ABSTRACT

Title of Dissertation:	MODELING AND SIMULATION OF NOVEL MEDICAL RESPONSE SYSTEMS FOR OUT-OF-HOSPITAL CARDIAC ARREST
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Dissertation directed by:	Professor Jeffrey Herrmann Department of Mechanical Engineering

Sudden Cardiac Arrest (SCA) is the leading cause of death in the United States, resulting in 350,000 deaths annually. SCA survival requires immediate medical treatment with a defibrillatory shock and cardiopulmonary resuscitation. The fatality rate for out-of-hospital cardiac arrest is 90%, due in part to the reliance on Emergency Medical Services (EMS) to provide treatment. A substantial improvement in survival could be realized by applying early defibrillation to cardiac arrest victims. Automated External Defibrillators (AEDs) allow lay rescuers to provide early defibrillation, before the arrival of EMS. However, very few out-of-hospital cardiac arrests are currently treated with AEDs.

Novel response concepts are being explored to reduce the time to defibrillation. These concepts include mobile citizen responders dispatched by a cell phone app to

nearby cardiac arrest locations, and the use of drones to deliver AEDs to a cardiac arrest scene. A small number of pilot studies of these systems are currently in progress, however, the effectiveness of these systems remains largely unknown.

This research presents a modeling and simulation approach to predict the effectiveness of various response concepts, with comparison to the existing standard of EMS response. The model uses a geospatial Monte Carlo sampling approach to simulate the random locations of a cardiac arrest within a geographical region, as well as both random and fixed origin locations of responding agents. The model predicts response time of EMS, mobile dispatched responders, or drone AED delivery, based on the distance travelled and the mode of transit, while accounting for additional system factors such as dispatch time, availability of equipment, and the reliability of the responders. Response times are translated to a likelihood of survival for each simulated case using a logistic regression model. Sensitivity analysis and response surface designed experiments were performed to characterize the important factors for response time predictions. Simulations of multiple types of systems in an example region are used to compare potential survival improvements. Finally, a cost analysis of the different systems is presented along with a decision analysis approach, which demonstrates how the method can be applied based on the needs and budgets of a municipality.

MODELING AND SIMULATION OF NOVEL MEDICAL RESPONSE SYSTEMS FOR OUT-OF-HOSPITAL CARDIAC ARREST

by

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Research Disclosures

The author of this dissertation is an employee of Philips Healthcare. Philips designs, manufactures, and markets both AEDs and monitor/defibrillator medical devices used by EMS. Philips also consults customers on the implementation of PAD programs, and other community response systems. Philips is providing tuition assistance for this degree. Philips is not providing funding to Professor Herrmann or any other faculty on this PhD committee.

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Table of Contents

List of Tables

List of Figures

List of Abbreviations

ACLS	Advanced Cardiac Life Support
AED	Automated External Defibrillator
AHA	American Heart Association
ALS	Advanced Life Support
ANOVA	Analysis of Variance
API	Application Programming Interface
BLS	Basic Life Support
BU	Bystander use
CARES	Cardiac Arrest Registry for Enhanced Survival
CDC	Center for Disease Control
CPR	Cardio Pulmonary Resuscitation
DES	Discrete Event Simulation
DOE	Design of Experiments
ECG	Electrocardiogram
EMS	Emergency Medical Services
ERC	European Resuscitation Council
FAA	Federal Aviation Administration
FDA	Food and Drug Administration
GIS	Geographic Information System
GPS	Global Positioning System
Lat	Latitude
Long	Longitude
MAUDE	Manufacturer and User Facility Device Experience
MCLP	Maximum Coverage Location Problem
MR	Mobile Responder
MSE	Mean Squared Error
NFPA	National Fire Protection Association
NPV	Net Present Value
OHCA	Out-of-Hospital Cardiac Arrest
PAD	Public Access Defibrillation
RMSE	Root Mean Squared Error
ROSC	Return of Spontaneous Circulation
RSM	Response Surface Methodology
SCA	Sudden Cardiac Arrest
UAV	Unmanned Aerial Vehicle
V&V	Verification and Validation
VF	Ventricular Fibrillation
VSL	Value of Statistical Life
VF	Ventricular Tachycardia

Chapter 1: Introduction

Sudden cardiac arrest is the leading cause of death in the United States. 350,000 people die from sudden cardiac arrest outside of the hospital each year [1]. When sudden cardiac arrest occurs, the heart ceases to beat in an organized, normally paced rhythm, instead, beating in a rapid, chaotic manner, known as fibrillation. While in this condition, the heart is not able to pump blood through the lungs to achieve oxygenation and exhalation of carbon dioxide, and is not able to provide perfusion to the brain and other vital organs. Loss of consciousness occurs immediately, neurological damage can occur within a few minutes, and the victim rarely survives longer than 10 to 15 minutes.

The treatment for sudden cardiac arrest is a defibrillatory shock and cardio pulmonary resuscitation (CPR). CPR is the act of compressing the cardiac arrest victim's chest by exerting repetitive force on the sternum. This action can compress the heart, causing the circulation of blood to occur. Mouth to mouth resuscitation or the use of a bag valve mask provides oxygen to the lungs during CPR. Defibrillation is the application of an electric shock across the torso of the victim, which interrupts the electrical activity of the heart muscles, and can restore a normal, organized heart rhythm. Both CPR and defibrillation must be provided within the first few minutes after the onset of cardiac arrest to provide a successful resuscitation. For every minute that elapses after the collapse of the victim the chances of survival are reduced by 5% to 10% [2][3][4]. Sudden cardiac arrest stands unique from other diseases and conditions in that much of the focus for improvement in survival is not on the clinical treatment of the condition, but on methods to reduce the time to get treatment to the patient.

1.1 Background

Sudden cardiac arrest can affect anyone, often occurring without prior indications. Although primarily affecting the elderly, sudden cardiac arrest can occur at any age, from neonatal, infants, children, teenagers, and through the adult years. The prognosis for cardiac arrest is very poor. When it occurs outside of the hospital, the survival rate in the United States is about 10% [3][1]. Even when it occurs within hospitals, where a quick response and professional care is standard, the survival to discharge is only 22% [5]. The primary source of treatment for out-of-hospital cardiac arrest (OHCA) is provided by Emergency Medical Services (EMS). This consists of paramedics and emergency medical technicians (EMT) dispatched to the cardiac arrest location in an ambulance. The national standard for EMS response times is to reach 90% of calls within 8 minutes [6], for the highest priority calls, although many municipalities and rural areas have significantly longer average response times. It is evident with these response times that survival from cardiac arrest will be very low.

Survival rates from sudden cardiac arrest have not shown significant improvement over time [7]. EMS systems have been optimized for quick response, but they are expensive to maintain, let alone to grow, in order to keep up with growing populations, congestion, and urban sprawl. Rural areas pose even greater challenges to achieve a fast EMS response time. Alternative approaches to response and treatment are needed to achieve quicker defibrillation in order to improve survival.

The invention of the Automated External Defibrillator (AED) has allowed bystanders to quickly and effectively respond to sudden cardiac arrests (Figure 1). An AED, when applied to a patient, will analyze the heart rhythm, algorithmically determine if the patient has a shockable arrhythmia, and deliver a defibrillatory shock. A “lay user”, i.e. a person without any medical training, can apply and operate the AED. When AEDs are available and used on a cardiac arrest patient, survival is increased to 25%, about 3 times the odds of survival as from EMS treatment [8]. Appendix B provides further description of the operation and function of an AED.

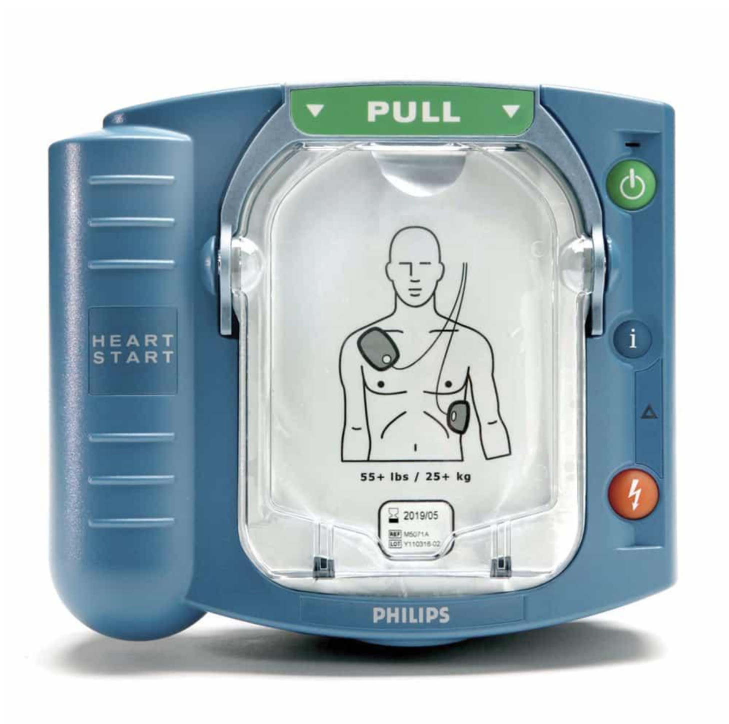


Figure 1. An Automated External Defibrillator (AED)

In locations where AEDs have been widely deployed, such as casinos, significant improvement in survival has been achieved. However, AEDs have failed to reach the level of dissemination needed to significantly improve overall survival rates for sudden cardiac arrest. Studies have shown only 2% to 5% of all sudden cardiac arrests are treated with an AED prior to EMS arrival [3]. Most AEDs are located inside buildings, many being private facilities, and unavailable for cardiac arrests in outdoor or public areas. Additionally, about two thirds of sudden cardiac arrests occur within homes, where AED adoption is nearly non-existent.

Recent advances in technology have led to the development of novel concepts to overcome these barriers to improved cardiac arrest survival. One such is the advent of the GPS equipped smartphone. Technology has been developed to dispatch volunteer responders who happen to be near a cardiac arrest location via a cell phone app. This allows a type of on-demand ”crowdsourcing” of a rescue response. Initially these programs have focused primarily on providing CPR until the arrival of EMS. Pilot studies are being explored where volunteers either carry an AED with them at all times, or are directed to the nearest AED in a community registry and then to the patient by an EMS dispatcher or by the app. While these programs have had sporadic success stories, it is not yet known how effective these programs will be in improving survival, nor what conditions would be required (e.g. responder density, AED access) to achieve a desired improvement.

The future of bringing early defibrillation to sudden cardiac arrest victims may lie in another emerging technology – the autonomous aerial drone. Drones have the capability to travel above traffic and buildings, use a straight line of navigation to the scene, and travel at speeds much faster than an ambulance on city streets. Development of drones for delivery purposes has been widely publicized, with some trials being performed by companies like Amazon [9]. Other companies and university researchers have directed research toward the development of drones specifically designed for AED delivery. Drones can quickly transport an AED from a central location, such as a fire station, to a cardiac arrest scene, to be used by a bystander or dispatched responder. Significant challenges – both technological and regulatory -- must be overcome before this type of response system becomes a reality. While technology exists for autonomous drone flights and routing, the FAA currently restricts drone flights to visual line of sight of the operator. The public is not yet accustomed to autonomous drones, and must have confidence in the reliability and safety of their use. There is currently research in drone AED delivery, and there have been a few simulated rescue demonstrations, however there is not yet any municipality using drones in actual medical responses.

Sudden cardiac arrest, by its very nature, is a difficult medical condition to study. Its occurrence is nearly impossible to predict, as many patients show no prior symptoms of cardiac issues. Clinical trials are not able to enroll patients with a known condition, in the traditional sense, as is typical with most disease studies. As the cardiac arrest victim is unconscious and unresponsive at the time of the arrest, informed consent cannot be obtained. Most studies of sudden cardiac arrest treatments have either employed a community based approach, where a community health agency provides the consent, often accompanied with a public notification, and a mechanism for citizens to opt out of the study. Other methods include identifying large numbers of high risk patients and monitoring them for a significant period of time. This too is difficult, because the standard of care is to provide implantable cardioverters to patients at the highest risk. Thus, such study approaches target patients with elevated risks, but not high enough to receive an implantable defibrillator.

The difficulties of studying cardiac arrest extend to the study of the efficacy of response systems. Formal studies of these new systems require several years to generate enough cases to assess the performance of the system. These studies are also expensive, particularly when provisioning large numbers of responders with AEDs. Other difficulties have arisen in these studies as well, such as liability for the actions of the responder, patient privacy concerns, the ability and authorization of responders to enter private residences, and responder safety. These make clinical studies rare, with only a small number having been commenced.

With the diversity of novel response systems proposed, EMS decision-makers will need to estimate costs, effectiveness, and reliability as they determine which type of enhanced system to implement within a community. Modeling and simulation is an approach that can synthesize information discovered from studies and trials, and provide predictions on system performance under conditions not available or achievable during a study or pilot program. It can also be used to extrapolate information obtained from existing systems, to make predictions about new, untested system concepts.

Modeling and simulation are widely used to analyze a system's capability when direct experimentation is difficult, costly, unsafe, or infeasible. A model is an abstraction of a real world item or system, which allows for simplified analysis or evaluation of the system. A model may be a physical representation of an item, or a functional representation, usually involving a computational or mathematical evaluation of the functions of a system. Modeling and simulation provide an approach to studying sudden cardiac arrest response concepts that can be both flexible and comprehensive in the analysis of factors that impact system performance. The benefits of modeling and simulation are the ability to predict the performance of a system under many different conditions, in order to define an optimal or ideal set of conditions, or most cost effective conditions to apply to the real system. Where direct studies of a response system may take several years and cover a single set of operating conditions, simulation experiments can be performed in a relatively short time and cover multiple conditions to provide a spectrum to system performance potential. Models can be applied prospectively as decision support tools, which inform the decision-makers of the most efficient, effective, and cost-effective type of system, and the optimal conditions of such a system.

1.2 Goals of this Research

The objective of this research is to generate new knowledge that can be used to design and realize better cardiac arrest response systems, such that more lives can be saved. The goal is to create a comprehensive approach and decision support tools that can help decision-makers predict the effectiveness and evaluate the costs and benefits of various novel response systems. This objective is approached through the development of a set of mathematical models which can simulate the cardiac arrest response times of different proposed response systems, and provide comparison to simulated EMS response times. The models were developed such that the effects of different attributes, or conditions of the system can be evaluated, including the reliability of the system, as pertaining to its ability to provide a response. Together, these are used to provide an estimated improvement in survival, i.e. the public health benefit of the system. The benefits of the various systems can be balanced against the cost of implementing such a system.

This research is intended to answer the following questions:

1. *Can alternative cardiac arrest medical response systems provide a substantial improvement in survival for out-of-hospital cardiac arrest?*

    - *What system structure and conditions are needed to achieve the improvement in survival?*

- *Can alternative response systems provide cost effective improvement in the survival rate for cardiac arrest?*

These alternative response systems, by design, can only improve survival, as they are an additional response system to augment the traditional EMS response system. The effectiveness of the traditional EMS response is assumed unaffected by the addition of an enhanced response system in these models, thus the overall survival could be no worse than with an EMS response only. If an adverse impact on EMS response efficacy did exist due to the additional response system (for example, EMS response slows because they believe help will already be on the scene), it is conceded that only an actual human trial could identify the effect. Hence, the more important question is *how much* of an improvement in survival could be achieved by these systems, and what conditions of the system would be necessary to realize the improvement.

A series of simulation experiments were used to explore each of the models, to understand the effect of each factor. The research also provides analysis of the overall cost of each proposed concept, as well as the costs associated with varying different conditions in the system.

2. *How could modeling and simulation methods be used to evaluate the benefits of various alternative response systems for specific municipalities or EMS organizations?*

EMS organizations vary greatly in their capabilities, response time performance, budgets, priorities, etc. Some municipalities could benefit more from one type of alternative response, while others may find greater benefit from entirely different systems. The culture of a community may provide a preferred choice. A close knit community may find volunteer responders easy to recruit. Other communities may not be comfortable with non-commissioned volunteer responders entering private residences, or having access to the location of cardiac arrest victims. Modeling and simulation would be a significant asset in decisions around improving response systems, and allocating budget. The predicted effectiveness of different options could be balanced against community preferences, values, and resources.

1.3 Outline of Dissertation

This dissertation is organized as follows: Chapter 2 provides a literature review of existing and proposed novel cardiac arrest response concepts, as well as the application of modeling and simulation to the area of emergency response systems. Chapter 3 provides an overview of the research approach, including the modeling and simulation that served as the basis for this dissertation. Chapter 4 describes the model, its inputs, outputs, and execution, as well as an approach for verification and validation. Chapter 5 examines the sensitivity of the model to input factors, as well as a response surface design of experiments (DOE) analysis of the response behavior and interactions of significant factors. Chapter 6 applies the model and simulation to compare the effectiveness of a diversity of systems, while Chapter 7 extends the comparison to include a cost analysis and cost-benefit decision approach. Chapter 8 summarizes the key points of the research, the limitations, and future directions of the research.

Chapter 2: Literature Review

2.1 Cardiac Arrest Survival

The American Heart Association defines sudden cardiac arrest as "the abrupt loss of heart function" where "the time and mode of death are unexpected". Cardiac arrest results in immediate failure of the circulatory system. Visible symptoms of cardiac arrest include a sudden collapse, loss of consciousness, lack of a pulse, and lack of breathing. The cessation of perfusion to the lungs, brain, and other organs causes tissue hypoxia, which if untreated, leads to death within minutes. The prognosis for victims of sudden cardiac arrest is poor, as the fatality rate in the United States is nearly 90% [3].

Cardiac arrest is caused by an irregular electrical rhythm of the heart. While there are many types of arrhythmias, the two that require immediate treatment to prevent death are ventricular fibrillation (VF) and ventricular tachycardia (VT). The treatment for a patient in VF or VT is CPR, defibrillation, and Advanced Cardiac Life Support (drug delivery, airway intubation, and other treatment provided by a medical professional). A detailed discussion of the physiology of cardiac arrest and its treatment is provided in Appendix A.

The time from patient collapse to defibrillation has a strong correlation to survival. An often quoted heuristic is the chances of survival decrease by 10% for each minute that passes before defibrillation [10]. More precise studies by Abrams *et al*. [3]and Wik *et al.* [11] have produced survival curves such as the one shown in Figure 2. Larsen *et al.* formed a linear regression model on time-to-CPR t_{CPR}, time-to-defibrillation t_{defib}, and time-to-Advanced Cardiac Life Support t_{ACLS} to produce the probability of survival P_s equation [2]:

$$P_s = 0.67 - 0.23t_{CPR} - 0.11t_{defib} - 023t_{ACLS} \quad (1)$$

This model is limited to the first 20 minutes after the arrest. Valenzuala *et al.* improved by using logistic regression to model survival. They reported a reduced model, consisting of only time to defibrillation and time to CPR, provided equivalent predictive accuracy to more complex models [12]:

$$P_s = \frac{e^l}{e^l + 1} \quad (2)$$

Where: $l = 0.26 - 0.106t_{CPR} - 0.139t_{defib}$

Others have reported significantly higher survival possibilities with very short time to defibrillation.

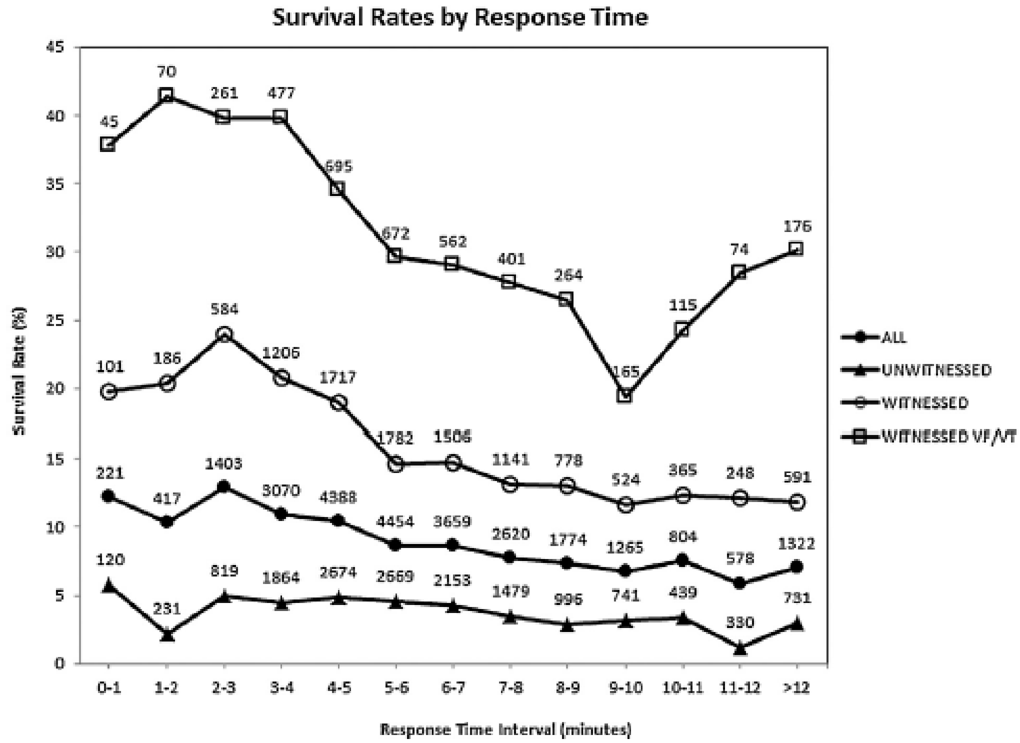


Figure 2. Cardiac arrest survival based on response time, whether the collapse was witnessed, and the presenting arrhythmia of the patient. Adapted from [3].

Treatment and survival of cardiac arrest are measured by both physiological states, as well as time or recovery event based. The most immediate measurement of treatment of cardiac arrest is known as Return of Spontaneous Circulation (ROSC). This is the conversion of a cardiac arrhythmia to a rhythm that is capable of providing perfusion without the aid of CPR. A second measurement is survival to hospital admission. This metric may be used to evaluate the effectiveness of an EMS response when ultimate patient outcome is not known or easily tracked. One of the most common used metrics in response and treatment studies is Survival to Hospital Discharge. This metric indicates that a medium term (several days) survival and some amount of recovery has occurred. Other metrics may track longer survival, such as 1-year survival, or the neurological state of the surviving patient. Often, survival rates are classified as pertaining to either witnessed or unwitnessed out-of-hospital cardiac arrest, or may be classified according to the presenting arrhythmia. Survival rates are sometimes quoted for the Utstein subgroup, i.e. cases of bystander witnessed out-of-hospital cardiac arrest with an initial shockable rhythm, as this is considered the most "savable" subset of all cardiac arrest cases [13].

2.2 EMS Response to Cardiac Arrest

Most out-of-hospital sudden cardiac arrest patients are treated by EMS. In response to a 911 medical emergency call, ambulances are dispatched to the arrest location. Some systems may dispatch ambulances or fire trucks to provide Basic Life Support (BLS) first, which consists of CPR and defibrillation, followed by an ambulance with paramedics to provide ACLS.

The National Fire Protection Association (NFPA) Standard 1710 requires "the fire departments EMS for providing ALS shall be deployed to provide for the arrival of an ALS company within an 8-minute response time to 90 percent of incidents" [6]. A study of 485 EMS agencies in the United States showed in urban and suburban areas median response times of 6 minutes with the 90th percentile responses within 12 and 14 minutes respectively [14]. However, in rural areas, the median response time dropped to 13 minutes with the 90th percentile reaching 26 minutes.

Cardiac arrest survival with EMS response is poor. Cram *et al.* report a survey of studies ranged from 2% to 20% survival, with an average of 10% [8]. A relative few, high performing EMS communities, have reached survival rates in excess of 50% with EMS treatment [15]. These communities, such as King County, WA, benefit from fast ambulance response times as well as a high likelihood of bystander CPR. However, the reality is that 95% of all major cities worldwide have survival rates less than 5%.

2.2.1 EMS Response Modeling and Simulation

EMS dispatch locations and ambulance resourcing presents a problem driven by medical objectives, economic considerations, as well as political influences. EMS policy makers have turned to operations research for decision support tools to find optimal solutions to these objectives. The EMS models may be categorized by two purposes: identification of optimal ambulance station locations to maximize coverage of demand points and to minimize response time, and simulation to assess the performance of an EMS system and evaluate potential operational strategies.

Optimal EMS location modeling was first introduced by Toregas *et al.* in 1971[16]. He proposed the use of a Set Covering Problem to identify the minimum ambulance locations nodes such that each demand node is within a certain response time or distance radius of an ambulance location node. Church and ReVelle developed a Maximal Covering Location Problem approach to optimize the service locations under a constrained number of location nodes [17]. The objective of their approach is to identify location points for a fixed number of facilities that provide the maximum coverage of demand points within a desired distance of the facilities (Figure 3). These approaches are limited by the fact that each demand node is covered by only one ambulance, and if the ambulance is on a call, a significant area of demand nodes is uncovered for a period of time.

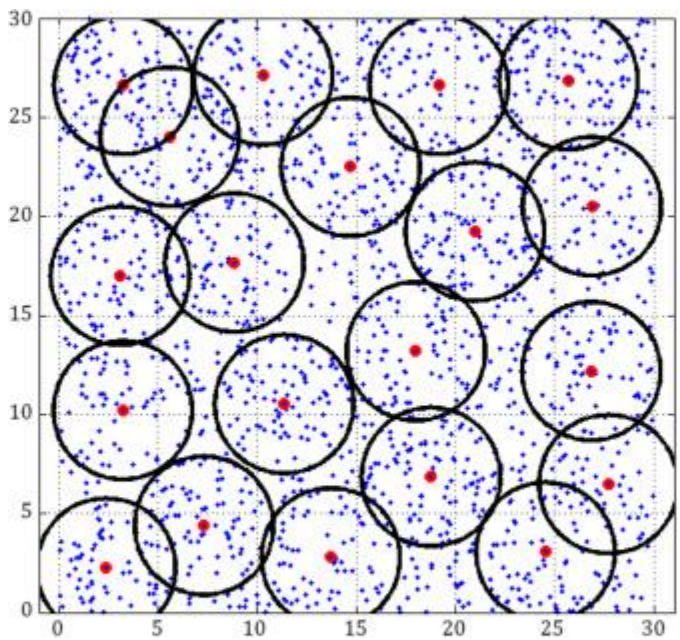


Figure 3. Maximum Covering Location Problem (from [18]). Red dots represent facility locations. Blue dots represent demand locations. Circles show the coverage area of each ambulance base facility.

To address this weakness, Gendreau *et al.* proposed the Double Standard Model, which applies two coverage radii, r_1 and r_2, where $r_1 < r_2$ [19]. This approach applies double coverage constraints to the optimization, with α proportion of demand points within the distance r_1 and all demand points covered within distance r_2. The model was later extended to the Dynamic Double Standard Model, where ambulances can be redeployed to new locations in real time when an ambulance is out on a call [20].

Another utilization of modeling and simulation for EMS systems is for the assessment of system performance. This enables optimization of EMS system configuration (e.g. the number of ambulances at each dispatch location) and operational strategy (e.g. when to perform maintenance on an ambulance). Ambulances are finite resources which may either be available or in service at any given time, while emergency calls are stochastic events which may be modelled as stationary or non-stationary Poisson arrival processes. As such, Discrete Event Simulation (DES) has been utilized for research in EMS system simulation. Larson describes the problem as a queuing system with spatially distributed servers [21].

Early use of computer simulations by Savas analyzed ambulance service improvements in New York city [22]. He evaluated the cost-effectiveness of changes to the number and location of ambulances, and identified low cost improvements in service by redistributing existing ambulances. More recently, Ingolfssen *et al.* used DES to evaluate a single start system (all ambulances located at the same base) against the existing multiple start system (10 existing ambulance base locations) for the city of Edmonton, Canada [23]. The simulations concluded that a single start system could improve average ambulance availability due to improved efficiency in ambulance cleaning and restocking between calls, and that an increase in the percentage of calls reached within a 9-minute target response time could be achieved. Wu used DES to create a simulation model for Tainin City, Taiwan [24]. The model was used to develop operational strategies to minimize disruption to normal service when ambulances are unavailable due to provisional events, such as festivals and races. Nogueria *et al.* used both optimization modeling to locate and allocate ambulances for the EMS service in Belo Horizonte, Brazil, together with a DES model to analyze the dynamic behavior of the system [25].

2.3 Public Access Defibrillation

Up until the early 1990s, defibrillation was a treatment which was only performed by doctors or other highly trained clinicians. The advent of the AED, and its ability to enable lay-responders, or those without medical training, to provide the lifesaving defibrillation therapy, brought new strategies to improve response times for cardiac arrests. The concept of Public Access Defibrillation (PAD) first came from the American Heart Association's "Future of CPR" task force in 1990 [26][27]. The term has since come to encompass the many strategies of untrained responders using AEDs to provide early defibrillation. The AHA's initial recommendations around PAD were [28]:

1. AEDs be widely available for appropriately trained people.
2. All firefighting units that perform CPR and first aid be equipped with and trained to operate AEDs.
3. AEDs be placed in gathering places of more than 10,000 people.

4. Legislation be enacted to allow all EMS personnel to perform early defibrillation.

In their second public access defibrillation conference in 1997, the AHA defined four levels of public access defibrillation [27].

Level 1 is traditional dispatched first responders (e.g. firefighters, police) which would carry AEDs in their vehicles.

Level 2 is non-traditional first responders (e.g. life guards, security personnel, flight attendants) who have a duty to respond.

Level 3 is civilian laypersons with first aid training (e.g. sport coaches) who have a desire to provide emergency care.

Level 4 is untrained civilian laypersons who may be a bystander to a sudden cardiac arrest.

Level 1 programs rely on transporting an AED to the scene, while Level 2, 3, and 4 PAD programs all rely on AEDs strategically located where a need may be likely.

Many countries have adopted national PAD systems (e.g. Japan [29], England [30], Austria [31]). In the United States, AED legislation has progressed on the national and state level. In 1998, Congress Passed the Aviation Medical Assistance Act, which directed the FAA to determine requirements for AEDs on passenger aircraft, and declared that carriers and individuals are not liable for damages when attempting to provide medical assistance during flight [32]. In 2000, congress passed the Cardiac Arrest Survival Act, providing Good Samaritan protection against civil lawsuits for good faith efforts to purchase or use AEDs in federal buildings, as well as providing $25 million in local grants for AED purchase [33]. In 2002, congress passed the Community Access to Emergency Devices Act, providing $30 million in grants to states and localities to purchase AEDs for public access placement [34]. 21 states have laws requiring AEDs placed in schools, while 18 states require or recommend AEDs in health clubs, sports clubs, and gyms [35]. Other requirements vary by state, such as dental offices, day care centers, swimming pools, places of public assembly, or buildings that exceed a minimum occupancy.

Public Access Defibrillation has shown improved sudden cardiac arrest survival in many implementations. Cram *et al.* performed a survey of several published studies, citing a probability of survival to hospital discharge range of 0.20 to 0.50 with use of a PAD AED, versus a survival range of 0.02 to 0.20 for treatment by EMS only [8]. Casinos have been one of the most successful applications of a PAD program. Valenzuela *et al.* performed a prospective study using trained security guards in Las Vegas casinos resulting in 53% survival to hospital discharge [36]. Through the use of video surveillance systems, strategic AED placement, and thorough training, the study found the average time from collapse to CPR was 2.9 minutes, and 4.4 minutes to defibrillation. Another successful PAD implementation has been equipping police with AEDs and dispatching to cardiac arrest scenes along with EMS. One of the pioneering communities in this approach is Rochester, Minnesota. White *et al.* carried out a retrospective observational study of atraumatic cardiac arrest treatments over a 5-year period, finding police responded faster than EMS (5.8 versus 6.3

minutes) and survival to discharge was higher for the police response (58% versus 43% for EMS) [37].

Despite the promising results in many applications of Public Access Defibrillation, the overall survival for cardiac arrest remains low and very few victims receive treatment prior to EMS arrival. Agerskov *et al.* report that in Copenhagen, Denmark, only 3.8% of all out-of-hospital cardiac arrests have an AED applied despite 15.1% of arrests occurring within 100m of a PAD AED [38]. Similarly, in Denmark, a longitudinal study of AED usage found an improvement in public locations from 1.2% in 2001 to 15.3% in 2012 after nationwide initiatives to increase bystander resuscitation [39]. However, the use of AEDs in residential locations remained at only 1.3% even after the awareness and training initiatives. Deakin *et al.* studied PAD efficacy in Hampshire, England, concluding only 4.2% of cardiac arrest calls had an AED available in the vicinity of the arrest, and only 1.74% were successfully retrieved and used [40]. In the United States, an analysis of the Cardiac Arrest Registry to Enhance Survival (CARES), established by the Center for Disease Control (CDC), found only 4.4% of out-of-hospital cardiac arrest cases had an AED used by a bystander [3].

2.3.1 Modeling and Simulation of PAD Systems

The locating of AEDs to maximize likelihood of use and geographical coverage has received significant research. Widespread dissemination of AEDs has been limited by the cost of the devices and as such AEDs may be considered a finite resource.

European Resuscitation Council (ERC) recommends placing an AED where cardiac arrest occur every two years [41] while the American Heart Association (AHA) recommends placement where a cardiac arrest occurs every five years [42]. Such guidelines may be cost prohibitive or may only cover a fraction of cardiac arrests. A study of the geographic locations of cardiac arrests in Copenhagen, Denmark, between 1994 and 2005 estimated that 19.5% of arrests would be covered under the ERC guidelines and 66.8% would be covered under the AHA guidelines [43]. The need for strategic placement of AEDs has led to the development of different optimization approaches.

Several attempts to identify high risk locations to place AEDs have identified certain building types as target locations. These are primarily facilities with high density of people -- transportation hubs, airports, sports venues, malls. Early work to identify such buildings was done by Becker *et al.* in Seattle, Washington [44]. The study classified buildings into 23 categories, with 2 additional categories for automobile and outdoors. The authors identified 10 location categories as high cardiac arrest incidence and thirteen as low incidence. Similar approaches to classifying high risk locations followed in Kansas City, Missouri [45], Toronto, Canada [46], and Copenhagen, Denmark [43]. These approaches yielded limited results due to the fact that only a few facility types had multiple cardiac arrests over the study period, with most types having only one arrest. The predictive power of this approach is limited, and beyond the identifications of a few sudden cardiac arrest “hot spots”, the method does not address where to place AEDs in lower incidence areas.

The locating of AEDs to maximize the spatial coverage of an area has employed similar approaches as used in locating ambulance bases. Two common demand measures for coverage problems are population based (i.e. covering the maximum proportion of a population within a defined distance of an AED) or historical arrest location based (i.e. covering the maximum number of locations of past cardiac arrests). Chan *et al.* used a model based on the Maximal Covering Location Problem to assess optimal locations for additional AED placement in Toronto, Canada [47]. They first assessed the coverage of the existing AED network through a location registry, determining the number of historical arrests within 100 meters of a registered AED (assumed to correspond to a 1.5-minute walk). They compared a population based placement approach, using building floors as a proxy population density, to an optimized approach with the MCLP model. The optimized model approach outperformed the population based approach under scenarios of various numbers of additional AEDs.

2.4 Emerging Concepts for Novel Response Systems

With the lifesaving potential of early defibrillation with an AED established, but the low likelihood of an AED being used in out-of-hospital cardiac arrests, researchers are proposing new methods to bring early defibrillation and CPR to cardiac arrest victims. Ringh *et al.* propose changing the definition of PAD from *who* defibrillates the patient to *how* the AED is brought to the patient [27]. The authors have proposed new definitions consisting of three levels of PAD:

> *Level 1* is dispatched professional first responders. This includes paramedics, fire fighters, and police, who transport an AED to the cardiac arrest location.
> *Level 2* is dispatched lay first responders. These are civilian responders who may or may not transport the AED to the scene (they may be guided by the dispatch center to retrieve an on-site AED), and may or may not be trained.
> *Level 3* is non-dispatched lay responders. These are random bystanders who retrieve a nearby AED.

This section summarizes some of the newer response concepts, pilot programs, and studies, as well as modeling and simulation research relevant to these systems. The systems are separated into two broad categories: Sections 2.4.1 through 2.4.4 discuss *mobile responder systems*, which are characterized as systems which rely on volunteers or off duty first responders, who are dispatched to the cardiac arrest location by phone app, and whose location at the time of dispatch is not predetermined nor specifically predictable. Sections 2.4.5 through 2.4.6 discuss *Aerial Drone* systems, which are characterized by the aerial transport of an AED from a fixed base location to the cardiac arrest location.

2.4.1 PulsePoint

PulsePoint is a non-profit organization that provides smartphone apps as well as EMS dispatch integration to alert CPR trained volunteers of nearby cardiac arrests [48]. Enrollment is on a voluntary basis, with no verification of responder training or background check, such that members of the system remain ”anonymous”. As such, the system is only used for cardiac emergencies that occur in public locations. A snapshot of the distribution of enrolled responders in Portland, Oregon, and the surrounding suburbs is shown in Figure 4. Pulse Point creates a network of mobile responders, which use a “crowdsourcing” approach to achieve quick CPR to cardiac arrest victims. PulsePoint is active in 3,815 communities around the globe, with most being in the United States.

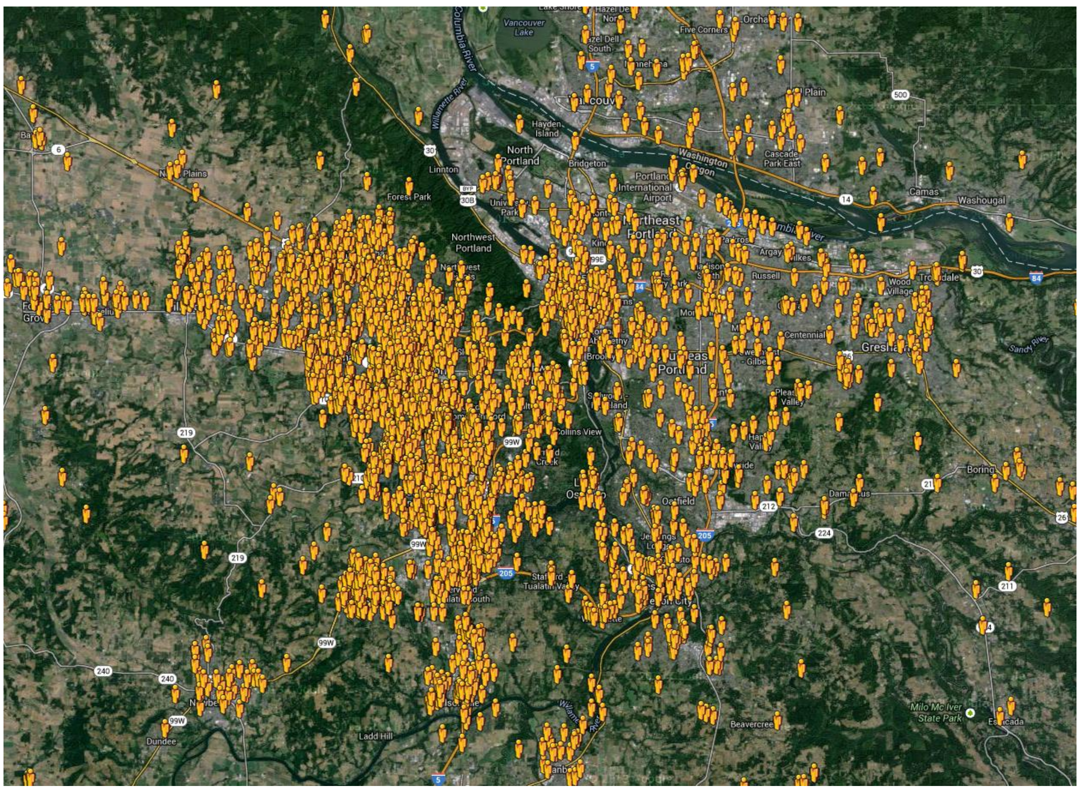
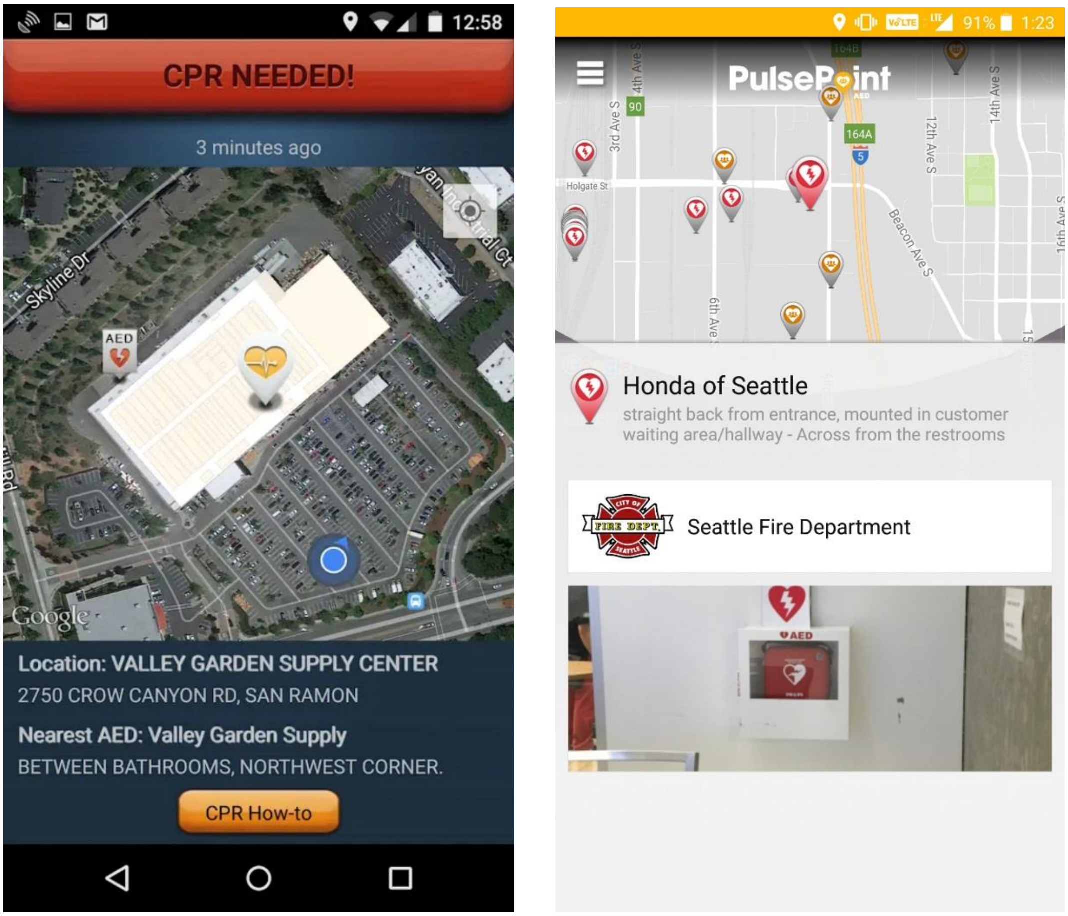


Figure 4. Snapshot of distribution of responders in PulsePoint system approximately 3260 sq. km region of Portland, Oregon and the surrounding area (from [48]). The orange figures show the locations of all PulsePoint responders within the area at a single point in time.

