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Emergency Medical Services Response Time and Mortality in an Urban Setting: A Retrospective Cohort Study

by

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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled " Emergency Medical Services Response Time and Mortality in an Urban Setting: A Retrospective Cohort Study" submitted by Ian Blanchard in partial fulfilment of the requirements of the degree of Masters of Science: Epidemiology.

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Abstract

Introduction: The Emergency Medical Services (EMS) standard is to respond to an emergency within eight minutes for 90% of events. Our hypothesis was that there would be no observable difference in all cause mortality stratified by an 8 minute response time.

Methods: Retrospective study of adult patients treated by Calgary EMS for a critical life-threatening event during one calendar year.

Results: The adjusted odds of mortality given a response time of ≥8 minutes is 1.19 times that of a response time <8 minutes (95% CI 0.97 – 1.47). The adjusted odds ratio of mortality for patients that die in the Emergency Department or as an in-patient were 1.07 (95% CI 0.76 – 1.53) and 1.30 (95% CI 1.00 – 1.69) respectively.

Conclusions: The eight minute response time was not associated with a difference in all cause mortality. Secondary analysis suggests some patients that might benefit from a rapid response.

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Dedication

To Anna, Petra, and Kyle for your love, patience, understanding, support, and guidance on what is really important in life.

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Symbol	Definition
AED	Automatic external defibrillator
ALS	Advanced life support
BLS	Basic life support
BLS-D	Basic life support with defibrillation
CAD	Computer aided dispatch
CFD	Calgary Fire Department
CHR	Calgary Health Region
CI	Confidence interval
CTAS	Canadian Triage and Acuity Scale
Determinant	The level of response assigned to the event (e.g., Echo, Delta, etc.)
ED	Emergency Department
EMD	Emergency Medical Dispatcher
EMS	Emergency Medical Services
EMT	Emergency Medical Technician
FMC	Foothills Medical Centre
HSAU	Health System Analysis Unit
IP	In-patient
IQR	Interquartile range
MB	Misclassification bias
MH	Mantel-Haenszel
MPDS	Medical Priority Dispatch System
NDMB	Non-differential misclassification bias
OR	Odds ratio
PCI	Percutaneous coronary intervention
PCR	Patient care record
PHAR	Prehospital arrest record
PHN	Personal health number
PLC	Peter Lougheed Centre
PRU	Paramedic response unit
RVH	Rockyview Hospital
SB	Selection bias
SD	Standard deviation
STEMI	ST elevation myocardial infarction
ULI	Unique lifetime identifier
VF	Ventricular fibrillation

Chapter One: Introduction

Modern Emergency Medical Services (EMS) systems are considered to have their origins with Jean Dominique Larrey, Napolean's chief physician.(1) He is credited with organizing a system to treat and transport injured French soldiers.

In the present day, many nations recognize the importance of EMS systems. Modern EMS bridges the gap between health and social systems and the community.(2)

A historically cherished aspect of EMS care is the urgent response to the scene of an emergency; in former times with bells and whistles and in contemporary times with lights and sirens.(3) EMS leaders continue to promulgate the clinical importance of rapid response capability. In North America, for example, a common response time target is an eight minute response time to life threatening emergencies on 90% of emergency events.(3-5) Recent research, however, calls into question the association between an expeditious response time and improved clinical outcome for the majority of patients attended by EMS systems.(6, 7) When these data are placed in the context of risk to the public and the mounting financial cost associated with maintaining and improving EMS operations, some EMS leaders have begun to question the need for rapid EMS response in the vast majority of cases.(8) Like many prehospital interventions, however, there is scant empirical data describing the impact of rapid response on patient outcome. There are no known studies in a Canadian

EMS system that have studied the association of response time with ED or in-patient mortality for the highest priority calls at the point of EMS activation.

This thesis will investigate the association between an EMS response time of 8 minutes and all-cause mortality in a large urban Canadian setting using a sample of events designated as critical life-threatening at the point of 911 call. It will further assess this association at the four and nine minute levels and restrict the analysis to emergency department patients, and patients subsequently admitted to the hospital.

Chapter Two: Literature Review

2.1 EMS system background and design

Two general types of EMS systems exist, one tier and two tiered. A one tier system dispatches a transport capable vehicle to all events, regardless of severity. A two tiered system dispatches a transport capable vehicle to all events, regardless of severity, and a first response (often non-transport capable) vehicle to certain events (i.e., usually life threatening). Both one and two tiered systems can be Basic Life Support (BLS), BLS with defibrillation capability (BLS-D), and/or Advanced Life Support (ALS) capable.(9) There are numerous combinations of two tiered systems, some examples include ALS transport capable vehicle dispatched on all calls and BLS transport capable vehicle dispatched if needed, both ALS and BLS transport capable vehicles dispatched on all calls, and ALS first response non-transport capable vehicle and BLS transport capable vehicle dispatched.(9)

BLS generally includes non-invasive procedures and limited pharmacology; BLS providers are often given the designation of Emergency Medical Technician (EMT). ALS generally includes a host of invasive procedures and pharmacology; ALS providers are often given the designation of Paramedic.(10)

Although myriad combinations of tier and level of care exist, for the purposes of this paper, EMS systems will be designated as either one or two tiered and BLS, BLS-D, or ALS. Two tiered system level of service will be designated with the first response level of service first, followed by the transport system level of service (e.g., BLS-D/ALS refers to a two tiered system with defibrillation capable BLS first responders and an ALS capable transport service). A common EMS system design in many major centres in Canada is a two tiered BLS-D/ALS system.

2.2 Study site characteristics

Calgary EMS is the sole provider of ambulance services to the citizens of Calgary. Its service area includes The City of Calgary, Tsuu T'ina Nation, the Town of Chestermere, and sections of the Municipal District of Rockyview.(2) In 2006 the population of The City of Calgary was 988,193, although the population serviced by Calgary EMS was likely higher due to visitors and service areas outside the city limits.(11)

Citizens access Calgary EMS through a 911 system. To meet demand Calgary EMS operates a total of 43 response vehicles.(2) Calgary EMS is an all ALS system, which means that every response vehicle is staffed by at least one Paramedic, and is equipped with ALS supplies. The City of Calgary Fire Department (CFD) provides a BLS-D first responder service that augments the Calgary EMS system; thus making the whole system two tiered BLS-D/ALS.

Calgary EMS provides all patient transports in this system using ambulances. In addition to ambulances, Calgary EMS operates vehicles that act as ALS first responders within the ALS tier of response. These vehicles are known as Paramedic Response Units (PRUs), and are staffed by one paramedic; as opposed to an ambulance which is staffed by two paramedics, or one paramedic and one EMT.(2) The rationale behind PRUs is the facilitation of rapid response at an ALS level of care at a lower cost relative to an ambulance (colloquially these vehicles are referred to as “clock stoppers” as they are generally deployed in areas where response times are long). The primary disadvantage of PRUs, however, is that they do not have the capacity to transport patients.

Calgary EMS response vehicles are dispatched according to event severity as assessed by a trained Emergency Medical Dispatcher (EMD) using the Medical Priority Dispatch System® (MPDS).(2, 12) The MPDS system prompts the EMD to ask key questions to elicit the event severity. Event severity is translated into a five level determinant ranging from Alpha (least serious) to Echo (most critical).(2, 12) The two highest priority events are Delta and Echo. In order to meet the criteria for this level of event, the caller must provide key information that would lead the EMD to conclude that this is a time-dependent life-threatening emergency. The primary difference between a Delta and Echo level event is that an Echo level event is a confirmed critical time-dependent life-threatening event (e.g., patient not breathing as confirmed by the EMD through the 911 caller, etc.).(2, 12)

The response to Delta and Echo level events is different to Alpha, Bravo, or Charlie events in that both tiers of the EMS system responds (i.e., CFD provides BLS-D first response and Calgary EMS provides ALS response and transport). In addition, to hasten ALS response a PRU may also be dispatched, depending on the proximity to the event location. All vehicles utilize lights and sirens to respond.(2)

Bravo and Charlie level events are potentially time dependent emergencies, and hence Calgary EMS vehicles are sent to the scene using lights and sirens. There is, however, only a single tier response (i.e., no response by CFD). Calgary EMS may dispatch a PRU to these events if an ambulance is not immediately available or close to the scene.(2)

Alpha level events are the lowest priority events and hence no lights and sirens are utilized. Vehicles responding to these events will be re-routed to higher priority events if required. (2)

The Calgary EMS response standards for these event types are summarized in Table 2.1.

Table 2.1: The City of Calgary Emergency Medical Services response standards.

MPDS Determinant	Response Time Standard	Response Time Standard Compliance Goal
Alpha	<15 min.	90% of all events
Bravo and Charlie	<10 min.	
Delta and Echo	< 8 min.	

Note: MPDS=Medical Priority Dispatch System®

2.3 Response time standards: A historical perspective

The current response time standard used in the majority of industrialized nations has its origins in findings from a 1979 retrospective cohort study by Eisenberg *et al.*(7, 13) This study was conducted in a two tiered BLS/ALS American EMS system. This influential study suggested that the time from collapse to the initiation of CPR and the time from collapse to definitive care should be less than 4 minutes and 8 minutes respectively to maximize survival to hospital discharge in patients with a witnessed cardiac arrest from primary heart disease. From this study a response time standard of less than four minutes for BLS units and less than eight minutes for ALS units was operationalized.(13) Although this standard was based on a study of witnessed adult prehospital cardiac arrest patients of a medical origin, the eight minute standard for ALS response was generalized to all patients requiring emergent response by EMS systems.(3, 14) In addition, the most common operationalized version of the recommendations from this study defines response time as the time from 911 call to arrival on-scene of an emergency vehicle, not time from patient collapse to administration of a critical intervention such as CPR or defibrillation as Eisenberg *et al.* describe.(2, 13).

More recent research has suggested that the most important prehospital intervention that increases the odds of survival from out-of-hospital cardiac arrest is defibrillation.(15, 16) Unlike EMS systems in 1979, defibrillation is no longer considered an ALS level intervention, and is available for use by BLS units and the lay public through automatic external defibrillators (AED's).(17) Other ALS interventions (e.g., endotracheal intubation, intravenous medication, etc.) have not been demonstrated to increase survival from prehospital cardiac arrest.(18, 19)

These contemporary EMS system characteristics and empirical cardiac arrest data, in addition to the common operationalized definition of response time as 911 call to arrival on-scene of an emergency vehicle, cast doubt on the clinical basis for the historical eight minute response time standard presently used as a quality assurance benchmark in ALS EMS systems. Moreover, some authors argue that emergent responses to prehospital cardiac arrest patients of a medical origin comprise less than 1% of emergency events in an EMS system; which further supports the need to explore the generalization of this rigid response time standard for the majority of EMS patients.(3, 7, 14, 20)

In addition to an eight minute response time standard, another aspect of the present standard is the percent compliance. Presently many systems use a 90% compliance target to the eight minute time standard. This 90% target has its origins in the work of Jack Stout and the public service utility model of EMS.(3) Locally, this criterion was a recommendation made in 1988 to Calgary City Council in a value for money audit.(21) This 90% target level has been widely adopted in spite of little empirical data supporting it.(3)

2.4 Components of an EMS response

Research involving EMS response intervals is problematic as inconsistent response time definitions have been used. To that end, Spaite *et al.* proposed a model of EMS time intervals that was validated by direct observation of emergency responses.(22) For the purposes of this study, some elements of this EMS time interval model will be applied. Specifically data exist for Calgary EMS that include time from 'call received' to 'alarm' (activation interval), time from 'alarm' to 'arrive scene' (response interval), time from 'arrive scene' to 'leave scene' (on-scene interval), and time from 'leave scene' to 'arrive hospital' (transport interval).

Response time is defined as the sum of the activation and response intervals; the post-arrival time is the sum of on-scene and transport intervals; and total prehospital time is defined as the sum of activation and response intervals (response time), plus the sum of on-scene and transport intervals (post-arrival time) (Figure 1).(22)

Some authors have suggested that EMS response time should include the time from arrival at scene to the time to initial patient contact (patient access interval) (N.B., not shown in Figure 1).(23, 24) Occasionally there are situations when EMS units are asked to "hold-back" until police services can arrive and ensure the safety of the scene. Moreover, there are situations where there may be a long patient access interval, such as a tall building or a patient located far from vehicular access. In any of these instances the recorded response time will underestimate the time from 'call received' to initial patient contact.

Others authors have suggested that response time should not only include time to initial patient contact, but also time to the application of a critical intervention.(3, 25) Moreover, it is not the time of the 911 call that may be important, but rather the exact time of injury or disease.(25, 26) Although these data would be useful, they are presently not available in most EMS systems including Calgary EMS.

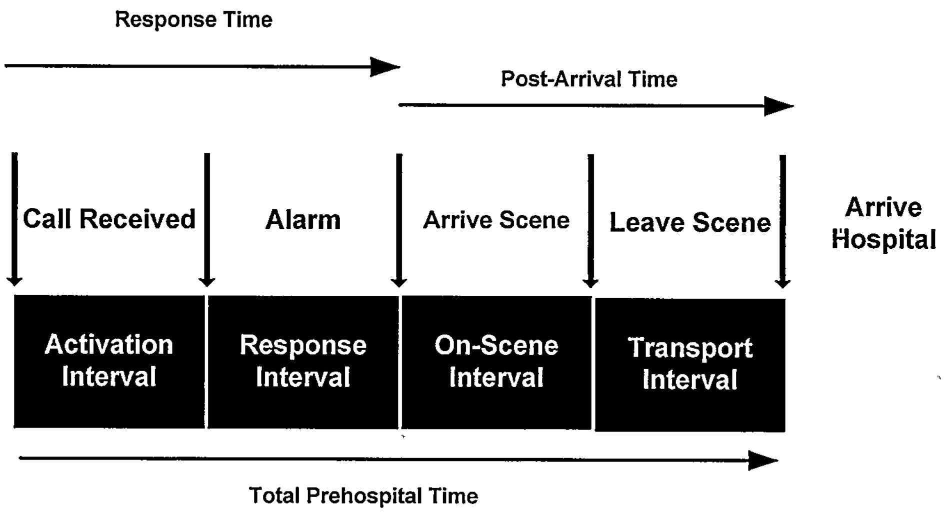

Figure 2.1: Time elements available from The City of Calgary Emergency Medical Services system. Adapted from Spaite *et al.*[20]

2.5 Response time and perspective

There are numerous perspectives that can be taken when assessing a response time standard. A response time standard, for example, may be logically viewed as a clinical intervention that can affect patient outcome (i.e., clinical perspective) or as a measure of citizen expectation (social perspective). Assessing the effectiveness of a response time standard may be dependent on the perspective. In the above clinical and social perspectives, what the general public perceives as the optimal response time standard may not necessarily correspond to what the empirical clinical evidence suggests. It therefore stands to reason that studies assessing response time standards should explicitly state the perspective(s) they are assessing.

2.6 The evidence for present response time standards from a clinical perspective

2.6.1 Response to all EMS patients

A summary of key findings from studies that include all EMS patients is found in Table 7.1.

