so far on the different aspects that together cover the proposed concept of operations of the MDS project. The literature study aims at creating a better understanding of the quantitative risks and benefits associated with the logistics of UAV assisted delivery system of medical goods, and enable decision makers to weigh these pros and cons in order to make informed strategic decisions. Because of the relative novelty and multidisciplinary nature of the subject an holistic overview of findings from different fields of studies is provided, which together can provide context on the proposed system.

1.2. Report structure

The proposed concept of operations covered in this research, combines knowledge from a wide variety of domains. In chapters 2-5 findings and research gaps of prior research of these domains are discussed. First, in chapter 2, an overview is provided of what has been studied in the specific topic of blood supply chain design. Next in chapter 3 we will introduce other medical goods and use cases and discuss findings from the general field of healthcare logistics. In chapter 4 the use of unmanned aerial systems (UAS) is introduced, investigating the most relevant aspects of drone operation research, as well as looking in depth at the current state of the art in studies covering drone assisted medical delivery systems. chapter 5 discusses what is known about the effectiveness of current road based operations. Finally modeling and solution techniques and methods used to tackle the problems from the domains covered in chapters 2-5 are reviewed in chapter 6.
The main findings of the literature study are summarized and tied together in chapter 7, including identified research gaps. These findings and gaps form the basis of the research plan presented in chapter 8, which elaborates on how this thesis relates to past research and contributes to the relevant fields of study.

#	Title	Purpose
2	Blood supply chain design	In depth analysis of quantative studies optimizing the supply chain network design of blood products , identifying modeling needs and best practices
3	Healthcare logistics	Provide a more holistic overview on healthcare logistic optimization and identify healthcare related trends relevant for UAV delivery systems
4	UAS delivery	Get to know drone delivery pros and cons in general and specific to healthcare. Reviewing methods aimed at optimizing and quantifying these
5	Road transport	Discuss the performance of the current road transport system
6	Modeling techniques	Present the different techniques that can be used in order to model and optimize the proposed system
7	Conclusion	Summarize the findings of the previous chapters emphasizing the found research gaps
8	Research plan	Provide the developed research plan for the MSc thesis, based on the conclusions from the literature study

Table 1.1: Purpose of the main chapters of the literature study

2

Blood supply chain design

A well functioning blood supply chain is of vital importance inside the body. However the dependency on fresh blood for medical treatments ranging from basic surgery to cancer therapy, makes having a reliable blood supply chain for hospitals and other medical institutions a pre-requisite for an effective healthcare system. In The Netherlands alone, having a population of around 17 Million, more then 700.000 units of blood are donated every year [209]. Which is above the average of 31.5 donations per 1000 people for high income countries, the averages of 15.9, 6.8 and 5.0, for upper-middle-income countries, lower-middle-income countries and low-income countries are even lower [233]. A sample of Whole Blood (WB) consists of multiple components that serve different purposes within the body. The main components are packed red blood cell concentrate (PRBC), platelet concentrate, plasma and cryoprecipitate [37]. These different components can be sourced from WB using different processes and filters during or after the donation process.

The blood supply chain (BSC) covers the flow of blood from donors to patients. Different views exists on how a BSC is defined in terms of its components. [176] argues that 5 echelons make up a BSC, distinguishing donors, mobile collection sites, blood centers, demand nodes and patients. However different countries and or regions can have different BSC structures, therefor a more general structuring of 4 echelons is used:

- **Collection**
- **Production**
- **Inventory**
- **Distribution**

Besides different products that can be derived from WB that were stated earlier, also compatibility of different blood types within the BSC is an interesting topic of study. The ABO and RH factors determine the interchangeability of different blood products [23]. Although different products can be part of this study, the problem is simplified by ignoring the possibility to use or convert product supply to serve a different type of demand. Details on research regarding this particular part of the BSC is thus not part of this literature review. Similarly the process of production regards separation of the different components and products from the blood. Since this is a mainly medical process it is considered out of scope for this research, and will not be discussed individually.

Several different aspects, applications and echelon operations, related to medical transport, have been studied extensively both individually and in the context of a BSC as a whole. In section 2.1 literature covering the collection process will be discussed. The perishable characteristic of blood products makes that optimizing inventory strategy is a crucial and well researched subject in BSC management. section 2.2 gives a brief overview of inventory management optimization research. Transport between layers or echelons of the BSC are most often considered in combination with other echelons. Most research regarding the topic of transportation within the BSC is focused on transport between (mobile) collection centers and blood centers, which is not part of the BSC covered in this research. Distribution of blood products towards end-users, hospitals in this case, is discussed in section 2.3.

Disaster relief is a well studied application of BSC design in which different needs and objectives are relevant

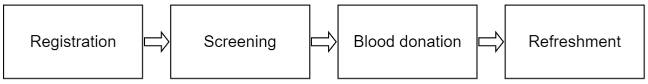


Figure 2.1: Blood collection process

compared to more traditional BSC design. Although this research is aimed at designing a BSC under regular operating conditions, concepts like resilience and vulnerability to disruptions have blown over from disaster relief since supply and demand for these products being is inherently variable. section 2.4 talks about how these concepts have been studied in the context of disaster relief, and how they could be applied to models of systems under regular operating circumstances.

2.1. Blood collection

The goal of supply chains in general are matching supply and demand. In the case of blood, supply is generated by collecting blood from healthy people who donate some of their blood. Williams et al. argue that within BSC research little focus has been on optimizing supply e.g. blood collection. [231]. The process of blood collection from a donor point of view can be divided into 4 phases illustrated in Figure 2.1. The screening and testing of blood is necessary because of the many safety related constraints involved with blood transfusion and donation.

The multi-disciplinary nature of the subject, causes research to come from different backgrounds, ranging from Health Policy and Services to Operational Research. Different studies try to optimize different phases and area's of the blood collection process. Reviewing the findings on this topic can provide insight in how supply can be modeled as well better understanding the characteristics of the BSC.

Appointment scheduling

Most healthcare systems have strong regulations on the maximum time between collection and processing. Mobasher et al. studied a case in which platelets need to be extracted from the blood within six hours of blood collection at a central processing center [153]. This is done by synchronizing donor appointments with collection schedules.

Seda Baş et al. provide an appointment scheduling framework showing the capability of balancing the production of different blood types among days[36]. Both booked and non-booked, so called walk-ins, slots are considered with the ability to readjust the number of slots which to preallocate. This research optimizes the amount of donations from the perspective of the collection facility, in contrast Van Brummelen aims to reduce waiting time for donors during the collection process [47]. Simulation experiments suggest a reduction of 40 to 80% in waiting donors to be achievable.

In general it is found that a research gap exists in combining different aspects and goals of appointment scheduling. A more holistic approach is needed in order to effectively source blood products such that it is convenient for both donors and most use full for the collection facility and the rest of the supply chain.

Donation process

Compared to appointment scheduling, the policies regarding the donation process, is better researched. Most research regards the optimal quantity of blood (products) to be collected per donation. Two methods of blood (product) collection exist, with regular donations WB is collected and stored in bags. These bags can be processed in a later stage in order to acquire specific blood products. Alternatively blood products, like PRBC or plasma, can be collected directly using apheresis [166]. Many innovations regarding collection techniques consequently require new research into how to use these most optimally. Multicomponent Apheresis allows altering the quantities of different blood products collected in a single donation. A technique that is shown, when used optimally, to be better able to match supply with the demand of specific blood products [170].

Strategies concerning quantities per donation strongly relate to inventory management, which will be discussed more extensively in the next section. It has been shown that always collecting the maximum amount of blood (product) is not always optimal, as it can cause increased costs and wastage [137].

Donor demographics

The dependency on human donors in sourcing blood products, makes studying donor behaviour, location, age, etc. an interesting field worth studying. By clustering and classification of historic donor patterns, a better understanding of donor behaviour can improve the predictability of blood supply [132].
It has been shown that both the day of the week and the hour of day are important variables when predicting donor arrival rates. Suggesting that resources, for instance workforce, can planned more effectively when accounting for these known arrival patterns [213]. Additional knowledge regarding donor behaviour could attribute to a more reliable and predictable supply of blood products greatly.
Additional to the behaviour, the location of donors has been studied extensively. This is often used as an input when optimizing the location of collection centers, main findings of research regarding these problems are discussed in the next paragraph.

Location planning

In optimizing the collection echelon of the blood supply chain, most research attention has been paid to the location of the collection centers. Often the optimal location of collection centers is determined as part of the problem of designing a BSC. In most literature this question is posed as a location-allocation problem, deciding on the location of the centers as well as determining who should go to which center. Both fixed and mobile collection centers have been studied extensively. In the context of this research transport from donor location to the collection center has been left out of scope. However it is has been found that having a more centralized system can save up to 40% compared to a highly decentralized collection system [167]. It has been acknowledged that the collection process is the echelon within the supply chain that might be the hardest to centralize because of the dependency of donors of whom one can not expect to travel a long time. Additionally, and specifically interesting for this research, it was found that travel time is the biggest influence for the degree of centralization that is feasible. Decreasing travel time through the use of drones is therefor expected to enable further centralization and thus cost savings. The degree of centralization also highly impacts the optimal inventory strategy, which will be discussed in more detail in section 2.2.

Vehicle routing

Often synchronous with determining the optimal locations of collection centers, the costs associated with transport between supply chain echelons is minimized. Such vehicle routing problem can significantly reduce costs, especially when a large amount of collection centers need to be covered. Lodree et al. specifically studied the vehicle routing problem for blood donation collection [136]. They found that in general longer routes are prefered over shorter routes, additionally collection centers with large accumulation rates should be visited last. Both findings can be explained by the representation of the system in the proposed linear integer programming model, in which collection centers collect blood at a specified rate, and the overall aim of the model is to maximize the amount of blood collected. Therefor it is beneficial to postpone collecting the blood at nodes with high accumulation rates. Additionally Lodree et al. recognize that, by simplifying the problem with assumptions in order to be able to generate optimal solutions, they limit the ability for implementation into practise. Thus models creating non-optimal but more representative solutions might be preferred over simplified models.

Studies on blood collection have shown that supply of blood products is impossible to be stable and or 100% predictable. It is needed to take into account the various aspects and complexity in future studies, whilst accepting that there will always remain a high degree of supply uncertainty. The observation, that in most research regarding blood supply chain collection optimization models need to become more complex in order to mimic real life application, is confirmed by Williams et al[231]. Although this research will not focus on blood collection specifically, we will see that this observation applies to many aspects of blood supply chain design. And more holistic approaches need to incorporate multiple echelons in order to make the entire supply chain more efficient.

2.2. Inventory strategy

Having received the blood, either directly by donation or by delivery from nodes earlier in the supply chain, it can be stored for a limited amount of time. The perishability of blood products combined with the literaly life threatening consequences of shortages makes inventory management within the BSC an interesting and well researched topic. A taxonomy evaluation conducted in 2019 suggested that inventory management has

received the most attention from past literature within the context of blood supply chain management [176]. Additionally it was observed that publications covering inventory management are relatively old compared to the BSC management average. This might be due to recent developments in IT systems and decreasing lead times, which both enable dynamic responsiveness and decrease the relevance of static inventory managements strategies.
Two specific problems that have been studied extensively are the optimal inventory policy, mostly deciding when to order, and order quantity, determining the size of orders. These problems have been covered from the point of view of different hierarchy levels. Optimal strategies can be determined for single institutions, which can be placed at different stages of the BSC, for instance individual hospitals or blood centers. Additionally inventory strategies can be adjusted in order to optimize the BSC as a whole.
Types of policies are often declared using one of or a combination of the letters, R, Q, S and s. In this system R represents periodicity, Q indicates fixed order quantities, lastly S and s represents inventory quantities which is the target level (S) or the point at which one should reorder (s).

Inventory policy

As a result of the perishable character of most blood related products, different inventory policies have been studied with mixed results. The two most common policies are first-in-first-out (FIFO) and last-in-first-out (LIFO). A comparison conducted by Abdulwahab and Wahab showed that FIFO performed better when aiming to minimize shortages, outdated products and inventory levels [8]. Additionally they found that more frequent deliveries are also favourable when optimizing the FIFO policy. Therefor it is expected that a new distribution system will impact inventory policies significantly.
Relatively new in BSC research are policies including the possibility for lateral-transshipment, meaning the ability to ship products between hospitals in addition to deliveries from blood banks. Multiple countries and hospitals have already adopted policies that make use of this option and have shown promising results. However Dehghani et al. showed that simple decision rules, that are currently best practise, deliver suboptimal results in terms of cost optimality [63]. A more cost-effective policy was found in a scenario with transshipment between two locations. They acknowledge that an increase in the number of locations and inventory information will make the problem more complex and challenging. Different policies for transshipment could be tested using simulation techniques able of simulating these more complex problems. A more in depth analysis of lateral transshipment is included in section 2.3.

Ordering quantity

Directly related to when to order is how much to order. In most literature both problems are evaluated simultaneously, but when considering a distribution network that might have limits on the quantities that can be delivered in one order, it is interesting to investigate possible consequences.
In a recent study meta-heuristic algorithms were tested in order to optimize blood allocation and ordering policies. A Symbiotic Organisms Search algorithm was shown to be use full when applied on real-life scenarios, where it able to take into account complex factors like social behaviour [88]. Besides showing the benefits of using meta-heuristic algorithms for better representing of real-life systems, it indicated that the effects of higher ordering quantities and the corresponding stock-piling policy depends highly on the blood product and its shelf life. Also imports and transportation of products were considered as undesirable.
Dillion et al. have proposed a two-stage stochastic programming model for optimizing inventory management under demand uncertainty [70]. When tested using a monte-carlo simulation case study, it was found that hospitals could reduce the amount of outdated products, ageing and holding cost by lowering their ordering reference point (S) without negatively impacting the service level. Having a more reliable, more frequent and quicker delivery system is expected to enable even lower ordering reference points and thus ordering quantities, resulting in fewer outdated products. Suggested further research includes, adding the possibility for transshipment in the model, as well as that a combination of optimization and simulation would be better capable of representing real life hospital operations. Additionally they emphasize the need to consider implementation when developing models, in order to promote real-world applicability. In chapter 6 these modeling criteria are further elaborated upon and its implication on which methods are best fitted.

Inventory centralization

Less well studied within the field of BSC is the effect of inventory centralization. These effects have been researched on different scales ranging from in-hospital centralization[73] up to macro-scale considering all

echelons of the BSC[167].
A reduction in blood product wastage of 90% was found to be feasible when using a intra-hospital centralization strategy. However optimal numbers are found to be strongly dependent on cost related parameters, such as holding and transportation fees. Additionally the authors suggest hospitals to further investigate possibilities to decrease blood product transportation costs in order to further minimize the effect of shortages[73].
In a study that considered the second echelon (hospitals) in a two echelon BSC (bloodbanks & hospitals), it was found that further inventory centralization could reduce shortages and outdate [104]. It could be argued that in such a BSC network hospitals actually take on some of the role that initially belonged to the first echelon. Thus increasing the ability for transshipments, is likely to further decrease the need for a multi-echelon BSC. Hosseinifard et al. recommend studying the effect of these transshipment policies, a subject that will be covered in the next section about distribution.
When centralization of multiple echelons within the BSC is considered, results are similar and favour a more centralized network configuration[167]. As mentioned earlier, although beneficiary from an BSC optimization perspective, centralization of collection centers might not be feasible when taking into account travel times of donors. Similar to other research, the main drivers for a more centralized systems were the costs of physical facilities and stock-outs. Regarding physical facilities the benefits of centralization have been identified in other healthcare sectors next to the blood supply chain as well, this is discussed more extensively in the chapter 3.

2.3. Distribution

Most research regarding the physical transport of blood products within the BSC is focused around the collection process, and already touched upon briefly in section 2.1. In this section literature is covered that regards transport of blood towards the end users, which in the context of the proposed concept of operations would be hospitals.

Lateral transshipment

In the section covering inventory management, lateral transshipment was already mentioned as a means to improve inventory management performance. Shokouifar et al. studied the effects of transshipments in the context of aged differentiated platelets, with uncertainty in both supply and demand[207]. Simulation results showed that lateral transshipments between hospitals can decrease shortage costs by 38.1% and wastage costs by 35.9%. This showed the cost saving potential of better balancing load between demand nodes enabled by these lateral transshipments .
However lateral transshipments can be implemented in different layers of the BSC. For instance, Zhou et al. showed that lateral transhipments between different blood centers, who later supply the demand nodes, can also be beneficial [242].
Whereas most research has focused on reactive lateral transshipment policies, meaning shipping when products are needed, proactive policies can also make the BSC more efficient[64]. This study suggest that cost savings introduced by current lateral transshipping policies can be improved by shipping proactively. However it is noticed that in this model emergency shipping costs are modeled 10 times greater then normal shipping costs, with drones delivering emergency orders this number is expected to decrease heavily. Since proactive lateral transshipment within the context of BSC has not yet gotten a lot of attention more research has to be done to gain better insight on its potential impact. Also the new modes of transport might significantly change the prerequisites and results of lateral transshipment research.

Hospital collaboration

It has been noted, among others in the context of lateral transshipment discussed in the previous paragraph, that the efficiency at which a BSC functions is heavily dependent on the degree of collaboration between different actors. The quality of decisions made by, for instance, inventory managers are not only a direct consequence of the adherence to theoretical inventory policies but are also highly influenced by the quality and quantity of information available to the manager[7] . Connecting actors and sharing information is a pre-requisite when designing a BSC with the goal of optimizing overall performance. For instance when an integrated inventory system to share the hospitals' inventory levels is suggested [23][22].
In addition to blood shortage and wastage, which is often the main indicator for BSC efficiency, service delivery time also decreases with increased collaboration between hospitals. Improved performance is shown to

be directly related with the amount of hospitals in collaboration. Real world implementation and realisation of such benefits are dependent on challenges related to among others transportation reliability [123].

Vendee or vendor

In the Dutch BSC, and common among international systems, hospitals or end-users order blood products at suppliers [209]. This is a so called vendee-managed inventory system, in which each vendee (hospital) manages its own inventory and orders when desired. Hemmelmayr et al. were the first to study the impact of shifting responsibility to the vendor, aiming to organize blood product delivery more cost-effectively in Austria [99]. Their proposed integer programming model determined when and how much products were delivered to each hospital by the vendor, resulting in significant cost savings.

A more in-depth study showed similar results, in which a vendor-managed inventory routing problem for blood products outperformed original distribution schemes[134]. Numerical analysis of the platelet distribution network in the city of Nanjing, China, indicates that transportation costs could be reduced with up to 75%. However uncertainty in supply, demand, travel time, etc. were not included in this study, and is regarded as a next research step on this topic.

Transportation modes

Within the field of regular BSC distribution, little attention had been paid to comparing different modes of transportation. In a study by Eskandari-Khanghahi et al. different types of vehicles were included in a mixed-integer linear programming formulation aimed at designing a sustainable BSC [81]. However comparing the impact of different fleet configurations was not part of this study, and little details on the exact types of vehicles were included in the paper. Similar observations hold for a second study that includes a heterogeneous fleet within modeled BSC [91].

Several studies have suggested the possibility of using drones for blood delivery, as will be elaborate on in chapter 4. However, these studies are often of a qualitative character, and little quantitative evidence exists on the effect of integrating drones in a BSC under normal operating conditions.

Additionally in the context of disaster relief BSC some quantitative oriented studies do suggest different transportation modes, including drones. Findings on the topic of disaster relief are discussed separately in section 2.4. However, apart from a study by Otero et al., who compared the costs of hospital delivery networks (which might include blood products) when using either drones, motorcycles or cars[168], little studies have been found that consider using different kind of transport modes in the BSC under regular operating circumstances. This is especially relevant when considering that congestion is acknowledged by Sanquin (responsible for the majority of the BSC in the Netherlands) as one of the main challenges to overcome when ensuring a reliable supply[209]. A possible explanation for this lack of literature is that until recently no viable alternatives were available worth studying. This might be considered as a research gap since it is unlikely that systems will transition from fully ground vehicle based to fully drone based (or another mode of transport) directly. A hybrid system, using multiple vehicle types for BSC distribution, is expected to be adopted at least during the transition phase, and might be the most efficient option in the long term.

Environmental impact

Environmental impact has become an important topic in many industries over the last decades, and often named as a benefit of using drones over current transport systems. Until recently environmental pollution had never been considered when designing a BSC. In 2018 the first studies regarding environmental impact of the BSC were published. Heidari-Fathian and Pasan- dideh were the first to model carbon emmissions of vehicles used in the BSC, aiming to design a sustainable BSC network[98]. The proposed multi-objective mixed integer mathematical programming model was used to minimize (I) total costs, (II) outdates & shortages and (III) Greenhouse gas emmissions of transportation. Using a bounded objective function the three objectives were converted into a single objective model, which was solved using a Lagrangian relaxation heuristic.

In a similar study energy used for transportation was represented as a source of costs, which was added to costs related to more conventional topics like: inventory, shortage, wastage, deterioration, operations and facilities. The model was tested with data from a case study in the city of Ansan in South Korea and determined optimal location-allocation of blood facilities in order to minimize total costs [112].

The study mentioned in the last paragraph by Eskandari-Khanghahi et al., which was first received at Elsevier in the same week as that of Heidari-Fathian and Pasan- dideh, also considers the environmental impacts of establishing blood facilities and centers [81]. Although multiple vehicle types are included in the model, using a different vehicle does not alter the modeled environmental impact of transportation.

Arani et al. argue that environmental impact, social benefit and costs all contribute to the sustainability of a BSC. Besides transportation and facility establishment, waste of blood also contributes to costs related to environmental impact[23]. Because in these studies minimizing environmental impact is just a part of the objective, either by converting it into costs or having multiple objective functions, the decrease of the environmental impacts is hard to distill from overall results. One is able to adjust the relative importance of environmental impact by altering the costs or weight of the objective function, however analysing the resulting effects on environmental issues specifically has been impossible so far. The criteria of taking into account multiple aspects in mathematical models and effective methods to do so will be discussed in chapter 6
An often named advantage of using drones for transportation purposes is the reduction in emissions, as will be discussed in more detail in chapter 4. The only other study that was found to include environmental impact of blood product distribution is that of Otero et al [168]. Their study shows the potential reduction in CO2 emissions as a result of switching to a drone based blood distribution system. In their results emissions costs, which are derived using a carbon emission charge, are almost negligible compared to others costs for both air and ground based transportation networks.
As a consequence of the research gap identified in the previous paragraph, regarding the lack of studies modeling heterogeneous transportation fleets, analysis of environmental impact of different fleet configurations is not present. Since concerns about climate change are receiving an increasing amount of attention, the ability to show the positive impact of drone usage on environmental issues, is expected to benefit adoption desirability.

2.4. Disaster relief

A special kind of BSC research considers post disaster situations. Although not directly applicable to the design of a distribution network operating under 'normal' uncertainty circumstances, use of drones have been considered more frequently for these applications. Also uncertainty being a key consideration within this field, simulation techniques have seen a bigger adoption rate as they are considered as more effective in reflecting these uncertainties as will be elaborated upon in chapter 6.
Much contribution in this field has come from Iran, where for instance the design of a blood supply chain network for post earthquake situations is considered[199]. This work that builds upon earlier findings from Sahin et al.[197] and Delen et al[65] and considers a three echelon BSC. Results emphasize that a robust model is more predictable in terms of costs when compared to a deterministic model, resulting in less deviation from the mean when different simulations are run.
The concepts of robustness and reliability of BSC design for disaster relief have been further investigated by Rahmani [187], who included disruptions in his model. The proposed model seems less sensitive to disruptions, and can therefor be considered as more robust and reliable. However only disruption within facilities were considered, including disruptions in BSC transport might be a relevant topic for future research.
In a study conducted by Wen et al. the use of drones is proposed in order to deliver blood directly to patients in emergency situations [230]. Because the quality of the product at arrival is heavily dependent on the temperature, this was part of the proposed capacitated vehicle routing problem.
If the marginal costs of blood transportation come down due to the integration of drones in the BSC, emergency transport might become more widely adopted. As stressed in most works regarding disaster relief, including uncertainty and disruptions in models is needed to create reliable BSC networks. It can be argued that in disaster relief it is more widely accepted that BSC optimallity should be inferior to the reliability of the system.

2.5. Conclusions

The unique characteristics and societal importance of blood products have caused the BSC to be the most extensively studied supply chain in healthcare. Optimization research have quantified the benefits of different BSC concepts and strategies. Recently the real life complexity of the BSC have caused researchers to acknowledge that problems should be solved more holistically, and that optimization of single elements within the system limits real life applicability due to the unrealistic assumptions and boundary conditions. Additionally their will always exist some degree of uncertainty within all echelons of the supply chain. Rather then trying to control every single aspect one should accept these uncertainties and design BSC's capable of coping with unexpected events and supply and demand fluctuations. Both these observations change the way in which problems are solved, chapter 6 elaborates on different methods and their pros and cons.
BSC studies have shown the potential benefits of inventory centralization and sharing through lateral trans-

shipment. The current modes of transportation have limited the degree and intensity in which these practices have been considered. Changing transportation abilities could prove to be an enabler for innovative practices within the different echelons of the BSC. In the next chapter it is discussed how these findings relate to the broader concept of healthcare logistics.

3
Healthcare logistics

The recent Covid-19 crisis has emphasized, the importance, dependence and vulnerability of our healthcare system. However, whilst the pandemic will likely come to an end, challenges and problems facing the healthcare system will not. The cost of the Dutch healthcare, often regarded as one of the best functioning systems worldwide, is expected to double to €174 billion by 2040 [86]. Material and its logistics pose the second highest source of costs, after labor, within the healthcare industry[193]. Non-surprisingly logistics problems have gained attention within the healthcare industry, with high potential for improved efficiency[222]. Drones will not only have to be integrated into the current healthcare system they might be part of the solution on some of the challenges currently facing healthcare logistics.
In the previous chapter trends and literature specific to the blood supply chain were discussed in detail. This chapter elaborates on how these relate to the topic of healthcare logistics in general. Main trends within the healthcare industry are discussed as well as the associated problems and literature. Additionally specific goods and their characteristics, next to the already discussed blood products, within medical delivery are outlined. First in section 3.1 the goal of healthcare is discussed, and how these general goals apply to the subject of logistics. Next in section 3.2 and section 3.3 the different problems and trends within the field of healthcare logistics are discussed. Lastly the different medical goods and products that might be suitable for drone delivery will be discussed in section 3.4

3.1. Objective of healthcare logistics

In order to conclude whether the use of drones for medical goods distribution will improve healthcare, first one should define when healthcare actually improves. Additionally it is needed to investigate how these general healthcare criteria relate to the subject of medical distribution. In 2001 a special committee from the United States, chosen by the governing board of the national research council, proposed a framework consisting of 6 principles one should aim to improve in the health care system of the 21-st century[147]. For any innovation within the healthcare industry, the perspective of the patient and their safety is widely considered to be the most important. Vincent adopted the 6 key principles in his book on how to improve patient safety [221]. Vincent is considered to be a leading figure on the topic of patient safety related topics, and his view along with that of the committee, on how one should improve the system is adopted as a framework against which to measure improvement potential. Magnussen and Peterson, with the help of industry experts have indicated how these 6 principles relate or translate to performance indicators within the medical logistics sector[141]. The 6 principles, their respective definition and how these relate to logistics are presented in Table 3.1. The indicators named in the last column can form a basis from which the added value of an improved logistical system can be assessed. It is argued that when such indicators are positively impacted by innovation, healthcare and society benefits from these innovation.

The Netherlands Organisation for applied scientific research (TNO) has published a vision report on what healthcare will look like in 2030 and what the envisioned role of logistics within this system will be [60]. It states that logistics in the Dutch healthcare system of 2030 will be efficiently and sustainably organized, by bundling and using cleaner vehicles. Logistics is recognized as an enabler for many other trends and innovations that can improve healthcare. These trends and the role of logistics and transport are discussed later in

Principle	Definition	Logistics related indicator
Safe	Avoiding injuries to patients from the care that is intended to help them	Percentage of deliveries conducted without deviations such as destroyed or lost goods, or dissemination of personal information.
Effective	Providing services based on scientific knowledge to all who could benefit and refraining from providing services to those not likely to benefit	Transport system is sufficient to meet the demand for deliveries of the customer.
Patient-centered	Providing care that is respectful of and responsive to individual patient references, needs, and values and ensuring that patient values guide all clinical decision	Flow efficiency. Value-adding activities in relation to the throughput time
Timely	Reducing waits and sometimes harmful delays for both those who receive and those who give care	Percentage of goods delivered on time. Can be put in relation to dependability, where the sequence of activities is of high importance.
Efficient	Avoiding waste, including waste of equipment, supplies, ideas and energy	Utilization rate of resources, such as modes of transport, or percentage of time healthcare professionals spends on non-patient related activities such as administrative tasks or goods handling.
Equitable	Providing care that does not vary in quality because of personal characteristics such as gender, ethnicity, geographic location and socioeconomic status	Availability of deliveries independent of location, day of the week or time of the day

Table 3.1: 6 aims for healthcare improvement and related logistics indicators

this chapter. The vision is developed in order to state how logistics should develop in order to make healthcare more effective, efficient and patient-oriented.

3.2. Healthcare logistics problems

As stressed in the introduction of this chapter, logistics in the healthcare industry is recognized as a relevant topic by both industry and academia. This section discusses quantitative research aimed at improving these logistics. Three main overarching topics are identified among this work[222]: Supply, Inventory management and Distribution & Scheduling, which are often combined in relevant healthcare facility location problems. Ahmadi-Javid et al. state that reducing costs of logistics is not a priority for producers and distributors since costs are often directly passed on to healthcare providers [12]. This might limit their willingness to adopt more innovative logistics methods, which in turn can explain the relative old fashioned methods currently in use.

3.2.1. Supply

Cost of many goods and supplies within the healthcare supply chain are significant. Therefor several studies have investigated how to purchase these goods against the most favourable prices and conditions. Increasing purchasing volumes has proven to be favourable because of higher purchasing power. Hospitals establishing group purchasing organizations, has proven to increase competition among manufacturers and reduce prices for the health providers [105]. Although largely out of scope of this research, purchasing power is another example of how increased collaboration can benefit all hospitals.

Next to horizontal (inter hospital), vertical collaboration has also found to increase system efficiency. Although a lack of studies exist quantifying the effect, outsourcing some of the ordering responsibilities to the vendor is considered to reduce costs. Azzi et al. used simulation to compare different levels of drug logistics outsourcing and found, in line with findings from the field of BSC and other supply chain sectors, the benefits of vendor managed inventory (VMI)[32]. VMI systems, where suppliers control hospital inventory levels, is the current state of the art in healthcare logistics. Removing these buffer inventories all together and suppliers directly providing goods where and when needed is referred to as just-in-time delivery (JIT). Although applied successfully in other supply chains, JIT has not yet been adopted in healthcare, most likely due to the fear and severe consequences of stock-out situations[128].

The uncertainty of demand is a related argument that has been named as a major hurdle in adopting more state of the art supply chain management techniques like JIT [58]. However, forecasting demand for medical supplies in hospitals is very hard or impossible [222]. A faster and more reliable done assisted distribution system might be considered as an enabler to adopt these more efficient supply chain management concepts. subsection 3.3.2 discusses what more qualitatively orientated research has stated about the adoption of these novel concepts in healthcare logistics.

3.2.2. Inventory management

Since JIT ordering is not yet adopted in the health care logistics system, hospitals mainly rely on their own inventory to fulfil demand. Inventory policies have been studied in literature, comparing different strategies comparable to the ones discussed in section 2.2. Ordering parameters like quantity and frequency have been optimized in various hospital inventory settings. Compared to the BSC, where perishability is often considered in ordering policy decision making, hospital inventory policy problems are often more simplistic. Often products with high and stable demands are considered for these kinds of problems, the effect of goods characterized by a more irregular demand on ordering policies have not been widely researched [133].
The impact and importance of delivery lead-times on inventory policies is stressed by Nicholson et al.[159]. They state that including realistic lead-times in models is especially important when products or goods need to come from outside suppliers and/or warehouses. Inventory policy is part of an system getting increasingly more complex, taking these complexities into account is crucial if real-life applicability is needed.
Danas et al. proposed creating a virtual hospital pharmacy inventory system, that would replace pharmacy inventories of several hospitals in geographical proximity of each-other [58]. At the time of writing (2001) this was still a mainly hypothetical concept, the authors combined findings from other studies on hospital inventories to conclude such system would be beneficial. Two decades later these systems have been adopted in several industries, but such shared inventory systems have not been found in inter-hospital settings.
A study on drug shortages identified 9 ways how drug shortages may negatively impact costs and quality of healthcare[117]. Collaboration and potential inventory sharing were named as a possible direction for preventing these shortages. As drugs become more specialized and rare, this becomes additionally relevant as demand at single locations will be extremely low.
Different studies on inventory related problems covering different healthcare products and goods have seen similar conclusions to that of the BSC covered in the previous chapter. Optimization results have shown the potential upside on more horizontal collaboration, and sharing inventory. These results have caused the industry to pursue further centralization and create a lean healthcare system, these trends will be discussed in more detail in section 3.3. Additionally it shows that inventory problems are part of a bigger supply chain system and should thus be modeled as such.

3.2.3. Distribution

Due to the sheer size of hospitals, several studies on the distribution of goods have purely focused on internal processes. Fragapane et al. proposed using automated guided vehicles to distribute goods inside the hospital[84].
The interference between inter- and external hospital distribution should also be taken into consideration and is especially relevant for emergency deliveries[33]. As hospitals become bigger, taking holistic approaches covering the entire distribution chain might be crucial for ensuring optimal results.
Kergosien et al. studied the logistics of commodities in a hospital complex in Tours (France)[122]. They considered 9 different goods to be distributed among different locations, managed by 7 logistical centers, each responsible for one or two of the considered goods. Because one of the hospitals modeled was particularly complex due to its composition of multiple units and limited delivery docks, a two-level vehicle routing problem was created. The first layer was tasked with routing a heterogeneous fleet of vehicles among the different depots and hospitals in order to deliver and pickup the different goods as efficiently as possible. In the second layer the logistics within the complex hospital of Bretonneau is optimized, focusing on how to allocate the limited staff available. Although results from the model suggested that a staff reduction would not be achievable, it did show that combining different good streams could reduce the amount of vehicles needed, reduce congestion and simplify logistics from a hospital perspective.
The actual transport and distribution of medical goods, especially outside the hospital has not been studied widely. Volland et al. found in their literature review in 2017 only 5 studies focused on hospital distribution of medical goods, and identified 3 areas for future research[222]:

1. Assess robustness of solutions, by incorporating discrete-event simulation [122]
2. Incorporating inter-hospital transportation issues into layout planning
3. Including emergency deliveries within hospital networks

3.2.4. Facility location

Deciding on where to place certain facilities is sometimes considered to be part of other optimization problems, like for instance inventory problems. However healthcare facility location is well studied also as stand alone problems or in other not yet covered contexts. For an extensive review of all work on healthcare facility location problems, the reader is referred to the work of Ahmadi-Javid et al.[12]. They concluded that most healthcare related problems are discrete location problems, in which the facilities can be located at a limited amount of pre-defined locations. Additionally they distinguish non-emergency and emergency healthcare facility location problems, further categorizing the types of facilities covered by research, ranging from entire hospitals to doctors' offices.
As multi-hospital systems have become more common, meaning a single organisation owns and operates multiple hospital locations in a specific region, studies have tried to optimize potential synergies. A study focusing on how to allocate different specialized medical services among a multi-hospital network, compared different scenario's both from a financial and patient perspective. The authors conclude that: "By allocating demand across fewer locations hospital networks can better utilize resources. Aggregating demand across hospitals can reduce cost and improve the quality of patient care as higher patient volumes enable medical personnel to become more efficient at providing the specialized service, build their cumulative experience and effectiveness in administering the service, and avoid a loss of learning between sporadic procedures. Beyond quality, economic savings from pooling demand for medical capacity can be passed to the patient in terms of lower expenses or used by the network to offer other services, thereby improving the hospital networks overall service offering." [143]. Published in 2011, opportunities for future research were identified in how technological advancements might enable pooling medical capacity over larger geographic regions. Transportation of blood samples could by drone might be considered an example of such enabling technological advancement.
A recent study minimized total system costs of specialized diagnostic services, by optimizing the decision on which hospital to offer which services[149]. This paper focused on how one could solve such problems for bigger networks, therefor not providing much insight in the actual results of the different optimization in terms of allocation. The authors state the intend of these models to be helping decision makers plan future infrastructure more effectively. Uncertainty in supply and demand is named as an opportunity to further extend the models.