The system is activated when a 911 call is determined to be for a possible cardiac arrest (such as symptoms of collapse, non-responsive, not breathing, etc.). All members within a quarter mile radius of the arrest scene are dispatched to the scene with an audible alert on the cell phone as well as a satellite image map showing the location of the user and the cardiac arrest location. An address or description of the location is provided as well.

PulsePoint also creates a registry of AED locations within an area. The registry is populated by a crowdsourcing approach, with members of the public uploading the geo-location of AEDs through the cell phone app, along with a picture of the AED and description of the location. When an activation occurs, users receiving the notification are provided with the location of the nearest AED as well as the cardiac arrest location (Figure 5).



a) b)

Figure 5. PulsePoint smartphone app showing a) cardiac arrest activation; and b) AED registry on cell phone app (from [48]).

PulsePoint has realized only limited success since its implementation in 2012. Although the organization reports over 1.9 million citizen responders, and over 98,000 activations [48], only a small percentage of these have resulted in actual responder treatment to the patient. A survey provided to responders shortly after an activation notice was sent indicated only 23% of activated responders attempted to travel to the cardiac arrest location, with only 11% arriving at the scene [49]. Reasons cited for not responding included:

- the cell phone being muted,
- the responder did not hear the alert due to a noisy environment,
- the responder was away from their phone,
- they were unavailable at the time of the call,
- the arrest location was considered too far away,
- a belief that EMS would arrive first,
- unable to get out of a vehicle at the time of a notification (e.g. on a bus),
- they did not understand how to get to the location.

2.4.2 ALERT Study

The ALERT study is a currently ongoing pilot program sponsored by Philips Healthcare, King County Public Health Department, the University of Washington, and PulsePoint. The program uses the PulsePoint system, adding to it the concept of a *verified responder* who carries an AED with or near them at all times (e.g. in a grab bag, or in their car). Verified responders represent a different class of responder within the PulsePoint system. These responders are targeted to be off duty professional health care workers or other public safety workers. This includes off duty firefighters, policemen, nurses, doctors, security officers, life guards, search and rescue volunteers, etc. These responders are trained in first aid and typically in AED use as part of their jobs, and are experienced in responding to critical and potentially chaotic events.

For the ALERT study, off duty firefighters were recruited from five EMS districts: Tualatin Valley Fire and Rescue (suburbs around Portland, Oregon), Sioux Falls Fire and Rescue (Sioux Falls, South Dakota), Spokane Fire Department (Spokane, Washington), Spokane Valley Fire Department (Spokane Valley, Washington), and Madison Fire Department (Madison, Wisconsin) [50]. The study recruited 621 verified responders across the five districts, with 550 AEDs provided to the responders. A survey taken during the recruitment process indicated that 54% would keep the AED in their car, while 38% would carry the AED on their person [51]. The verified responders would be dispatched by the same PulsePoint cell phone app as the lay responders, but would be dispatched into private residences as well as public locations. The dispatch radius could also be increased for the verified responders.

Interim results from the study indicate that verified responders have been activated to a scene 137 times, however 39% were on duty at the time of the activation. Of those that were off duty, 31% attempted to respond to the activation, with 14% making it to the scene prior to EMS. An AED was applied in 3 cases, and there has been one resuscitation attributable to the program.

2.4.3 Other Mobile Responder Systems

A number of other systems employing the concept of the mobile responder are in various stages of trial or implementation throughout the world. The GoodSAM app operates similar to PulsePoint, and has the largest citizen network in the United Kingdom [52]. The phone app has the added functionality to stream video back to the EMS agency, a feature called "Instant On Scene", to further aid the response. Through the sponsorship of the Singapore Heart Foundation, the "AED on Wheels" program has equipped 150 taxi cabs in Singapore with AEDs, fire extinguishers, and first aid kits [53]. Dispatched through a phone app, the system has responded to 149 cardiac arrests since its implementation in 2015. Hartslagnu (Heartbeat Now) in the Netherlands is a phone app dispatch system that will send the closest citizen responder to the cardiac arrest location to start CPR, while directing other nearby responders to public access AED locations to retrieve an AED before going to the cardiac arrest [54]. They have recently partnered with Volvo as a pilot study to have AEDs installed in cars and the app integrated with the car's navigation system.

2.4.4 Modeling and Simulation of Mobile Responder Systems

Mobile responder systems incorporate the dispatch of a BLS responders simultaneously with the dispatch of an EMS ambulance. Marshall *et al.* used a Monte Carlo simulation model to predict both volunteer response times and EMS response times to sudden cardiac arrest locations in North and West Belfast, Ireland[55]. The simulation accompanied a two year trial in which mobile volunteers and police carried AEDs and were dispatched to cardiac arrests scenes by an alphanumeric pager [56].

The Belfast study region was divided into seven zones, with each zone having a single volunteer responder ”on duty” at any given time. EMS response times were modeled using a log-logistic distribution fit to historic response time data for each of the seven zones. Responder times were pre-calculated using road network information (Microsoft MapPoint Europe 2004) for response times between the centroid of each of the 7 zones to the centroid of each of 434 Census Output Areas within the region. For the simulations, variation around the expected volunteer response times was added using a log-logistic distribution. Their model also accounted for the likelihood of availability of each of the seven responders for each cardiac arrest simulations.

The simulation resulted in volunteers arriving ahead of EMS 18.8% of events, with an average improvement of 56 seconds over the EMS response. This compared against the actual study results of 15%. The survival regression model presented by Larsen *et al.* [2] was incorporated into the model to predict survival for witnessed cases with an initial rhythm of VF or VT. The authors used the model to predict an improvement of the volunteer arrival first by an additional 18% if the availability doubled, and 32% if it is tripled.

Khalemsky *et al.* created an Emergency Response Community Effectiveness Model (ERCEM) to simulate response times for cell phone app alert systems for anaphylaxis, hypoglycemia, and opioid overdose [57]. They estimated the number of responders in the systems based on population density and the percentage of the population prescribed to carry the medicine for each condition. They used additional factors to account for the fraction of this subpopulation who would participate in the community responder program. They then applied a Monte Carlo simulation for the number of responders within a 1km or 2km radius of the patient in need, and estimated response times base on the travel distance and some system delay values. They compared these response times to actual EMS response times recorded in the NEMSIS database for specific events, or to benchmark EMS response times. Their model was limited to walking mode responses only, and considered only the Euclidean distance for the transit. Their simulation found that phone dispatched responders a EMS in 13% of cases. They proposed the ERCEM as a decision support tool for communities considering augmentation of their EMS response with these citizen network systems.

2.4.5 Aerial Drone Response Systems

A significant drawback of PAD systems is that coverage of low demand areas within a quick retrieval distance, i.e. 150 meters, is not cost affective. Static AED placement is most effective in buildings or areas with a high concentration of people. Even when an AED is near the cardiac arrest scene, it is often difficult for bystanders to locate and retrieve the nearest AED. A method to deliver the AED quickly to the scene, which is currently being researched, is the use of Unmanned Aerial Vehicles (UAV), also known as drones.

UAV drones have the capability to transport an AED quickly to a cardiac arrest scene, flying above traffic, buildings, and other obstacles. Drones can travel from 50 km/h to 150 km/h. AED weight is currently well within the payload capability of existing drones, however once the feasibility of a drone response system is demonstrated, AEDs could be designed specifically for integration with drones. Cameras on the drone could provide situational awareness to en route EMS responders, as well as the potential for CPR coaching and AED application feedback from the 911 operator. AED deployment concepts being explored include dropping with a small parachute near the arrest scene, landing the drone with the AED attached, or lowering the AED by a cable and winch. The AED can be received and applied by a bystander, or potentially the 911 caller. Such a system could suffer from the same apprehension of bystanders or laypersons to apply the AED [58], however recent small scale human simulations have produced promising results [59] . A drone system paired with a dispatched mobile responder system has been proposed to address this issue [60]. GoodSAM will begin offering an AED Drone Delivery service to communities supported by its responder network by the end of 2020 [61].

Drone medical supply transport systems have currently only been implemented in remote, isolated areas. Zipline uses fixed wing drones to fly blood supplies and vaccines to remote areas in Rwanda and Tanzania [62]. In Stockholm, Sweden, researchers obtained temporary permission to perform aerial drone rescue simulations over unpopulated areas [63] (Figure 6). The simulated rescues included three AED deployment methods: parachute; dropping the AED from a 3 to 4-meter height, and landing the drone. The authors concluded dropping the AED was the safest and most practical method. A similar mock rescue study by researchers from the University of Toronta, using response beyond line of visual sight navigation, found that drones responded 2.1 to 4.4 minutes faster than EMS for distances from 6.6 to 8.8 km [64]. Outside of Ottawa, Canada, in Renfrew County, drones are used to deliver medicine, and recently the first drone was dispatched to a cardiac arrest scene with an AED [65]. In the United States, the city of Reno Nevada was recently selected as one of 10 designated drone test areas by the Federal Aviation Administration as part of the Unmanned Aircraft Systems Integration Pilot Program [66]. The drone startup company Flirtey has partnered with the Reno EMS department to pilot an AED transport system to cardiac arrest locations [67].

Figure 6. Drone dropping AED in simulated cardiac arrest rescue (adapted from [63]).

Drone delivery of AEDs has garnered much recent attention due to the potential to significantly improve access to an AED and time to defibrillation, particularly in rural areas or difficult geographic areas where EMS response times are very long. There are, however, significant barriers that need to be overcome to implement a drone response system. Most countries have regulations around the flight of drones, including limiting flights to visual line of sight distances, requiring an active pilot, airspace restrictions, and nighttime flight restrictions [68]. Commercial drones have a maximum flight elevation of 400 ft, and a maximum speed of 100 mph. There are additional concerns for public safety, both with potentially landing drones in crowded public spaces, and in the event of a drone malfunction or loss of power. Other public resistance to drones has come from concerns with noise and privacy [69]. Advances in drone technology are addressing some of these concerns, with redundant flight systems, autonomous piloting, and collision avoidance sensors. The early pilot programs, as well as the use of simulation to predict the potential benefits of the systems, will likely drive regulatory decisions. It is expected that the public will likely view the benefits of such a system as outweighing the risks.

2.4.6 Modeling and Simulation of Drone Response Systems

Modeling of drone response systems has been limited primarily to a few specific regions and based on optimizing coverage around historical cardiac arrest locations. Similar approaches to those used for optimizing ambulance base locations and AED placement locations have been used to model drone responses. Pulver *et al.* used an MCLP approach to configure a network of drone locations in Salt Lake City, Utah, with the objective of providing one minute travel time to all demand locations [70]. The approach modeled the effect of using existing EMS locations as drone launch sites, as well as adding new launch sites to the system. The analysis found that while EMS can reach only 4.3% of demand within one minute, drone responses from existing EMS locations increased to 80.1% the locations reached within one minute, and 90.3% if new launch sites were added.

Boutilier *et al.* used a two stage approach to modeling drone response systems for Toronto, CA and outlying areas [71]. The first stage used a coverage based optimization algorithm to determine the minimum candidate drone locations (ambulance, fire, and police stations) to provide a 1-minute, 2-minute, and 3-minute improvement over EMS response times. After determining the optimal drone locations, the second model used a continuous-state Markov Chain queuing algorithm to determine the number of drones required at each location. The Markov model included states of busy and available for drones, based on demand following a Poisson process, and busy time based on flight time, treatment time, return time, and a drone reset time. The modeling indicated that 81 drone bases with 100 drones would be required for a median improvement of 3 minutes over EMS response time.

Claesson *et al.* used a modeling approach to identify drone locations in Stockholm, Sweden [72]. With use of a GIS tool (ArcGIS), the city was broken into a discrete grid, with a raster layer of EMS response time for each area, as well as a raster layer of incidence of cardiac arrests for each area. A 50/50 weighting was used for the two layers to find optimal locations in the urban area of Stockholm, while an 80/20 weighting (80% to EMS response time, 20% to OHCA incidence) was used for outlying rural regions. Using this method, 20 locations were identified which could cover 72% of all historic cardiac arrest locations. The model predicted drone arrival before EMS in 32% of urban cases, and 93% of rural cases.

2.5 Discussion

Although new concepts for responding to sudden cardiac arrest are being developed, previous research on these systems and the related topics of EMS response and AED positioning have not yielded useful techniques that estimate the costs and benefits of new response systems. Much of the prior modeling has focused on optimal locations for EMS bases and AED placement. While valuable for maximizing the efficiency of limited resources, this optimization is only expected to have a marginal impact on survival. There is little research using modeling and simulation to provide comparisons of the emerging, novel response systems under similar assumptions. Additionally, most modeling approaches neglect the reliability aspects of elements within the response system, and their impact on system effectiveness. This dissertation will help to fill that gap by developing and demonstrating models that can simulate different types of response systems under various operating conditions.

Chapter 3: Research Approach

To address the fundamental questions posed by this dissertation, a set of models was developed to incorporate both the predictable factors in out-of-hospital cardiac arrest response as well as the aleatory uncertainty associated with the location of the arrest and responding agents. The models simulate the response time to a cardiac arrest event for different types of responding agents, based on distance travelled, additional delay times associated with the logistics of dispatching the responding agent, and the reliability and availability of the responding agent or required equipment. The response times for CPR and defibrillation provide the inputs to a logistic regression survival model, allowing for a survival likelihood prediction for each simulation. The Monte Carlo method using a large number of simulations was employed to assess the variation in response times due to stochastic factors, and develop summary statistics to represent the performance of a response system. Chapter 4 presents the model structure, underlying assumptions in the model, input factors to the model, output responses, execution, and validation. The chapter also discusses sources of information and analytical methods used to provide the model inputs.

In order to understand the system structure and factors that have the largest impact on response time and survival, sensitivity analysis experiments were performed on the inputs to the model. Simulation experiments were performed on each type of responding agent, EMS, mobile responders, and drone response, independently, to understand the most significant factors in each response time. Overall system sensitivity experiments were then performed, to characterize the interaction of multiple responding agents in the cardiac arrest treatment, as well as the impact of reliability and available of responding agents. Additionally, simulation experiments were run to assess the sensitivity of response time predictions to the type of geo-spatial distribution used to generate both the cardiac arrest location and the mobile responder locations. Chapter 5 presents the results of these experiments, with in-depth analysis of the most significant factors using a response surface design of experiments.

A primary objective of this research is to use the modeling and simulation to predict and compare the performance of different types of emerging response systems within a specific region, and evaluate the potential improvement over the traditional EMS response paradigm. Chapter 6 discusses results of simulation experiments used to compare several systems with a range of system conditions. The results demonstrate that augmentation of EMS with emerging systems, under the right conditions, can provide meaningful improvement in the time to defibrillation and survival rate of cardiac arrest. Chapter 7 expands on the analysis from chapter 6, providing a cost model for each of the systems, and presents the results in a cost-benefit decision analysis format. Chapter 8 provides a summary of the learnings, and their relevance to the primary research questions, as well as a discussion of limitations of the research and future work. Figure 7 shows a flowchart of the steps in this research approach, the chapters which provide their description, and the relationship to the research questions.

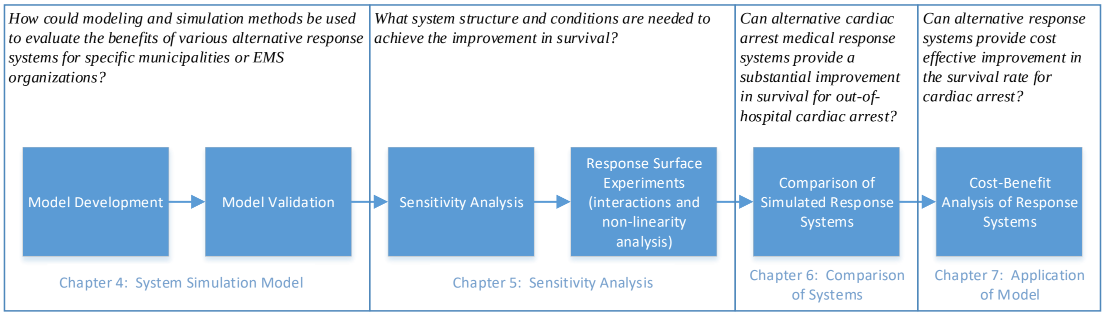


Figure 7. Steps in research approach.

The modelling approach was to create a geographically flexible model, which could be applied to urban, sub-urban, and rural areas, and integrate region specific geospatial attributes, such as the location of existing fire stations, ambulance bases, and potential drone bases. Throughout this research, the city of Bellevue, located in King County, Washington, was used as the example region for model experimentation. Bellevue is the fifth largest city in the state of Washington, consisting of 82.8 sq. km of land, with a population of 147,000 [73]. It is primarily a suburban city, with a moderate downtown area with a few high rise buildings. It is in King County, the most populated county in Washington, and lies just east of the city of Seattle. Bellevue was chosen as the example city due to proximity and familiarity, as well to leverage my relationships with EMS leaders, cardiac arrest response researchers, and access to data from King County EMS. The modelling approach, however, is extendable and customizable to any region.

Chapter 4: System Simulation Model

The approach to predicting the performance of the emerging cardiac arrest response systems utilized the creation of a set of models to simulate the types of response systems described in Chapter 2. Geo-spatial Monte Carlo Simulation models were developed to simulate response times and predicted survival likelihood for each cardiac arrest response system. Modeling and simulation approaches can quickly generate insights into a system that could take years to learn from studying and experimentation with a real world system. However, models and simulations are only a representation, or approximation of a real world system. As such, the full complexity of the system was not intended to be replicated in a model. The goal was to identify the minimal necessary complexity of a system to provide useful, actionable insights into the system. With too little complexity, the model loses the capability to provide accurate predictions, while too much complexity results in an intractable model.

This chapter begins with an overview of the model in Section 4.1, followed by the introduction of the input factors in Section 4.2. Section 4.3 provides the detailed formulas and mathematical calculations used in the model. Section 4.4 describes the implementation and execution of the model. Section 4.5 provides a discussion of the model inputs, the sources of data, and analytical methods used to derive the inputs. Finally, Section 4.6 presents approaches to validation of the models.

4.1 Model Overview

This modeling and simulation approach relies on the following axioms:

1. Out-of-Hospital Cardiac arrest occurs at random locations on a geographical space that can be represented by a 2-dimensional Cartesian terrestrial surface.
2. A network of "mobile responders" can be represented by random locations in a similar geographical space at the time of a cardiac arrest occurrence.
3. The time to respond to a cardiac arrest location can be predicted based on a distance metric from the origin to destination, the travel speed, and additional time components independent of the distance from origin to destination.

The models' primary simulation responses are the times for various responding agents to provide each of the two primary methods of treatment for sudden cardiac arrest, i.e. CPR, and defibrillation (either with an AED or by an ALS provider with a defibrillator/monitor device). These response times are strong predictors of survival to hospital discharge for out-of-hospital cardiac arrest. The response may originate from a fixed location, such as an EMS ambulance base location or drone base, from a random location, such as a mobile responder at the time of the cardiac arrest, or a combination of fixed and random locations, such as a bystander from a random location retrieving an AED transported by a drone from a fixed location.

The response times for CPR and defibrillation treatment methods are used to predict a survival probability for each simulated cardiac arrest event. The logistic regression equation provided by Valenzuela *et al.* is used to predict survival. The survival equation provides a probability of survival estimate only for the "Utstein subgroup" of all cardiac arrest cases, i.e. adult patients with witnessed collapse of cardiac etiology, with an initial shockable rhythm (VF or VT).

As these response systems include actions by both human and machine components (e.g. ambulances, AEDs, volunteer responders), the reliability and availability of these components are integral to the efficacy of a system. Ambulances may be out on another call or being cleaned and restocked at the time of a cardiac arrest, AEDs may have a dead battery or other functional failure, and volunteer responders may not notice an alert on a cellphone, or may be unable to respond for various reasons. The nature of these systems provides redundancy for each of these components; however, the response time may suffer when a backup is needed. An unavailable ambulance may require an EMS response from a more distant base location, a non-functional AED would delay defibrillation until EMS arrives at the scene, or an unreliable responder would result in a delay until the next closest responder arrives. These reliability and availability aspects of the modeling of various response systems are incorporated as additional stochastic events.

The influence diagram in Figure 8 shows the conceptual relationships of these components of the model. The model simulates several intermediate events in order to ultimately predict survival for each simulated cardiac arrest event. First, the model simulates the distance from the origin of the responding agent to the cardiac arrest location. The distances are influenced by the locations of the responding agents, both fixed and random, the number of agents in a system, and the availability of each agent within a system at the time of the cardiac arrest. The distance, along with the velocity of the responding agent and some non-transit, system specific time constants (e.g. dispatch times), determine the time for the first responder of each type. The modelled therapy capabilities of each response system, i.e. CPR and/or defibrillation, together with response time, determine the time-to-defibrillation and the time-to-CPR. These are then used as inputs into the logistic regression model to predict the survival likelihood for the simulated cardiac arrest.

There are system design factors such as the number of ambulances and number of drones, and the locations of these within the region. The number of responders within the system, which determines responder density, is a design factor as well. The values of these decision factors influence both the response time and survival predictions, as well as the cost of operating the system. The costs of these systems is discussed in Chapter 7.

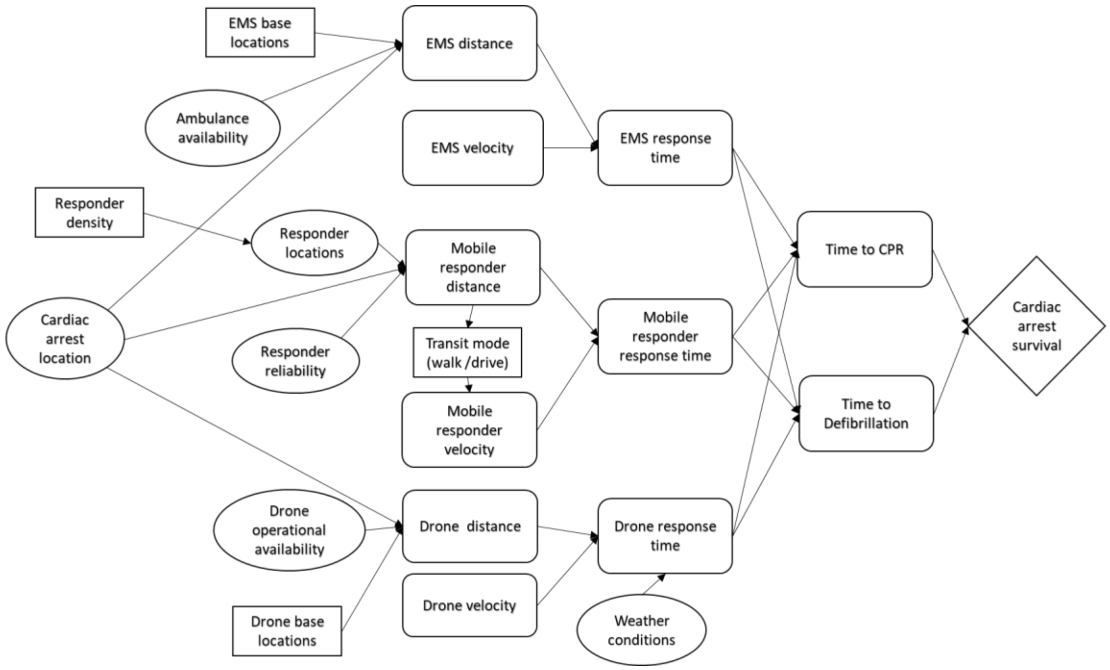


Figure 8. Influence diagram showing the relationship between chance inputs (ovals), decision inputs (rectangles), intermediate event calculations (rounded rectangles), and the output of survival prediction (diamond). Additional inputs describing time constants (discussed in Section 4.2) are omitted from the diagram.

Each simulation results in a different response time for each of the responding agents in the simulation (e.g. EMS, mobile responders, drones, etc.), due to the random location of the cardiac arrest event as well as random locations of mobile responders. Any single simulation does not represent the performance of the system, as chance may favor one type of response over another. The Monte Carlo method is used to find the distribution of responses over a large number of simulations. The distribution of responses defines the performance and efficacy of a system, and the impact of changes to components or factors in the system are measured by the effect on the response time distributions.

The structural approach to the model was to parameterize all mathematical components which may vary among specific systems, such that these parameters are independent input factors to the model. This approach enables flexibility in the model to simulate many different systems, as well as to tune the model to known attributes of a specific system (e.g. tune the model to match EMS response times for a specific region or municipality). This also facilitates sensitivity analysis on the various factors in the model.

4.2. Model Factors

The model factors, or model inputs, are the variables within the models that are set to define the specific attributes and conditions of a response system. These factors define the geographic region of the simulation, the response characteristics of the different agents being modeled, the distance travelled between origin and destination points, and the reliability and availability of elements within the systems. The nomenclature for all model input factors is summarized in Table 1, and are briefly described in the following sections.

Table 1. Nomenclature for model factors.

Factor	Description
x_{NW}, x_{SE}	Longitude points to define region
y_{NW}, y_{SE}	Latitude points to define region
p	Minkowski distance order
A	Cardiac arrest location
R_i	Location of the *i*th mobile responder
E_i	Location of the *i*th EMS base
t_{ED}	EMS dispatch delay time
t_{EC}	EMS chute time
v_E	Ambulance velocity
E_A	Ambulance availability
t_{RD}	Responder dispatch delay time
t_{RW}	Responder walk delay time
t_{RDr}	Responder drive delay time
v_{RW}	Responder walking velocity
v_{RD}	Responder driving velocity
R_R	Responder reliability
R_{AED}	AED mission reliability
D_i	Location of the *i*th drone base
t_{DD}	Drone dispatch delay time
t_{DV}	Drone vertical flight time
v_D	Drone velocity
t_{DDe}	Drone descent time
D_{AO}	Drone operational availability
D_{AW}	Drone weather availability

4.2.1 Simulation Region Inputs

Geographic region: Let (x_{NW}, y_{NW}) be the longitude and latitude of the northwest corner of the simulation region. Let (x_{SE}, y_{SE}) be the longitude and latitude of the southeast corner of the simulation region.define the Northwest and Southeast Longitudes and Latitudes of the simulation region. The model may be used to define any EMS district or region of interest by two pairs of geographic coordinates (latitude and longitude).

Minkowski Distance Order (p): Let p_w, p_d, and p_f be the Minkowski distance orders for a walking, driving, and flying route of transit respectively. The Minkowski distance order is used to approximate the actual travel distance between the origin of the responding agent and the cardiac arrest location.

Cardiac Arrest location and Mobile Responder location distributions: Let A represent the latitude, longitude location of the cardiac arrest victim, and R_i be the latitude, longitude location of the ith mobile responder.

4.2.2 EMS System Inputs

EMS Dispatch Locations: Let E_i be the location of the ith EMS dispatch location within the simulation region. EMS dispatch locations such as fire stations, ambulance bases, hospitals, etc. are defined by their latitude, longitude coordinates. Where multiple ambulances are stationed at the same location, each ambulance is treated as an independent model entity.

EMS Dispatch Delay: Let t_{ED} be the time interval that accounts the short time for the 911 operator to identify the call as a medical emergency and dispatch the closest ambulance unit.

Chute time: Let t_{EC} be the time from the sounding of the alarm in the fire station (or other ambulance base) until the ambulance begins transit, which is known as "chute time".

Ambulance Speed: Let v_E be the average velocity at which an ambulance can travel in a type of region.

Ambulance availability: Let E_A provide the probability that a specific ambulance is available for dispatch at the time of a cardiac arrest.

4.2.3 Mobile Responder System Inputs

Mobile Responder dispatch delay time: Let t_{RD} be the mobile responder dispatch delay. Similar to the EMS dispatch delay time, the mobile responder delay is the time interval from the 911 call to the receipt of the alert activation on a cell phone.

Walk delay time: Let t_{RW} be the time that accounts for a potential short delay from the alert activation until the responder begins transit by walking to the cardiac arrest scene.

Drive delay time: Let t_{RDr} be the time that accounts for a potential short delay from the alert activation until the responder begins transit by driving to the cardiac arrest scene.

Responder walking speed: Let v_{RW} be the average speed at which a responder would walk to a cardiac arrest location.

Responder driving speed: Let v_{RD} be the average speed at which a responder can drive to a cardiac arrest location.

Responder reliability: Let R_R be the reliability of the responder, which is the probability that upon receiving an alert of a nearby potential cardiac arrest victim, the responder attempts to travel to the scene and provide medical assistance if needed.

AED reliability: Let R_{AED} be the reliability of the AED. The AED reliability factor in the models specifically refers to the *mission reliability* of the AED, i.e. the conditional probability, given that an AED is deployed for a patient use, that the AED is able to perform its functions for the duration of the use (e.g. analyze the heart rhythm and provide a shock if necessary).

4.2.4 Drone System Inputs

Drone location: Let D_i be the latitude, longitude location of the ith drone in a drone response system. Similar to EMS, if multiple drones are stationed at the same dispatch location, each drone is modeled as a separate entity.

Drone dispatch delay: Let t_{DD} be the drone dispatch delay. This denotes the time interval from the start of the 911 call until the drone takes flight.

Drone vertical takeoff time: Let t_{DV} be the time for the drone to ascend to a safe flight elevation (e.g. 120 meters).

Drone travel speed: Let v_D be the lateral velocity of the drone.

Drone descent/AED drop time: Let t_{DDe} be the descent time of the drone. Similar to the drone vertical takeoff time, this time interval accounts for the descent of the drone to a safe level to deploy the AED, and the time required to deploy the AED (e.g. lower by a cable and winch, land and release, etc.) to a waiting recipient.

Drone operational availability: Let D_{AO} be the operational availability of the drone. This factor accounts for the time a drone may be unavailable due to maintenance, or is out on another call.

Drone weather availability: Let D_{AW} be the weather availability of the drone. This factor accounts for the proportion of time a drone system would be inoperable due to weather conditions. While operational availability affects individual drones independently, weather availability affects all drones in the system.

4.3 Mathematical Formulas and Calculations

This section discusses the mathematical calculations used within the simulation model.

4.3.1 Distance calculations

4.3.1.1 Coordinate to distance conversion

Locations of the cardiac arrest event and responding agents (EMS stations, mobile responder locations, and drone bases) are defined by geographic coordinates within the simulation region. The model uses geographic coordinates based upon the World Geodetic System (WGS84 reference system). Distances between points (latitude, longitude coordinates) are converted from angular degrees in the coordinate system to kilometers using the following conversion formulas, where d_{lat} is the distance in kilometers per degree latitude, d_{long} is the distance in kilometers per degree longitude, and l is the latitude at the conversion location [74]:

$$d_{lat} = 111.13292 - 0.55982\cos\left(2l\frac{\pi}{180}\right) + 0.001175cos\left(4l\frac{\pi}{180}\right) - 0.0000023cos\left(6l\frac{\pi}{180}\right) \quad (1)$$

$$d_{long} = 111.41284cos\left(l\frac{\pi}{180}\right) - 0.0935cos\left(3l\frac{\pi}{180}\right) + 0.000118cos\left(5l\frac{\pi}{180}\right) \qquad (2)$$

4.3.1.2 Calculations of travel distances between locations

The response model for driving modes of transit was developed to use either the actual best transit route distance, queried from the Google Maps API, or an approximation of the actual route distance. Although the actual distance is preferred for accuracy of the model prediction, there is a high cost (both monetary and in computational efficiency) with using the Google Maps API. Querying distances from the Google Maps API resulted in simulation runs of over 1 minute each, which would require several days to run a 5000 run Monte Carlo simulation. Additionally, each distance request costs $0.005. With up to 500 requests per simulation run, the cost of a single Monte Carlo simulation of 5000 runs could cost $12,500. An approximation of the actual route distance is used for the large number of simulations required with the Monte Carlo method. The Google Maps generated distance is reserved for training the approximation method for a specific region, and for validating the accuracy of the approximations.

The shortest distance between two points in a Cartesian space is the Euclidean distance, which is the distance of a straight line between the points, or "as the crow flies" distance in two dimensions. However, the actual route distance travelled between two geographic points is rarely defined by the Euclidean distance, as obstacles must be avoided, and road networks must be traversed. Many urban and suburban areas use a grid type road network, with roads aligned in a North-South and

East-West manner. In such a network, the Manhattan (or rectilinear) distance may provide the best transit distance estimate. However, few regions have a perfect grid system of roads. The Minkowski distance is a generalization of the path between two points, where D is the defined distance between points X and Y, each of dimension *n*, and *p* is the distance order:

$$D\ (X, Y) = \left(\sum_{i=1}^{n} |x_i - y_i|^p \right)^{\frac{1}{p}} \tag{3}$$

The formula returns the Euclidean distance for p = 2, and the Manhattan distance for p = 1. The formula can provide distances between the Euclidean and Manhattan for 1 < p < 2, and distances greater than the Manhattan distance for p < 1 (Figure 9).

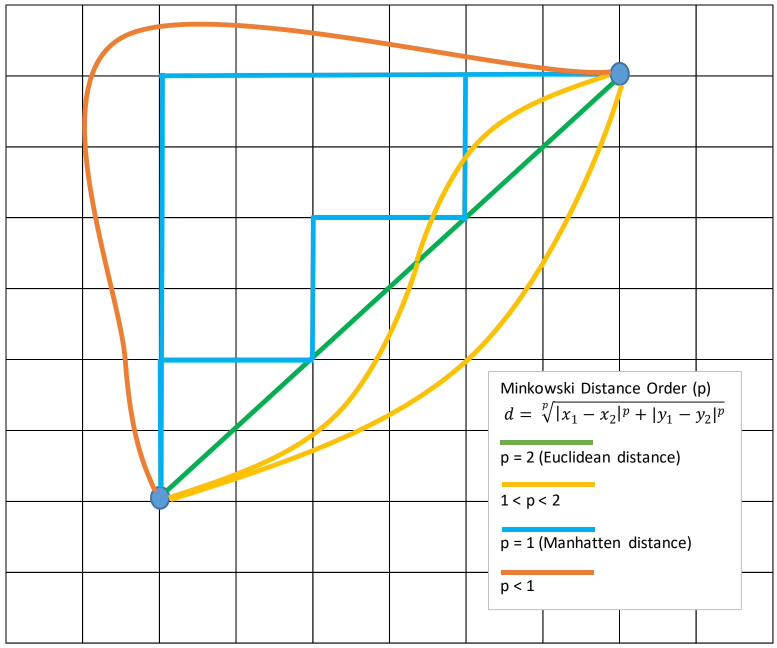


Figure 9. Minkowski distances between two points. The colored lines correspond to different values of the Minkowski order value.

4.3.2 Response time calculations

4.3.2.1 EMS response time

The model simulates response time for the three basic types of responding agents: EMS, mobile responders, and aerial drones. The response time is divided into distinct components for each of these agents. For the EMS response calculation, the time components are shown in Figure 10.

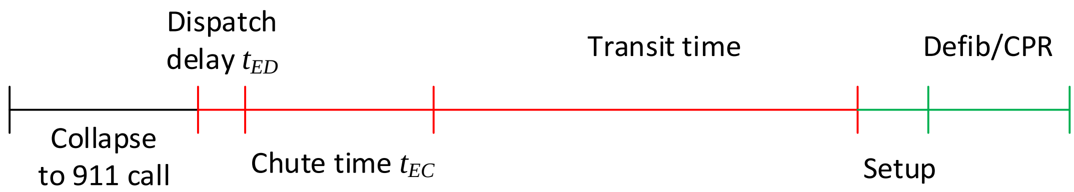


Figure 10. EMS response time components

All response times begin with the time interval from the collapse of the victim at the onset of the cardiac arrest, to the point at which 911 is called (shown in black). This time is difficult to measure in actual cardiac arrest responses, as it must be relied upon for the caller to estimate this elapsed time after the rescue has concluded. Such estimations of time when a cardiac arrest witness is undergoing high stress and emotion result in unreliable estimates. Minimizing this time is crucial for survival, as this explains the dramatic difference in survival between witnessed and unwitnessed cardiac arrests. However, this time interval is identical for all responding agents, and thus not included in the modeled response time.

The EMS response time, after the collapse to 911 call interval, contains the dispatch delay time, the chute time, and transit time to the cardiac arrest location. (This is often accounted for as the arrival time at curbside of the cardiac arrest location. There may be additional "vertical time", i.e. time required to climb stairs, if the victim is indoors and not on the ground floor, however this time would apply equivalently to all types of responders). These times, which are shown in red in the timelines, are simulated within the models with the following formula as a function of distance *d*:

$$t_{\mathrm{ReE}} = t_{ED} + t_{EC} + d/v_E \tag{4}$$

The final time intervals in the timeline (shown in green) are the time from arrival on scene until treatment, which includes the time to assess the patient, setup the equipment (e.g. remove clothes, apply defibrillation pads), and finally the treatment consisting of alternating applications of defibrillation and CPR. For model simplicity and consistency, the setup time is assumed to be 1 minute, similar to the approach by Larson *et al.* [2].

4.3.2.2 Mobile responder response time

The mobile responder timeline components are shown in Figure 11. Following the time interval to call 911, there is a dispatch delay time, and an additional delay which accounts for the time from the responder receiving the alert until the responder begins transit. The model incorporates two modes of transit for the mobile responder, walking and driving. The model can be evaluated for either mode of transit, or under a scenario where the responder knows the best mode of transit (e.g. if the arrest location is within 150 meters, the responder may choose to walk, otherwise they would drive). The following formulas are used to calculate the mobile responder's response time, where t_{ReDi} is the driving response time, t_{ReWi} is the walking response time, and t_{ReBi} is the best possible time between the two transit modes for the *i*th closest responder as a function of d_i:

$$t_{\mathrm{ReDi}} = t_{RD} + t_{RDr} + d_i/ v_{RD} \tag{5}$$

$$t_{\mathrm{ReWi}} = t_{RD} + t_{RW} + d_i/v_{RW} \tag{6}$$

$$t_{\mathrm{ReBi}} = \min \{t_{\mathrm{ReDi}} , t_{\mathrm{ReWi}}\} \tag{7}$$

The treatment times following arrival are identical to those used for EMS.