A qualitative study on a purposive sample of Paramedics and EMT's in the United Kingdom reported by Price describes the effects on patient and prehospital personnel's health and safety while attempting to meet an eight minute response time standard.(27) Semi-structured interviews were conducted on 20 experienced paramedics with a mean level of service of 19 years. This group of paramedics reported that response time standards were not adequate as a performance indicator of EMS systems. Moreover, other quality indicators are not being considered because of the need to meet government response time standards. These paramedics feel that the response time standard is detrimental to patient care, and also has adverse effects on the health, safety, and morale of prehospital personnel. The authors conclude that the eight minute response time standard appears to lack an evidence base and may be putting patients and paramedics at risk.(27)

The most recently published quantitative study examining the relationship between response time and survival for all patients served by an EMS system is from a two tiered American BLS-D/ALS system.(7) This retrospective cohort study from Pons *et al.* (2005) defined response time using the previously presented definition of the sum of activation and response intervals. Mortality was defined as all-cause mortality measured at hospital discharge. The authors attempted to control for potential confounders, such as on-scene interval, transport interval, and age, sex and level of severity of patient. The exposure variable was determined *a priori* to be response time as a continuous variable and dichotomized at four and eight minutes. All emergency calls, defined as the use of lights and sirens, were considered for inclusion. The exposure outcome relationship was explored using multivariable logistic regression. The authors conclude that there was a survival benefit in this EMS system when response times were dichotomized as less than or greater than or equal to 4 minutes (OR=0.70; 95% CI=0.52 – 0.95). There was no statistically significant difference between the less than, or greater than or equal to 8 minute categories (OR=1.06; 95% CI=0.80 – 1.42), or with response time as a continuous variable (OR=1.01; 95% CI=0.98 – 1.04).(7)

Limitations to this study were that only events transported to a trauma centre were included in the sample, and events were stratified into risk categories based on dispatch call taker and emergency department (ED) diagnosis.(7) In addition, no sensitivity analyses were provided to assess the potential for misclassification of response time. Moreover, how multiple ambulance responses to the same event were handled was not explicitly provided (i.e., was it the response time of the first unit on-scene or the individual response time of each responding unit).

Blackwell and Kaufman (2002) examined the same relationship also using a retrospective cohort design in a two tiered BLS-D/ALS American EMS system.(6) The authors defined response time as the time from deriving the chief complaint or address of the patient, or 30 seconds after call receipt (whichever was shortest) to the time of arrival on-scene. Mortality was defined in the same manner as Pons *et al.* All emergency events (defined as the use of lights and sirens) that resulted in either a priority one (emergency life-threatening) or priority two (emergency non-life threatening) transport to the ED of the trauma centre were included. The authors found no significant difference between the median response time of survivors and non-survivors (6.4 and 6.8 minutes respectively; p=0.10). The response time mortality relationship was further explored by comparing the observed and expected (which assumed a uniform death proportion across all strata) proportion of death at each minute of response time. When observed minus expected deaths were plotted by response time categorized by minute, the observed deaths exceeded expected deaths at the five minute response time level. Further *post hoc* analysis revealed a significant difference between the response times of survivors versus non-survivors when response times were stratified at the five minute mark.

A secondary analysis in this study employed a convenience sample of physicians to determine if those that died would have survived if there had been a faster response time. The physicians agreed that 83% of non-survivors would not have survived with a faster response time. The positive effect of a faster response time on the remaining non-survivors was espoused by some of the physicians, but there was not universal agreement. This secondary analysis suggested that regardless of the length of the response time, certain patients may not survive.

Limitations of this study included: no multivariable analysis, important findings were based on exploratory analyses, and a full calendar year of data were not included in the sample (as types of events often have a seasonal variation).(6) Like Pons *et al.*, no sensitivity analyses were provided to account for possible systematic bias in the study design.

An early retrospective cohort study by Mayer based on data derived from a two tiered BLS/ALS American EMS system described a response time exposure and all-cause mortality relationship in a large urban setting.(28) Response time in this study was defined as the time from dispatch to arrival on-scene (i.e., response interval). Mortality was examined as an outcome, but it is unknown if all-cause mortality included those patients that died in the field, or only patients that received a transport. Moreover, the definition of mortality appeared to be outcome at hospital arrival, not at hospital discharge. When the response interval of the first arriving unit (which is BLS), categorized in three broad time strata from 0 to 3.99 minutes, 4 to 6.99 minutes, and greater than 7 minutes was stratified by all-cause mortality, there was no statistically significant difference ($p>0.25$). When response interval was categorized from 0 to greater than 15 minutes in one minute increments, the proportion of death increased from 31% in the under one minute category to 59% in the 1 to 2 minute category.

When these data were restricted to the ALS unit response only, and categorized as per the aforementioned three broad time strata, there was a significant difference between those that lived and died ($p<0.001$). When the ALS unit was stratified as per above in one minute increments, the obvious difference in proportion of death was between the 8 to 9 and 9 to 10 minute categories (60% to 83% mortality respectively).

Although this study has interesting results, EMS systems and the role of the public as a first responder have both changed substantially since 1979. Moreover, this study defines mortality at handover from EMS to the hospital system, not discharge from the hospital system. Finally, this study does not take into account potential confounders and effect measure modifiers such as age, gender, and post-arrival time. Nor does this study provide a quantitative assessment of potential systematic biases such as misclassification of response interval.(28)

2.6.2 Cardiac arrest patients

There is no single medical condition that has received more research in EMS than that of prehospital cardiac arrest. Despite the low prevalence of prehospital cardiac arrest events, when compared to the myriad other medical and traumatic conditions that EMS systems respond to, prehospital cardiac arrest has been well studied. Indeed, as mentioned previously, the eight minute response standard has its origins in prehospital cardiac arrest research.

Broadly, a cumulative meta-analysis of prehospital cardiac arrest studies in 1999 revealed interesting trends with respect to EMS system design.(15) The authors suggest that patients were more likely to survive when treated in a BLS-D/ALS EMS system. In addition, survival was improved with increased rates of bystander CPR, early defibrillation, and the provision of early ALS.(15) These findings suggest that ALS response time is important.

In stark contrast to these data, the Ontario Prehospital Advanced Life Support (OPALS) study group has suggested that systems with BLS-D /ALS, compared to BLS-D alone did not improve survival from cardiac arrest.(18, 19) The authors conclude that ALS does not improve survival from cardiac arrest, but bystander CPR and rapid defibrillation does. These findings suggest that ALS in general may not be an important factor in survival, regardless of response time.(18, 19)

When assessing the impact that response time has on cardiac arrest, it is often difficult to distinguish the role that ALS response time has on outcome.(29) For example, in many instances, but not all, a BLS-D first responder may arrive prior to the ALS ambulance. In instances where this does not occur, the arrival of the ALS ambulance may provide the initial defibrillatory shock; time to defibrillation has been demonstrated to be an important predictor of survival in certain cardiac arrest situations.(15, 18) In this instance the ALS ambulance response time may have been associated with survival, but does this support the notion of decreasing ALS ambulance response times or rather does it support bolstering the existing BLS-D first response program? Some authors would suggest the latter, due to the cost of the former.(30, 31)

One study has attempted to delineate this relationship. This prospective cohort study in a large urban two tiered BLS-D/ALS system concluded no benefit to a decreased interval of time between the arrival of the BLS-D unit and the arrival of the ALS unit.(32)

The debate in the literature regarding the contribution of ALS to cardiac arrest survival and the lack of causal evidence in the ALS ambulance response time and survival relationship has not altered the Chain of Survival model espoused by the International Liaison Committee on Resuscitation (ILCOR). This committee continues to recommend early ALS care as the fourth link in the chain of survival, but does not explicitly quantify 'early'.(17, 33)

The response time of an ALS ambulance may be important in this clinical sub-group. Not because the ambulance is ALS (19, 32), but rather because the ambulance carries a defibrillator, and time to defibrillation has been demonstrated in numerous systems (using varied methodology) to be associated with increased survival from hospital in some cardiac arrest patients.(29, 31, 34-36)

There are authors that would propose that response time defined as activation and response intervals may not be an appropriate proxy measure for the clinically important time from collapse to defibrillation.(25, 29, 34) The rationale for this is that certain key intervals as defined by Spaite *et al.* are missing (i.e., notification interval, patient access interval, and initial assessment interval).(22, 29) Notification interval, which is the interval from recognizing an emergency to contacting 911, is very difficult to measure, especially in cardiac arrest as the arrest must be witnessed, and the witness must recognize an emergency and contact 911. It is very rare to have a valid and reliable measure of this interval in the prehospital environment, except in instances where video surveillance has been used.(34) Patient access interval has been demonstrated to be a sizeable source of additional time in several EMS systems.(23, 24) It also follows logically that arriving to the patient's side is only one step in getting a defibrillator attached and charged for shock. To further complicate this time interval, once a defibrillator is attached a defibrillatory shock may be delayed for a period of time as many services are now performing a span of CPR prior to shock.(37)

2.6.3 ST elevation myocardial infarction (STEMI) patients

There is a beneficial effect of reperfusion strategies on mortality in patients presenting with myocardial infarction (MI).(33) Two general strategies for reperfusion have emerged, percutaneous coronary intervention (PCI) and fibrinolytic therapy.(33, 38) Although debate exists in the literature as to which intervention is most efficacious for which patient situation, both treatments are beneficial compared to the situation in which the patient receives neither. Therefore the critical issue for EMS systems is that time to definitive treatment is important for STEMI patients.(39-43)

It follows logically that the most clinically important measure of time for an EMS system in responding to a patient with STEMI would depend on the intervention chosen. Prehospital fibrinolytic therapy, for example, may depend on EMS response time, as the longer the response time, the longer the delay until fibrinolytic therapy. Conversely, total prehospital time may be more important in

EMS systems that utilize rapid identification and transport of patients to a PCI centre.

Calgary EMS transports patients to the Foothills Medical Centre (FMC) for PCI and does not perform prehospital fibrinolytic therapy.(37, 43) de Villiers *et al.* (43) studied consecutive patients transported by Calgary EMS during a 16 month period after the implementation of a multi-disciplinary expedited pathway for STEMI patients. This study found that the interval of time between EMS arriving on-scene to the STEMI patient arriving at the catheterization laboratory was shortened. However this study did not explicitly associate response time or total prehospital time with clinical outcome in this patient subset.(43)

The American Heart Association (AHA) reports that delays in time to reperfusion can be divided into three causes. The causes and their contribution in percent to total presentation delay are: interval from symptom onset to decision for patient to act (60% to 70%), interval from arrival of EMS personnel to arrival at the ED (5%), and the interval from ED arrival to treatment (25% to 30%).(33) These data suggest that the two largest categories for presentation delay are prior to EMS contact and after EMS handover of patients to the health care system. It follows that any delay in response time should not affect patient outcome to the same extent as delays in the notification interval or in-hospital delays. This is especially true in a system that relies on rapid transport to a PCI centre for definitive treatment in STEMI patients, as response time may only be detrimental in its contribution to total prehospital time. There were no studies found that explicitly associated EMS response time with clinical outcomes in this clinical sub-group.

2.6.4 Stroke patients

A stroke can be classified as either ischemic or hemorrhagic in nature. The former aetiology is responsible for the majority of strokes, but is amenable to treatment by thrombolytic therapy.(33) There is, however, a small time window in which this treatment can be applied.(33, 44)

The AHA recommends that EMS systems should have an active role in the treatment of stroke patients. Specifically the first three steps in the chain of survival for stroke patients are Detection, Dispatch, and Delivery. The AHA recommends rapid dispatch of ambulances to potential stroke patients and rapid delivery with hospital notification by EMS systems. There is no explicit time standard, however, attached to these recommendations.(33)

A systematic review on barriers to the delivery of thrombolysis for stroke patients concluded that paramedical staff did not appropriately triage the patient, and therefore avoidable delays occurred in response and transport intervals.(44) It did not, however, provide quantified differences in time between the delayed and non-delayed group, nor did it associate these delays with clinical outcome.

Other studies have noted a marked improvement in time to ED arrival, and often time to thrombolysis with the use of EMS.(45-47) These studies, however, fail to delineate the relationship between EMS system response time and post-arrival time, and outcome.

2.6.5 Severe trauma patients

The notion of time and trauma care has been an important theme in the rationale for trauma systems and training of paramedics. Terms such as the "golden hour" have originated from trauma practitioners, and describe the ideal goal for trauma patients to reach definitive care.(48) Much debate still exists in the literature over appropriate on-scene treatment for trauma patients, and ideal prehospital time intervals.(49, 50) A great deal of literature has focused on the scene interval, and total prehospital time, but not response time.(50, 51)

A recent review article reported by Liberman *et al.* does not report any studies that looked explicitly at the association between response time and clinical outcome.(50)

A study by Pons *et al.* explicitly assessed the association between trauma patient outcome and response time in a two-tiered BLS-D/ALS American EMS system.(52) This study employed similar methodology in the same system as the study reported in section 2.6.1. The notable exception was that response time was defined as response interval only and did not include the activation interval. The authors conclude that the mortality OR for an eight minute response interval exposure is 0.81 (95% CI 0.43 – 1.52).(52)

This study had numerous limitations such as the definition of response time (i.e., using response interval only), the omission of post-arrival time in the multivariable analysis, and the lack of a quantitative assessment of potential systematic bias.(52)

A study in the UK by Jones and Bentham examined the association between ambulance response interval, post arrival time, and the sum of response, scene, and transport intervals (total prehospital time not including activation interval) and outcome.(53) This study estimated all response intervals by EMS using geographic information systems (GIS) technology. The authors concluded no statistically significant difference in the odds of mortality in response interval either as a continuous or categorical variable.(53) This study did not control for any treatment or severity measures for patients.

Another UK study explored the association between mortality, length of hospital stay, intensive treatment unit (ITU) admission and length of stay and the location of the injury (i.e., rural or urban).(54) This study used various prehospital intervals as potential explanatory variables. Response time was not statistically associated with mortality, or any of the other outcome measures.(54)

2.6.6 Other conditions

Intuitively other medical conditions may be amenable to improved outcome by rapid EMS system response or total prehospital intervals (e.g., airway obstruction, gastrointestinal bleeding, asthma, etc.). No other studies could be located that explicitly associated EMS response time to clinical outcome.

Chapter Three: Research Questions

3.1 Primary question

Is there an association between an ALS emergency vehicle (unit) response time of greater than eight minutes and all-cause mortality in events designated as critical life-threatening in an urban two tiered EMS system with BLS-D first response?

3.2 Secondary questions

Is there an association between an ALS emergency vehicle (unit) response time of greater than eight minutes and all-cause mortality in a subset of subjects who die in the ED or who die in hospital after being admitted from the ED?

Is there an association between an ALS emergency vehicle (unit) response time of greater than four minutes and all-cause mortality for events designated as critical life-threatening in an urban two tiered EMS system with BLS-D first response?

Is there an association between an ALS emergency vehicle (unit) response time of greater than four minutes and all-cause mortality in a subset of subjects who die in the ED or who die in hospital after being admitted from the ED?

Is there an association between an ALS emergency vehicle (unit) response time of greater than nine minutes and all-cause mortality for events designated as critical life-threatening in an urban two tiered EMS system with BLS-D first response?