Similar to quantitative models from the blood supply chain, other healthcare logistics models come to similar conclusions. The benefit of more centralization and extensive collaboration between hospitals and other logistics stakeholders is suggested to be beneficial, the next section elaborates on how this relates to real-life healthcare. Additionally uncertainty is stated as important to include in future research to ensure real life applicability.

3.3. Trends

From the industry, sometimes strengthened by findings from academics, several trends have emerged that are defining the healthcare system for the future. In this section these trends are discussed by reference to mostly qualitative publishing's, different to the previous section where quantitative optimization problems were discussed. Exact naming of the trends and changes in the healthcare industry differ among authors, in this section two related trends are distinguished and discussed, centralization and lean healthcare.

3.3.1. Centralization

In the context of BSC problems, the concept of lateral transshipment was introduced. Research covered in section 2.3 and the previous section proved the potential to save costs and reduce waist, by sharing and moving inventory within the supply chain. Additionally the healthcare industry becomes capable of increasingly sophisticated procedures and diagnosis. As a result the costs of providing these services rise rapidly at locations that decide to offer them. Reducing the amount of locations where these services are offered is referred to as centralization. As fewer hospitals offer a certain service, the hospital(s) that does remain or start offering it can become more specialized on this service. Centralization of services often results in further specialization.
In order to gain a better understanding on how further centralization of specialised healthcare services will impact society, Svederud et al. conducted interviews and took surveys from different stakeholders [211]. Non-surprisingly all groups, patient association members, patient association representatives and health-

care decision makers, all named quality of care as the most important factor in relation to centralization. Patients named the geographic location most often as a negative effect. As facilities will become sparser it can be expected that patients will have to travel further and longer in order to reach the hospital with the required facilities. However technical improvements in transportation might mitigate this disadvantage and thus enable even further centralization.
In Denmark a restructuring in 2007, among others, reduced the amount of hospitals from 40 to 21. A study analysed the results of this hospital centralization after being in use for 10 years and found a stable cost reduction [52]. The authors also recognized that Danish governmental institutions have accomplished something extraordinary, in adopting these centralization strategies democratically. Understanding of the centralization concept and possible impact on quality, is of crucial importance when acquiring the needed societal support. In subsection 4.6.1 the role of drones and its impact on healthcare centralization is discussed in more detail.

3.3.2. Lean healthcare

The term lean originates from the Toyota production processes during the 90's, which were revolutionary at the time and enabled their rapid growth within the car industry[232]. In general it refers to processes where maximum customer value is pursued whilst minimizing wastage and thus stock inventory. Such system alter their production based on the observed demand, so called 'pull' production strategies. In recent decades entire bookshelfs have been written on how Toyota has revolutionized supply chain management. Others from both the car and other industries have since adopted 'lean' without fully understanding the underlying idea. Ironically enough Toyota was the only major car manufacturer who held a back-up inventory of computer chips when a big shortage occurred during the Covid-19 pandemic [217]. This has emphasized the need to take into account factors like reliability of delivery times when considering implementing these strategies.
Although proven to be beneficial in many industries, the term is relatively new in healthcare. Souza & Pidd have identified some barriers that have prevented adoption of lean thinking in healthcare at the same level that has been found in manufacturing [61]. A similar but more recent literature review stated the various categories within healthcare where lean thinking can be found [57]. Borges et al. listed the different forms of wastage, aimed to be minimized by lean thinking strategies, found in the hospital environment to be: overproduction, excessive transport, excessive motion, over-processing, rework of defects, waiting and inventory[42]. The authors stressed that half of hospital supply chain costs might be eliminated due to adopting lean practices. Compared to other value streams within healthcare, logistic functions, like medicine delivery, showed the most positive result for lean thinking implementation.
Just-in-time ordering policies discussed earlier are a particularly good example of how lean philosophies can be applied in the hospital setting. Pakdil et al. argue that healthcare delivery systems naturally run based on "pull" principles, a term commonly used in lean context to state that demand "pulls" productions levels [171]. Although one is able to produce a car before selling is, a 'push' system, one cannot provide healthcare to someone who is not yet sick. Most literature on lean healthcare state the hesitance of stakeholders to be one of the main barriers to overcome in adopting lean in medical (delivery) processes. Creating clearer insight in possible benefits and reliability is crucial to overcome this barrier and gain trust among practitioners. Antony et al. named the following research gap in their literature review: "Assessment methods based on simulation: assessment methods based on simulation with realistic assumptions have a huge potential to deliver great insights for firms implementing Lean in healthcare, as the past research lacks such usage. Simulation experiments provide a field to test for different possibilities and help firms in making an informed decision." [20]

3.4. Medical products

Hospital logistics is a broad term that covers a wide range of processes within a hospital. These processes can concern both people or goods, which can be further subdivided. Figure 3.1 shows a full categorization of hospital logistics [126].

The U in UAV automatically rejects the person part of the tree in the context of a drone based logistics system. Goods are further subdivided into medical and non-medical goods, the latter is also not considered in this report since the high volume and low value of these goods is most likely why no previous literature was found suggesting drone use for these logistics. This research thus focuses on the medical goods category. Magnusson & Hagerfors studied the delivery system of medical goods in Gothenburg (Sweden) [141], which is found to be similar to most current systems in the Netherlands. Using literature, secondary data and expert interviews, they obtained a better understanding of the specif characteristics and needs of the different prod-

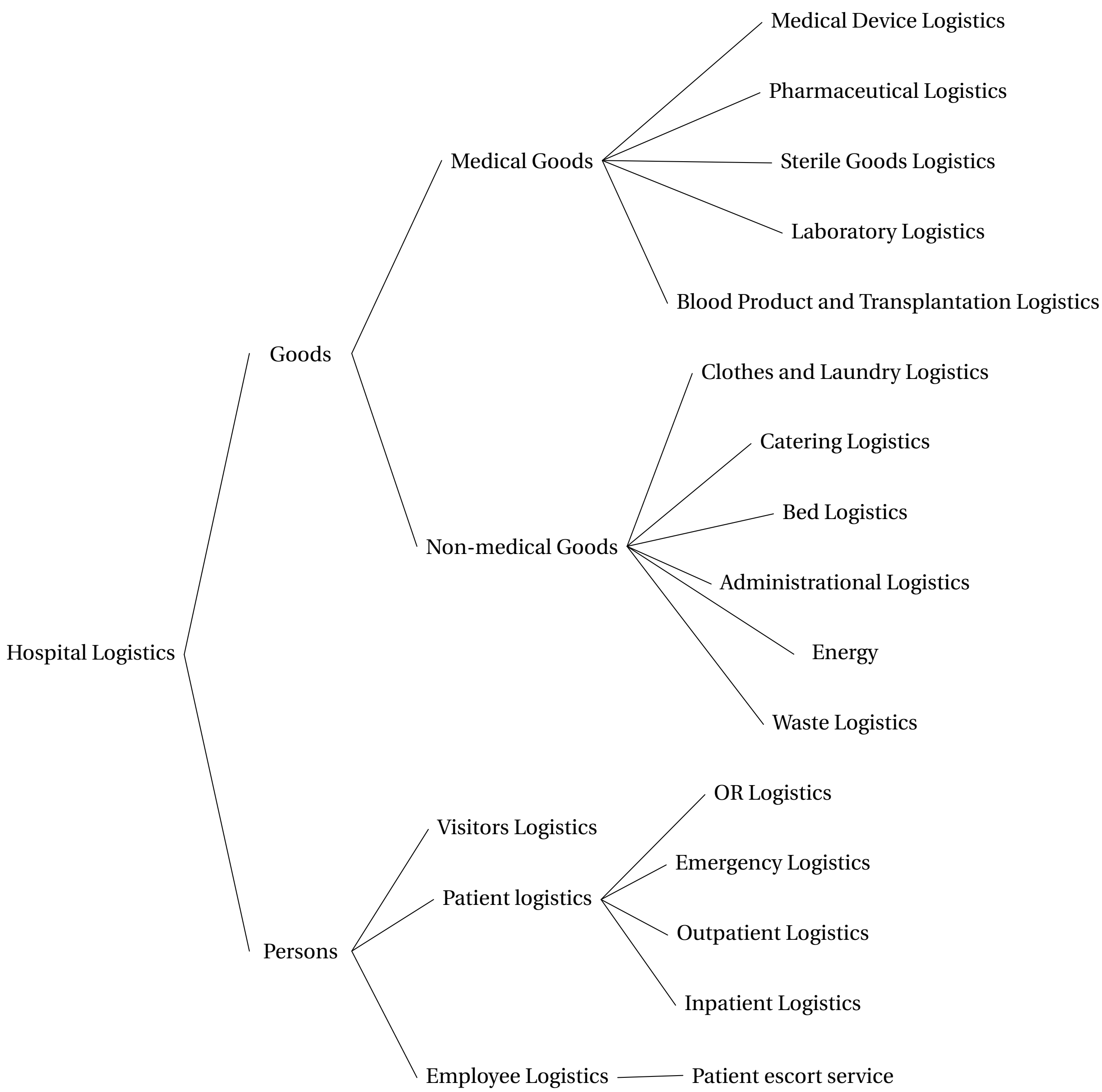


Figure 3.1: Categorization of hospital logistics, Source: [126]

ucts. Their findings are summarized in Table 3.2, merging their defined subgroups into the 5 main categories of medical goods. Goods within the category varying can cause some indicators to be a range, additionally some characteristics may not be relevant for all goods within a certain category.
First the weight, size and economic value of the goods are stated, which can be used to assess suitability for drone transport. A product with low weight comes in under 0.5kg, high weighing products are over 5kg and medium being in between. Size is indicated as either small, medium or large, with medium referring to goods that can fit inside a shoe-box. Economic value is stated as low when under €50 and high when over €1000 per product.
Next the frequency at which these goods on-demand delivery occurs, instead of using the alternative of scheduled deliveries, is stated. Daily states that on an average day this product is delivered on-demand at least once in the Gothenburg study of a 3 hospital system. Goods that are predominantly transported by scheduled delivery but sometimes require on-demand delivery are labeled sometimes, which indicates more frequent on-demand deliveries then the rarely category.
In the transport requirements column, details on how these products need to be handled during transport are presented. This can cover packaging but also environmental condition requirements. Studies that have investigated if these conditional requirements can be maintained during potential drone flights will be covered later in subsection 4.6.1.
Lastly it is indicated wether the product can be replaced by another item when it for instance gets lost. The inability to replace some of the goods makes these logistical problems somewhat unique and re-emphasizes the natural "pull" characteristic of the supply chain.

Medical goods	Size	Weight	Economic value	On-demand deliveries	Transport requirements	Replaceability
Medical devices	Small to large	Low to high	Low to high	Rarely	-	Yes
Pharmaceuticals	Small to large	Low to high	Low to high	Sometimes	Traceability Temperature Humidity Stability Security	Yes
Sterile goods	Small to medium	Low to medium	Low to medium	Rarely	Three layer packaging	Yes
Laboratory samples	Small	Low to medium	Low	Daily	Traceability Temperature Stability	No
Blood products	Small	Low	Medium	Sometimes	Traceability Temperature	Yes

Table 3.2: Medical goods characteristics. Source: [141]

The economic value of laboratory samples is low since it holds little intrinsic value for entire society, however for the individual patient to which the sample belongs it can be of lifesaving value, hence the irreplaceability. So although economic value is considered low it can be argued that value to society of these samples is actually higher then some other goods.

In past literature products suggested for drone transport do not always overlap exactly with the categorization of Kriegel et al.[126]. The list below gives an overview of general product groups that have been encountered in past literature as potentially fit for drone transportation.

- Blood products[215] [194] [79] [238] [15] [208] [131][168] [125] [203] [68] [141]
- Laboratory samples [14] [194] [17] [161] [16] [18] [131] [224][125] [68] [114] [141]
- Defibrillators[215] [203] [184] [194] [38][125]
- Vaccines [92] [194] [79] [127] [186] [185] [214] [203]
- Medicine[215] [203] [194] [160] [100] [131] [186] [224] [168][125] [141]
- Organs [202] [79] [212]

It should be noted that not all mentioned research have suggested inter hospital transport by drone, but might intend for instance at home delivery. As can be seen some literature indicates multiple medical goods to be interesting for drone delivery, although not all suggest actually combining the UAS for multiple use cases, it is argued that doing this will significantly improve the viability from an economic perspective. Although transportation requirements might prevent combining different products inside one drone transport, supporting infrastructure and personnel at a hospital can be shared.

3.5. Conclusions

Healthcare logistics differ from general logistics in that the medical environment requires not only pursuing efficiency or cost savings, but evaluate the impact of the system on the quality of healthcare. Whilst in other industries it can make economic sense to allow shortages once in a while, this can have lethal consequences in healthcare logistics. Quantitative optimization studies have so far failed to provide holistic information to decision makers, which has caused reluctance when considering adopting novel logistics concepts. For now the impact of further centralization and lean thinking in healthcare logistics remain mainly hypothetical and unclear, this is especially unfortunate considering the immense costs associated with hospital and healthcare logistics.

The small size and low weight combined with relatively high economic and societal value, make medical goods particularly interesting for drone distribution. Multiple specific goods have been mentioned to be fit for UAV transport, combining these different use cases is expected to improve the business case. In the next chapter past findings on UAS delivery are discussed, including what has been published on medical goods drone delivery specifically.

4

UAS delivery

As already briefly touched upon in previous chapters, the use of Unmanned Aerial Vehicles (UAV) for medical purposes has been investigated sporadically. In section 4.6 a more comprehensive overview is provided on drone applications in healthcare. In the first sections of this chapter a birds (or drone) eye view is taken on applications and problems covered in recent drone related literature.
Drone technology has, both literally as figuratively, taken flight in the last decades. First different flavours and types of UAV's are reviewed in section 4.1. Next in section 4.2 a brief overview is provided on how drones can be of added value in different fields of application. The biggest challenges preventing large scale adoption of UAS for the different are discussed in section 4.3. The next two sections, subsection 4.3.2 and section 4.4, cover quantitative studies on drone related optimization studies and drone risks.

4.1. UAV designs

Whilst often used interchangeably, it is necessary to distinguish the different official definitions and abbreviations, drones, UAS, UAV and RPA. The European Commission defines any aircraft operating or designed to operate autonomously or to be piloted remotely without a pilot on board as an 'Unmanned Aircraft' (UA)[82]. More commonly used and very similar to the definition of an UA is the term 'Unmanned Aerial Vehicle' (UAV). When equipment and/or personnel needed for remote control is taken into consideration it is defined as an unmanned aircraft system (UAS). If the UA or UAV used in the UAS is remotely controlled by an external pilot this is referred to as a Remotely Piloted Aircraft Systems (RPAS). The popular term of 'Drone' can be considered in a wider variety of contexts and knows many definitions. Drones mostly refer to autonomous vehicles, which can also include ground- or water-based vehicles. Following from these definitions it can be argued that an UAV can always be considered a drone, however a drone does not necessarily has to be an UAV.

UAV's come in many different size and forms. Often an initial categorization based on the vehicle weight is introduced. Brooke-Holland[46], Arjomandi et al.[25] and Weibel and Hansman[227], provide three different categorizations based on weight. Brooke-Holland proposes 3 main classes partly based on intended use which are further subdivided into a total of 6 categories ranging from Nano drones to Strike drones. Arjomandi et al.and Weibel and Hansman adopt comparable, mainly weight based, classifications, both classifying the smallest drones as micro. The biggest drone categories considered are, Super Heavy (> 2.000 kg) and Heavy (> 30.0000 lbs) respectively. Besides weight and intended use, other criteria with whom one can divide drones in different categories are for instance range, speed, wing span, engine type, flight aerodynamics and landing capabilities.
The latter two originally resulted in a similar categorization, but recent technological development has created a rapid rise in drone design configurations. In 2017 Hassanalian and Abdelkefi distinguished over 50 different types of air drones[97]. When we focus on UAVs commonly encountered in delivery use cases, a main separation can be made based on the take-off and landing procedures. Drones that posses the ability of vertical takeoff and landing (VTOL) are well suited for urban and crowded environments where space for takeoff and landing is limited. Alternatively, horizontal takeoff and landing (HTOL) UAVs often benefit from higher cruising speed and range.

Figure 4.1: UAV for intended use in Medical Drone Service project

The most common types of drones with VTOL capabilities are multirotor or rotorcraft models, who use multiple (often 4 or 8) rotors to stay in the air. Similar to helicopters, who use a single rotor for vertical lift, these drones benefit from the ability to hover relatively stable at a certain position in the air. Thiels et al. proposed using a special quad-copter UAV to transport blood in a feasibility study in 2015 [215]
Sticking to a more traditional airplane-like design, are the so-called fixed-wing drones, that rely on the lift generated by the combination of horizontal speed and wings to keep flying. Especially for bigger designs much knowledge from the aviation industries, has transferred to both the design and manufacturing phase of such drones.
Fixed-wing designs are often HTOL drones, however recently new designs have tried to combine the benefits of speed and range of fixed-wing configurations with the ability of VTOL. Some research suggest encapsulating configurations, benefiting from both VTOL and speed/range capabilities, in a hybrid category. A rather simple example are fixed-wing designs with nose-rotor propulsion capable of generating enough thrust to lift the weight of the vehicle by itself. More sophisticated designs often tilt the, rotor(s), wing(s) or body of the drone, in order to take of vertically and fly efficient and fast in the cruising phase of operation. As suggested by the name, tilt-rotor drones have rotors in a vertical orientation during lift-off and landing, after which they are tilted 90○ during cruising flight phase. When not only the rotors but also wings, to which rotors may be attached, can have different orientations, these vehicles are referred to as tilt-wing drones. Getting increasingly complex, the tilt-body category, refers to design concepts where both wing and fuselage can rotate freely [191].
The drone currently proposed for the Medical Drone Service project in the Netherlands is produced by Avy, a relatively new Dutch drone producer, and is presented in Figure 4.1. This fixed-wing design, has 4 vertical rotors, in addition to the horizontal rotors that are common to fixed-wing concepts, in order to have VTOL capabilities. Zipline, a pioneering company in blood delivery by drone, uses a fixed-wing UAV which in combination with a launch and catch installation. This UAS enables a relatively simple drone design since take-off and landing is partially done by supporting infrastructure.

Official classification of drones is very much location depended. In the Netherlands official regulations defined by the European Commission in 2019 are adopted since 2020. Different UAS flight operations categories are based on the amount of risk involved with the intended drone usage, as will be elaborated upon in. subsection 4.3.2 will discuss how ground specific risk can be evaluated.
As will become clear in the remainder of this chapter, drone characteristics and parameters are often a crucial part of academic models. The assumed values of these inputs highly affect the real life relevance and applicability of these models. Research, that aims to represent actual UAS has to use relevant and realistic drone

parameters. Unfortunately drone innovations rapidly remove past limitations and significantly change the boundary conditions of the model through drone characteristics. It can be argued that a model that can be updated with the latest drone characteristics ensures longer real life relevance and applicability.

4.2. Applications

The use of drones has been proposed in many different fields and industries. This section gives a brief overview of the different applications that have been considered for drone usage. This provides context on how the medical goods distribution usage relates to other applications in terms of market potential. Also it is aimed at giving background information on the challenges facing drone applications described later in section 4.3, and which are most relevant for the different use cases. Merkert and Bushell identify 4 main categories of use cases: monitoring/inspection and data acquisition, photography, recreation, and logistics (including passenger) [150].

Monitoring and data acquisition

Agriculture and construction, were one of the first industries to make use of satellite imagery becoming more easily available. Although resolution and quality has improved greatly, these still form limitations on the amount and quality of data that can be collected with these sources. Drones can overcome this issue, by providing similar data but with significantly better quality and resolution, enabling for instance farmers to gain insights in the growth of their crops [156]. Easing the adoption of drone for such use cases is the fact that flights often occur above the area owned by the commissioning party, minimizing impact on third parties. As will be discussed in section 4.3 third party risk is a major hurdle in large scale civil drone applications.
Similar industries that historically rely on regular manual inspections to ensure reliability and or maintenance, have started using drones to perform this costly and repetitive task. Flights with such missions often take place above and around vulnerable or dangerous infrastructure like power lines, resulting in additional challenges to ensure safety. Drones could for instance be used to inspect railway tunnels or culverts more efficiently [223].
Next to private institutions, government has started using drones for surveillance purposes. It is easy to imagine dystopian societies using drone surveillance, in which we are helped by books like 1984 and other science fiction work. Although we should be aware and prevent such use cases, government drone surveillance can also bring good to the world. It can monitor large corporations on their adherence to standards on emissions and land rehabilitation [116]. The range of stakeholders impacted by such operations is large, however often benefit from regulatory backing by supporting governmental institutions.

Photography

The use cases mentioned in the previous paragraph rely greatly on imagery, however the gathered visuals are converted into other sorts of data. In this paragraph we focus on use cases where the imagery captured by the drone is already the main purpose of operation.
Drones have enabled us to watch a wide range of events or scenery's, from a new angle or perspective. The birds-eye-view that can be provided by drones are used for small scale private events (like weddings), shooting marketing commercials and sport events. Feasibility of such use cases is highly case-specific, and dependent on many, mainly environmental, factors. Some cases might only require flying above private property but come with additional difficulties regarding a large amount of people beneath the drone. In other cases flying over public properties or domains might be required, which also introduces regulartory complexities [150].

Recreational

Drone technology has developed at a high pace in the last decade, whilst simultaneously bringing down costs. More people can now afford private drones for recreational purposes. It can be argued that such increase in (potential) users benefits the familiarity of people and the public with drone technology. This in turn can have a positive effect on the acceptance of drones by and in society. These additional use cases can also provide valuable insights and data that can be applied in a wider scope of drone applications. Analysis of crashes in drone racing events, for instance, can create additional knowledge on how one should evaluate risks [35].

Logistics

Initial interest for the use of drones in the logistics sector have come from several major corporations like UPS. Many use cases have been suggested delivering everything from your amazon order to your domino's

pizza [34]. It is believed that drones will have a big impact on the supply chain of the future[72]. Whilst last mile delivery might be the part of the supply chain on top of mind for most people. Upstream use cases can increase effectiveness and design of the entire supply chain system as we know it. Ayamga et al. state that further studies are required on how drones can be integrated in existing transport systems, highlighting issues around payload, range and social acceptance[29]. Some suggest that logistics and more specifically urban parcel delivery, will be the first widely used UAS for civilian purposes, highlighting the dependency of our current society on stuff to be delivered to us[19].
Even the sky is not the limit when thinking of potential goods or services that can be distributed through the air. And although initial tests have been successfully conducted in many areas, large scale roll-out of these applications have not been observed. Most stakeholders point to lagging regulations as one of main causes for this observation. Therefor 30 minute delivery of Amazon orders is, although tested successfully in 2016, for now still a future prospects for most[229]. Later in section 4.6 the use of drones for medical logistics is covered more extensively.

When extrapolating trends and observations, the number of use cases will likely expand further in the years to come. The list and examples of applications covered in this section, already indicates the potential impact that drones can have on the society of the future. How to manage this revolution is an interesting topic of debate that has no clear cut answers[150]. Several issues and questions will be covered in the next section. To enable strategic decision makers to decide on different use cases and how to incorporate them, it is necessary to provide them with the opportunity to weigh societal benefits and costs of these applications. Additionally knowledge from other from other fields might apply to novel or other applications as well.

4.3. Challenges

The positive effects that UAV's can have on our society do not come unaccompanied. Although commercial drone technology is expected to increase efficiencies in many industries an may improve personal lifestyles, it is needed to invest more attention in understanding negative consequences [139]. Qualitative research based on interviews with medical drone program managers and field staff found that the majority of challenges faced were of non-technical nature[113]. Already quite a significant amount of research has been focused on optimizing problems around UAS as will be discussed more elaborately in section 4.4. Note that use cases of such problems are often still mainly hypothetical, as we have seen so far, actual large scale adoption of UAS's has not yet seen the light of day. Some challenges and barriers have to be overcome first, which are the main point of discussion of this section. In general challenges regarding drone usage are highly interdependent and the barriers covered in this section are acknowledged to be far from exhaustive.

4.3.1. Regulation

One of the main factors holding back large scale commercial drone activity is regulation. A study that prioritized barriers for drone implementation in the logistics sector using an analytic hierarchy process, showed that regulations as the barrier with the highest priority [195]. Pathak et al. appoint that at the time of writing (2019) commercial drone activity is considered illegal in both the United States and Canada[174]. In this perspective the lack of regulations often results in more restrictions holding back drone potential. The inability of operators to get licences to operate drones is not limited to western and highly developed countries. A survey conducted in Sub-Saharan Africa showed the need for more awareness among authorities to establish and enforce regulations[30]. For the full potential of drone technology to be used, regulations that enable UAS operations are needed worldwide[29]. Additionally users should be made aware when such regulations are in place, to prevent large scale unauthorized usage creating potentially dangerous situations. Rao et al. acknowledge that regulations heavily lack behind the pace at which drone technology is being developed, which they state causes confusion among potential users[189]. A survey showed that most respondents are not aware of the regulations that do exist or are confused on which apply to them. The lag of regulations and for now often entire prohibition of commercial drone usage is often said to be due to safety issues. The reluctance of governmental institutions to regulate and allow commercial drones can be understood when considering that long term risks are indeed still to a large degree unknown.

The increased focus on UAS related risks can be observed in the regulatory categorization implemented by the European commission. Whilst more traditional categorizations, covered in section 4.1, used to form the foundation for airworthiness certification. The core of the new framework comprises of UAS categories solely based on risk related to the proposed concept of operations[101]. The certification needed to operate an UAS, within a certain category, increases in number and complexity with these categories. The three main categories as defined the European commission and adopted in the Netherlands are[82]:

1. Open
2. Specific
3. Certified

Due to the rapid rise in UAS technology and its adoption, regulations will and need to change in the upcoming decade. Bradley states: "There is potential for dramatic steps forward to be taken as a country's authority may simply decide to issue more exemptions." [44]. Research on the added value of drone delivery and that of medical goods specifically can help authorities make these steps forward as informed as possible. Risks should be taken into consideration when evaluating potential UAS, however limiting current research to current regulations would not drive innovation and regulatory changes.

4.3.2. Safety

A literature review on commercial drone usage states that safety was mentioned most often as the biggest concern around drone usage [139]. It is thus crucial to quantify safety risks associated with potential concept of operations. The need for better understanding of future risks posed by drone technology has indeed gained in attention recently. Risk and safety are broad terms that have been interpreted differently and inconsistently across literature. In this section we will cover 3 specific concerns that are often associated with safety and risk.

Privacy

As discussed in section 4.2 many application rely or benefit from the ability of UAV's to capture visual data from the air. Even UAV's flying with missions that do not primarily aim at capturing such data, are often equipped with camera's to help with navigation and or landing. The ability of drones to capture video's or images of people who are not aware or do not consent, is a risk that should be taken seriously. Cavoukian highlighted the issue of privacy associated with drone technology back in 2012, advocating for privacy impact assessments to gain better understanding of these concerns[49]. He suggests using a so called "Privacy by Design" approach to ensure privacy is considered in early parts of UAS development.
Concerns about privacy can be divided into three main categories as suggested by Yaacoub et al.[237]:

1. **Physical privacy** - Gathering personal imagery of somebody
2. **Location privacy** - Tracking and detection of people
3. **Behaviour privacy** - The presence of drones altering behaviour and thus restricting freedom

Although privacy might be less of a concern when the use of drones to deliver medical goods is concerned, it should not be discarded and be taken into consideration early on when designing the concept of operations.

Cyber-security

Because UAV's are by definition unmanned they rely on wireless communication for most part of their operation. The signals transmitted and received by the drones form an additional risk that should be considered. When these signals are intercepted this can result in for instance data to be stolen, which might contribute to the privacy concern mentioned above. In general cyber-attacks on drones can have two purposes, firstly one could hack the control system in order to conduct a physical attack (of which the possible dangers will be discussed in the next paragraph). Secondly attackers can use the communication system itself to do harm[13]. Similarly to privacy, these concerns are very much relevant and should be considered in the design process. For more detailed discussions on the security risks, limitations and possible solutions the reader is referred to studies and reviews specifically aimed at these topics [237].

Physical risks

Collisions of drones with either other users of the airspace or actors on the ground poses another risk. As civilian drone usage is expected to grow around the world, the risk of physical accidents is destined to multiply [189]. Preventing mid-air collisions is both the responsibility of individual drones that should require collision avoidance system, but also on a higher level air space control needs to adopt for high number of drones taking flight. subsection 4.3.3 goes deeper into the challenge of (re)structuring the airspace, in order to prevent mid air collisions.

The other major risk of drones crashing into the ground might be due to the control system being hacked as discussed above, however technical malfunction might also cause such accidents. Either way people or objects on the ground are vulnerable to the drone coming down and hitting them. The perceived danger of air-travel, which in some cases is not proportional to actual risks, has led to strict standards around physical safety of aircrafts. These standards are often expressed in a maximum amount of fatalities or incidents per operating hour and compliance with these standards is checked extensively using statistical analysis.

In aviation one has been capable of computing these incident or fatality rates quite reliably. Although the occurrence of such events is luckily still rare, the intensive use of airtravel over several decades has produced enough data for statistical significance risk estimations. However total operating hours of drones have been limited so far, hindering reliable risk estimations. In 2004, when drone technology was still very much under development, the US Department of Defense compared mishap rates of their military UAV's with that of regular aircrafts [163]. They found that their best performing UAV was 3,200 times less reliable, in terms of mishap occurrences, compared to large airliners. However the computed rates for the UAV's, expressed in mishaps per 100.000 flight hours, were all based on less then 100.000 actual flight hours. Hirling and Holzapfel identify this lack of historic data regarding UAS incidents, to generate unreliable statistics on drone safety[101]. They state that cross industry comparison of such risks is thus impossible, which makes it difficult to put safety numbers like fatalities per operating hour into perspective.

Since data does not offer a viable solution when estimating physical drone risks, scientists have developed more theoretical models that aim to quantify risks posed by drones. These models are covered in section 4.5.

4.3.3. Airspace structuring

Similar and related to regulations, the structuring of the airspace will need to adopt to large scale UAV usage. This paragraph briefly describes the challenge of airspace structuring and possible solutions.

Our current airspace structures are primarily designed for safe operation of a relative low number of big airspace users like commercial aviation and helicopters. These structures are, especially in dense urban environments, not capable of accommodating a growing number of users such as commercial drones. A collaborative project by Delft University of Technology, the National Aerospace Laboratory in Amsterdam, Ecole Nationale de l'Aviation Civile from France and the Deutsches Zentrum für Luft- und Raumfahrt did an extensive investigation on different airspace structures[210]. Four airspace structures were considered and compared using simulation.

The four concepts, increasing in the level of structure that were evaluated are:

- Full mix - Unstructured airspace with no restrictions on flight plans
- Layers - Vertically stacked altitude layer, flight altitude is imposed based on heading and speed
- Zones - Mainly horizontal segmentation based on city topology, circular zones similar to ring roads
- Tubes - Fixed routes, origins and destinations are connected with pre-defined routes or tubes

This project provides regulators with an initial menu from which they can pick their preferred option. In the end it is up to strategic decision makers to weigh costs and benefits of different options. Often one needs to balance efficiency, capacity and safety, which research can help to quantify to some degree. In the context of urban low altitude airspace structure research is expected to play a big role in strategic planning[236].

4.3.4. Other barriers

Apart from the challenges mentioned above, some but not all issues impeding drone implementations regard[195][113]:

- Public perception
- Environmental impact

- Economics
- Technical
- Practical challenges

A main trend that can be observed among these challenges, is that the stance of researchers on these issues is highly dependent on the perspective. This is especially relevant for broad and not well defined concepts like environmental impact and economics.
Taking the latter one as an example: As discussed in section 4.2 implementing drones in the logistics sector is expected to have a beneficial effect on the efficiency and thus economics of supply chains. Studies focusing on improving the economics of the logistics sector might therefor conclude that drones will have a positive economic effect. Whilst others, who take the perspective of (un)employment, may state that drones will cause job losses of for instance truck drivers. From such perspective conclusions can suggest drones will have a negative impact on economics, increasing economic polarization[129].

As we have seen, UAV's can have great potential benefits across a number of applications and industries. However when developing the business case for different drone applications, one should adopt a holistic view considering both economical and social values. Quantifying trade-offs may be challenging and even induce new ethical questions, but without increased understanding of both benefits and costs, adaptation of drones in society will be slow [169]. A property of emergent technology, which drones might still be considered as, is that social and ethical implications are largely unknown before technology is used in a particular context[93]. Overcoming the challenges and barriers covered in this section mostly rely on strategic decision making and deliberately designing the future. Research providing decision makers with an holistic overview of costs and benefits, enables more informed and less lacking decisions.

4.4. Optimization problems

So far mainly qualitative studies have been discussed, highlighting the potential and barriers of drone use. The rise of drones has also started a new field of research among optimization sciences. Some characteristics that make drones unique, create new problems or add new constraints or criteria on existing problems. This section discusses some of the most relevant problems among drone optimization research.
Three types of drone related optimization problems can be distinguished: problems that consider individual drone operation, problems about collaboration between multiple UAV's and problems that cover the supporting aspects needed around drone operations. Additionally one can categorize problems based on the time horizon they consider. Listed in order from short-term and specialized to long-term and high-level analysis, the three categories are:

- Operational
- Tactical
- Strategic

4.4.1. Individual drone

Given a flight mission, individual drone behaviour can be optimized so to accomplish the given mission as efficiently as possible. One problem related to this goal that has been studied extensively in the context of drones is path planning.
The higher mobility and different operating conditions compared to conventional transportation vehicles, that have often been road or at least ground bound, makes UAV path planning an interesting topic. Recently, together with the popularity, the application range of UAV's has grown rapidly, with this the need for planning algorithms with special requirements has also grown. Especially the need for planning in a 3-D environment, makes the problem more complex compared to conventional path planning methods.[40]
Since flight operations are out of scope of this research many flight planning problems are not considered relevant, two high level terms with a more logistical nature are[62]:

- Navigation

- Global path planning

Both are to a large degree about how one should get from A to B, and concern relative long distances and use simplified models of the vehicle. Such path planning is often part of the solution to a bigger logistical problem, of which examples are given in in the remainder of this section and in section 4.5. The novelty in such research lays often in the non-path planning section of the paper, most state of the art research on individual UAV path planning optimizes flight operations[11]. As the name suggests flight operation optimization can be categorized as an operational problem and thus less relevant for strategic decision processes.