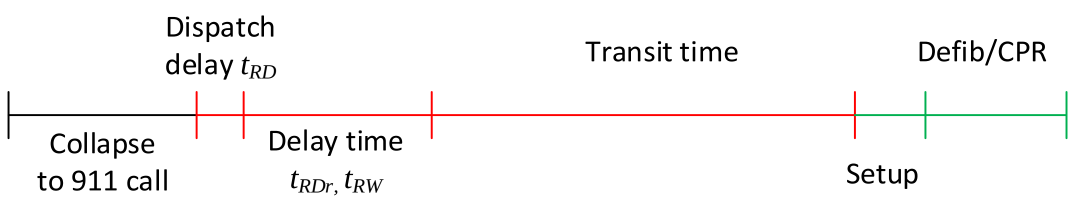


Figure 11. Mobile responder response time components

4.3.2.3 Drone response time

The timeline for the drone transit of an AED to the cardiac arrest location, after the 911 call, begins with a dispatch delay, followed by the vertical ascent time, the lateral flight time interval is the time to reach location of the arrest scene, and the vertical descension and AED deployment (Figure 12). The formula for the drone response time as a function of the distance for the *i*th closest drone is:

$$t_{Di} = t_{DD} + t_{DV} + d_i/v_D + t_{DDe} \quad (8)$$

The treatment times are identical for all responding agents.

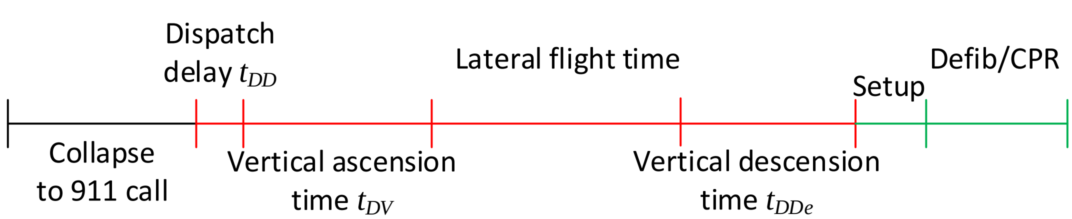


Figure 12. Drone response time components

4.3.3 System response time

The system response time is determined for the two types of cardiac arrest therapy. The CPR response time is the minimum of all responding agents capable of providing CPR. This includes mobile responders and EMS.

$$t_{CPR} = \min\{t_{ReE}, t_{ReBi}\} \tag{9}$$

The time to defibrillation is the minimum time at which there is a defibrillator at the scene and a person to operate the defibrillator. The structure of this is dependent on assumptions in the modeled system. A system with mobile responders carrying AEDs, together with the EMS system would follow a similar formula for CPR response time:

$$t_{defib} = \min\{t_{ReE}, t_{ReBi}\} \tag{10}$$

A system which uses a drone delivered AED, and requires a cell phone dispatched mobile responder to operate it, together with the EMS response, would follow the equation:

$$t_{defib} = \min\{\max\{t_{ReBi}, t_{Di}\}, t_{ReE}\} \tag{11}$$

4.3.4 Simulation survival prediction

Cardiac arrest treatment requires both CPR and defibrillation, although CPR may be provided before the defibrillation by a different responder. Each run of a simulation provides a survival probability prediction by applying the system response times of each type of therapy to the survival logistic regression equation:

$$p_{survival} = \frac{e^l}{e^l+1} \quad (12)$$

where: $l = 0.26 - 0.106t_{CPR} - 0.139t_{defib}$

4.4 Model Implementation and Execution

4.4.1 Model Implementation

The models are implemented using Microsoft Excel 2016 with Oracle Crystal Ball add-in[75]. The model uses only native Excel functions and formulas, with the exception a Visual Basic macro used in the version that accesses the Google Maps API for distances between locations (which was used only for validation purposes). Model inputs are stored in spreadsheet cells, with the mathematical operations described in Section 4.3 applied as Excel formulas. The set of system models are combined into a single Excel file for efficiency of execution. Henceforth, the set of system models is collectively referred to as the *model*.

Crystal Ball is used to define the sampling distribution type (e.g. Uniform, Beta, Binomial) and provide random sampling for the Monte Carlo simulations. Distribution parameters are stored in cells as model inputs. Crystal Ball controls the execution of simulations, and stores the resulting outputs of each simulation. Additionally, Crystal Ball provides basic graphing and summary statistics of the stored outputs.

Crystal Ball was used for the generation of all stochastic data within the model, including random locations of the cardiac arrest event and mobile responders, as well as defining reliability and availability outcomes for each simulation. A random number generator constant seed value of 999 was used for all simulation experiments to provide a common sequence of random numbers across different sets of runs to reduce variation of the results.

4.4.2 Model Execution

The model is executed by running a series of simulated cardiac arrest events in the defined region, with response times and predicted survival likelihood calculated for each type of response system. The accumulation of several thousand simulation runs, designated and controlled by Crystal Ball, under the same conditions (i.e. input factors) generates a distribution of response times and survival predictions. These can then be used to evaluate each system and compare the effectiveness of different systems.

Execution of simulations are performed with the following sequence of steps.

1. Simulation run initialization. EMS responders (i.e. ambulances) and drones start at their input base locations E_i and D_i.
2. A random location *A* (latitude, longitude) is assigned for the cardiac arrest based on the geo-spatial input distribution within the region defined by $x_{NW}, y_{NW}, x_{SE}, y_{SE}$.
3. Random locations R_i are assigned for each of N mobile responders sampled from the responder geo-spatial distribution.
4. For each mobile responder, the model stochastically determines if they are "able and willing to respond" based on the responder reliability input R_R.
5. Both the walking and driving travel distance d_i is calculated for each available responder.
6. The response time t_{ReBi} is calculated for each of the 3 closest mobile responders using Equation 7
7. The operational state of the AED is stochastically determined based on the AED reliability input R_{AED}. The mobile responder time-to-CPR is defined by the first arrival. The time-to-defibrillation is defined by the first arrival with an operational AED.
8. For each EMS ambulance E_i, the model stochastically determines if it is available based on the ambulance availability input E_A.
9. The travel distance d_i is calculated for each available ambulance. The closest available ambulance is determined.
10. The response time t_{ReE} is calculated for the closest available ambulance using Equation 4..

11. For each drone D_i, the model stochastically determines if it is available based on the drone operational availability input D_{AO}. For all drones, the system availability is stochastically determined based onthe drone weather availability input D_{AW}.
12. The travel distance d_i is calculated for each available drone. The closest available drone is determined.
13. The response time t_{Di} is calculated for the closest available drone using Equation 8.
14. Response time to CPR t_{CPR} is calculated using Equation 9.
15. Response time to defibrillation t_{defib} is calculated using Equations 10, 11, etc. depending on the system being modeled.
16. The survival probability prediction $p_{survival}$ is calculated using Equation 12.
17. The model output values are stored, and the model is returned to initialization step 1 for the next simulation, repeating the process until all simulations are complete.

The location definition of the cardiac arrest and distance calculations for responding agents are depicted in Figure 13. After completion of a Monte Carlo simulation (i.e. execution of many simulation runs under the same input conditions), the stored output data can be displayed as histograms, from which additional statistical analysis can be applied. Figure 14 shows example histograms for time to defibrillation from a Monte Carlo simulation, with the median time, 5^{th} percentile, and 95^{th} percentile annotated.

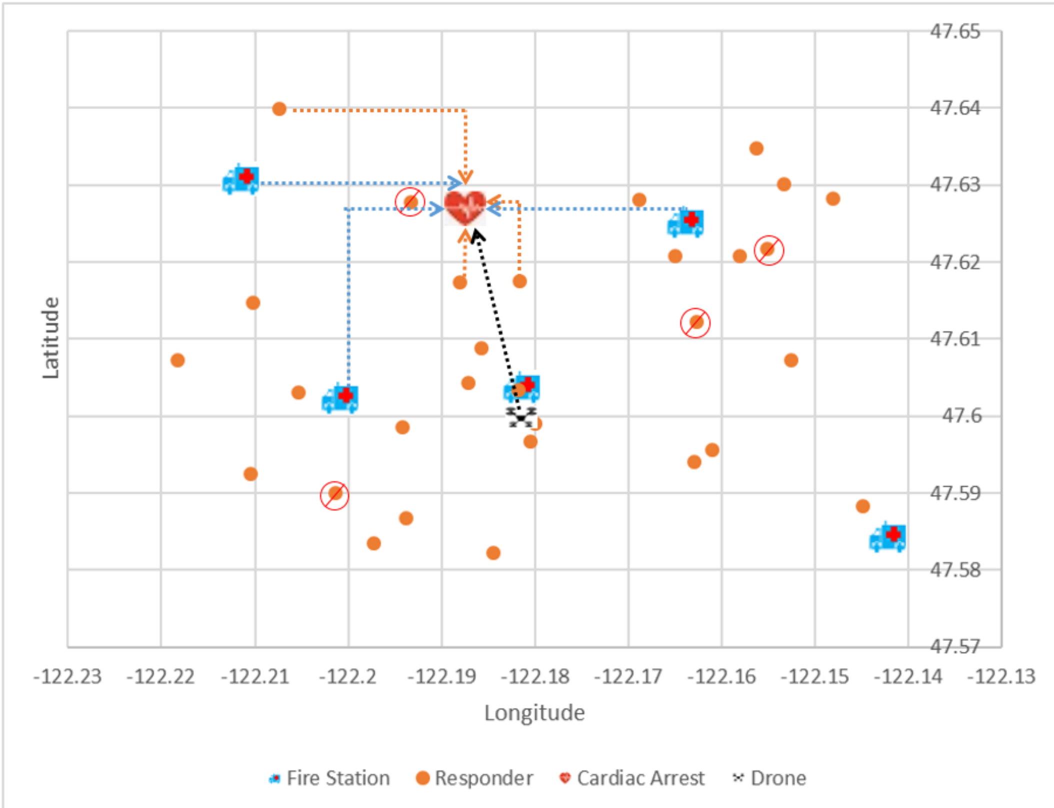
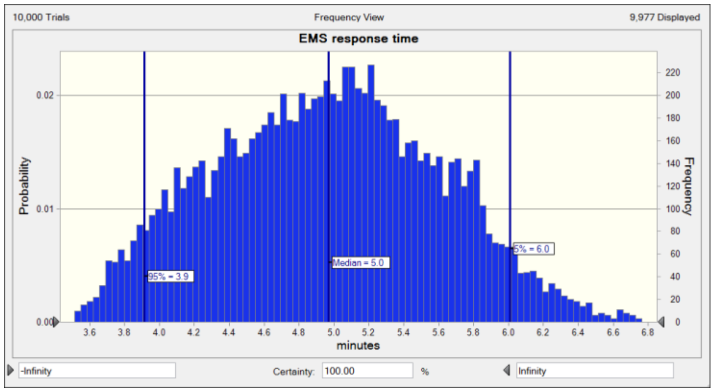
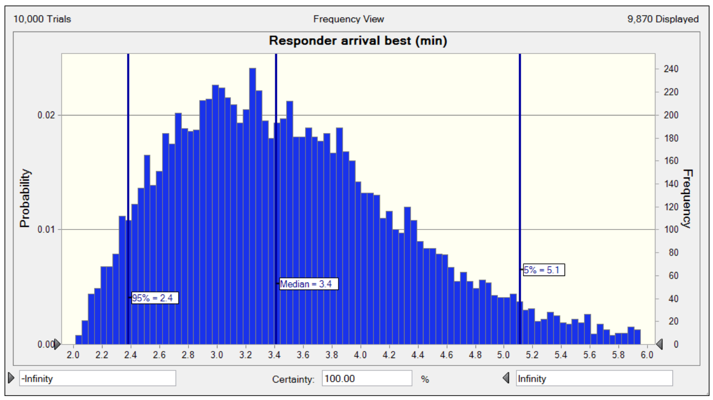


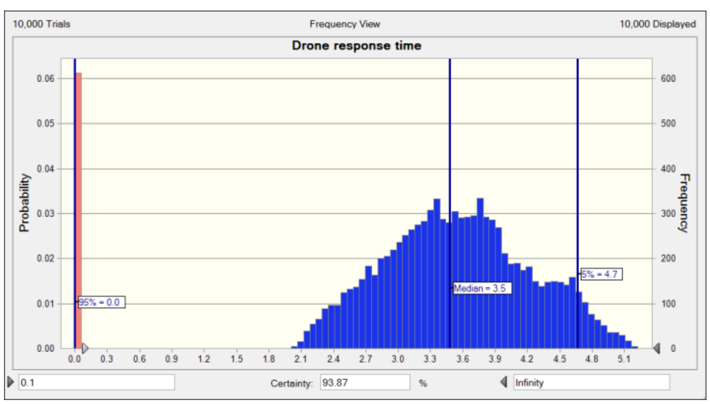
Figure 13. Diagram depicting model execution with EMS, mobile responders, and a drone response. Crossed out responders represent those that are stochastically determined as unable to respond.



a) Example EMS response time to defibrillation distribution



b) Example mobile responder time to defibrillation distribution



c) Example drone response time to defibrillation

Figure 14. Histograms generated by Crystal Ball for the response time-to-defibrillation distributions. The results shown are from a 10,000 run Monte Carlo simulation in the Bellevue, Washington region.

The differences in response time between systems can be calculated for each simulation run, and displayed as a distribution of time differences. In the example output in Figure 15, the difference between the EMS response time and the first mobile responder arrival time is displayed. In the distribution shown, a negative time difference (salmon colored) indicates simulations where EMS arrived first, while a positive time difference (blue) denotes simulations with the mobile responder arriving ahead of EMS. In the example, the responder arrives faster than EMS in about 89% of cases, with a median time of 1.5 minutes ahead of EMS, and 5% of the time at least 3 minutes ahead.

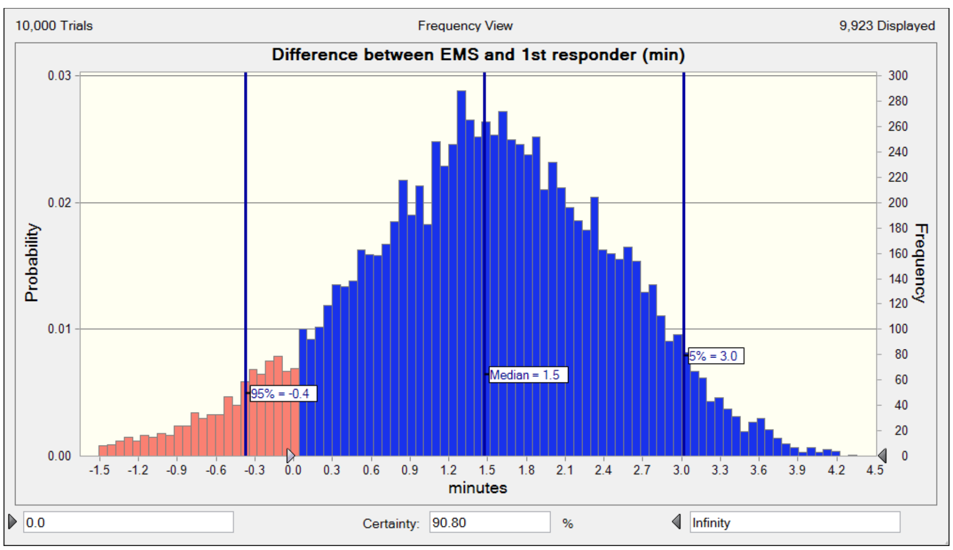


Figure 15. Example distribution of difference in response times between EMS and mobile responders. Negative times indicate EMS arrived ahead of responders.

4.5 Discussion of Inputs

4.5.1 Simulation region inputs

4.5.1.1 Method for Minkowski Distance Approximation

The Minkowski distance order value p is used to approximate the transit distances in the model. This value can vary with modes of transportation as well as among types of regions. A responder travelling by foot to the scene would likely take a very direct route, with p close to 2. A responder who drives to the scene would have a distance with p close to 1, as they would navigate a road network. A drone flying above buildings may be best approximated by a Euclidean distance ($p = 2$).

Different approaches to approximating travel distances have been reported in literature. Nogueira *et al.* used the Euclidean distances multiplied by a factor of 1.366 to approximate the actual travel distances of ambulances in Sao Paulo, Brazil [25]. Rabe *et al.* compared approximations to real distances by Euclidean, Manhattan, Minkowski ($p = 1.15$), weighted Euclidean, and exponential Euclidean [76]. The authors conclude that "the different distance metrics achieve surprisingly good results according to the real distances." Shahid *et al.* use the Minkowski distance to model travel distances from patient homes to the nearest hospital [77]. In their evaluation, the road network distance data set provided a mean distance of 11.82 km, with a standard deviation of 5.27, while the Minkowski approximation provided a mean of 10.45 km, with a standard deviation of 5.18. The authors argue "distance metrics typically produce less accurate estimates than actual measurements, but each metric provides a single model of travel over a given network. Therefore, distance metrics, unlike actual measurements, can be directly used in spatial analytical modeling." The authors modeled the city of Calgary, Canada, and found that a Minkowski order value p of 1.31 best approximated the transit distances from homes to the hospitals.

In this model, drone response distances are assumed to be Euclidean unless the region has a restricted airspace. The model approximates driving distances using the Minkowski distance. For a driving response (by EMS ambulance or mobile responder), depending on the nature of the road network, the Minkowski order may range from 0.5 to 1.5.   For any particular trip, there is a specific value of p that yields an accurate estimate. For example, Figure 16 shows the Minkowski distance (shown in red) to approximate the actual street network distance between two points in Baltimore, Maryland. The actual road network distance (shown in blue), as provided by Google Maps [78], is 3.1 km. The Euclidean distance (green) is 2.6 km, the Manhattan distance (purple) is 3.4 km, while the best Minkowski distance, with p = 1.21, is 3.1 km, matching the road network distance.

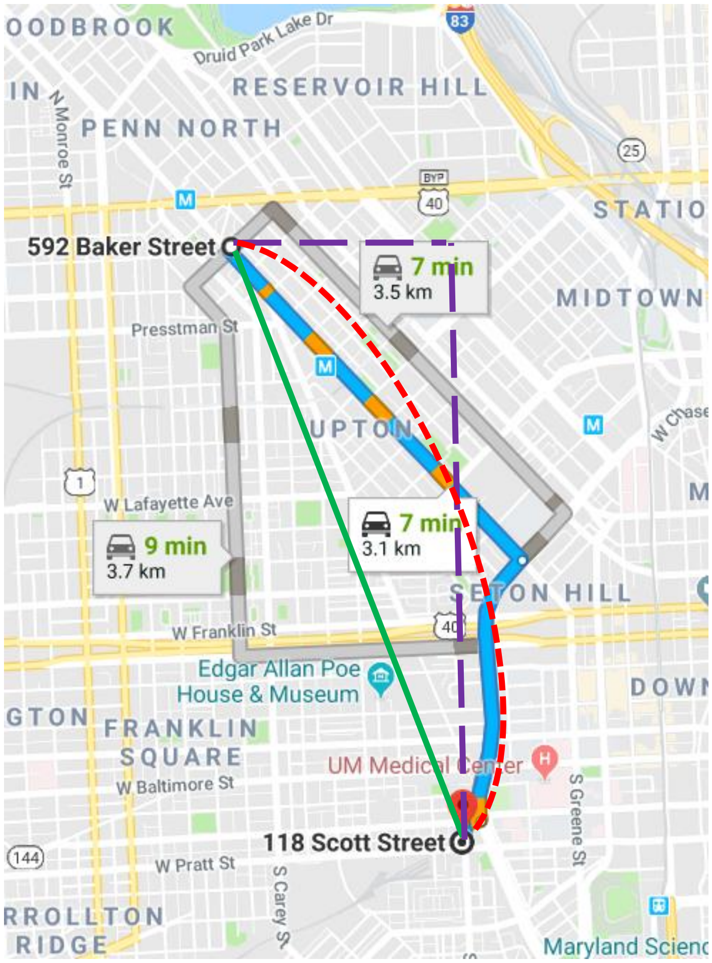


Figure 16. Google Maps street network route (blue), Euclidean distance (green), Manhattan distance (purple), and Minkowski distance p = 1.21 (red)

The model uses a single value of p for all driving distances in a region, however. Different values of p were used for different regions. For each of eight regions I determined the best value of p by conducting a calibration study. Table 2 lists the regions that were examined; these regions represent diverse geographies within the United States. The regions were classified as urban, suburban, and rural. Within each of these regions, a geographic rectangle was defined from which 30 location pairs (origin and destination locations) were randomly sampled; I then used the Google Maps API to determine the actual driving distance for each location pair. Areas with large geographic obstacles such as lakes, rivers, etc. were excluded. For sixteen values of p from 0.5 to 2.0, I estimated the driving distances for the 30 location pairs using the Minkowski distance with that value of p, calculated the difference from the actual driving distances, and determined the Root Mean Squared Error (RMSE) for that value of p for that region based on this training dataset. Figure 17 shows the training results, from which I chose, for each region, the value of p that had the smallest RMSE (these are shown in Table 2). For example, for Bellevue, Washington, p equals 0.8.

Table 2. Best identified Minkowski distance order p and validation results for eight regions.

City	Region type	p	Bias	MSE	RMSE
Bellevue WA	Suburban	0.8	0.35	1.53	1.24
Baltimore MD	Urban	1.0	0.28	0.70	0.84
College Park MD	Suburban	0.9	0.54	1.38	1.18
Spokane WA	Urban	0.8	0.28	6.63	2.58
Ellensburg WA	Rural	0.7	0.03	4.24	2.06
Tualatin Or	Suburban	0.7	-0.90	3.29	1.82
Sioux Falls SD	Suburban	0.7	0.04	6.08	2.47
Seattle	Urban	0.9	0.30	0.50	0.71

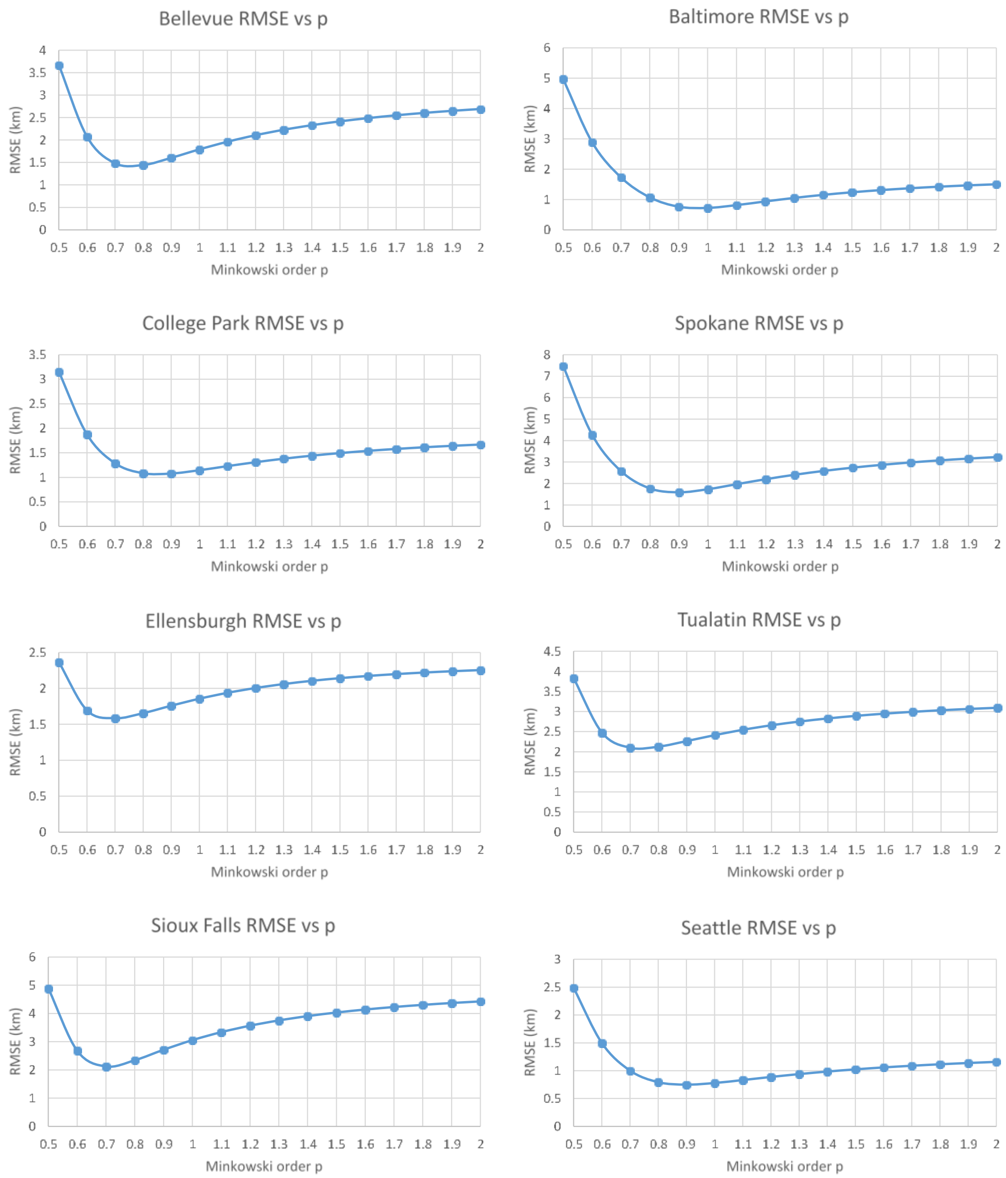


Figure 17. Plots of RMSE versus Minkowski order p for training data from eight regions.

Then, for each region, 30 additional validation location pairs were sampled. The bias and root mean squared error were calculated for each region using that region's p value. The results with the validation dataset are shown in Table 2 and Figure 18. The results indicate the accuracy of the approximation and show that the RMSE for the validation dataset is close to the RMSE for the training dataset. For example, for Bellevue, Washington, with p = 0.8, the RMSE for the training dataset was approximately 1.4 (as shown in Figure 17), and the RMSE for the validation dataset is 1.24. The validation results provide evidence that the approximation was not overfitted to the training dataset.

To assess the sufficiency of the sample size of the training data, one region, Seattle, had the Minkowski order trained with 30, 100, and 300 sample location pairs. The trained order p was then validated against the same validation sample set of 30 location pairs. The results are shown in Table 3.

Table 3. Sample size sensitivity of training method.

City	Region type	p	Bias	MSE	RMSE
Seattle 30 samples	Urban	0.9	0.30	0.50	0.71
Seattle 100 samples	Urban	0.8	0.08	0.49	0.70
Seattle 300 samples	Urban	0.9	0.30	0.50	0.71

The different sample sizes in the training data produce very consistent Root Mean Squared Error values. The bias shows no directional trend with increased sample size. It is thus concluded that 30 samples is sufficient a training data set

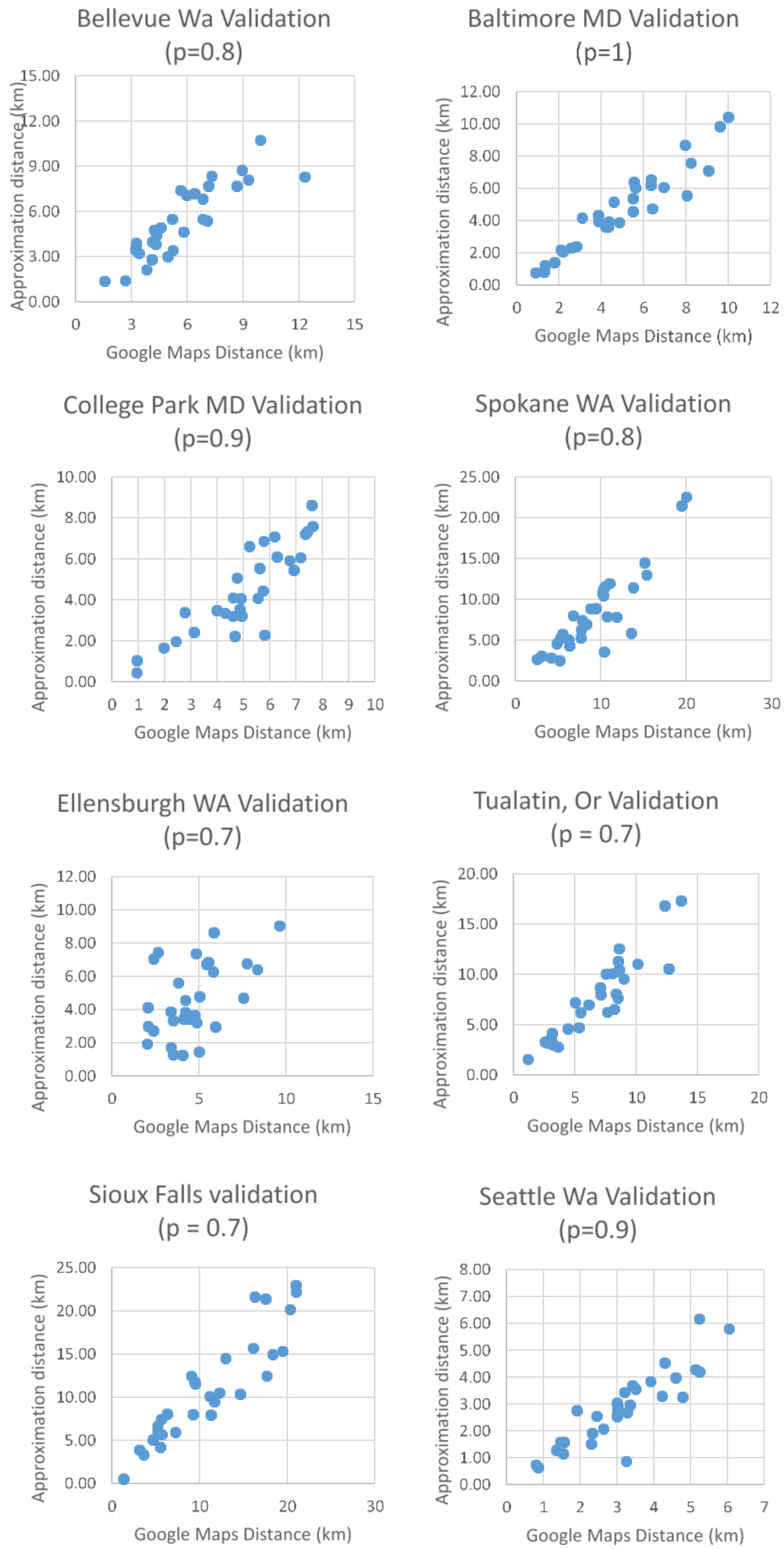


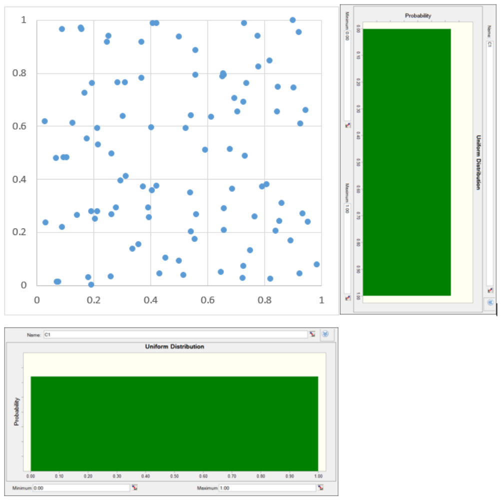
Figure 18. Plots of validation data showing the Minkowski approximated distance versus the Google Maps distance.

4.5.1.2 Cardiac Arrest and Mobile Responder location distributions

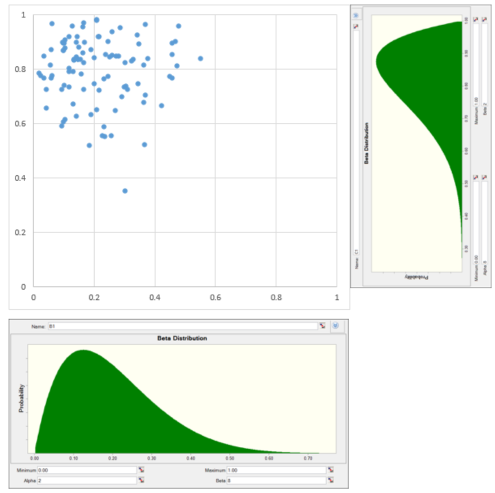
The Monte Carlo simulations randomly sample a cardiac arrest location *A* and a defined number of mobile responder locations R_i from 2-dimensional spatial distributions. The model can accommodate any bivariate distribution with finite support. Four types of distributions are described in Table 4, along with an example application. The first three types of spatial distributions are defined by a latitude generating distribution, and a longitude generating distribution. The latitude and longitude locations are randomly sampled from their respective generating distributions to create the two dimensional spatial distribution. The uniform, triangular, and beta distributions are chosen due to their finite support interval and ease of defining the mode. An example of 100 random sample locations and the pictured generating distribution are shown in Figure 19.

Table 4. . Location sampling distribution descriptions.

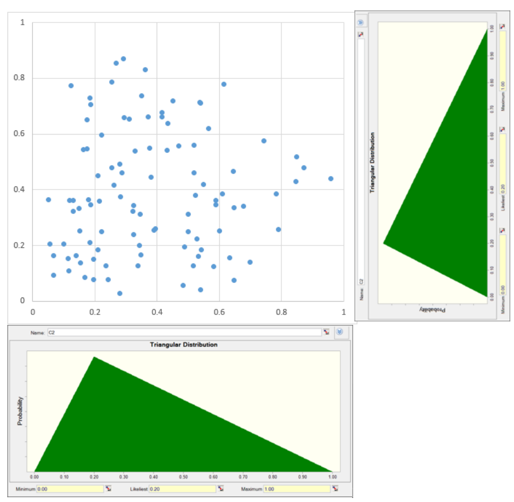
Distribution type	**Example Application**	**Generating distribution**
Uniform	Rural or suburban area, or small model regions with a uniform population density	Uniform
Concentrated	Large areas that have a densely populated central location	Beta
Diffuse centered	Rural or suburban areas that have a gradient of population density emanating from a central location	Triangular
Custom	Prior known or complex clustering of population or historic cardiac arrest locations	Heat map / density map



a) Uniform



b) Beta



(c) Triangular

Figure 19. Example random spatial sampling and sample generating distributions for (a) Uniform, (b) Beta, (c) Triangular.

The fourth type of distribution, the *Custom* distribution, is generated from a heat map or density map. The map could be based on population density, historic cardiac arrest density, or responder location density. The 2 dimensional sampling distributon is generated by first dividing the density map into a grid of discrete cells, each representing a single latitude, longitude location for the model and a value (e.g. a count, probability, frequency). A probability is calculated for each cell in the grid which is proportional to the value of the cell. Latitude, longitude locations are then sampled from the discrete number of grid cells based on the probability of each cell. Figure 20 shows an example density map, and an example of 100 spatial samples.

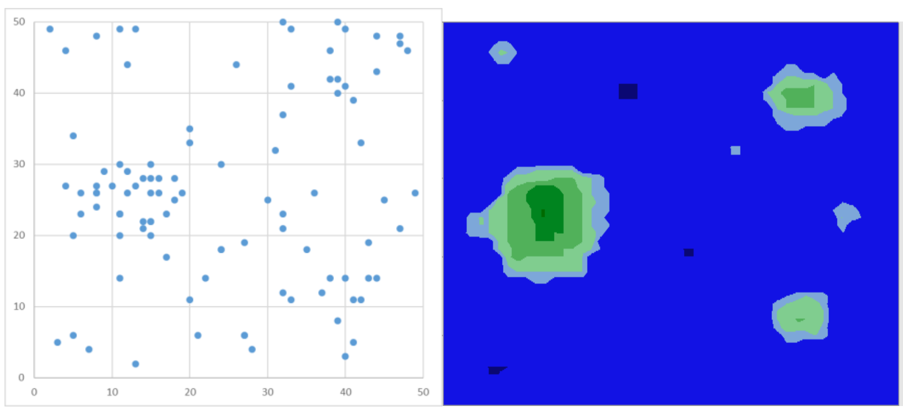


Figure 20. Example *Custom* random spatial sampling, sample generating density map.

4.5.2 EMS System Inputs

EMS inputs were obtained from both literature sources and empirical analysis of available response data. The dispatch delay t_{ED}, i.e. the time required to identify a 911 call as a medical emergency requiring EMS response, is assumed to be between

0.25 and 1 minute. Ingolfsson *et al*. used an average chute time t_{EC}, i.e. the time from dispatch alarm to "wheels rolling", of 2.5 minutes with standard deviation of 1 minute, and an average ambulance speed of 69.4 kn/h in the DES modeling of Edmonton, Canada EMS response [23]. King County EMS reports that the dispatch time is less than 90 seconds for 93% of calls [79]. The chute time typically ranges from 30 seconds to 2 minutes.

Regression analysis of actual EMS response time and distance data was also be used to calculate travel speed v_E, as well chute time t_{EC}. The data plotted below was provided by King County Public Health Department. The data set includes response times to cardiac arrest events over a 1-year period in the city of Bellevue, Washington, along with the Manhattan (rectilinear) distance from the dispatch station to the patient location. After outlier removal, a least squares linear regression line was fitted to the data (Figure 21). The regression equation for response time t (minutes) with respect to distance d (meters) is:

$$t = 3.537 + 0.000869d \tag{13}$$

The y-intercept of 3.537 minutes may be interpreted as the combination of dispatch delay time t_{ED} and chute time t_{EC}. The slope is the inverse of ambulance velocity, which when converted to km/hour is 69 km/h, which is nearly identical to the speed cited by Ingolfsson.

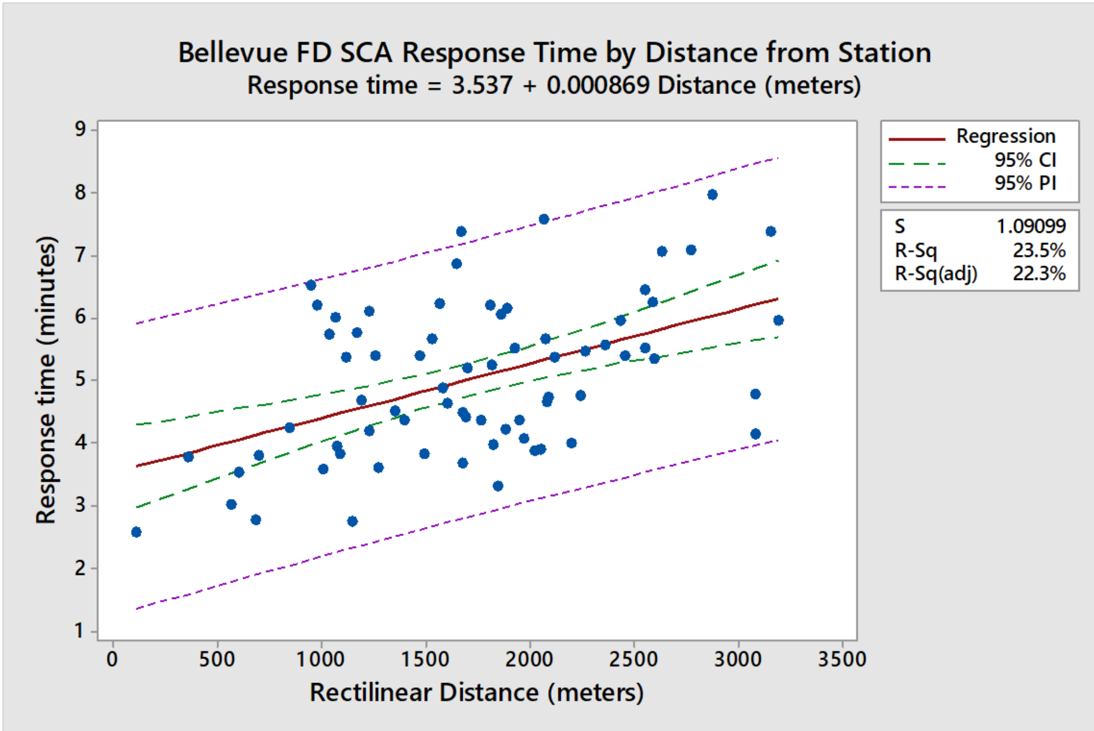


Figure 21. Regression analysis of Bellevue, Washington EMS response time to cardiac arrest events.

The ambulance availability E_A input includes unavailability due to the ambulance being out on another call, the ambulance being cleaned or restocked after a call, or longer-term issues such as vehicle maintenance. Ambulance availability is typically high, even in busy districts with high call rates. Ambulance availability is the mathematical complement of *commitment factor*, a measure of the proportion of time an ambulance is on a call. This can range from 0.16 (ideal) to 0.3 (unsustainable) [80], translating to an availability range of 0.7 to 0.84.

4.5.3 Mobile responder inputs

The mobile responder dispatch delay t_{RD} may differ from the EMS dispatch delay, as an ambulance dispatch is initiated once the call is determined to be any medical emergency, while the responder activation may require additional time for the operator to determine that the call is likely a cardiac event. The input range for this constant is estimated to range from 0.5 to 2 minutes. This delay time may be significantly reduced in the near future with the employment of voice recognition and artificial intelligence into the 911 dispatch system. The Danish startup company Cordi has tested its artificial intelligence technology in Copenhagen on 161,000 emergency calls, finding it was 93% accurate in identifying cardiac arrests, where human dispatchers were only 73% accurate [81].