Is there an association between an ALS emergency vehicle (unit) response time of greater than nine minutes and all-cause mortality in a subset of subjects who die in the ED or who die in hospital after being admitted from the ED?

3.3 Exploratory analysis questions

Is there an association between an ALS emergency vehicle (unit) response time of greater than eight minutes and all-cause mortality for critical life-threatening events which are subsequently identified or result in cardiac arrest, ST elevation myocardial infarction, stroke, or severe traumatic injury in an urban two tiered EMS system with BLS-D first response?

Chapter Four: Methods

4.1 Study population and sample

All adults who, at the time of a 911 call, required a two-tiered (BLS-D/ALS) emergency response (Delta or Echo level event) and who were transported to hospital. Our sample is a convenience sample of one year of data from January 1st, 2006 to December 31st, 2006. A year of data was utilized so that seasonal fluctuations in event type and severity do not introduce bias into the study sample.

4.1.1 Study inclusion criteria

Study inclusion criteria included:

1. Patients who were18 years of age or older.
2. Emergency unit response that resulted in a transport to an acute care facility within The City of Calgary municipal boundary (i.e., Foothills Medical Centre [FMC], Rockyview Hospital [RVH], or Peter Lougheed Centre [PLC]). The only exception was for the exploratory analysis on cardiac arrest patients, where transported and non-transported patients were included because many cardiac arrest patients have resuscitation attempts terminated at the scene without transport.
3. Patients that received a Delta or Echo level of response (critical or life-threatening emergency) as defined by the Medical Priority Dispatch System® (MPDS, Medical Priority Consultants Inc.).

4.1.2 Linkage exclusion criteria

Individual subject specific data were excluded from linkage if the following variables were missing from the EMS data:

- arrival at scene time

Or

- age

Or

- sex

Or

- other (missing acute care facility name or shared linkage variable [i.e., Patient Care Record (PCR) number], event started in 2006 and ended in 2007, duplicated or conflicting line of data).

4.2 Data sources

All prehospital data were supplied by The City of Calgary EMS; all hospital data were supplied by the Calgary Health Region (CHR).

Prehospital data included variables needed to calculate response time (exposure), response level (MPDS), post-arrival time, and demographic and linkage variables.

Hospital data included variables needed to calculate the primary outcome (all-cause mortality), secondary outcomes (all-cause mortality from the Emergency Department [ED] and as an in-patient [IP]), demographic and linkage variables:

Broadly, the study sample was constructed as follows. All EMS events were identified in the calendar year and inclusion criteria one and two were applied. Any records missing data as outlined above were excluded and EMS data were then linked to the CHR ED data employing a deterministic linkage strategy using PCR#, difference between EMS and ED time of hospital arrival, and first and last name. Linked EMS-ED data were then linked to IP data employing a deterministic linkage using unique lifetime identifier (ULI), hospital site, and difference between ED discharge and IP admit time. From the EMS-ED-IP linked data, inclusion criteria three was applied, and a logic test (i.e., arrival at scene time was not ≤30 seconds from initiation of transport time) and final data review completed (i.e., data not missing exposure, outcome, or covariates) (Figure 4.1).

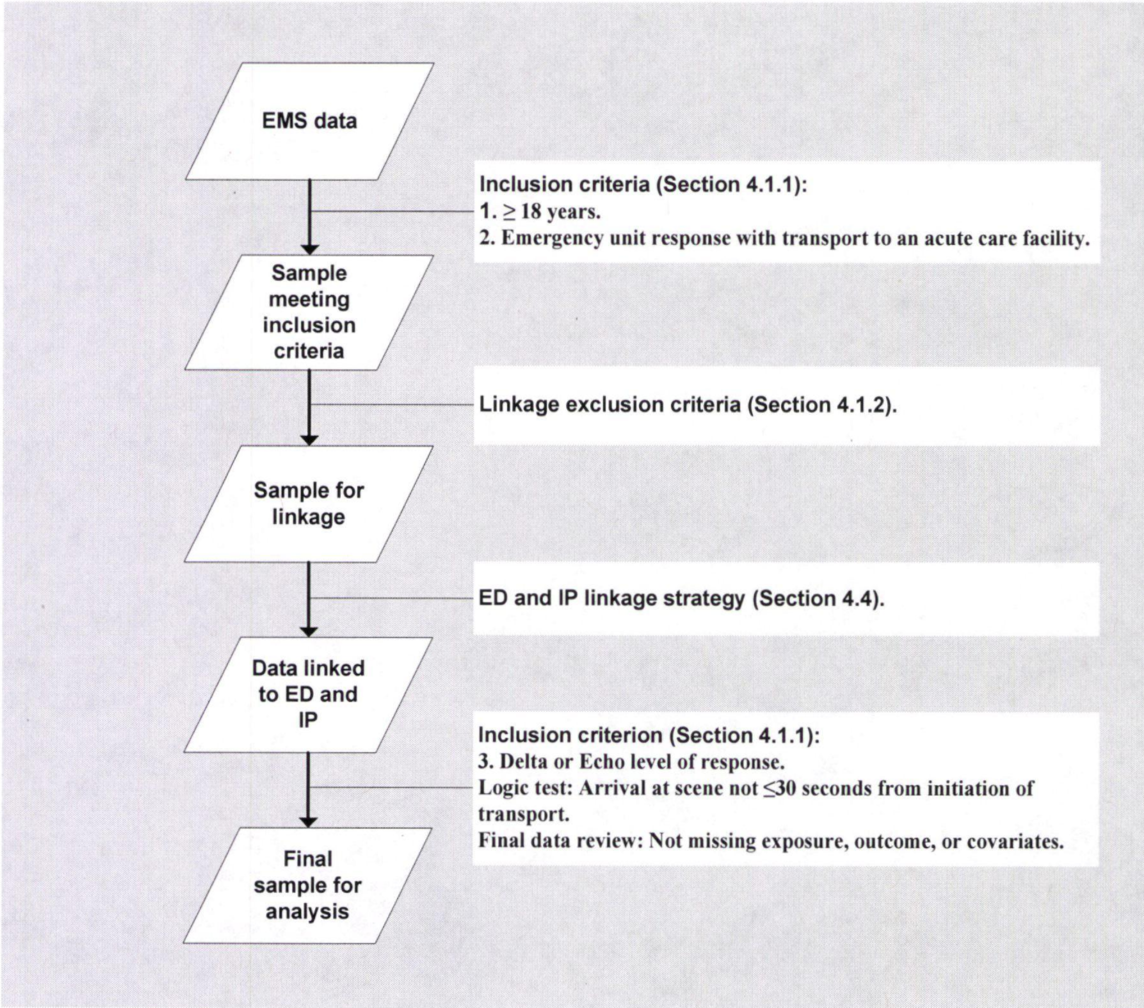

Figure 4.1: Overview of methods used to arrive at the final sample for analysis.

4.3 Data preparation

4.3.1 Prehospital data

The City of Calgary EMS uses a computer aided dispatch system (CAD) to capture all prehospital time variables. This system also captures basic demographic data such as patient name, sex, and age, event information such as MPDS level, and linkage data such as PCR number.

These data are structured first by event number, then by unit response to the event, then by patient. One event, for example, may require multiple unit responses and will therefore have multiple lines of data (theoretically one per unit response). Each unit response, however, may also result in the assessment of one patient or multiple patients, therefore each unit response may have numerous lines of data associated with it.

Multiple lines of data may also be created for one event, requiring one unit response, for one patient. This happens when patient demographic data is updated as more information becomes available. An additional line of data is automatically generated identical to the original line, except for the changed demographic variable. As a consequence multiple lines of data may pertain to the same event, unit response, and patient. To add to this complexity, multiple events may be created that pertain to the same event (i.e., from multiple 911 calls from different sources), resulting in multiple unit responses (i.e., until it can be confirmed that there is only one event and that other resources can be cancelled), and multiple patients (i.e., some patients may refuse care, accept care but refuse transport, and accept both care and transport, or be declared dead on-scene, abscond from scene etc.).

Due to their complexity all EMS data were manually reviewed, and extraneous lines of data removed. This resulted in 107,562 unit responses where one line of data referred to one unit response.

The City of Calgary EMS defines response time compliance as the proportion of events where the shortest response time by an EMS unit to the event met the response time criterion. When multiple units are responding to the same event, some units may be dispatched at a later time as the scene is assessed and resource needs are determined. It is therefore important to attach the initial response time of the first unit to arrive on-scene to all subsequently arriving units. This ensures that the true response time to the event is reflected in all units, not the individual response times of all units.(2, 15) The 107,562 unit responses were manually reviewed to determine the shortest response time for each event. This response time was then attached to all subsequently arriving units for each event.

4.3.2 Hospital data

Hospital data was prepared by the CHR Health System Analysis Unit (HSAU). The HSAU searched the Ambulatory Care Classification System (ED database) and In-patient discharge (IP) databases for all records of patients that arrived by ground ambulance and where the EMS patient care record (PCR) number was present for the one year study interval.

4.4 Data linkage

EMS data were linked with ED and IP data using a deterministic linkage strategy that included the following two steps:

1. Linkage with ED data:
    a. Linkage with PCR number (a shared patient tracking number), last name, and first name. If all three variables match then the record was considered linked.

b. If less than three variables match then the data were manually checked. The record was considered linked if the following manual check rules were met:

    i. Arrival at hospital time by EMS minus arrival at hospital time by CHR ≤120 minutes

    ii. Two of three of PCR#, last name, first name match.

2. Linkage with IP data:

    a. Linkage with ULI. (N.B. Alberta residents ULI=personal health number (PHN) assigned by Alberta Health Care. Non-Alberta residents are assigned a ULI at the time of registration)

    b. Hospital site

    c. Difference between time of ED discharge and IP-admit ≤24 hours.

4.5 Data measurement

4.5.1 Exposure

The primary exposure was response time dichotomized as greater than or equal to eight minutes and less than or equal to seven minutes and 59 seconds. Patients were considered exposed if they received an EMS response time of greater than or equal to eight minutes, and unexposed if the response time was less than or equal to seven minutes and 59 seconds.

Secondary exposures included response time dichotomized as greater than or equal to four minutes and less than or equal to three minutes and 59 seconds, and dichotomized as greater than or equal to nine minutes and less than or equal to eight minutes and 59 seconds (Table 4.1).

4.5.2 Outcome

The primary outcome was a dichotomous variable that describes all-cause mortality, which included patients that died in the ED and patients that died as an IP.

The secondary outcomes were dichotomous variables that describe ED all-cause mortality and, for patients that survived to be admitted to hospital (IP's), their subsequent in hospital all-cause mortality (Table 4.1).

4.5.3 Covariates

There were three clinically plausible covariates in this analysis and are described in detail in Table 4.1.

Table 4.1: Summary of variables included in the primary and secondary research questions.

Variable Name	Function	Type	Variable Description	Rationale
8 minute response time	Primary exposure	Dichotomous	Time interval from EMS dispatch call receipt to EMS vehicle arrival at scene (activation and response intervals). Dichotomized at ≥8 minutes or ≤7 minutes, 59 seconds.	Ideally this time interval would also include patient access interval. These data were not available from The City of Calgary EMS. Previous studies on this topic have not included these data.(6, 7, 52)
All-cause mortality	Primary outcome	Dichotomous	Dead or alive at hospital discharge. This includes patient all-cause mortality in the ED and in those that may have subsequently become an IP.	From a clinical perspective, reducing mortality is the rationale behind decreasing EMS response time.(6, 7, 13, 27, 52)
4 minute response time	Secondary exposure	Dichotomous	Time from EMS dispatch call receipt to vehicle arrival at scene (activation and response intervals). Dichotomized at ≥4 minutes or ≤3 minutes, 59 seconds.	Two previous studies have noted reduced all-cause mortality effect at four minutes and five minutes respectively.(6, 7)
9 minute response time	Secondary exposure	Dichotomous	Time from EMS dispatch call receipt to vehicle arrival at scene (activation and response intervals). Dichotomized at ≥9 minutes or ≤8minutes, 59 seconds.	Many EMS systems in Canada and the rest of the world use this standard instead of an 8 minute response time standard.(2)
ED all-cause mortality	Secondary outcome	Dichotomous	All-cause mortality at ED discharge. Patients may have also been discharged and immediately admitted as an IP.	Certain patient conditions may not respond to any treatment, regardless of how quickly it is applied. It follows logically that there may be different associations between response time and mortality in patients that die in the ED versus those that die as an IP.
IP all-cause mortality	Secondary outcome	Dichotomous	All-cause mortality in patients that survived to be admitted to hospital (IP's).	See above.
Age	Covariate	Measured	Age of patient in years.	Aging changes the pathophysiology of disease and injury, and therefore may influence the response time mortality relationship.(55)
Sex	Covariate	Dichotomous	Sex of patient.	Unpublished Calgary EMS data suggests that males suffer different traumatic injuries than females.(56)
Post-arrival time	Covariate	Measured	Length of time spent on-scene and in the transport of patients to an acute care facility (on-scene and transporting intervals).	Although response time may be theoretically important for conditions to which a time-critical life-saving intervention may be applied by paramedics in the prehospital environment, many conditions require interventions that can only be applied in the hospital.(40, 46, 49, 57) For these conditions, total prehospital time may be more closely associated with all-cause mortality than response time. It follows logically that total prehospital time may be an important covariate in this exposure outcome relationship. Post-arrival time consists of on-scene and transporting intervals, which when added to response time encompass total prehospital time.

Note: EMS=Emergency Medical Services; ED=Emergency Department; IP=In-patient.

4.6 Data analysis

All data were analysed using Stata (version 8.2) statistical software (StataCorp., College Station, Texas). A descriptive analysis of demographic and other key variable is first presented. Continuous data were described using means and standard deviations for normally distributed variables and categorical data were described using proportions.

All statistical tests were considered significant at the 0.05 level.

4.6.1 Primary question

The primary analysis examined the proportion of all-cause mortality between patients that received a response time greater than or equal to eight minutes (exposed) versus patients that received a response time of less than eight minutes (unexposed) and were compared using a two-sided Fisher's exact test.(58)

Classic stratified analysis was used to further examine the relationship between the exposure (response time of 8 minutes) and outcome (all-cause mortality). A crude odds ratio was calculated with a 95% confidence interval. The potential modifying effects of covariates were assessed by comparing effect estimates across exposure strata and testing with the Mantel-Haenszel test of homogeneity. In addition, results were compared to previous study findings, and considered within the context of clinical significance.(59) Table 4.2 describes how the covariates were operationalized.

Table 4.2: Summary of variables included in the stratified and multivariable analyses of the primary and secondary research questions.

Variable Name	Function	Coding	Variable Coding Description	Operational Rationale
Age	Covariate	Ordinal	Age 18 to <40 years = 0 Age ≥40 to <65 years = 1 Age ≥65 = 2	It was determined that using age as a measured variable was problematic due to the assumption of linearity. It was deemed clinically implausible that a one year change of age in a young adult would have the same effect as a one year change of age in an older adult. There exists no known data that describes the age related survival changes in a heterogeneous population of patients receiving EMS care. Age was therefore divided into clinically plausible age cut-points.
Sex	Covariate	Categorical	Female = 0 Male = 1	Standard categorization of this variable.
Post-arrival Time	Covariate	Ordinal	Post-arrival <30 minutes = 0 Post-arrival ≥30 & <36minutes = 1 Post-arrival ≥36 & <45minutes = 2 Post-arrival ≥45 minutes = 3	There exists no known data that describes the post-arrival time related survival changes in a heterogeneous population of patients receiving EMS care. Therefore quartiles were used to categorize post-arrival time.