4.4.2. Collaboration

Logistic UAS problems are mostly used to discover how different actors or vehicles interact competitively or cooperatively. Focusing on problems relevant to delivery applications, we find that much research has been conducted on drone vehicle routing problems. Vehicle Routing Problems (VRP) are a well known and studied subject in operations research. VRP are often confused and mixed up with Traveling Salesman Problems (TSP). Introduced in 1959 VRP is an generalization of TSP because it can use multiple vehicles (or salesman) and are not forced to return to its origin[59]. VRP aim at optimizing the allocation and sequence of tasks to different vehicles.

Vehicle routing problems often aim at representing real-life applications in order to find cost efficient solutions. However in practice usually multiple stakeholders are involved pursuing different goals. "Optimizing multiple objectives can more accurately reflect the reality of decision making in routing problems"[241]. Because multiple objectives, that often have some conflicting interest, are optimized for simultaneously, in most scenarios no optimal solution exists. Rather it gives decision makers the ability to weigh the the different objectives and pick the most desired solution.

A shift to more holistic approaches, taking into account different and more sophisticated objectives, has been identified during recent years. Two surveys, conducted in 2021 and 2008, covering all kinds of vehicle routing problems identified 105 different objectives in the most recent survey, of which 39 were new since 2008[118][241]. This shift causes research to better reflect and support real life decision making, increasing industry relevance.

Within delivery focused vehicle routing problems, drones enable more reliable and precise estimation of delivery time. The trade-off between increased customer service and costs is recognized to be an interesting topic for future research [241].

Drone delivery vehicle routing problems can be categorized by the type of collaboration they cover. Here we distinguish between problems of systems that only include UAVs and systems in which multiple types of vehicles collaborate.

Multi drone operations

VRP that consider a vehicle fleet of only drones can also be referred to as drone delivery problems (DDP). Studies in this field have an increased focus on issues that are unique to UAV's such as maximum payload and battery charge limitations[140]. Especially relevant is the work of Liu who optimizes drone dispatch in an on-demand meal delivery system [135]. The model represents real-world situations well, by incorporating factors like, unknown and varying demand, different order sizes, drones' mobility range, carrying capacity and constraints on combining different types of goods carried by a single drone. Similar to the distribution of medical goods, novel food delivery concept of operations using UAV's would also (partly) replace road-based vehicles. The goal of this routing problem is to dispatch drones near-real-time to live incoming orders, with minimum waiting time and maximum efficiency. Whilst the concept of operations used in this paper shows a lot of similarities with one that would cover the distribution of medical goods to medical centers, some differences were noticed. The location of both pick-up and destination were unknown and could be placed anywhere, whilst the possible locations for supply and demand are limited to the locations of medical centers in the scenario of medical goods distribution. This forced Liu to use a grid representation of the covered area, whilst a graph representation might be more beneficial in a scenario with a limited amount of prior known locations. This paper showed the novelty of dynamic DDP, as well as its complexity and its relevance for future agile transportation systems.

Heterogeneous vehicle operations

Recently a significant share of drone related routing problems, consider systems with different kind of vehicles [192]. Especially well studied are problems that combine drones and trucks in a single delivery system.

Drones benefit from speed and route flexibility over regular trucks. However they are limited in terms of travel range and load capacity. Using drones in collaboration with trucks, who do not have the latter limitations, creates synergy and could further enhance drone utility [53]. Next to academia, industry has also recognized possible benefits of combined operations. In 2017 UPS piloted a system in which delivery drones take off and return to the roof of a relatively normal looking delivery truck[3]. Drone delivery models considering combined operations with other vehicles can be further categorized in 4 main types op operations[169]:

- Vehicles supporting drone operation
- Drones supporting vehicle operation
- Drones and vehicles performing independent tasks
- Drone and vehicle synchronized operation

In this literature review we will focus on work published on the third topic. Research on the remaining 3 options mainly focuses on how to synchronize and align operations of the two kinds of vehicles which is not in scope of this particular research.
Most work on independent drone and truck systems, deal with the problem of which task to assign to which vehicle. These problems are therefor sometimes classified as task allocation or task assignment problems instead of routing problems, however often there exist no clear-cut differences between the two[53]. In the context of delivery and logistics, most problems regard deciding on who should perform a last-mile delivery task. Ulmer and Thomas studied a concept of operations where orders come in throughout the day and should be delivered within a certain time window [218]. They showed the benefit of using heterogeneous fleets, only requiring 6 trucks and 17 drones to serve their case study sufficiently. The scenario required 12 trucks or 47 drones when homogeneous fleets were adopted. In these scenario's a single base hub was considered from where all deliveries were conducted. Ham extended this problem by considering multiple hubs and also introducing pickup tasks for drones, representing order returns by customers[94]. Although this still regards concept of operations based on consumer last-mile delivery, the introduction of pickups resembles a hospital distribution problem more closely. Ham mainly focused on how to model such problems so that (near) optimal results could be generated in reasonable time, ensuring real life usability. Differences in modeling techniques will be discussed in detail in chapter 6.
Little studies were found that covered systems where different (heterogeneous) fleet configurations were compared. There exists a need for research that can support in making strategic decisions on fleet configurations[169].

4.4.3. UAS support

Some studies have taken an optimization approach to UAS design, considering the supporting roles and infrastructure needed. Operational and tactical problems from this field focus on for instance scheduling of the operating personnel. Of a more strategic nature are papers taking an optimization approach to the challenge of airspace structuring covered extensively in subsection 4.3.3.
Most widely studied among UAS support problems cover the location of physical supporting infrastructure. Such facility location problems mostly regard the placement of launching sites, charging stations, warehouses or hubs. A study by Shavarani et al. aimed at estimating total costs of a drone delivery system by Amazon in the city of San Fransisco [205]. Minimizing for the investments related to both fleet size and infrastructure it tried to give an indication on economical viability of such system.
Other studies that regard medical application of drone-delivery focus on reliable availability of the to be delivered goods. The range limitations of drones make this an interesting but also more complex problem compared to more traditional facility location problems [50]. To enable decision makers to weigh the cost and benefits of their investments, Kim et al. proposed an economic analysis tool [124]. They recognize that benefits are often hard to directly quantify because of their societal nature. It can be argued that, in order to express improvement of for instance medicine availability in monetary quantities, one has to make ethical decisions on how to value human well being.
Note that the above mentioned studies differ from the use case of hospital distribution since it regards delivering to patients, or customers more generally, at their homes. More studies specifically aimed at medical distribution will be discussed in section 4.6.

Overall is has been noted that drone optimization problems tackled in recent literature are mostly operational or tactically oriented and aimed at cost minimization of supposedly already existing systems. Otto et

al. recognized a lag of drone operation research considering strategic issues like fleet size and composition determination [169]. This emphasize on operational and tactical problems by existing literature is also recognized in the context of drone logistics by Sah et al[195].
Additionally most drone delivery optimization problems do not focus on using realistic drone parameters. This might be due to the fact that these problems not yet reflect real life scenario's, since these are not implemented yet. Future research could focus on integrating more realistic parameters to enable comparison of different technologies and weigh costs and performance more realistically [140]. "Optimization is a valuable tool to examine the best-case and the expected potential of emerging innovations, and it, thus, can help guide engineers and managers in investment and research decisions."[169]

4.5. Risk modeling

As discussed in subsection 4.3.2 the physical risks drones pose to people on the ground is one of main concerns around large scale drone operations. Regardless of the question weather these concerns are deserved, they are likely partly due to the military nature of drone perception. A SWOT analysis on UAV use for public health, stated drones falling out of the sky and injuring people as one of the major threats. "Assessment of public safety and privacy has to be done before scaling up of drones in public health" concludes Laksham. [131]. This concern has subsequently led to research aimed at quantifying the risks in order to prevent undesired effects of large scale drone usage. In this section results from these attempts to quantify the risk to people on the ground are discussed.
With the already high number of drone configurations and environments they can operate in, the ways in which they might induce harm to people on the ground are almost endless and growing. The UAS Ground Collision Severity Evaluation report that covered over 300 publications on several types and usages of drones, listed all possible UAS ground collision options in 2017, resulting in 23 identified knowledge-gaps [26]. In order to tackle this problem systematically, most researchers have tried to compute the probability of fatality or heavy injury for people on the ground in a way that is widely applicable. Melnyk et al. named two primary reasons for expressing risk as fatality rate instead of for instance economic impact[148]. First it is argued to be the most important aspect of safety. Secondly deriving fatality rates is already difficult considering the lack of data available and needed assumptions, introducing additional metrics are likely to increase this difficulty. Although exact implementation of the equation differ, most studies use something to similar to Equation 4.1 to compute the risk and subdivide the problem. Here the simple and clear formulation found in a study aimed at quantifying small UAV risk is provided [130].

$$p_{\text{fatality}} = p_{\text{event}} \cdot p_{\text{impact person}} \cdot p_{\text{fatal impact}} \tag{4.1}$$

In the remainder of the section findings on the three factors individually are evaluated.

4.5.1. Probability of failure event

The probability of failure states the likelihood of an UAV malfunction happening. This metric is mostly expressed as a probability per flight hour, and can differ for different failure modes. These failure rates are a characteristic of the modeled drone, and would ideally be derived from analysis of large amount of conducted flights. However not enough flight hours have been made by UAVs to enable reliable derivation of these failure rates. Washington et al. state: "There is limited reliability data available on UAS owing to the relative infancy of the technology and the diversity that exists amongst these systems. Thus the use of a system/functional approach to determine the failure rate of the system might prove to be more suitable for UAS."[225]
Melnyk et al. therefor propose a framework using a Target Level of Safety approach in order to derive the required safety levels for a UAV to comply with regulations [148]. Resulting from such framework are maximum failure rates that would lead to an overall acceptable probability of fatality for a certain drone in operation. Such frameworks could serve regulators setting minimum operating requirements that applicants need to comply with in order to receive certification.
The lack of historical data has caused other scientists to take values from other fields of study or make expert based assumptions. A literature review on 17 models showed that all used a constant failure rate [225]. With assumed failure rates ranging from 0.01 to 10^{-6} failures per flight hour. The authors only identified two models that considered different types of failures, whilst stressing the significance of the type of failure in determining the risk.

Since 2017 more literature has taken the approach of modeling different failure types. These heterogeneous failures subsequently lead to different ways in which the UAV descents to the ground. Four descent event types that are commonly encountered [182] [130] [181] :

- Ballistic descent
- Uncontrolled glide (UG)
- Parachute descent
- Flyaway

Table 4.1 shows the assumed probabilities of these events as a consequence of a drone failure for two studies that use general aviation data.

	Ballistic	**UG**	**Parachute**	**Flyaway**
la Cour-Harbo (2019) [130]	1/125	1/150	1/100	1/200
Primatesta et al. (2020) [181]	1/200	1/200	1/100	1/250

Table 4.1: Probabilities of events (per flight hour)

4.5.2. Probability of impact

Given that a malfunction has occurred, the next step in deriving the probability of fatality or injury, is expressing the probability that this malfunction leads to somebody being impacted. This can generally be subdivided in two additional steps. First one needs to determine where the UAV will come down, secondly the probability of somebody being impacted at that certain place needs to be estimated.

Models that assume the four different descent events from last paragraph, also produce four ground impact footprints that state, given that UAV will start one of these descents at a certain the location, the probability the vehicle will hit the ground at a variety of locations. A study that elaborated on the descent models for a fixed wing UAV of 3.75kg showed the dependency of input parameters like heading and wind on the resulting footprints [181]. Taking into account this uncertainty they found that the distance from failure occurrence to the drone hitting the ground was almost always within 90, 900 and 125 meters for ballistic, uncontrolled flight and parachute decent models respectively. Fly-away descents could cover greater distances before hitting the ground in these models, however one could argue that in such event the drone and or its operator can still actively influence the outcome.
The importance of uncertainty among the input parameters and other variables is stressed by Washington et al., in their literature review [225]. To better understand the impact of uncertainties Morio et al. studied the footprint for a fixed-wing UAV in a uncontrolled glide after main engine failure [154]. To account for uncertainty, they used simulation to produce the footprint focusing on rare events. It is expected that in the coming years more accurate representations of the different descent models will be developed, integrating higher levels of uncertainty.

These ground impact footprints are combined with maps or grids representing the amount of people at risk at a certain location. The accuracy of the descent model should be in the same order of magnitude as the grid size of the risk map. It is of no use predicting where an UAV will hit the ground up to a single meter accuracy, when the ground risk map is divided into a grid of 100m by 100m tiles. The to what is often referred to as risk-map can integrate multiple layers in order to estimate the risk at certain locations. As mentioned, this map is often represented as a grid of square tiles rather then a continuous map, partly because of computing scalability reasons and partly because of the granularity of the available input data. The different layers generally contain risk associated values for the different grid points. This structured method of representing the environment with a risk-map was first proposed by Primesta et al. and build upon by sequential papers [179].
The risk-map representation allows for risk-aware path planning, minimizing the risk of getting from A to B.
Different factors that determine the probability of people being impacted at a certain location and their associated risk map layer are discussed below.

Population density

Ideally one knows the exact number of people present at every grid cell at every given moment. Although suggestions have been made to integrate other data sources, like mobile location data of cellular carriers[66], so far privacy related regulatory have prevented such use in practice.
Often uniform population density distributions are used, depended on national available data sources this is often obtained through national census data. Whilst population density is a relatively easy to obtain parameter to estimate people at risk on the ground, it is sometimes processed further before combined with other risk layers. Ortlieb et al. proposed normalizing the population density so differences in more sparsely populated areas are also taken into account[164]. To compensate for human behaviour throughout the day, going to work or public spaces, Melnyk et al suggested incorporating data from human activity pattern studies [148]. It could be argued that such knowledge is only effective when used in combination with location specific data on the composition of a certain area in terms of land use. In most other studies no such modification was used on the population density layer of the risk map [225].

Sheltering factor

Melnyk et al. state: "A more accurate representation of the population density takes into account whether people are in the open, in their homes, in a car, or in some type of commercial building." [148]. The sheltering layer tries to quantify to what extend people at a certain location are sheltered from, in this particular situation, drones falling from the sky. Different models have been suggested to determine the sheltering factor, ranging from binary non- or fully-protected to implementing probability studies used to determine impact of fragments on roof[225].
Primesta et al. have somewhat simplified this layer by assigning one of 5 sheltering factor values to each grid cell according to what is (most) present within that area, and these are presented in Table 4.2. The authors argue that this factor is part of the probability of fatality rather than impact, but emphasize that it is most essential that it is only used once in the entire risk estimation. Especially when this factor is used to alter the kinetic energy of the person being impacted it is agreed that is most relevant when computing the severity of the injury, however since often the value is location specific one might include it in the risk map value, since in the end the two factors are multiplied anyways as seen in Equation 4.1.

Area	**Sheltering factor**
No obstacles	0
Sparse trees	2.5
Vehicles and low buildings	5
High buildings	7.5
Industrial buildings	10

Table 4.2: Sheltering factors as defined by Primatesta et al. Source:[181]

Often the extend to which someone is protected from a drone does not only depend on the environment, but also on the decent type with which the drone is coming to the ground. La Cour-Harbo proposes different shelter factors for the aforementioned four types of decent models [130].

Obstacle layer

Next to protection, discussed in the previous paragraph, buildings can also hinder drone missions as they are regarded as obstacles. Recent studies have tried to quantify the risk of obstacles for drone missions, and integrate this risk factor as another layer in the risk map. Next to buildings additional obstacles have been considered that form a particularly big risk to drone operations. Primatesta et al. used an open source model of the environment to define an obstacle layer consisting of objects reaching higher then 30 meters in the air [179].
Ortliep et al. propose a more comprehensive approach and classify objects into distinct obstacle classes [164]. The different classes contain an impact score that indicates the danger of out-of-control drones above or around such obstacles. This score is then combined with the height of the obstacles, similar to the approach of Primatesta et al., creating the desired 2D risk map.
These approaches have only been used on small scale case studies. Since it requires building by building analysis of 3D environment models the scalability of this approach is questionable. Additionally the availability of such data is not guaranteed in many instances.

Impact area

The area in which people might be impacted by a drone crashing, might be bigger then the surface area directly hit by the drone. Research that takes this into account in their model might refer to it as impact area. It was noted that other ground risk model research refer to impact area when considering all possible places where a drone might crash given a failure. In this section we focus on what has been found on additional affected area around a given crash location when mentioning the impact area.
Methods used to quantify the impact area can be divided into two main categories: hypothetical and empirical models [148]. The hypothetical methods use geometry of the UAV to estimate the impacted area, for which 3 main decent models are distinguished: planform, gliding and vertical decent models. The planform approach simply assumes that the impacted area is equal to the planform area of the UAV. The gliding approach uses the angle at which the vehicle is predicted to hit the ground, which has become dominant in recent years. The vertical decent model often assumes the impacted area to be a circle with a diameter related to the wingspan of the UAV.
In Equation 4.2 and Equation 4.3 two equations applicable to fixed-wing drones are presented. In both equations the impacted person is modeled as a standing cylinder, in which r_{p} and h_{p} are the radius and height of this cylinder. r_{uav} is the radius of a sphere that contains the drone and finally the glide angle is represented by θ. Equation 4.2 from [181] is argued to overestimate the impact area when the glide angle approaches zero. Therefor Equation 4.2 was proposed by Primatesta et al., which, the authors argue, lacks this limitation[179].

$$A_{exp}(\theta) = 2\left(r_{\mathrm{p}} + r_{\mathrm{uav}}\right)\frac{h_{\mathrm{p}}}{\tan(\theta)} + \pi\left(r + r_{\mathrm{p}}\right)^2 \tag{4.2}$$

$$A_{exp}(\theta) = \pi\left(r_p + r_{uav}\right)^2\sin(\theta) + 2\left(r_p + r_{uav}\right)\left(h_p + r_{uav}\right)\cos(\theta) \tag{4.3}$$

La Cour-Harbo has taken a more pragmatic approach and assumed the impact area to be $25cm^2$, $25cm^2$ and $200cm^2$ for uncontrolled glide, fly away and ballistic decent models respectively [130]. These area's were defined for a 16kg Penguin C fixed wing UAV, similar to the one proposed for the Medical Drone Service project in the Netherlands.
Emprical models use historic data to determine the impact area of drone crashes. Mostly a categorization is done based on the UAV weight or size, for which each category has a pre-defined expexted impact area. A comparison of different methods to estimate the impact area showed that weight was a better predictor then size based methods [148]. Since not sufficient UAS crash data exists, researchers have often turned to general aviation incident reports. However, since crash data of big aircrafts were used and similar behaviour is just assumed for smaller drones, its applicability for UAV risk assessment is questionable[225].

No fly zones

The final layer that is often used in creating ground risk maps for UAV's considers no-fly zones. No-fly zones can be defined by different institutions for different reasons, four common examples are:[181]

- National regulation agencies, like the FAA in the United states. These no-fly zones can often be found around airports
- Nature sensitive areas, these can for instance be national parks or other protected areas. These no-fly-zones are less common in the Netherlands.
- Security zones, where flying is not allowed because of safety reasons. This can be above highly populated urban areas, or industrial areas which pose dangers.
- Zones defined as inaccessible by the operator, which can have a wide variety of reasons.

Often no-fly-zones are modeled as a binary layer into the ground risk map. Either a location is part of a no-fly-zone and can therefor not be accessed by drones or it is not part of any no-fly-zone which means the drone can in theory fly over this location. No-fly zones can either be static, meaning that flights are not allowed at any moment in time, or dynamic which indicates that these locations can only be accessed during certain hours [164]. In case studies often API's of regulatory agencies are used as a primary source of this ground risk map layer.
As established earlier no-fly-zones can be defined for many reasons. Whilst some of these reasons are not covered in other ground risk map layers, like airport vicinity, others might overlap with other layers. Some

zones that have been defined as too dangerous to fly over by operators or regulators, were done so because of population density or the presence of high buildings. Since at the time these were defined no such thing as a drone ground risk map existed, these were mainly defined manually. Analysis of no-fly-zone locations of the previously named literature as well as Dutch drone no-fly-zones confirm that the location of some highly correlate with areas associated with high risk scores from other layers of the ground risk map. Therefor is it argued that one should analyse no-fly-zones more thoroughly before adding them as a binary value into the risk map, to prevent this overlap. Excluding areas, which might have a high risk value in other layers hence the no-fly-zone, can ultimately results in drone flights planning routes avoiding these no-fly-zones that ultimately create larger risks then when flying over the manually established no-fly-zone. No-fly-zones should be classified along the reason for establishment, if this reason is already covered in a different layer it can be argued that it could either be ignored all together or its risk value should be altered accordingly.

4.5.3. Probability of injury

In 2014 it was noticed that research focused on deriving the probability of fatality mostly assumed that all impacts would cause a fatality[148]. But this assumption can be considered as over-conservative [181]. In recent years more attention has been spend on determining this probability more accurately. Two common methods are discussed next.

Blunt Criterion

The blunt criterion uses a relatively simple approach converting the kinetic energy (E) into the expected injury severity (BC). Taking into account characteristics of the hitting object and the object, or in this case person, being hit. Equation 4.4 to Equation 4.6 define the blunt criterion[130]. With W representing the mass of the casualty, k being 0.6 and 0.7 for females and males respectively, D the diameter of the hitting object and AIS representing the severity of the injury. More details on the AIS scale will be discussed in section 5.2. A certain AIS threshold represents a fatality in most drone risk related studies, but the blunt criterion might be especially use full when also taking into account probability of serious injury[55].

$$\mathrm{T} = kW^{1/3} \tag{4.4}$$

$$\mathrm{BC} = \ln \frac{E}{W^{1/3} T D} \tag{4.5}$$

$$\mathrm{AIS} = 1.33 \cdot \mathrm{BC} + 0.6 \tag{4.6}$$

Area Weight Kinetic Energy

In contrast to the blunt criterion the area weight kinetic energy method focuses on where somebody is hit by the object instead of the size of impacted area [130]. Equation 4.7 shows how the FAA computes the weighted kinetic averages taking into account four different body parts: head, thorax, abdomen and limbs [26]. A represents the area and KE the kinetic energy treshhold specific to that part of the body.

$$KE_{\mathrm{avg}\,|\,\mathrm{lethal}} = \frac{(KE_{\mathrm{head}}\, A_{\mathrm{head}}) + (KE_{\mathrm{Abdo}}\, A_{\mathrm{abdo}}) + (KE_{\mathrm{thrx}}\, A_{\mathrm{thrx}}) + (KE_{\mathrm{limb}}\, A_{\mathrm{limb}}).}{A_{\mathrm{head}} + A_{\mathrm{abdo}} + A_{\mathrm{thrx}} + A_{\mathrm{limb}}} \tag{4.7}$$

This highly elaborated work of the FAA implements the general equation of Janser as proposed back in 1982 [111]. It can define the kinetic energy thresholds that induce a specific probability of fatality for different human postures, of which two are presented in Table 4.3.

Probability of Fatality	KE threshold (joules) Standing	KE threshold (joules) Sitting
1%	43	39
10%	66	61
30%	92	83
50%	114	100
90%	194	169

Table 4.3: Area weighted kinetic energy thresholds for different postures; Source: [26]

4.5.4. Path planning

This section so far discussed the ability to better model the risk involved with drone operations by increased understanding of the probability of an event, a person being impacted and the consequences of somebody getting hit. This increased knowledge is used by some to determine the ideal routes drones should take in order to minimize the risk associated with going from A to B. In drone risk modeling related research this is often referred to as path planning. However this term is not well defined in the context of drones and is used differently across literature to refer to a certain problem. To distinguish different kinds of drone path planning problems, 3 key terms that are often encountered in drone path planning research can be used to provide guidance:[11]

- **Navigation:** This the most high level term which mostly refers to how an UAV should roughly plan its route in order to avoid big collisions etc.
- **Trajectory planning:** Given a rough route, this covers the exact speed, time and kinematics of the UAV at the different locations along the route.
- **Motion planning:** Based on the trajectory this is the most in detail planning term which states how the plane should actually move and act in order to follow the desired route.

Drone path planning problems are argued to form a spectrum in terms of details taken into consideration. With navigation being on one end of the spectrum with the fewest specifics and motion planning being located at the other end. As a drone path planning problem moves along the scale towards motion planning more drone specific parameters and flight abilities are taken into consideration. This added complexity creates more difficult problems that require more in depth knowledge and analysis. Because path planning is not the primary problem considered in drone risk modeling research often little of such complexity is considered. Although some research evaluate and plan 3[71] or 4[235] dimensional flight trajectories, which is common in general drone path planning problems, this is rare for risk related drone path planning problems. In the previous paragraphs of this section, the development of a 2-dimensional risk map was discussed. Finding optimal paths in 3 or more dimensions based on a 2-dimensional risk profile does not make a lot of sense, thus risk optimal paths are also only described in 2 dimensions.
Primatesta et al. add a path smoothing step in their 2 dimensional path planning algorithm to take constraints of the radius of curvature into account.[180]. However the authors do so in a second phase of path planning because the radius of curvature is similar to the resolution of the risk map used in order to find the optimal path. Thus taking into account this flight operation constraint would not alter the result in the previous step. To find the optimal path across the previously determined risk map grid, mostly well known path finding algorithms are used. Relatively simple algorithms are well suitable since the risk map has a limited resolution and thus the grid consists of a manageable amount of cells. Most commonly encountered algorithms among earlier risk related work are based on:

- Dijkstra [106]
- A* [180] [106]
- Rapidly-exploring Random Tree [179]
- Ant Colony algorithm [106]

For a more in-depth review of different drone path planning algorithms readers are referred to the work of Aggarwal & Kumar [11].

In this section models have been discussed that can be used to quantify ground risks imposed by drone operations, whilst historical data is not yet available. Sensitivity analysis have shown that weight, population density and the failure rates are dominant predictors for fatality rates[148]. However differences still exists on how different factors and drone characteristics are taken into account. A literature review from 2017 emphasized the need for clearer documentation of assumptions in research on UAV risk models [225]. The divergence in base assumptions, especially when not documented well, prevents decision makers and regulators to determine the applicability of the proposed model on the specific concept op operations. Integrating these risk models into drone delivery problems is recognized to be important in future scientific research. Currently in drone delivery routing problems, integrating no-fly zones is already considered state-of-the-art[140].

4.6. Medical Delivery

In section 4.2 some general fields of application for drones have been discussed. The versatility of drones also translates to UAV's being considered for various use cases within the healthcare industry. Rosser et al. identified three applications where drones can add value in healthcare[194]:

- Public Health and Medical Surveillance
- Telemedicine
- Drones as Medical Transport Systems

The first category mainly concerns gathering health related data. This can range from assessing the number of people in danger resulting from disasters to detecting hazardous substances on the ground or in the air. Drones can also create reliable communication streams where these may (temporarily) be not available, in the context of healthcare this application is referred to as telemedicine. Using drone assisted telecommunication, medical experts can perform more advanced diagnosis at a distance and instruct people at the sight what to do. Even more innovative, are concepts where robots perform surgery on a remote patient, operated by a surgeon in a control centre, which communicate through drone assisted networks[96].
In this research we will focus on applications that consider the transport of medical goods with drones. Thiels et al. were one of the first to explicitly explore demand, feasibility and risks associated with UAV based medical delivery back in 2015[215]. They concluded that UAVs could be a particularly viable option for medical transport in situations of critical shortages. Industry experts state that medical transportation may hold the largest market potential, both within civil drone delivery context and drone applications in general[169]. One of the most relevant studies, investigating a drone based medical goods delivery system in Gothenberg, Sweden, focuses on assisting strategic decision making. Their findings are intended to be used by healthcare organizations considering the use of drones for medical deliveries. The suggested concept of operations regards an urban delivery system between three major hospitals, and is thus of limited scale, but qualitatively proves the high potential of a drone-based medical logistics system [141].
First the main advantages and disadvantages of this specific use case named in past literature is discussed. Next different proposed concepts of operations from studies most similar to that of the MDS project are presented and will provide better understanding how drones would actually be used. Finally some real world existing projects will be shortly covered.

4.6.1. Pros and cons

From different qualitative and feasibility studies considering delivery of medical goods by drones, often named pros and cons were identified. In the remainder of this section both qualitative and quantitative backing for these pros and cons are discussed. Having a good understanding on both benefits and potential downsides is crucial for decision makers to make well informed decisions. Additionally communities should be informed on both positive and negative consequences as well. Jeyabalan et al. state: "It would be unethical to implement drones for health projects based on the consent provided by individuals who have not considered the risks and fully understand the nature of these drones for health projects."[113].

Economics

The primary objective of most quantitative studies is to minimize total system costs. Some pros and cons that will be discussed later can also result in additional economic benefit in the end, however this paragraph focuses on cost reduction possibilities that result directly from transportation.
Ochieng et al. analysed the economic viability of UAS transport of laboratory samples in Liberia [161]. They found that drone assisted delivery was more expensive per transport compared to motorcycle based operations. However costs were relatively comparable, and the authors emphasize the effects of changing parameters on the resulting cost effectiveness. Having more reliable data on the lifetime performance will likely increase the relevance of results. Amukele agrees that these findings are hard to generalise, but emphasizes the importance of such head-tot-head cost comparisons.[14]
To hedge against the uncertainty of some drone and scenario parameters, Haidari et al. performed extensive sensitivity analysis[92]. Their model described an UAS vaccine distribution concept and compared the cost with traditional land-based transport. In contrast to the findings of Ochieng et al. they found that the UAS system to be on average 20% cheaper for most settings and circumstances.
A case study on the London blood supply chain, suggested that operational costs of current transport means

are up to three times higher compared to a drone based hospital distribution network [168]. Fuel specific costs could be reduced by almost 90% according to this study. The authors suggest that additional benefits may come from considering heterogeneous fleet, and an increase in overall demand levels. The dependency of economic viability on scale is confirmed by Wright et al. [234]. They state that combining different use cases into a single system can increase cost-effectiveness.
The work of Dhote & Limbourg on the Drone4Care project in Brussels that does consider multiple use cases, estimates total costs of the system[68]. They conclude that total system costs increase significantly when higher demand satisfaction is assumed. However no comparison is made with costs of current or alternative systems, which impedes putting the total cost numbers into perspective.
Although most research suggest cost savings using drones for medical transport, the few actual implemented projects have not shown cost reduction in practise. Ersson and Olsson state about UAS for medical purposes: "To fully understand the potential utility and obstacles that the system poses, more research is needed."[79]

Environmental impact

Although opposing opinions exist, the majority of literature and experts suggest replacing traditional delivery methods with drones reduces carbon emissions. However little to no studies exist analysing system wide differences, estimating total differences is recognized as an open field of interest[192]. Some studies were found more recently that try and fill this literature gap. A study that focused on comparing truck and drone based delivery suggested that a blended system, using both trucks and drones would be most beneficial[87]. The used approach was found to be most extensive in estimating both truck and drone emissions. However they recognized the dependency of the results on the assumed characteristics of the drone, which prevented having clear cut conclusions on environmental favourability of either truck or drone. Additionally there assumed delivery model, based on at home package delivery, is significantly different from hospital distribution models.
The relevant work of Otero Arenzana et al. suggested that a hospital delivery network using UAV's would indeed produce less CO2 emissions, even when production emissions were taken into account[168]. In their model CO2 emissions were converted into additional costs through a carbon emission cost parameter, that might be imposed by governments in the future. However the additional emission tax imposed costs contributed to less then 0.01% of total costs for a UAV based system thus most likely not impacting optimization results greatly. Additionally exact emission numbers and costs of the baseline scenario's were not explicitly mentioned. Since the relative share of environmental costs was not significant they were non distinguishable in provided figures. Instead of converting emissions into costs and minimizing total costs, one could provide the values of different evaluation criteria so decision makers can decide for themselves on the relative value of for instance reducing emissions.

Centralization

The main benefits of centralization in healthcare and BSC have been discussed previously in chapter 2 and chapter 3. Drone delivery enabling further centralization is named as a major source of potentially increasing system wide efficiency[141]. However quantitative studies that provide numerical insight in the effect of this enabling does not exist to the best of our knowledge.
Centralization benefits can be argued as most relevant for more developed healthcare industries, since their main objective is often making the system more efficient. Whilst most medical drone delivery studies have focused on increased accessibility of healthcare in less developed contexts. Two studies that cover the effect of drone enabled healthcare centralization in developed setting indirectly are covered next.
Analysis of the results on the case study of blood supply network in London conducted by Otero Arenzana et al., showed that with big hub capacity, the model preferred placing hubs at hospitals over blood banks[168]. This suggests that indeed a horizontal on-demand delivery system of blood products supported by drones, could save transportation costs in the end.
A model representing a full-scale drone logistics system, for centralization of a large Laboratory within Oslo University Hospital was created by Johannessen, Comtet & Fosse[114]. They stress the potential benefit of merging laboratories with duplicate facilities enabled by drone delivery. Data on current diagnostic demand and transport derived from the hospitals' history showed the vast amount of daily samples to be analysed. In their model both regular transport and emergency transport were introduced, initially transporting all incoming requests with flights on a regular schedule. If this would lead to samples taking longer then the maximum allowed 60 minutes, an emergency transport was conducted. Although no estimation on the costs of the UAS was provided, it did suggest cost savings between 10 and 20 Million euros annually by reducing

duplicate facilities. This small scale (transport between two hospitals) shows the potential of drone enabled facility centralization. The authors suggest that future work could investigate the effects of regular trips versus on demand transport, or a combination of the two.

Product quality

Ever since transport of biomedical products with drones have been proposed, concerns about the quality preservation during flight have been prevalent. So far many pros and cons discussed previously rely mainly on theoretical and modeling research to provide insights in possible effects. In contrast, several real life test have been conducted in order to see the effect of drone transportation on the to be transported goods. This section covers the results from these studies for different use cases, which to a large extend determines the suitability of the product for drone transport.
In 2015 the first tests were conducted to evaluate the effects of drone transport on diagnostic clinical laboratory specimens. Samples transported via small UAVs showed no significant differences compared to samples kept on the ground for routine chemistry, hematology, and coagulation tests[16]. A follow up research, looked at the impact of longer 3 hour flights, on the stability of biological samples. Most analytes showed no or small differences, only glucose and potassium tests showed significant biases. These biases were related to the duration and magnitude of temperature difference of the product during the flight, which led to the conclusion that long drone flights are feasible when environmental control measures are in place[18]. Both of these studies conducted real drone flights to obtain results, Johannessen et al. however simulated turbulence through a shaker creating vibrations[115]. Their findings on whole blood samples were inline with previous studies, meaning no negative effects could be observed. For plasma samples, which have been centrifuged and separated using gels before 'flight', test results differed significantly. This resulted in the recommendation not to perform centrifugation before transporting these samples via drone.
Blood products for transfusion purposes have been studied using real-life flight testing methods similar to that mentioned above. Amukele et al. found no adverse impact of drone flights on the quality of Red blood cell, apheresis platelet and frozen plasma products[15]. A more extensive study on red blood cell products in Japan, confirmed that quality is preserved during flight. Although a multi-copter drone was used during these tests, the authors are more concerned with external risk of UAV transport then with product quality when fixed-wing drones are concerned [238].
Hii et al. tested medicine quality after drone transport on insulin characteristics. For this particular case they found quad-copter drones to be safe for medicine transport. Since the amount of possible drone and medicine combinations is extensive, the authors propose 5 tests that should be applied when medicine transport by drone is considered[100]:

1. Determine safe flight range and time, considering the weight of the product and UAV characteristics
2. Performing medicine quality test post-delivery
3. On board environment monitoring of temperature, pressure, vibrations and g-forces
4. Ensuring medicine security within the supply chain
5. Understanding effects of drone failure during flight on product and environment

A 2021 study tested the effect of drone flights similar to Hii et al., but used both multi-copter and fixed-wing drones[160]. Vibrations were found to be less in the fixed-wing vehicles, although product vibrations depended heavily on the type of packaging used. Overall vibrations were higher then with road transport, but because these vibrations have significantly other frequencies current knowledge on medicine vulnerability to vibrations cannot be used. All samples past quality tests after flight, which reconfirms the thought that medical products in general do not deteriorate in terms of quality during UAV flights.