Additional mobile responder delays account for the time between receipt of the alert via a cell phone app, and the start of transit to the cardiac arrest location. This may be time to grab the AED or a gear bag, or inform their present company that they are leaving. When the mode of transit is walking, this delay, t_{RW}, is estimated to be from 0.5 to 1 minute. When driving, the delay t_{RDr} it is estimated at 0.5 to 2 minutes, as additional time may be needed to get to the responder's vehicle.

The speed of the responding agent is also dependent on the mode of transit. The Center for Disease Control (CDC) defines a brisk walking pace from 3 to 4.5 mph (4.8 to 7.25 km/h) [82]. It is assumed that a healthy responder travelling to a medical emergency would typically achieve the upper end of this range. Driving speed v_{RD} is dependent on many factors. The type of road network, traffic conditions, and time of day all affect the speed of vehicle transit. A study of estimated travel speeds in 50 US cities using the Google Maps distance and duration between sampled origin and destinations resulted in an grand average of 48 km/h (30 mph) with a standard deviation of the average speeds of 9 km/h (5.6 mph) [83].

The mobile responder reliability R_R is the probability that upon receiving an alert of a nearby potential cardiac arrest victim, the responder attempts to travel to the scene and provide medical assistance if needed. Prior research on task acceptance for on-demand mobile crowdsourcing (e.g. citizen journalism, citizen science) has identified *situational factors*, such as weather, and convenience of location, as well as *temporal factors*, such as time of day, and immediacy of the task [84][85]. Brooks *et al.* found only 23% of PulsePoint responders attempted to travel to the location of the cardiac arrest [49]. The authors identified primarily technological barriers, such as muted phones, or lack of cell reception, as impediments to response rate. Early results from the ALERT study indicate only about 31% of verified responders (off duty firefighters) actually responded to alert activations. Other communities with similar systems under trial have achieved marginally better responder reliability. A trial system on the small island of Langeland, Denmark, found that at least one of 9 dispatched verified first responders arrived to the cardiac arrest scene in 96% of the cases [86].

There are barriers to responding that are unique to volunteer treatment of cardiac arrest victims. Ozcan *et al.* performed a mobile volunteer responder simulation study, in which human study volunteers were asked to carry an AED with them for a week, and were notified at random times of a simulated cardiac arrest nearby [87]. Four types of barriers were identified which could prevent successful response to an alert (Figure 22). *Barriers to commitment* include issues that prevent a responder's ability to respond (e.g. sickness) or their willingness to respond (e.g. the phone is placed in mute due to an important meeting, or spending time with family) *Barriers to notification* include technical issues such as cell reception, being in a loud environment, and not waking when notified while sleeping. *Barriers to leave* involve either situational reasons (the responder is in an important meeting, or at a doctor appointment), or judgement reasons, such as believing it would be unsafe to travel to certain neighborhoods at night. Finally, *barriers to perform* include concerns about credibility (e.g. fear of entering a chaotic, crowded setting), liability, or lack of mental preparation (e.g. fear of removing a victim's clothes, or delivering a shock). The study found a 49% response rate from the simulation; however, the authors noted that the study was designed more around understanding barriers to response than accurately quantifying a response rate.

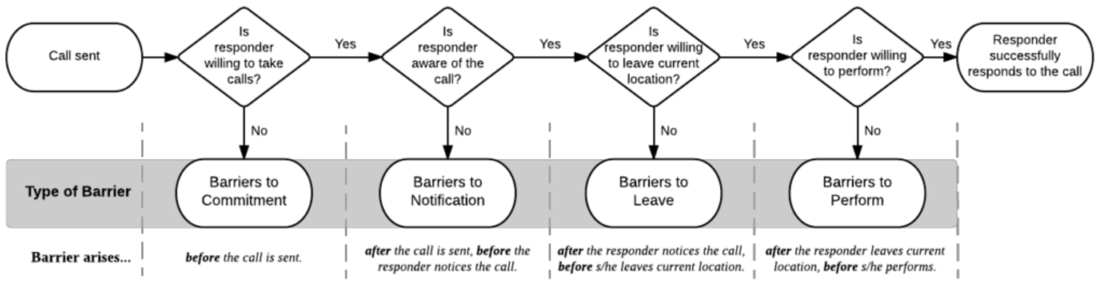


Figure 22. Barriers for a mobile responder to respond to a cardiac arrest scene (from [87])

The AED reliability factor R_{AED} in the model specifically refers to the *mission reliability* of the AED, which is the conditional probability, given that an AED is deployed for a patient use, that the AED is able to perform its functions for the duration of the use (e.g. analyze the heart rhythm and provide a shock if necessary).

AEDs are inherently highly reliable devices. Their relatively narrow scope of intended functions allows for a design that is highly customized to a single purpose. Additionally, AEDs perform automated self-diagnostic tests daily, which verify their readiness for use, further increasing the mission reliability. Most AED hardware failures are detected by the self-test and the device is repaired or replaced without impacting any patient use.

AEDs require only minimal maintenance – the battery must be replaced every 3 to 4 years, and the electrode pads must be replaced every 2 to 3 years. Overdue maintenance, particularly devices with depleted or low batteries at the time of a therapy need, is one of the leading drivers of reduced AED mission reliability.

Deluca *et al.* discuss a review of AED patient use failures in the FDA MAUDE database, reporting that battery and power problems are the "most likely cause" in 23% of cases and a "possible contributor" in 53% of cases [88]. A University of Louisville study tested 322 AEDs at 190 different sites and found that 5% had depleted batteries [89].

Maintenance related AED mission failures are primarily applicable to static located public access AEDs. These AEDs may be in remote locations (relative to the responsible maintenance manager), and inspected infrequently. It is unlikely that a responder carrying an AED with them would have this issue, as the AED emits audible and visible alerts for several days when it reaches a low battery state or requires other maintenance. Hence, the reliability model input can be very specific to the type of response system being simulated. As AED manufacturers are exploring designs for very low cost AEDs, one attribute that may be reduced is the mission reliability (e.g. an AED with no self diagnostic functionality would have reduced mission reliability due to lack of failure detection). The impact of AED reliability on different response systems can be explored with this factor, as it can range from 95% to greater than 99.9%.

4.5.4 Drone Inputs

The drone dispatch delay t_{DD} is similar to the EMS dispatch delay and mobile responder dispatch delay, denoting the time interval from the start of the 911 call until the drone takes flight. This delay time could, in theory, not exist, as the drone could be dispatched automatically upon receipt of a medical 911 call, and returned to the base at any point if it is determined not to be needed. There may however be physical constraints to an immediate takeoff, such as opening storage garage doors, time for an on duty pilot to man the flight controls (if required by regulations), etc. The expected range for this factor is thus 0 to 2 minutes [90].

The time for the drone to ascend vertically to a safe flight elevation (e.g. 120 meters), t_{DV}, can be modeled as a constant, as it is assumed there would be a standard minimum elevation requirement based on regulations and the regions topography, bounded by the current maximum legal flight elevation of 400 ft. The time required to reach this elevation would be based on the vertical ascension speed of the drone, but would remain constant across flights. This factor can be determined from drone performance specifications, and ranges from 0.25 minutes to 1 minute [91]. Rotary-wing drones have typical lateral flight speeds of 50 to 100 km/h, although custom designed drones could reach speeds up to 150 km/h [90]. Similar to the drone vertical takeoff time, the drone descent time interval, t_{DDe}, accounts for the descent of the drone to a safe level to deploy the AED, and the time required to deploy the AED (e.g. lower by a cable and winch, land and release, etc.) to a waiting recipient. This too is assumed constant within a system, and is expected to range from 0.5 to 1 minute.

Like all complex equipment that perform a critical function and must operate safely, drones will require periodic maintenance, both preventive and corrective. The downtime is minimal relative to the operational time; however, this operational availability D_{AO} is incorporated into the model to assess the impact, as it could drive decisions on redundant drone capability. The availability of a drone is a fraction between 0% and 100%, and is applied stochastically and independently to each drone within the system for each simulation. Typical drone availability is estimated at 95% [90].

The model accounts for the occurrences when a drone would not be able to respond to a cardiac arrest scene due to weather conditions. Drone flight may be restricted during periods of high winds, heavy rain, heavy snow, or poor visibility. This factor, D_{AW}, would be unique for the geographic region being modeled. An nominal weather availability estimate is 90% [90]. The weather availability factor is a fraction between 0% and 100%, and is applied stochastically and equivalently to all drones within the system for each simulation (i.e. if the weather is not permitting, no drones in the system model are able to respond in the particular simulation).

4.5.5 Excluded Factors

Modeling and simulation relies upon the simplification of the complexities of real world systems. Many factors which could influence the response time were not included in the model. Some of these factors provide additional stochastic variance to response times and survival, but were applied as constants representing average values. Others represent uncommon events or situations, with little impact on the macro-scale evaluation of system performance (i.e. the mean response time). These factors are noted here:

- *Driving velocity variation over time of day*. The velocity inputs used represent the average velocity, across all times of day and driving conditions. Specific responses may result in faster or slower driving speeds, depending on time of day, traffic, and weather.
- *Simultaneous cardiac arrest events.* The model does not explicitly simulate multiple cardiac arrest responses occurring at the same time. Based upon the frequency of cardiac arrests, it is very unlikely more than one concurrent response would be required within the same geographical vicinity. The ambulance availability factor accounts for the possibility that some ambulance are unavailable due to response to other medical emergencies, and likewise the drone operational availability considers time deployed for other calls.
- *Restricted air space.* The model assumes a Euclidean distance for drone flight. There may be restricted airspace within a region of simulation. This could be compensated by a reduction in the Minkowski order value, below the value of 2. A training approach similar to that described for the driving distance approximation could be applied to determine the value of p.
- *AED use related errors.* AED use errors are rare, occurring in about 4% of all cases, with about 72% of errors caused by the operator [92]. Not all errors result in the patient being deprived of therapy, some may result in delaying

the time to defibrillation. This factor could be combined with the AED reliability factor to include all causes for AED mission failures.

- *Additional geo-spatial distributions*. Section 4.5.1 discussed the models requirement for distributions with finite coverage intervals, to provide boundaries for the distribution. Uniform, triangular, beta, and heat-map distributions were discussed. This could be extended to include the use of truncated distributions.

4.6 Model Verification and Validation

Model validation is the "substantiation that a computerized model within its domain of applicability possesses a satisfactory range of accuracy consistent with the intended application of the model"[93]. Model validation is necessary to provide credibility to the predictions and insights gained from simulation experiments, and to build confidence in conclusions and decisions made from simulation analysis. The state of implementation of the cardiac response systems modelled in this research range from concepts, to small pilot studies and experimental trials, to fully implemented but still in their infancy. In the context of validation, these can be considered non-existent systems, as there is a lack of available real system data. As such, the validation approach relies heavily on rationalism and only minimally on empiricism (employing it when real system data is available).

The goal of the model validation is to support the credibility of the results of the virtual system experimentation and application performed as part of this research. Carson notes that a model cannot be completely verified or validated. “When we (loosely) say that a model has been verified or validated, we mean that we have explicitly carried out a series of tasks to verify and validate our model to the degree necessary for our purpose. Such V&V is always a matter of judgment to a large extent”[94]. The degree of accuracy sought in this project is the sufficiency to understand the effect of system factors on the system behavior, and to predict the potential improvement in response time and survival that different response systems may provide.

The model validation consisted of four aspects, as described by Sargent [93], each employing a number of techniques. The four aspects -- conceptual model validation, data validation, computerized model verification, and operational validation, are summarized in the following sections.

4.6.1 Conceptual Model Validation

A conceptual model is an abstraction and simplification of a real world system or problem into a set of assumptions and logical relationships. The conceptual model provides the foundations for the logic and mathematical algorithms that are implemented in the computerized model. Sections 4.1 through 4.4 provide the conceptual model for the cardiac arrest response system simulation model.

Validation of the conceptual model was performed using the technique of *face validity*. Face validity is a review of the conceptual model with experts knowledgeable with the system or system concept. The experts review assumptions, input-output relationships, and model logic to assess whether the models behavior is reasonable. This was performed on both the individual event level, i.e. the response time prediction of a specific agent, as well as at the global model response level.

I selected experts in the EMS domain who have significant knowledge and experience in both the clinical aspects of cardiac arrest resuscitation, as well as the operational details of out of hospital cardiac arrest response systems, such as EMS and PAD systems. These are the type of positions that could ultimately be consumers of analysis generated by the model, as they are decision-makers in the deployment of EMS systems as well as augmentation with additional cardiac response systems. The following sections summarize my review with the experts.

4.6.1.1 Dr. Mickey Eisenberg review

One expert reviewer was Dr. Mickey Eisenberg, MD, MPH, PhD. Dr. Eisenberg is a professor of Emergency Medicine at the University of Washington, and the former Medical Director for King County EMS. His perception following our review of the conceptual model is that the logical foundation of the response time predictions is sound, and the model produced response time outputs that were consistent with his personal experience and expectations for the novel systems.

One notable comment was the apparent discrepancy in the simulated Bellevue survival predictions (a city within King County, Washington) with actual King County survival rates for witness VF cardiac arrest. Further discussion resulted in possible explanations: (1) the logistic regression model used to predict survival was based on data from 1976 to 1993. Although time to defibrillation and time to CPR are still considered the predominant factors in survival, there have been many advances in the quality of CPR, advanced life support treatment, and hospital care which increase the overall survival for all systems. Additionally, this data predates the widespread adoption of AEDs for public access. (2) The model does not include the potential for bystander CPR, which typically results in very short times from collapse to the initiation of CPR. Bystander CPR is a random event which would apply to all cardiac arrest response systems equivalently. The occurrence of bystander CPR is significantly higher in King County than in most cities or communities.

4.6.1.2 Dr. Greg Ayers review

A second face validity review was performed with Dr. Greg Ayers, MD, PhD. Dr. Ayers is a cardiologist, the Head of Clinical Affairs for Philips Healthcare, and also a trained firefighter, EMT, and ALS responder, serving as a volunteer with Orcas Island Fire and Rescue.

Similar to Dr. Eisenberg, Dr. Ayers found the model and simulation approach to be logical and produce believable results. We had a discussion about the delays in mobile responder sequence of response actions. The drive mode of response, in particular, would expect delays both upon receipt of the cell phone app alert, as well as a potential delay upon arrival at the location to find parking. The average of these delay times, which is used in the model, may vary amongst the type of responder of the system modeled. As an example, an off duty firefighter, as a verified responder, would likely have a shorter delay, as they would be authorized to park at any safe location. A citizen responder system may have a longer average delay, as they would likely be inclined to find legal parking close to the scene. Dr. Ayers believed that the range of drive delay time proposed for the simulations was valid, however he believed it would commonly be toward the upper end of the range (i.e. 1.5 minutes). He also commented that the drone dispatch delay time should be no greater than the mobile responder dispatch delay. However, it could be much shorter, similar to the EMS dispatch delay, if the drone is launched immediately upon determination of a medical 911 call. The drone would be recalled if the dispatcher subsequently learned that the call is not a cardiac arrest and the AED is not needed.

Dr. Ayers also had similar comments to Dr. Eisenberg's on the survival prediction for EMS response in Bellevue. While this prediction would be typical of average survival in the United States, certain communities, such as King County, Washington, have achieved significantly high survival based on high bystander CPR likelihood, advancements in Advanced Cardiac Life Support and post arrest hospital care. He agreed that an updated survival model would be beneficial, but it would need to factor in these region specific variables. These would result in a unique intercept in the model for different regions, although the effect of time to CPR and time to defibrillations would likely be similar to the model published by Valenzuela et al.

4.6.1.3 Dr. Tom Rea review

A third face validity review was performed with Dr. Tom Rea, MD, MPH. Dr. Rea is a Professor of Internal Medicine at the University of Washington, a Section Head at Harborview Medical Center in Seattle, Washington, the Medical Director of King County Emergency Medical Services, and the Director of the Center for Progress in Resuscitation. He is one of the thought leaders behind the ALERT study, the concept of a verified mobile responder (i.e. off duty medical professional or first responder), and is active in the oversight of the study.

Dr. Rea's overall impression of the model and simulation approach was that the method provided credible predictions, and would be valid for the comparison of different response systems. Like the other reviewers, Dr. Rea noted that the predicted survival from the Bellevue simulations was lower than that currently observed. He believed similar factors result in the higher survival, particularly the large percentage of cardiac arrests with bystander CPR in King County. As King County is one of the highest regions for bystander CPR in the United States, with approximately 65% of cardiac arrest cases having CPR prior to EMS arrival, he believed the survival prediction, while understating the King County survival, would be fairly accurate for a typical region. Further, he agreed that the effect of bystander CPR would result in an equivalent increase of survival for all systems, and thus the relative differences in survival predicted by the model and simulations would remain valid.

Dr. Rea also had a few comments on estimated nominal values used for some of the model factors. He believed that the time between responder arrival and starting the patient treatment is about 90 seconds, compared to the nominal 1 minute used in the model. He did not believe this would have a large effect on accuracy of the survival prediction, and would have no effect on relative comparisons. He commented that chute times for EMS and delay times for mobile responders are longer at night than in daytime hours. However, the velocity of a driving responder (ambulance or mobile responder) is higher at night, and these two effects would likely offset each other. He noted that in King County, ambulance availability was typically 80% to 90%, however he believed that King County was higher than a typical EMS system, and the 70% nominal value seemed reasonable.

When reviewing the results of comparison of system response times and survival, he noted that the Pulse Point system only responds to public location cardiac arrests. As 70% of arrests occur in private residences, the Pulse Point response is only available for a minority of occurrences. The model does not account for this limitation of the Pulse Point system, and thus would overstate the benefit of Pulse Point when compared to systems that provide a response to all cardiac arrest locations. He stated the overall, the predicted improvements in survival from these response systems appeared "grounded and likely conservative". He noted that in using Bellevue, Washington, as the base level for survival comparison, I was using one of the best performing regions in the country. If the comparisons were against a region of much lower average survival, the improvements would be more dramatic.

4.6.2 Data Validity

Data validity is the assurance that the model input values reasonably reflect actual real world system values. A fully valid model may produce unrealistic or inaccurate predictions if the inputs are not realistic values or distributions. This research leveraged published data to the extent available for model inputs. Sourced model inputs are considered valid data without further proof. Sources of input data are discussed in Section 4.5.

Where available, empirical data was used to confirm or supplement published sources. A source of empirical data is the Bellevue EMS response times and distances, which through regression analysis provides an estimated ambulance velocity and delay time (the sum of EMS dispatch delay and chute time). The Minkowski distance order input and bias correction used a cross validation with Google Maps determined distance, as described in Section 4.5.1.1. The velocity ranges for walking and driving by cellphone dispatched responders are reported by Auricchio [95] from a pilot study in Switzerland. Data from these validations is provided in Appendix D.

Where neither reference data nor empirical data was available, face validity was used. Knowledgeable experts reviewed the range of values considered reasonable for the mdel. Table 5 provides the method of validation used for each model input.

Table 5. Data validity source for model inputs.

Factor	Description	Publication	Empirical Data	Face Validity
t_{DD}	Drone dispatch delay time (minutes)			x
R_d	Responder density per sq km			x[1]
v_{RD}	Responder driving velocity (km/h)	x		
v_D	Drone velocity (km/h)	x		
t_{DDe}	Drone descent time (minutes)			x
t_{RD}	Responder dispatch delay time (minutes)			x
t_{RDr}	Responder drive delay time (minutes)			x
M_{dbc}	Minkowski distance bias correction		x	
R_R	Responder reliability	x	x	
t_{DV}	Drone vertical flight time (minutes)		x	x
t_{EC}	EMS chute time (minutes)		x	
p_d	Minkowski drive distance order (p)		x	
v_E	Ambulance velocity (km/h)	x	x	
D_{AW}	Drone weather availability			x[2]
E_A	Ambulance availability	x		
p_a	Minkowski drone distance order (p)			x
D_{AO}	Drone operational availability	x		x
p_w	Minkowski walk distance order (p)			x
t_{RW}	Responder walk delay time (minutes)			x
v_{RW}	Responder walking velocity (km/h)	x		

1. Responder density can take any value.
2. The weather availability factor is specific to the region under simulation.

4.6.3 Computerized Model Verification

The computerized model verification provides assurance that the conceptual model is correctly coded and implemented into computer software or programming language. The model used in this research was implemented in Microsoft Excel, using entirely native functions within the spreadsheet. The verification of the model relied upon three facets: peer review of implementation, operational graphics and formula auditing tools, and tests with extreme scenarios.

The process of creation of the Excel model from the conceptual involved the creation of a pseudocode description. The pseudo code provides mathematical formulations and logic operations in an algorithmic format, which is not specific to a programming language or simulation software. The pseudo code is an intermediate step in the process of constructing the computer model, which allows easy review of the model algorithms without the need to read detailed code syntax. The pseudocode also accommodates the translation into the Excel coding. This two stage process facilitates the peer review of the model mathematics, logic, as well as the coding of the algorithm. Peer review of both the model pseudo code and the Excel implementation was performed by Professor Jeffrey Herrmann, the author's academic advisor. The pseudo code for the model can be found in Appendix C.

To trace the flow of data from model inputs to outputs in the spreadsheet cells, I used Excel formula auditing tools. The Trace Precedents function was used to verify the source cell of each formula variable, and to verify against the pseudo code. The

Trace Dependents function was used to verify that each cell value or calculation was used in the subsequent operation of the algorithm. I used *Operational graphics*, the real time charting of model data as simulations are executed, to verify the geospatial sampling function implementation. I used a graph showing the latitude and longitude location of each agent within each simulation run to verify implementation of both the random located agents (e.g. mobile responders, the cardiac arrest location) as well as static located agents (e.g. EMS stations, drone bases).

Extreme value and degenerate cases of model inputs were used to verify the model provided the expected behavior as inputs were set to their physical limits or extremely high values. Examples of degenerate case verification include setting responder reliability to zero or responder density to zero and verifying the response time distribution became identical to an EMS only response. Similarly, setting drone operational availability to zero or weather availability to zero produces the same response as a system without drones, whereas setting these values to one negates the effect of these factors. Setting the responder density to increasingly high values results in the response time asymptotically approaching the walk delay time, which is the minimum possible response time. These tests verify that the model was implemented sufficiently to perform over the entire applicable range of inputs.

4.6.4 Operational Validation

The operational validity of a model is the ability of the model to provide sufficient accuracy for its intended purpose. In this research, most of the described systems are classified as non-observable systems, particularly in terms of a lack of data available to perform empirical validation. In cases such as this, a thorough analysis of the behavior of the model, as well as comparison to other models, can be used for validation.

The operational validation of the response system model used face validity, event validity, and sensitivity analysis. Face validity, as in the conceptual model validation, was accomplished through expert review of the model outputs. While the experts could not quantify the precision of the model predictions, they were able to support the output behaviors as reasonable and of the expected magnitude.

Event validity is the validation of intermediate calculations, or "events" within the model, that together provide the global model response. While no empirical data is available for validation of the global modal responses of time to CPR, time to defibrillation, or survival, limited published data was used for empirical validation of events within the model. Events such as response time for individual responding agents, percentage of mobile responders which walk versus drive, were explored with sensitivity analysis and comparison to available empirical data in literature. Auricchio *et al* published results from a pilot study of cell phone app dispatched mobile responders in southern Switzerland. While many of the model factors are not reported in the publication, applying a responder density of 2 per sq. km, and using the average responder velocity from the distribution reported, provides a response transit time distribution which is very similar to the distribution reported from the study. The model also closely predicted the percent of responders which walked to the cardiac location versus those which drove.

The EMS system is the only system in the model which had sufficient empirical data to provide a comparison. While the model provided good response time simulation of the Bellevue EMS system, the survival prediction underestimated observed survival. The EMS response time predicted by the model for Bellevue, Washington was compared to mean and median response times provided by King County EMS. The mean and median simulated response times were 5.8 minutes and 5.6 minutes respectively, while the King County EMS provided response times for cardiac arrest cases in 2014 was 4.9 minutes (mean) and 4.7 minutes (median). The reasons for the underestimate of survival are discussed in Section 4.6.1, and are likely somewhat specific to King County, due to the high likelihood of bystander CPR. Inclusion of this factor would provide a similar magnitude of survival increase for all systems, and does not affect response time prediction.

Sensitivity analysis was performed at both the event level and global response level. This analysis confirmed intuitive predictions about the direction of change of a response as a model input was changed. Examples include increasing responder velocity results in decreased response time. Decreasing delay times results in decreased response times. Increasing drone operational availability increases the percentage of drone arrivals before EMS.

4.7. Summary of Research Model

This chapter has described the creation and execution of a model designed to simulate the response times of different out-of-hospital cardiac arrest response systems. The model incorporates the stochastic nature of the cardiac arrest location with respect to responding agents. As such, the output of the model is best analyzed using the Monte Carlo method, with the system efficacy being described by summary statistics of a distribution of thousands of simulated responses.

As one of the goals of this research is to understand the contribution of various factors in different response systems to the effectiveness of the system, the model was structured in such a manner that these factors could readily be explored through model experimentation. Each factor in the model was presented, with a following discussion of how a realistic range of values can be obtained for the factor. Chapter 5 follows this with an analysis of the sensitivity of model predictions to each factor in these systems.

The model was verified and validated through multiple methods, with reviews and tests directed at the conceptual level, the input data, the computer implementation, and the operational outputs. This included comparisons to empirical data when available, as well as face validity reviews with experts in the cardiac arrest response system operations and research, as well as drone operations. The results of the validation exercises suggest that the model is capable of producing credible predictions of response time and the effect on survival. These predictions enable the analysis of the potential response time and survival improvements provided by these systems.

Chapter 5: Sensitivity Analysis

A primary objective of this research is to utilize modeling and simulation to better understand factors that affect response time and survival in the various emerging cardiac arrest response systems. Understanding the magnitude of influence that each model input has on the model response provides the following two benefits. First, when improving the descriptive or predictive precision of the model and simulations, tha accuracy of highly sensitive inputs can be prioritized over insensitive factors. Minimizing the uncertainty to these inputs will reduce the uncertainty in the model predictions. Second, to improve existing response systems, or when planning the deployment of new systems, resources can be applied toward improving factors that have the greatest impact on the response time.

Sensitivity analysis is the practice of executing a complex model with one input varied among the executions, while all other inputs are held constant, typically at their nominal values. This chapter presents the results from a series of sensitivity analysis simulation experiments. Section 5.1 focuses on the sensitivity of the response *time to defibrillation* of each type of primary responding agent, i.e. EMS, mobile responders, and drone transport of an AED. Section 5.2 then applies sensitivity analysis to the global response time at the system level model, which incorporates the effects of multiple agents responding to a cardiac arrest, as well as reliability and availability factors that affect each agent's ability to respond. The sensitivity of the response times to the types of geo-spatial distributions used to simulate random cardiac arrest locations and mobile responder locations are presented in Section 5.3. With the identification of the most important factors in the model, Response Surface Methodology experiments were run to provide an in depth understanding of interactions between factors and non-linearity of the response. The results of these simulation experiments are presented in Section 5.4. Finally, a discussion and conclusions from the sensitivity analysis are provided in Section 5.5.

5.1 Response Time Sensitivity

Sensitivity analysis experiments were generated to specifically evaluate the response time of each type of agent in the model, independent of system level factors. Bellevue, Washington was used as an example region for the sensitivity analysis. Factors specific to the region, such as the Minkowski distance order and the Minkowski distance bias correction were identified through the process described in Section 4.5.1.2. Only factors that directly influence the responders time to defibrillation were assessed in these experiments. Factors that dictate the ability of an agent to respond, such as reliability or availability factors, as well as the effect of multiple responding agents vying for the best response time, were excluded from this analysis.

The experimental range for which each factor was varied was based on either a reasonable range of variation around a nominal value, or a reasonable uncertainty in the estimate of the nominal value. The experimental points do not represent necessarily the extreme of possibility for each factor, but a reasonable range that may exist within a single region. Factors were symmetrically varied around the nominal value, with each factor evaluated at five set points. 5000 simulations were run at each experimental setting, with the mean of the response time to defibrillation distribution used to characterize the sensitivity. Tornado diagrams were used to graphically interpret the results. Each experiment was automated using Crystal Ball software [75].

5.1.1 EMS Response Time Sensitivity

The factors evaluated for the sensitivity of the EMS response time, along with the low, center (nominal), and high settings, are shown in Table 6. The results of the sensitivity analysis are shown as a Tornado Diagram in Figure 23.

Table 6. EMS sensitivity analysis factors and ranges.

Factor	**Description**	**Low**	**Center**	**High**
p_d	Minkowski drive distance order (p)	0.7	0.8	0.9
M_{dbc}	Minkowski distance bias correction	0.15	0.35	0.55
t_{EC} / t_{ED}	EMS chute time / dispatch delay (minutes)	2	3	4
v_E	Ambulance velocity (km/h)	60	70	80

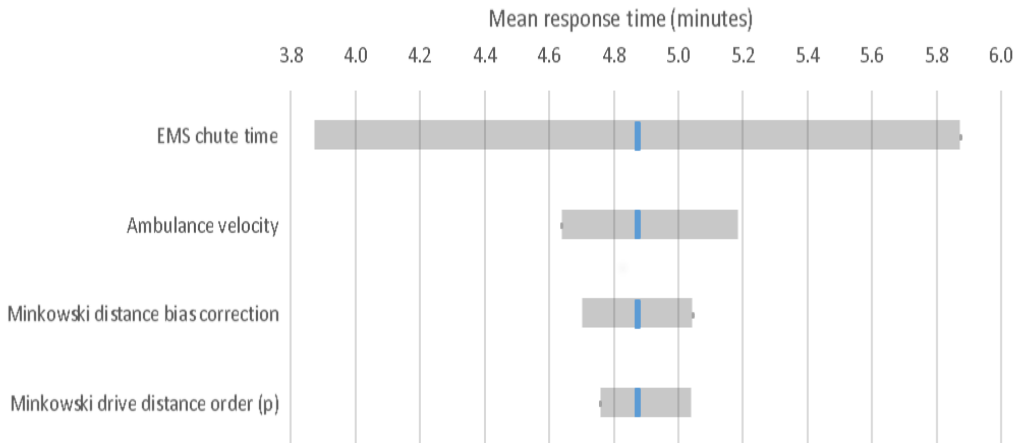


Figure 23. Tornado diagram of EMS sensitivity. The blue mark is the response with all factors at nominal values. The grey bars show the range of the response across the range of factor input values.

5.1.2 Mobile Responder Response Time Sensitivity

The factors evaluated for the sensitivity of the mobile responders' response time, along with the low, center (nominal), and high settings, are shown in Table 7. The results of the sensitivity analysis are shown as a Tornado Diagram in Figure 24.

Table 7. Mobile responder sensitivity analysis factors and ranges.

Factor	Description	Low	Center	High
p_w	Minkowski walk distance order (p)	1.5	1.7	1.9
p_d	Minkowski drive distance order (p)	0.7	0.8	0.9
M_{dbc}	Minkowski distance bias correction (km)	0.15	0.35	0.55
R_d	Responder density per sq km	2	5	8
t_{RD}	Responder dispatch delay time (minutes)	0.5	1	1.5
t_{RW}	Responder walk delay time (minutes)	0.5	0.75	1
t_{RDr}	Responder drive delay time (minutes)	0.5	1	1.5
v_{RW}	Responder walking velocity (km/h)	6	7	8
v_{RD}	Responder driving velocity (km/h)	24	32	40

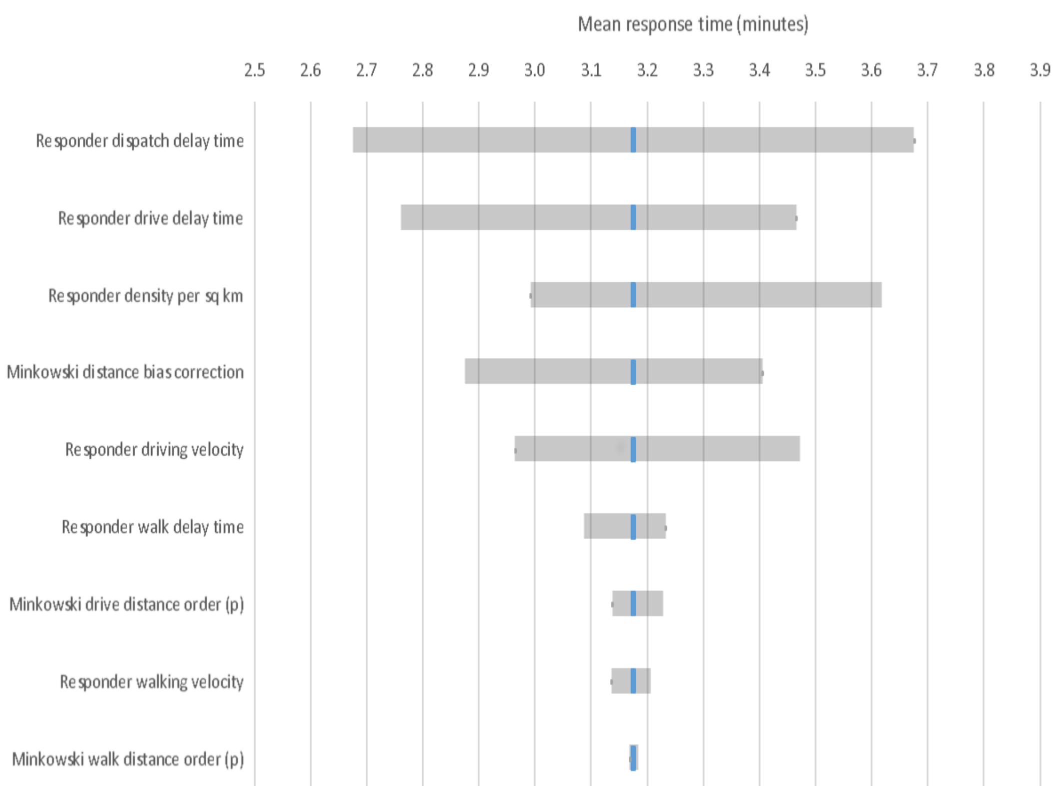


Figure 24. Tornado diagram of mobile responder sensitivity. The blue mark is the response with all factors at nominal values. The grey bars show the range of the response across the range of factor input values.

5.1.3 Drone Response Time Sensitivity

The factors evaluated for the sensitivity of the drone response time, along with the low, center (nominal), and high settings, are shown in Table 8. The results of the sensitivity analysis are shown as a Tornado Diagram in Figure 25.

Table 8. Drone response time sensitivity analysis factors and ranges.

Factor	Description	Low	Center	High
p_a	Minkowski drone distance order (p)	1.8	1.9	2
t_{DD}	Drone dispatch delay time (minutes)	0.5	1	2
t_{DV}	Drone vertical flight time (minutes)	0.25	0.5	0.75
v_D	Drone velocity (km/h)	64	80	96
t_{DDe}	Drone descent time (minutes)	0.5	1	1.5

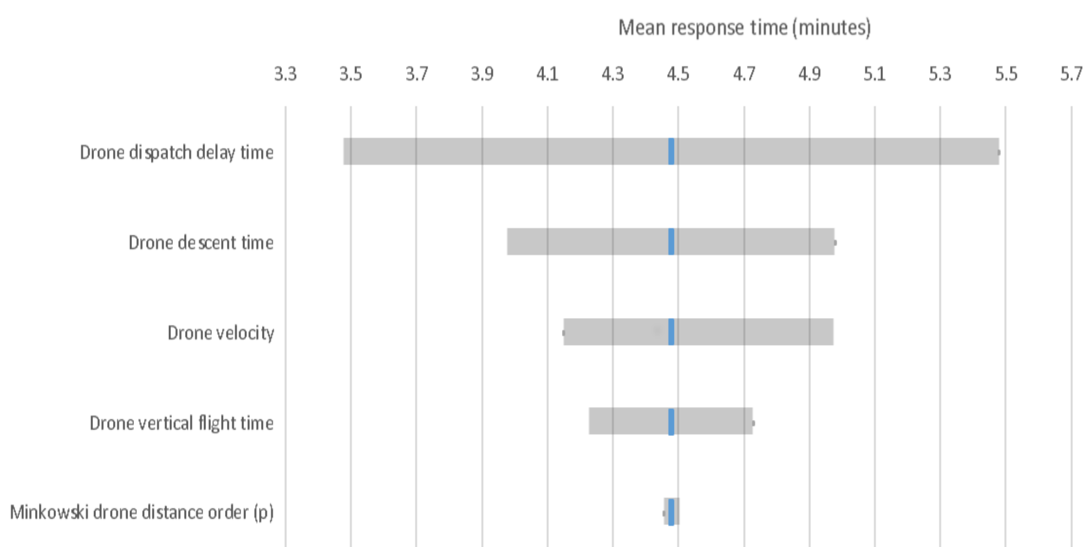


Figure 25. Tornado diagram of drone response time sensitivity. The blue mark is the response with all factors at nominal values. The grey bars show the range of the response across the range of factor input values.

5.1.4 Discussion of Response Time Sensitivity

The response time sensitivity of all responding agents in the model is dominated by the various "delay" factors, which are modeled as constant values, and added to the distance based time calculation. In reality, these delays would have some small stochastic variance in each cardiac arrest response; however, this variance is likely small relative to the variance in response distances. Some delay factors may vary significantly based on system protocols and strategies, even between similar types of response systems. As the sum of the EMS Dispatch Delay and Chute time was increased from 2 to 4 minutes, the mean response time increased from 3.9 to 5.9 minutes. While EMS dispatch delay is likely similar across agencies, chute time can vary, based on station readiness protocols. Increasing the mobile responder Dispatch Delay from 0.5 to 1.5 minutes resulted in a response time increase from 2.7 to 3.7 minutes. Responder dispatch delay could take an aggressive approach by activating a mobile responder network at first indication of a possible cardiac event, or a more conservative approach, waiting until the 911 operator is highly confident that the call is a cardiac arrest. An aggressive approach would result in some false activations, while a conservative approach would result in a slower response time. This emphasizes the importance of minimizing these delays to achieve the best system performance.

The velocity of the responding agents was the next strongest factor; reducing ambulance velocity form 80 to 60 km/h increased the average response time by 0.6 minutes. When distances from origin of the responding agent to the cardiac arrest are not great, such as in an urban or suburban region, the velocity of the response has less of an impact than the delay factors. In a real system, the largest impact on velocity would likely be traffic conditions. Ambulances have the benefit of using lights and sirens, which reduces the impact of traffic, and thus variance in the velocity. As mobile responders have a choice of walking or driving to the cardiac arrest location, a dispatch app that could provide guidance to the responder on the best mode of travel, accounting for traffic conditions and distance, would reduce the impact of traffic on response time and provide improved system performance.

The density of mobile responders in the region was also influential on the response time. Increasing the density of responders from 2/sq. km to 8/sq. km provided an improvement of the mean response time from 3.6 minutes to 3.0 minutes. High densities of responders increases the likelihood of responders being close to the cardiac arrest location.

The distance approximation factors, i.e. the Minkowski distance order and the Minkowski bias correction, had the least impact on response times. Varying the Minkowski drive order by 0.2 only resulted in a 0.07 minute change in mean response time, and varying the Minkowski walk order by 0.4 resulted in a change of 0.02 minutes. This suggests that the model is robust to some imprecision in the estimates of these values and the difference between the approximated distance and the actual distance.

5.2 System Response Time Sensitivity

When multiple types of responding agents are incorporated into the system response for a region, additional calculations occur in the model. The model is essentially finding the minimum response time to provide therapy to the cardiac arrest victim amongst the different responding agents. However, in some manifestations of a system, multiple agents are needed to provide therapy. For example, a system that has a drone AED delivery but requires a dispatched mobile responder to operate the AED involves the interaction of these agents, with EMS providing a parallel response effort. Additional factors affect the availability of responding agents, including reliability of human responders, as well as that of the drone and AED, and the availability of an ambulance, or weather prevention of drone flight.

To assess this additional system complexity, a series of system sensitivity analysis experiments were conducted using a hypothetical system in which the three types of responding agents all participate. Bellevue, Washington was again used as the example region. The hypothetical system used a drone delivery of the AED from a single drone stationed at the most centrally located fire station in the region, along with a network of dispatched mobile responders who retrieve the AED and apply it to the patient. The responders do not carry AEDs, and thus rely on the drone delivery. This is backed up by the standard EMS response for the region.

The sensitivity analysis included all model factors, with five set points for each factor (Low, Center, High, and the midpoints between Low-Center and Center-High). Each experimental condition had 5000 simulations run. The response analyzed was the mean of the time to defibrillation distribution over the 5000 simulations. ANOVA was used to identify statistically significant factors, using a p-value of 0.05. The R-squared value from the ANOVA provides a quantitative measure of the effect of each factor on the response time to defibrillation. The ANOVA was performed using Minitab statistical analysis software [96]. The experimental conditions, along with the ANOVA p-value and R-squared, are provided in Table 9, sorted by highest to lowest R-squared value.