Note: Post-arrival time= time interval from arrival on scene to arrival at hospital.

Confounding was assessed by comparing the crude to adjusted odds ratios. Previous study findings and clinical significance also informed this assessment of confounding.(59)

To further address the primary research question a multivariable logistic regression model was developed. The clinically plausible model is represented schematically by:

$$\ln\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 Exp + \beta_2 Age + \beta_3 Sex + \beta_4 Post\_Arrival$$

The modelling procedure included the following steps (26, 58, 60):

1. Clinically appropriate categorization of covariates.
2. Univariable assessment of covariates:

a. assess impact on exposure outcome relationship
b. identify zero cells in stratified covariate subgroups
c. clinically plausible collapsing of covariate categories as needed to eliminate zero cells.

3. Fit the clinically plausible model.

4.6.2 Secondary questions

The methods described above were used to further explore the response time and all-cause mortality relationship by substituting the eight minute response time exposure (primary exposure) with four and nine minute exposures (secondary exposures). Moreover the primary outcome (all-cause mortality) was substituted with ED and IP mortality for the eight, four, and nine minute dichotomous exposure levels.

4.6.3 Exploratory analysis questions

4.6.3.1 Cardiac arrest patients

4.6.3.1.1 Data sources

The data sources for this exploratory analysis was as described above in section 4.2, with some exceptions. Prehospital data, in addition to variables needed to calculate response time (exposure), response level (MPDS), post-arrival time, and demographic variables, also included the outcome of patients that were not transported. The rationale for including the outcome of non-transported patients for this subgroup is that numerous patients in cardiac arrest are not transported by EMS if the resuscitation was not successful. It follows logically that non-transported patients should be included in the analysis. In addition, this is the only subgroup where detailed information exists describing the outcome of non-transported patients.

The City of Calgary EMS maintains a prehospital arrest record (PHAR) database that is a subgroup of the larger CAD database. All patients contained in this database for the 2006 calendar year were confirmed as being in cardiac arrest by the attending paramedic.

4.6.3.1.2 Data preparation

The City of Calgary EMS supplied cardiac arrest data in the PHAR database. This included age, bystander CPR, pre-EMS arrival defibrillation, and death in the field. PHAR data were manually reviewed to ensure there were no duplicate events, no patients less than 18 years of age, or events with missing age.

Upon successful data linkage, the data were further prepared by removing all events that were not Delta or Echo responses.

4.6.3.1.3 Data linkage

The EMS PHAR database was linked with the thesis database using a deterministic linkage strategy that included the following two steps:

1. Linkage by event number (a City of Calgary EMS unique proprietary number for every event created in the CAD database).
2. All non-linked data from step 1 resulted in a linkage attempt by invoice number (a City of Calgary EMS unique proprietary number for patients assessed by EMS).

All non-linked events where the patient died on scene were then linked to the City of Calgary CAD system by event number to obtain event determinant and response time variables.

The resulting database contained event determinant, response time (exposure), and mortality (outcome) information for cardiac arrest patients identified in the PHAR database.

4.6.3.1.4 Data measurement

Exposure and outcome data were the same as described in section 4.5, except they included those patients who died in the field. Therefore the new exposure variables included the response time of events corresponding to patients who died in the field, and the new outcome variable included all-cause mortality in the field, all-cause mortality from the ED, and all-cause mortality as an inpatient. In addition, cardiac arrest specific covariates are described in Table 4.3.

Table 4.3: Summary of variables included in the exploratory analysis for the subgroup cardiac arrest.

Variable Name	Function	Type	Variable Description	Rationale
Bystander CPR	Covariate	Dichotomous	Dichotomized as either bystander CPR present or absent.	Previous literature would suggest that bystander CPR may have an effect on mortality.(61)
Pre-EMS Defibrillation	Covariate	Dichotomous	Dichotomized as either pre-EMS defibrillation provided or not provided.	Previous literature would suggest that the interval of time between cardiac arrest and the application of a defibrillatory shock effects all-cause mortality in some cardiac arrest situations.(34, 61)

Note: EMS=Emergency Medical Services

4.6.3.1.5 Data analysis

The analysis proceeded as per the primary research question described in section 4.6.1. The notable difference was in the multivariable logistic regression analysis, where the clinically plausible model was represented schematically by:

$$\ln\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 Exp + \beta_2 Age + \beta_3 Sex + \beta_4 Byst\_CPR + \beta_5 PRE\_EMS\_defib$$

Post-arrival time was omitted from this model as it was deemed to have little influence on the outcome of cardiac arrest patients, as the majority of key resuscitation interventions for most cardiac arrest patients are delivered in the prehospital phase of treatment.(37)

4.6.3.2 ST elevation myocardial infarction (STEMI) patients

4.6.3.2.1 Data sources

The data sources for this exploratory analysis were as described above in section 4.2.

The City of Calgary EMS maintains a STEMI database that is a subgroup of the larger CAD database. All patients contained in this database for the 2006 calendar year are recorded as a STEMI patient by the attending paramedic, and confirmed by the Calgary STEMI Quality Improvement and Health Information group.

4.6.3.2.2 Data preparation

The City of Calgary EMS STEMI database was manually reviewed to ensure there were no duplicate events, no patients younger than18 years of age, or events with missing age.

Upon successful data linkage, the data were further prepared by removing all unit responses where the determinant was not a Delta or Echo.

4.6.3.2.3 Data linkage

The EMS STEMI database was linked with the thesis database using a deterministic linkage strategy that included the following two steps:

1. Linkage by event number (a City of Calgary EMS unique proprietary number for every event created in the CAD database).
2. All non-linked data from step 1 will result in a linkage attempt by invoice number (a City of Calgary EMS unique proprietary number for patients assessed by EMS).

4.6.3.2.4 Data measurement

Data measurement was as described above in section 4.5.

4.6.3.2.5 Data analysis

The analysis proceeded as per the primary research question described in section 4.6.1.

4.6.3.3 Stroke patients

4.6.3.3.1 Data sources

The data sources for this exploratory analysis were as described above in section 4.2 for a subgroup of stroke patients that were identified using the International Classification of Disease (ICD) 10 Canadian enhancement (CA) codes supplied in the ED and IP data. ICD-10 CA codes from the ED and IP data were used in this instance because Calgary EMS does not maintain a prehospital stroke database.

The primary ED and IP diagnosis were used to identify patients with stroke. The validation of these ICD-10 CA codes in the CHR is described elsewhere.(62)

4.6.3.3.2 Data preparation

Data for this exploratory analysis were prepared as described above in section 4.3.

4.6.3.3.3 Data linkage

No data linkage was required for this exploratory analysis.

4.6.3.3.4 Data measurement

Data measurement was as described above in section 4.5.

4.6.3.3.5 Data analysis

The analysis proceeded as per the primary research question described in section 4.6.1.

4.6.3.4 Severe trauma patients

4.6.3.4.1 Data sources

Severe trauma patients were identified using the CHR Trauma Services regional trauma registry. Patients entered into this registry have an Injury Severity Score (ISS) greater than or equal to 12.(63) Trauma registry data for these patients were linked to the thesis database to obtain exposure, outcome, and other variables described in Table 4.1.

4.6.3.4.2 Data preparation

Data was prepared for this exploratory analysis as described above in section 4.3. In addition, using the variable "ems_id" (a thesis specific unique identifying variable), PHN was attached to patient records in the thesis database by the CHR HSAU.

4.6.3.4.3 Data linkage

The CHR Trauma Services regional trauma registry was linked with the thesis database using a deterministic linkage strategy that included the following two steps:

1. Linkage with PHN.
2. In records where the linkage was not successful, a linkage strategy with last name using the SAS Soundex function (SAS Institute, Cary, NC) and sex.

4.6.3.4.4 Data measurement

Data measurement was as described above in section 4.5. In addition, a severe trauma mechanism of injury (MOI) specific variable was created (Table 4.4).

Table 4.4: Summary of variables included in the exploratory analysis for the subgroup severe trauma.

Variable Name	Function	Type	Variable Description	Rationale
Trauma type	Covariate	Polychotomous	Categorized as blunt, penetrating, or burn trauma.	The mechanism of traumatic injury causes different injury patterns and hence may influence the outcome.(64)

4.6.3.4.5 Data analysis

The analysis proceeded as per the primary research question described in section 4.6.1. The notable difference was in the multivariable logistic regression analysis, where the clinically plausible model was represented schematically by:

$$\ln\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 Exp + \beta_2 Age + \beta_3 Sex + \beta_4 Post\_arrival + \beta_5 Trauma\_type$$

Trauma type will be converted to an indicator variable using the xi command in STATA version 8.2 (College Station, Texas).

Chapter Five: Ethical Concerns

Prior to data acquisition ethical review and approval was granted by the Conjoint Health Research Ethics Board (CHREB) of the University of Calgary and Calgary Health region. In addition, approval was obtained from the City of Calgary to ensure that Freedom of Information and Protection of Privacy (FOIPP) legislation was met. Waiver of patient consent was granted for this study.

Upon successful data linkage, data were rendered de-identified to protect against potential privacy issues. Access to study data was restricted to the principal investigator and the author of this thesis as his designate.

Chapter Six: Results

6.1 Overview of final sample

Final sample results are outlined in Figure 6.1.

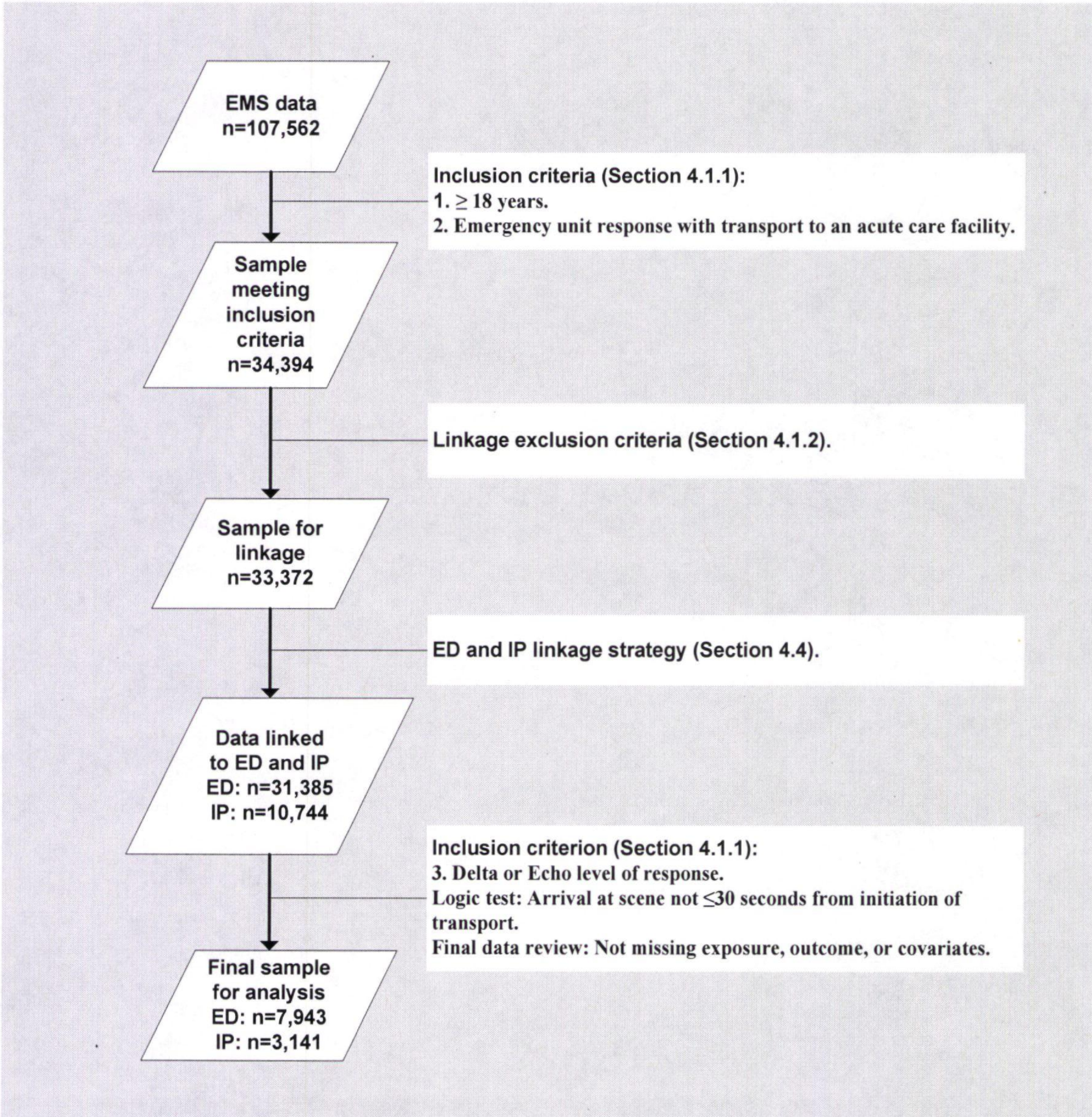

Figure 6.1: Overview of final sample.

6.1.1 Data preparation

An initial sample of 34,394 Calgary EMS unit responses met study inclusion criteria one and two. A total of 1,022 unit responses met linkage exclusion criteria (Box 6-2-1, Figure 6.2), leaving 33,372 unit responses for linkage (Figure 6.2).

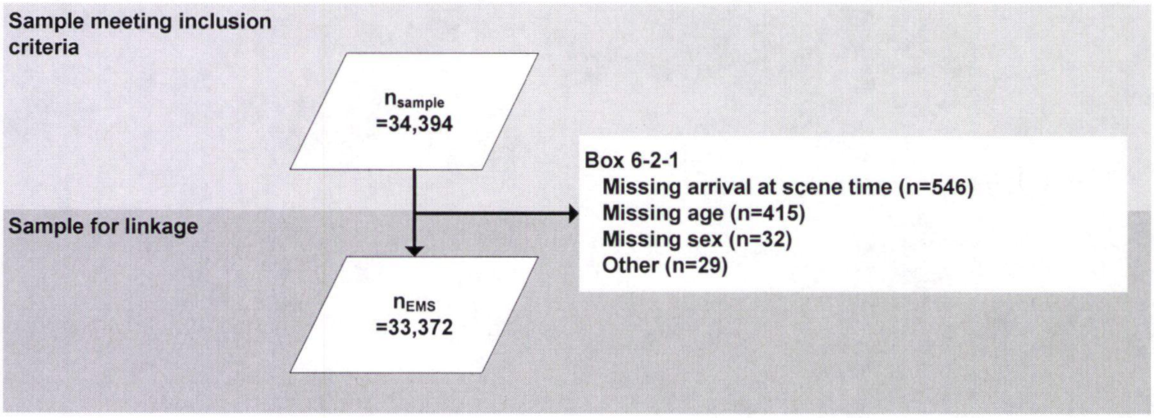

Figure 6.2: Final sample for linkage for The City of Calgary Emergency Medical Services (EMS) for the 2006 calendar year.