Although not yet considered in this research, initial findings suggest even organs to be save to be transported by multi-copter drones[202]. Since organ quality deteriorates when vibrations are introduced, the authors suggest fixed-wing flight to be less suitable. However the research from Hii et al. suggests that vibration in fixed-wing drones are less compared to multi-copter configurations[100].

Reliability

The first projects concerning drone delivery of medical goods are mainly located in regions with less well developed infrastructure. A main benefit of UAS in these regions is an increase in healthcare accessibility for the rural areas [79]. In more developed countries like the Netherlands, healthcare accessibility is already of sufficient level, and the added value of drones would not be in increased accessibility. Additionally projects that improve accessibility mainly consider delivery of medical goods directly to the patient, whilst this concept of operations proposes delivery to a medical institution. However related to the concept of accessibility is reliability. One might have good access to medical services, but if these services can not provide you with the right care because for instance no medical supplies are present, such system is not reliable.

Feasibility studies identify both risks and benefits in terms of medical good availability due to drone delivery. A reliable distribution is critical for the long term viability of any supply chain, but especially true when lives potentially depend on a delivery. Some state that drones increase reliability of the system because delivery times are more stable and predictable [141]. A simulation study by Haidari et al. suggests that vaccine distribution using drones reduces costs and increases vaccine availability, compared to land transport systems [92]. The authors state that the simplification of their model is one of the main limitations of their study. Limited availability of system wide operational costs are available, which is stated to be due to lack of large scale commercial implementation. However it can be argued that this lack of implementation is also due to missing reliable estimations on the long term effects of the big investments needed to create such systems.

The value adding character of drones in terms of product availability is dependent on the quality of the current infrastructure, terrain and remoteness of the area[79]. Due to increasing congestion in developed regions, the added value drones can bring in terms of reliable product availability is also relevant in these contexts.

Simulations on the possibility for laboratory centralization for hospitals in Oslo, showed the reliability of drone delivery times for sample transportation [114]. All occurrences where the maximum total time in the system was exceeded were due to delays in the laboratory or other in-hospital processes.

4.6.2. Concept of operations

In short the concept of operations suggested for the MDS projects is as follows. Both urgent and non-urgent transport of medical goods will be (partially) conducted by drones. Drones are stationed at or on top of medical centers it will distribute to and from. A control center will operate all drone operations from a single location 24 hours a day, 7 days a week. Three different use cases are considered namely blood products, diagnostic samples and medicine. For now transport to and from large healthcare facilities like hospitals and blood-banks is considered, but integration of smaller entities like general practitioners is seen as a long term objective. At the medical centers who are part of the system, drone supporting infrastructure is present as well as employees who are trained at handling the loading, maintenance and communication around the drone operations.

Although some studies have suggested a system that resembles the concept of operations proposed for the MDS project, no previous work was found that exactly matches. Dhote & Limbourg presented a study based on a Belgium project called Drone4Care which can be regarded very similar to the Medical Drone Service project in the Netherlands[68]. The authors investigated the logistical issues around an UAV network for biomedical material transportation. Although in the model no distinction could be observed, the proposed network is designed for different biomedical products like blood units, medical samples and medicines/vaccines. In the proposed concept of operation, a shipper makes an order at a centralized control center, which assigns the order to an UAV, based on all current network parameter values. After which the UAV flies to the pick-up location where the order gets loaded by personnel, who are able to track the drone using mobile applications. A similar process is conducted at the delivery location where the product is unloaded and its delivery confirmed to the control center. The possible locations of demand and supply, and therefor all transportation occurs between, hospitals, laboratories and blood transfusion centres, which is in line with the MDS concept. After delivery the drone returns to its base station, during the entire mission drones are allowed to stop and recharge at dedicated charging stations. Note that the location of base or charging stations do not have to correspond to the locations of medical institutions.

The goal of the study was to place these base stations, and the optional charging stations in order to minimise total costs. This network design problem was based on the work by Shavarani et al. who performed facility location problem for Amazon drone delivery in San Fransisco [205]. In such problem a large emphasis of the study is on the impact of the range constraints that come with drone use, partly because a quad-copter UAV

with a range limit of 23 km was assumed. This is a significantly more limiting range compared to that of the VTOL drones proposed for the Dutch project. Additionally the use of base and charge stations seems more rational in the Amazon delivery context, where a limited amount of warehouses need to be placed in order to serve demands that can be placed anywhere in the network. By contrast the MDS concept of operations suggests that drone-supporting infrastructure is placed at medical centers, reducing the need for additional supporting bases.
Otero Arenzana et al. who designed an UAV hospital delivery network for blood products, assumed a similar concept of operation[168]. The, to be placed, hubs function as blood product warehouses, from where deliveries are performed. However they assumed that hubs would be placed at existing hospitals or blood bank locations.
Additionally in both before-mentioned proposed concept of operations drones were forced to return to their base station after delivery which caused superfluous flight kilometers[68][168]. Removing this constraint will likely cause challenges in terms of UAV fleet imbalances, however it is believed that it will enable large efficiency gains in a more horizontal orientated supply chain. Increasing emphasize on how medical institutions could divide inventory and facilities so to benefit most from the capabilities of the UAS.

4.6.3. Implemented systems

In the past decades the first UAV-based medical delivery systems have been deployed at various places around the world. Some ongoing examples are discussed below as well as some planned projects.

Zipline

The first large scale medical UAS was implemented in Rwanda, where the local government partnered up with Zipline, a start-up from San Francisco, in 2016. Local spacing between medical centers is limited when considering the crow flies distances, however this is not reflected in road travel time because of indirect routes caused by the hilly environment. This in combination with a progressive local political regime created the ideal circumstances to implement these novel technologies. Zipline built a drone aided blood delivery system that has since proven to be very effective. In 2019, having delivered 2700 emergency and 8000 regular deliveries, access to rare blood products had already increased by 175 %.[145] Recently, having proven its capabilities in Rwanda, Zipline has expanded rapidly, first into neighbouring Ghana. However, partly helped by the pandemic, it has also started delivering medical goods in the United states and is planning to do so in Japan in the near future. Mainly because of these successes the company managed to raise another $250 million recently which increased their valuation to around $2.75 billion.[4] The rising valuation and financial backing by well known brands like Toyota, shows that these medical delivery drones are believed to be(come) commercially viable.

DHL

As a major logistics company DHL, as well as some of its direct and indirect competitors like UPS and Amazon, is interested in drone delivery not only for medical goods but for parcel delivery in general. The drone developed by DHL is thus not specifically designed for medical purposes, but has been used for such use cases successfully. First a (non medical) trial of the proposed UAS in the German region of Bavaria was successfully completed in 2016.[67]
Currently the drones are used to transport medical goods to Tanzania's remote Ukerewe island district of Lake Victoria. This real life implementation emphasizes the benefit of combining use cases, transporting medicines, blood samples and blood products meant for transfusion. Additionally it proves that small and more remote medical institutions can help a wider variety of patients locally due to the support of drones. Local satisfaction with the innovative system is expressed by the local commissioner: "We are very much satisfied by the service provided by these drones. We call upon other innovative companies to invest in such services".[2]

WeRobotics

This NGO, backed by among others the famous Gates foundation[5], aims at increasing local knowledge on novel technologies like drones, robotic and artificial intelligence. Recently it partnered up with a delivery drone provider named Wingocopter, in their Flying Labs project. The goal of the project is to provide hard-to-reach areas access to medical goods by delivering these goods via drones. The project has already run in Brazil, Democratic Republic of the Congo, Dominican Republic, Fiji, Nepal, Papua New Guinea and Peru.[1]

This approach of generating local knowledge and supporting locally led and owned projects might not lead to the most innovative implementations from a technological perspective. However it can support sustainability and affordability of the projects. It can be argued that, especially for developing countries where medical infrastructure is lacking, hiring western companies to install a medical delivery UAS is not viable.

Recently a lot of projects have been suggested distributing Covid-19 vaccines or other medical goods to fight the pandemic [214][185][173]. Although the pandemic has increased the interest and relevance of drone based medical deliveries massively, most projects encounter similar challenges as pre-pandemic projects. However the pandemic has stressed the importance and vulnerability of the medical supply chains.
As medical drone delivery has gained in attention recently and the first implemented systems have been running for a decent amount of time, little attention has been paid to how these have actually performed. Ersson and Olsson state in their literature review: "there are big gaps in research regarding the already implemented systems which contributes to uncertainties in the discussion about the potential of the technology."[79]

4.7. Conclusions

The use of drones have been proposed for a wide range of applications, even within healthcare they could provide value in several ways. The delivery of medical goods is considered to be an application that generates a lot of value for society. However several challenges have so far prevented large scale civil drone implementations in society. Governments are hesitant to introduce consenting regulations, since they are afraid for possible negative consequences. One of these potentially negative consequences that is often regarded as most prevalent, is the risk posed to people on the ground by drone operations. Since no historical data is available, theoretical models have been developed in order to quantify these risks. Next to general drone application challenges, concerns about system reliability are legitimate when the delivery of medical goods is considered. Other criteria that have been stated as important are the economics, environmental impact, and product quality preservation. Holistic approaches and models taking into account multiple objectives and criteria are needed in order to cover these different long-term consequences. However most drone related optimization research has focused on single and specific tactical or operational issues, increased attention should be paid to major and all-encompassing strategic problems. Although strategically orientated simulation models might not be able to estimate effects with high accuracy it can enable decision makers to weigh pros and cons more informed.
Both academics and industry have mentioned the high potential of drone based medical deliveries from both economic as healthcare perspectives. However little evidence exists that shows the benefit of UAV's over road or other transport modes. More specifically early research suggests that an heterogeneous fleet configuration might be more optimal then using only one mode of transport. Extending models to explore heterogeneous vehicle fleets is thus promising for future research on hospital delivery systems[168]. Similarly the enabling effect of drones on healthcare centralization and JIT delivery is still largely unknown in terms of its magnitude. For now one can only rely on the assessments of experts when considering the use of drones for medical delivery.

5
Road transport

In the previous chapter the possibility to distribute medical goods with drones was proposed. As mentioned little research exists that directly compares different modes of transportation. In order to do so not only knowledge on drone operations needs to exist, a better understanding on the effectiveness of traditional road transport is needed. Since often drone operations would replace emergency road transport, it is needed to further investigate the impact of these current emergency transports. A drone focused paper that considered medical good transport from a warehouse to a drone-deployment-station by road, estimated the distance land based vehicles to be 1.6 times the euclidean distance between warehouse and station[203]. The authors recognized this simplification may not represent real road networks well, and suggest changing this in future research. Johannessen et al. argue that current logistics has still room for improvement and state: "We conclude that comparing drone transport with existing solutions, the logistics may require substantial refinement if the true potential of drone transport is to be achieved."[114]

Currently in the Netherlands different medical goods rely on different transport operators to distribute products across the network. Sanquin ensures availability of blood products at medical centers by performing both standard and emergency deliveries from two central warehouses. In 2019, 1.570 scheduled deliveries were performed every week, an additionally conducted on average around 3 emergency deliveries daily [209]. Some medical goods, like for instance blood products, being of life saving importance in some situations, emergency deliveries are common in this industry. Although exact procedures differ between nations and transport providers, in general emergency deliveries mean that the vehicle will execute the delivery as fast as possible. In this process it can often violate traditional traffic regulations and can use other measures to warn other road users about their presence. Currently transport of all different medical goods is often conducted by different operators, whilst the proposed MDS concept of operations combines transportation of different goods in one system. Thus this literature study will not elaborate on differences and interactions between different operators.

This chapter describes the effectiveness of road based distribution of medical goods, focusing on research covering emergency vehicles. Pure optimization studies on ground transportation on similar problems as described in section 3.2 and section 4.4 are not covered in this literature study. In general it is concluded that observations on drone related optimization studies to a large extend also apply to ground transportation logistics. Focus in transportation science research has predominantly been on tactical and operational problems, like for instance vehicle routing problems. Strategic orientated problems, like facility location, has received relatively less attention whilst these kind of problems often concern large capital and time investment[10]. This could be due to the high degree of uncertainty inherent with long-term strategic models according to the authors.

Instead section 5.1 elaborates on how models can estimate the time needed to perform a road delivery. Especially when emergency deliveries are concerned regular travel time predictors are inapplicable. Experts from within the medical industry stress the problem and even potential dangerous consequences related to an increase in urban road congestion. Emergency transport of medical products by car or motor, often comes with additional permissions and allowances aimed at reducing travel time. However, measures like, higher speed allowances and priority right of way at crossings, are not able to fully mitigate congestion related issues. Additionally these measures might involve increased road risk. As discussed in the previous chapter, the risk posed to third parties by drone operations is a major concern preventing large scale adoption, therefor it is tried to quantify the risks of road transport enabling comparison of the two systems. These road related risks are covered in section 5.2.

5.1. Time

The response time of emergency vehicles is defined by the time interval between receiving the emergency information to the arrival of the vehicle to the desired location, and can be of life or death importance in emergency situations. Minimizing this response time can have high societal impact, and has been the topic of several researches worldwide. Little is known about emergency delivery of medical supplies specifically, however it is expected that findings on other emergency vehicles with priority of way like police, firetrucks and ambulances, are applicable on emergency delivery vehicles as well.

5.1.1. Theoretical findings

In route optimization problems for emergency vehicles, traffic networks are often represented as graphs. Weights associated with edges can either represent distance or travel time of that specific road segment. Thus, optimising will either find the shortest or the fastest paths. In both cases previous work has suggested several ways in which weights should be adjusted in order to represent real-life emergency vehicle scenarios. Brady and Park for instance, created a custom road network representation that includes roadway geometry, like lane count and construction work, to generate edge weights [45]. Additionally they labeled intersections as either having a stop sign, traffic signal or a pre-emption signal. By doing so a regular road network representation was adjusted to take into account possibilities for emergency vehicles to gain time.

Pre-emption refers to the ability of emergency vehicles to get priority of way at intersections. Probably the most well known example is the lights and sirens with which many emergency vehicles are equipped nowadays, but more advanced infrastructure may include traffic lights that respond to approaching emergency vehicles. Optimizing the usage of such responsive traffic lights has been studied with different approaches, mainly focusing on when and how the pre-emption should be triggered. In a recent study the problem of both conflicting pre-emption requests and overall traffic delay were tackled. Applying transit signal priority techniques was proposed and simulations suggested a reduction of 8% of total travel delay to be feasible [27]. Studies, on route optimization, pre-emption strategies or a combination of both, are research based and thus the feasibility of real-world implementation is still unclear [107]. Supported by the fact that although considerable amount of research is conducted on decreasing response time with promising simulation results, actual response-time has not decreased so far.

5.1.2. Practical findings

The highly dynamic situations and unpredictability encountered in real-life emergency vehicle transportation have motivated some researchers to take a more pragmatic approach. Different studies have looked at how actual emergency vehicles trips compare to predictions, or driving with or without sirens. Petzäll et al. investigated 30 emergency ambulance transportations, and re-rode the same route at the same time of week under normal driving conditions [175]. They found an average travel time in urban environment of 8.0 and 10.9 minutes for emergency and non-emergency driving, a 26.6% reduction. In rural areas emergency driving was found to be 23.6% faster compared to normal driving.

In Thailand the effect of lights & sirens (L&S) on pre-hospital times in emergency medical services were investigated in a recent study. They found an average transport time of 11.1 and 17.1 minutes for L&S and non-L&S rides respectively [21]. However the suggested 35% reduction in transport time should be put into perspective, since this study took a patient perspective, also including non-ambulance transport. Driving behaviour of road users might be different when transporting people in emergency situations. Also it has been argued that when transporting patients, as was the case in the above mentioned papers, driving behaviour is eased to increase patient comfort and ability of paramedics to treat the patient. Since the use cases covered in this research do not involve patient transportation, differences in response time are more relevant. With response time being defined as the time it takes an emergency vehicle to reach the scene of the accident after getting the distress call.

Two similar studies from 1998 and 2001, looked at the response time differences for ambulances using warning lights and sirens compared to vehicles traveling without. The first study conducted in the urban part of an US metropolitan area with a population of 378,000, found a 38.5% reduction in response time when using lights and sirens[102]. The second paper found a 30.9% reduction when analyzing the differences in the rural area of Becker County, Minnesota[103]. However the method of both studies used a vehicle not using lights and sirens directly following the ambulance with sirens. The authors acknowledge that the second vehicle might have benefited from the so called wake effect left behind by the ambulance. This wake effect covers events that are the result of the passage of an emergency vehicle, like for instance other cars moving over [155].

A more reliable method was used in a study conducted in Syracuse in 2000, where they re-rode the route that an ambulance had driven during an emergency response situation. The rerun was conducted at a similar moment in terms of road occupation and other influential conditions. Using this method they found a 26.5% reduction in response time, since this study was conducted in a similar environment as the before mentioned, this lower value is most likely due to the lack of wake effect benefits.

However a study by Rehn et al. on rapid response vehicles in London found a bigger difference[190]. The suggested 54.9% reduction in response time might be partly due to congestion regularly experienced in London traffic.

This problem of congestion and the resulting unreliability of ambulance dispatching time, was one of the main drivers for Poulton et al. in their attempt to model and predict ambulance movement [177]. They used an extensive data set of a 2-year period from the London ambulance service, containing ambulance gps data of over 2.3 million L&S journeys. The proposed algorithm was found to be the first when it comes to predicting travel times for emergency ambulatory vehicles based on a data-driven approach. When they compared recorded trips from the data set with estimates retrieved from the Google Maps Distance Matrix API, they found that that the API overestimated travel times by a factor of 1.4 and 1.5 for ambulance and first response units respectively. The size of the data set enabled Poulton et al. to develop the Blue Lights Road Network, a graph representation of London's road network. The edges within graph, representing road segments, have weights associated with 5 different speed-metrics of increasing complexity. With metric 1 and 2, using a standard speed profile for all roads or road profiles respectively, are similar to what is used in common routing engines. Metrics 3 till 5 use historic data, altering for location and time of week, resulting in better estimates.

Regarding patient transportation, the use of ambulances versus helicopters has also been studied in the context of Pennsylvania's trauma response. Historical data suggested a threshold distance from the hospital beyond which the use of helicopters was faster under different conditions. On average this threshold was found to be 7.7 miles or 12.4 km, however this threshold was shown to be highly regionally dependent, with values ranging from 5.4 to 35.3 miles[51]. This may support the idea that a hybrid system using both air and ground travel might improve overall delivery performance.

5.2. Risk

When considering risk, a major advantage of using UAVs in emergency transport, as encapsulated in the name, is the absence of a crew in the vehicle. This is often qualitatively mentioned in papers on both disaster relief situations and regular emergency delivery of medical supplies [215]. In section 4.5 research on the risks involved with UAS operations were discussed. In order for decision makers to make well informed decisions, they should be able to both qualitatively and quantitatively compare options and potential risks. Little or no research has been found that specifically covers risks involved with ground (emergency) transportation of medical supplies. In this section we will focus on both road risks in general and increased risks caused by emergency situations.

In order to quantify road risks, often metrics like injuries or fatalities per kilometer or mile are used. When considering injuries, one has to define a lower bound in terms of severity from which people are considered injured after an accident. An internationally adopted tool to indicate severity is the Abbreviated Injury Scale (AIS) which is developed by the Association for the Advancement of Automotive Medicine[28]. The AIS can score all individual injuries of a casualty, the Maximum Abbreviated Injury Scale (MAIS) takes the maximum of all AIS scores to indicate the severity of injury of the casualty. Both the AIS and MAIS range from 1, representing a minor injury, to 6 indicating the most severe injuries. The Netherlands were one of the first to adopt these scales to casualties of road accidents. Since 2010 casualties from accidents with a MAIS score of 2 or higher which have not died within 30 days after the accident are considered as seriously injured [43].

5.2.1. Regular road risk

Road accidents and measures to decrease them have been studied and discussed in society a lot, which is non-surprising when considering the societal impact and costs involved. In the Netherlands costs of road crashes in 2009 were believed to be 2.2% of the gross domestic product[228]. In this literature report only the observed statistics will be discussed, since research on the causes and other factors are considered non-

Year	2015	2016	2017	2018
Fatalities	621	629	613	678
MAIS 3+	6000	6400	6500	6900
MAIS 2	14400	14800	14300	15300
Fatalities per billion vehicle kilometers	4.6	4.6	4.4	4.8
Injuries per billion vehicle kilometers	152.1	153.8	148.7	156.5

Table 5.1: Fatalities and injuries caused by road accidents in the Netherlands

relevant for this particular research. Road infrastructure and behaviour greatly differs from country to country, resulting in different statistics and limiting cross-country relevance of findings. A benchmark that compared road safety of 10 European countries showed not only the differences in metrics used per country, but also performance differences when compared equally[206]. Additionally the authors emphasize that, instead of only considering fatalities, serious injuries caused by accidents should be taken into account when measuring road safety.

In the Netherlands the institute of scientific research on road safety called SWOV gathers data from different sources in order to derive the performance in terms of road safety. Their publications mostly measure performance in terms of total numbers of both injured and fatalities. Similar to industry standards this is converted to a risk rate using total kilometers driven by road users. These numbers are obtained from International Traffic Safety Data and Analysis Group (IRTAD), which tracks these for a range of countries, and used for the rates presented in Table 5.1 [162]. In the Netherlands accidents are mostly tracked by the Central Bureau of Statistics (CBS). The average number of traffic accident fatalities in the period 2015-2018 has been 635 per year, which makes the Netherlands, when corrected for population, one of the top performing countries in Europe [6]. In terms of injuries a rising number of total injuries caused by road accidents have been mainly due to increased numbers of the more severe injuries of a MAIS score of 3 or higher[43]. The above references statistics have been summarized and converted to a per km rate in Table 5.1. Total injury rate covers all injuries of MAIS score 2 or above. Exact results, especially for rates, differ slightly between publication dependent on sources used and assumptions made. The SWOV report for instance uses the average number of fatalities of the 2015-2018 period, but divides this by average number of motor-vehicle kilometres of only 2015,2016 and 2017, resulting in a 5% difference in average fatality rate compared to the results presented here[43].

5.2.2. Increased emergency risk

In section 5.1 it has been described how use of pre-emption methods indeed decrease travel time significantly. To do so often regular road regulations are violated, which might cause dangerous situations by itself. This section focuses on research on this effect, with the aim of quantifying the risk of emergency transport.

Emergency transport of medical goods being rare, data and studies on the involved risks are non-existent. However, ambulances and other emergency vehicles have been studied in this context, providing the most reliable insights into the risks involved. The applicability and reliability of generalized ambulance data should be put into perspective. Watanebe et al. stated in 2019: "The relative rarity of ambulance crashes hampers single-system analyses: smaller systems with low response volumes could go several years without a crash, even though the underlying crash rate and association with lights and sirens use could be the same as in larger systems. Even relatively large systems could have too few crashes to detect any effect of lights and sirens use, and data from extremely large systems with high response volumes are not necessarily generalizable to other systems."[226]. Although ambulance crash statistics should be viewed as estimates, they provide the best and most relevant indicators of emergency medical goods transport-risks. First findings from global studies are discussed, next statistics for the Netherlands will be presented.

Global findings

Still used in practise almost everywhere around the world, the utility of emergency transport is questionable. Murray and Kue state: "A review of the available literature surrounding ambulance L&S use, patient and provider safety, and ambulance design has consistently demonstrated improved response and transport times, but fails to show any clinically significant impact on patient outcomes. It has, however, demonstrated unfavorable effects on the safety of patients, emergency medical services providers, and the general public during ambulance L&S response operations."[155]
An extensive study on ambulance accidents between 1987 and 1997 showed that emergency ambulances crashed more often in emergency use compared to non-emergency use [120]. Additionally it was shown that most fatal injuries happened with people in the back of the ambulance. This is non-surprising given the conditions in which both patients and medical personnel find themselves in the back of an ambulance. In 2002 Maguire et al. were one of the first to study the occupational fatality rates of emergency medical services personnel [142]. They found that transportation incidents were the leading cause of occupational fatalities, within an occupation that had an overall fatality rate more then twice that of United States averages. The difference in transportation specific fatality rate, 9.6 and 2.0 per 100.000 for emergency medical services workers and national average respectively, was found to be even bigger. The authors suggested that more attention and effort had to be spend on tackling this issue, since these people literally risk their lives to save that of others.
To facilitate comparison between years, countries and transport modes, one needs to look at incident, injury or fatality rates. San-Fransisco's ambulances in a 27 month period prior to 1994, showed statically different injury rates between non L&S travels and L&S travels[201]. 22,2 injuries per 100.000 travels were recorded during emergency ambulance trips, versus 1,46 out of 100.000 non-emergency travels. A similar analysis of the 2016 National EMS Information System from the United States showed that the use of lights & sirens in the transport phase of ambulance rides increased crash rates from 7,0 per 100.000 rides to 17,1/100.000[226]. The metric in which risk statistics are expressed vary greatly between studies. Emergency vehicle risk exposure is often not expressed in risk per mile or time driven, which is common among normal road risk estimates. This is likely due to a lack of necessary data to derive these numbers reliably [152].
To take into account the entire societal risk involved with road emergency transport, it is not enough to only include crashes where the emergency vehicle is directly involved. Clawson et al. were the first one to recognize this need for broader perspective in their paper published in 1997[56]. Surveying 73 paramedics in and surrounding Salt Lake City, they found the number of, what they referred to as, wake-effect collisions to be as much as four times higher than collisions where the emergency vehicle was directly involved. The limitations of their methods make for limited reliability of the actual numbers, however it shows the need for further research and attention into potential third party risks involved with these wake-effect collisions.

Dutch statistics

In the Netherlands the "Insituut Fysieke Veiligheid" (IFV), has studied accidents involving emergency vehicles over the last decade. Their most elaborate study from 2014 analysed emergency vehicle accident data from the period between 2010 and 2013 [90]. IFV differentiates the three main categories of emergency vehicles in most of the statistics, police vehicles, firetrucks and ambulances. Considering the small sample sizes of the individual crash statistics, some numbers are derived from the combined dataset. Although most emergency driving time-gain is won by having priority at crossings, this comes at a cost. 75% of accidents involving emergency vehicles occur at crossings, for ambulances specifically this number is slightly higher at 79%. Unique for this study is that the amount of trips and the average trip length using L&S have been used to derive risk rates per million driven hours. The total hours driven, over the studied period of 4 years, along with the number of fatality and seriously injured, and the resulting rates are given in Table 5.2.

	Ambulance	Police	Firebrigade	**Total**
Total driven hours driven with L&S	**222.037**	193.193	24.483	**440.713**
Number of emergency vehicle drivers involved in deathly accident per million driven hours	**9**	10	39	**11**
Number of emergency vehicle drivers involved in accident causing major injuries per million driven hours	**59**	67	78	**64**

Table 5.2: Emergency vehicle accident rate 2010-2013 in the Netherlands

In 2018 and 2020 IFV published updated statistics that only stated accident totals, not as a per hour rate[75][76]. The total amount of accidents involving an emergency vehicle and that of ambulances specifically are presented in Table 5.3. The numbers from the years 2010 to 2013 have been used to derive the before mentioned rates. Ambulance specific numbers for the years 2016 and 2017 were only stated to be 55 in total, which is similar to the total of 2018 and 2019. A rising trend can be observed for both ambulance specific and total emergency vehicle accident numbers.
In order to see if and or to what extend this is due to an increase in total driven hours with L&S by ambulances, a similar calculation to the one used in Table 5.2 was conducted using data provided by the Dutch ambulance operator for the period 2016 till 2019 [31]. Resulting in an total hours driven with L&S by ambulances of 291.164 in the 2016-2019 period, a 31% increase compared to the 2010-2013 period. Whilst the total accidents only increased by 9% when the same periods are compared. Deriving the same rates as provided in Table 5.2 including the number of major injuries and fatalities was not possible due to changes in published statistics.
Due to the small sample size, individual events have large impacts on the statistics resulting in variability in the numbers over the years. However when analysing aggregated numbers over larger periods it is argued that the provided rate of emergency vehicles involved in fatal or major injury accidents per hour is the most realistic representation of reality.

	2010	2011	2012	2013	2016	2017	2018	2019
Ambulance	20	24	22	35	-	-	27	28
Total emergency vehicles	38	49	58	56	68	80	99	66

Table 5.3: Number of accidents involving emergency vehicles in the Netherlands

The latest study also confirmed the hypothesis that emergency vehicle risks also applies to emergency transport of medical goods. As two drivers of Sanquin, the blood bank in the Netherlands, were involved in a recorded accident[76].

5.3. Conclusions

Current delivery of medical goods mainly relies on different forms of road transportation. Often different products are distributed by different operators, and specific procedures and systems vary greatly among different operators and countries. In order to compare road and air transportation means fairly, the risk and time it takes to transport a medical product should be estimated for both instances. Because emergency transport of medical goods is a niche and little/no specific data exists, findings on other emergency vehicles like ambulances are assumed to be most relevant.
Different studies comparing response times of ambulances and quantifying the effectiveness of pre-emption methods have suggested various time saving percentages. The most elaborate study relying on the biggest dataset of trips in an environment that can be considered similar to the road system of the Netherlands found

a consistent 33% reduction in travel time. Also this is in accordance to the average of all conducted research in this field combined.

Although travel time is reduced this comes with significant increase in risks created by these emergency vehicles. An inconsistency is identified in how regular road risk is measured and expressed, countries as well as year on year comparison is therefor difficult. Combining different sources risk related rates have been found to be around 4.5 fatalities and 150 MAIS2+ injuries per billion vehicle kilometers in the Netherlands.

Direct comparison of Dutch statistics on regular road risk and that of emergency vehicles is impossible due to different metrics that have been used. Regular road risk is expressed as a rate per kilometer, whilst emergency vehicle use is measured in time thus resulting in a accident per hour metric. The IFV has used an average speed of 45km/h to convert the regular road risk rates to an per hour metric in order to compare the two more directly [90]. For all types of emergency vehicles they found that emergency vehicles rates of both fatalities and injuries were more then 30 times higher then regular road vehicles. It should be noted that this comparison is based on multiple rough assumptions that make the exact factors of risk increase for emergency vehicles, ranging from 36 to 156, non accurate. However it does clearly indicate that driving with L&S in the Netherlands indeed increases the risk involved greatly. Additionally both initial qualitative research and Dutch experts have indicated that so called wake-effect incidents might pose an even greater risk to third party road users. All in all risk of human injury can thus relatively safely be stated to be a factor of 30 bigger for emergency delivery compared to regular road transport.

6

Modeling techniques

In the previous chapters mainly the results of previous research on the relevant topics have been discussed. Additionally requirements related to what needs to be taken into account when deriving these results have been elaborated upon. In some examples from previously discussed work the used method that led to the results have been briefly touched upon. In this chapter different methods that can be used to solve the problems and answer the questions posed in chapter 2 till chapter 5 are discussed in more detail.
The focus of this chapter is on techniques and methods used in quantitative studies, frameworks and methods used in qualitative and feasibility studies are considered out of scope. First the observations related to past research in terms of methods used as well as requirements for new studies will be discussed in section 6.1. Next, with these requirements in mind, different modeling environments are elaborated upon in section 6.2. Actual modeling methods that use these different environments are discussed in section 6.3. Different solutions methods that are used to solve the models are presented in section 6.4. Finally a more detailed evaluation is presented on the methods that might be considered as most suited in section 6.5.

6.1. Requirements

Analysis of the covered research as well as observations and recommendations stated in these papers, have led to several reoccurring trends and suggestions for future work. This section covers these trends and describes the resulting requirements posed on modeling methods. Note that detailed elaboration on the actual methods is covered later in this chapter, this section aims to determine the criteria and requirements needed to evaluate different methods on their suitability. This section focuses on trends and characteristics that may set apart the needs for a model, specific to the proposed concept of operations of medical goods drone distribution, of other models.

Uncertainty

When one want to model any real-life system effectively, one needs to take into account the uncertainty of several elements within the system. Although humanity has the tendency to prefer controlling everything, the current pandemic is an example of how this is still very much unrealistic and it could be argued as non desirable. Acknowledging that randomness is an inevitable part of life leads to the conclusion that models without any uncertainty might not be a good representation of processes in life. Especially in the healthcare industry systems should not only perform optimal in average operating conditions, at least equally important is its ability to handle changing conditions. In subsection 3.3.2 it was described how 'lean' supply chain practices, may increase efficiency but can also increase its vulnerability to disturbances. Studying how a system performs under different scenarios and for instance fluctuating supply and demand, is very much needed when considering distribution of vital medical goods. Using only average values might have highly undesired consequences. After all one can still drown when crossing a river with an average depth of 30 centimeters. In order to evaluate the effectiveness of a system to handle outliers, uncertainty is a pre-requisite in the model that represents the system.
The most straightforward example of a source of uncertainty within a medical goods distribution system is the fluctuation in supply demand. In section 2.1 research entirely focused on optimizing bloods supply showed the difficulty to so reliably. Many studies on healthcare inventory systems have often incorporated some kind

of supply and demand fluctuations already because of the importance within this specific topic, but future models are advised to replace relatively simple methods of introducing uncertainty with more complex and practical methods [196]. When inventory policy is not the main focus in healthcare facility location studies, incorporation of uncertainty becomes rarer. Whilst the authors state in their literature analysis that noticed this scarcity: "uncertainty is an important modeling factor which should not be simplified" [12]. Incorporating fluctuations in demand is also recommended by Prodhon & Prince in their evaluation of location-routing research [183]. Techniques and methods that can cater for uncertainty in demand and more realistic data-quality is thought of as a requirement of future research into medical deliveries using UAV's [80].
Variability in supply and demand have been widely adopted among BSC literature, however it was noticed that this is not the only source of uncertainty relevant in this context. Fluctuating transportation times are relevant in a field where transportation is already lacking in attention[176]. In drone operations different sources of uncertainty are also very much present. For instance the susceptibility to weather conditions is recognized as an important factor of uncertainty that future research might consider[169].