Table 9. System sensitivity analysis set points, along with ANOVA p-value and R-squared value.

Factor	Description	Low	Center	High	p-value	R sq (%)
t_{DD}	Drone dispatch delay time (minutes)	0	1	2	0	14.36
R_d	Responder density per sq km	2	5	8	0	11.61
v_{RD}	Responder driving velocity (km/h)	24	32	40	0	7.67
v_D	Drone velocity (km/h)	64	80	96	0	4.3
t_{DDe}	Drone descent time (minutes)	0.5	1	1.5	0	4.1
t_{RD}	Responder dispatch delay time (minutes)	0.5	1	1.5	0	3.4
t_{RDr}	Responder drive delay time (minutes)	0.5	1	1.5	0	3.39
M_{dbc}	Minkowski distance bias correction	0.15	0.35	0.55	0	2.53
R_R	Responder reliability	0.2	0.3	0.4	0	2.32
t_{DV}	Drone vertical flight time (minutes)	0.25	0.5	0.75	0	1.41
t_{EC}	EMS chute time (minutes)	2	3	4	0	1.26
p_d	Minkowski drive distance order (p)	0.7	0.8	0.9	0	0.77
v_E	Ambulance velocity (km/h)	60	70	80	0	0.15
D_{AW}	Drone weather availability	0.8	0.9	0.99	0	0.14
E_A	Ambulance availability	0.7	0.76	0.84	0.035	0.04
p_a	Minkowski drone distance order (p)	1.8	1.9	2	0.397	0.02
D_{AO}	Drone operational availability	0.9	0.96	0.98	0.437	0.02
p_w	Minkowski walk distance order (p)	1.5	1.7	1.9	1	0
t_{RW}	Responder walk delay time (minutes)	0.5	0.75	1	1	0
v_{RW}	Responder walking velocity (km/h)	6	7	8	1	0

An example ANOVA results for the factor EMS chute time are shown in Table 10. The analysis provides the means and 95% confidence intervals for each level of the factor setting. Additionally, the statistical significance (p-value) of the difference in mean values of the settings shown. The R-squared is a measure of the percentage of variation in the response time that is explained by the factor setting. Higher R-square values indicate a stronger impact on response time relative to factors with lower R-square values. A graph of the mean and 95% confidence intervals for each factor setting, as well as box and whisker plots of the entire distribution of simulation responses, is shown in Figure 26. The statistical significance is sensitive to the number of simulations run at each factor level, as this directly dictates the *error degrees of freedom* in the analysis. Thus, the p-value merely indicates which factors are significant to the response for a given number of simulation runs. The R-squared value, however, is not sensitive to the number of simulations, and is thus a strong indicator of the relative importance of each factor.

Table 10. ANOVA results for EMS Chute time.

Factor Information

Factor	Levels	Values (minutes)
EMS Chute time	5	2, 2.5, 3, 3.5, 4

Analysis of Variance

Source	DF	Adj SS	Adj MS	F-Value	P-Value
EMS chute time	4	212.6	53.1380	80.04	0.000
Error	24995	16593.0	0.6639		
Total	24999	16805.6			

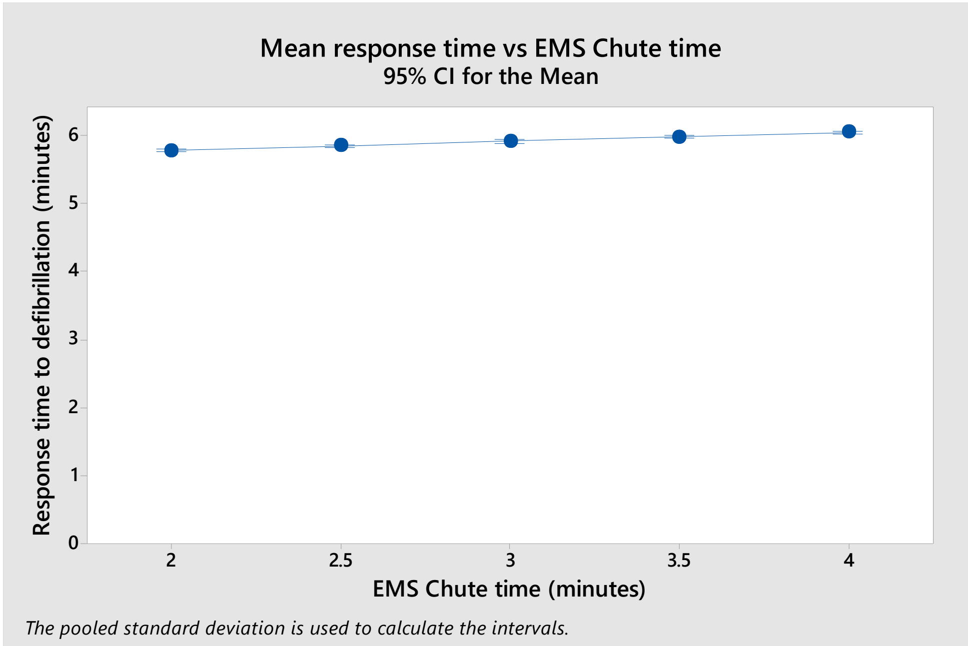
Model Summary

S	R-sq	R-sq(adj)	R-sq(pred)
0.814772	1.26%	1.25%	1.23%

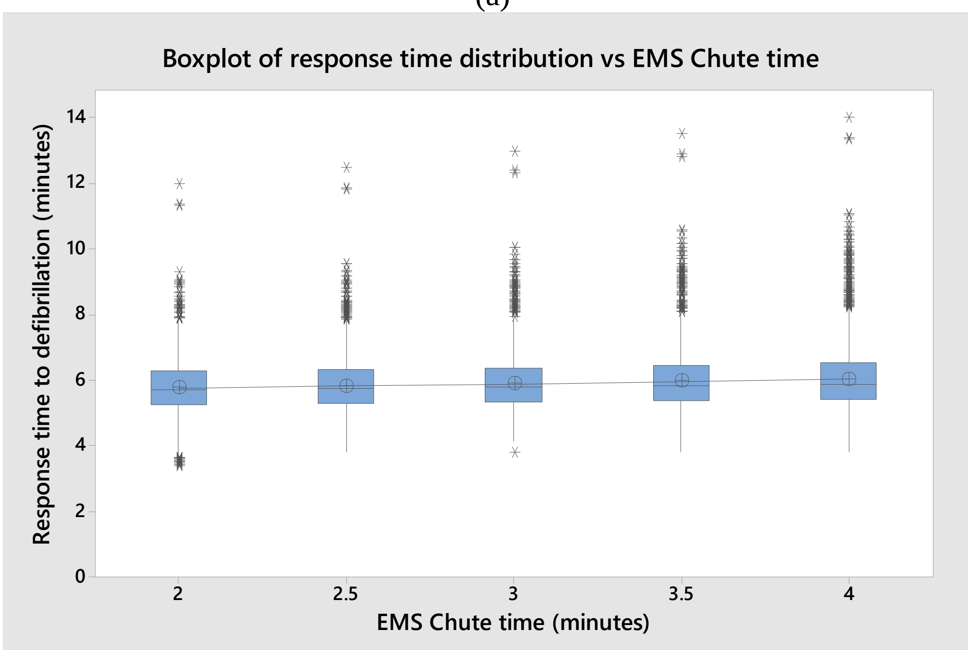
Means

Factor	N	Mean	StDev	95% CI
2	5000	5.7759	0.7876	(5.7533, 5.7985)
2.5	5000	5.8411	0.7651	(5.8185, 5.8637)
3	5000	5.9063	0.7792	(5.8837, 5.9289)
3.5	5000	5.9715	0.8280	(5.9489, 5.9941)
4	5000	6.0367	0.9060	(6.0141, 6.0593)

Pooled StDev = 0.814772



(a)



(b)

Figure 26. (a) Chart of means and confidence intervals, and (b) boxplot of distribution, for each setting value for EMS Chute time.

The tornado diagram in Figure 27 shows a graphical comparison of the relative impact of each model input across a reasonable range of settings. The relative range of the each factor in the tornado diagram correlates to the R-square value from the ANOVA.

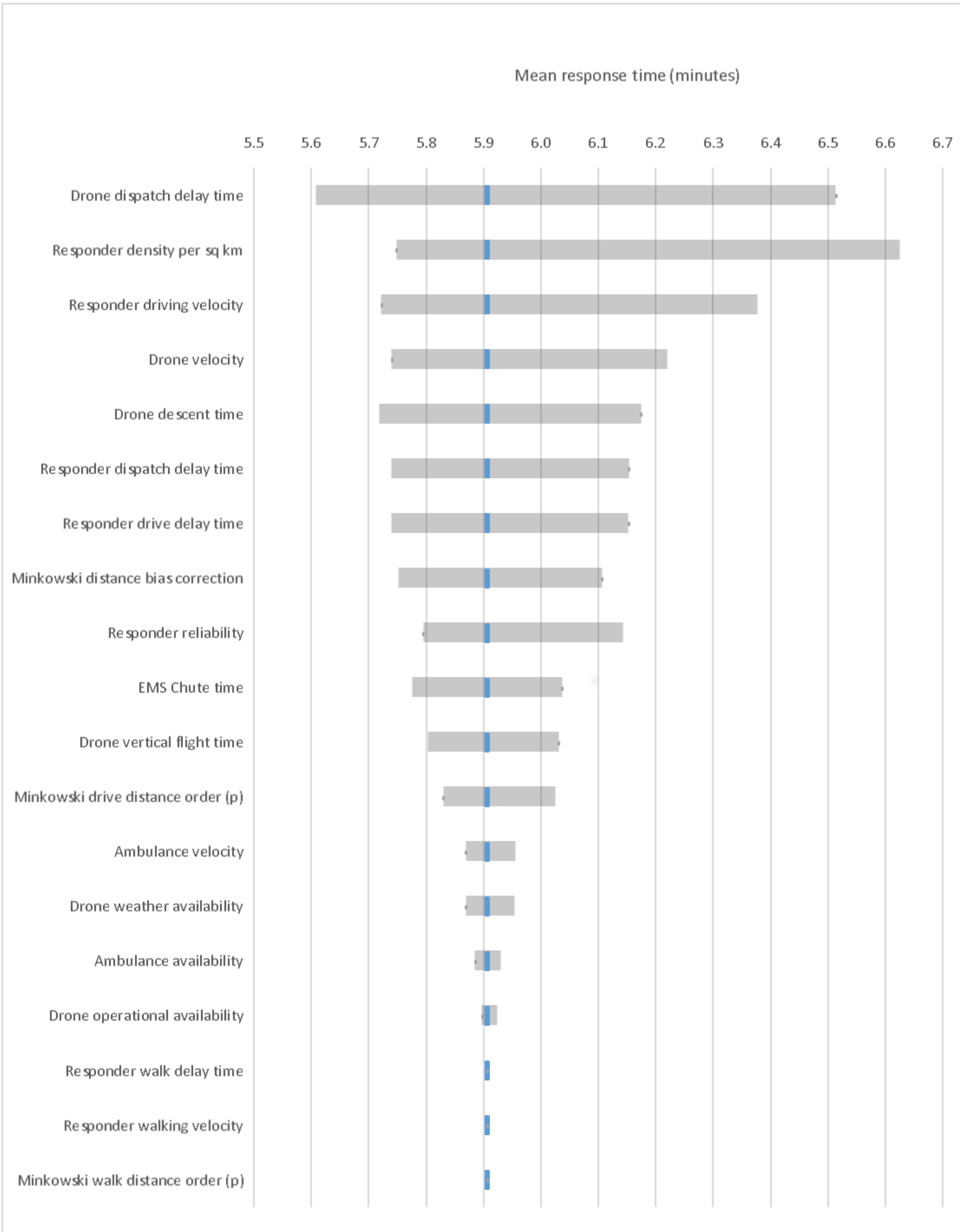


Figure 27. Tornado diagram of system sensitivity analysis results. The blue mark is the response with all factors at nominal values. The grey bars show the range of the response across the range of factor input values.

5.2.1 Discussion of System Sensitivity

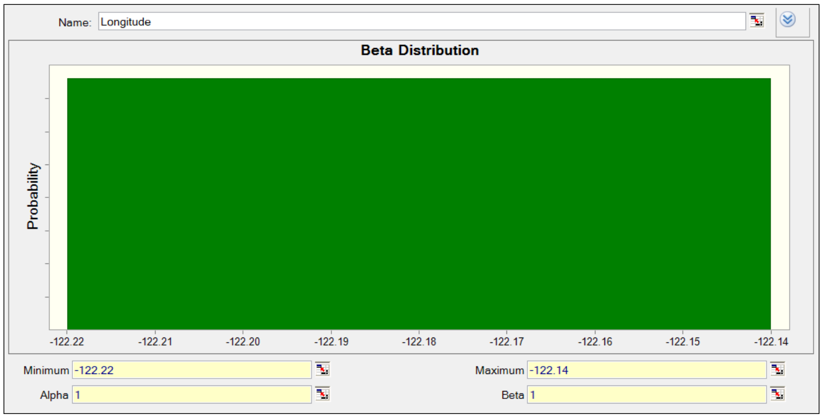
The specific system on which the sensitivity analysis was evaluated relied on two agents, both a mobile responder and a drone, arriving at the cardiac arrest location in order to provide defibrillation ahead of the arrival of EMS. The drone dispatch delay time, t_{dd}, remains as the most sensitive factor for response time, by virtue of the wide range of potential values. This time may contribute from zero to two minutes to the response time of the drone. Other delay times, such as mobile responder dispatch delay t_{RD}, which constitute a smaller range of potential values (0.5 to 1.5 minutes), are less sensitive, only resulting in a change of 0.5 minutes. This is because both the drone and mobile responder experience a delay time before beginning transit to the cardiac arrest location, while the longest response time of the two agents determines the effective time to defibrillation. Even complete elimination of the delay time of one type of agent would have a minimal impact if the other agent's response time were unchanged. The analysis indicates efforts would be best placed on minimizing the delay in the drone taking flight. This would favor a strategy such as an automated drone launch on the first determination of any medical call, with the drone being recalled to the base if not needed for a cardiac arrest emergency.

Mobile responder density has nearly as strong of an effect as the drone dispatch delay time, with the mean response time decreasing from 6.6 to 5.7 minutes as the density increased from 2/sq. km to 8/sq. km. A high density of responders provides a high likelihood that an available responder will be within close vicinity of the cardiac arrest. The transit time of mobile responders, even when driving to the location, is generally longer than that of the drone, due to the slower velocity and need to use the road network. Ensuring a mobile responder is near the arrest location, when both are random events, is achieved by having a large number of responders.

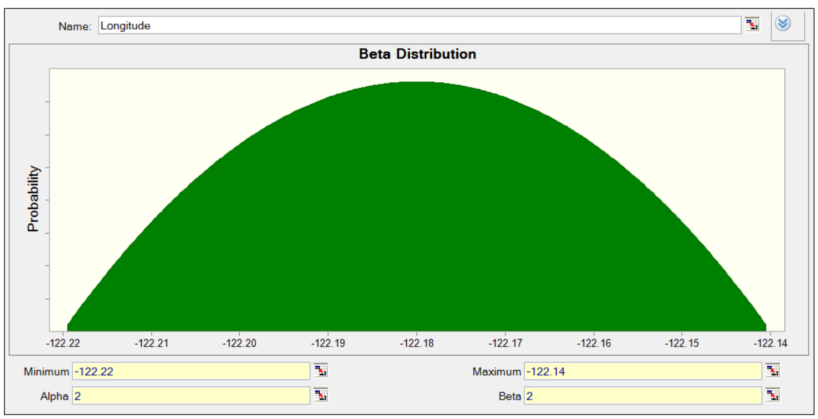
Compensating for the mobile responder proximity to the cardiac arrest is the velocity at which the responder can travel to the arrest. Driving velocity, v_{RD}, is the third most sensitive factor. As velocity was increased from 24 to 40 km/h, the mean response time decreased from 6.2 to 5.7 minutes. This factor would be dictated by the road conditions of the region (e.g. traffic, stop lights, etc.), and would be difficult to improve upon without adversely affecting the responder and general public safety.

5.3 Sensitivity to Geo-spatial Distributions

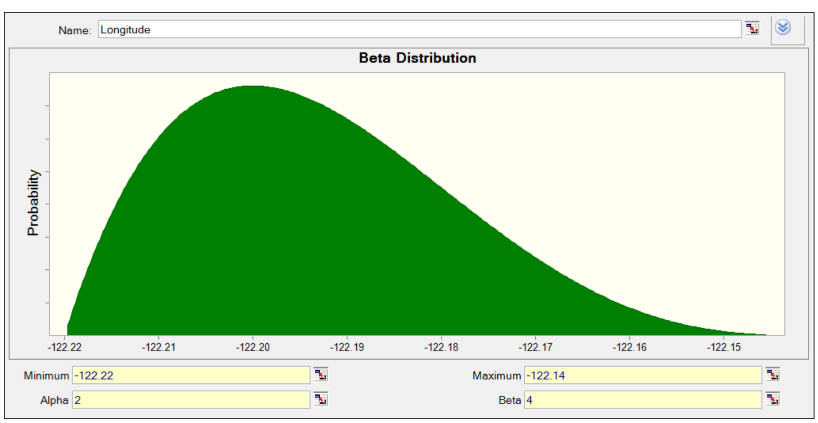
The sensitivity analysis in the prior sections was performed using a bivariate uniform distribution to generate both the random cardiac arrest location as well as the location of each mobile responder. The assumption of uniform dispersion may not be valid in real world systems. The distribution could take on infinite forms in reality. To evaluate the influence of the assumed geo-spatial distribution, sensitivity analysis was conducted by varying the alpha and beta parameters of a bivariate Beta distribution. Three forms of a Beta distribution were used; Beta(1, 1), which is equivalent to the uniform distribution, Beta(2, 2), a symmetric, somewhat bell shaped distribution, and Beta(2, 4), a skewed distribution. The three distributions are shown in Figure 28. The bivariate location generating distributions used the same Beta parameters for both the latitude and longitude locations, e.g. when the latitude was generated with Beta(1, 1) the longitude was also generated with Beta(1, 1).



(a) Beta(1, 1)



(b) Beta(2, 2)



(c) Beta(2, 4)

Figure 28. Three Beta distributions used in sensitivity analysis.

Sensitivity experiments were conducted using the same hypothetical system in the Bellevue, WA region as the analysis described in Section 5.2. First, the cardiac arrest generating distribution was held constant at Beta(1, 1) while the mobile responder generating distribution was varied over the three Beta distributions. Next, the mobile responder distribution was held constant at Beta(1, 1) while the cardiac arrest distribution was varied. Finally, both distributions were varied across the three distributions. ANOVA was used to analyze the statistical significance of the difference in distribution, with a p-value of 0.05 used as the threshold. Equal variance across the distribution settings was not assumed for the ANOVA. Graphical analysis was used to assess the practical implication on model sensitivity.

The ANOVA results for holding the cardiac arrest location distribution constant at Beta(1, 1) while changing the mobile responder distribution are shown in Table 11. Graphs of the mean response time and boxplots of the distribution are shown in Figure 29. While the change in distribution was statistically significant to the mean of the time to defibrillation, the R-squared value indicated that these changes only accounted for 6.46% of the variation across the simulations. This variation amounted to about 0.8 minutes in the mean response times.

Table 11. ANOVA results for the mobile responder geo-spatial distributions.

Factor Information

Factor	Levels	Values
Mobile responder distribution	3	MR Beta 1 1, MR Beta 2 2, MR Beta 2 4

Welch's Test

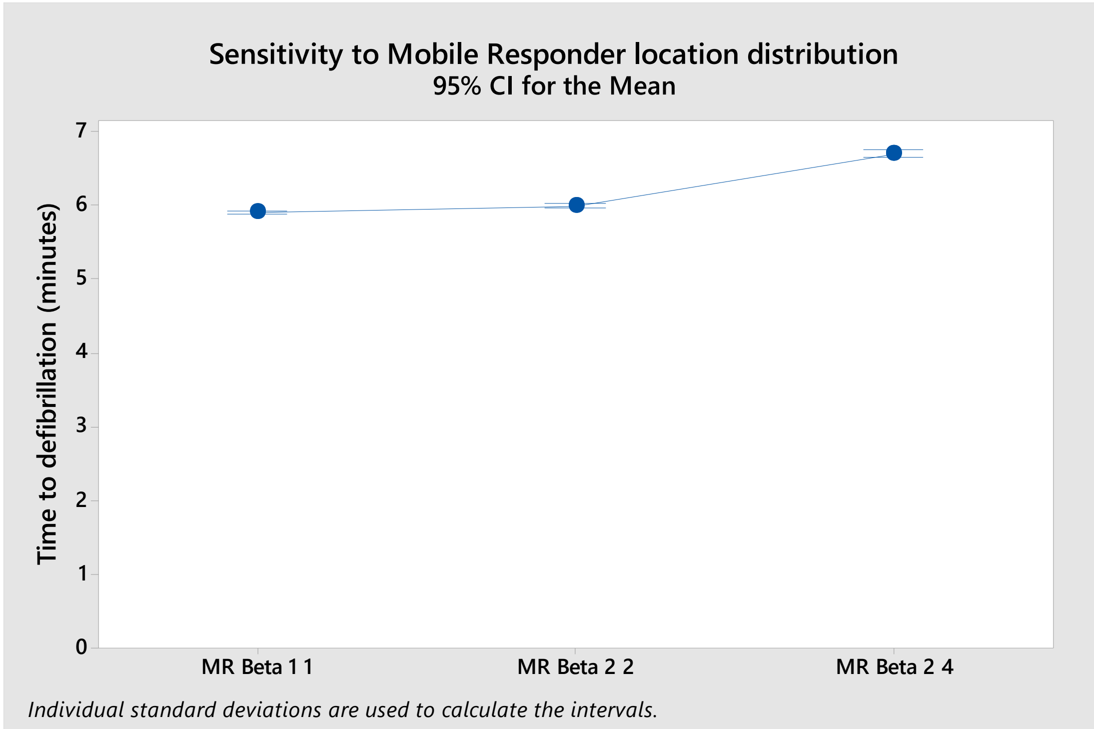
Source	DF Num	DF Den	F-Value	P-Value
Mobile responder distribution	2	9202.77	349.78	0.000

Model Summary

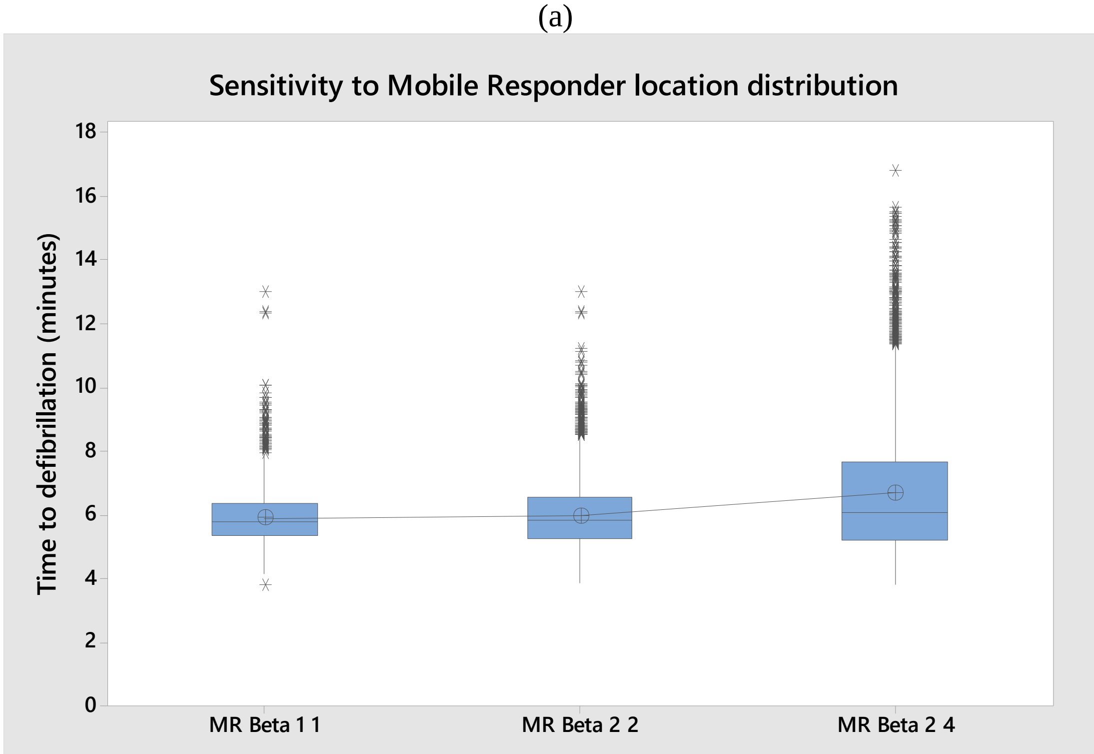
R-sq	R-sq(adj)	R-sq(pred)
6.46%	6.44%	6.42%

Means

Factor	N	Mean	StDev	95% CI
MR Beta 1 1	5000	5.9065	0.7793	(5.8849, 5.9281)
MR Beta 2 2	5000	5.9845	1.0065	(5.9566, 6.0124)
MR Beta 2 4	5000	6.6960	1.9658	(6.6415, 6.7505)



(a)



(b)

Figure 29. Plot of changes in (a) mean and (b) distribution of response time to defibrillation as a result of changing in the mobile responder distribution.

The results for holding the mobile responder location distribution constant at Beta(1, 1) while changing the cardiac arrest distribution are shown in Table 12. Graphs of the mean response time and boxplots of the distribution are shown in Figure 30. Similar to the results of varying the mobile responder distribution, changing the cardiac arrest distribution was statistically significant, but did not have a strong effect on mean response time giving a range of about 0.4 minutes.

Table 12. ANOVA results for cardiac arrest geo-spatial distribution.

Factor Information

Factor	Levels	Values
Cardiac arrest distribution	3	CA Beta 1 1, CA Beta 2 2, CA Beta 2 4

Welch's Test

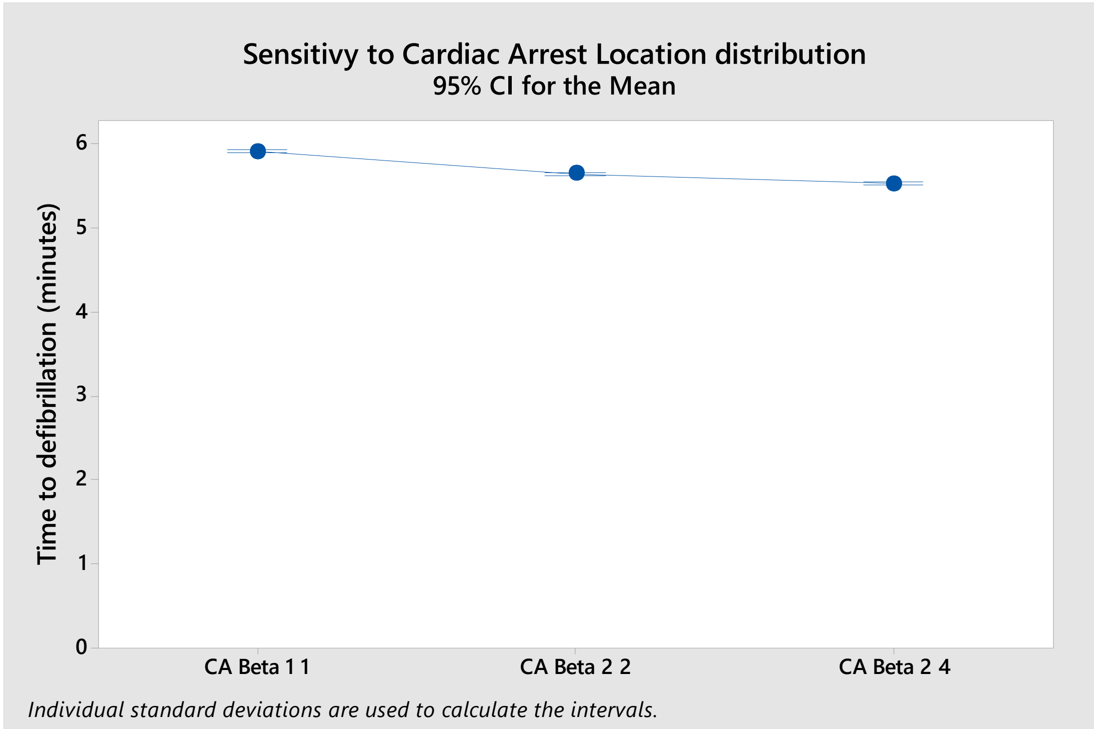
Source	DF Num	DF Den	F-Value	P-Value
Cardiac arrest distribution	2	9953.14	355.56	0.000

Model Summary

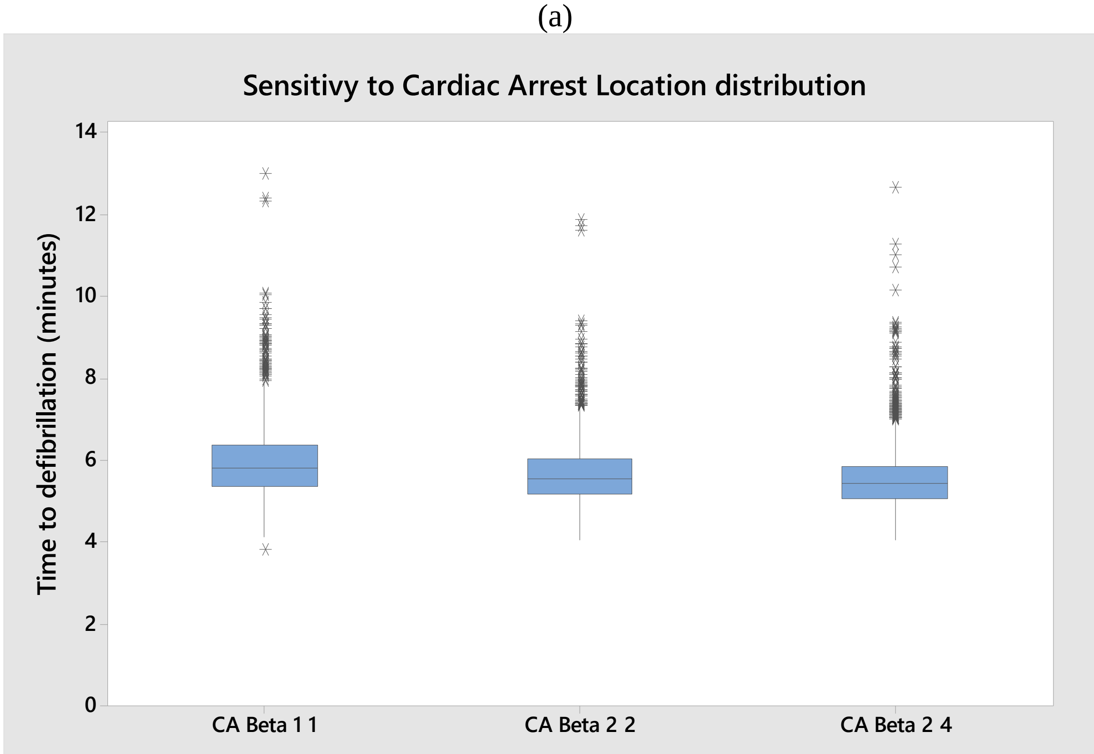
R-sq	R-sq(adj)	R-sq(pred)
4.88%	4.87%	4.85%

Means

Factor	N	Mean	StDev	95% CI
CA Beta 1 1	5000	5.9072	0.7799	(5.8856, 5.9289)
CA Beta 2 2	5000	5.63964	0.67100	(5.62104, 5.65825)
CA Beta 2 4	5000	5.52356	0.67072	(5.50496, 5.54216)



(a)



(b)

Figure 30. Plot of changes in (a) mean and (b) distribution of response time to defibrillation as a result of changing in the cardiac arrest location distribution.

The final location distribution sensitivity experiment measured the effect of both the cardiac arrest generating distribution and the mobile responder distribution changing. Three experimental conditions were evaluated; first with both distributions using the Beta(1, 1), second, with both using Beta(2, 2), and third, with both using Beta(2, 4). The effect of the distribution was statistically significant, with about a 0.7 minute impact on the mean response time. The ANOVA results are shown in Table 13 and graphs of the mean response time and boxplots of the distribution are shown in Figure 31.

Table 13. ANOVA results for changes in both cardiac arrest location and mobile responder location distributions.

Factor Information

Factor	Levels	Values
All location distributions	3	Beta 1 1, Both 2 2, Both 4 4

Welch's Test

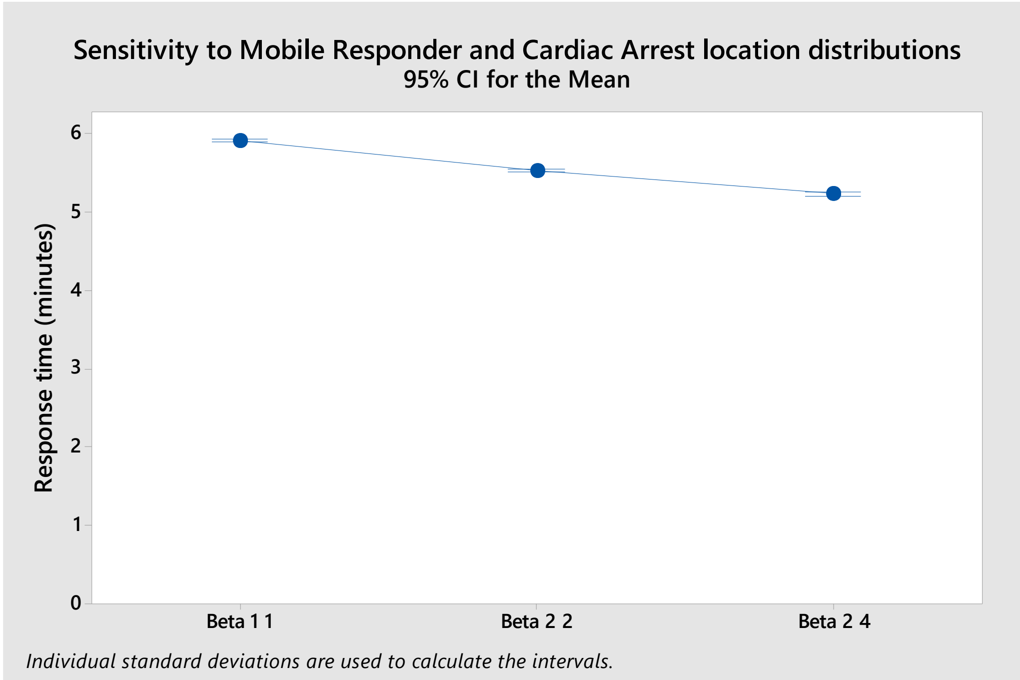
Source	DF Num	DF Den	F-Value	P-Value
All location distributions	2	9997.55	961.59	0.000

Model Summary

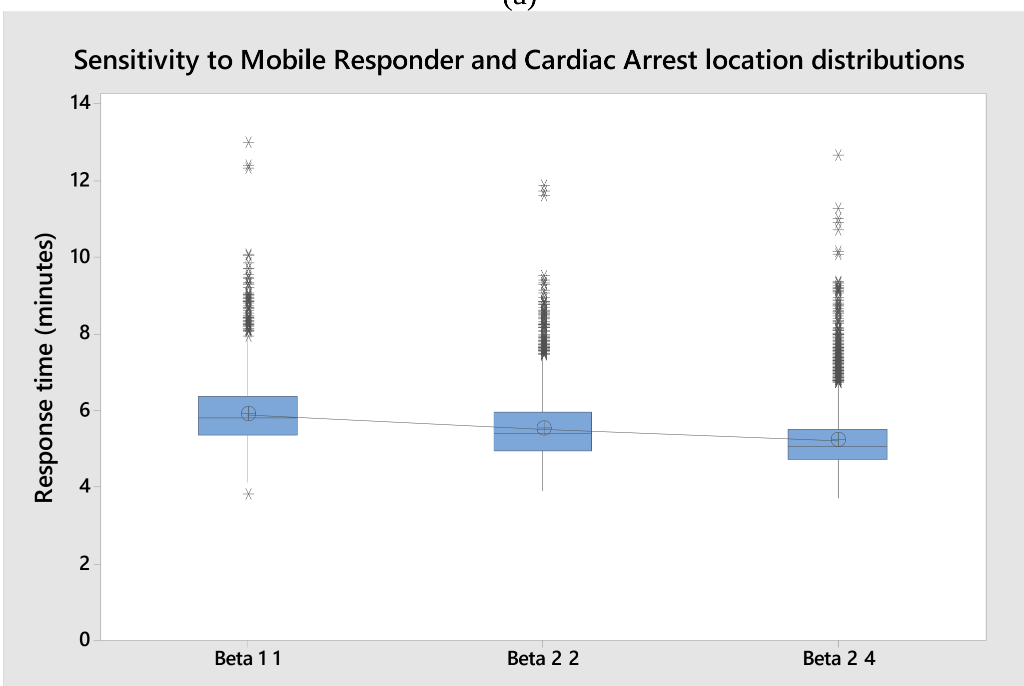
R-sq	R-sq(adj)	R-sq(pred)
11.46%	11.44%	11.42%

Means

Factor	N	Mean	StDev	95% CI
Beta 1 1	5000	5.9065	0.7793	(5.8849, 5.9281)
Both 2 2	5000	5.5244	0.7666	(5.5031, 5.5456)
Both 4 4	5000	5.2272	0.7733	(5.2058, 5.2486)



(a)



(b)

Figure 31. Plot of changes in (a) mean and (b) distribution of response time to defibrillation as a result of changing both the cardiac arrest location distribution and the mobile responder distribution.

5.3.1 Discussion of Sensitivity to Geo-spatial Distributions

The sensitivity analysis to the geo-spatial distribution showed minimal sensitivity to for the mean response time to defibrillation within the system. In all cases, changing from a uniform distribution, to a symmetric bivariate peaked distribution, to a skewed bivariate distribution, resulted in less than a one minute difference in the mean response time. When varying the mobile responder distribution, the mean response times changed from 5.9 to 6.7 minutes. When varying the cardiac arrest distribution, the mean response times changed from 5.9 to 5.5 minutes. When changing both distribution together, the mean response time changed from 5.9 to 5.2 minutes. This supports the model robustness to imperfect replication of real world distributions of both the cardiac arrest location and mobile responders.

The largest effect of the location distributions is found in the upper tail of the response time distribution. This is noticeable when the cardiac arrest distribution is Uniform, i.e. Beta(1, 1), and the mobile responder distribution is skewed, i.e. Beta(2, 4). In such a case, the number of very long response times (> 10 minutes) is much larger, than when the distributions are identical or even both symmetric. However, this effect is not observed when the mobile responder distribution is uniform and cardiac arrest distribution is skewed. The effect of the mobile responder distribution is asymmetric with respect to the effect of the cardiac arrest distribution. This is because the cardiac arrest distribution generates a single location for each simulation, while the mobile responder distribution generates many locations; however, the response time depends only on the responder location with the minimum distance to the cardiac arrest. This suggests a system using mobile responders would be best served by recruiting responders who naturally spread themselves uniformly over a region. This could be achieved through occupational targeting, such as postal carriers, Uber drivers, or other recruitment strategies.

5.4 Response Surface Analysis

The sensitivity analysis identified the factors with the greatest effect on the model response of average time to defibrillation, while all other factors were held constant at nominal values. The strongest factors were further explored for interactions and non-linearity of the output using response surface methodology. A central composite design of experiments (DOE) was used to assess five significant model factors, distributed over the three types of responding agents. The factors were t_{dd} drone dispatch delay, R_d density of mobile responders, V_{rd} velocity of mobile responders when driving, V_d drone velocity, and T_{ec} EMS chute time.

An experimental design that utilized a half fraction factorial cube with a center point and ten axial points was chosen such to provide an efficient number of experimental runs (27 total runs). 1000 simulations were performed for each experimental run. The responses analyzed were the mean of the time to defibrillation distribution and the 95th percentile. The points in the upper tail of the response time distribution were analyzed to understand how these factors affect not only the average time to defibrillation, but also the longest times.

The results of the DOE were analyzed using ANOVA and Stepwise Linear Regression. The stepwise regression used backward elimination with an alpha-to-remove value of 0.05. The final model contained only terms with a p-value less than 0.05 after including all removed terms in the error estimate. The results of each analyzed response are provided in Sections 5.4.1 and 5.4.2.

5.4.1 RSM Results for Mean of Time to Defibrillation

The final reduced model for the mean of the system time to defibrillation included four significant main effect terms, one quadratic term, and one interaction term. The final ANOVA results and the regression equation are shown in Table 14. Figure 32 shows the plots of the four main effect factors, with the slope indicating their relative impact on the response time, as well as showing the non-linearity of the response to the responder density R_d input. Figure 33 shows the interaction of the drone dispatch delay time t_{dd} and the driving velocity of the mobile responder V_{rd}.