6.1.2 Data linkage

A total of 31,385 out of 33,372 (94%) unit responses were successfully linked using the previously described deterministic strategy to corresponding ED data. Of the 31,385 unit responses, there were 11,441 corresponding to a patient that subsequently was recorded as becoming an in-patient. A total of 10,744 out of 11,441 (94%) unit responses were successfully linked to CHR IP data (Figure 6.3).

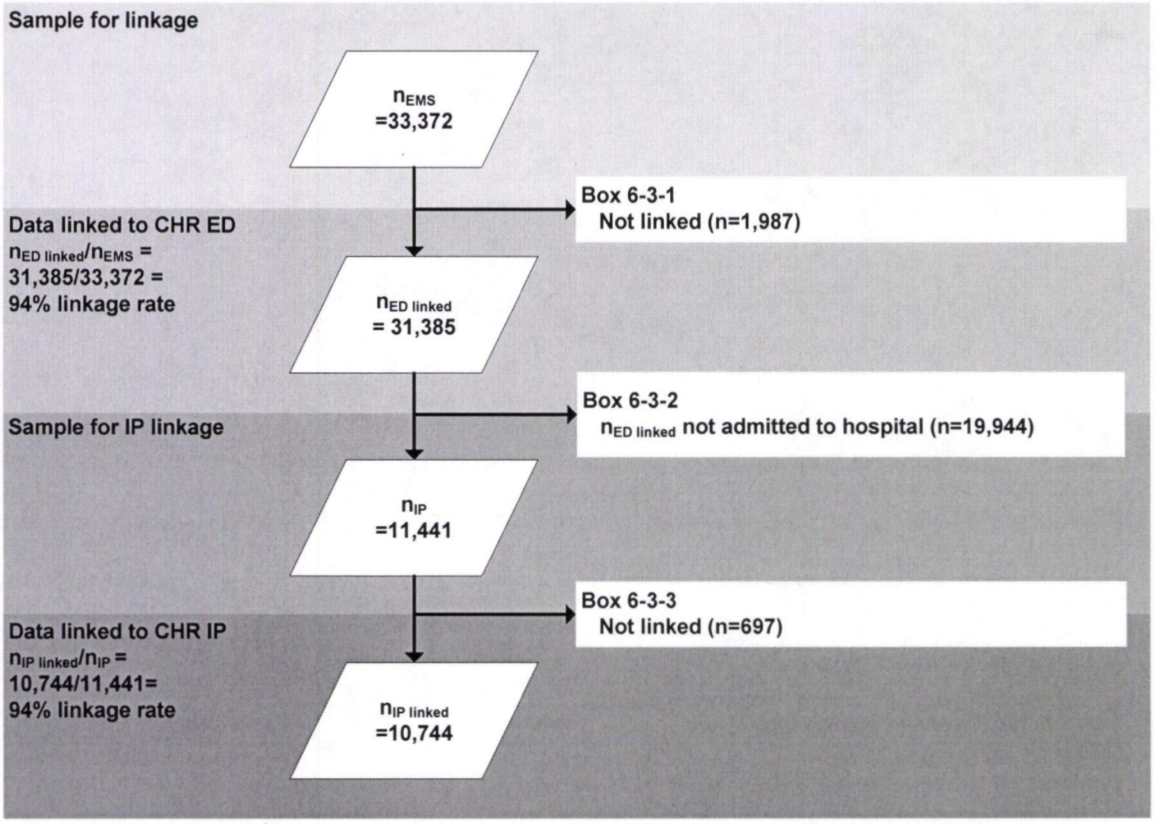

Figure 6.3: Linkage rates for The City of Calgary Emergency Medical Services (EMS) unit response data to the Calgary Health Region Emergency Department (ED) and in-patient (IP) data.

6.1.3 Final data

The 31,385 unit responses that were successfully linked to the CHR ED data included 7,976 unit responses determined to be a Delta or Echo (inclusion criteria three). After logic testing and final data review, the final sample for analysis consisted of 7,943 unit responses (Figure 6-4). Of these 7,943 Delta and Echo level unit responses successfully linked to the CHR ED database, 3,141 unit responses were subsequently linked to the CHR IP database. There were 183 unit responses that pertained to a patient with an IP disposition from the ED that could not be linked to the CHR IP database. In addition, there were 142 unit responses that were linked to IP data, but were not recorded as being an in-patient.

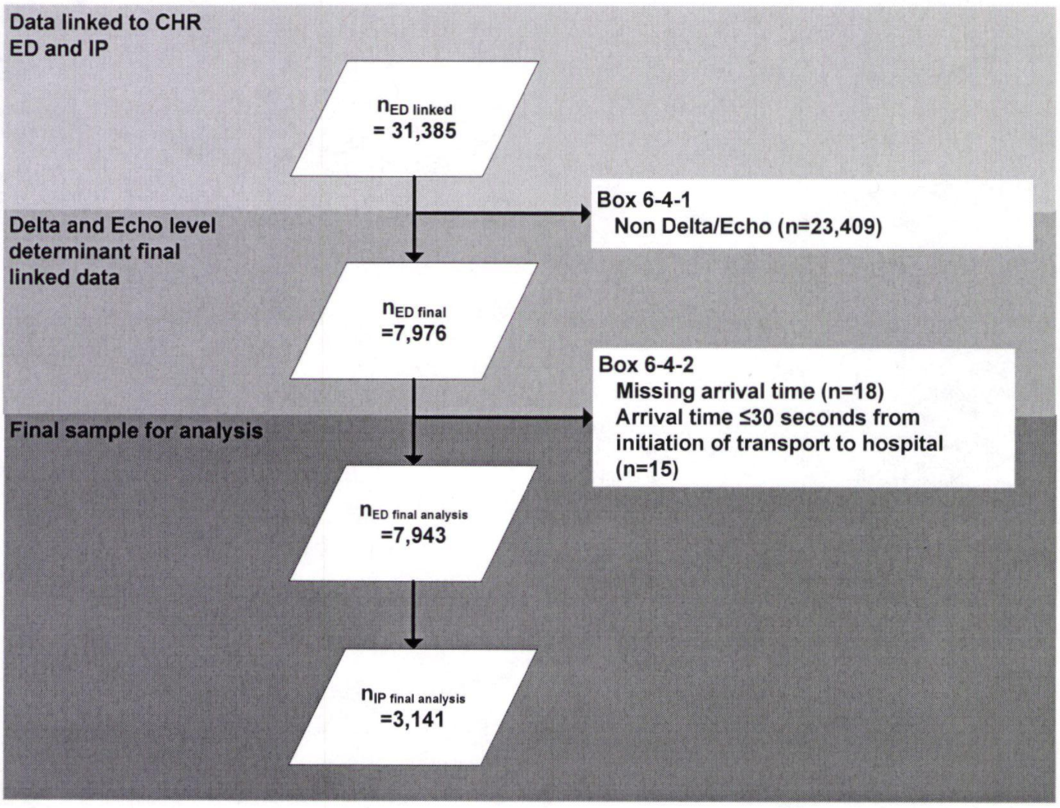

Figure 6.4: Description of the final sample size for The City of Calgary Emergency Medical Services Delta and Echo level unit response data linked to the Calgary Health Region Emergency Department (ED) and in-patient (IP) data.

6.2 Patient characteristics

6.2.1 Included versus excluded unit responses

A comparison of event and patient characteristics between Delta and Echo level unit responses that were included and those unit responses that were excluded are outlined in Table 6.1.

In Table 6.1 included unit responses correspond to the value of $n_{ED\ final\ analysis}$ in Figure 6.4 and the excluded unit responses correspond to the Delta and

Echo level unit responses in Box 6-2-1 (Figure 6.2), Box 6-3-1 (Figure 6.3), and Box 6-4-2 (Figure 6.4).

Table 6.1: Comparison of baseline characteristics for included and excluded Delta and Echo level unit responses.

Description	Included (n=7,943)	Excluded (n=776)
Mean response time in minutes (±SD)	6.7 (3.1)	6.8 (3.1)
≥8 minutes [n (%)]	1,916 (24.1%)	195 (26.3%)
Mean age in years (±SD)	56.9 (21.5)	46.6 (21.8)
Sex		
Male [n (%)]	4,325 (54.5)	290(42.2)
Median post-arrival time in minutes (IQR)	36.7 (14.8)	33.9 (19.6)
ALS vs. BLS level of care‡		
ALS [n (%)]	3,914 (49.5)	279 (37.3)
Transport location		
FMC [n (%)]	3,807 (47.9)	314 (40.5)
MPDS® priority		
Echo [n (%)]	235 (3.0)	25 (3.2)

Note: SD: Standard Deviation; IQR: Inter-Quartile Range; ALS: Advanced Life Support; BLS: Basic Life Support; FMC: Foothills Medical Centre; MPDS: Medical Priority Dispatch System®; Post-arrival time= time interval from arrival on scene to arrival at hospital.
‡ All City of Calgary EMS response units are ALS capable, but patient condition does not always warrant ALS level care. ALS level of care criteria include: patients with a prehospital index≥4; medication administered including fluid bolus; endotracheal intubation or attempted intubation; electrical counter shock; surgical intervention; all other patients categorized as BLS.

There are obvious differences between included and excluded unit responses with respect to mean patient age, sex, median post-arrival time, ALS care, and transport location. There were, however, no obvious differences between mean response time, proportion of unit responses greater than or equal to eight minutes, and MPDS priority. Another measure of patient severity, which is estimated by the Canadian Triage and Acuity Scale (CTAS), could not be compared as there were no CTAS scores for excluded patients.

In summary, unit responses excluded from the analyses had the following characteristics when compared to those included in the study: younger mean age, decreased proportion of males, lower mean post-arrival time, less ALS level care, and fewer transports to FMC.

There were, however, no obvious differences over mean response time, and response time dichotomized at the eight minute level (primary exposure). There were also no obvious differences over the proportion of unit responses that were Echo level.

There were 183 patients who received a Delta or Echo level unit response that could not be linked from the ED but were coded as having become an IP. The characteristics of these patients in terms of the exposure and potential covariates are summarized in Table 6.2.

Table 6.2: Comparison of exposure and covariates in linked and unlinked groups for Delta and Echo level unit responses between the Calgary Health Region Emergency Department and In-Patient databases.

Description	Linked (n=3,141)	Unlinked (n=183)
Mean response time in minutes (±SD)	6.7 (3.0)	6.7 (2.5)
≥8 minutes [n (%)]	724 (23.1)	51 (27.9)
Mean age in years (±SD)	64.5 (19.5)	64.2 (18.8)
Sex		
Male [n (%)]	1,777 (56.6)	95 (51.9)
Median post-arrival time in minutes (IQR)	37.1 (14.8)	36.3 (18.0)
CTAS		
Level 1 [n (%)]	446 (14.2)	22 (12.0)

Note: SD: Standard Deviation; Post-arrival time= time interval from arrival on scene to arrival at hospital; IQR: Inter-Quartile Range; CTAS=Canadian Triage Acuity Scale.

These data suggest that the unlinked patients were not obviously different to those patients linked to the IP database over exposure and potential covariate variables.

6.2.2 Successfully linked data

There were 7,943 unit responses with a Delta or Echo level determinant that were linked to the CHR ED data. Patient characteristics stratified by the primary exposure (8 minute response time) are summarized in Table 6.3.

Table 6.3: Patient characteristics of included unit responses.

Variable	< 8 min. (n=6,027)	≥8 min. (n=1,916)	Total
Sex			
Female	2,771 (46.0%)	847 (44.2%)	3,618 (45.6%)
Male	3,256 (54.0%)	1,069 (55.8%)	4,325 (54.5%)
CTAS*			
Level 1	531 (8.8%)	160 (8.4%)	691 (8.7%)
Level 2	3,102 (51.5%)	994 (51.9%)	4,096 (51.6%)
Level 3	2,244 (37.2%)	707 (36.9%)	2,951 (37.2%)
Level 4	148 (2.5%)	55 (2.9%)	203 (2.6%)
Level 5	2 (0.03%)	0 (0.00%)	2 (0.03%)
Mean age in years (±SD)	57.4 (21.6)	55.5 (21.1)	56.9 (21.5)
18 to 39	1,492 (24.8%)	499 (26.0%)	1,991 (25.1%)
40 to 64	1,962 (32.6%)	686 (35.8%)	2,648 (33.3%)
≥65	2,573 (42.7%)	731 (38.2%)	3,304 (41.6%)
Median post-arrival time in minutes (IQR)	36.1 (14.1)	39.1 (16.6)	36.7 (14.8)
MPDS® priority			
Delta [n (%)]	5,836 (96.8%)	1,872 (97.7%)	7,708 (97.0%)
Echo [n (%)]	191 (3.2%)	44 (2.3%)	235 (3.0%)
ALS vs. BLS level of care†			
ALS [n (%)]	2,970 (49.5%)	944 (49.4%)	3,914 (49.5%)
BLS [n (%)]	3,033 (50.5%)	966 (50.6%)	3,999 (50.5%)

Note: CTAS=Canadian Triage and Acuity Scale; SD=Standard Deviation; MPDS=Medical Priority Dispatch System; ALS=Advanced Life Support; BLS=Basic Life Support; Post-arrival time= time interval from arrival on scene to arrival at hospital..

* Canadian triage and acuity scale is used to prioritize patient care in Canadian emergency departments. It is applied on arrival at the ED by the triage nurse. CTAS level 1 is defined as resuscitation, level 2 as emergent, level 3 as urgent, level 4 as less urgent, and level 5 as non urgent.

† All City of Calgary EMS response units are ALS capable, but patient condition does not always warrant ALS level care. ALS level of care criteria include: patients with a prehospital index≥4, medication administered including fluid bolus, endotracheal intubation or attempted intubation, electrical counter shock, surgical intervention, all other patients categorized as BLS.

6.3 Primary research question

A total of 133 out of 1,865 (7.1%) patients that received a response time of greater than or equal to 8 minutes died, compared to 375 out of 5,895 (6.4%) patients that received a response time of less than 8 minutes (Table 6.4). A two sided fisher's exact test failed to reject the null hypothesis (p=0.238) that the crude proportion of mortality is not different for exposed and unexposed patients. The estimated odds ratio of mortality is 1.13 (95% CI 0.91 to 1.39).

A stratified analysis was performed to examine any potential contribution of the covariates age, sex, and post-arrival time to the observed relationship between 8 minute response time and all-cause mortality (Table 6.4).

Post-arrival time was separated into four strata and age into three strata as described in Table 4.2. The stratum specific OR's between the strata with the covariates sex and post-arrival time were relatively homogeneous suggesting no effect measure modification. Likewise the pooled OR's for sex and post-arrival time were similar to the crude OR, suggesting that these variables were not confounders to the effect estimated by the crude OR.

However, a large difference in stratum specific OR's was seen for age with the stratum specific OR for 18 to 39 year olds being 0.57 (95% CI 0.14 – 1.71) compared to 1.28 (95% CI 0.84 – 1.92) for ages 40 to 64 years and 1.22 (0.94 – 1.59) for ages greater than or equal to 65 years.