Complexity

Uncertainty is often considered as one element how models become more complex, however a need for models to become more complex is identified more widely in several fields of study. Additionally as multiple fields of study are combined this in itself increases the complexity, for instance by introducing multiple modes of transport into the model. The need for decision makers to be able to weigh pros and cons quantitatively directly implies that all pros and cons to be weighed should be expressed and integrated in the model. More holistic approaches have been mentioned multiple times in previous chapter as relevant for future research.
In drone aided healthcare distribution combining different use cases and products into a single model has been identified as promising when cost-effectiveness is required as discussed in subsection 4.6.1. Or as Saha & Ray put it in future healthcare inventory management research modeling suggestions: "An integrated model considering all types of healthcare product may open new avenues for further investigation." [196].
This merging of different use cases will as a result increase the complexity of the model. Adding more parameters, and thus complexity, is also posed as a future model requirement for models specifically designing a drone aided medical distribution system[68].
The 2017 literature survey by Ahmadi-Javid stated: "It seems that the healthcare facility literature has mostly tended to use a modeling approach that results in simple models, which can be optimally solved using existing optimization solvers within reasonable times , but sacrifices or dilutes the validity of the models. This shows that there is much room for operational research experts to use more advanced modeling approaches."[12].
In BSC research it was recognized that by papers often only covering single or a limited amount of echelons models become more simplified[176]. This limits the ability to analyse interactions between echelons as well as the impact of individual actors on the system as a whole. Thus even when a single actor or element of the system needs to be optimized, it can be argued that in order to do so effectively one needs to model the entirety of the system that is somehow influenced by that element.

Scalable

As systems and their models become more complex, often this negatively impacts the scale that a model can handle. In the previous paragraph combining of use cases was already stated as beneficial for economic viability, this could be seen as a dimension in which the system can scale. However other ways systems can scale are for instance demand and geographical coverage. In order to ensure the relevance of a method for cases where a large scale implementation is needed, the model needs be able to handle this scale. The ability of different models to do so is discussed in section 6.3.
One trend that has been observed to ensure methods being capable of handling large scale problem instances is moving from central coordination to decentralized control. "As more and more drones, wheeled robots and other autonomous vehicles are deployed in the logistics system, routing will inevitably become too complex to perform centrally. Central dispatch is especially impractical when traffic conditions, such as corridor congestion and collision avoidance, are explicitly considered. Future work will also focus on extending the proposed framework to allow for decentralized decision-making, more tolerance for uncertainty and improved computational parallelism, therefore adapting the framework to production-scale systems." [135]

Multi-objective

Historically many optimization studies have focused on optimizing for a single metric, which is often found to be costs. Because of the rising complexity of systems that should be reflected in the models that repre-

sent them, more parameters and metrics become available in these models. We have seen how issues like sustainability and risks have gained attention amongst various industries and are more often desired to be taken into consideration by decision makers. The involvement of multiple stakeholders in an increasingly complex environment requires transportation optimization research to develop multi-objective models[10]. Additionally the authors state: "To be successful, transportation researchers will need to rethink traditional ways of modeling, particularly objectives, and also boldly explore new problems."
In section 3.1 different metrics that can be used to evaluate the (positive) impact of an system on healthcare have been listed. It shows that one should not only formulate a problem more holistically but also take a more holistic approach in what should be aimed for. Dhote & Limbourg agree that more holistic approaches to medical goods drone delivery concepts should be developed using models that reflect this multi perspective approach. They state: "As a research outlook, this work could be further developed by considering the impact of other attributes of transport such as quality of service, reliability, accessibility, safety, security, flexibility, or environmental impact."[68]

Strategic

In previous chapters a lack of strategically orientated research was identified in both drone and medical fields. Although strategic mainly refers to the type of problem rather then the model to solve it, it does impact the requirements and criteria to which a methods should be evaluated. Agatz et al. states in one of three themes identified as relevant for addressing big challenges in transportation problems: "Measuring the impact of long-term investments often requires models that consider long planning horizons, which in turn necessitate recognizing uncertainty."[10] It should be noted that this uncertainty is different from what has been discussed at the beginning of this section and mainly refers to long term uncertainty of parameters. At the end of section 4.1 it was explained how drone design and capabilities is likely to change over time. Due to this uncertainty in model parameters obtaining optimal solutions becomes less of a priority since its relevance will be mitigated once conditions change. In section 2.4 it has been stated how in the context of disaster relief, optimality is less important then ensuring a well-working distribution system under future conditions that are not fully known. Strategic decision making might be considered to be subject to similar future unknowns, leading to prioritisation of other criteria then optimality.
Similarly, whilst most traditional models aim to serve all demand, strategic models might benefit from not being constrained to this need. In determining where to place launch facilities in the proposed medical drone distribution network of Brussels costs increased significantly when the so called demand satisfaction rate rose [68].
Additionally when considering long term planning, often one needs to decide on several strategic decisions simultaneously, since little is pre-defined. Ahmadi-Javid, Seyedi & Syam suggest the following: "Integrating location decisions with other strategic, tactical, or operational decisions in healthcare facility location models"[12].

Adaptability

In addition to what has been stated in the previous paragraph, the long term uncertainty of some system parameters also require adaptability of the model to ensure long term relevance. Models that are hard to adapt will be of limited use to decision makers considering systems not identical to the initial configurations of the model. Ideally decision makers can access a tool that is adaptable to the specifics of considered system. Several studies have shown the dependency of for instance economic viability to the environment and other location specific factors. Ochieng et al. state, having compared UAV and road based laboratory sample delivery: "The issues raised in this study suggest that cost- effectiveness of UAS depend on a country's geographical and health-system design context. For example, South Pacific islands with high road densities might still need UAS to serve isolated islands, even if the intra-island road networks are reliable."[161] Closer to home, the study on the proposed use of drones for biological material transport in Brussels suggested analyzing other regions as well, to be able to distinct context variations [68].
In designing a drone assisted hospital delivery network, the dependency of costs on operational parameters was shown to be significant. In Figure 6.1 the total costs of the designed hospital distribution system for the London test case is shown for changing values of three operational parameters. The figures emphasizes the need for an adaptable model when representing a system of which its operating conditions are still to a large extend unknown.

In this section criteria were stated that can be used to evaluate different modeling techniques on their suitability to the purpose of the proposed research. It is acknowledged that different criteria listed above are

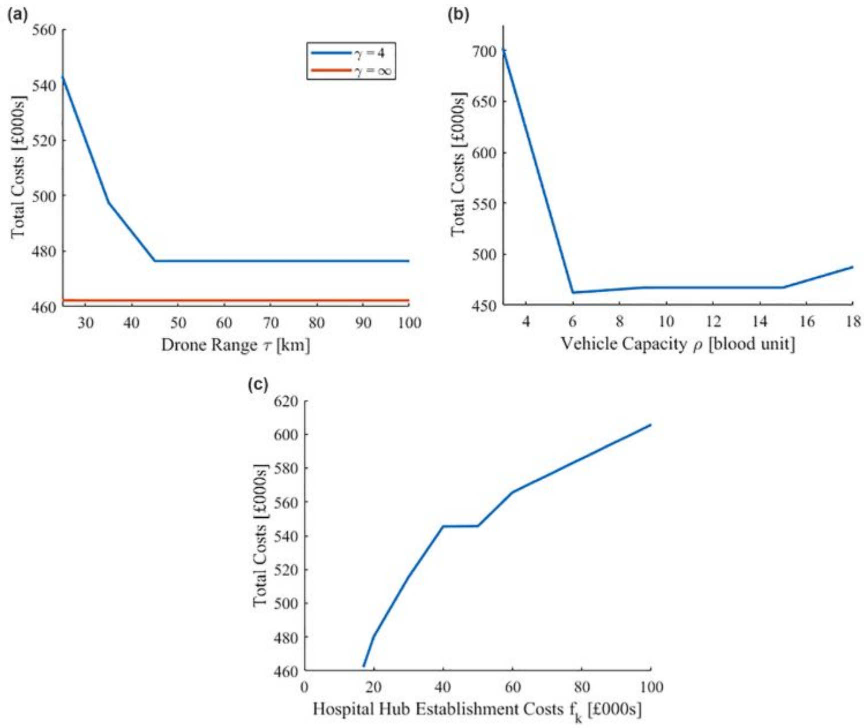


Figure 6.1: Result sensitivity to model parameters. Source: [168]

often related and not mutually exclusive. As will become apparent later in this chapter, some criteria lead to trade-offs, because methods can improve models to accommodate for a criteria by conceding on others. The next three sections will cover different aspects of models and methods used in prior research and how they relate to the criteria posed here.

6.2. Modeling environment

Mainly to incorporate different degrees of uncertainty, different modeling environments exists. In this section different environments used in past studies are distinguished. On a high level environments can be either deterministic or uncertain, in which the latter can be further divided into three groups, namely: stochastic, unknown and fuzzy[176]. Below the different environments are briefly discussed and finally evaluated for their suitability along the criteria posed in the previous section.

Deterministic

When all parameters within the modeling environment are known, these models are considered deterministic. These models are often considered as unrealistic since these are a simplified representation of real life. Nevertheless, when a large environment is modeled, deterministic models can provide insight when comparing a large number of complex scenario's. Bruno et al. used a deterministic environment to optimize a facility location problem within the BSC [48]. Using known parameters the proposed model is capable of supporting decision makers in the network design of real-life big and complex scenario's. A case study of the Campania Region in Italy, with originally 22 blood centers, shows that simplified deterministic models can benefit real life applicability by its ability to handle scaled problems.

Since the need to take uncertainty into account in healthcare has been expressed multiple times in previous literature, Ahmadi-Javid, Seyedi & Syam were surprised to find that the majority of non-emergency healthcare facility location problems were modeled in a deterministic environments[12].

Also drone aided medical distribution models are currently dominated by deterministic models. The facility location model, used to determine optimal drone facility locations for the London hospitals to be supplied by drones, considered deterministic demand levels[168]. Transforming the model so to become stochastic was stated as an important next step of this research. Similarly Dhote & Limbourg used a deterministic demand model, and compared different scenario's in terms of drone range, minimum demand satisfaction and the obligation to return to the base station after delivery[68]. Incorporating demand uncertainty was named in their conclusion as possible enhancements of their model.

Stochastic

In contrast to what has been discussed in the previous paragraph, uncertain environments contain parameters that have no fixed value. Stochastic, which is covered in this paragraph, unkown and Fuzzy, which will be discussed in the following paragraphs, are 3 commonly used methods to introduce these uncertain parameters.
In Stochastic models, which are most common in BSC problems, the probability distribution of the uncertain parameters are known, and often described by a Poisson distribution. Blake et al. used a known Poisson distribution of both supply and demand to simulate the effects of reduced shelf life for blood products on the BSC [41]. This proved effective as the network model of the production and distribution was validated on a case study in the Canadian province of Quebec. Mestre et al. were one of the first in 2015 to adopt stochastic modeling in hospital network planning, and emphasized its usefulness to such strategic problems: "Planning hospital networks requires making long-term decisions under uncertain conditions about the future configuration of the system. Nevertheless, extensions of stochastic location models for planning hospital systems considering uncertainty appear to be relatively new, unlike in other research fields such as supply chain management."[151] The stochastic demand used in their model is derived from expectations about future population size and utilization rate, both subject to uncertainty.

Unknown

When the probability distributions of uncertain parameters are unknown we non-coincidentally include these in the uncertain environment subgroup labeled as unknown. Uncertain or random parameters in this group can be either continuous or discrete. Although the exact probability distribution of the parameter is unknown, often a pre-defined interval is defined when continuous parameters are included in a model. Where as scenario approaches are the standard for modeling discrete unknown variables[89].
The latter scenario based approach is often used to assess the robustness of for instance a supply chain network design. In a study that aimed at making retail supply chains more future ready, numerical results showed that the a model relying on several unknown future scenarios outperformed the deterministic model in designing a resilient network[200].
In another paper, determining optimal blood donation facility locations, continuous unknown parameters were used to model uncertainty in demand and transportation costs. This study showed that costs, represented in the resulting objective function values, become higher as one models more conservatively [188]. In this context, being more conservative means being able to cope with more extreme values of the unknown uncertain parameters.

Fuzzy

The last method to incorporate uncertainty, discussed in this literature review, is using fuzzy numbers. The concept of fuzzy numbers was fist introduced by Zabeh in 1975 and later elaborated upon by Dijkman et al. in 1983 [239] [69]. In fuzzy modeling environments uncertain parameters are represented by fuzzy numbers and constraints as fuzzy sets. Violation of constraints is allowed in the latter, and the extend to which the constrained is adhered to is represented in the membership function of the constraint [198]. This use of fuzzy goals and sets can also be referred to as flexible programming, since is might be useful when the goals of decision makers are vague and unclear. Alternatively, possiblistic programming is considered when fuzzy numbers are used to manage lacking information on model parameters [89].

When the four mentioned environments are evaluated for its applicability to the problem posed in this literature study, we conclude that deterministic environments are less fit due to their inability to incorporate uncertainty. The suitability of the other environments is argued to be dependent on the quality of data available about the uncertain environments. If for instance the demand of certain medical goods can be represented by a normal distribution stochastic environments might be the best fit. When a discrete number of uncertain future scenarios need to be compared by decision makers unknown models are preferred. Fuzzy methods are assessed as unlikely to be useful since they are less fitted to evaluate reliability and robustness to disruptions.

6.3. Models

In the previous section different modeling environments that can be used to incorporate uncertainty were discussed. This section will elaborate on the actual models used to mathematically represent systems. Often the modeling environments are a key differentiate of different models, thus naming and model characteristics are often inherited from the environment they are modeled in.
In this section models are classified in one of two groups, either optimization or simulation models. As will become apparent later the latter can also be used for optimization purposes as well, however the models in these groups differ in their mathematical formulations as discussed next. Although maybe somewhat confusing it is has been chosen to stick to more traditional group naming so that this work relates better to previous literature. Rather then giving an extensive overview of all techniques, the aim of this section is discuss the main characteristics, benefits and drawbacks of different approaches.

6.3.1. Optimization

The group of models covered in this group are referred to as optimization since the goal of the mathematical model of the system is to optimize it. This is somewhat trivial, especially in optimization research however it was found that no other consistent group naming exists. We further distinguish this group into model(families) most encountered in literature.

Integer programming

For problems modeled in a deterministic environment, linear programming-based approaches are most commonly used as they are relatively straight forward. Ganesh et al. used a linear programming (LP) approach to model a vehicle routing problem of the delivery and collection echelon of a BSC. This simplified representation still resulted in a NP-hard problem that was solved using a more innovative solution method, combining heuristic and meta-heuristic approaches [85].
More often mixed integer linear programming (MILP) models are encountered, in which some (decision) variables are forced to be integers. This is the model most frequently encountered among the various fields of research covered in this literature review.[12] [89] [176]
The UAV network design problem in line with the Drone4Care program in Brussels used 4 MILP models of increasing complexity. In Equation 6.1 until Equation 6.4 their first model is presented. In which the first equation states the objective of minimizing total system costs[68].

$$\min\left(\sum_{i=1}^{n}\sum_{j=1}^{m} f_i\left(\alpha\left(d_{ij}^{p}+d_{ij}^{d}\right)+\beta d_i\right)x_{ij}+\sum_{j=1}^{m} b_j w_j\right) \tag{6.1}$$

$$\sum_{j=1}^{m} x_{ij} = 1 \forall i \in N \tag{6.2}$$

$$\sum_{i=1}^{n} x_{ij} \leqslant w_j \sum_{i=1}^{n} f_i \forall j \in M \tag{6.3}$$

$$w_j, x_{ij} \in \{0,1\} \forall i \in N, j \in M \tag{6.4}$$

The purpose of providing the mathematical formulation is not to go into detail describing it, thus the parameters are also not further explained. Rather it shows the simplicity of such models, with just 4 equations one can already create a rough drone assisted medical delivery system model. Admittedly the other 3 models were more elaborate by adding or altering constraints. This is a basic fundamental of these model, each element within the concept of operation needs to reflected with a linear formulation in a constrained and/or the objective function, inside the representing model. It is argued that this limits the ability of the model to represent more complex systems since non-linear relationships are present all around us, for instance when wants to model the drone range as a function of its payload.[80].
To mitigate this problem some models introduce non-linear relationship in integer programming models by first linearizing the non-linearity. The mixed integer nonlinear programming (MINLP) model proposed by Mobasher et al. was first linearized using auxiliary integer variables to a MILP before optimization was conducted [153]. Other MINLP models are combined with other programming techniques like stochastic programming covered in the next paragraph.

Stochastig programming

When modeled in an stochastic environment MILP and MILNP methods are almost always combined with other optimization techniques. Shapiro et al. give an elaborate overview of different stochastic programming (SP) techniques used on models with uncertain variables [204]. Chance constrained programming (CCP), for instance, can be used to convert a model with constraints including uncertain parameters related to blood inventory levels, to a deterministic counterpart [158]. Using CCP, rather then always being enforced, constraints have to be adhered to with a particular probability.
Supply chain design decision-making often knows different phases, namely strategic, tactical & operational decisions. Two-stage stochastic programming (TSSP) having a similar distinction makes it a popular method in design problems including uncertainties [89]. During the first stage parameters are uncertain and exact values unknown to the decision maker. Strategic decisions on for instance facility locations are made during this initial phase. When the values of parameters become known in the second stage of TSSP tactical & operational decisions can be made on the basis of this increased knowledge. For instance routing and transportation can be optimized, taking the facility location (outcome of the first phase) as a fixed input to the problem. Hamdan and Diabat used this technique to minimize the number of outdated units, system costs and blood delivery time, for a BSC with four echelons [95]. During the first stage the amount of mobile blood centers in the collection echelon is decided, whilst the second stage determines inventory related strategies.
If more stages are added to the model these models are referred to as multi-stage stochastic programming (MSSP). Similar to TSSP at each stage more is known about the realization of the uncertain parameters, which, together with decisions from earlier stages, is used as an input to make new decisions. Strategies in MSSP models may not use realizations of parameters from the future when making decisions, strategies need to be non- anticipative [74]. It is shown that when a MSSP approach is used on a supply chain design problem, the model becomes highly complex and difficult to solve for large scale applications[240]. Although MSSP approaches might be better in representing real life systems, the increased model complexity limit usability for decision makers. Note the difference between system and model complexity, whilst representation of a complex system is desired, complex models are not necessarily beneficial and are often even disadvantageous.

Robust optimization

MILP problems modeled in an unknown environment, in which the probability distribution of uncertain parameters is unknown, are often combined with a robust optimization (RO) approach. In a RO approach one needs to make a trade-off between robustness of the solution or that of the model. Where robustness of the solution refers to the degree in which optimality remains under different input scenarios and robustness in the model suggests feasibility of the different scenarios[110]. If uncertain parameters are discrete, specific scenario's can be used and evaluated, whereas continuous parameters the pre-defined range discussed earlier is used. By varying the cost associated with the violation of constraints in a RO objective function, this trade-off can be altered in both directions. A solution for a platelet supply chain design problem, preventing demand under-fulfilment in all possible scenarios was shown to be significantly more expensive then a less robust solution[78]. RO is recognized to be effective in evaluating to which extend solutions can handle disturbances in Location-routing problems[183]. Thus it is not surprising that RO models are relatively often encountered when designing supply chains with some kind of uncertainty[216].
However it should be noted that robust optimization is often combined with an integer programming model and thus inherits most benefits and downsides of these models.

Other optimization models

An approach that is less widely applicable and therefore less frequently encountered in literature, are queuing models (QM). In research conducted together with Sanquin, the organization responsible for blood collection in the Netherlands, it was used to improve donor experience by reducing waiting times in the collection echelon [219].
Civelek et al. evaluated different inventory policies by modeling the related problem as a markov decision process (MDP). In order to have a manageable state action space, simplifications were needed that might hinder real life representation accuracy [54].
Fuzzy programming was already elaborated upon when the fuzzy modeling environment was discussed in the previous section. Often fuzzy models are first transformed into regular mathematical models which in turn are then optimized. A big difference of fuzzy compared to stochastic models, is the ability of fuzzy methods to handle complex probability distributions[109].

It is concluded that the optimization models and accommodating methods discussed above are currently most widely spread among literature. It is found that more complexity and uncertainty is added in the models by adding more constraints and (uncertain) variables or making the constraints or objective function itself more complex. The increasing amount and rising complexity of constraints, variables and objective functions has resulted in the need to develop more sophisticated solution methods, which will be discussed in section 6.4.
Multiple objectives can be simultaneously optimized for, but this is mostly done by transforming a multi-objective problem to a single-objective one, which is called a scalar method. Less often pareto approaches are implemented in which the model is aimed at obtaining the pareto front. These two methods comprise the vast majority of models that implement multiple objective, however both do not significantly change the underlying model characteristics and thus the models score at other criteria discussed in section 6.1. For an elaborate review on different methods to deal with multi-objective models one is referred to the work of Zajac & Huber [241].
Optimization models are created to find optimal solutions which limits the possibility of strategic decision makers to evaluate and weigh different solutions. Stochastic and RO models do provide decision makers better opportunities to do so, however comparing results to specific scenario's and evaluate personally created solutions remains difficult. Additionally optimization can sometimes be somewhat of a black box where analysing elements within the bigger system is difficult.
Finally these models, especially simple ones, are relatively adaptable by simply altering constraint or objective function parameters. However this adaptability is again limited by the difficulty of these models to adapt to increasing complexity. Integrating new, case specific, constraints becomes non-trivial as the model grows.

Some research relying on traditional optimization methods have incorporated simulation tools mainly to validate their findings. However the optimization model is still at the base of their research, in contrast next section will cover research where simulation is the main mathematical model used.

6.3.2. Simulation

The second and final flavour of mathematical models discussed in this literature study is simulation. In contrast to the optimization models, the primary purpose of these models is to imitate a system mathematically as realistic as possible instead of optimzing it. This can be an existing system or a proposed new system. This section provides a short overview of three simulation techniques commonly encountered in healthcare and drone transportation research. Note that, similar to the previous section, the different techniques discussed below can and are often combined when creating simulation models.

Discrete event simulation

In a Discrete-Event Simulation (DES) the state of the model is changed every time an event happens, in between events the model state does not change. Therefor a model can 'jump' directly to the next event after having finished altering its state, alternatively one can make fixed jump in times. Bélanger et al. developed a DES model to compare 4 different ambulance fleet management strategies[39]. The model archichecture is shown in Figure 6.2 and includes the four main simulation components as well as the three input databases. It shows how different simulation components are combined to create a single model, which can be adjusted individually. The component referred to as 'Simulation Engine' drives the discrete event simulation by going trough the chronologically ordered list of events. The developed simulation tool enabled the authors to perform an in depth comparative analysis with the aim of quantify pros and cons of the different strategies. They explain there model choice by stating: "Simulation can help in dealing more adequately with different stochastic aspects inherent to emergency medical services that cannot be addressed easily in the formulation of mathematical models." The mathematical models named here by the authors refer to what is categorized as optimization models in this literature study.
In BSC research on the effect of transshipment only two papers were found using a simulation approach, both opting for a variation of discrete event simulation techniques[242][22]. The latter one by Arani et al. highlights its use fullness when considering how to deal with uncertainties, and suggest future work should continue in the direction of simulation.
In transport related applications the event of a vehicle departing is followed by an event of the same vehicle arriving somewhere else, thus the actual movement of a vehicle is not part of a DES model[24]. Additionally DES as a stand alone model is best fitted for operational or tactical problems[77].

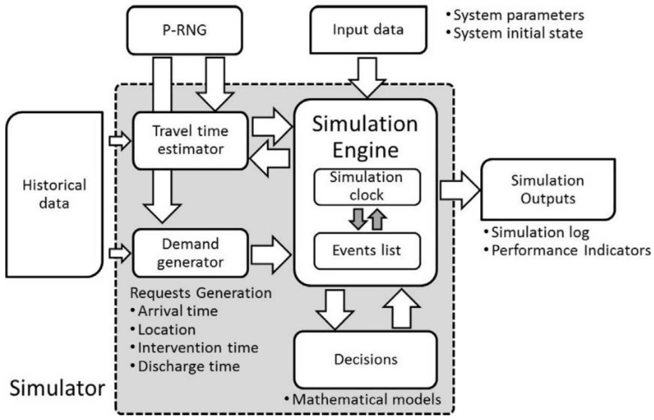


Figure 6.2: DES simulation model architecture of Bélanger et al. Source: [39]

Agent-based simulation

When one want to model the behaviour of, and interaction between, individual actors within a system, one can develop an Agent-Based Simulation (ABS) model. By adding multiple of these self regulating agents into a model, one can represent a system 'bottom-up'. A model can thus be scaled by simply adding more agents into the model, however modeling all agents and possible interactions may be a time consuming process.
Aringhieri, Carello & Morale used an ABS for similar purposes as the DES model of Bélanger et al. described in the previous paragraph [24]. Their model existed of two agent types: "Operation Centre" and "Ambulance". Ambulance agents were either of the "standard" or "smart" type, the latter was able to start a new mission before having returned to their base. This ability to change the destination of an ambulance whilst en route distinguishes ABS from DES based models where such flexibility is not possible.
The use fullness of ABS to compare different vehicle fleet configurations, including innovative types like drones, was emphasized recently by Palanca et al.[172]. Their ABS tool enables thorough evaluation of different urban mobility systems, which have become increasingly complex. The authors state another benefit of their ABS tool to be its ability to be altered to new configurations or scenarios.

Monte carlo simulation

Monte carlo simulation, which implies re-running a simulation for a set amount of times, is well suited for systems that contain uncertainty. Input variables can be randomly created from a pre-defined probability distribution at each simulation run. Johannessen et al. created a simulation model of a large-scale laboratory sample drone transport system, and concluded that the system has the potential to save cost and improve service time[114]. In order to come to this conclusion the authors simulated the complete transport system for 10.000 times and looked at both the average and extremes of the results.
Ochieng et al. took a similar approach to compare the economics of labatory sample delivery by motorcycle versus drone[161]. A base scenario relying on motorcycles only was compared with 9 drone scenarios in which drone range and lifespan was varied, all scenarios were simulated 10.000 times using monte carlo simulation. In this study no optimization of the fleet configuration was conducted, rather the model provides a ball park estimation on the economic viability of the proposed system.

A main benefit of simulation is its ability to reflect complex and uncertain systems. Figueira and Almada-Lobo state: "the core advantage of simulation is its ability to deal with complex processes, either deterministic or stochastic, with no mathematical sophistication."[83] Many models are found to be modular in their architecture, which enables adding or altering single elements relatively easy. Additionally simulation models can support strategic decision makers by enabling extensive analysis of different scenario's and quantify both benefits and drawbacks of different system configuration. Analysis can be performed on the system as a whole but more in depth analysis of single elements is also possible, especially in ABS. For these reasons using simulation approaches is encouraged in inventory management literature for complex systems that cannot be solved analytically[196]. Similar opinions, arguing for simulation models, exist in other industries, El Raoui et al state: "Stand-alone optimization models cannot overcome the complexity because they are usually built on a very abstract level, neglecting the dynamic behavior of real-world supply chain systems."

[77].
Monte carlo simulations are, although requiring simulation of a single configuration a large amount of times, well fitted to cope with uncertainty in systems. Most DES and or ABS models can be scaled relatively easily, with the added benefit of ABS to enable even more flexibility in ways individual actors can me modeled.
Simulation does not by itself search for an optimal solution, which makes it difficult for decision makers to evaluate the potential, which in turn can lead to the design of a sub-optimal system. This major drawback of simulation models have been tried to overcome by combining simulation models with optimization algorithms. This and other solution techniques are described in the remaining sections of this chapter.

6.4. Solving method

In subsection 6.3.1 different methods were described that enabled describing a system mathematically in order to optimize it. However this mathematical representation does not generate knowledge on its own, to do so the model still has to undergo the actual optimization process. Several techniques that are aimed at obtaining optimal decision variables, and thus solving the model, are described in this section.
Alternatively the simulation models described in subsection 6.3.2 can be of added value as is. Comparing different pre-defined scenarios using simulation is by some already considered a solving method and referred to as Statistical Selection Methods. More advanced methods have been created that are aimed at combining the advantages of simulation models with techniques that strive for optima, which is the topic of section 6.5.
Because developing efficient solution methods is often not part of the covered papers, many researchers use commercial software in order to find solutions for their proposed models. In more than half of supply chain design research commercial solvers are invoked, because of the progress made by these solvers to solve problems fast[89]. The drone assisted hospital delivery network proposed by Otero Arenzana et al. used the CPLEX commercial solver on an Intel Xeon E5-1650 with 64GB machine[168].

Exact

Exact algorithms are capable to find the exact optimum for relatively simple models. Examples of such algorithms that have been encountered in literature are: ',Branch and Cut'[121], 'Euler Method'[157] and 'Bender's decomposition'[166]. These algorithms will not always find the exact optimum within the desired time, instead it can provide the bounded-error which states the interval in which the solution will be. This directly highlights one of the major disadvantages of these solution approaches, as models grow in complexity exact algorithms often take (too) long to find a solution. Ahmadi-Javid et al. claim that several healthcare facility location problems are NP-hard, elaborating by stating: "These are problems with no known polynomial-time exact solution algorithms. It means that the time required to exactly solve an instance of these problems may increase very rapidly as the size of the problem instance grows, often well beyond any reasonable time frame." [12]. Pirabán et al. state something similar about blood supply chain problems: "Exact procedures can only solve models for small-sized instances within a reasonable computation time." [176]

Heuristics

To overcome the lacking ability to find solution for large models by exact methods, heuristic methods were introduced. Heuristic techniques are more pragmatic in the sense that they primarily aim at finding a feasible solution rather then the optimal. Agatz, Bouman & Schmidt developed a route-first, cluster-second procedure to solve a drone and truck traveling salesman problem [9]. First they construct a solution where no deliveries are performed by drone, which creates a regular TSP. Having found a solution they start assigning deliveries to drones, using a fast greedy heuristic, and an exact partitioning algorithm based on dynamic programming. Whilst the first option is faster, the latter guarantees finding the optimal solution for the TSP solution found in the first step.

Meta-heuristics

Heuristic methods often require some knowledge about the to-solve problem in order to generate a feasible solution, however this knowledge is not always present. Meta-heuristic (MH) techniques do not require any problem specific knowledge in order to find solutions, which generally makes them more generally applicable. "Meta-heuristics are applied to I know it when I see it problems. They're algorithms used to find answers to problems when you have very little to help you: you don't know beforehand what the optimal solution looks like, you don't know how to go about finding it in a principled way, you have very little heuristic information to go on, and brute-force search is out of the question because the space is too large. But if you're

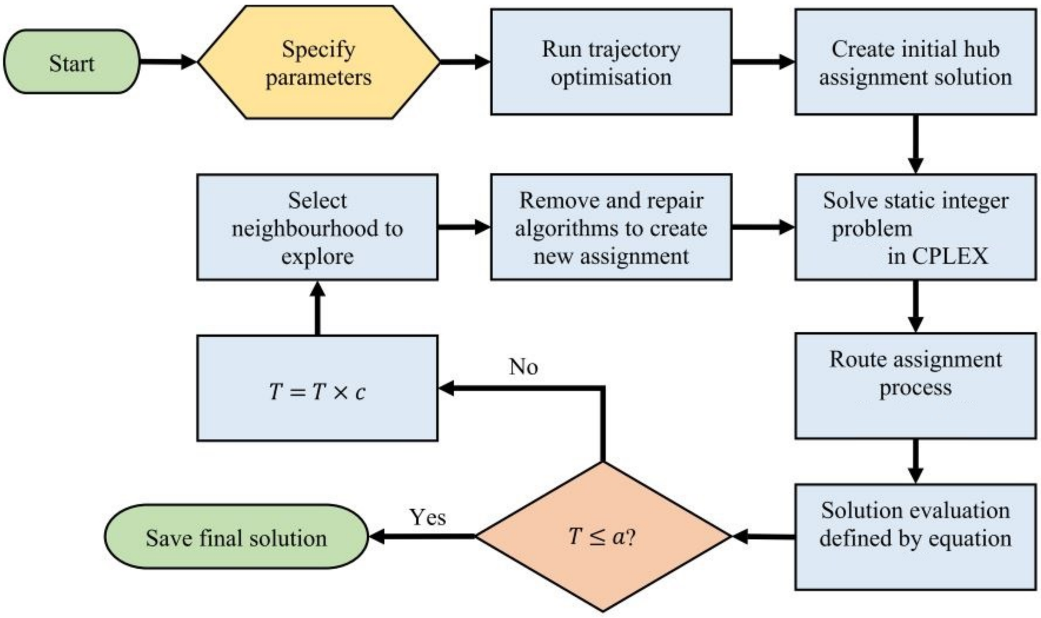


Figure 6.3: LNS meta-heuristic solution approach. Source: [80]

given a candidate solution to your problem, you can test it and assess how good it is. That is, you know a good one when you see it." [138]
Over 100 different meta-heuristic algorithms exist, all with their own characteristics and use cases. The simplest meta-heuristic technique is random search, in which random model configurations are tested and the best result, found within the time the algorithm is run, is returned.
Escribano Macias, Angeloudis & Ochieng used a metaheuristic solution algorithm to solve their optimal hub selection for rapid medical deliveries model[80]. Their model consisted of two stages, first optimizing the drone trajectories of the different routes to make them as energy, cost and length efficient as possible. After this stage, which can be considered as pre-processing, the optimal location of the warehouses and UAV itineraries are modeled in a hub selection-routing problem. A custom Large Neighbourhood Search (LNS) metaheuristic algorithm was created in order to find the best solution of this complex problem. This algorithm navigates through different 'neighborhoods' of the search space where it finds an optimal solution, by randomly moving to another neighbourhood sticking to local optima is avoided. Their solution approach is visualized in Figure 6.3, where the "temperature" (T), "cooling rate" (c) and "absolute temperature" (a) together define the progress, speed and duration with which the algorithm is run. The algorithm found better solutions compared to Simulated Annealing (SA) and bi-level SA, two other meta-heuristic algorithms, whilst taking less time to do so. This emphasizes both the effectiveness of meta-heuristics to optimize large problems as well as the importance of using fitted algorithms in order to produce the best results.

Above mentioned solution techniques have originally been developed in order to find solutions for the optimization models described in subsection 6.3.1. Increased model size and complexity have caused exact algorithms to be incapable of computing results in reasonable time. To ensure solution finding, priority for optimality is moved more to feasibility in the developed heuristics and meta-heuristic methods. These more advanced solution approaches can mitigate some disadvantages of optimization models like those related to scale and solving complex models, however adding complexity and adaptability of models remain major cons to the use of these models for the posed problem.