Table 14. ANOVA and Regression results for mean value response surface.

Analysis of Variance

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Model	6	2.91891	0.48648	65.52	0.000
Linear	4	2.76333	0.69083	93.04	0.000
t_{dd}	1	0.37500	0.37500	50.51	0.000
R_d	1	1.12667	1.12667	151.74	0.000
v_{rd}	1	1.12667	1.12667	151.74	0.000
t_{ec}	1	0.13500	0.13500	18.18	0.000
Square	1	0.11557	0.11557	15.57	0.001
R_d*R_d	1	0.11557	0.11557	15.57	0.001
2-Way Interaction	1	0.04000	0.04000	5.39	0.031
t_{dd}*v_{rd}	1	0.04000	0.04000	5.39	0.031
Error	20	0.14850	0.00743		
Total	26	3.06741			

Regression Equation

$$\text{Mean} = 8.880 - 0.550\, t_{dd} - 0.4370\, R_d - 0.0792\, v_{rd} + 0.1500\, t_{ec} + 0.02926\, R_d^2 + 0.0250\, t_{dd}v_{rd}$$

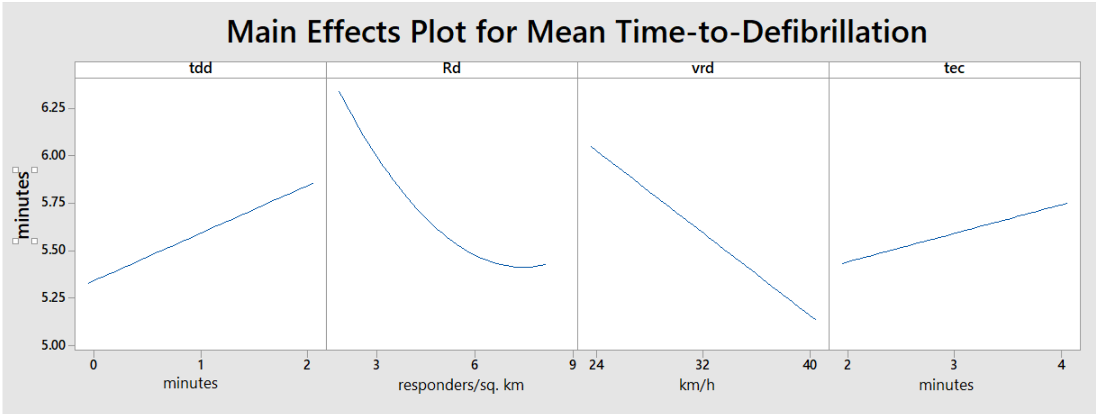


Figure 32. Plot of main effects of significant factors for the mean of the distribution of time to defibrillation. The experimental space is defined by the range of uncertainty or variability for each factor. t_{DD} = drone dispatch delay time; R_d = responder density; v_{RD} = responder driving velocity; t_{EC} = EMS chute time.

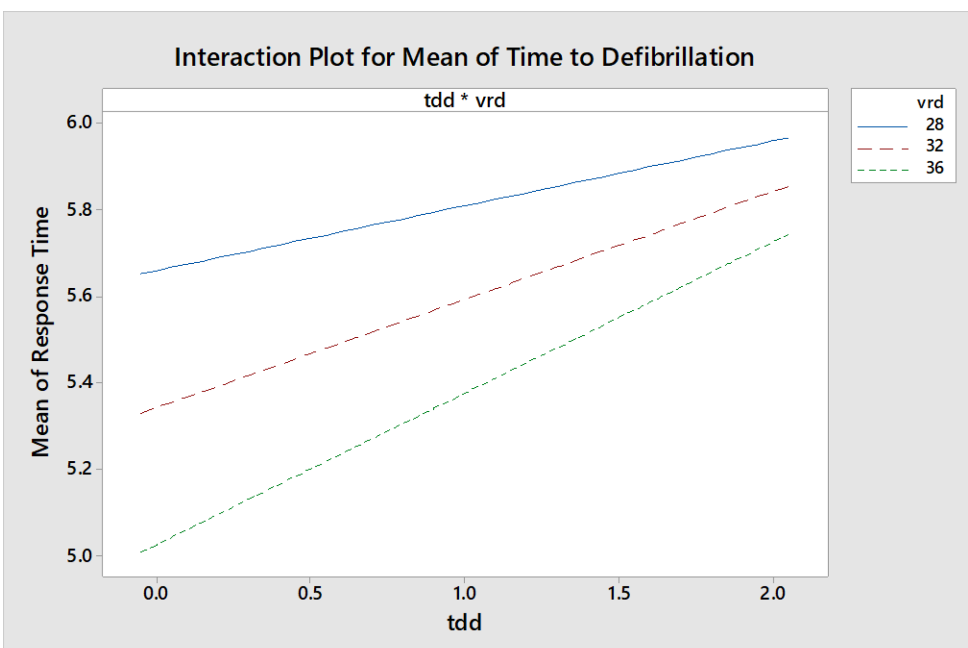


Figure 33. Plot showing the interaction between drone dispatch delay and responder driving velocity on the mean of the time to defibrillation.

5.4.2 RSM Results for 95th Percentile of Time to Defibrillation Distribution

The 95th percentile of the distribution was analyzed to assess not only the sensitivity of the mean response time, but also the sensitivity of very long response times. The final reduced model for the 95th percentile of the system time to defibrillation included three significant main effect terms, one quadratic term, and one interaction term. The interaction term is different from the interaction identified as significant in the mean response time. The final ANOVA results and the regression equation are shown in Table 15. Figure 34 shows the plots of the three main effect factors, with the slope indicating their relative impact on the response time, as well as showing the non-linearity of the response to the responder density R_d input. Figure 35 shows the interaction of the mobile responder density R_d and the driving velocity of the mobile responder V_{rd}.

Table 15. ANOVA and Regression results for 95th percentile response surface.

Analysis of Variance

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Model	5	6.6785	1.33571	62.18	0.000
Linear	3	6.0079	2.00264	93.23	0.000
R_d	1	3.1537	3.15375	146.82	0.000
v_{rd}	1	2.2204	2.22042	103.37	0.000
t_{ec}	1	0.6338	0.63375	29.50	0.000
Square	1	0.3400	0.34000	15.83	0.001
R_d*R_d	1	0.3400	0.34000	15.83	0.001
2-Way Interaction	1	0.3306	0.33062	15.39	0.001
R_d*v_{rd}	1	0.3306	0.33062	15.39	0.001
Error	21	0.4511	0.02148		
Total	26	7.1296			

Regression Equation

$$95^{th}\ \text{percentile} = 14.56 - 1.510\, R_d - 0.1958\, v_{rd} + 0.3250\, t_{ec} + 0.0502\, R_d^2 + 0.02396\, R_d v_{rd}$$

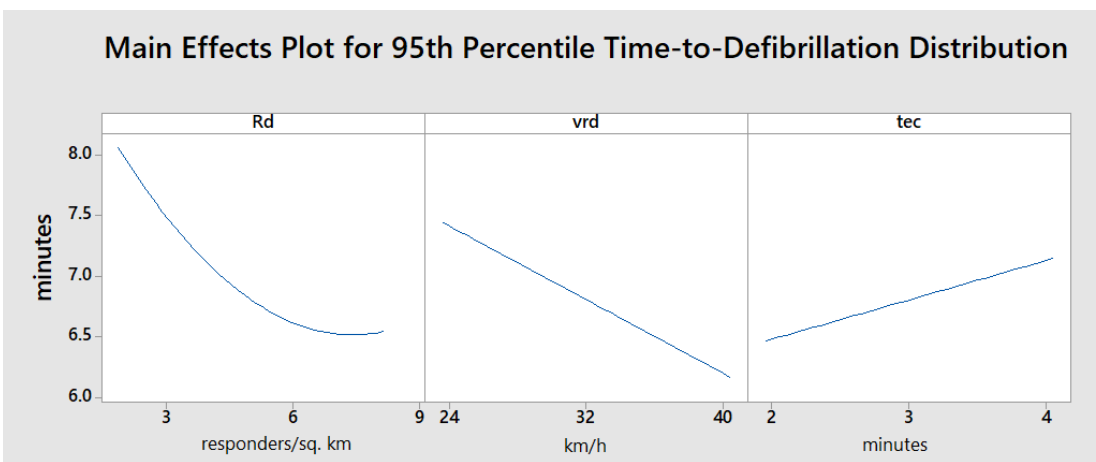


Figure 34. Plot of significant main effects for the 95th percentile of response time distribution. The experimental space is defined by the range of uncertainty or variability for each factor. R_d = responder density; v_{RD} = responder driving velocity; t_{EC} = EMS chute time.

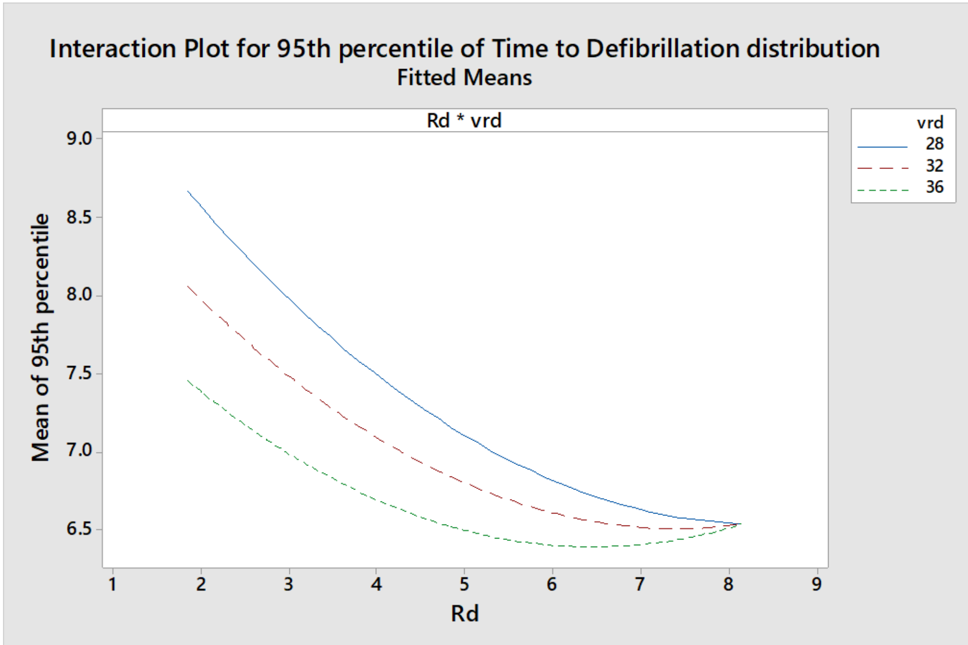


Figure 35. Interaction plot of 95th percentile of response time distribution.

5.4.3 Discussion of Response Surface Analysis

Conducting a response surface DOE on a stochastic simulation model results in a "model of a model" of a real system. Montgomery discusses the application of Design of Experiments (DOE) to computer simulation models [97]. He describes the approach as "the data from the experimental design is used to build a model of the system being modeled by the computer simulation – a meta model – and optimization is carried out on the meta model. The assumption is that if the computer simulation model is a faithful representation of the real system, then optimization of the model will result in adequate determination of the optimum conditions for the real system". The meta model provides some analytical advantages over the full simulation model. The meta model, being a regression model with quadratic and interaction terms, is much more computationally efficient than running Monte Carlo simulations on the full model. An estimated mean response time to defibrillation, or 95th percentile time, can be directly calculated with only knowing a few of the model inputs. Additionally, the full simulation model is intended to be a predictive model, and not an optimization model. However, the field of Design of Experiments has established tools for optimizing the factors in the RSM experiment to achieve specific outputs. Optimization can be performed on the meta model and verified on the full simulation model.

In this analysis, the response surface identified a non-linear response as the density of mobile responders increased. As more mobile responders are added to a system, the minimum distance from the randomly located responders to the arrest location decreases, but with diminishing returns. The RSM indicated that beyond 7 to 8 responders per square kilometer, additional improvement in response time is not expected. Once this density is achieved, resources would be better spent improving other factors in the system.

The analysis also identified important interactions in factors. In regions where the mobile responder is able to drive fast e.g. rural locations, the drone dispatch delay becomes more impactful to the response time. Where driving speeds are lower, this has less of an impact, as the drone will still arrive ahead of the mobile responder even with long dispatch delays.

For the 95th percentile of the time to defibrillation distribution, i.e. the longer response time, the responder density and responder driving speed have a significant interaction. At low densities of responders, the driving speed has a much larger impact than with a high density of responders. This is because with fewer responders, the driving distances can become significantly longer.

5.5 Sensitivity to Independence of Factors

The modelling approach assumes each of the input factors is independent of other factors. This allows for model simplification of factors that have only modest stochastic variance (relative to the variance of response distance) by using an average value for these factors. This approach is applied to the constant time components of each response system, as well as the velocity of the responding agents. However, the variation of these values may be correlated in a real world system.

A likely correlation is the velocity of driving responders, i.e. EMS and mobile responders, to the weather conditions, which also impact the availability of the drone system to provide a response. Poor weather, e.g. snow or heavy rain, would result in no drone response, and would also likely result in slower driving speeds by both EMS and mobile responders.

A sensitivity experiment was used to evaluate the effect of the assumption of independence of these factors. A stochastic factor, "weather effect", w, was added to the model for this experiment. This factor value was sampled from a Beta (4, 4) distribution ranging from zero to one. This factor was used to determine the drone availability outcome for each simulation, based on the weather availability factor D_{AW}. This factor was set to the nominal value of 90% weather availability, with the result determined by any sampled value of w below 0.2786 (the 10th percentile of the Beta distribution) resulting in the drone system being unavailable.

The driving velocity of both EMS and mobile responders were defined as a function of the factor w. Both factors applied a scaling and location shift of the Beta distribution to produce a velocity between 70% and 130% of the nominal value, maintaining the nominal value as the average speed.

$$v_E = 40w + 50 \tag{14}$$

$$v_{RD} = 19.2w + 22.4 \tag{15}$$

These functions resulted in a perfect correlation (i.e. correlation coefficient of 1) of driving velocities between EMS and mobile responders, as well as a perfect correlation between drone system unavailability and the slowest driving velocities.

To compare the correlated factors to uncorrelated factors, the model was separately modified to create stochastic inputs for EMS and mobile responder driving velocities.

These inputs used the same Beta (4, 4) distribution, with EMS v_E ranging from 50 to 90 km/h, and mobile responder velocity v_{RD} ranging from 22.4 to 41.6 km/h.

The experiment considered two types of systems; the drone delivery system with the mobile responder application of the AED; and the drone delivery with bystander use. Each system was evaluated under two conditions; first with 1 drone in the system, and then with 5 drones. The drones were located at the most central fire station (1 drone) and all fire stations (5 drones) in the Bellevue region. The experiments consisted for 5000 simulations runs with the correlated and uncorrelated factors.

5.5.1 Results and Discussion

The results of the experiment are shown in Figure 36. The boxplots show the distribution of time-to-defibrillation for 5000 simulations. Table 16 shows the comparison of mean, 5th percentile, and 95th percentile between the model using uncorrelated inputs and the model with correlated inputs. The effect of the correlated inputs is minimal on the overall distribution. The difference is most notable in the longest few simulations, with the range of the data extended up to 2.8 minutes. However, even at the 95th percentile, the change is minimal, with the most extreme difference of 0.3 minutes. These results suggest that the model is not sensitive to an assumption of independence in inputs, and the use of average values to simplify small stochastic variations has a minimal effect on the predictive capability.

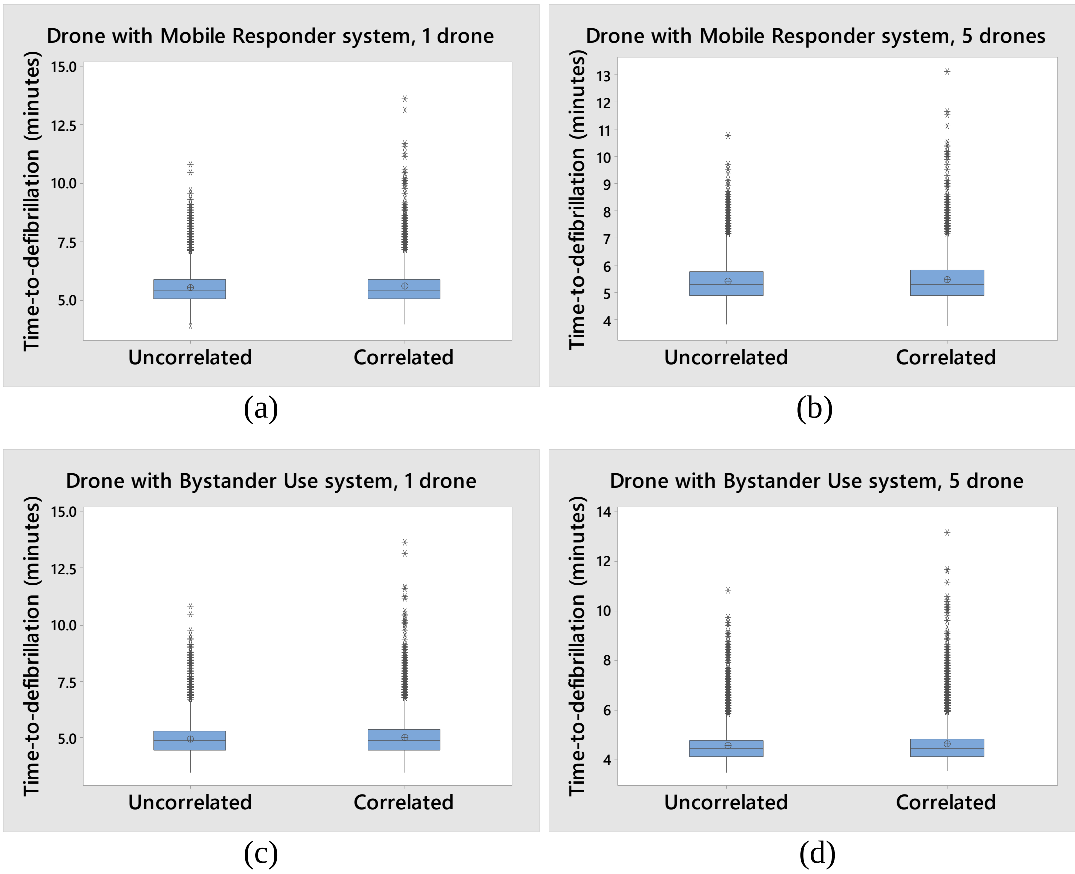


Figure 36: Boxplots of time-to-defibrillation distributions using uncorrelated and correlated factors for (a) drone mobile responder system with 1 drone; (b) drone mobile responder system with 5 drones; (c) drone bystander use system with 1 drone; and (d) drone bystander use with 5 drones.

Table 16. Comparison of time-to-defibrillation (minutes) distribution statistics between uncorrelated and correlated inputs.

	Uncorrelated Inputs			Correlated Inputs		
System	Mean	5th Percentile	95th Percentile	Mean	5th Percentile	95th Percentile
Drone Mobile Responder, 1 drone	5.5	4.6	6.8	5.5	4.6	6.9
Drone Mobile Responder, 5 drones	5.4	4.5	6.7	5.5	4.5	6.8
Drone Bystander Use, 1 drone	5	3.9	6.3	5	3.9	6.5
Drone Bystander Use, 5 drones	4.6	3.8	5.9	4.6	3.8	6.2

5.6 Summary and Conclusions of Sensitivity Analysis

The sensitivity analysis described in this chapter has generated valuable insights into the model and simulation approach to predicting the efficacy of different cardiac arrest response systems. When assessing the fidelity of the model to the real world system, and minimizing the error in predictions, the analysis has shown that the model is tolerant to some error in the regional and geospatial characteristics of a system. The Minkowski distance metric is robust to small errors in the selection of the optimum p value for a region. Additionally, assuming a uniform distribution of both the cardiac arrest locations and the mobile responder distribution will result in only small predictive errors in the mean and 95th percentile response times if the actual distributions depart from uniformity. The exception to this is that the model may underestimate the magnitude of the longest response times (i.e. upper tail of the distribution) in cases where the true mobile responder distribution is highly skewed or clustered.

The analysis highlighted the importance of the delay time prior to the transit of responding agents to the cardiac arrest location. Accurately assessing these times, including both the delay due to the dispatching process, and other delays post dispatch, is important to the predictive accuracy of the modeling. Additionally, when improving or optimizing such systems as a drone AED transport, or cellphone dispatched responders, the focus should be on technological or operational methods to reduce and minimize these delay times.

Chapter 6: Comparison of Systems

A powerful benefit of modeling and simulation of systems is the ability to predict the performance of different cardiac arrest response systems, as well to estimate the performance of systems operating under varying operating conditions. A goal of this research is to use the developed modeling approach to compare the performance of different new and emerging cardiac arrest response systems, hypothetically operating in the same region, to gain an understanding of the potential impact on survival from the different response concepts.

This chapter presents simulation experiments comparing several different cardiac arrest response systems modeled in the region of Bellevue, Washington. Four of the emerging systems that were discussed in Chapter 2 are compared through simulation, with both the time to defibrillation and the survival probability evaluated as system responses. The systems modeled were:

1. Pulse Point: cellphone dispatched citizen responders providing CPR only
2. ALERT: cellphone dispatched verified responders providing AED and CPR (similar to the ALERT study)
3. Drone – BU: drone AED delivery with bystander use, similar to the Flirty and Reno, Nevada drone pilot program.
4. Drone – MR: combination of drone AED delivery with cellphone dispatched responders to apply AED, proposed by GoodSAM.

These systems range in their implementation maturity from fully established, to moderate scale trial, to small pilot study, to concept only. The systems were compared to the baseline simulated response of EMS in the region. Section 6.1 describes the conditions of each system that were evaluated, including those that were tested under multiple settings. The results of the simulation experiment are shown in Section 6.2. Section 6.3 provides a discussion of the experiment results.

6.1 Experimental Conditions

The conditions for each of the systems being compared are described in the following sections. Global conditions used for the Bellevue, Washington simulations were a Minkowski drive distance of 0.8, with a bias correction distance of 0.35 km.

6.1.1 EMS System Conditions

The Bellevue, Washington region of the simulations is supported by ambulances in five fire stations distributed over the region shown in Figure 37. The region extends from latitude 47.58 to 47.64, and from longitude -122.14 to -122.22, covering an area of approximately 40 square kilometers. The EMS specific model parameters are 3.5 minutes for the combined dispatch delay and chute time, and an ambulance velocity of 70 km/h, which has been empirically determined for Bellevue as discussed in Section 4.5.2. The ambulance availability was set at the nominal 0.76. These conditions were used both to provide time to defibrillation and survival predictions for EMS response alone, as well as for EMS operating in conjunction with the other modeled systems.

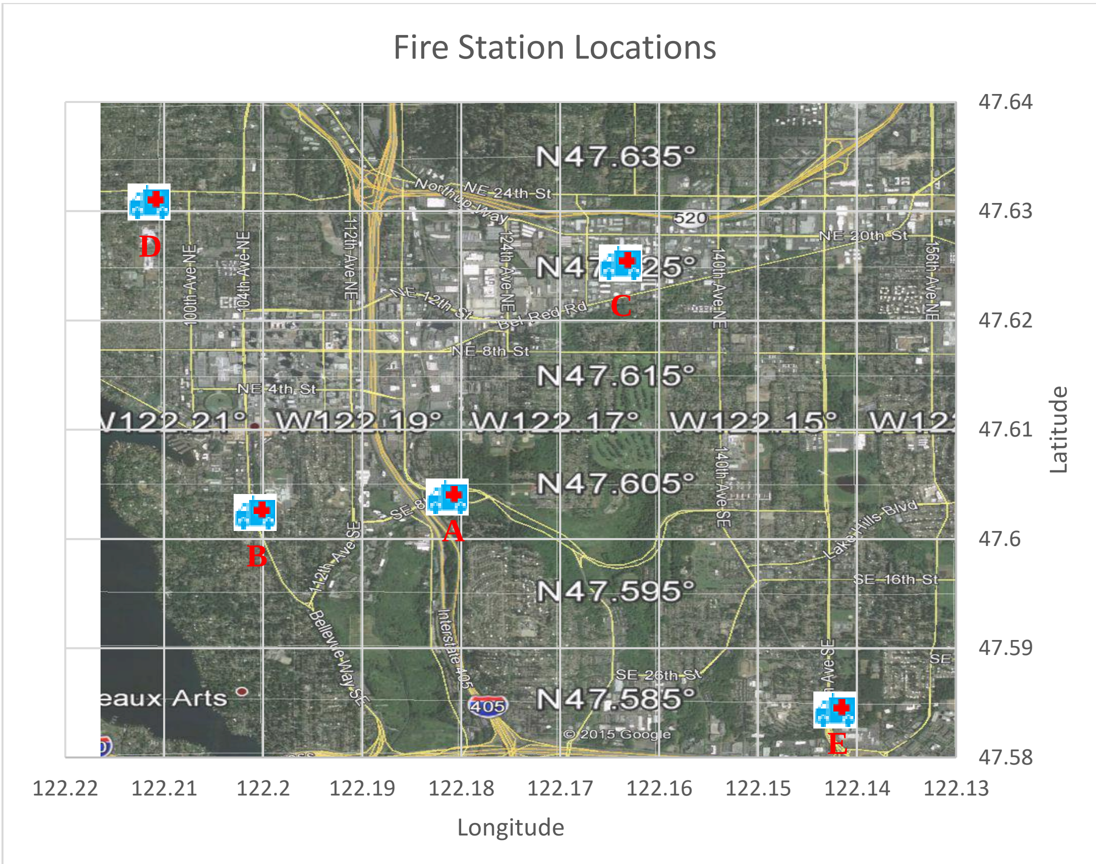


Figure 37. Fire station and drone base locations in Bellevue, Washington simulations.

6.1.2 Pulse Point Conditions

The Pulse Point system was modeled with three different densities of mobile responders. The simulation experiments were run with 80, 200, and 320 mobile responders, corresponding to a responder density of 2/km^2, 5/km^2, and 8/km^2. Aside from responder density, factors that are specific the mobile responder were set at nominal conditions shown in Table 17.

Table 17. Conditions used for the Pulse Point simulation.

Factor	Description	Setting
p_w	Minkowski walk distance order (p)	1.7
t_{RD}	Responder dispatch delay time (minutes)	1
t_{RW}	Responder walk delay time (minutes)	0.75
t_{RDr}	Responder drive delay time (minutes)	1
v_{RW}	Responder walking velocity (km/h)	7
v_{RD}	Responder driving velocity (km/h)	32

The Pulse Point mobile responders provide only CPR. Thus the experiment responses of time-to-defibrillation is unchanged by the Pulse Point, as EMS is relied upon to provide defibrillation. The Pulse Point response affects the survival likelihood by providing early CPR, which has been shown to increase survival. This system is included in the comparison study because it is the most established and widely implemented of the emerging response systems. It currently represents the "state of the art" of augmentation to EMS response.

6.1.3 ALERT Study Conditions

The ALERT study is a large-scale study of enhancing the Pulse Point system with the concept of a *verified responder*. In the case of the study, these responders are off-duty fire fighters. However, the verified responder concept can be extended to other off-duty healthcare workers and first responders (nurses, doctors, police, security guards). The primary improvement in this system over the standard Pulse Point application is that the mobile responders carry AEDs with them at all times. Thus, in this system the mobile responder provides both CPR and defibrillation, in contrast to the Pulse Point system above which only provides CPR.

The conditions of the ALERT simulation are identical to the Pulse Point conditions above. Similarly, the system is evaluated at three responder densities; $2/km^2$, $5/km^2$, and $8/km^2$.

6.1.4 Drone with Bystander Use System Conditions

The drone with bystander AED use system emulates a FAA approved pilot program involving the drone delivery company Flirty and the city of Reno, Nevada. This type of system is generically characterized by a drone delivery of an AED, while relying on bystander retrieval of the AED and application to the cardiac arrest victim. The simulation experiment included the conditions of one, two, and five drones. The drone stations were located at existing fire stations within the Bellevue region. For simulations with a single drone, the drone was located at the most central fire station, annotated as A in Figure 36 in Section 6.1.1. When two drones were modeled, the base locations were set at fire stations annotated as B and C, as these locations minimize the average response distance over the region. Drones were located at each fire station when five drones were simulated.

Additional drone specific factors settings are shown in Table 18.

Table 18. Drone factor settings.

Factor	Description	Setting
p_a	Minkowski drone distance order (p)	1.9
t_{DD}	Drone dispatch delay time (minutes)	1
t_{DV}	Drone vertical flight time (minutes)	0.5
v_D	Drone velocity (km/h)	80
t_{DDe}	Drone descent time (minutes)	1

6.1.5 Drone with Dispatched Mobile Responder System Conditions

A system using a drone AED delivery together with mobile responders dispatched to the cardiac arrest scene has not yet tested, but has been proposed in literature as well as by GoodSAM. In this system, both CPR and defibrillation are applied by the mobile responder; however, the responder may arrive before or after the drone delivery of the AED. It is thus assumed that the time to both CPR and defibrillation treatment is the maximum of the response time for both the drone and the mobile responder.

For the system comparison study, the mobile responder system conditions were identical to those described in the Pulse Point simulation, and the drone conditions were identical to those described in the drone with bystander use. Similar to the experimental conditions for Pulse Point and the drone response, the mobile responder density was varied as well as the number of drones in the system.

6.2 Results of System Comparison Experiments

The results of the system comparison are presented in Figure 38 for time to defibrillation and Figure 39 for survival prediction. The notation on the x-axis of the charts describes the system, with the specific conditions (number of mobile responders and the number of drones) in brackets. The graphs show the median of the response distribution, with the bars showing the range of the 5th percentile to the 95th percentile of the distribution.

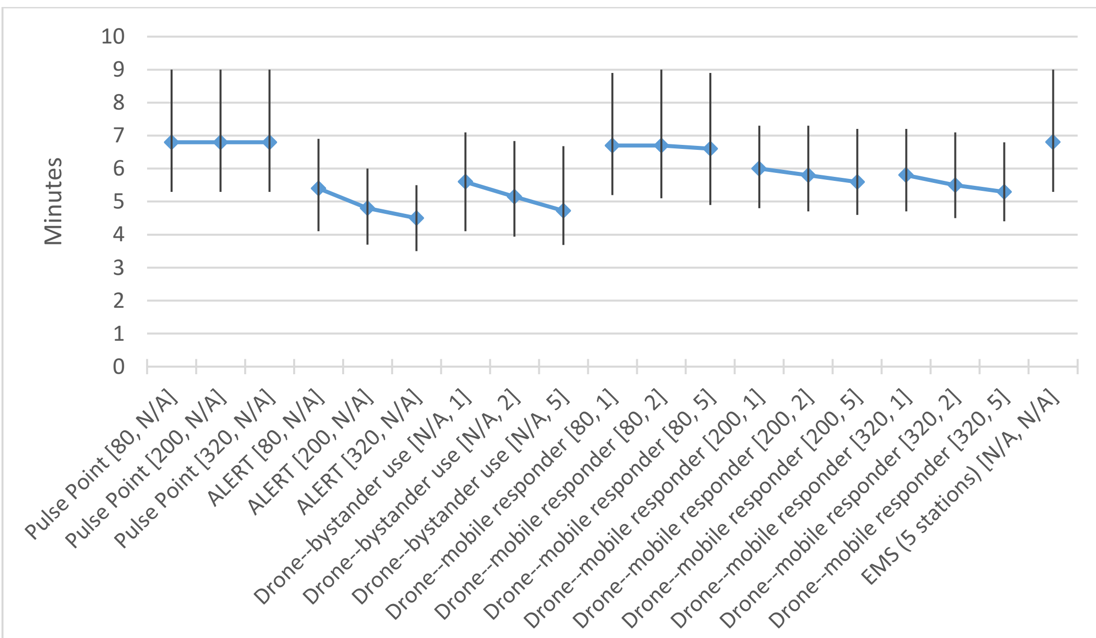


Figure 38. Comparison of systems for time to defibrillation. The blue marker indicates the mean response time. The interval bar indicates the 5th and 95th percentiles of the response time distribution.

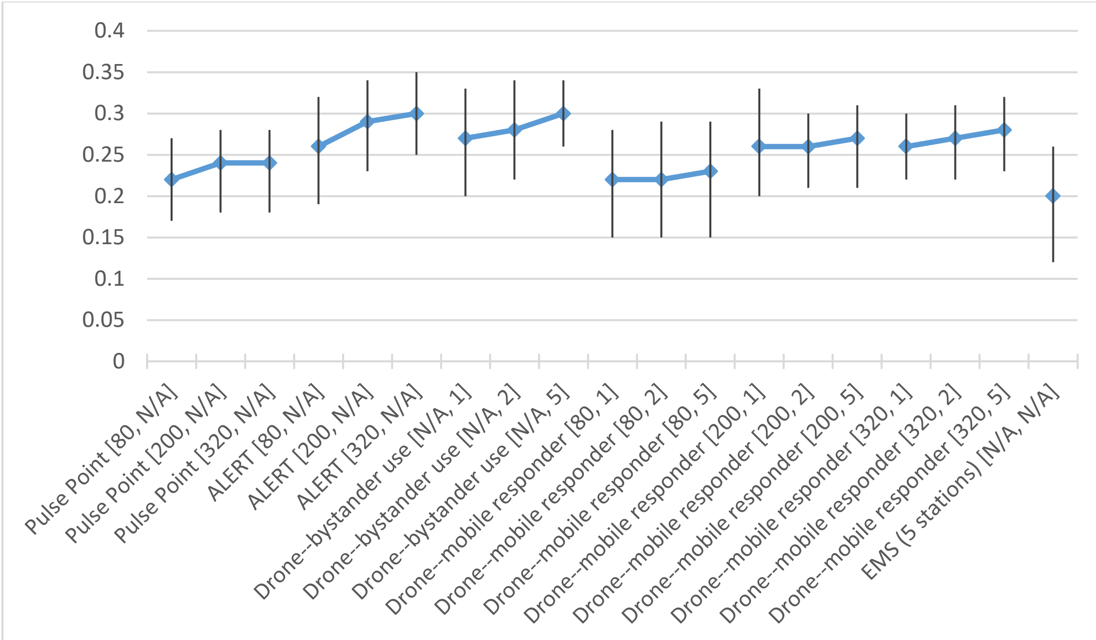


Figure 39. Comparison of systems for survival. The blue marker indicates the mean predicted survival probability. The interval bar indicates the 5th and 95th percentiles of the predicted survival distribution.

6.3 Discussion of System Comparison Results

The study provided comparisons of each system to a baseline performance of EMS, as well as for performance comparisons between the different types of systems. Trends in experiment responses are identifiable from the changes in conditions within each system. All systems provided an improvement in survival over the baseline EMS, with the mean survival improvement ranging from 2%, for a low responder density Pulse Point system, up to 10%, for both a high density ALERT type system and a drone delivery – bystander use system . This improvement is expected, as all systems have the existing EMS operating in parallel, and it is presumed that the systems have no detrimental impact on the EMS response. The results also confirm that adding more resources to a system, whether they be additional responders or additional drones, will improve the performance of the system. However, as discussed in Section 5.4, the effect of these additional resources is non-linear, and thus provide diminishing returns as they are increased.

The best performing systems were the ALERT system and the drone AED delivery with bystander use. The ALERT system performs best with a relatively high density of mobile responders. Achieving this density may be challenging for some communities, as the pool of potential verified responders to recruit from may be limited. Further, this type of system requires a high level of commitment by the responder to constantly carry an AED. While this has been achieved in the study, the long term compliance is unknown. The drone transport with bystander use relies upon a willing and capable bystander providing CPR and applying the AED. The success rate of this is largely unknown, although some inference can be gathered from studies of the willingness of bystanders to use public access AEDs. This system also assumes the bystander will provide CPR until the drone arrives with the AED, resulting in an earlier time to CPR treatment and the associated survival benefit.

The drone AED transport with application by a dispatched mobile responder solves these potential issues. The mobile responder does not need to carry the AED with them at all times, as it is now delivered by the drone. The application of CPR and the use of the AED for defibrillation is assured with this system, and will be performed by a trained professional, which could produce better results (independent of response time).

This system suffers in response time relative to the other systems because the responder may have to wait for the AED arrival, or the AED may arrive well before a responder. Figure 40 shows an analysis of this wait time for the nine conditions under which this system was modeled. The histograms of 1000 simulations show the difference in response time between the mobile responder and the drone. The blue colored bins indicate simulations where the mobile responder had to wait for the AED to arrive (i.e. a positive time difference). The orange colored bins are simulations where the drone arrived before the mobile responder (i.e. a negative time difference). Conditions resulting in symmetric wait times (where the mean wait time is near zero) indicate the most efficient resourcing of the system. Asymmetric distributions around zero wait time indicate either the mobile responder or the number of drones is under resourced, resulting in either the drone or the mobile responder frequently waiting for the other to arrive. Under these experimental conditions, the most symmetric distributions around zero fall on the diagonal. These are the conditions that result in the drone and the mobile responder arriving at about the same time most often, suggesting that balancing drone and mobile responder resources is needed for optimal performance.

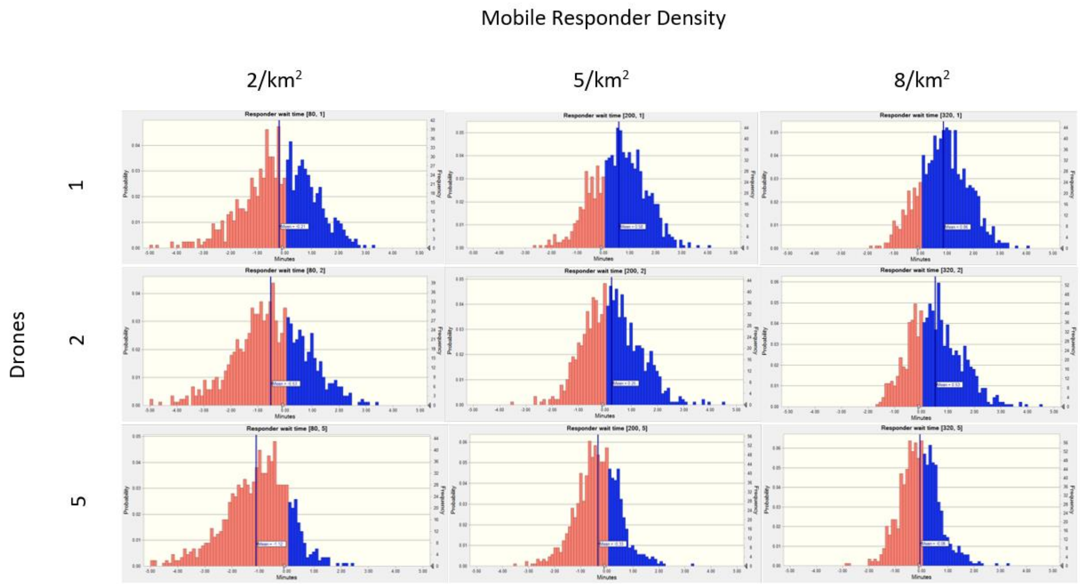


Figure 40. Time difference between arrival of mobile responder and arrival of drone. Mean time difference is annotated with the black bar.

The drone response systems do not always provide an AED to the cardiac arrest scene. In such cases, the mobile responder can perform CPR but the defibrillation is delayed until EMS arrives. The chances of the drone being unable to respond are dictated by the operational availability of the drones, and the weather in the region. Under the conditions of this simulation, (96% operational availability and 90% weather availability), a drone was available to respond in 84.5% of simulations with 1 drone, 89.0% of simulations with 2 drones, and 89.3% of simulations with 5 drones. Thus, there is a benefit to having redundant drones in the system, however additional redundancy beyond two provides very little improvement on capability to respond (however, it does improve response time).

As both the time to defibrillation and survival performance of these systems are strongly dependent on the resources of the system, i.e. density of mobile responders and number of drones, the cost of these resources must be considered when evaluating the potential options to improve cardiac arrest survival in a community. The performance versus cost of these systems is discussed in Chapter 7.

Chapter 7: Application of Model

The ultimate utility of predictive modelling and simulation is to inform decisions, such to maximize the likelihood of the best outcome. A primary question which this research proposed to answer is how the application of the predictive model can be used to evaluate the benefits and costs of various alternative response systems. Chapter 5 discussed an experimental determination of the important factors within each type of responder system, as well as the interaction of these factors and how they might be optimized for the maximum increase in survival. Chapter 6 discussed usage of the model to compare survival improvements of several currently active or proposed alternative systems, under varying conditions within each system. This chapter expands upon the results of Chapter 6 to demonstrate how these system comparisons can inform decisions faced by communities and EMS systems throughout the world.