A reasonable biologically plausible hypothesis could not be found to account for this observation. Likewise, an examination of available literature did not demonstrate a similar finding. In examining the 18 to 39 year old data, it was observed that the cell comprising deaths in the strata with a response time greater than or equal to eight minutes was small. To examine the effect of the cell size on the stratum specific estimate we moved two individuals from alive to dead in the greater than or equal to eight minute stratum, and two individuals from dead to alive in the less than eight minute stratum (four individual outcomes reassigned out of 1,967 observed unit responses). These changes resulted in a movement of the stratum specific OR for the 18 to 39 year old group to 0.96.

In the absence of a biologically plausible explanation, or previous observed similar phenomena, it is unlikely that this is effect measure modification. In addition, as the pooled OR is similar to the crude, reporting of the crude OR would seem appropriate (Table 6.4).

Table 6.4: Stratified analysis for the primary research question.

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥8 < 8	133 375	1,732 5,520	1.13	0.91 – 1.39
Age	18-39	≥8 < 8	4 21	484 1,458	0.57	0.14 – 1.71
	40-64	≥8 < 8	38 86	632 1,833	1.28	0.84 – 1.92
	≥65	≥8 < 8	91 268	616 2,229	1.22	0.94 – 1.59
	MH Pooled	≥8 < 8	---	---	1.20	0.97 – 1.48
Sex	Female	≥8 < 8	62 162	760 2,546	1.28	0.93 – 1.75
	Male	≥8 < 8	71 213	972 2,974	1.02	0.76 – 1.35
	MH Pooled	≥8 < 8	---	---	1.13	0.92 – 1.39
Post-arrival time (minutes)	<30	≥8 < 8	26 98	371 1,456	1.04	0.64 – 1.65
	30-35	≥8 < 8	24 74	315 1,296	1.33	0.79 – 2.18
	36-44	≥8 < 8	33 86	519 1,581	1.17	0.75 – 1.79
	≥45	≥8 < 8	50 117	527 1,187	0.96	0.67 – 1.38
	MH Pooled	≥8 < 8	---	---	1.09	0.89 – 1.34

Note: OR=Odds ratio; CI=Confidence interval; MH=Mantel-Haenszel; Post-arrival time= time interval from arrival on scene to arrival at hospital.
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The exposure outcome relationship was further analyzed using logistic regression. The planned model is represented schematically by:

$$\ln\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 Exp + \beta_2 Age + \beta_3 Sex + \beta_4 Post\_Arrival$$

The final model results are summarized in table 6.5. This model would suggest that there is no statistically significant difference in the estimated mortality between patients who received a response time greater than or equal to eight minutes versus patients who received a response time under eight minutes (OR=1.19; 95% CI 0.97 – 1.47) while controlling for the effects of age, sex, and post-arrival time. It would also suggest that for a given response time, there is a statistically significant increased odds of mortality with increasing age (OR=2.87; 95% CI 2.46 – 3.35), and a statistically significant increased odds of mortality in males when compared to females (OR=1.22; 95% CI 1.02 – 1.47).

Coding age as a measured variable or as a categorical variable using the same age cut-points did not change the association between the exposure and outcome.

Table 6.5: Results of the final model for the primary research question.

Variable	OR	CI	p-value*
Response ≥8	1.19	0.97 – 1.47	0.103
Age	2.87	2.46 – 3.35	<0.001
Sex	1.22	1.02 – 1.47	0.033
Post-arrival time	1.05	0.97 – 1.15	0.236

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.4 Secondary research questions

6.4.1 Eight minute response time and ED and IP all-cause mortality

6.4.1.1 Eight minute response time and ED mortality

A total of 43 out of 1,916 (2.2%) patients that received a response time of greater than or equal to 8 minutes died in the ED, compared to 127 out of 6,027 (2.1%) patients that received a response time of less than 8 minutes (Table 6.6). A two sided fisher's exact test failed to reject the null hypothesis (p=0.717) that the crude proportion of mortality in the ED is not different for exposed and unexposed patients.

The estimated odds ratio of mortality is 1.07 (95% CI 0.73 to 1.53). A stratified analysis similar to the primary research question described previously was performed. No evidence of effect measure modification or confounding by sex or post-arrival time could be demonstrated. Similar to the primary research question the OR for the 18 to 39 year old stratum differed from other age stratums. The frequency of observation of death in the 18 to 39 year old stratum for response times greater or equal to eight minutes was only 1 out of 499 unit responses. Again given no similar observation in previous studies, and no obvious biologically plausible explanations it is likely an effect of small sample size. We estimated the odds-ratio if we moved two individuals from alive to dead in the greater than or equal to eight minutes, and 2 individuals from dead to alive in the less than eight minute strata (4 individual outcomes reassigned out of 1,991 observed unit responses), these changes resulted in a movement of the stratum specific OR for the 18 to 39 year old group to 1.0.

In the absence of a biologically plausible explanation, or previous observed similar phenomena, it is unlikely that this is effect measure modification. In addition, as the pooled OR is similar to the crude, reporting of the crude OR would seem appropriate (Table 6.6).

Table 6.6: Stratified analysis for the secondary research question (eight minute response time and ED mortality).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥8 < 8	43 127	1,873 5,900	1.07	0.73 – 1.53
Age	18-39	≥8 < 8	1 11	498 1,481	0.27	0.01 – 1.87
	40-64	≥8 < 8	14 38	672 1,924	1.06	0.52 – 2.01
	≥65	≥8 < 8	28 78	703 2,495	1.27	0.79 – 2.00
	MH Pooled	≥8 < 8	---	---	1.11	0.78 – 1.57
Sex	Female	≥8 < 8	18 43	829 2,728	1.38	0.74 – 2.45
	Male	≥8 < 8	25 84	1,044 3,172	0.90	0.55 – 1.44
	MH Pooled	≥8 < 8	---	---	1.06	0.75 – 1.50
Post-arrival time (minutes)	<30	≥8 < 8	7 30	396 1,562	0.92	0.34 – 2.16
	30-35	≥8 < 8	7 25	344 1,374	1.11	0.79 – 2.68
	36-44	≥8 < 8	13 26	551 1,671	1.51	0.75 – 3.09
	≥45	≥8 < 8	16 46	582 1,293	0.77	0.41 – 1.40
	MH Pooled	≥8 < 8	---	---	1.09	0.89 – 1.34

Note: OR=Odds ratio; CI=Confidence interval; MH=Mantel-Haenszel; Post-arrival time= time interval from arrival on scene to arrival at hospital.
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The final model results for the primary exposure (8 minute response time) and ED mortality are summarized in Table 6.7. The conclusions from this model are unchanged from the primary research question model described above, except post-arrival time. In this model for a given response time the odds of mortality increases with increasing post-arrival time (OR=1.16; 95% CI 1.01 – 1.34).

Table 6.7: Results of the final model for the secondary research question (eight minute response time and ED mortality).

Variable	OR	CI	p-value*
Response ≥8	1.07	0.76 – 1.53	0.688
Age	2.09	1.66 – 2.63	<0.001
Sex	1.69	1.23 – 2.33	0.001
Post-arrival time	1.16	1.01 – 1.34	0.038

Note: OR = Odds Ratio; CI = 95% Confidence Interval; ED=Emergency Department
* Wald test

6.4.1.2 Eight minute response time and IP mortality

A total of 90 out of 724 (12.4%) patients that received a response time of greater than or equal to 8 minutes died as an IP, compared to 248 out of 2,417 (10.3%) patients that received a response time of less than 8 minutes (Table 6.8). A two sided fisher's exact test failed to reject the null hypothesis (p=0.101) that the crude proportion of survival from the IP is not different for exposed and unexposed patients.

The estimated odds ratio of mortality is 1.24 (95% CI 0.95 to 1.61). A stratified analysis similar to the primary research question described previously was performed. No evidence of effect measure modification or confounding by sex or post-arrival time could be demonstrated. Similar to the primary research question the OR for the 18 to 39 year old stratum differed from other age stratums. The frequency of observation of death in the 18 to 39 year old stratum for response times greater or equal to eight minutes was only 3 out of 104 unit responses. Again given no similar observation in previous studies, and no obvious biologically plausible explanations it is likely an effect of small sample size. We estimated the odds-ratio if we moved two individuals from alive to dead in the greater than or equal to eight minutes, and 2 individuals from dead to alive in the less than eight minute strata (4 individual outcomes reassigned out of 410 observed unit responses). These changes resulted in a movement of the stratum specific OR for the 18 to 39 year old group to 1.88.

In the absence of a biologically plausible explanation, or previous observed similar phenomena, it is unlikely that this is effect measure modification. In addition, as the pooled OR is similar to the crude, reporting of the crude OR would seem appropriate (Table 6.8).

Table 6.8: Stratified analysis for the secondary research question (eight minute response time and IP mortality).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥8 < 8	90 248	634 2,169	1.24	0.95 – 1.61
Age	18-39	≥8 < 8	3 10	101 296	0.88	0.15 – 3.51
	40-64	≥8 < 8	24 48	205 635	1.55	0.88 – 2.65
	≥65	≥8 < 8	63 190	328 1,238	1.25	0.90 – 1.72
	MH Pooled	≥8 < 8	---	---	1.30	1.00 – 1.69
Sex	Female	≥8 < 8	44 119	262 939	1.33	0.89 – 1.94
	Male	≥8 < 8	46 129	372 1,230	1.18	0.81 – 1.70
	MH Pooled	≥8 < 8	---	---	1.25	0.96 – 1.61
Post-arrival time (minutes)	<30	≥8 < 8	19 68	140 525	1.05	0.58 – 1.83
	30-35	≥8 < 8	17 49	114 494	1.50	0.78 – 2.77
	36-44	≥8 < 8	20 60	191 654	1.14	0.64 – 1.98
	≥45	≥8 < 8	34 71	189 496	1.26	0.78 – 1.99
	MH Pooled	≥8 < 8	---	---	1.22	0.94 – 1.58

Note: OR=Odds ratio; CI=Confidence interval; MH=Mantel-Haenszel; Post-arrival time= time interval from arrival on scene to arrival at hospital.
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The final model results for the primary exposure (8 minute response time) and IP mortality are summarized in Table 6.9. This model would suggest that there is a statistically significant difference in mortality between patients who received a response time greater than or equal to eight minutes versus patients who received a response time under eight minutes while controlling for the effects of age, sex, and post-arrival time (OR=1.30; 1.00 – 1.69). It would also suggest that for a given response time there is a statistically significant increased odds of mortality with increasing age (OR=2.04; 1.67 – 2.51) (Table 6.9).

Table 6.9: Results of the final model for the secondary research question (eight minute response time and IP mortality).

Variable	OR	CI	p-value*
Response ≥8	1.30	1.00 – 1.69	0.046
Age	2.04	1.67 – 2.51	<0.001
Sex	0.90	0.71 – 1.13	0.355
Post-arrival time	1.00	0.90 – 1.11	0.966

Note: OR = Odds Ratio; CI = 95% Confidence Interval; IP=In-Patient
* Wald test

6.4.2 Four minute response time and all-cause mortality

A total of 460 out of 6,784 (6.8%) patients that received a response time of greater than or equal to 4 minutes died, compared to 48 out of 976 (4.9%) patients that received a response time of less than 4 minutes (Table 6.10). A two sided fisher's exact test rejected the null hypothesis (p=0.032) that the crude proportion of mortality is not different for exposed and unexposed patients.

Table 6.10: Crude results for the secondary research question (four minute response time and all-cause mortality).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥4 < 4	460 48	6,324 928	1.41	1.03 – 1.95

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The estimated odds ratio of mortality is 1.41 (95% CI 1.03 to 1.95). A stratified analysis similar to the primary research question described previously was performed (results not shown). No evidence of effect measure modification or confounding by age, sex, or post-arrival time could be demonstrated.

The final model results for the secondary exposure (4 minute response time) and all-cause mortality are summarized in Table 6.11. This model would suggest that there is not a statistically significant difference in mortality between patients who received a response time greater than or equal to four minutes versus patients who received a response time under four minutes while controlling for the effects of age, sex, and post-arrival time (OR=1.35; 0.99 – 1.83) (Table 6.11). For a given response time there was also a statistically significant increase in mortality with increasing age (OR=2.85; 95% CI 2.45 – 3.32) and a statistically significant increased odds of mortality in males when compared to females (OR=1.22; 95% CI 1.02 – 1.47).

Table 6.11: Results of the final model for the secondary research question (four minute response time and all-cause mortality).

Variable	OR	CI	p-value*
Response ≥4	1.35	0.99 – 1.83	0.060
Age	2.85	2.45 – 3.32	<0.001
Sex	1.22	1.02 – 1.47	0.035
Post-arrival time	1.06	0.97 – 1.15	0.215

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.4.3 Four minute response time and ED and IP all-cause mortality

6.4.3.1 Four minute response time and ED mortality

A total of 152 out of 6,947 (2.2%) patients that received a response time of greater than or equal to 4 minutes died in the ED, compared to 18 out of 996 (1.8%) patients that received a response time of less than 4 minutes (Table 6.12). A two sided fisher's exact test failed to reject the null hypothesis (p=0.484) that the crude proportion of mortality in the ED is not different for exposed and unexposed patients.

Table 6.12: Crude results for the secondary research question (four minute response time and ED mortality).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	**Crude**	≥4 < 4	152 18	6,795 978	1.23	0.73 – 2.12

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The estimated odds ratio of mortality is 1.23 (95% CI 0.73 to 2.12). A stratified analysis similar to the primary research question described previously was performed (results not shown). No evidence of effect measure modification or confounding by age, sex, or post-arrival time could be demonstrated.

The final model results for the secondary exposure (4 minute response time) and ED all-cause mortality are summarized in Table 6.13. This model would suggest that there is not a statistically significant difference in ED mortality between patients who received a response time greater than or equal to four minutes versus patients who received a response time under four minutes while controlling for the effects of age, sex, and post-arrival time (OR=1.14; 0.70 – 1.87) (Table 6.13). For a given response time there was also a statistically significant increase in ED mortality with increasing age (OR=2.08; 95% CI 1.65 – 2.63), a statistically significant increased odds of ED mortality in males when compared to females (OR=1.69; 95% CI 1.23 – 2.33), and a statistically significant increase in ED mortality with increasing post-arrival time (OR=1.16; 95% CI 1.01 – 1.34).

Table 6.13: Results of the final model for the secondary research question (four minute response time and ED mortality).

Variable	OR	CI	p-value*
Response ≥4	1.14	0.70 – 1.87	0.600
Age	2.08	1.65 – 2.63	<0.001
Sex	1.69	1.23 – 2.33	0.001
Post-arrival time	1.16	1.01 – 1.34	0.036

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.4.3.2 Four minute response time and IP mortality

A total of 308 out of 2,766 (11.1%) patients that received a response time of greater than or equal to 4 minutes died as an IP, compared to 30 out of 375 (8.0%) patients that received a response time of less than 4 minutes (Table

6.14). A two sided fisher's exact test failed to reject the null hypothesis (p=0.075) that the crude proportion of survival as an IP is not different for exposed and unexposed patients.