6.5. Simulation-optimization

In many fields of research like healthcare logistics and supply chain management, quantitative studies have used either optimization or simulation approaches as discussed in section 6.3. The solving methods described above were thus only used in studies adopting optimization approaches. However, to combine the advantages of the different approaches and mitigate their individual downsides, simulation-optimization (S-O) methods have increased in academic popularity in recent years. Note that S-O can be considered a generic term that is used differently in a wide range of contexts. S-O frameworks can be further categorized based on for instance the interaction structure between simulation and optimization, the purpose of simulation and search method. Four main simulation purposes can be distinguished as follows:[83]:

- **Evaluation function (EF)** - iterative procedures that use simulation to evaluate solutions
- **Surrogate Model Construction (SMC)** - methods which apply simulation for the construction of a surrogate model
- **Analytical Model Enhancement (AME)** - approaches making use of simulation to enhance a given analytical model
- **Solution Generation (SG)** - methods where a simulation model generates the solution

Whereas the first two purposes originate most often from simulation research, the latter two rely more on analytical optimization models and thus are often from optimization backgrounds. Since most drone and healthcare logistics problems covered in this literature study have been mainly studied by optimization researchers, this is likely to have caused AME and SG approaches to be the most common S-O approaches in these fields. An example of this optimization focused approach is that of Osorio et al. who took a solution generation approach to improve BSC performance by better matching the blood products and group quantities to the demand [165]. In this study a DES model was used to generate input for an integer linear programming optimization algorithm aimed at optimizing daily decision making. It was shown that, by using a combination of Simulation and Optimization techniques, the complexity and uncertainty of the BSC could be analysed more effectively. It enables analysis of different aspects and special features within the system through one methodology. Resulting in the ability to reduce the overall quantity of blood that needs to be collected.
Next to the simulation purpose but somewhat related is the distinction in hierarchical structure, which defines the relation between simulation and optimization within the model. The main four flavours defined by Figueira and Almada-Lobo are:[83]

- **Optimization With Simulation-Based Iteration (OSI)** - in which iterations of simulation runs are performed as part of system optimization.
- **Alternate Simulation—Optimization (ASO)** - simulation and optimization modules run alternately and in each iteration, either both simulation and optimization run completely or both run incompletely.
- **Sequential Simulation—Optimization (SSO)** - both modules run sequentially in which both simulation or optimization can start.
- **Simulation with Optimization-based Iterations (SOI)** - where the overall model is a simulation model, and in all or part of iteration, optimization model is called to compute some parameters.

Martins et al. also took a SG approach, in which they adopted an SSO hierarchy, to the problem of redesigning the supply chain network of pharmaceutical wholesalers[144]. They support their choice for a S-O method with the following elaboration: "Because a wholesaler activity is very time sensitive, with multiple orders taking place at the same time and in a large scale, modeling the different operations and their relationships in one mathematical programming model would be very complex and lead to an intractable model. In these types of systems, simulation is a popular approach, since it deals with complex flows with no mathematical sophistication. On the other hand, by using solely simulation models, the number of decision scenarios is rather limited, and hence the optimization can be compromised. Therefore, in order to truly optimize the wholesaler's network and at the same time obtain a clear image of the impact of implementing a new design, both from the operational and marketing points of view, this paper develops an optimization-simulation approach." In Figure 6.4 the interaction between the optimization and simulation model used by the authors is presented. Note that in this sequential scheme an MIP optimization model is used to make the strategic and tactical network design problem decisions. Next the simulation model replicates stakeholder activities and thus computes additional operational indicators like delays. The results from the simulation model are not used as input to further optimize the strategic decisions in the MIP model, which causes the SSO hierarchy. Thus strategic decisions still rely on the full mathematical representation of the system in an optimization model, this solution generation approach is therefor argued to not fully exploit the benefits of combining simulation and optimization. Further integration, which in literature is often referred to as hybridization, is encountered more frequently in studies with an OSI or ASO hierarchical structure. Putting it differently, the above mentioned examples of S-O usage are although rare, still relatively simple since the level of S-O hybridization is low, a lot of room for improvement is thus observed.

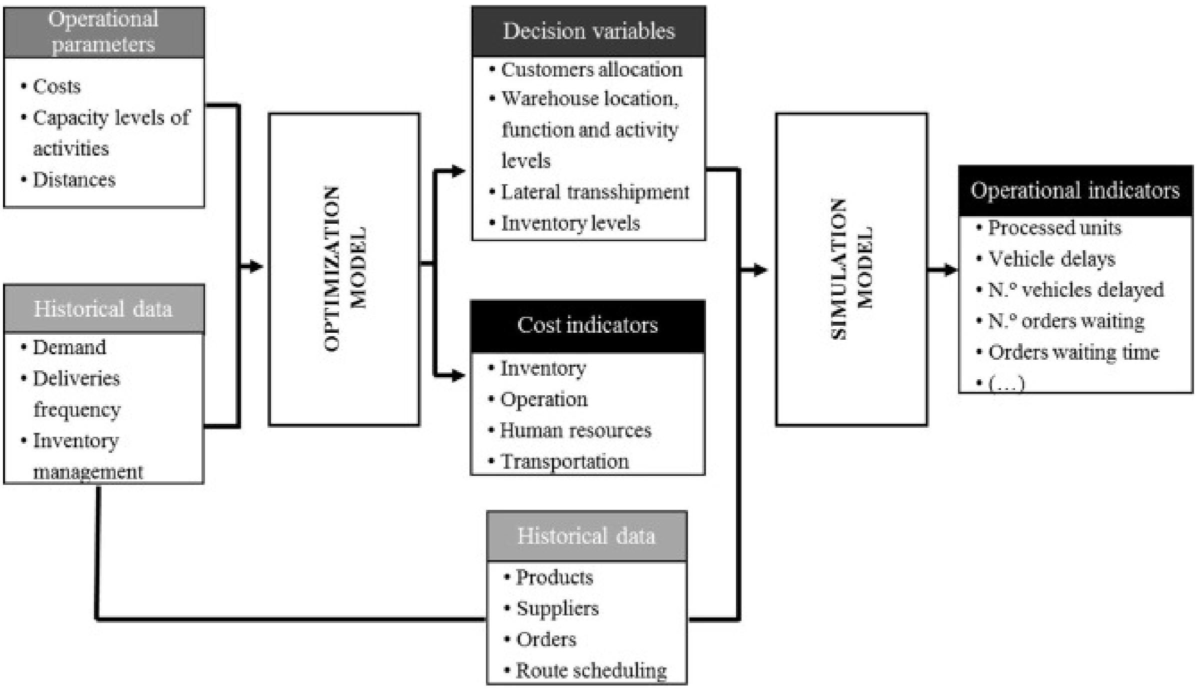


Figure 6.4: Example interaction scheme between optimization and simulation model. Source: [144]

Focusing on simulation based approaches, recall the first two simulation purposes named earlier, the general simulation optimization problem can be defined as:[83]

$$f(\theta) = Y[F(\theta,\omega)] \tag{6.5}$$

$$g(\theta) = Z[G(\theta,\omega)] \geqslant 0 \tag{6.6}$$

$$\theta \in \Theta \tag{6.7}$$

In this definition θ represents the input variables to the simulation model, and Θ being the domain of possible values of these variables. With ω being a sample path of the simulation, which causes the simulation outputs F and G being the objective function and constraints generated by the simulation model respectively. These are thus dependent on both the input variables, which are controllable, and random stochastic processes within the simulation. Finally Y and Z are statistical assessments of the simulation outputs.
As shown by El Raoui et al. this EF simulation purpose (SMC approaches are more complicated) is most often combined with OSI hierarchies[77]. The authors argue that for strategic supply chain design problems where an analytical model is difficult to construct an OSI hierarchy using, Statistical Selection Methods (SSM) or Meta-heuristics (MH) are best practices. With SSM being most fitted for problems having a discrete and limited solution space, where a limited amount of pre-defined scenario's can be compared extensively. MH methods, are better fitted when one aims at finding (near) optimal solutions in problems where Θ consists of a continuous range of input parameters.

A main advantage of S-O methods in supply chain design is its ability to study system reliability and resilience. However in supply chain design studies it was noticed more frequently that this increased ability to study the sustainability and resiliency of supply chain design enabled by S-O methods was not yet fully utilized as of 2016[178]. In the following years S-O methods were sparsely used to design and assess resilient

supply chain networks. More hybrid S-O approaches were found to be particularly useful for such applications because (1) it can better represent real-world uncertainties and the potential effects of disruptions on the system; and (2) besides solely measuring the risk, resilience and costs of system configurations, one can actually optimize for these system characteristics [216].
Next to the need for increased S-O integration other trends in S-O approaches have been identified that are in line with was found as interesting for future research for drone assisted medical delivery systems in this literature study. Juan et al list among others the following relevant S-O trends:[119]

- Multi-objective optimization
- Increased system complexity
- Use of innovative simulation models

Hunter et al. provide an introduction on multi-objective simulation optimization problems, and acknowledge the increasing the amount of objectives makes the problem often harder to solve [108]. The latter two points can be achieved by taking a more simulation based approach rather then the more commonly used optimization based option.

6.6. Conclusion

The dynamics around a future drone assisted distribution system of medical goods imposes several requirements on methods that try to model such system, in order to assist strategic decision making. The dependency on a reliable medical distribution system has become increasingly clear lately and different modeling environments that can incorporate uncertainty have become more relevant. Whereas different optimization models can include uncertainty, using these modeling environments, they often lack the ability to represent complex and scalable systems. Additionally optimization methods provide less insight in internal processes and dependencies, which is argued to make them less fit for supporting strategic decision makers. By contrast simulation methods were found to better fit the criteria, however not by itself searching for optimality. Monte Carlo simulation techniques can provide the desired insight in the resilience and sustainability of systems under uncertainty. DES jumping from one event to another, is less taxing on computing resources, however internal processes are more difficult to include. In contrast ABS 'bottom-up' models enable more in depth analysis of internal processes and emergent behaviour. It is expected that one needs to combine different simulation techniques in order to best meet posed criteria.
The suitability of different methodologies on criteria similar to the ones listed in section 6.1 have been visualized by Juan et al.[119] and is presented in Figure 6.5. The criteria named 'Modeling'in the work of Juan et al. refers to a criteria similar to what is referred to as the complexity criteria in this literature study. Here we can (again) observe the suitability of simulation and simheuristics (which in the work of Juan et al. is defined similar to what is described here as S-O methods) in dealing with the different criteria posed by the stated problem supporting the conclusion preferring a simulation based approach.

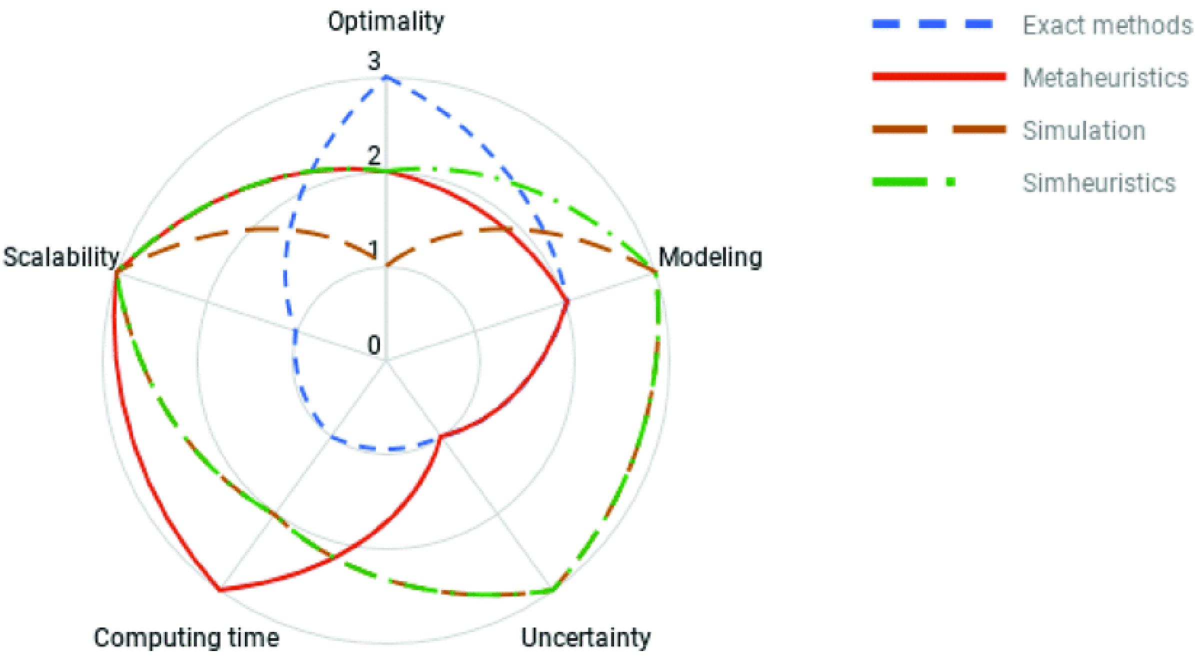


Figure 6.5: Comparison of methodologies Source: [119]

Whilst these simulation based methods have not been observed widely among the relevant fields of study, they are recognized as relevant directions of future work. Ahmadi-Javid et al. state as one of their suggested future research directions: "Using the simulation approach for modeling healthcare facility location problems which cannot be mathematically modeled or their mathematical models cannot be solved efficiently."[12]
Computing power having increased rapidly in recent years, S-O methods have gained in popularity among researchers in the last decade. Within the S-O methods covered in this literature review, more simulation based approaches like EF and SMC are preferred because of similar reasons to what has been stated as the benefits of simulation. In the field of BSC Williams et al. observed that simulation is mostly used as support of the mathematical models [231]. Using simulation as a primary tool is not yet used widely, and holds potential according to the authors. This fitness of simulation based S-O methods is confirmed for general supply chain optimization research by Pourhejazy and Kwon who state: "The main purpose of an S-O framework as a solution approach is to solve large-scale mathematical problems in a stochastic environment. According to the present review, analytic model enhancement and function evaluation types of simulation-based optimization frameworks are well suited to overcoming the complexities associated with solving large-scale, stochastic, multi-objective and nonlinear problems"[178].
OSI and ASO hierarchical module structures are found to be best fitted and most common for these simulation oriented approaches. The simulation module of such method can strongly resemble that of a stand-alone simulation model. In terms of optimization, SSM methods are preferred to enable in depth comparison of different scenario's. Since this approach provides decision makers with the statistical differences among multiple criteria between these different options, decision makers can weigh the criteria themselves leaving them with better opportunities for assessment. Although officially stated as an S-O method, little optimization is done in SSM approaches, however having the benefit of not needing to weigh different objectives among each other. Since eventually one would want to obtain more or near optimal configurations of the considered system, S-O MH methods are found to be most ideal. Hybridized MH methods in resilient supply chain network design are recognized to hold great future potential [216].

7 Conclusion

The importance of a reliable medical distribution systems has become especially clear lately. The inherent characteristics of blood products: scarcity, perishability and supply/demand fluctuations, has made BSC design a popular field of study that combines knowledge from medical and operational fields. Recent BSC system design studies have shown the rising complexity of these problems, even when focusing on single actors/echelons within the BSC. More holistic approaches and the possibility for lateral transshipment of blood products have shown potential cost savings and suggested to be studied further, however with it problem complexity rises requiring new modeling methods. The benefits of collaboration and having horizontal ties within medical supply chains/networks are not exclusive to blood products. Medicines and sample diagnosis distribution for instance is also expected to benefit from such strategies. Studies that have quantified this potential ran into the costs and delivery speed limitations of ground transport. Drones are expected to enable further centralization of facilities and inventory; and increasing 'lean' practices like JIT delivery.

Because potentially life-saving goods are considered, the main objective in this field is often to minimize costs whilst maintaining the required service level under any circumstance. This requires taking into account high levels of uncertainty. Recently, other factors like wastage and environmental impact have gotten increased attention, requiring multi-objective system modeling.

With the coming of age of the technology, using UAVs for medical deliveries is often acknowledged as an application with high potential. First real-life implementations, mostly in developing countries, have confirmed these hypothesis. Qualitative feasibility studies have pointed out both costs and benefits associated with drone aided delivery systems in more developed and urban environments. However, large scale implementation requires strategic long-term investments with large possible impacts. Most quantitative and optimization studies on drone delivery have focused on single tactical or operational problems like path finding, task allocation or collaboration strategies. A gap is identified between high level qualitative feasibility studies, pointing out risks and benefits of drone assisted medical delivery and quantitative tactical and operational research focusing on a single criteria or element of the system. Thus, strategic decision makers lack the possibility to weigh potential benefits like cost savings and reduced emissions, with potential downsides like the risk of drones colliding into the ground. Because little or no large scale drone implementation exists, quantifying these third-party ground risks cannot rely on statistical analysis, rather mostly theoretical methods are needed to create best estimates.

Conventional means of transportation from the medical industry can rely on analysis of historic operations to get insights into performance in terms of risk and delivery time on the road. Research on emergency vehicles using pre-emption methods shows that a decrease in travel time comes with significant additional risks. Experts suggest that current emergency deliveries cause more risks both to those directly involved and third-party road users compared to drones performing the same task. No quantitative comparison exists of a delivery system using current road transport versus a system relying (partially) on drones in terms of risks, costs and reliability.

The high complexity, uncertainty and long term nature of the proposed system needs to be reflected in a model that will represent it. A combination of different simulation techniques can together create a realistic representation of the proposed concept of operation resulting in a model that can support strategic decision makers weigh pro's and cons. A modular agent-based framework enables further research and optimization on both local and system wide emergent behaviour, ensuring long term relevance due to adaptability.

8
Research plan

Based on the results of the literature study, a research plan is constructed which is described in this chapter. section 8.1 describes the objective and sub-objectives of the proposed research, elaborating on the relevance and contribution to industry as well as academics. section 8.2 covers in more detail how this objective is intended to be achieved by elaborating on the intended work plan.

8.1. Research objective

Distribution of medical goods using an UAS is expected to have large benefits in terms of, amongst others, cost reductions and speed of delivery. Potential downsides and challenges of drone delivery have withheld large scale implementation so far. Strategic decision makers lack the possibility to make informed assessments, quantitatively weighing costs and benefits that would result from high upfront investments in a large scale medical delivery UAS.

Several qualitative studies have listed the main expected pros and cons of large scale UAV assisted medical delivery systems [141][215][208][131][194][113]. These studies support stakeholders by providing guidance on which pros and cons might be expected but do not enable fully informed decision making, since quantitative understanding of the size of the listed pros and cons is lacking. This research aims at broadening the quantitative understanding of the these pros and cons, extending on what has been found in earlier works and what has been suggested as interesting for future research[168] [161] [68] [114]. From what has been concluded in the literature study as a whole and these previous works specifically, as well as input from initial stakeholder interviews the following 4 criterion have been defined that aim at ensuring its relevance. This research should:

- Support strategic decision makers
- Provide a holistic approach covering the major pros and cons
- Reflect the complexity of the envisioned system
- Create a foundation from which future research can extend

In addition and sometimes related to these core criterion, the knowledge gaps identified in the literature study have been used to develop the research objective and its supporting sub-objectives. The main objective of the MSc thesis covered in this research plan is formalized as follows:

Create a quantitative understanding of the expected sustained impact in terms of costs, reliability, emissions, risks and efficiency, of large scale implementation of an UAV assisted medical distribution system.

This main research objective is further subdivided into 3 sub-objectives that are more specific and together support the main objective. The sub-objectives are collectively exhaustive to the main objective, which means if these objectives are reached, the main objective is automatically considered successful as well. The sub-objectives are focused more on individual research gaps identified in the literature study.

(A) **Create a modular simulation-model that can simulate the daily operations of an medical delivery UAS, reflecting the system complexity and operating uncertainties.**
From chapter 6 is was concluded that traditional mathematical optimization methods do no longer meet the criteria posed by the problem characteristics. Simulation models can better reflect the complexity of the (future) systems as well as take into account uncertainty and the resulting reliability of these distribution systems. The proposed model will simulate the logistics of daily operations, with tasks coming in 'live' as the day progresses. The model criteria defined in section 6.1 are used as guidelines on what should be focused on for the model. As described in one of the model criteria, the to be developed model should be adaptable to different systems since every considered medical distribution UAS differs in use cases, environment and other preconditions. For this research a case study based on the MDS project is used as input for the simulation-model. This research aims at, next to creating generally applicable knowledge, providing support to the medical drone service project by modeling the long-term impact of the proposed project. A more detailed elaboration on the model is provided in the related second work package presented in the next section.

(B) **Compare different fleet configurations in a drone and/or road based distribution system**
Previous studies have mainly focused on potential cost savings of transporting medical goods by drone and found mixed results as was elaborated upon in chapter 4. Only a handful of studies have directly compared (current) road transport fleets with drone fleets in their models, and although suggested by some as interesting for future research no previous work has been found investigating the effects of heterogeneous fleet configurations. Additionally, the risk posed by a rising number of drones flying through our airspace to third parties has until know prevented large scale adoption. Novel research focusing on these drone related risks enables quantifying these risks without the need to rely on (unavailable) historical data, and directly comparing these to the risks created by ground transportation which might be underestimated as discussed in chapter 5.

(C) **Analyze the effect of healthcare centralization enabled by drone delivery**
Centralization and moving towards a more 'lean' healthcare system are (related) trends that have found stronger anchorage in both industry and academics recently. In chapter 2 mathematical models found early quantitative support for these trends in the blood specific supply chain. In chapter 3 similar quantitative backing of these ideas in the broader field of healthcare logistics was provided but also covered qualitative studies emphasizing that drones might act as a catalyst for further adoption of these trends in healthcare. This research wants to investigate this effect, which has been named frequently as the main benefits of using drones by stakeholders from a non-logistical but healthcare background. Next to filling academic gap of quantitative understanding of this drone enabling factor, this knowledge can support project leads in getting medical institutions on board.

8.2. Workplan

In order to achieve the desired objectives covered in the previous section, a workplan has been developed that provides an overview on the foreseen tasks needed to be fulfilled. These tasks have been bundled into different work packages, that together comprise the entire research. Although some tasks and or entire work packages are dependent on results from other work packages, the sequence in which the work packages are presented here does not imply they will be performed in this order. As much of the suggested research is of a novel nature, predicting exact time spend on different tasks is very much unreliable. Thus the majority of tasks will be executed in an iterative process to ensure timely result delivery, referring to the famous example of building a skateboard first instead of setting of to directly build a car. Rather then an exact timeline on when what task will be performed, this workplan is aimed at providing structure and making the project more manageable. Note that the work packages are subject to changes, as new findings and challenges are expected to come up which requires altering or adding work to be done. Rather than an exact to do list, the different work packages are outlined by expressing their main contribution to the project.

WP 1: Concept of operations & assumptions

As described in the research objective A, this research aims at creating a realistic mathematical simulation model that reflects the complexity of the system as closely as possible. In order to do so the concept of operations first has to be defined. Since a not yet existing system is considered, this is mainly done by having stakeholder interviews with different members of the MDS team. It is expected that still many unknowns

exist in the envisioned concept of operations and that it will evolve as the project reaches new phases later. In consultation with the stakeholders a concept of operations will be formulated which in this research will be translated into a simulation model.
Along with the concept of operations, assumptions and scoping decisions have to be made to keep the MSc thesis research feasible. To do so the research objective and sub-objectives form a guideline on what is most important to focus on. A list of assumptions and scoping decisions is kept and added to throughout this research. 5 important points that have been defined so far are listed below, note that this is not an exhaustive list of all assumptions and scoping decisions.

- Flight operations are out of scope of this research
- All stakeholders are fully cooperative within the concept of operations
- 3 use cases of medical goods are considered for drone transport, with no additional distinction within the use case (group)
- Drone risks are modeled using methods and supplementary assumptions from [181]
- Car risks are modeled using average road crash rates for normal delivery, multiplied by an additional risk factor derived from [90]

WP 2: Simulation model development

The concept of operations needs to be translated into a simulation model that reflects it as closely as possible. Different simulation techniques need to be combined in order to reach the desired effect. The criteria that the model needs to satisfy as well as the conclusion that a simulation model is most fit for this problem has been discussed in chapter 6. The model is expected to be divided into two main sections, a pre-processing section and the main simulation section.
The pre-processing model will include the drone risk model and its integrated path finding algorithm, additionally this section will include methods that determine the routes of ground vehicles. The input for this pre-processing section are the speed and range of a fully charged drone and the locations of all medical centers within the area of the case study. The output will include a set of matrices that state, for every combination of medical centers, the drone route along with the associated distance and risk, the road route, distance and expected travel time.
The main simulation model will take these matrices as input, after which it is able to run independently. This makes the total simulation more efficient since the output of the pre-processing will be the same for each run preventing repetitive computation with the same results. As stated in the research objectives a modular simulation system is preferred, enabling future research and in depth optimization of the different modules. The main modules envisioned for the model are:

- Demand generation
- Inventory and facility allocation
- Supply & demand matching
- Task allocation
- Route & schedule generation
- Transport execution

Next to the model itself it is important to keep track of the KPI's during simulation as well as creating the necessary simulation output. What will be measured and how these results will be used is part WP 3 and discussed next.

WP 3: Running simulation & results analysis

Research objectives B and C are converted into the following two research questions. The two questions are formulated below in a concise form for ease of reading, different terms within the questions are elaborated upon next.

1. What are the effects when switching from current land-based transport to a drone or hybrid system?
2. What are the effects of healthcare facility centralization and inventory sharing enabled by drone transportation on the system?

The concept of operations that is considered in this research is referred to as **the system** in the research questions. This system can have different configurations, which will be compared when trying to answer the posed questions. **Land-base transport** is what is used currently for transport of medical goods, and in this research cars are the only land-based vehicles that are used in the system. These cars are however capable of driving in two different modes, emergency and non-emergency, similar to the current concept of operations. The mentioned **hybrid** system configurations refers to a concept of operations in which both cars and drones are used to perform deliveries. **Healthcare facility centralization and inventory sharing** both refer to the degree in which inventory and or facilities are located in a limited number of medical centers. In a non-centralized system all medical centers posses the ability to process blood samples and have plenty of inventory for blood products and medicine. The **effects** stated in both research questions relate to the measured KPI's and derivatives. Below the main indicators that are used in this research are presented:

- Fixed system configuration costs [€]
- Variable/returning system costs [€ / year]
- Risks [expected injuries / year]
- Emission's [Kg of CO2 / year]
- System usage [# of deliveries]
- Delivery performance [avg delivery time]
- Delivery performance [# of late/non deliveries]

To answer the posed research questions different system configurations are tested by running the simulation and comparing the results. The main decision variables that are being tested in this research are the number of drones and cars and the degree of supply centralization as explained in the previous paragraph. The stochastic processes integrated in the different model modules require the model to be ran multiple times for each system configurations to generate reliable results. The coefficient of variation can be used to indicate the amount of simulation runs required per system configuration. Partially based on the results of the initial comparative simulations, further in depth analysis on specific emergent behaviour can provide suggestions on how the system can be further optimized. Additionally sensitivity analysis on the input parameters like drone range and costs provide insight in how future technical developments on drone hardware might alter the conclusions from this research.

WP 4 (optional): System configuration optimization

As discussed in chapter 6 simulation models in itself do not provide optimal solutions. In the two research questions, that will be answered in WP 3, the optimallity of the system configuration is solely dependent on the self created input configurations. Although this does provide insight in how individual trends influence different system results, other decision variable configurations might result in better system performance. To uncover which combination of input variables leads to the most optimal system outputs a third research questions is formulated to be:

3. What is the most optimum facility location and fleet configuration for a drone assisted hospital distribution system

To answer this research question the simulation model can be combined with MH optimization techniques in a Sim-opt model as elaborated upon in section 6.5. Whilst for research questions 1 and 2 the different performance indicators do not have to be prioritized, multi-objective optimization needs to be performed in order to define and find optimality. Assigning weights to different performance indicators, which will be needed when the most common multi-objective optimization technique of simple additive weighting is applied, is based on the stakeholder discussions from WP 1. Finding the most optimal solution is not the main focus of this research, since it is only applicable to the assumed case study and will change as drone characteristics evolve. Thus this work package is optional and will only be performed if time and resources allow to do so without compromising the quality of other work packages.

WP 5: Reporting & conclusions

The final work package consists of presenting the methods and results from the other work packages. It is important to distinguish results that are case study specific as well as results that are more generally applicable. Because of the last research criterion listed in section 8.1 stating the aim to form a base for future research, a critical analysis of the model and methods can provide insights in how is can be improved by future researchers. Lastly in this work package time will be spent on advising the MDS project on how the results from this study could be interpreted and used in the project.

III

Supporting work

A

Routes elaboration

The Agent-based simulation model relies on pre-determined routes as an input, defining length, TPR, travel time, and emissions. As described in the scientific paper, the pre-processing phase of the model performs this pre-determination of the routes for both drones and cars. In this chapter we further elaborate on this pre-processing module of the model, focusing on additional insights that can be derived from the routes found. First, in section section A.1 we provide additional insights on the routes derived for drones. Next in section section A.2 we further analyze the routes found for cars. Lastly, we provide a brief analysis, comparing the routes of both vehicle types in section section A.3.

A.1. Drone routes

In this section, we build on top of what has been stated in the scientific paper on drone routes. For the exact implementation of the model described in the paper, we refer the reader to the code repository available on Github[220]. The direct and thus routes found by the model are visualized in Figure A.2 and the safer routes are presented similarly in Figure A.3. Both maps show the hospitals and all routes connecting them. The background indicates the ground risk based on the population density as described in the methodology of the paper. From this, we can clearly distinguish the major urban areas of the province of South-Holland. Adding an additional layer on the risk map, that would incorporate no-fly zones was tested. However, it was decided to not weigh no-fly zones in the risk map because of several reasons. First, if all no-fly zones would be strictly adhered to, the majority of hospitals could not be reached since they lay within such no-fly zone. Secondly, these no-fly zones are often indicated as a circle around an airport which is argued to be quite arbitrary resulting in routes precisely following the edge of the circle as shown in Figure A.1. A solution might be weighing different (parts of) no-fly zones differently, however, this is argued to require having to make even more unsubstantiated assumptions. This brings us to our last and maybe most important argument, namely that for our proposed system to be implemented, a new airspace structuring is likely to be required. Creating routes based on the old structuring would thus be a little inconsistent.

The numbers on the axis provide an indication of the grid cells of the risk map. In this case study, an area of 40 by 40 kilometers was represented by square cells of 100 by 100 meters, resulting in a 400 by 400 grid map. The different colors of the hospitals and routes are used so that different routes are easier to differentiate, and are thus not indicative of any additional information.
In Figure A.2 we can clearly see why the distances of the routes found in our model are not equal to the absolute distances between hospitals. Our path-finding algorithm only allows for horizontal, vertical, and diagonally movements. The fact that the routes mostly consist of multiple straight lines, one being horizontal or vertical and one being diagonal, is due to the way the algorithm is implemented. To minimize computation time a hospital starts searching for routes to all hospitals simultaneously, although optimal routes are guaranteed for all destinations often parts of the routes to different hospitals overlap. The combination of multiple heuristics leads the algorithm to first go into the direction in which it minimizes the direct distance to all hospitals it has found no route to yet. This causes the effect that when considering neighboring cells a cell in the same direction as that was previously traveling in is often preferred. The resulting overlap and straight lines are thus merely an effect of the model implementation. Since no effort is made to minimize TPR

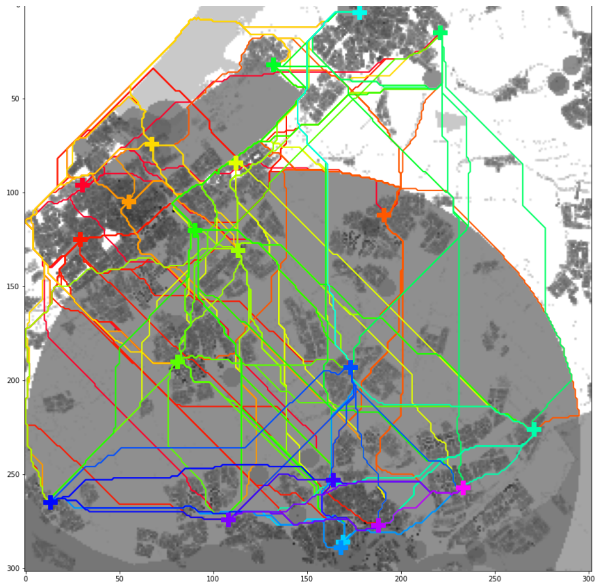


Figure A.1: Done routes based on ground risk map including no-fly zones

by the algorithm it is likely that less risky routes exist between hospitals with the same amount of straight and diagonal movements, resulting in the exact same distance. This is actually part of a broader limitation of our approach. Only two types of routes are being evaluated being the two most extreme options, either fully minimizing TPR or only focusing on finding the shortest and thus fastest route. The decision to only use these two extreme options, and similar decisions on the modes of operations, were made so we could provide insights into the operational limits of the proposed system on either side of the spectrum. By modeling what would happen if one were to solely focus on either TPR or speed of delivery, we generate a range for the different measured KPIs within which one might expect performance to be. In the results of the different modes of operation, we can see how more deliberate strategies can result in above-average performance on all indicators. A similar less polarized method of deriving drone routes, by taking into account both TPR and travel distance is expected to have similar benefits. The implementation of our methods allows for any ratio, weighing the two extreme options, resulting in different routes that might encapsulate this benefit. However since the main focus of this study was also to compare drones and cars, having a more sophisticated route generation model for drones balancing both TPR and travel time minimization, would require similar levels of sophistication in developing routes for cars. As will be discussed in the next section this would require data or theoretical models that are currently not available.