Communities around the globe are faced with the challenge of improving the currently poor survival for sudden cardiac arrest. As discussed in Chapter 2, numerous novel response systems are being conceptualized, researched, and piloted. Communities looking to improve cardiac arrest survival rates would likely choose amongst these emerging systems. The modelling and simulation approach in this research dissertation can be used to provide insights on which system, and under which conditions, the highest survival improvement could be realized. However, the decision would not be based upon the survival improvement alone, as the cost of implementing and operating such systems would also need consideration. The Value of a Statistical Life (VSL) is frequently used as a benchmark by government agencies when performing a cost-benefit analysis of policy or program decisions [98][99]. The VSL allows for the comparison of the mortality reduction benefit and program cost to the monetary value which a society at large is willing to pay to reduce health risks.

This chapter provides a method of cost estimation for each of the systems compared in Chapter 6, which used Bellevue, Washington as an example community. Section 7.1 provides a general cost structure for citizen mobile responder systems, with consideration of systems which provide only CPR (Pulse Point) and systems which equip responders with AEDs (e.g. ALERT study). Section 7.2 provides a general cost model for a drone AED delivery systems. Section 7.3 discusses costs of a system with both drone AED deliver and dispatched mobile responders. Section 7.4 estimates the costs of an alternative choice to these novel systems, which is the provision of an additional BLS Ambulance to an EMS system. Finally, section 7.5 provides a cost benefit analysis and comparison of a hypothetical set of system options, with a discussion of the application in Section 7.6.

This analysis evaluates the *marginal cost* of the additional response system, and does not include the cost of the existing EMS system. A 10 year timeframe was selected for the cost analysis, which roughly represents the service life of the capital assets required by the systems (e.g. ambulances, defibrillators/AEDs, and drones). The Net Present Value method is used to account for the time value of costs over the 10 year timeframe, such that a single 10 year cost is calculated for each option. A standard discount rate of 5% is used for the analysis. The analysis assumes 100 cardiac arrest responses per year in the city of Bellevue (in 2014 there were 79 cardiac arrests).

Unless specifically cited, cost estimates were gathered from discussions with subject matter experts, including cell phone app system developers, King County EMS, and University of Maryland Unmanned Aircraft Systems Test Site.

7.1 Cost analysis of mobile responder systems

Mobile responder systems are those in which non-EMS responders are dispatched to cardiac arrests which occur nearby by a cell phone app. The responders may be citizen volunteers, as in the Pulse Point system, off duty first responders or medical professionals, e.g. the verified responders in the ALERT study, or taxi cab drivers, such as with the AED on Wheels system. Other variations on these concepts, such as the use of Uber drivers, have been proposed as well. Mobile responders may be provided with AEDs (e.g. ALERT system), or may be dispatched to provide CPR only (e.g. Pulse Point system).

The primary costs of these types of systems are the app dispatch system integration with the 911 system, and the AEDs, if provided to the responders. Additional lesser costs include the cost of recruiting volunteer responders, training costs (if provided), and potentially small compensation when a response occurs. Although once implemented, the systems are operated by existing 911 dispatch personnel, it is also expected that a small administrative cost exists.

The dispatch software and cell phone app are provided as turnkey solutions by a few existing companies or non-profits. Pulse Point is the most widely implemented system in the United States, while Good Sam system is the most widely used in Europe. The approximate costs of these systems in the United States are $25,000 for the initial software integration with the 911 dispatch system, with $10,000 per each year after for ongoing support.

The Pulse Point volunteer citizen responder system provides CPR therapy only as the standard response. There is no training or compensation provided, with the only costs being the system integration and ongoing support costs. Table 19 provides the 10 year cost estimate for the Pulse Point system. The number of responders is essentially an uncontrolled factor in this system, as it is determined by the number of citizens who choose to enroll. Thus, there is no incremental cost for each responder. The 10 year NPV estimated cost of the Pulse Point system is $91,503.

Table 19. 10 year cost of Pulse Point system.

	Year									
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Dispatch software integration	$ 25,000									
Recurring costs										
System support	$ -	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000
Total annual cost	**$ 25,000**	**$ 10,000**	**$ 10,000**	**$ 10,000**	**$ 10,000**	**$ 10,000**	**$ 10,000**	**$ 10,000**	**$ 10,000**	**$ 10,000**
Discount rate	5%									
10 year NPV cost	($91,503)									

The ALERT system uses the PulsePoint app and dispatch system, however it recruits off-duty first responders, and provides them with an AED to carry nearby at all times. In addition to the cost of the Pulse Point system integration and support, the system also has the cost of providing an AED to each responder. The Philips HS1 is a low cost AED which is well suited for this type of responder. The retail cost of the AED is $1275.00 [100]. Along with the AED is consumable costs of replacing the pads ($70) every 2 years or upon use, and the battery ($170) every 4 years. It is assumed the ALERT type system would also require local administration support, separate from Pulse Point support, estimated at $25,000 per year (25% full time employee). It is also assumed a small training cost of $50 per year would apply to each responder. Table 20 shows the 10 year cost estimate for an ALERT system with 80, 200, and 320 responders. The NPV cost is estimated at $448,814 for 80 responders, $695,215 for 200 responders, and $941,616 for 320 responders.

Table 20. 10 year cost of ALERT system with (a) 80 responders, (b) 200 responders, and (c) 320 responders.

Number of Responders	80									
	Year									
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Dispatch software integration	$ 25,000									
AEDs	$ 102,000									
Consumables costs										
Pads	$ -	$ -	$ 5,600	$ -	$ 5,600	$ -	$ 5,600	$ -	$ 5,600	$ -
Battery	$ -	$ -	$ -	$ -	$ 13,600	$ -	$ -	$ -	$ 13,600	$ -
Recurring costs										
System support	$ -	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000
Administrative costs	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000
Training	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000
Total annual cost	**$ 156,000**	**$ 39,000**	**$ 44,600**	**$ 39,000**	**$ 58,200**	**$ 39,000**	**$ 44,600**	**$ 39,000**	**$ 58,200**	**$ 39,000**
Discount rate	5%									
10 year NPV cost	($448,814)									

(a)

Number of Responders	200									
	Year									
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Dispatch software integration	$ 25,000									
AEDs	$ 255,000									
Consumables costs										
Pads	$ -	$ -	$ 14,000	$ -	$ 14,000	$ -	$ 14,000	$ -	$ 14,000	$ -
Battery	$ -	$ -	$ -	$ -	$ 34,000	$ -	$ -	$ -	$ 34,000	$ -
Recurring costs										
System support	$ -	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000
Administrative costs	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000
Training	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000
Total annual cost	**$ 315,000**	**$ 45,000**	**$ 59,000**	**$ 45,000**	**$ 93,000**	**$ 45,000**	**$ 59,000**	**$ 45,000**	**$ 93,000**	**$ 45,000**
Discount rate	5%									
10 year NPV cost	($695,215)									

(b)

Number of Responders	320									
	Year									
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Dispatch software integration	$ 25,000									
AEDs	$ 408,000									
Consumables costs										
Pads	$ -	$ -	$ 22,400	$ -	$ 22,400	$ -	$ 22,400	$ -	$ 22,400	$ -
Battery	$ -	$ -	$ -	$ -	$ 54,400	$ -	$ -	$ -	$ 54,400	$ -
Recurring costs										
System support	$ -	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000
Administrative costs	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000
Training	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000
Total annual cost	**$ 474,000**	**$ 51,000**	**$ 73,400**	**$ 51,000**	**$ 127,800**	**$ 51,000**	**$ 73,400**	**$ 51,000**	**$ 127,800**	**$ 51,000**
Discount rate	5%									
10 year NPV cost	($941,616)									

(c)

7.2 Cost Analysis of Drone AED Delivery System

A drone AED delivery system which relies on bystanders to apply and operate the AED requires several system components. The drones in the system must be high reliability, able to fly autonomously or by remote piloting, and carry a payload of at least 5 kg. Example drones that meet this criteria are the Freefly Alta 8 [101] and the xFold Cinema X8 U7 [102]. These drones, when fully equipped, cost about $25,000. The drone system would require a ground control station, with software that integrates with the EMS dispatch system, to activate the drone response. A single ground control station can support a system of multiple drones. The cost of the ground control station is estimated at $15,000. Additionally, telemetry hardware is required for communication with the drone while deployed, via radio communication or integrated with a 4G or 5G cellular network. The cost of this hardware is estimated at $5000 to cover a city the size of Bellevue, Washington. Each drone in the system requires a drone nest, which is an enclosure that protects the drone while in standby, provides charging to the drone battery, and has automated doors that open for deployment. The nest could be located on the roof of a fire station, or other location within the region. The cost of the nest is estimated at $10,000 per drone.

Each drone carries an AED and a drop mechanism as its payload. The AED should be one that is both simple to use, designed for bystander use, as well as rugged enough to survive flight in the weather elements and the drop from the drone. The Philips FRx device meets these criteria, at a retail price of $1600 [103]. Each drone would require an AED, and the system would also require a spare AED for every 5 drones in the system. After deployment, the AED would be unavailable for a period of time while event data are recovered, and the AED is cleaned, tested, and new pads are installed.

The consumable costs in the system are the AED drop mechanism, the drone battery, the AED pads, and AED battery. The drop mechanism, likely a winch with a light weight cable, is estimated to cost $100 and have a service life of 100 deployments. The drone battery is estimated to cost $500, with a service life of 300 deployments. The AED pads replacement would occur with each deployment, as the pads are single use accessories to the AED. Each pad replacement for the FRx AED costs $60. With a few drones responding to many cardiac arrest events each year, the pads would not be expected to reach the 2 year shelf life expiration before use. With the significant amount of AED applications, it is expected that the battery would be replaced about every 6 months, at a cost of $170 per battery.

The recurring costs within the system are the drone pilot, drone and nest maintenance costs, and system administration costs. A proposed concept for piloting the drone is the use of a subscription pilot service [104]. With such a service, the pilot is not part of the local EMS system, but a remote located pilot that may support many geographically distant drone systems. Such a service is estimated to cost around $3000 each year per ground station. Maintenance costs are estimated at $1500 each year per drone/nest for semi-monthly servicing. Administrative costs for a system supporting a city the size of Bellevue is $25,000 per year (25% full time employee).

Table 21 provides the 10 year cost analysis for a system consisting of 1, 2, and 5 drones. The 10 year NPV cost is estimated at $337,368 for 1 drone, $386,528 for 2 drones, and $534,009 for 5 drones.

Table 21. 10 year cost analysis for drone AED system with (a) 1 drone, (b) 2 drones, and (c) 5 drones.

Number of Drones/nests in system	1									
Annual deployments	100									
					Year					
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Drone	$ 25,000									
Telemetry hardware	$ 5,000									
Ground control station/EMS dispatch	$ 15,000									
Drone nest	$ 10,000									
AED	$ 3,400									
Consumables costs										
Payload drop mechanism	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100
Drone Battery	$ 500	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167
AED Pads	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000
AED Battery	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680
Recurring costs										
Drone pilot (subscription)	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000
Drone/Nest Maintenance	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500
Administration	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000
Total annual cost	**$ 95,180**	**$ 36,447**	**$ 36,447**	**$ 36,447**	**$ 36,447**	**$ 36,447**	**$ 36,447**	**$ 36,447**	**$ 36,447**	**$ 36,447**
Discount rate	5%									
10 year NPV cost	($337,368)									

(a)

Number of Drones/nests in system	2									
Annual deployments	100									
					Year					
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Drone	$ 50,000									
Telemetry hardware	$ 5,000									
Ground control station/EMS dispatch	$ 15,000									
Drone nest	$ 20,000									
AED	$ 5,100									
Consumables costs										
Payload drop mechanism	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100
Drone Battery	$ 500	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167
AED Pads	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000
AED Battery	$ 1,020	$ 1,020	$ 1,020	$ 1,020	$ 1,020	$ 1,020	$ 1,020	$ 1,020	$ 1,020	$ 1,020
Recurring costs										
Drone pilot (subscription)	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000
Drone/Nest Maintenance	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000
Administration	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000
Total annual cost	**$ 133,720**	**$ 38,287**	**$ 38,287**	**$ 38,287**	**$ 38,287**	**$ 38,287**	**$ 38,287**	**$ 38,287**	**$ 38,287**	**$ 38,287**
Discount rate	5%									
10 year NPV cost	($386,528)									

(b)

Number of Drones/nests in system	5									
Annual deployments	100									
					Year					
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Drone	$ 125,000									
Telemetry hardware	$ 5,000									
Ground control station/EMS dispatch	$ 15,000									
Drone nest	$ 50,000									
AED	$ 10,200									
Consumables costs										
Payload drop mechanism	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100
Drone Battery	$ 500	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167
AED Pads	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000
AED Battery	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040
Recurring costs										
Drone pilot (subscription)	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000
Drone/Nest Maintenance	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500
Administration	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000
Total annual cost	**$ 249,340**	**$ 43,807**	**$ 43,807**	**$ 43,807**	**$ 43,807**	**$ 43,807**	**$ 43,807**	**$ 43,807**	**$ 43,807**	**$ 43,807**
Discount rate	5%									
10 year NPV cost	($534,009)									

(c)

7.3 Cost Analysis of Drone AED Delivery with Mobile Responder System

A system which incorporates the delivery of the AED by drone, with the application of the AED by a mobile responder, has a cost structure that combines the elements of the drone delivery with bystander use, and the ALERT system of trained mobile responders. However, in such a system the mobile responders are not provided AEDs, as these are delivered to the location by drone.

As there are 9 combinations of number of drones (1, 2, 5) and number of responders (80, 200, 320) under evaluation, only a sample of 3 cost analysis is shown in Table 22. The three examples demonstrate the changes in the cost model as the number of drones is increased from 1 to 5, and as the number of responders are increased from 80 to 320. A full summary of the 10 year NPV costs for all system combinations is shown in Table 23.

Table 22. 10 year cost analysis for system with (a) 1 drone and 80 mobile responders, (b) 1 drone and 320 mobile responders, and (c) 5 drones and 80 mobile responders.

Number of Drones/nests in system	1									
Number of responders in system	80									
Annual deployments	100									
					Year					
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Drone	$ 25,000									
Telemetry hardware	$ 5,000									
Ground control station/EMS dispatch	$ 15,000									
Drone nest	$ 10,000									
AEDs	$ 3,400									
Dispatch software integration	$ 25,000									
Consumables costs										
Payload drop mechanism	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100
Drone Battery	$ 500	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167
AED Pads	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000
AED Battery	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680
Recurring costs										
Drone pilot (subscription)	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000
Drone/Nest Maintenance	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500
App dispatch system support	$ -	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000
Training	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000
Administration	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000
Total annual cost	**$ 124,180**	**$ 50,447**	**$ 50,447**	**$ 50,447**	**$ 50,447**	**$ 50,447**	**$ 50,447**	**$ 50,447**	**$ 50,447**	**$ 50,447**
Discount rate	5%									
10 year NPV cost	($459,758)									

(a)

Number of Drones/nests in system	1									
Number of responders in system	320									
Annual deployments	100									
					Year					
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Drone	$ 25,000									
Telemetry hardware	$ 5,000									
Ground control station/EMS dispatch	$ 15,000									
Drone nest	$ 10,000									
AEDs	$ 3,400									
Dispatch software integration	$ 25,000									
Consumables costs										
Payload drop mechanism	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100
Drone Battery	$ 500	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167
AED Pads	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000
AED Battery	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680
Recurring costs										
Drone pilot (subscription)	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000
Drone/Nest Maintenance	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500	$ 1,500
App dispatch system support	$ -	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000
Training	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000	$ 16,000
Administration	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000
Total annual cost	**$ 136,180**	**$ 62,447**	**$ 62,447**	**$ 62,447**	**$ 62,447**	**$ 62,447**	**$ 62,447**	**$ 62,447**	**$ 62,447**	**$ 62,447**
Discount rate	5%									
10 year NPV cost	($552,419)									

(b)

Number of Drones/nests in system	5									
Number of responders in system	80									
Annual deployments	100									
					Year					
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Drone	$ 125,000									
Telemetry hardware	$ 5,000									
Ground control station/EMS dispatch	$ 15,000									
Drone nest	$ 50,000									
AEDs	$ 10,200									
Dispatch software integration	$ 25,000									
Consumables costs										
Payload drop mechanism	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100	$ 100
Drone Battery	$ 500	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167	$ 167
AED Pads	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000	$ 6,000
AED Battery	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040	$ 2,040
Recurring costs										
Drone pilot (subscription)	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000	$ 3,000
Drone/Nest Maintenance	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500	$ 7,500
App dispatch system support	$ -	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000	$ 10,000
Training	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000	$ 4,000
Administration	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000	$ 25,000
Total annual cost	**$ 278,340**	**$ 57,807**	**$ 57,807**	**$ 57,807**	**$ 57,807**	**$ 57,807**	**$ 57,807**	**$ 57,807**	**$ 57,807**	**$ 57,807**
Discount rate	5%									
10 year NPV cost	($656,400)									

(c)

Table 23. 10 year NPV cost for combinations of drones and responders in system.

		Mobile Responders		
		80	200	320
Drones	1	$459,758	$506,088	$552,419
	2	$508,918	$555,249	$601,579
	5	$656,400	$702,730	$749,060

7.4 Cost Analysis of Additional BLS Ambulance for Cardiac Arrest Response

An alternative approach that an EMS system could take to improving cardiac arrest survival is increasing the number of ambulances in its fleet. The greatest impact on response time would be to locate the ambulance at a new base location, which would be geometrically optimal, where the response distance from existing bases is the greatest. The most economical ambulance solution is a BLS Response Ambulance, as this can provide both the CPR and defibrillation therapy where response time is critical. Many EMS systems, including King County EMS, use a two tier response strategy, dispatching a BLS Ambulance and an ALS Ambulance to all cardiac related calls as a matter of protocol.

As a comparison point to the implementation of the novel response systems in Sections 7.1 -7.4, a cost benefit analysis of a single additional BLS ambulance in the Bellevue region was estimated. Estimating the marginal cost of operating an additional ambulance in an existing EMS system is complex and subject to wide variation. Lerner *et al.* describe a framework for estimating the cost of an EMS system [105]. The components of the cost framework include vehicles, equipment, training, medical oversight, administration, communications, ambulance crew, and the physical plant. The authors note “Although throughout the United States most calls to 911 will result in a response, the staff and equipment that are sent to the scene will vary according to chief complaint and geographic location.” Many of the costs of the EMS system would not apply to the *marginal* cost of an additional ambulance. The primary marginal costs are vehicle, crew, equipment, maintenance, insurance, and fuel. A physical base location may exist, or may need to be procured.

The cost of a new ambulance vehicle can range from $100,000 to $200,000 [106] [107]. This analysis used the midpoint of this range, $150,000. Equipment in a BLS ambulance is an additional $40,000 [108]. The median salary of an emergency medical technician (EMT) in the United States is $34,320 per year [109]. An ambulance operating 24 hours a day requires 4 crews of 2 EMTs. Maintenance and insurance costs are estimated to add another $5000 per year, and fuel another $7500 per year. While an additional ambulance would provide BLS response to cardiac arrest events, it would also respond to other medical emergencies as well, providing an additional benefit to the EMS system beyond the cardiac arrest survival improvement. In King County, 24% of BLS responses were for life threatening emergencies (cardiovascular, respiratory, and neurological), with the remaining 76% distributed over a variety of medical needs [110]. To create an equivalent comparison to other cardiac arrest response systems, the BLS ambulance capital and recurring costs are multiplied by a factor of 0.24, while the defibrillation specific consumables are accounted at full cost. The 10 year NPV cost, shown in Table 24, is $589,003.

Table 24. 10 year NPV marginal cost analysis for adding 1 additional BLS ambulance to EMS system, with 24% allocation to cardiac arrest response.

Ambulances	1									
Cardiac Arrest Response allocation	0.24									
Annual deployments	18									
					Year					
	1	2	3	4	5	6	7	8	9	10
Capital costs										
Ambulance	$ 36,000									
Equipment	$ 9,600									
Consumables costs										
AED Pads	$ 1,080	$ 1,080	$ 1,080	$ 1,080	$ 1,080	$ 1,080	$ 1,080	$ 1,080	$ 1,080	$ 1,080
AED Battery	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680	$ 680
Recurring costs										
Crew	$ 65,894	$ 65,894	$ 65,894	$ 65,894	$ 65,894	$ 65,894	$ 65,894	$ 65,894	$ 65,894	$ 65,894
Maintenance/Insurance	$ 1,200	$ 1,200	$ 1,200	$ 1,200	$ 1,200	$ 1,200	$ 1,200	$ 1,200	$ 1,200	$ 1,200
Fuel	$ 1,800	$ 1,800	$ 1,800	$ 1,800	$ 1,800	$ 1,800	$ 1,800	$ 1,800	$ 1,800	$ 1,800
Total annual cost	**$ 116,254**	**$ 70,654**	**$ 70,654**	**$ 70,654**	**$ 70,654**	**$ 70,654**	**$ 70,654**	**$ 70,654**	**$ 70,654**	**$ 70,654**
Discount rate	5%									
10 year NPV cost	($589,003)									

To analyze the survival improvement, the additional ambulance was simulated with the existing Bellevue EMS response system. The new ambulance was based at the location of maximum distance from existing fire stations and the region boundary, such to maximize locational impact. This location was identified by finding the centroid of the 3 most distant fire stations, and the region boundary. I used an online geographic location calculator, Geo Midpoint [111], to obtain the centroid coordinates. Figure 41 shows the location of the additional ambulance base (latitude 47.604794, longitude -122.153048). The result of the simulation (5000 trials) was a mean survival probability of 0.21, with the 5th percentile at 0.15, and the 95th percentile at 0.26. This represents an increase in the mean survival probability of 0.01 over the existing 5 ambulance EMS system.

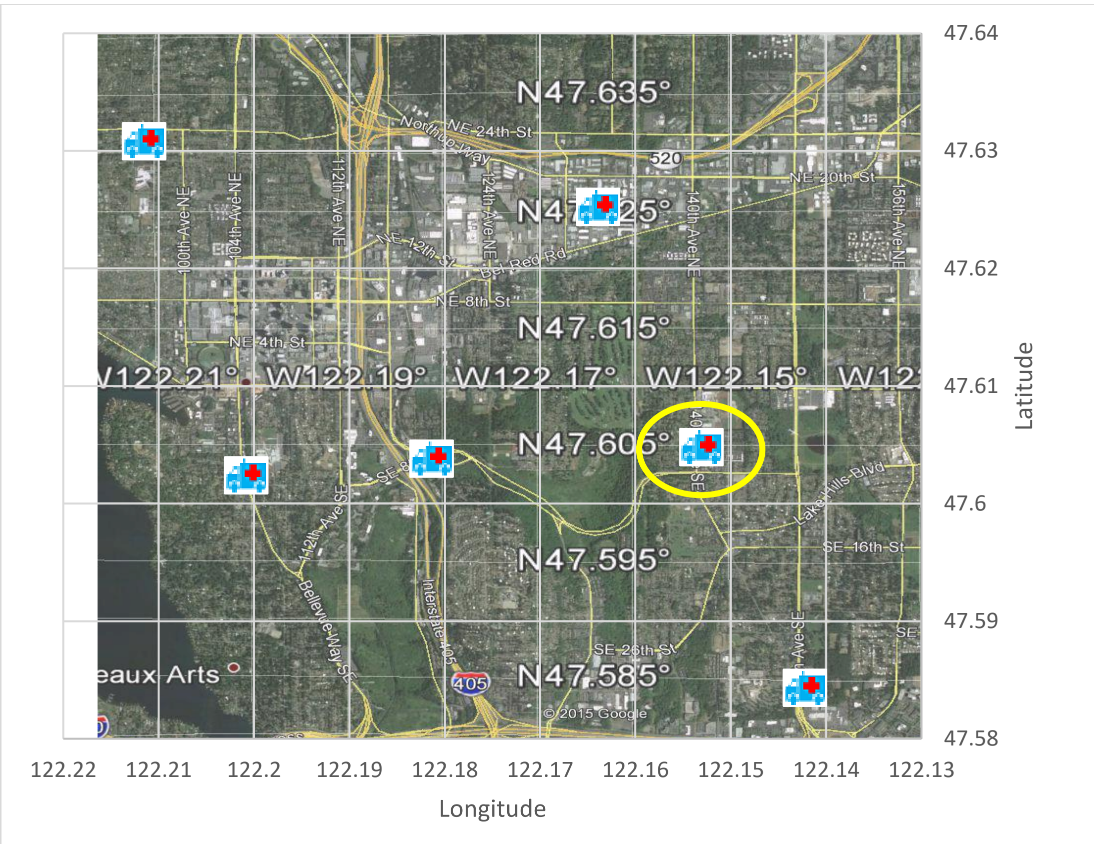


Figure 40. Location of additional ambulance base (shown circled).

7.5 Cost-benefit Comparison of Response System Alternatives

The predicted survival of each of the response system options was plotted against the 10 year NPV cost of implementing and operating the system. The results are shown in Figure 42. The red dashed line represents the Pareto frontier of the solution set. All systems not on this line are preferentially dominated by another system. The Pareto optimal solutions include the Pulse Point responder system, and the drone delivery systems in which a bystander applies and operates the AED.

It is noted that the Pulse Point system limits responses to cardiac arrest in public locations. The accounts for about 30% of all cardiac arrests, as the other 70% occur in private residences. The benefit in survival of the PulsePoint system determined in Chapter 6 has been reduced by 70% for this analysis. The survival improvement prediction is shown for the Pulse Point system with 320 responders (8 per sq. km) in the Bellevue region. With the current Pulse Point system, this amount is readily achievable, however it is not controlled. The Pulse Point system relies on community oriented volunteers to download the app in order to become a member of the system.

The drone AED delivery with bystander use system represents the most cost effective opportunity for improvement in survival. This advantage is primarily driven by the cost of the AEDs. The drone system requires only 6 AEDs, while a similarly performing ALERT system requires 320 AEDs. The drone system, however, is also the least mature of all options. It is only beginning to be piloted in limited locations. Some decision-makers may opt to pay a premium for a more mature system.

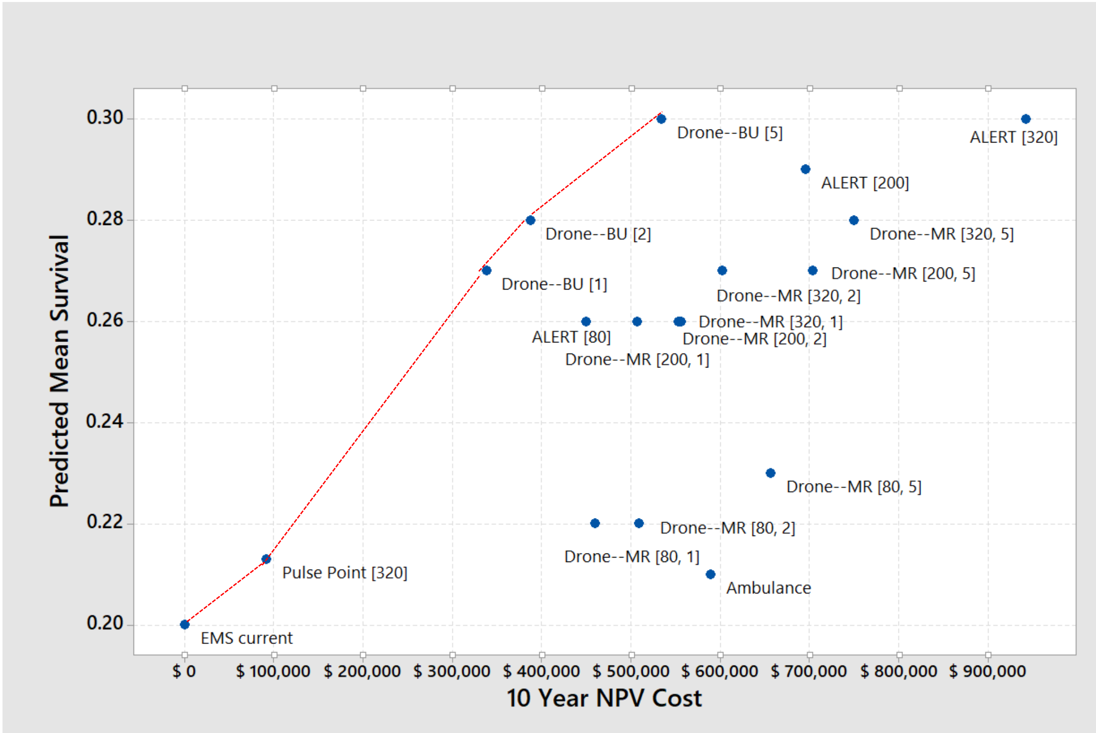


Figure 41. Decision chart of predicted mean survival against 10 year NPV cost. The red dotted line represents the Pareto frontier. The bracketed numbers indicate the mobile responders in the system (80, 200, or 320) or the number of drones in the system (1, 2, 5) or both in the drone – mobile responder system. Abbreviated system names are *Drone – BU* (Drone with bystander use of AED) and *Drone – MR* (Drone with mobile responder providing AED).

The costs associated with these systems are subject to significant variation and dynamic market conditions. For example, a large quantity purchase of AEDs could receive a significant discount over the retail price. As commercial drone package deliveries become more common, the cost of a drone's hardware and operations will likely decrease. Mobile responder networks which are organically grown, such as through non-profits, may be operationally less expensive than government funded systems. With such variation in these factors, the uncertainty of the costs is difficult to estimate. However, many of these systems share similar costs in their structure, and thus the system costs would scale equivalently with component cost variation. Figure 43 shows a stacked bar chart of each system 10 year NPV cost broken out by component 10 year NPV costs.

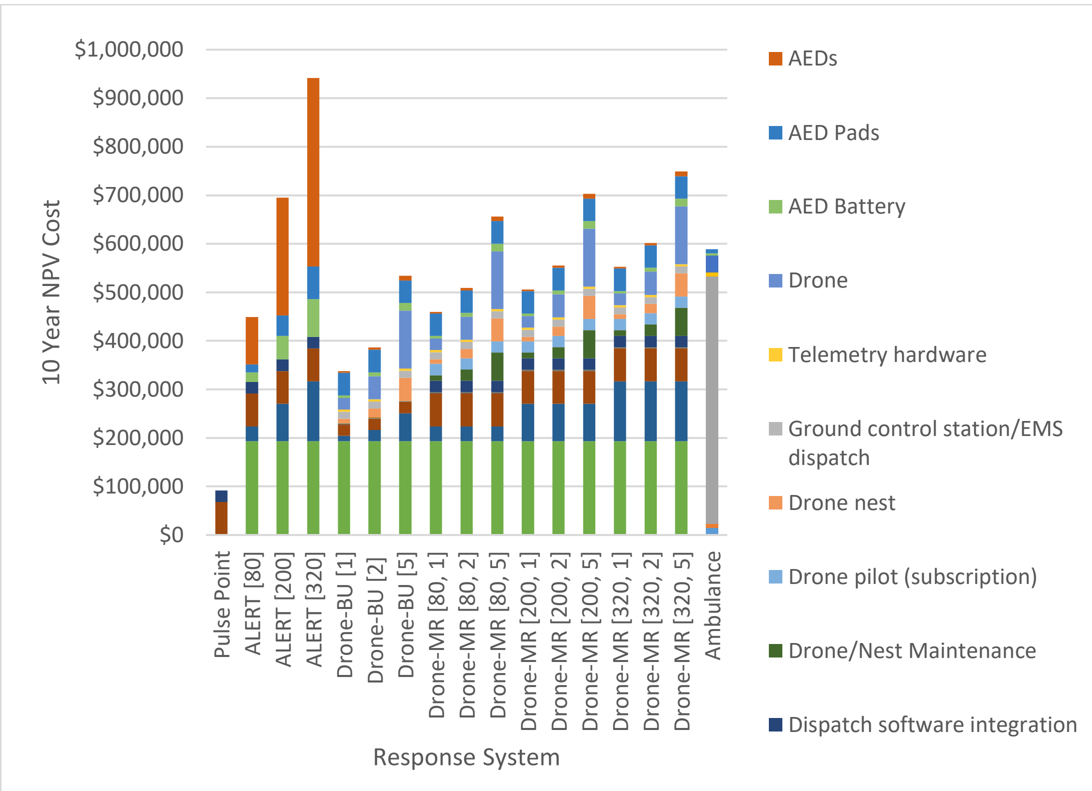


Figure 42. Stacked bar chart of response systems 10 year NPV costs.

7.6 Discussion of Model Application

This chapter described an approach to using the predictive survival model together with a cost analysis to determine the most efficient alternative to improve survival in a region. Above the current 20% survival rate, the marginal survival improvements from the Pareto optimal system choices range from 0.01 for a 10 year cost of $91,503(Pulse Point) to 0.1 with a cost of $534,009 (5 drones with bystander use). Budget availability, local drone regulations, and community preferences would dictate the choice of system from the Pareto optimal solutions. With an assumed 100 cardiac arrests per year within the Bellevue area, a marginal survival improvement of 1% (Pulse Point) would save an additional 1 life per year, while the maximum marginal improvement of 10% (5 drone system) would save 10 lives per year. With current United States VSL estimates ranging from $7 million to $12 million [99], all systems provide a strong benefit for the associated cost based on societal preferences. For the non-dominated alternatives, the expected cost (NPV) per life saved should be less than $100,000, which is much less than these values, which suggests that the benefits of these alternatives are worth the additional cost.

The use of Bellevue, Washington, as the example case region, essentially defines the low end of marginal survival improvement, as it has one of the top performing EMS systems in the United States. Regions with longer EMS response times, and lower survival, would realize significantly higher survival improvements. This would also apply to regions with low rates of bystander CPR, or minimal Public Access defibrillators. A study of 132 counties in the United States from the Resuscitation Outcomes Consortium found 50% had survival rates of 9.7% or less [112]. The greatest benefits of these types of systems could eventually be realized in developing countries, where EMS services are very limited. Hauswald, *et al.* estimated the cost of operating an EMS system in Kuala Lumpur, Malaysia, at approximately $2.5 million USD per year [113], and concluded "developing countries would do well to consider alternatives to a North American EMS model."

Chapter 8: Summary and Conclusions

Sudden cardiac arrest survival rates have remained stubbornly low despite decades of improvements in clinical therapy, along with the advent of the AED and public access defibrillation. While the treatment has been proven effective, the challenge remains providing the treatment in very short time to the cardiac arrest victim. It is widely recognized that EMS systems alone cannot provide this rapid treatment consistently and cost effectively. Public health and emergency medicine researchers, as well as operations research and systems engineering research, are now collaborating to develop systems that bring an AED to the cardiac arrest location quickly.

8.1 Summary of Research

The primary objective of this research was to develop a modelling and simulation approach to predict the response times and the corresponding survival likelihood. This work developed a geospatial model which was used to simulate the random locations of cardiac arrest events, which then predicted response times from nearby ambulance bases, drone bases, and randomly located mobile responders. The modelling approach included stochastic factors such as human reliability, AED reliability, ambulance availability, and drone availability to improve the fidelity to real world system operation. The approach applied Monte Carlo simulations to obtain distributions of simulated response times under stated system conditions. The model used the response time for CPR and defibrillation therapy as inputs into a logistic regression survival prediction model. The modelling and simulation approach was validated through event validity comparisons to published data, as well as face validity with subject matter experts in the emergency medicine domain.

I then used the validated model to both explore the conditions that most impacted response times, as well as compare the response times and predicted survival, both within a system, as conditions are varied, and between types of systems. Sensitivity analysis experiments revealed the most influential factors both at the event level of response times for the various responding agents, as well as at the system level, for the global response time to CPR and time to defibrillation predictions. With the strongest factors identified through the sensitivity analysis, an in-depth response surface method (RSM) design of experiments (DOE) was performed to identify interactions among factors, as well as characterize non-linear responses.

The objective of modelling and simulation is to provide insight for decisions where real world system data is not available. This research demonstrated that the modelling and simulation approach could be used to compare the effectiveness and potential improvement in survival of different types of response systems operating in a specific region. Several currently implemented or proposed system concepts were compared using the city of Bellevue, Washington as an example region, with their EMS response time and survival as a baseline. I estimated the implementation and operating costs of these various systems over a 10 year period. This thesis then presented a cost benefit analysis of the simulated response systems in a format which would aid decision-makers seeking to improve cardiac arrest survival within a community.

8.2 Conclusions

The motivation for this research was to answer the question: Can alternative cardiac arrest medical response systems provide a substantial improvement in survival for out-of-hospital cardiac arrest? The over-arching conclusion from this research is that the novel response systems, when operated synergistically with EMS, have the potential to take a significant step in improving cardiac arrest survival. Even further, they have the potential to do so in a very cost effective manner. The comparison of simulated systems in Bellevue, Washington, predicted an increase in probability of survival up to 10%. When compared to the current state of 20% survival, this represents an improvement ratio of 50%. As this simulation was compared against the baseline survival of a high performing EMS system, most communities could realize even greater survival improvement. As these response systems are implemented and mature, additional lifesaving treatments could be easily added, such as epinephrine auto-injectors to respond to anaphylactic shock, or naloxone (Narcan) nasal spray for rapid treatment of opioid overdoses [114][115]. These will even further magnify the life-saving potential of these systems.

Experimental exploration of the simulation model provided valuable information on how system attributes affect response time and survival. The significant conclusions are highlighted for each general type of response system.

Mobile Responder Systems

- Responder density in these types of systems intuitively affects response time, and such was demonstrated in model experiments. However, the response time is non-linear with responder density, and densities above 7 responders per square kilometer provide little additional improvement.
- Responder reliability essentially decreases responder density. Innovative or technological methods to improve responder reliability may be more efficient and effective than recruiting additional responders.
- Predictions of the mean response time of such systems is rather insensitive to the assumed geo-spatial distributions of cardiac arrest events and responder location. However, if the focus is on analyzing the longest of response time, the simulation will gain accuracy with better replication of the responder geospatial distribution. Further, to minimize the number of long response times, a system is best served by a responder location distribution that is similar to the cardiac arrest location distribution.

Drone AED Delivery Systems

- The time between the 911 call and the drone takeoff has a significant effect on the drone response time, particularly where the distances are relatively short (less than 5km). System operational strategies which minimize this time, such as initiating takeoff at the earliest identification of the medical call location, would optimize response times.

- Drone systems with multiple drones, even when based at different locations, provides redundancy benefit for the operational unavailability of the drones. However, the overall reliability of drones to respond is limited by the weather factor. The benefit of drone systems would be reduced in regions with low weather availability.

Drone AED delivery with Mobile Responder Systems

- Response systems which use drones to deliver an AED and dispatch mobile responders to the scene to apply the AED offer many operational advantages. The mobile responders are not required to carry an AED with them. The drone is always met by a trained responder who is experienced in applying the AED and CPR. However, this type of systems suffers in response time, as treatment is not started until both the drone and the responder have arrived at the location.
- Optimal use of this type of system requires balancing the number and location of drones with the density of mobile responders. An imbalance of either resource results in one agent arriving significantly faster, only to wait for the other to start treatment. The simulation model can be used to determine the appropriate balance between the number of drones and the mobile responder density.

This research additionally demonstrated that these novel response system concepts can deliver a cost efficient survival improvement, when evaluated with respect to the Value of Statistical Life (VSL). The comparison study indicated that both an ALERT type system and a drone AED delivery system with bystander AED use can deliver similar survival improvements, up to 10% incremental improvement. The drone system can provide this at a significantly lower lifecycle cost, which is primarily driven by the cost to provide each mobile responder with an AED in the ALERT system, while the drone system requires only a few AEDs.

8.3 Contributions

Significant prior work in the application of modelling and simulations to EMS response is reported in the literature, however, there is a dearth of published modelling applications to the alternative cardiac arrest response systems addressed in this dissertation. This research approach is the first to provide simulation capabilities of a diversity of types of response systems (drone, mobile responder, and combinations of each), such that comparisons of the performance and effectiveness of systems can be made. Further, this approach provides greater flexibility in tailoring the simulation to specific regional attributes (e.g. specific ambulance base locations and drone base location, weather patterns which affect drone availability), and system attributes (e.g. dispatch times, mobile responder reliability, ambulance availability) than existing simulation approaches.

The most consequential contribution of this research is likely the adaptability of the modeling approach to simulate a diverse variety of both existing and emerging response systems working together, as well as the integration of a cost model. Existing literature generally provides analysis to characterize the potential response time improvement that specific alternative response system approaches may provide. This research expands upon this, by applying the simulation of multiple alternative systems to a specific region, to predict which system, and under what conditions, would provide the best survival improvement. This is further expanded to include not only the survival improvement, but a cost benefit analysis of the improvement, in a decision analysis framework. It is this capability that will enable public health decision-makers to make better informed decisions around the allocation of resources, and ultimately increase the number of lives saved from cardiac arrest in their communities.