Table 6.14: Crude results for the secondary research question (four minute response time and IP mortality).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥4 < 4	308 30	2,458 345	1.44	0.96 – 2.20

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The estimated odds ratio of mortality as an IP is 1.44 (95% CI 0.96 to 2.20). A stratified analysis similar to the primary research question described previously was performed (results not shown). No evidence of effect measure modification or confounding by age, sex, or post-arrival time could be demonstrated.

The final model results for the secondary exposure (4 minute response time) and IP all-cause mortality are summarized in Table 6.15. This model would suggest that there is not a statistically significant difference in IP mortality between patients who received a response time greater than or equal to four minutes versus patients who received a response time under four minutes while controlling for the effects of age, sex, and post-arrival time (OR=1.44; 0.97 – 2.13) (Table 6.15). For a given response time there was also a statistically significant increase in IP mortality with increasing age (OR=2.03; 95% CI 1.65 – 2.49).

Table 6.15: Results of the final model for the secondary research question (four minute response time and IP mortality).

Variable	OR	CI	p-value*
Response ≥4	1.44	0.97 – 2.13	0.072
Age	2.03	1.65 – 2.49	<0.001
Sex	0.90	0.71 – 1.13	0.346
Post-arrival time	1.01	0.91 – 1.12	0.900

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.4.4 Nine minute response time and all-cause mortality

A total of 70 out of 1,210 (5.8%) patients that received a response time of greater than or equal to 9 minutes died, compared to 438 out of 6,550 (6.7%) patients that received a response time of less than 9 minutes (Table 6.16). A two sided fisher's exact test failed to reject the null hypothesis (p=0.255) that the crude proportion of mortality is not different for exposed and unexposed patients.

Table 6.16: Crude results for the secondary research question (nine minute response time and all-cause mortality).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥9 < 9	70 438	1,140 6,112	0.86	0.65 – 1.12

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The estimated odds ratio of mortality is 0.86 (95% CI 0.65 to 1.12). A stratified analysis similar to the primary research question described previously was performed (results not shown). No evidence of effect measure modification or confounding by age, sex, or post-arrival time could be demonstrated.

The final model results for the secondary exposure (9 minute response time) and all-cause mortality are summarized in Table 6.17. This model would suggest that there is not a statistically significant difference in all-cause mortality between patients who received a response time greater than or equal to nine minutes versus patients who received a response time under nine minutes while controlling for the effects of age, sex, and post-arrival time (OR=0.93; 0.72 – 1.21) (Table 6.17). For a given response time there was also a statistically significant increase in all-cause mortality with increasing age (OR=2.85; 95% CI 2.45 – 3.32), and a statistically significant increased odds of all-cause mortality in males when compared to females (OR=1.23; 95% CI 1.02 – 1.47).

Table 6.17: Results of the final model for the secondary research question (nine minute response time and all-cause mortality).

Variable	OR	CI	p-value*
Response ≥9	0.93	0.72 – 1.21	0.597
Age	2.85	2.45 – 3.32	<0.001
Sex	1.23	1.02 – 1.47	0.031
Post-arrival time	1.06	0.97 – 1.15	0.182

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.4.5 Nine minute response time and ED and IP all-cause mortality

6.4.5.1 Nine minute response time and ED mortality

A total of 22 out of 1,238 (1.8%) patients that received a response time of greater than or equal to 9 minutes died in the ED, compared to 148 out of 6,705 (2.2%) patients that received a response time of less than 9 minutes (Table 6.18). A two sided fisher's exact test failed to reject the null hypothesis (p=0.392) that the crude proportion of mortality in the ED is not different for exposed and unexposed patients.

Table 6.18: Crude results for the secondary research question (nine minute response time and ED mortality).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥9 < 9	22 148	1,216 6,557	0.80	0.49 – 1.27

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The estimated odds ratio of mortality is 0.80 (95% CI 0.49 to 1.27). A stratified analysis similar to the primary research question described previously was performed (results not shown). No evidence of effect measure modification or confounding by age, sex, or post-arrival time could be demonstrated.

The final model results for the secondary exposure (9 minute response time) and ED mortality are summarized in Table 6.19. This model would suggest that there is not a statistically significant difference in ED mortality between patients who received a response time greater than or equal to nine minutes versus patients who received a response time under nine minutes while controlling for the effects of age, sex, and post-arrival time (OR=0.83; 0.53 – 1.31) (Table 6.19). For a given response time there was also a statistically significant increase in ED mortality with increasing age (OR=2.07; 95% CI 1.64 – 2.61), a statistically significant increased odds of ED mortality in males when compared to females (OR=1.69; 95% CI 1.23 – 2.33), and a statistically significant increase in ED mortality with increasing post-arrival time (OR=1.17; 95% CI 1.02 – 1.35).

Table 6.19: Results of the final model for the secondary research question (nine minute response time and ED mortality).

Variable	OR	CI	p-value*
Response ≥9	0.83	0.53 – 1.31	0.430
Age	2.07	1.64 – 2.61	<0.001
Sex	1.69	1.23 – 2.33	0.001
Post-arrival time	1.17	1.02 – 1.35	0.030

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.4.5.1 Nine minute response time and IP mortality

A total of 48 out of 469 (10.2%) patients that received a response time of greater than or equal to 9 minutes died as an IP, compared to 290 of 2,672 (10.9%) patients that received a response time of less than 9 minutes (Table 6.20). A two sided fisher's exact test failed to reject the null hypothesis (p=0.747) that the crude proportion of survival as an IP is not different for exposed and unexposed patients.

Table 6.20: Crude results for the secondary research question (nine minute response time and IP mortality).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥9	48	421	0.94	0.66 – 1.30
		< 9	290	2,382		

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The estimated odds ratio of mortality is 0.94 (95% CI 0.66 to 1.30). A stratified analysis similar to the primary research question described previously was performed (results not shown). No evidence of effect measure modification or confounding by age, sex, or post-arrival time could be demonstrated.

The final model results for the secondary exposure (9 minute response time) and IP mortality are summarized in Table 6.21. This model would suggest that there is not a statistically significant difference in IP mortality between patients who received a response time greater than or equal to nine minutes versus patients who received a response time under nine minutes while controlling for the effects of age, sex, and post-arrival time (OR=1.02; 0.73 – 1.41) (Table 6.21). For a given response time there was also a statistically significant increase in IP mortality with increasing age (OR=2.03; 95% CI 1.65 – 2.49).

Table 6.21: Results of the final model for the secondary research question (nine minute response time and IP mortality).

Variable	OR	CI	p-value*
Response ≥9	1.02	0.73 – 1.41	0.911
Age	2.03	1.65 – 2.49	<0.001
Sex	0.90	0.72 – 1.13	0.366
Post-arrival time	1.01	0.91 – 1.12	0.870

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.5 Summary of primary and secondary research question results

A summary of the findings from the primary and secondary research questions are presented in Table 6.22.

Table 6.22: Summary of results for the primary and secondary research questions.

Exposure	Outcome	OR (95% CI)	
		Crude	Adjusted*
8 minutes	Total Mortality	1.13 (0.91 – 1.39)	1.19 (0.97 – 1.47)
	ED Mortality	1.07 (0.73 – 1.53)	1.07 (0.76 – 1.53)
	IP Mortality	1.24 (0.95 – 1.61)	1.30 (1.00 – 1.69)
4 minutes	Total Mortality	1.41 (1.03 – 1.95)	1.35 (0.99 – 1.83)
	ED Mortality	1.23 (0.73 – 2.12)	1.14 (0.70 – 1.87)
	IP Mortality	1.44 (0.96 – 2.20)	1.44 (0.97 – 2.13)
9 minutes	Total Mortality	0.86 (0.65 – 1.12)	0.93 (0.72 – 1.21)
	ED Mortality	0.80 (0.49 – 1.27)	0.83 (0.53 – 1.31)
	IP Mortality	0.94 (0.66 – 1.30)	1.02 (0.73 – 1.41)

Note: OR = Odds Ratio; CI = 95% Confidence Interval; ED = Emergency Department; IP = In-Patient; post arrival interval=time interval from arrival on scene to arrival at hospital.
* Adjusted for age, sex, and post-arrival time

With an eight minute exposure, the adjusted odds ratio of mortality is close to statistical significance for all patients, marginally statistically significant for IP's, but not close to statistical significant for ED patients. At a four minute response time exposure the adjusted odds ratio of mortality is close to statistical significance for all patients and IP's, but not close for ED patients. At a nine minute exposure it is not close to statistical significance for all patients, IP's, and ED patients.

6.6 Exploratory analysis questions

6.6.1 Cardiac arrest patients

6.6.1.1 Data preparation and linkage

There were 364 unit responses recorded in the prehospital arrest database (PHAR) maintained by Calgary EMS. A total of 193 non-duplicated unit responses were for a delta or echo unit response resulting in transport to hospital. A total of 171 out of 193 (89%) unit responses were successfully linked to the thesis database.

6.6.1.2 Stratified analysis

A total of 58 out of 66 (87.9%) of patients that received a response time of greater than or equal to 8 minutes died, compared to 182 out of 212 (85.6%) of patients that received a response time of less than 8 minutes (Table 6.23). A two sided fisher's exact test failed to reject the null hypothesis (p=0.838) that the crude proportion of mortality is not different for exposed and unexposed patients.

The estimated odds ratio of mortality is 1.20 (95% CI 0.50 to 3.19). A stratified analysis similar to the primary research question described previously was performed (Table 6.23). Sizeable differences in stratum specific OR's were seen for all variables. Similar to the situation with age in the primary research questions, there are multiple cells with a small sample size. A reasonable biologically plausible hypothesis could not be found to account for these observations. Likewise, an examination of available literature did not demonstrate a similar finding. In the absence of a biologically plausible explanation, or previous observed similar phenomena, it is unlikely that this is effect measure modification. In addition, as the pooled OR is similar to the crude, reporting of the crude OR would seem appropriate (Table 6.23).

Table 6.23: Stratified analysis for the exploratory research question (8 minute response time and all-cause mortality for the sub-group cardiac arrest).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥8 < 8	58 182	8 30	1.20	0.50 – 3.19
Age	18-39	≥8 < 8	6 15	2 3	0.6	0.54 – 9.08
	40-64	≥8 < 8	24 64	4 16	1.5	0.42 – 6.76
	≥65	≥8 < 8	28 103	2 11	1.50	0.30 – 14.62
	MH Pooled	≥8 < 8	---	---	1.29	0.55 – 3.00
Sex	Female	≥8 < 8	21 62	2 11	1.86	0.36 – 18.55
	Male	≥8 < 8	37 120	6 19	0.98	0.34 – 3.21
	MH Pooled	≥8 < 8	---	---	1.20	0.52 – 2.75
Bystander CPR	Yes	≥8 < 8	27 75	3 7	1.31	0.43 – 4.79
	No	≥8 < 8	30 101	5 22	0.84	0.18 – 5.40
	MH Pooled	≥8 < 8	---	---	1.13	0.49 – 2.62
Pre-EMS defibrillation	Yes	≥8 < 8	3 7	2 3	0.64	0.04 – 11.91
	No	≥8 < 8	54 167	6 26	1.40	0.53 – 4.38
	MH Pooled	≥8 < 8	---	---	1.26	0.53 – 2.96

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

6.6.1.3 Multivariable analysis

The exposure outcome relationship was further analyzed using logistic regression. The planned model is represented schematically by:

$$\ln\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 Exp + \beta_2 Age + \beta_3 Sex + \beta_4 Byst\_CPR + \beta_5 PRE\_EMS\_defib$$

Bystander CPR was not included in the multivariable model as it was found to be associated with increased mortality when compared to patients who did not receive bystander CPR. Further analysis revealed that the majority of cases of witnessed arrest by EMS (n=36) did not receive bystander CPR. When crude mortality is compared to witnessed arrest status, it was found that 35.9% of all cardiac arrests that were witnessed by EMS survive, compared to 17.2% that survive when witnessed by bystanders, and 4.8% that survive when not witnessed. Moreover, the final results of the model did not change when bystander CPR was included.

Therefore the final model is represented schematically by:

$$\ln\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 Exp + \beta_2 Age + \beta_3 Sex + \beta_4 PRE\_EMS\_defib$$

The final model results for the primary exposure (8 minute response time) and all-cause mortality for patients in cardiac arrest are summarized in Table 6.24. This model would suggest that there is not a statistically significant difference in all-cause mortality between cardiac arrest patients who received a response time greater than or equal to eight minutes versus patients who received a response time under eight minutes while controlling for the effects of age, sex, and pre-EMS defibrillation (OR=1.35; 0.57 – 3.19) (Table 6.24). For a given response time there was also a statistically significant increase in all-cause mortality with increasing age (OR=1.80; 95% CI 1.08 – 3.02), and a statistically significant decrease in mortality with pre-EMS defibrillation (OR=0.31; 0.10 – 0.99).

Table 6.24: Results of the final model for the exploratory research question (eight minute response time and all-cause mortality for the sub-group cardiac arrest).

Variable	OR	CI	p-value*
Response ≥8	1.35	0.57 – 3.19	0.495
Age	1.80	1.08 – 3.02	0.024
Sex	1.04	0.49 – 2.19	0.922
Pre-EMS Defibrillation	0.31	0.10 – 0.99	0.048

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.6.2 ST elevation myocardial infarction (STEMI) patients

6.6.2.1 Data preparation and linkage

There were a total of 242 unit responses that corresponded to a patient with a confirmed STEMI for the 2006 calendar year, of which 137 unit responses were for a delta or echo unit response and not a duplicate unit response in the database. A total of 119 out of 137 (87%) unit responses were successfully linked in this database.

6.6.2.2 Stratified analysis

A total of 1 out of 25 (4.0%) patients that received a response time of greater than or equal to 8 minutes died, compared to 3 out of 91 (3.3%) patients that received a response time of less than 8 minutes (Table 6.25). A two sided fisher's exact test failed to reject the null hypothesis (p=1.000) that the crude proportion of mortality is not different for exposed and unexposed patients. A stratified analysis similar to the primary research question described previously was performed. It is impossible to assess for effect measure modification or confounding due to the presence of zero cells.

Table 6.25: Stratified analysis for the exploratory research question (8 minute response time and all-cause mortality for the sub-group ST Elevation Myocardial Infarction).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥8 < 8	1 3	24 88	1.22	0.02 – 16.0
Age	18-39	≥8 < 8	0 0	3 3	---	---
	40-64	≥8 < 8	0 1	16 50	0	0
	≥65	≥8 < 8	1 2	5 35	3.5	0.05 – 76.57
	MH Pooled	≥8 < 8	---	---	1.73	0.17 – 17.48
Sex	Female	≥8 < 8	0 1	3 20	0	0
	Male	≥8 < 8	1 2	21 68	1.62	0.03 – 32.38
	MH Pooled	≥8 < 8	---	---	1.27	0.12 – 13.37
Post-arrival time (minutes)	<36	≥8 < 8	1 2	9 45	2.5	0.38 – 51.94
	≥36	≥8 < 8	0 1	12 43	0	0
	MH Pooled	≥8 < 8	---	---	1.49	0.15 – 15.03

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The estimated odds ratio of mortality is 1.2 (95% CI 0.02 to 16.0). There are only four patients in this cohort that died. There are zero cells in at least one strata for each covariate. The covariates cannot be further collapsed in a clinically appropriate manner, therefore no covariates were included in the analysis.