Analyzing Figure A.3more closely we clearly see that routes avoid highly populated areas, validating the functioning of our model. The effect of this is seen most clearly when looking at the routes between hospitals in The Hague, located on the left of the map. Multiple hospitals are geographically located relatively close to each other in different parts of one densely populated area. However, in order to fly to another hospital within the same city, we can see that the path-finding algorithm first seeks a route out of the city. Next, it flies around the city to a point on the city border close to its destinations from which it flies a more or less direct route into the city towards the hospital. This last part of the route is often similar for all routes going towards that hospital and might even be referred to as an approach path. A similar effect of overlapping routes is also observed in routes between populated areas. Multiple routes from and to a populated often converge and fly similar routes avoiding populated areas. The combination of these two effects causes a relatively structured route map to emerge, even though it contains 171 unique routes. Thus we argue that one might create a fixed 'road map' in the sky of paths a drone can fly. Combining different 'roads' it is likely that one can create a route from a to b that has similar TPR values as the most ideal route for that particular origin-destination combination. By fixing these roads in the sky, we suspect that getting both governmental and societal approval might be eased.
The diversions seen on the map and described above are quantified and visualized in Figure A.4. This heatmap shows the ratio between the length of the safe routes and the absolute distances between hospitals, which in this research is referred to as the diversion factor. The hospitals located within the same urban area or city

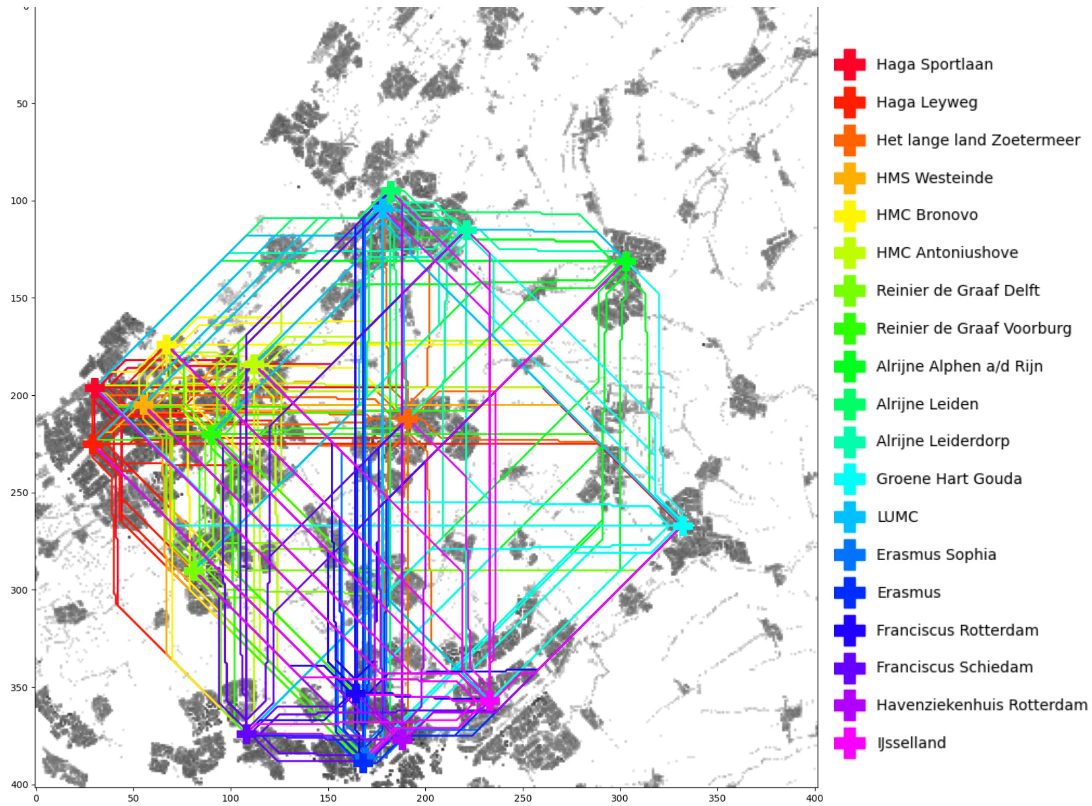


Figure A.2: Fast drone routes derived from the pre-processing module

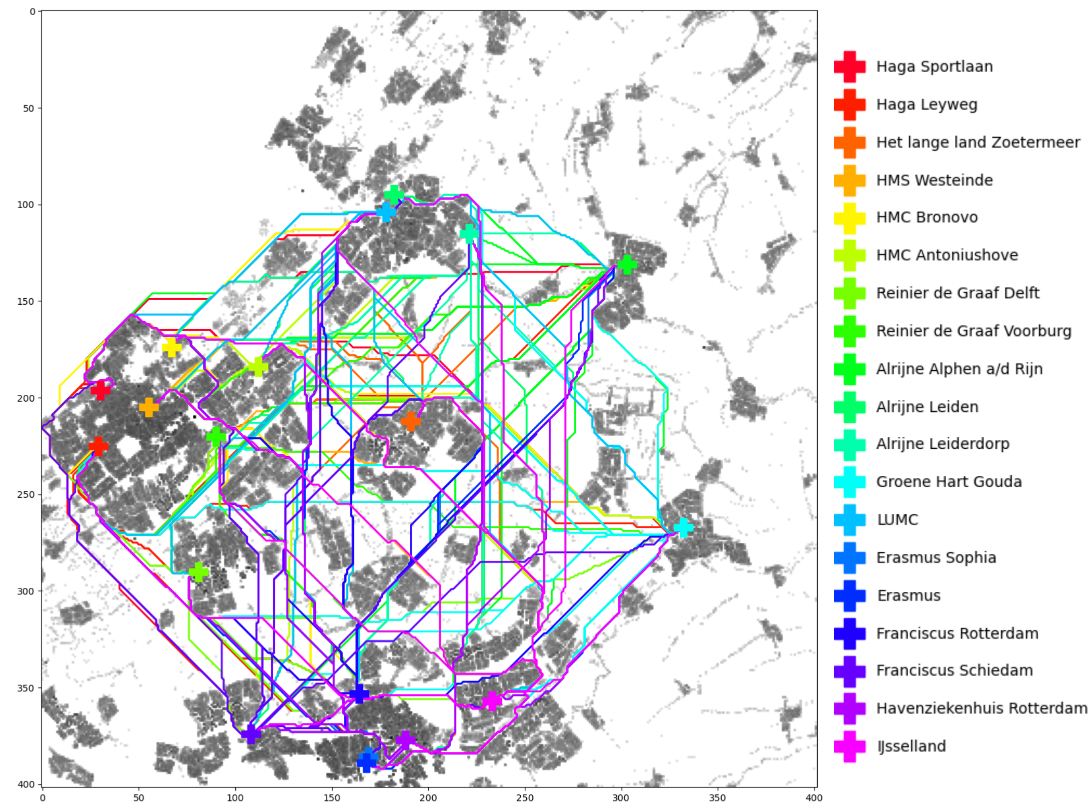


Figure A.3: Safe drone routes derived from the pre-processing module

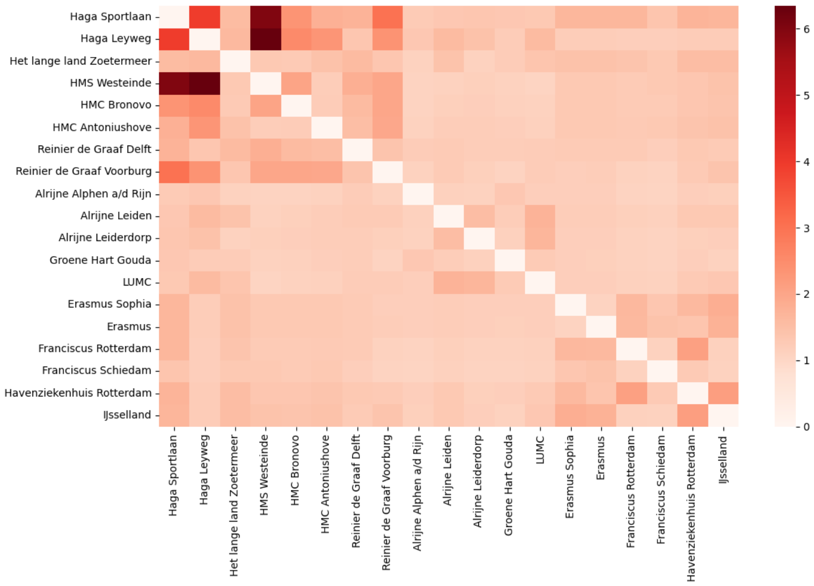


Figure A.4: Diversion factor of safe drone routes

are grouped and can be distinguished quite clearly. The top left corner of the heatmap represents hospitals within The Hague, which in accordance with our observations from Figure A.3, have the biggest diversion in their routes. Additionally, we see increased diversion factors, although less severe, within the urban areas around Leiden and Rotterdam, in the middle and bottom right corner of the heatmap.

In our research we assumed drones, after taking 30 seconds to vertically take-off, fly at a constant cruising speed during the entire route. In section C.2 we present a sensitivity analysis showing the impact of different, among others, take-off/landing times and cruising speeds. The methods used to derive emissions have been discussed in more detail in both the scientific paper and its supporting work in the literature study.

A.2. Car routes

As described in the paper, the routes that cars use are generated with an API that requests route details from Bing. Initially, a Google API was used, however in order to measure the effect of congestion we wanted to get route details for different moments during the week. It was found that this was not possible for the Google API, thus the switch to Bing was made. A verification analysis showed little differences between the two when route details were requested for the same origin, destination and time. By collecting and analyzing data for a variety of time, day, and month combinations, we found that the time needed to complete a trip and to a lesser extent the route distance, is only dependent on the time of day and day of the week. In other words, the expected travel time on any route would be the same for every Monday at 14:00, no matter the week or month of the year. Thus we requested data for every hour of the week for each hospital pair. Although in reality, we expect external factors like holidays and extreme weather conditions to generate differences with respect to the week or month, we assumed the 7*24 data points collected to be representative of an average week. In the remainder of this section, we will evaluate these data points in more detail.

In Figure A.5 the expected travel times in minutes are shown for several hospital combinations during different hours of the week. The lines labeled with a day of the week represent the expected travel time by car at different hours of that particular day. As a reference, the time it takes a drone to take either the safe or fast route is included as well. note that these drone travel times include two thirty-second take-off and landing time-frames. As indicated by the straight line, these are not time-dependent. The next section will go into detail on the comparison between car and drone travel times, whilst here we will mainly discuss insights on car routes specifically.
Although plots differ for different origin/destination combinations, we see some recurrent patterns emerging. We can clearly distinguish the morning and afternoon rush hours, indicated by the peaks around 8:30

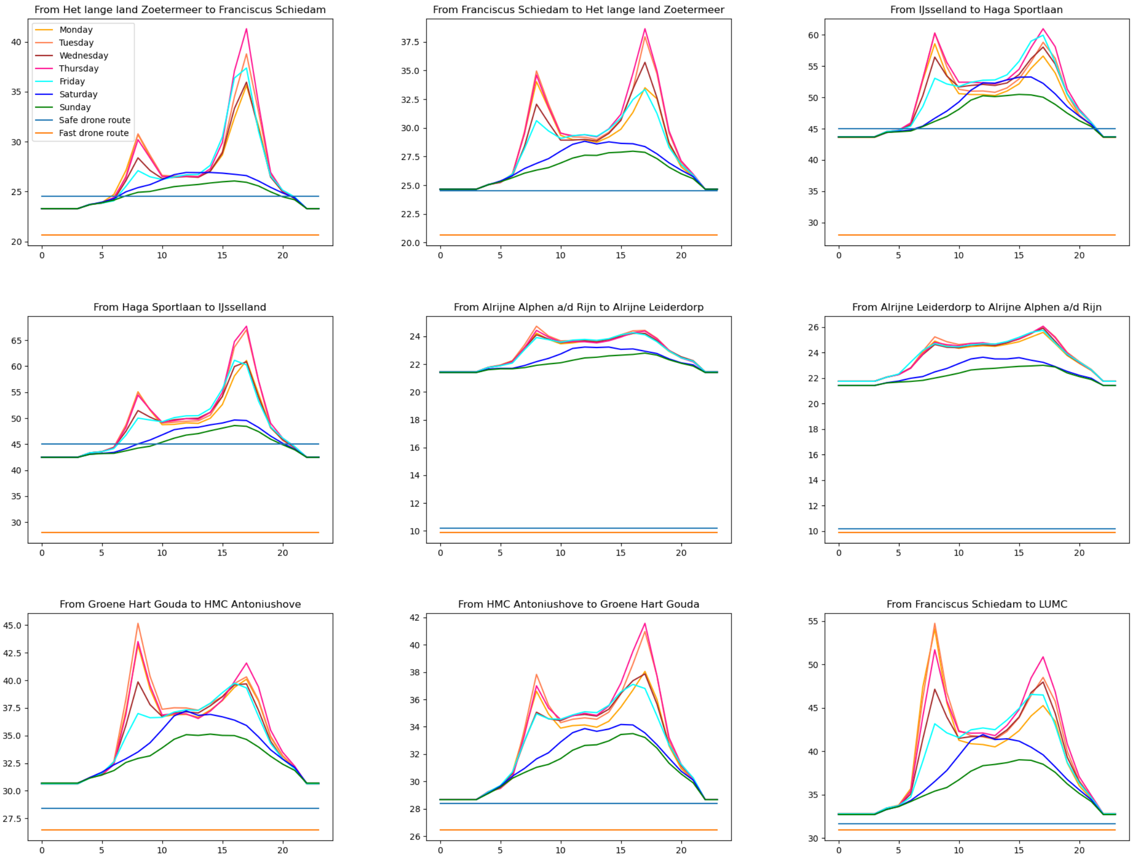


Figure A.5: Car travel times in minutes at different times during the week and 17:30 during weekdays. During the weekend we observe a single spread out peak, Saturday generally being slightly more congested than Sunday. Congestion being a major problem for emergency delivery of medical goods, as suggested by medical stakeholders within the MDS project, can be confirmed from this data. In the bottom right graph, we see that a trip by car between the Franciscus hospital in Schiedam and the LUMC only takes a little more than 30 minutes on empty roads, which is well within the required hour. However during peak morning rush hour expected travel time becomes over 50 minutes, which means that in order to deliver within the hour a car should be ready to depart immediately and little room for any other delay exists. Probably most interestingly the afternoon rush hour peak tends to begin earlier on Fridays, an indication of the Dutch working culture of leaving for home a little earlier to start the weekend. When looking at the graphs on the bottom (left) we see how the severity of congestion during morning and afternoon rush hour depends on the general direction of the commute. People living outside the city in smaller towns or in more rural areas like the region around Gouda often work in cities like The Hague where the HMC is located. Thus during the morning, we see higher congestion from Gouda to the HMC whilst in the afternoon congestion is worse in the other direction.

Comparing the different graphs within Figure A.5 we see how the problem of congestion is highly dependent on which route is considered. In Figure A.6 the travel time in minutes is shown for all hospital combinations during the least congested time of the week as well as the longest expected travel time. The increase of travel time due to congestion as a percentage is provided in Figure A.7, indicating on which routes the problem of congestion is most significant. We see that in our case study all routes between hospitals can be driven within an hour when doing so at night when the roads are least congested. However, at peak congestion, the heatmap turns red and several routes are expected to take more than an hour to be completed by car. Naturally, hospital pairs that are located further apart tend to have longer expected travel times. Thus we can clearly distinguish the two major cities that contain multiple hospitals: The Hague and Rotterdam, by the green(er) big squares on the top left and bottom right of the heatmaps in Figure A.6 respectively. Additionally, we see that Rotterdam as a city seems to suffer the most from congestion, as indicated by the fact that the bottom right of Figure A.7 is primarily red. Upon further investigation, we could explain the horizontal red line of routes departing from the LUMC in Leiden. The majority of routes lead from the LUMC onto either the N206 or A44, both roads are notorious for being congested during the afternoon rush hour. A problem that has actually led to the planning and current construction of a new connecting road.

As described in the scientific paper we assumed that emergency vehicles using lights and sirens are expected to be one and a half times faster than normal vehicles. In the study this speeding factor was derived from, they compared actual travel times with estimates from a similar API as used in this research[177]. They found that this factor was relatively stable and not highly dependent on the time of day or route length. Thus in order to create the car travel time estimates for the fast routes all expected travel times were divided by this 1.5 speeding factor. From the presented numbers on congestion and this speeding factor derived from earlier research, we conclude that one might actually expect an emergency vehicle driving during rush hour to take longer to travel certain routes compared to a normal car driving the same route during the night. Next to providing interesting insights into Dutch infrastructure and road travel behavior, this data confirms the problem of congestion for the proposed system and makes the simulation model using this data as an input better representative of real-life than other methods.

The steps taken to determine TPR and emissions associated with the different routes have been described in the scientific paper. For a more detailed discussion on where the numbers used in these calculations have been derived from we refer readers to the related section in the literature study.

A.3. Comparison

So far we have discussed the two different methods used to derive the routes individually. Based on these methods matrices were derived for both vehicle types containing the distance, TPR, travel time, and emissions associated with each route. To reiterate these route KPIs were dependent on the hour of the week for cars, whilst for drones, they were assumed to be constant. We acknowledge that both methods and their direct comparison might be somewhat reductive, however, the aim of the study is not to provide a perfect model deriving the route KPI('s) for a single vehicle. We want to provide a holistic overview providing ballpark estimates on different medical delivery distribution system configurations.

In Table A.1 we provide the average travel time, TPR, and emissions for all routes for both drones and cars. Since car values are time-dependent we provide a range by stating the averages in the best and worst-case scenarios. It should be noted that taking the averages of all routes, the differences presented here can differ

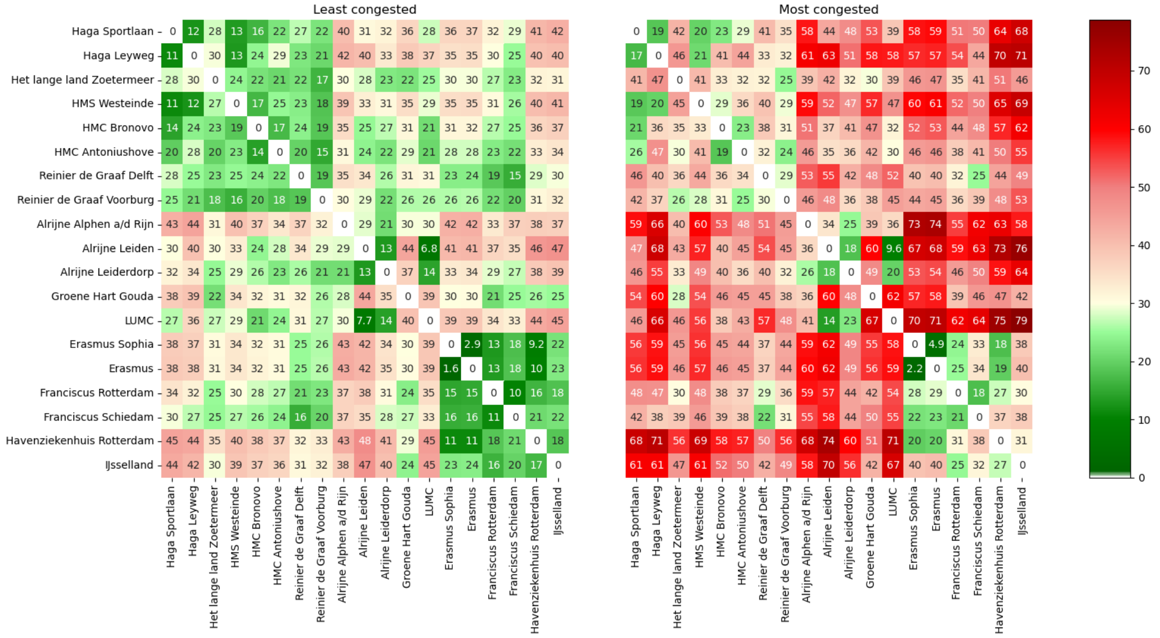


Figure A.6: Car travel times at the least and most congested time of the week

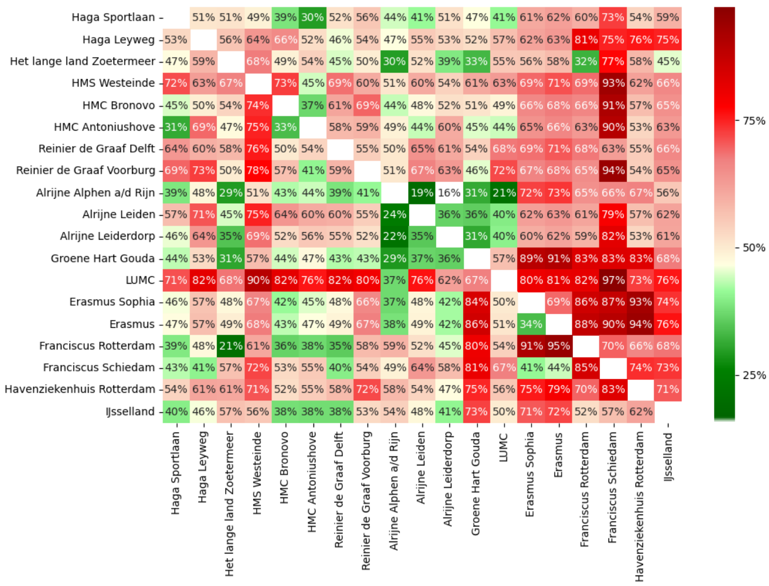


Figure A.7: Increase in car travel time due to congestion

	Drone		Car least congested		Car most congested	
	Fast	Safe	Fast	Safe	Fast	Safe
Travel time [min]	19.0	23.2	19.1	28.7	29.9	44.9
TPR [expected casualties]	$5.11 * 10^{-6}$	$0.26 * 10^{-6}$	$29.9 * 10^{-6}$	$0.56 * 10^{-6}$	$19.1 * 10^{-6}$	$0.56 * 10^{-6}$
Emissions [kgCO2]	0.29	0.36	2.87	2.87	2.87	2.87

Table A.1: Average route KPI comparisons

(heavily) from system-wide performances. Some routes and hospitals are more heavily used during operation simulation, whilst other routes between two distant hospitals are never used.
The relatively small difference in average travel time for drones between the safe and fast option can be explained by the fact that the majority of diversion factors shown in Figure A.4 are close to zero. Again we see the impact of congestion on travel time, during the night emergency vehicles are on average almost as fast as the fastest drone option. However, in less ideal conditions car travel times are significantly longer than drones, no matter which option is taken. In terms of average TPR, we see big differences between the safe and fast options for both cars and drones. However, for both options, drone routes result on average in less TPR. It should also be noted that although TPR derivation methods are vastly different for cars and drones, the resulting values are actually in the same order of magnitude. Although precise numerical differences might not be very reliable, these findings strengthen our belief that the physical risks of drones falling out of the sky might not be that different from risks we are already (subconsciously) tolerating. The differences in emissions between car and drone routes are not surprising and very much in accordance with previous research presented in the literature study. Since in our methods emissions are derived from the route distance, these values do not change for cars with respect to how fast one is able to complete the trip. The fact that these average emissions for cars are the same between the least and most congested hours of the week, tells us that the route planner API actually suggests taking the same route during congestion but it just takes longer to complete this trip.

B

Statistical substantiation

In this chapter, we will discuss in more detail the statistical analysis conducted on our presented results. We build upon what has been stated in section 5.1 in the provided paper. First, we will elaborate on the number of simulations run for each configuration in section section B.1. Next, we discuss how the results were tested on normality in section section B.2. Lastly, in section section B.3 we present details on the statistical significance of the results presented in the paper.

B.1. Number of simulations

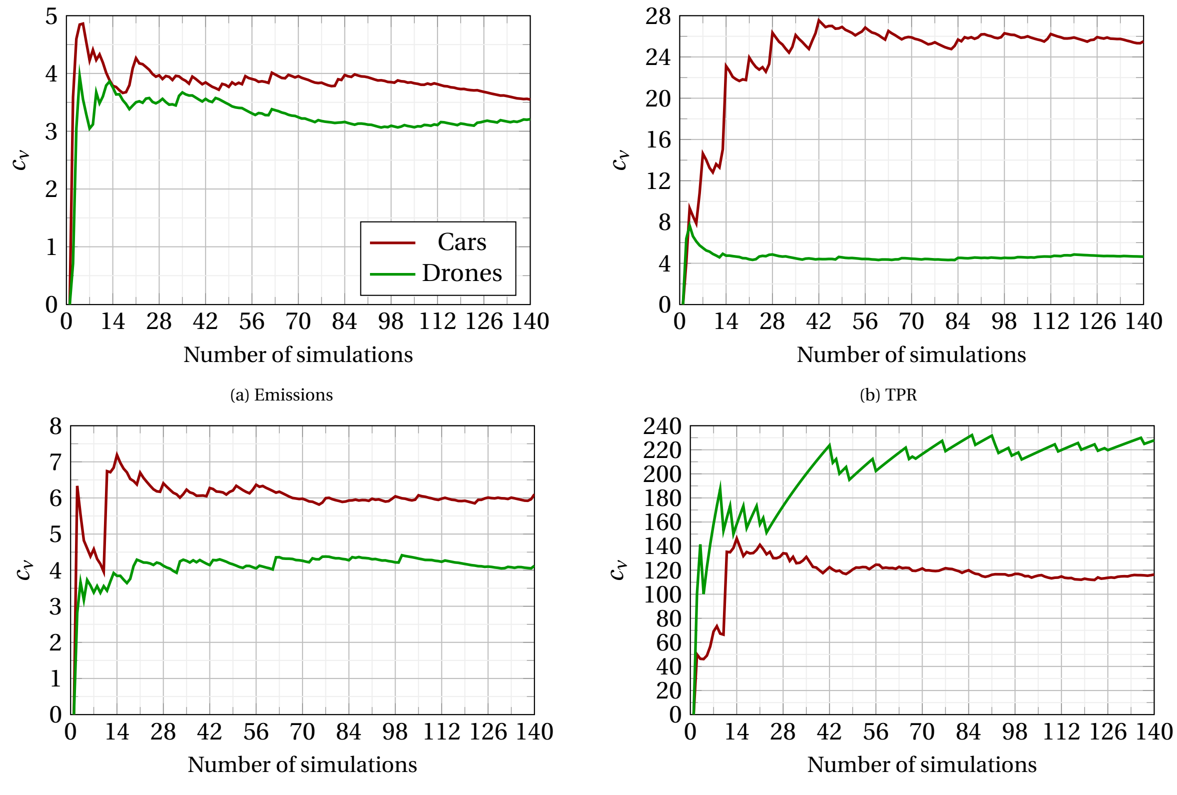
Visual behavioral and initial results analysis showed that simulation results are volatile and may not be normally distributed. Multiple requests occurring simultaneously could for instance induce long-term disruption of the delivery system, negatively impacting performance results. To get a better sense of the severity of this volatility and assess the number of simulations needed to obtain representative results for each simulation setup we analyzed the coefficient of variation, which is presented in Equation B.1.

$$c_v = \frac{\sigma(o)}{\mu(o)} \tag{B.1}$$

In Figure B.1 we present the coefficient of variation after an increasing amount of simulation runs. We present this graph for multiple parameters for both a Cars only and Drones only fleet with $N_{total} = 12$ and $\lambda / N_{total} = 2.5$. We see that between 70 and 140 simulations c_v values become relatively stable. With the exception of Figure B.1d, which we will discuss later, we observe that variation in results is less for configurations with Drones only fleets. This is due to the travel times of cars being time and more importantly, day dependent. Note that a single simulation run represents a single day so that every 6th run simulates a Saturday and every 7th a Sunday. This also explains the small jumps observed in the red lines at a relatively constant frequency of around 7 runs most clearly seen in Figure B.1b and Figure B.1c. As pointed out in the last discussion point in the scientific paper, one might obtain less varying and more normally distributed results when simulating an entire week per run. However, it should be noted that this would likely not impact mean resulting values heavily. Actually, the results of a single simulation run are already the means of all deliveries within that day. In Figure B.1d we show the coefficient of variation of the number of deliveries that are not fulfilled within the hour deadline. This parameter was used to determine the reliability of the system. Since the priority of the proposed system is getting this number as low as possible the mean of this number is often close to zero for systems performing under their capacity. This also explains why the Drones only line is less stable and higher in absolute value, since $\lambda / N_{total} = 2.5$ is further from the maximum capacity of a $N_{Drone} = 12$ fleet compared to its Cars only counterpart. The high absolute value coefficient of variation for this parameter is thus due to the nature and meaning of the parameter.

B.2. Normality of results

Having established that obtained results were representative using the coefficients of variation the distribution of the results was tested. In order to determine the normality of the results, we visually inspected the QQ-plot of the results and performed the Shapiro-Wilk test. In order to compare different scenarios fairly,

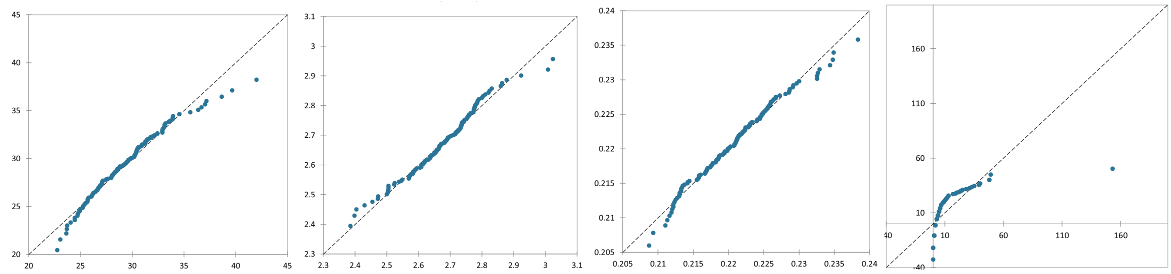


(a) Emissions (b) TPR (c) Delivery time (d) Number of overdue deliveries

Figure B.1: Coefficients of variation

we introduced the window of optimal operation described in the paper and defined it as reliability between 98% and 99.5%. We acknowledge that filtering results based on other results may not be optimal from a scientific perspective and can introduce biases. These biases, as discussed in the paper, are most severe at very low demand levels, and should be addressed in future studies. In Figure B.2 we present the QQ-plots of different parameters for a fleet of $N_{Drone} = 12$. We show plots for a fixed demand scenario as well as results obtained through the optimal operation window filter. The fixed demand results are from the scenario with $\lambda / N_{total} = 3.5$ which resulted in average reliability of 99.1%, thus the mean of this fixed demand lies within the window of optimal operation. Comparing Figure B.2a to Figure B.2c and Figure B.2e to Figure B.2g we can also see that the obtained values are of similar magnitudes for all three parameters. Additionally, both data sets are of similar size ($N = 140$ for the fixed demand data set and $N = 134$ for the data from the operational window filter). Alongside the QQ-plots we also included the results from the Shapiro-Wilk test from the corresponding data sets, with the null hypothesis being that the data follows a normal distribution.

From both the QQ-plot and the W and p values we conclude that results from the fixed demand data set are more skewed and assuming $\alpha = 0.05$ evidence exists that none of them are normally distributed. We can clearly see the effect of outliers in Figure B.2d where we show the number of late deliveries from a single day of operation. As stated in the report we are more interested in comparing typical days of operation, and operational capabilities of different system configurations. Thus we applied the filter including only results from days in which between 98 and 99.5% of deliveries were completed within the hour. The minimum of 98% removes the days in which operation got behind and a significant amount of orders could not be completed on time. The 99.5% upper limit discards days in which the system was operating (far) beneath its capacity, which results are less interesting because using such a system would not be cost-efficient. The approach of filtering based on this window was preferred over simply discarding outliers because this would likely result in a bigger positive bias of results. Using this method we included both positive and negative (small) outliers from demand levels lower and higher than the demand level that on average performed within the operational limit. We see this being confirmed in Figure B.2h where we plot the number of deliveries performed on a day with reliability between 98 and 99.5%.

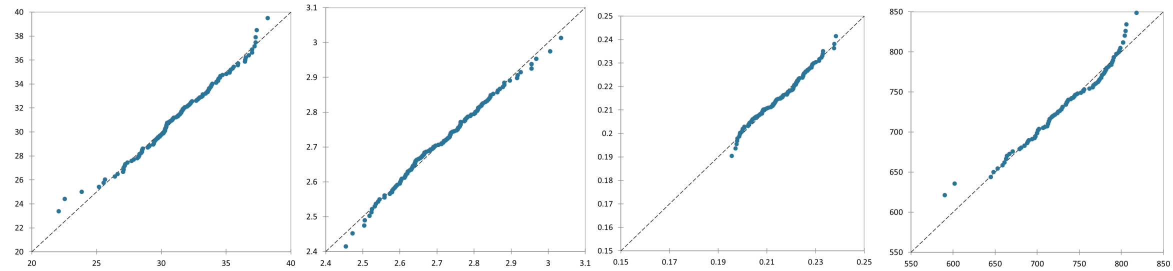


(a) Fixed demand, delivery time
$W = 0.97$, $p = 0.002$

(b) Fixed demand, TPR
$W = 0.98$, $p = 0.045$

(c) Fixed demand, emissions
$W = 0.98$, $p = 0.0098$

(d) Fixed demand, late deliveries
$W = 0.46$, $p = 0$



(e) Window of optimal operation delivery time
$W = 0.99$, $p = 0.29$

(f) Window of optimal operation TPR
$W = 0.99$, $p = 0.607$

(g) Window of optimal operation emissions
$W = 0.98$, $p = 0.078$

(h) Window of optimal operation system capacity
$W = 0.97$, $p = 0.008$

Figure B.2: QQ plots for different parameter results from a fixed demand scenario and from the window of optimal operation filter

Although the results shown in Figure B.2e to Figure B.2h still contain outliers, we can see from both the QQ-plots and p-values that these parameters are more normally distributed. Again assuming $\alpha = 0.05$ we might conclude that all parameters except the system capacity are normally distributed. Exact distribution and corresponding Shapiro-Wilk test results differed from scenario to scenario, and results from Cars only system configurations would more often result in $p < 0.05$. These findings were used in deciding which statistical tests to use when assessing the significance of the results, which will be discussed in more detail in the next section.

B.3. Significance and relevance

The goal of our study is to create a quantitative understanding of different KPIs for large-scale implementation of a UAV assisted medical distribution system. Throughout our study we compare different configurations and strategies, this is mostly aimed at giving decision-makers an indication of how different decisions might impact system performance. Thus our study is not trying to scientifically prove that one option is undeniably better than another since this would also force us to weigh different KPIs. This does not mean we should not be considered whether our results and conclusions are caused by actual system differences or chance. To validate our results we looked at the consistency of our findings when varying other system inputs than the ones tested. Additionally, we looked at the spread and distribution of all individual result parameters, creating a 95% confidence interval (CI) we could instinctively judge whether two result values would be significantly different. In Table B.1, Table B.2, Table B.3 and Table B.4 we present the results along with their respective CI broken down in the different scenarios that were combined into the results shown in the scientific paper. We noticed that when comparing different modes of operation on a single scenario, for instance, $\lambda = 36$ for a mixed fleet, observed differences would be regarded significant quicker. Either because no overlap would exist between the confidence intervals, or when overlap did exist, because a t- or Mann-Whitney test would indicate statistical significance. However, one strategy performing significantly better on a single configuration is argued to be less relevant. When comparing two individual result data sets with overlapping CI we consistently used a t- or Mann-Whitney test, based on the normality of the distribution as described in the previous section, assuming $\alpha = 0.05$. The vast amount of possible result combinations and thus the number of CI combinations and/or conducted tests means there is a high probability that one of the test results contains a Type 1 error (False positive). But since the difference in a combination is argued to be less relevant we accept this probability. Instead, we encourage readers to acknowledge the complexity and nuances in our results and be aware that individual differences may be caused by chance or other assumptions. In summary, we tested the validity and relevance of findings, by looking at whether they are of an interesting magnitude and consistent, and if not how/if that could be explained. We argue that this enables us to serve our goal best, by focusing on findings that are most meaningful for people wanting to assess the capabilities of a (UAV assisted) emergency medical delivery service.