Prior modeling work has used finite, predetermined cardiac arrest locations in the models, either based on historic locations, or the centroid of small divisions of a region (e.g. census tracts). While such simplifications perform adequately for simulating response from fixed locations, the method does not extend well to modeling the location of randomly roaming responders. This modelling approach is unique in the replication of the aleatory uncertainty of cardiac arrest locations and the locations of cell phone dispatched mobile responders. The geospatial location sampling approach, from flexible spatial distributions generated by the Beta distribution, is not found in prior approaches. This approach enables greater accuracy to actual transit distance replication, both through the integration with the Google Maps routing API, and the use of the Minkowski distance approximation. These approaches support both the flexibility and fidelity of the model predictions.

The focus of much prior research has been on determining the optimal location for EMS dispatch bases, AEDs, and drone bases. Limited work has been published on the performance of these emerging systems, specifically when accounting for additional factors other than simply origin and destination locations. Some models incorporate the time of the day into the response equation, but very little work has been done around the reliability of both the human and machine elements within the system. These factors impact system performance, and neglecting these effects could result in overly optimistic predictions of system efficacy. This research addressed this gap by incorporating the effects of ambulance availability, responder reliability, drone operational availability, and drone weather availability into the distance based response time simulation.

8.4 Limitations

8.4.1 Model Limitations

The developed model makes a number of assumptions which simplify the logic and algorithms. One such assumption is the choice of a mobile responder to walk or drive to the cardiac arrest location. This aligns with the operation of most current real world citizen responder systems. The model applies the minimum of the walking and driving response times, implying the responder has perfect knowledge of the best mode of transit. While with most actual cases the best transit mode would be intuitive to the responder based on distance to the cardiac arrest location, there would be some cases where the responder chooses the non-optimal transit mode.

A simplifying assumption applied is that all events occur on a two dimensional surface, i.e. the "ground floor". In the real world, cardiac arrests may occur in buildings above the first floor. Additionally, mobile responders my originate in locations above the first floor at the time of the cell phone app alert. This would result in additional vertical transit time, which is not accounted for in the model. Thus, the actual response time, and corresponding survival likelihood, would be optimistically predicted in such cases. However, this simplification applies to all types of responding agents, including EMS, and thus has little effect on relative comparisons of response times and survival probability.

Assumptions around the drone response factors assume some exemptions are granted to current FAA drone regulations. This includes flying beyond the visual line of site, flying at night, and autonomous or remote piloting. Thus the model assumes *anticipated* drone system conditions, but not necessarily current drone conditions.

In the simulation of a system with drone AED delivery and bystander application of the AED, it is assumed that there is always a bystander available and willing, and that this person immediately retrieves the AED upon drone arrival. Real world test programs will reveal the prevalence of these conditions, and any potential additional delay times that should be included.

The Minkowski distance approximation method is computationally efficient, but works best in regions with a fairly uniform road network, and with no significant geographical obstacles (e.g. lakes, rivers, mountains) that must be circumnavigated. Application of this modeling and simulation approach to regions with such features should use an actual street network routing algorithm (e.g. Google Maps API). This research demonstrated this capability, but only applied this for validation purposes.

The logistic regression survival prediction model was published in 1997. It is based on data collected between 1976 and 1993. Improvements in Advanced Cardiac Life Support (e.g. high quality CPR) and post cardiac arrest hospital care have resulted in a modest survival improvement. Thus the logistic model marginally underestimates current survival rates. The possibility of bystander CPR and a nearby PAD AED are not accounted for in this research approach, as these are uncontrolled, random events, which would occur with all systems. The survival improvement from these effects can range from negligible to very significant, based on regional characteristics. This represents another source of underestimation of the actual survival rate in a region, however it has little effect on relative comparisons of systems (i.e. the marginal survival improvement).

8.4.2 Research Approach Limitations

The validation approach to the model was to assume these are non-existent system concepts. While accurate in some cases, e.g. the drone-mobile responder system, other systems have been implemented (PulsePoint) or are in trial studies (ALERT). For those systems which are implemented, very limited data is available to use for empirical model validation. This was limited a small number of "events", or intermediate calculations. The global responses could not be empirically validated, and thus there is no measure of precision of the predictions. Face validation provided a subjective support for the credibility of the model predictions.

Sensitivity analysis experiments were performed with all factors at "nominal", or best estimate settings for the city of Bellevue, Washington. The range of factor variation in the experiments were based on reasonable ranges for the system and region. Thus the sensitivity analysis evaluated both factor uncertainty, as well as the mathematical functions in the model, and should be interpreted accordingly. Reducing uncertainty in some factors, such as drone dispatch delay, would likely result in the factor being less influential on response time, with other factors rising on the tornado diagram. Further, as sensitivity analysis is a one-factor-at-a-time type experiment, important interactions would not be apparent in the analysis.

Factor interactions were analyzed in the Response Surface Method Design of Experiments. However, even when choosing efficient experimental designs, the number of experimental runs increases exponentially with the number of factors evaluated. This resulted in limiting the DOE to 5 factors, with some factor interactions and non-linear responses potentially unidentified.

The use of Bellevue, Washington as the example region for the model experimentation and application analysis could lead to conclusions that are not extendable to all regions. The most significant regional differences are the locations, and quantity, of EMS ambulance bases, as well as road network variations. Additional system specific variations, such as dispatch delay times, and chute times, likely exist as well.

Many of the components in the cost analysis have significant variation. For example, an ambulance vehicle cost may range from $100,000 to $200,000, depending on the type of ambulance. Drone costs have a broad range as well, depending on level of autonomy, redundancy, and durability, as well as payload and flight range specifications. This research used general estimates from published sources or discussions with subject matter experts.

8.5 Future Work

8.5.1 Model Enhancements

This research demonstrated the capability to incorporate road network routing algorithms (e.g. Google Maps API) into the simulation. The limitations of this approach, both in relatively high cost and computational efficiency, led to the development of the Minkowski distance approximation approach. The approximation approach is not adequate for regions with large geographical barriers, such as rivers, lakes, and hills. The road network route approach may become more economically and computationally feasible as new cloud based routing services are available, such as Mapbox [116] and the Open Source Routing Machine [117], which both provide APIs utilizing the Open Street Map [118].

Although Public Access Defibrillation (PAD) was not incorporated into the simulation model for this dissertation, due to the focus of this research on new, emerging systems, there is still significant interest and research on improving PAD systems. This includes optimizing the location of publically available AEDs [119] [120], and using cell phone apps to dispatch citizen responders to retrieve PAD AEDs [54]. The simulation model could be enhanced to provide predictions for such a system, and this system in conjunction with other types of response systems.

Real world studies and piloting of these novel systems may uncover additional stochastic factors, which could be added to improve the precision of the model predictions. This would include the likelihood of bystander CPR, and the time reduction in CPR therapy it would provide. It may also include additional human reliability factors, such as the likelihood that a bystander is capable and willing to retrieve and use a drone delivered AED.

8.5.2 Model Validation

This research approach relied upon face validation with some support from empirical event validation. As data is collected from studies of these novel systems, an empirical validation of the global responses could be performed. "Breadcrumb" data (GPS tracks) from actual mobile responder transits, along with timestamps of 911 call, EMS dispatch, and cell phone app alert activation, and arrival times, can be collected by systems such as PulsePoint. This data can be used to perform an empirical validation for the response times.

Appendices

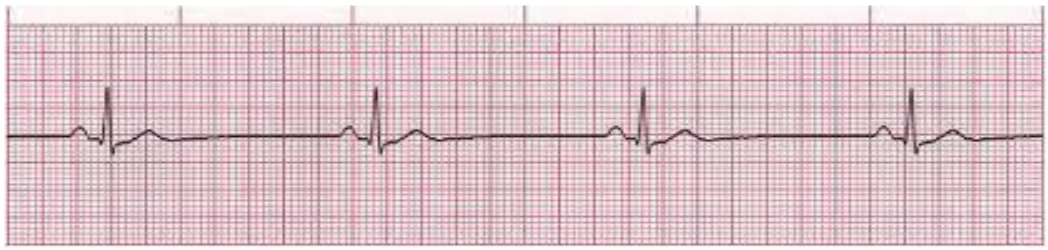
Appendix A: Physiology and Treatment of Cardiac Arrests

The human heart may be described by a mechanical analog as two side by side two-stage pumps. The right atrium and right ventricle act as a two-stage pump to draw oxygen depleted, carbon dioxide rich blood that has circulated to organs within the body, and provide high pressure to circulate the blood through the lungs. The left atrium and ventricle draw freshly oxygenated blood from the lungs to circulate throughout the body. The pumps share an electrical control system called the Sinoatrial node, which are cells that spontaneously produce an electrical impulse. The electrical pulse travels first across the right and left atria, causing the muscle to contract and force the blood content of the atria into the ventricle. After passing over the atria, the electrical pulse flows through the Atrioventricular node, briefly delaying the signal before it conducts across the ventricles, causing contraction of the muscle cells forcing the blood to the lungs and bodily organs. It is the precise timing and coordination of the contractions that allow for efficient generation of sufficient systolic pressure to circulate blood throughout the body. The electrical potentials created by the impulse propagating around the heart can be measured with an electrocardiogram (ECG).

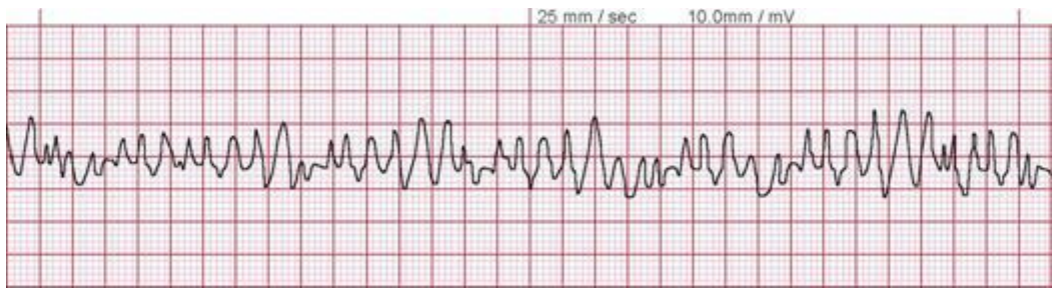
Normal, healthy functioning electrical conduction of the heart is known as a Sinus rhythm. An irregular electrical rhythm of the heart is known as a cardiac arrhythmia. Arrhythmias fall into four categories:

1. Premature heart beats, where extra or early atrial or ventricular contractions occur
2. Supraventricular tachycardia, an abnormally fast rhythm in the atria e.g. atrial fibrillation
3. Bradyarrhythmias, an abnormally slow heartrate e.g. bradycardia
4. Ventricular arrhythmias, which include ventricular fibrillation and ventricular tachycardia.

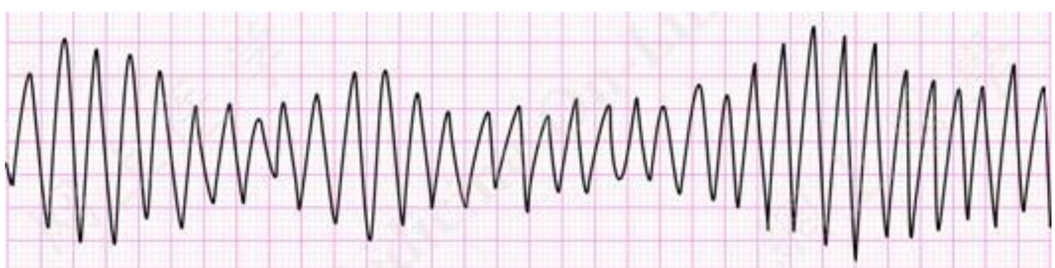
Most arrhythmias are treatable conditions through medication or the use of a pacemaker, and do not represent an acute medical risk, however the ventricular arrhythmias are the most common cause of cardiac arrest and require immediate medical treatment. In ventricular fibrillation (VF), the heart muscles are quivering rapidly and chaotically, preventing them from fully contracting and moving blood. Ventricular tachycardia (VT) is another arrhythmia in which the heart beats very rapidly, with a heart rate greater than 120 beats per minute. Both VF and VT require a defibrillatory shock to return the heart to a normal sinus rhythm.



a) Normal Sinus Rhythm



b) Ventricular Fibrillation (VF)



c) Ventricular Tachycardia (VT)

Figure 44. ECG strips of a) normal sinus rhythm; b) VF; and c) VT.

The arrhythmias are identified through the use of an ECG. The lack of a heart rhythm is known as asystole, and is commonly called a “flat line” due to its appearance on an ECG. A patient in asystole will have receive no benefit from a defibrillatory shock.

Modern day treatment for patients with out-of-hospital occurrences of cardiac arrest can be described by the “Chain of Survival”. In 1991, the American Heart

Association published a state of the art review titled *Improving Survival From Sudden Cardiac Arrest: The "Chain of Survival" Concept* [121]. It describes a sequence of actions that need to occur as quickly as possible after the onset of the cardiac arrest in order to maximize the likelihood of survival. The sequence of actions, depicted as links of a chain, are 1) Early recognition of the arrest and activation of the emergency response system; 2) immediate application of Cardiopulmonary Resuscitation (CPR); 3) early defibrillation; 4) and early Advanced Cardiac Life Support services.

The first action requires the cardiac arrest to be witnessed. Unwitnessed arrests have little to no chance for survival, as the victim is unconscious and unable to call for help. Unless the victim is quickly discovered, the prognosis for survival likelihood is essentially zero.

The second action is the application of high quality CPR. The act of compressing a patient's chest forcefully with the palm of the rescuers hands can induce blood flow from the heart through the lungs and from the heart to the brain, even while the heart is incapable of pumping blood on its own. The artificial ventilation provides oxygenation of the blood through the lungs. CPR can delay neurological damage due to hypoxia and can extend the brief time period for effective defibrillation.

The third action, early defibrillation, is critical to the chances of survival. Defibrillation is the application of an electrical shock across the torso, with the intent of disrupting the arrhythmia and restarting a normal sinus rhythm. Modern defibrillators administer the shock through the discharge of a high voltage capacitor through electrode pads coupled to the patient's skin with a conductive gel. Defibrillation dosage is measured by the energy of the shock delivered. Early defibrillators delivered a monophasic shock waveform, typically in the 200 to 300 Joule energy dosage. More recently, defibrillators have used a biphasic shock waveform, in which the discharged current direction is reversed midway through the shock. Biphasic shocks provide improved defibrillation efficacy at a lower energy (150 Joules), with reduced potential for burns to the skin or damage to heart tissue.

The fourth action is the early administration of Advanced Cardia Life Support (ACLS) by EMS. ACLS is a collective term for a range of clinical interventions for cardiac arrest by providers with advanced training in cardiac care. This includes the ability to read and interpret an ECG and a patient's vital signs, the intravenous delivery of pharmacological drugs, and endotracheal intubation. Drugs used on cardiac arrest patients include epinephrine, atropine, and antiarrhythmic drugs. In the United States, ACLS for out-of-hospital cardiac arrest is primarily provided by paramedics, while other countries may use nurses, or physician manned ambulances.

Appendix B: AED Function and Operation

The invention of the Automated External Defibrillator (AED) created a potential breakthrough in treatment and survival for sudden cardiac arrest. AEDs allow untrained “lay responders” to provide the same medical defibrillation shock treatment that previously was only provided by clinically trained professionals. The devices are relatively inexpensive ($800 to $2500), easy to use with minimal or no training, and extremely safe to operate. AEDs offer a simple user interface, often with guidance by voice prompts and visual icons. Many AEDs will provide CPR coaching through voice prompts and metronome tones in addition to providing a defibrillatory shock. One study showed that sixth grade students could operate an AED as well as adults [122].

At its basic functional level, an AED will acquire an ECG from the patient, algorithmically analyze the ECG to determine if the patient has a “shockable rhythm” (ventricular fibrillation or ventricular tachycardia), and deliver an electrical shock to the patient’s heart if needed. The ECG is acquired through the placement of adhesive electrode pads on the patient’s torso (upper right chest and left ribcage). An impedance measurement across the pads ensures that the pads are properly adhered to a human body. An analog micro-voltage signal detected by the pads is converted into a digital signal, upon which filtering and signal processing can remove signal artifacts due to patient’s muscular movements, capacitive coupling of the device to other electrical potentials, and implantable pacemaker signal. A shock decision algorithm then analyzes the ECG signal for a shockable rhythm, and if found readies the device to deliver a shock. A capacitor is charged to around 2000 V. The device will prompt the user to clear hands from the patient and press a button to deliver the shock. After shock delivery, the device will either resume ECG analysis, to determine if the shock successfully restored a normal sinus rhythm or if additional shocks are needed. If configured, the device may pause the analysis for 2 minutes to provide CPR to the patient. Recent advances in algorithms and have allowed the analysis of the ECG during the provision of CPR, resulting in faster shock delivery when required, and less “hands off time”, i.e. time without CPR performed.

AEDs are designed with features that enable safe and reliable operation. They operate off low voltage battery sources, and while in standby, do not store any high voltage energy. They only charge the capacitor to high voltage seconds before the shock is delivered, and if the shock is not delivered or the algorithm detects a change to a non-shockable rhythm, the device will discharge the capacitor into an internal load. The algorithm provides high specificity in its shock decision, while sacrificing some sensitivity, such as to prevent the possibility of delivering a shock when not needed. The devices run periodic self diagnostic tests when stored in standby, which exercise and verify the essential functions of the device, including the charging of the capacitor and delivery of a shock into an internal load. The high frequency of self tests relative to the low frequency of clinical therapy uses ensures that rare failures are detected and addressed without impacting a therapy use.

AEDs are designed to minimize user required maintenance. The device itself is maintenance free, with the exception of the periodic replacement of the pads and batteries. These must be replaced every two to four years. The pads contain a hydrogel adhesive that will lose conductivity and adhesion as it dries over time. Even stored in a sealed package, the useful life the pads ranges from 2 to 4 years. The pads must also be replaced after a patient use. The battery will deplete over a period of about 4 years, due primarily to energy consumption to run the periodic self diagnostics.

Appendix C: Pseudocode for Model

```
Program Uniform Random Responder
//Define simulation region
READ nwLatitude, nwLongitude, seLatitude, seLongitude
//Calculate conversion of degrees latitude and longitude to km
        COMPUTE convertLat=111.13292-
        0.55982*Cosine(2*nwLatitude*Pi/180)+0.001175*
        Cosine(4*nwLatitude*Pi/180)-0.0000023* Cosine(6*nwLatitude*Pi/180)
        COMPUTE convertLon=111.41284* Cosine(1*nwLatitude*Pi/180)-0.0935*
        Cosine(3*nwLatitude*Pi/180)+0.000118* Cosine(5*nwLatitude*Pi/180)

//Assign cardiac arrest location
READ alpha, beta
GENERATE random number cardiacArrestLat=Beta distribution [nwLatitude,
seLatitude, alpha, beta]
GENERATE random number cardiacArrestLon=Beta distribution [nwLongitude,
seLongitude, alpha, beta]

//Assign responder locations, compute distance to cardiac arrest location and travel
time
READ numberResponders, MinkdistWalk, MinkdistDrive, MinkBias, walkSpeed,
driveSpeed, dispatchDelayTime, walkDelayTime, driveDelayTime,
responderReliability, alpha, beta
Set i=1
WHILE numberResponders<=i
        GENERATE random number respLat(i)=Beta distribution [nwLatitude,
seLatitude, alpha, beta]
        GENERATE random number respLon(i)=Beta distribution [nwLongitude,
        seLongitude, alpha, beta]
        GENERATE random number respReliability(i)=Uniform distribution[0,1]
//Calculate the walk distance between responder i and cardiac arrest location
        COMPUTE walkdist(i)=[|(cardiacArrestLat- respLat(i))* convertLat|^
        MinkdistWalk +|(cardiacArrestLon- respLon(i))* convertLon|^
        MinkdistWalk]^(1/ MinkdistWalk)
//Calculate the walk time for responder i to cardiac arrest
        COMPUTE walkTime(i)= dispatchDelayTime+
        walkDelayTime+walkdist(i)*60/walkSpeed
        IF respReliability(i)>responderReliability
        THEN "N/A"← walkTime(i)
        ELSE walkTime(i)
// Calculate the drive distance between responder i and cardiac arrest location
        COMPUTE drivedist(i)=MinkBias*[|(cardiacArrestLat- respLat(i))*
        convertLat|^ MinkdistDrive +|(cardiacArrestLon- respLon(i))* convertLon|^
        MinkdistDrive]^(1/ MinkdistDrive)
```

```
//Calculate the drive time for responder i to cardiac arrest
        COMPUTE driveTime(i)= dispatchDelayTime+
        driveDelayTime+walkdist(i)*60/driveSpeed
        IF respReliability(i)>responderReliability
        THEN "N/A"← driveTime(i)
        ELSE driveTime(i)

i ← i+1
END WHILE

//Find fastest responder and assign AED functionality
READ aedReliability
COMPUTE firstArriveWalk= min {walkTime(i): i=1, …, numberResponders}
COMPUTE firstArriveDrive= min {driveTime(i): i=1, …, numberResponders}
COMPUTE firstArriveBest= min {firstArriveWalk, firstArriveDrive}
GENERATE random number aedReliabilityFirst=Uniform distribution[0,1]
IF aedReliabilityFirst<aedReliability,
        THEN WRITE "YES"
        ELSE WRITE "NO"

//Find second fastest responder and assign AED functionality
DEFINE function SMALL(m) to return the m^th smallest value in set of i values
COMPUTE secondArriveWalk= SMALL(2) {walkTime(i): i=1, …,
numberResponders}
COMPUTE secondArriveDrive= SMALL(2)  {driveTime(i): i=1, …,
numberResponders}
COMPUTE secondArriveBest= min {secondArriveWalk, secondArriveDrive}
GENERATE random number aedReliabilitySecond=Uniform distribution[0,1]
IF aedReliabilitySecond<aedReliability,
        THEN WRITE "YES"
        ELSE WRITE "NO"
//Find third fastest responder and assign AED functionality
COMPUTE thirdArriveWalk= SMALL(2) {walkTime(i): i=1, …,
numberResponders}
COMPUTE thirdArriveDrive= SMALL(2)  {driveTime(i): i=1, …,
numberResponders}
COMPUTE thirdArriveBest= min {thirdArriveWalk, thirdArriveDrive}
GENERATE random number aedReliabilityThird=Uniform distribution[0,1]
IF aedReliabilityThird<aedReliability,
        THEN WRITE "YES"
        ELSE WRITE "NO"

//Calculate number or responders within 1 km walk distance
k=0
i=1
WHILE i<=numberResponders
```

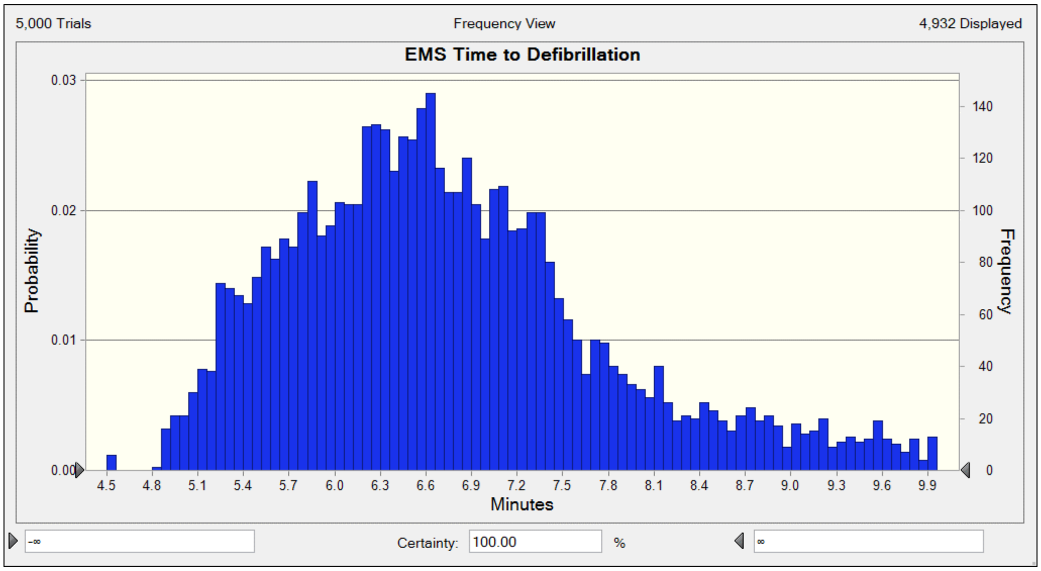
```
        IF walkDist(i)<1 THEN k←k+1
        ELSE k=k
        i←i+1
END WHILE

//Calculate number or responders within 1 km drive distance
m=0
i=1
WHILE i<=numberResponders
        IF driveDist(i)<1 THEN m←m+1
        ELSE m=m
        i←i+1
END WHILE

//Compute distance from EMS dispatch stations to cardiac arrest and compute
response time
READ numberEMS, emsLat(j), emsLon(j), chuteTime, emsDriveSpeed,
ambulanceAvail
Set j=1
WHILE numberEMS<=j
// Calculate the distance between EMS location j and cardiac arrest location
        COMPUTE emsDist(j)=[|(cardiacArrestLat- emsLat(j))* convertLat|^
        MinkdistDrive +|(cardiacArrestLon- emsLon(j))* convertLon|^
        MinkdistDrive]^(1/ MinkdistDrive)

//Calculate the drive time for EMS location j to cardiac arrest
        COMPUTE emsDriveTime(j)= chuteTime+emsDist(j)*60/ emsDriveSpeed
        GENERATE random number ambAvail=Uniform distribution[0,1]
        IF ambAvail(i)>ambulanceAvail
        THEN "N/A"← emsDriveTime(j)
        ELSE emsDriveTime(j)

j ← j+1
END WHILE
//Find fastest EMS response time
COMPUTE emsArrive= min{emsDriveTime(j): j=1,…, numberEMS}

//Calculate difference between EMS arrival time and first responder arrival time
COMPUTE deltaArriveTime=emsArrive- firstArriveBest
WRITE deltaArriveTime

//Calculate probability of survival with responder system
COMPUTE timeToCPR=minimum[emsArrive,firstArriveBest]
COMPUTE timeToDefib=minimum[emsArrive, lowest rank[firstArriveBest,
secondArriveBest, thirdArriveBest, where AED reliability =”YES”]]
COMPUTE systemL=0.26-0.106*timeToCPR-0.139*timeToDefib
```

```
COMPUTE probSurvival=(e^systemL)/(e^systemL+1)
WRITE probSurvival

//Calculate probability of survival of EMS only system
COMPUTE emsL=0.26-0.106*emsArrive-0.139*emsArrive
COMPUTE emsSurvival=(e^emsL)/(e^emsL+1)

WRITE emsSurvival
```

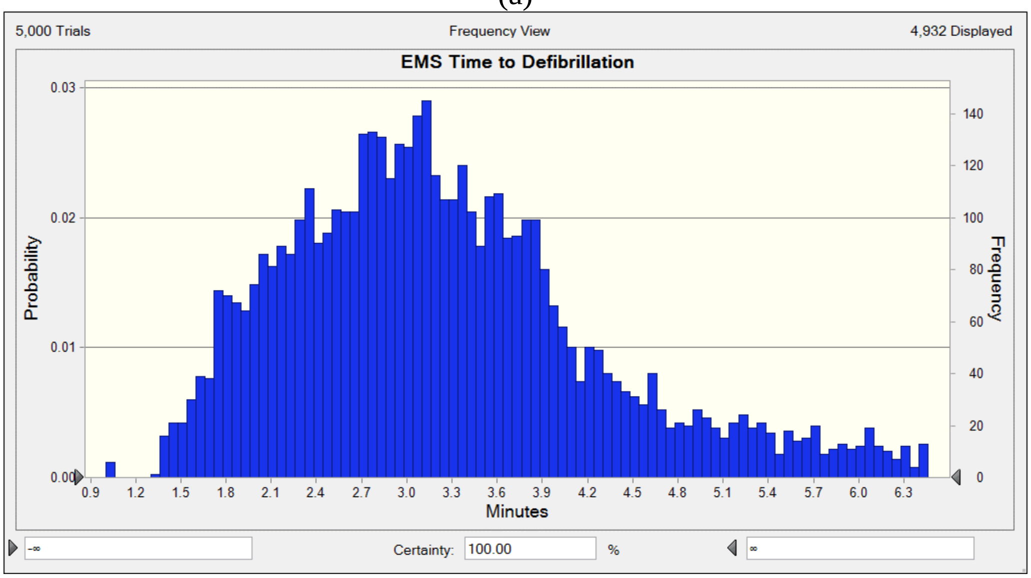
Appendix D: Select model verification and validation results

This appendix provides graphs that show the data from select validation tests. This includes representative results from extreme value tests, degenerative tests, and event validity tests used for the verification and operational validation of the model.

Extreme value tests were used to demonstrate the model provides stability and predictable results at the limiting values of model inputs. Figure 45 shows the effect of setting delay time to the limit of zero, i.e. no delay, on the time to defibrillation for EMS. Changing this delay (the sum of the EMS dispatch delay and the chute time) from 3.5 to 0 minutes results in an identical distribution of response times, shifted downward by 3.5 minutes. This same effect was observed when evaluating the response times of mobile responders and drones, when changing the various delay constants to 0.



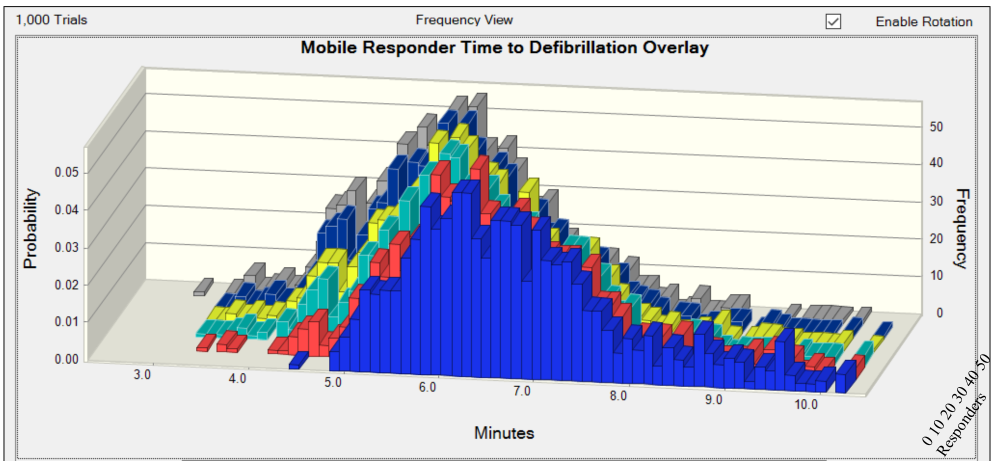
(a)



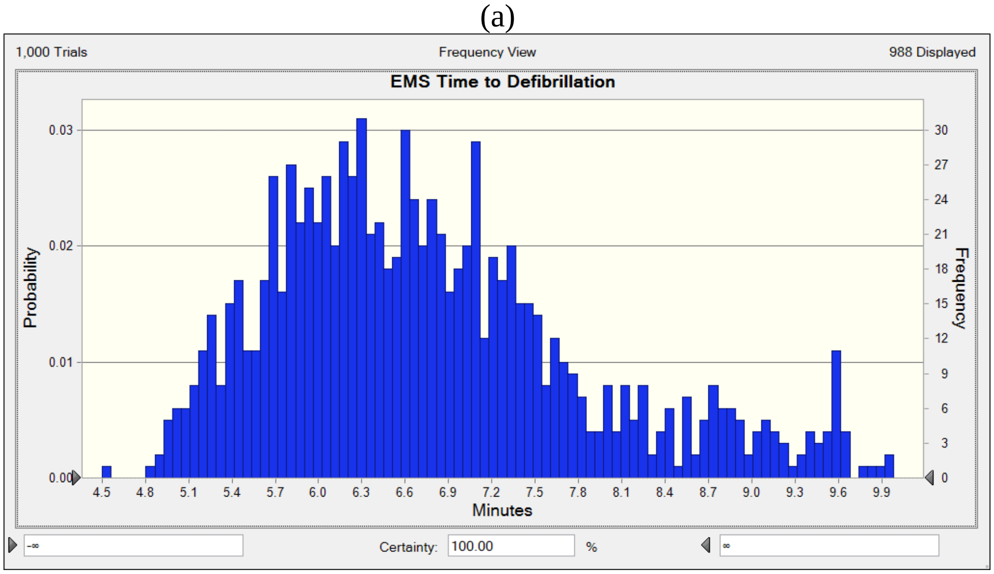
(b)

Figure 43. Extreme value verification test results showing EMS delay of (a) 3.5 minutes and (b) 0 minutes.

Degenerative tests are used to verify that as certain inputs to the model move toward extreme values, the model degenerates into a simpler system. In a system with mobile responders and EMS, as the number of mobile responders approaches zero, the system degenerates to a response system with only EMS. Figure 46 shows the test data that demonstrates this behavior. The time to defibrillation distribution with 0 mobile responders (the frontward, blue histogram) is identical to the model results for EMS alone. Similar results were obtained when reducing the number of drones to zero in a drone and EMS system, or when reduction the drone operational availability or weather availability to zero.



(a)



(b)

Figure 44. Data from degenerative test showing the effect of (a) reducing number of mobile responders from 50 to 0, with the distribution converging to (b) the EMS response distribution.

Event validity is the empirical validation of intermediate functions of the model when the global outputs cannot be empirically validated. Event validation consisted of comparison of simulated Bellevue EMS response times with response time statistics provided by King County EMS. Figure 47 shows simulated response time distribution for Bellevue, Washington, with the mean time of 5.8 minutes and the median time of 5.6 minutes. This compares closely with the actual response time of 4.9 minutes (mean) and 4.8 minutes (median).

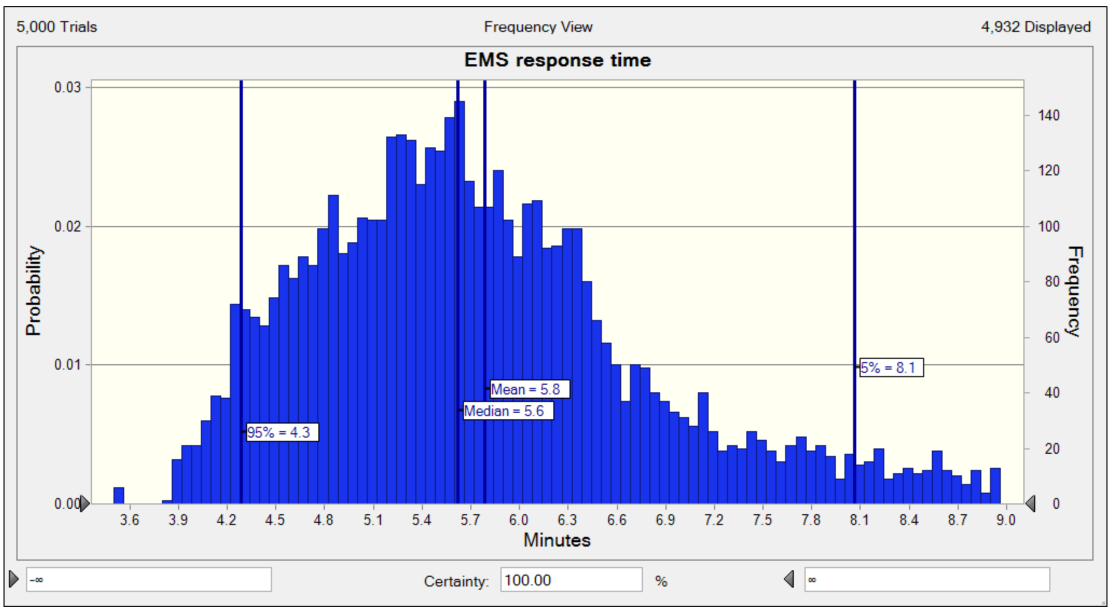
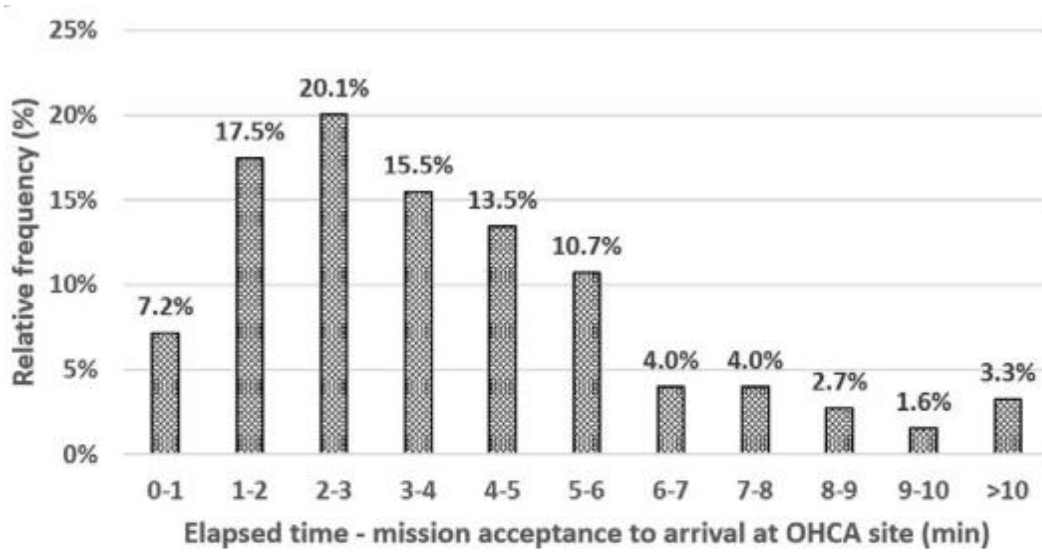
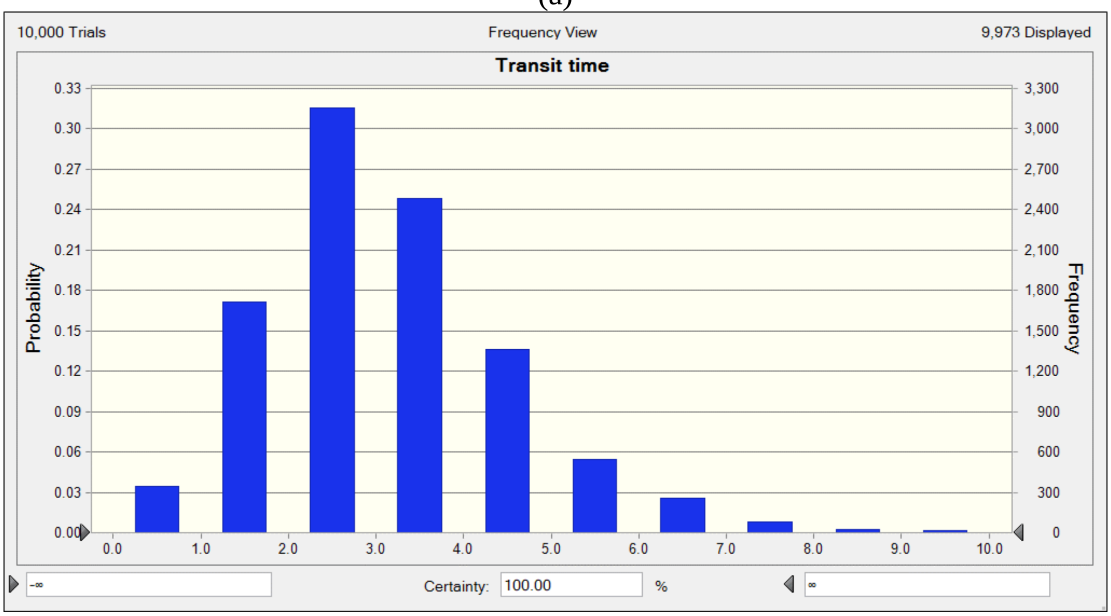


Figure 45. Distribution of simulated EMS response times in Bellevue, Washington.

Data published by Auricchio *et al.* [95] from a mobile responder study in Switzerland provided event validity comparisons for a couple of model functions. Although the article did not provide all the sufficient information to replicate the region with the model, some factor information was available, such as the distribution of response velocity, including both walking and driving responses. The distribution of response times after receiving the cell phone alert was also provided. Using reasonable assumptions for factors not discussed in the article, such as 2 responders per square km, and nominal delay times, the model predictions of cases where the mobile responder walked to the scene, versus cases where the responder drove, was compared to the data from the study. The study found 4.4% of cases resulted in the responder walking to the cardiac arrest location, with 95.6% choosing to drive. The simulation predicted 7% of the responses would be by walking, with 93% being by driving. A comparison of the distribution of response times reported in the article to the distribution of simulated response times is shown in Figure 48. The results show similar distributions.



(a)



(b)

Figure 46. Event data from the mobile responder study in Switzerland. (a) Data published by Auricchio et al. [95] response time distribution, with comparison to (b) simulated response time distribution.

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