		Combi				Fast				Safe			
		Forced	None	Closest Hub	Simple	Forced	None	Closest Hub	Simple	Forced	None	Closest Hub	Simple
$\lambda = 24$	Drones only	1 [1 , 1]	1 [1 , 1]	1 [1 , 1]	1 [1 , 1]	1 [1 , 1]	1 [1 , 1]	1 [1 , 1]	1 [1 , 1]	0.979 [0.978 , 0.981]	0.992 [0.991 , 0.993]	0.991 [0.991 , 0.992]	0.992 [0.991 , 0.993]
$\lambda = 24$	50% Drones	0.995 [0.994 , 0.997]	1 [1 , 1]	0.999 [0.999 , 1]	0.999 [0.999 , 0.999]	0.999 [0.999 , 0.999]	1 [1 , 1]	1 [1 , 1]	1 [1 , 1]	0.975 [0.973 , 0.977]	0.982 [0.98 , 0.984]	0.985 [0.984 , 0.986]	0.986 [0.985 , 0.987]
$\lambda = 24$	Cars only	0.954 [0.946 , 0.961]	0.999 [0.998 , 0.999]	0.996 [0.995 , 0.997]	0.994 [0.992 , 0.996]	0.994 [0.993 , 0.995]	1 [0.999 , 1]	0.998 [0.998 , 0.999]	0.998 [0.997 , 0.998]	0.938 [0.935 , 0.941]	0.903 [0.895 , 0.912]	0.945 [0.942 , 0.949]	0.943 [0.939 , 0.947]
$\lambda = 30$	Drones only	0.997 [0.996 , 0.998]	1 [1 , 1]	1 [1 , 1]	1 [0.999 , 1]	1 [1 , 1]	1 [1 , 1]	1 [1 , 1]	1 [1 , 1]	0.932 [0.929 , 0.936]	0.958 [0.954 , 0.963]	0.971 [0.967 , 0.974]	0.966 [0.962 , 0.97]
$\lambda = 30$	50% Drones	0.968 [0.962 , 0.974]	0.999 [0.998 , 0.999]	0.998 [0.997 , 0.998]	0.997 [0.997 , 0.998]	0.997 [0.997 , 0.998]	1 [0.999 , 1]	0.999 [0.999 , 0.999]	0.999 [0.999 , 0.999]	0.941 [0.938 , 0.945]	0.95 [0.945 , 0.955]	0.964 [0.962 , 0.967]	0.961 [0.958 , 0.965]
$\lambda = 30$	Cars only	0.832 [0.816 , 0.848]	0.994 [0.992 , 0.996]	0.988 [0.986 , 0.991]	0.984 [0.981 , 0.987]	0.988 [0.986 , 0.99]	0.999 [0.999 , 0.999]	0.997 [0.997 , 0.998]	0.997 [0.996 , 0.997]	0.915 [0.911 , 0.919]	0.888 [0.879 , 0.897]	0.918 [0.913 , 0.924]	0.909 [0.902 , 0.915]
$\lambda = 36$	Drones only	0.954 [0.944 , 0.965]	0.999 [0.998 , 0.999]	0.999 [0.999 , 0.999]	0.998 [0.998 , 0.999]	0.998 [0.997 , 0.998]	1 [0.999 , 1]	1 [1 , 1]	1 [0.999 , 1]	0.881 [0.878 , 0.885]	0.83 [0.815 , 0.844]	0.848 [0.834 , 0.861]	0.835 [0.821 , 0.849]
$\lambda = 36$	50% Drones	0.891 [0.877 , 0.906]	0.997 [0.996 , 0.997]	0.996 [0.995 , 0.997]	0.994 [0.994 , 0.995]	0.995 [0.993 , 0.996]	1 [0.999 , 1]	0.999 [0.999 , 0.999]	0.999 [0.999 , 0.999]	0.912 [0.909 , 0.915]	0.915 [0.909 , 0.922]	0.931 [0.926 , 0.936]	0.924 [0.918 , 0.929]
$\lambda = 36$	Cars only	0.765 [0.751 , 0.779]	0.987 [0.983 , 0.991]	0.978 [0.973 , 0.983]	0.967 [0.96 , 0.974]	0.979 [0.976 , 0.982]	0.998 [0.998 , 0.999]	0.997 [0.997 , 0.998]	0.996 [0.995 , 0.997]	0.899 [0.895 , 0.903]	0.867 [0.859 , 0.876]	0.895 [0.888 , 0.902]	0.886 [0.879 , 0.893]

Table B.1: Reliability, share of requests served within 60 minutes, mean and [95% CI]

		Combi				Fast				Safe			
		Forced	None	Closest Hub	Simple	Forced	None	Closest Hub	Simple	Forced	None	Closest Hub	Simple
$\lambda = 24$	Drones only	19.2 [19 , 19.3]	24.2 [24 , 24.3]	18.5 [18.4 , 18.7]	18.7 [18.5 , 18.8]	16.9 [16.8 , 17]	21.9 [21.8 , 22.1]	16.7 [16.6 , 16.8]	16.8 [16.7 , 16.9]	46.8 [46.4 , 47.2]	44.2 [44 , 44.4]	43.7 [43.5 , 43.8]	42.4 [42.2 , 42.6]
$\lambda = 24$	50% Drones	26.9 [26.6 , 27.2]	29.5 [29.2 , 29.7]	23.7 [23.5 , 23.9]	24.8 [24.6 , 25]	19.4 [19.2 , 19.5]	23.7 [23.5 , 23.9]	18.4 [18.3 , 18.5]	19 [18.9 , 19.2]	45.1 [44.6 , 45.5]	43.1 [42.8 , 43.4]	41.6 [41.4 , 41.8]	41.2 [41 , 41.5]
$\lambda = 24$	Cars only	38.9 [38 , 39.8]	38.4 [38.1 , 38.6]	33.9 [33.6 , 34.2]	34.8 [34.4 , 35.1]	23.9 [23.7 , 24.2]	27.5 [27.2 , 27.7]	23.3 [23.1 , 23.5]	23.3 [23.1 , 23.5]	58.8 [56.8 , 60.9]	55.5 [52.8 , 58.2]	44.1 [43.6 , 44.7]	43.6 [43.1 , 44.1]
$\lambda = 30$	Drones only	22.4 [22.2 , 22.7]	25.5 [25.3 , 25.7]	20.1 [20 , 20.3]	20.6 [20.5 , 20.8]	18.1 [18 , 18.3]	23 [22.8 , 23.2]	17.6 [17.5 , 17.7]	17.9 [17.7 , 18]	76 [71.9 , 80]	48.2 [47.8 , 48.6]	46.5 [46.2 , 46.9]	46.7 [46.3 , 47.2]
$\lambda = 30$	50% Drones	34 [33.3 , 34.7]	32.6 [32.3 , 33]	27.5 [27.1 , 27.8]	29.2 [28.9 , 29.6]	21.6 [21.4 , 21.9]	25.1 [24.9 , 25.4]	19.8 [19.7 , 20]	20.9 [20.7 , 21.1]	58.1 [56.1 , 60.1]	47 [46.5 , 47.5]	44.6 [44.3 , 44.9]	44.9 [44.5 , 45.3]
$\lambda = 30$	Cars only	61.8 [58.3 , 65.4]	39.5 [39.2 , 39.8]	36.8 [36.5 , 37.2]	38.2 [37.7 , 38.6]	26.3 [26 , 26.7]	28.2 [27.9 , 28.4]	24.4 [24.1 , 24.6]	24.9 [24.7 , 25.2]	87.3 [82.5 , 92.1]	57 [54.8 , 59.2]	48.4 [47.5 , 49.4]	49.8 [48.6 , 51]
$\lambda = 36$	Drones only	32.2 [31 , 33.5]	27.6 [27.3 , 27.8]	22.9 [22.7 , 23.2]	24.5 [24.2 , 24.8]	20.8 [20.5 , 21]	24.5 [24.3 , 24.7]	19.1 [18.9 , 19.2]	19.8 [19.6 , 20]	189 [178.7 , 199.3]	62 [59.9 , 64.1]	59.7 [57.7 , 61.6]	60.9 [58.9 , 62.9]
$\lambda = 36$	50% Drones	45.4 [43.5 , 47.2]	35.4 [35.1 , 35.7]	31.5 [31.2 , 31.9]	33.4 [33 , 33.8]	24.5 [24.1 , 24.8]	26.3 [26.1 , 26.5]	21.5 [21.3 , 21.7]	23 [22.8 , 23.3]	85.2 [81.1 , 89.4]	51.3 [50.5 , 52.2]	48.3 [47.7 , 48.8]	49.3 [48.7 , 50]
$\lambda = 36$	Cars only	92.8 [87 , 98.7]	40.7 [40.3 , 41.1]	39.5 [39 , 40.1]	41.4 [40.6 , 42.2]	28.9 [28.4 , 29.3]	28.7 [28.4 , 28.9]	25.6 [25.3 , 25.8]	26.6 [26.3 , 26.8]	119.4 [112.7 , 126.1]	63.9 [61.1 , 66.7]	53.1 [51.8 , 54.5]	54.4 [53.1 , 55.8]

Table B.2: Speed of delivery, average delivery time in minutes, mean, and [95% CI]

		Combi				Fast				Safe			
		Forced	None	Closest Hub	Simple	Forced	None	Closest Hub	Simple	Forced	None	Closest Hub	Simple
$\lambda = 24$	Drones only	0.41 [0.4 , 0.41]	0.42 [0.41 , 0.42]	0.43 [0.42 , 0.43]	0.42 [0.42 , 0.43]	0.96 [0.96 , 0.97]	0.78 [0.77 , 0.79]	0.96 [0.95 , 0.97]	0.96 [0.95 , 0.97]	0.05 [0.05 , 0.05]	0.03 [0.03 , 0.03]	0.04 [0.04 , 0.05]	0.04 [0.04 , 0.04]
$\lambda = 24$	50% Drones	0.32 [0.32 , 0.33]	0.36 [0.35 , 0.36]	0.38 [0.37 , 0.38]	0.33 [0.33 , 0.34]	1.76 [1.74 , 1.78]	1.34 [1.32 , 1.35]	1.67 [1.65 , 1.69]	1.72 [1.7 , 1.74]	0.04 [0.04 , 0.04]	0.03 [0.02 , 0.03]	0.04 [0.04 , 0.04]	0.03 [0.03 , 0.03]
$\lambda = 24$	Cars only	0.38 [0.37 , 0.4]	0.41 [0.38 , 0.44]	0.35 [0.33 , 0.37]	0.37 [0.35 , 0.39]	3.65 [3.61 , 3.69]	2.63 [2.6 , 2.66]	3.41 [3.38 , 3.44]	3.6 [3.56 , 3.64]	0.04 [0.04 , 0.05]	0.03 [0.03 , 0.04]	0.04 [0.04 , 0.04]	0.04 [0.04 , 0.04]
$\lambda = 30$	Drones only	0.48 [0.48 , 0.48]	0.53 [0.52 , 0.53]	0.52 [0.52 , 0.53]	0.51 [0.51 , 0.52]	1.19 [1.18 , 1.2]	0.98 [0.97 , 1]	1.17 [1.16 , 1.18]	1.18 [1.17 , 1.19]	0.07 [0.07 , 0.07]	0.04 [0.04 , 0.04]	0.05 [0.05 , 0.05]	0.05 [0.05 , 0.05]
$\lambda = 30$	50% Drones	0.43 [0.42 , 0.44]	0.48 [0.47 , 0.49]	0.46 [0.45 , 0.47]	0.41 [0.4 , 0.42]	2.38 [2.35 , 2.41]	1.78 [1.75 , 1.8]	2.2 [2.17 , 2.23]	2.33 [2.3 , 2.36]	0.05 [0.05 , 0.06]	0.03 [0.03 , 0.03]	0.04 [0.04 , 0.04]	0.04 [0.04 , 0.04]
$\lambda = 30$	Cars only	0.34 [0.32 , 0.36]	0.56 [0.52 , 0.59]	0.51 [0.49 , 0.53]	0.55 [0.53 , 0.58]	4.36 [4.32 , 4.4]	3.2 [3.17 , 3.23]	4.06 [4.03 , 4.1]	4.3 [4.27 , 4.34]	0.05 [0.05 , 0.06]	0.04 [0.04 , 0.04]	0.05 [0.05 , 0.05]	0.05 [0.05 , 0.05]
$\lambda = 36$	Drones only	0.52 [0.52 , 0.53]	0.63 [0.62 , 0.63]	0.6 [0.59 , 0.6]	0.59 [0.59 , 0.6]	1.39 [1.38 , 1.4]	1.18 [1.17 , 1.19]	1.36 [1.36 , 1.37]	1.37 [1.37 , 1.38]	0.08 [0.08 , 0.08]	0.05 [0.05 , 0.05]	0.06 [0.06 , 0.06]	0.06 [0.06 , 0.06]
$\lambda = 36$	50% Drones	0.5 [0.49 , 0.51]	0.6 [0.59 , 0.62]	0.54 [0.53 , 0.55]	0.51 [0.5 , 0.53]	2.87 [2.84 , 2.89]	2.16 [2.14 , 2.19]	2.65 [2.63 , 2.67]	2.82 [2.8 , 2.85]	0.06 [0.06 , 0.06]	0.04 [0.04 , 0.04]	0.05 [0.05 , 0.05]	0.05 [0.05 , 0.05]
$\lambda = 36$	Cars only	0.3 [0.28 , 0.32]	0.71 [0.67 , 0.74]	0.65 [0.63 , 0.68]	0.68 [0.66 , 0.71]	4.81 [4.78 , 4.84]	3.65 [3.62 , 3.68]	4.53 [4.5 , 4.56]	4.76 [4.73 , 4.78]	0.06 [0.06 , 0.06]	0.05 [0.05 , 0.05]	0.05 [0.05 , 0.06]	0.06 [0.06 , 0.06]

Table B.3: TPR, Expected number of casualties per operating year, mean, and [95% CI]

		Combi				Fast				Safe			
		Forced	None	Closest Hub	Simple	Forced	None	Closest Hub	Simple	Forced	None	Closest Hub	Simple
$\lambda = 24$	Drones only	103 [102 , 104]	75 [74 , 76]	96 [95 , 97]	101 [100 , 102]	76 [75 , 77]	65 [64 , 66]	73 [72 , 74]	76 [75 , 76]	153 [151 , 154]	123 [122 , 125]	135 [134 , 136]	144 [143 , 146]
$\lambda = 24$	50% Drones	275 [269 , 281]	189 [185 , 192]	247 [242 , 252]	260 [255 , 265]	307 [301 , 313]	244 [239 , 248]	288 [282 , 294]	300 [294 , 306]	335 [330 , 340]	208 [204 , 211]	312 [307 , 317]	292 [287 , 296]
$\lambda = 24$	Cars only	774 [766 , 783]	579 [574 , 584]	741 [735 , 747]	785 [777 , 793]	846 [836 , 857]	631 [625 , 637]	801 [793 , 808]	840 [831 , 850]	629 [622 , 636]	490 [485 , 495]	614 [609 , 619]	615 [609 , 622]
$\lambda = 30$	Drones only	134 [132 , 136]	96 [95 , 97]	121 [119 , 122]	129 [127 , 130]	99 [97 , 100]	83 [82 , 84]	92 [91 , 93]	98 [97 , 100]	187 [185 , 189]	155 [153 , 157]	164 [162 , 165]	173 [172 , 175]
$\lambda = 30$	50% Drones	414 [406 , 421]	273 [268 , 278]	360 [354 , 366]	385 [378 , 392]	462 [454 , 471]	340 [334 , 347]	410 [403 , 417]	450 [441 , 459]	428 [422 , 433]	287 [282 , 291]	379 [374 , 384]	389 [383 , 395]
$\lambda = 30$	Cars only	939 [929 , 950]	702 [695 , 708]	862 [856 , 868]	922 [915 , 929]	1062 [1051 , 1074]	776 [768 , 783]	976 [966 , 985]	1057 [1046 , 1068]	773 [763 , 783]	589 [583 , 595]	711 [705 , 717]	728 [722 , 735]
$\lambda = 36$	Drones only	163 [161 , 164]	116 [114 , 117]	141 [140 , 142]	152 [150 , 153]	120 [119 , 122]	101 [100 , 102]	110 [109 , 111]	119 [118 , 120]	214 [213 , 216]	181 [179 , 182]	186 [185 , 187]	190 [190 , 191]
$\lambda = 36$	50% Drones	507 [502 , 513]	355 [350 , 360]	449 [444 , 454]	476 [470 , 482]	596 [589 , 604]	427 [421 , 433]	522 [515 , 529]	590 [582 , 598]	486 [482 , 490]	354 [349 , 358]	429 [425 , 433]	450 [446 , 455]
$\lambda = 36$	Cars only	1070 [1056 , 1083]	791 [785 , 797]	928 [922 , 935]	983 [977 , 989]	1211 [1200 , 1221]	889 [882 , 896]	1105 [1098 , 1113]	1209 [1201 , 1217]	885 [877 , 893]	665 [659 , 671]	773 [768 , 779]	792 [786 , 798]

Table B.4: Emissions, kg of CO2 emitted, mean, and [95% CI]

C

Additional results and analyses

This appendix contains additional results that were not fully presented or discussed in the scientific paper. These results provide context and further clarifications of the main findings of our research.

C.1. Vehicle capacity

This section contains an elaboration on how many deliveries a single vehicle can complete each day. In subsection subsection C.1.1 we analyze how the vehicle type and size of a fleet influence the delivery capacity of a vehicle. Next in subsection subsection C.1.2 we look at how a vehicle spends its time in order to make these deliveries.

C.1.1. Fleet composition

Building upon what has been shown in the paper, we present a more detailed graph on the reliability of different fleet configurations in Figure C.1. We show for fleets ranging from $N_{total} = 1$ to $N_{total} = 14$ for both cars how reliably they can perform a certain amount of deliveries. Note that the amount of deliveries performed is also a simulation output which is influenced by χ, λ, the hospital-selection methods, and the number and size of hospitals. However, by plotting the reliability along this axis we hope to create some perspective that is difficult to grasp when looking only providing λ / N_{total} numbers. For both vehicle types the reliability increases with the number of vehicles, so the red and green light on the left represent fleets $N_{car} = 1$ $N_{drone} = 1$ respectively. Additionally, we highlight the fleets existing of 4, 8 or 12 vehicles.
We can observe that drones have a higher per-vehicle daily delivery capacity. It should be noted that in order to derive the daily capacity of the entire system one should multiply these per vehicle numbers by the number of vehicles in the fleet. This explains the more than linear growth of system capacity when increasing fleet size. In the assumed facility allocation scenario, which was the same as the experiments described in the fleet composition section of the paper, a fleet of 14 drones is able to reliably perform 65 deliveries per vehicle in 24 hours. Which is equivalent to an average of 2.7 deliveries per hour. In the next subsection, we go into more detail on how a drone spends its time during such a day. Additionally, this gives some explanation on why the per vehicle capacity for cars is lower.

C.1.2. Vehicle occupancy

To gain better insight into the delivery capacity of the system, and how by which factors this is limited, we analyzed the occupancy of the vehicles. In Figure C.2 we show the share of time during the day a vehicle is actually moving. This is shown for both vehicle types by the solid lines, the dashed lines state the percentage of time a vehicle is performing a delivery. The difference between the solid and dashed line thus represents the time the vehicle is on the move, for instance towards a pick-up location, whilst not actually transporting any goods. Naturally, these percentages increase when the number of deliveries performed during the day, indicated on the horizontal axis, becomes greater. For this analysis, we filtered simulation results so that only days with +95% reliability were included. Therefore, this plot does not show how often or how reliably a vehicle fleet can actually perform these amounts of deliveries per vehicle per day (which was shown in Figure C.1). It only shows when it does do so reliably, how vehicles are spending their time during that day.
We can see that for both vehicle types the total share of time a vehicle is on the move starts to plateau. This

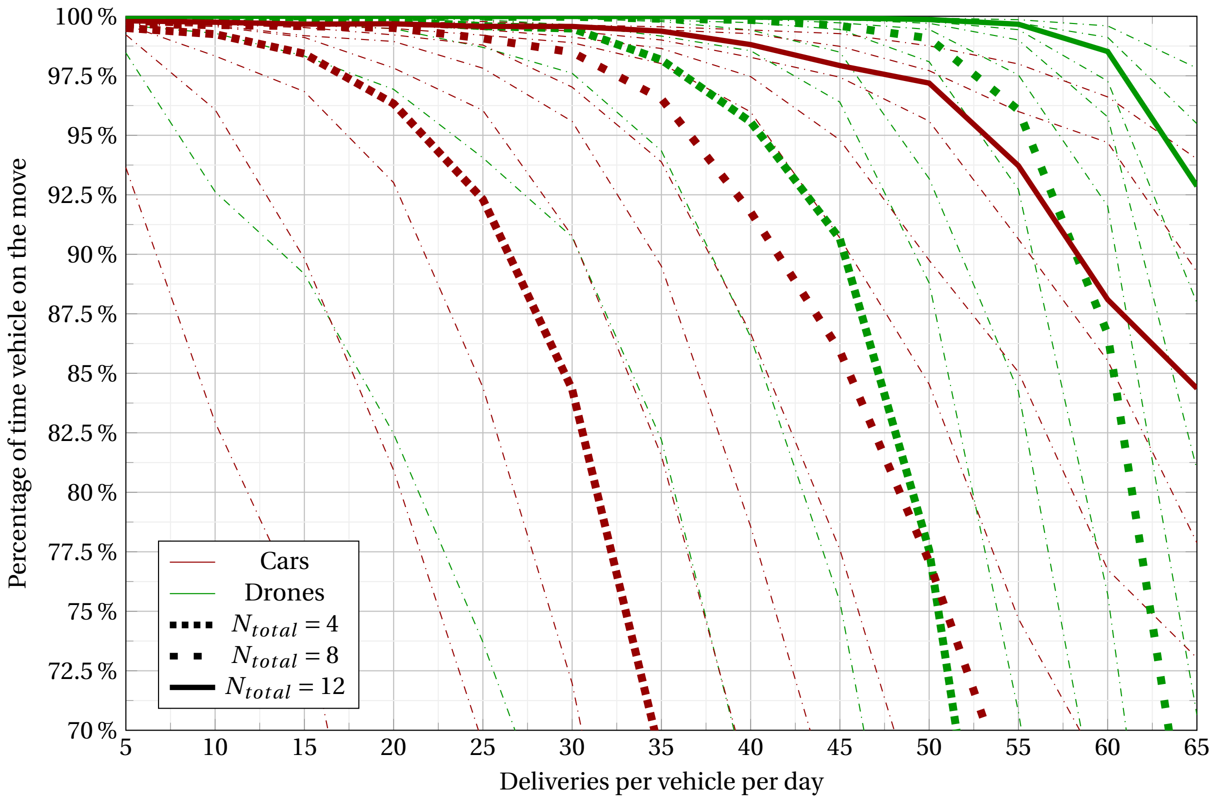


Figure C.1: Vehicle capacity

asymptote forms naturally around the average length of the routes in minutes, divided by this same number plus the vehicle turn-around-time. This average trip time of the routes used is longer for cars, indicated by the steeper slope of the dashed lines at the left of the graph. Additionally, cars are assumed to have a shorter turn-around-time compared to drones, three and five minutes respectively.
Since drones are only able to perform one delivery per flight, the share of time a UAV is carrying a product has a consistently linear relation with the number of deliveries performed. In contrast, because cars are assumed to be able to carry up to ten goods per trip, they can perform multiple deliveries in a single ride. Thus cars are able to keep increasing the number of daily deliveries whilst the share of time it is on the road carrying products does not grow at the same rate.

C.2. Drone sensitivity analyses

In our research, several assumptions were made on how drones would be able to operate. To test how robust the presented findings are to changes in these assumptions we conducted sensitivity analyses. In this section, we cover two drone-related experiments.

C.2.1. Travel time

Figure C.3 shows in a matrix of contour-plots how average delivery times would be impacted by four different parameters. Firstly the cruising speed of the drone, it should be noted that for this analysis the same drone route input was used. In order to determine the route distance and more importantly TPR in the pre-processing model, the initial assumption of a 60km/h cruising speed was assumed. Exact route distances and risk levels are expected to be slightly different when generating new routes based on other drone speed assumptions, however, we argue that this would not heavily influence the conclusions and findings one can derive from this sensitivity analysis. Secondly, the time needed to execute all procedures between landing and taking off on a new flight was varied. This turn-around-time (TAT) includes for instance (un)loading, swapping batteries, and performing a pre-flight checklist. Thirdly we changed the time needed to vertically ascend or descend before or after following the flight route. Since a VTOL drone is likely to be used that can

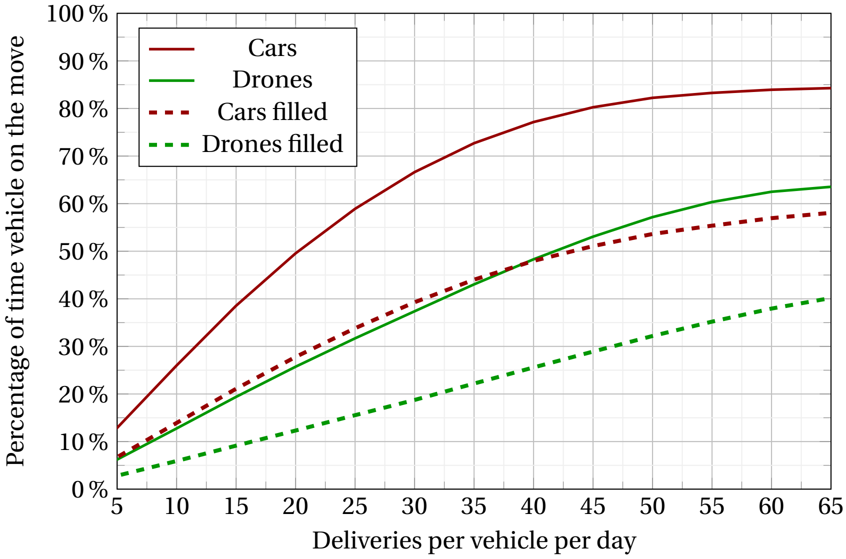


Figure C.2: Vehicle usage

land vertically on a drone platform on top of or near a hospital, time is needed to cover the vertical distance between the platform and cruising flight altitude. Lastly, we tested 3 levels of centralization, a term described more extensively in the paper. We set χ to 3, 6, or 9 representing a high, medium, or low degree of centralization respectively. Other model inputs were $N_{Drones} = 9$, $\lambda = 30$ and facilities were allocated using the Concentrated and Location method.

This analysis shows that although we encounter much emphasis on drone speed both in academics and industry, it is at least equally important to consider how these drones are handled at the hospital. It is not rational to opt for a drone model capable of flying 20 km/h faster, if this model is more difficult to (un)load by hospital-personal, thus increasing the TAT by several minutes. For the same reasoning take-off and landing times could be put into perspective by directly comparing their absolute values with the TAT. Although it is tempting to look at this system from mainly engineering perspectives, like drone flight performance indicators, we argue that one should engage medical stakeholders in the design of the proposed system.

Additionally, this sensitivity analysis stresses the dependency of our results on the assumptions made in this research. It can be argued that one can simply compensate for the effects of changes in these assumptions by altering other system parameters one can control, like for instance the fleet size or centralization. However, we want readers to be aware that results might not be directly applicable to other concepts of operations and encourage others to conduct research specific to other settings and environments.

C.2.2. Third-party-risk

Our model determines TPR for Cars based on historical statistics. The methods used to process these statistics into TPR values for all car routes for both safe and fast driving might be subject to debate. However, we argue that this method based on statistics requires less rough assumptions compared to the theoretical model used to derive drone route TPR. Thus we conducted a sensitivity analysis to gain insights into what would happen if, for instance, the probability of event would be twice as high.

In Figure C.4 we show the results of this sensitivity analysis. A Drones only and Cars only fleet of $N_{Total} = 12$ under a demand level of $\lambda = 25$, which for both fleets is beneath its operating limit. Similar to the above-mentioned sensitivity analysis, high, medium, and low degree of centralization is represented in the model as χ being 3, 6, or 9 respectively. The drone risk multiplication factor plotted on the horizontal axes of the graphs indicates how much bigger TPR values are on every single route compared to the results from the theoretical model. Thus this factor being 2^0 TPR values are not changed, whilst if the factor is 2^2 we expect four times as many casualties per flight route.

We see how drone-induced TPR is relatively independent of the degree of centralization in terms of average risk per flight. Note that with less centralization fewer flights are needed and total TPR does decrease. This is due to the fact that drone route TPR has little correlation with its distance, since the majority of risk is present

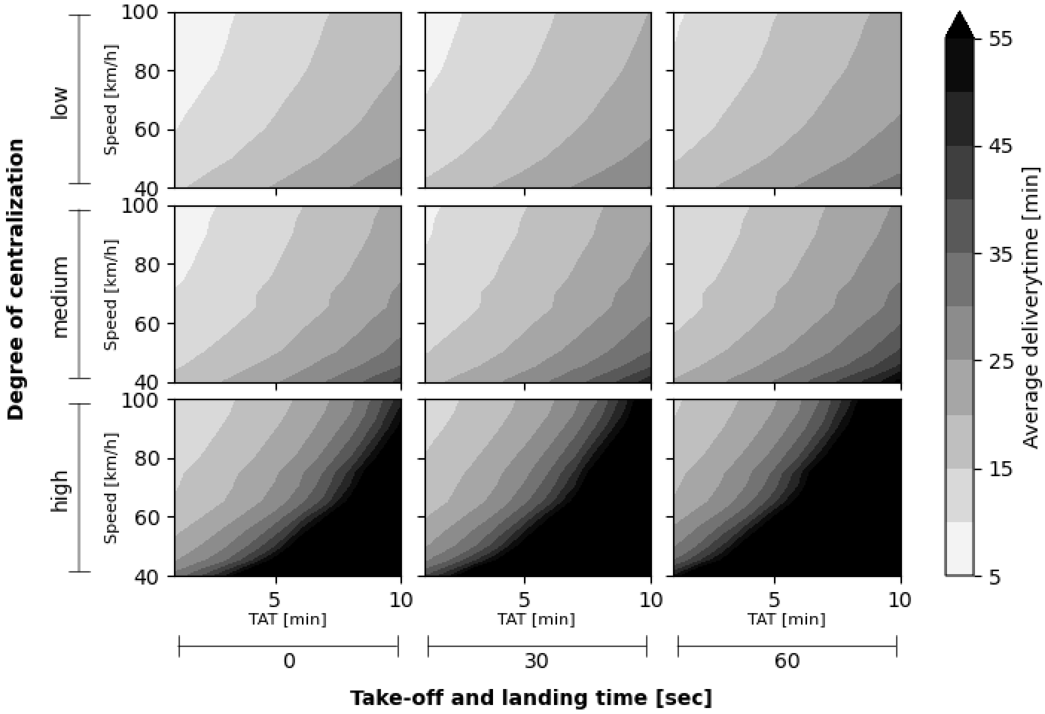


Figure C.3: Sensitivity analysis of drone assumptions

at the beginning and end of the route, above urban areas near the hospital. A future study might optimize the facility allocation algorithms further, so hospitals are not prioritized based on distance but on TPR minimization. Cars, on contrary, do benefit from having to cover less distance per route in terms of reducing TPR. Put differently, for more centralized medical systems drones are preferable when minimizing TPR compared to less centralized systems where only deliveries over short distances are needed.

Looking at the drone risk multiplication factor value where both lines intersect we see that actual drone TPR per flight can be up to six times higher, than what has been derived theoretically, for drone risks to be equally high as that of cars. For less centralized systems actual risk should be around 10% more than based on our assumption to reach this equilibrium. Since both fleets operate below their capacity, and car risk tends to increase more when getting nearer to its operating limit, we except that other scenarios will not be significantly more favorable for cars. What we actually want readers to take from this graph, and our research in general is not the exact factor that our risk models could be off by in order for our findings to uphold. Rather we want to emphasize the benefit of being able to put risk levels into perspective. Although exact casualty expectations might be off for both models, we are confident in saying that a UAV assisted distribution system would not cause an order of magnitude more TPR than what we are already (subconsciously) accepting from road transport.

C.3. Route usage

As mentioned at the end of the results section of the paper, a naturally emerging behavior exists that most flights happen within a single region. In Figure C.5 we visualize this effect by showing how often a route is flown as a percentage of all flights taken. We show here the heatmap created in a configuration with demand near system capacity, in such high demand situations it was found that both flights between different regions and flights not going to or coming from a hub occur more often compared with lower demand situations.

We can clearly distinguish which hospitals share the same hub and can be argued to form a region. Additionally, we see which hospitals are bigger and thus require more deliveries. We see that a significant share of flights depart from the Franciscus Rotterdam hub to the Reinier de Graaf hospital in Delft. However, the return flight is less frequently used but the route from Delft back to the Voorburg hub is actually used more than the outgoing route between the two Reinier de Graaf locations. This could be seen as an indication of

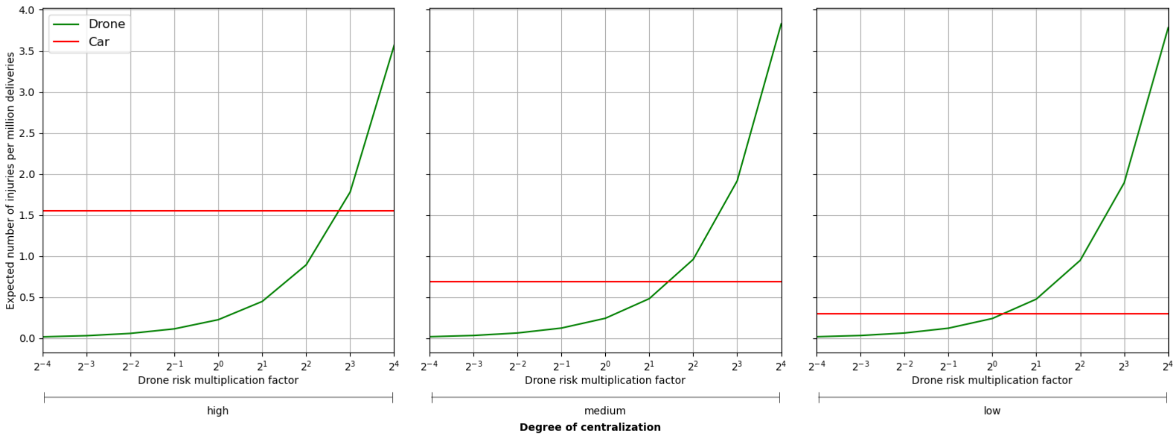


Figure C.4: Sensitivity analysis of drone risk

the self-balancing characteristic of system behavior, by reallocating delivery capacity in the form of vehicles to regions where they might lack them. A phenomenon that can only occur and be observed in more complex simulation models like the proposed agent-based framework.

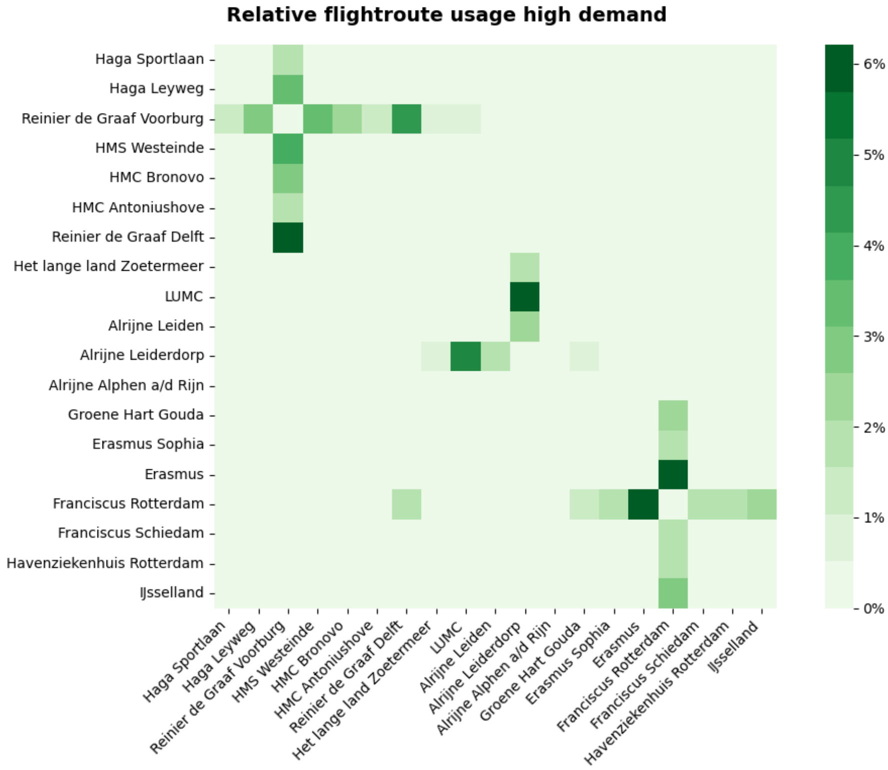


Figure C.5: Route usage heatmap

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