6.6.2.3 Multivariable analysis

As described previously, no covariates were included in this model due to zero cells in the strata of each covariate.

6.6.3 Stroke patients

6.6.3.1 Data preparation

The stroke subgroup did not require linkage, as locally validated ICD 10 CA codes were used to identify patients.(62) There were 7,943 unit responses, 147 corresponded to an ICD 10 CA code that pertains to stroke.

6.6.3.2 Stratified analysis

A total of 21 out of 41 (51.2%) patients that received a response time of greater than or equal to 8 minutes died, compared to 33 out of 103 (32.0%) patients that received a response time of less than 8 minutes (Table 6.26). A two sided fisher's exact test rejected the null hypothesis (p=0.037) that the crude proportion of mortality is not different for exposed and unexposed patients.

Table 6.26: Stratified analysis for the exploratory research question (8 minute response time and all-cause mortality for the sub-group stroke).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥8 < 8	21 33	20 70	2.23	1.0 – 4.98
Age	18-39	≥8 < 8	1 1	0 3	0	0
	40-64	≥8 < 8	3 9	4 21	1.75	0.21 – 12.67
	≥65	≥8 < 8	17 23	16 46	2.13	0.84 – 5.40
	MH Pooled	≥8 < 8	---	---	2.18	1.03 – 4.58
Sex	Female	≥8 < 8	11 17	12 34	1.83	0.59 – 5.62
	Male	≥8 < 8	10 16	8 36	2.81	0.81 – 9.80
	MH Pooled	≥8 < 8	---	---	2.22	1.06 – 4.66
Post-arrival time (minutes)	<29	≥8 < 8	4 7	5 20	2.29	0.34 – 14.13
	≥29 & <37	≥8 < 8	6 10	3 16	3.2	0.52 – 23.58
	≥37 & <47	≥8 < 8	6 7	6 18	2.57	0.49 – 13.43
	≥47	≥8 < 8	5 9	6 16	1.48	0.27 – 7.80
	MH Pooled	≥8 < 8	---	---	2.26	1.07 – 4.78

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

The estimated odds ratio of mortality is 2.23 (95% CI 1.0 to 4.98). A stratified analysis similar to the primary research question described previously was performed. Due to the presence of zero cells in the 18 to 39 year stratum, age could not be assessed for effect measure modification or confounding. Sizeable differences in stratum specific OR's was seen for sex and post-arrival time. Similar to the situation with age in the primary research question, there are multiple cells with a small sample size. A reasonable biologically plausible hypothesis could not be found to account for these observations. Likewise, an examination of available literature did not demonstrate a similar finding. In the absence of a biologically plausible explanation, or previous observed similar phenomena, it is unlikely that this is effect measure modification. In addition, as the pooled OR is similar to the crude, reporting of the crude OR would seem appropriate (Table 6.26).

6.6.3.3 Multivariable analysis

The exposure outcome relationship was further analyzed using logistic regression. The planned model is represented schematically by:

$$\ln\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 Exp + \beta_2 Age + \beta_3 Sex + \beta_4 Post\_arrival$$

Age category as defined in the stratified analysis contained zero cells in the 18 to 39 year old category. Therefore age was dichotomized at 65 years of age, as this broadly divides the cohort into younger and older.

The final model results are summarized in table 6.27. The main findings from this model would suggest there is a statistically significant difference in the estimate of mortality between patients with an ICD 10 CA code corresponding to stroke who received a response time greater than or equal to eight minutes versus those patients who received a response time less than eight minutes while controlling for the effects of age, sex, and post-arrival time (OR=2.17; 95% CI 1.02 – 4.58).

Table 6.27: Results of the final model for the exploratory research question (eight minute response time and all-cause mortality for the sub-group stroke).

Variable	OR	CI	p-value*
Response ≥8	2.17	1.02 – 4.58	0.043
Age	1.18	0.54 – 2.57	0.681
Sex	0.99	0.49 – 1.98	0.971
Post-arrival time	1.05	0.77 – 1.44	0.750

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.6.4 Severe trauma patients

6.6.4.1 Data preparation and linkage

There were a total of 466 patients that received a transport from the City of Calgary EMS registered in the CHR Trauma Services regional trauma registry for the 2006 calendar year. A total of 236 out of 466 (51%) patients were linked to the thesis database.

6.6.4.2 Stratified analysis

A total of 7 out of 56 (12.5%) patients that received a response time of greater than or equal to 8 minutes died, compared to 23 out of 175 (13.1%) patients that received a response time of less than 8 minutes (Table 6.28). A two sided fisher's exact test failed to reject the null hypothesis (p=1.000) that the crude proportion of mortality is not different for exposed and unexposed patients.

The estimated odds ratio of mortality for severe trauma patients is 0.94 (95% CI 0.32 to 2.45). A stratified analysis similar to the primary research question described previously was performed. Due to the presence of zero cells in the penetrating trauma stratum, trauma type could not be assessed for effect measure modification or confounding. Sizeable differences in stratum specific OR's were seen for age, sex, and post-arrival time. Similar to the situation with age in the primary research question, there were multiple cells with a small sample size. A reasonable biologically plausible hypothesis could not be found to account for these observations. Likewise, an examination of available literature did not demonstrate a similar finding. In the absence of a biologically plausible explanation, or previous observed similar phenomena, it is unlikely that this is effect measure modification. In addition, as the pooled OR is similar to the crude, reporting of the crude OR would seem appropriate (Table 6.28).

Table 6.28: Stratified analysis for the exploratory research question (8 minute response time and all-cause mortality for the sub-group severe trauma).

Variable	Category	Exposure (minutes)	Dead	Alive	OR*	95% CI
---	Crude	≥8 < 8	7 23	49 152	0.94	0.32 – 2.45
Age	18-39	≥8 < 8	1 9	26 80	0.34	0.01 – 2.70
	40-64	≥8 < 8	2 2	18 48	2.67	0.18 – 38.74
	≥65	≥8 < 8	4 12	5 24	1.6	0.26 – 8.96
	MH Pooled	≥8 < 8	---	---	1.09	0.41 – 2.86
Sex	Female	≥8 < 8	5 10	11 35	1.59	0.35 – 6.54
	Male	≥8 < 8	2 13	38 117	0.47	0.05 – 2.25
	MH Pooled	≥8 < 8	---	---	0.90	0.35 – 2.30
Post-arrival time (minutes)	<29	≥8 < 8	2 5	10 41	1.64	0.14 – 11.90
	≥29 & <37	≥8 < 8	1 6	12 39	0.54	0.01 – 5.26
	≥37 & <47	≥8 < 8	1 5	14 38	0.54	0.01 – 5.56
	≥47	≥8 < 8	3 7	12 34	1.21	0.17 – 6.46
	MH Pooled	≥8 < 8	---	---	0.95	0.38 – 2.36
Trauma type	Blunt	≥8 < 8	6 17	45 134	1.05	0.32 – 3.01
	Penetrating	≥8 < 8	0 4	3 18	0	0
	Burns	≥8 < 8	1 2	1 0	0	0
	MH Pooled	≥8 < 8	---	---	0.84	0.32 – 2.17

Note: OR=Odds ratio; CI=Confidence interval
*Odds of mortality given a response time greater than or equal to eight minutes over the odds of mortality given a response time less than or equal to eight minutes

6.6.4.3 Multivariable analysis

The exposure outcome relationship was further analyzed using logistic regression. The planned model is represented schematically by:

$$\ln\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 Exp + \beta_2 Age + \beta_3 Sex + \beta_4 Post\_arrival + \beta_5 Trauma\_type$$

Trauma type contained zero cells for penetrating trauma and other trauma stratum, but could not be collapsed in a clinically plausible manner so was omitted from the model.

$$\ln\left\{\frac{p}{1-p}\right\} = \beta_0 + \beta_1 Exp + \beta_2 Age + \beta_3 Sex + \beta_4 Post\_arrival$$

The final model results for the primary exposure (8 minute response time) and all-cause mortality for severe trauma patients are summarized in Table 6.29. This model would suggest that there is not a statistically significant difference in all-cause mortality between severe trauma patients who received a response time greater than or equal to eight minutes versus patients who received a response time under eight minutes while controlling for the effects of age, sex, and post-arrival time (OR=0.92; 0.35 – 2.41) (Table 6.29). For a given response time there was also a statistically significant increase in all-cause mortality with increasing age (OR=2.27; 95% CI 1.37 – 3.76), and a statistically significant decreased odds of all-cause mortality in males when compared to females (OR=0.36; 95% CI 0.16 – 0.83).

Table 6.29: Results of the final model for the exploratory research question (eight minute response time and all-cause mortality for the sub-group severe trauma).

Variable	OR	CI	p-value*
Response ≥8	0.92	0.35 – 2.41	0.868
Age	2.27	1.37 – 3.76	0.001
Sex	0.36	0.16 – 0.83	0.016
Post-arrival time	1.06	0.74 – 1.52	0.747

Note: OR = Odds Ratio; CI = 95% Confidence Interval
* Wald test

6.6.5 Summary of exploratory analysis

A summary of the findings from the exploratory analysis are presented in Table 6.30.

Table 6.30: Summary of results for the exploratory analyses.

Subgroup	OR (95% CI)	
	Crude	Adjusted
Cardiac Arrest	1.20 (0.50 – 3.19)	1.35 (0.57 – 3.19)*
STEMI	1.22 (0.02 – 16.0)	--
Stroke	2.23 (1.00 – 4.98)	2.17 (1.02 – 4.58)†
Severe Trauma	0.94 (0.32 – 2.45)	0.92 (0.35 – 2.15)†

Note: OR = Odds Ratio; CI = 95% Confidence Interval.
* Adjusted for age, sex, and pre-EMS defibrillation.
† Adjusted for age, sex, and post-arrival time.

There were no statistically significant differences between those patients that received a response time under 8 minutes versus those who received a response time greater than or equal to eight minutes in cardiac arrest, STEMI, and severe trauma patients. There was a statistically significant difference in stroke patients.

Chapter Seven: Discussion

7.1 Primary research question

For patients who require the highest level of EMS response (Delta and Echo level which results in a 2 tiered BLS-D/ALS response using lights and sirens) the adjusted odds of dying given a response time greater than or equal to eight minutes is 1.19 times that of dying given a response time of less than eight minutes. This OR may be as high as 1.47 or as low as 0.97. A difference of 1.19 or greater cannot be excluded due to chance alone.

These data are similar to the findings from Pons *et al.* that there is no statistically significant difference in mortality at an eight minute dichotomous exposure level (Table 7.1), although our estimate (and variance in estimate) had narrower confidence intervals and approached significance.(7) They differ from the results presented by Mayer (1979), but this is likely explained by differences in definitions for response time and mortality, and fundamental differences in the era in which the data were collected.

A key feature of this study relative to other studies listed in Table 7.1 is the restriction to Delta and Echo level unit responses. Both Delta and Echo level unit responses are reserved for patients reported to be in a critical life-threatening situation. Restriction to Delta and Echo level unit responses in this study was utilized to minimize the number of patients where EMS response time would not make a difference in mortality because their condition was not sufficiently critical to benefit from a rapid EMS response, and therefore, improve the potential to detect a “signal” through the “noise”.(65, 66)

Table 7.1: Summary of primary study findings and key secondary findings on response time and clinical outcome in the general population of patients receiving Emergency Medical Services care.

	Mayer (1979)	Blackwell and Kaufman (2002)	Pons *et al.* (2005)	Price (2006)	Blanchard *et al.* (2009)
Study Design	Descriptive	Retrospective cohort	Retrospective cohort	Qualitative	Retrospective cohort
Setting					
Country	USA	USA	USA	UK	Canada
System	2 tiered	2 tiered	2 tiered	N/P	2 tiered
Level	BLS/ALS	BLS-D/ALS	BLS-D/ALS	ALS	BLS-D/ALS
Population	All emergency unit responses where a paramedic unit was dispatched for one calendar year	All emergency unit responses defined by the use of lights and sirens that resulted in transport to one hospital in emergency life-threatening or non-life-threatening condition for 6 months	All emergency unit responses defined by the use of lights and sirens to one adult hospital for one calendar year	Purposive sample of ambulance Paramedics	All Delta and Echo level unit responses transported to all adult hospitals for one calendar year
Exposure					
Definition	Response interval	Activation* and response intervals	Activation and response intervals	N/A	Activation and response intervals
Measurement	Polychotomous	1 minute increments and 5 minute dichotomous	4 and 8 minute dichotomous and measured	N/A	4,8, and 9 minute dichotomous
Outcome					
Definition	Alive or dead at hospital arrival	Alive or dead at hospital discharge	Alive or dead at hospital discharge	N/A	Alive or dead at hospital discharge
Conclusion					
8 min.	1.54 (1.27 – 1.87) §	N/P	1.06 (0.80 – 1.42)‡	Eight minute target not evidenced based	1.19 (0.97 – 1.47)†
4 min.	1.15 (0.94 – 1.39) §	N/P	0.70 (0.52 – 0.95)‡		1.35 (0.99 – 1.83)†
Other findings		*post hoc* 5 min. dichotomous exposure: $Chi^2_{(df=1)}$ p = 0.002	measured exposure: 1.01 (0.98 – 1.04)‡	Response time targets placing ambulance crews and patients at risk	9 min. exposure: 0.93 (0.72 – 1.21)†

Note: N/P=Not provided; N/A=Not applicable
*activation interval was measured as time from obtaining an address or 30 seconds after 911 call receipt, whichever was shortest.
† Adjusted odds of mortality; ‡ Adjusted odds of survival
§ Crude odds of mortality. Calculated based on data provided in the study using the CCI command in STATA version 8.2 (College Station, Texas)

7.2 Secondary research questions

There are many patients in whom response time of an ALS ambulance will make no difference (i.e., there are patients who will likely die regardless of response time).(6) There are other patients where the response time of an ALS ambulance may make a difference (e.g., airway obstruction, severe allergic reaction or asthma, etc.). These patients will invariably be transported and likely be admitted as an in-patient. We therefore performed a secondary analysis examining only death in the ED and death in patients subsequently admitted as an in-patient in an attempt to further improve the potential to detect a "signal" in the dataset.

Our secondary analysis using an eight minute dichotomous exposure indicates that response time was not associated with mortality in the ED (OR=1.07; 95% CI 0.76 – 1.53). However, response time was associated with mortality for those who were subsequently admitted as an in-patient (OR=1.30; 95% CI 1.00 – 1.69). Mortality in the ED may in some way identify patients who are too sick to benefit from EMS intervention and therefore response time may not contribute to survival.

The adjusted odds of dying given a response time greater than or equal to four minutes is 1.35 times that of dying given a response time of less than eight minutes. This OR may be as high as 1.83 or as low as 0.99. The same trend noted above for ED and in-patient mortality with an eight minute dichotomous exposure level are also present in the 4 minute dichotomous exposure level

(OR=1.14; 95% CI 0.70 – 1.87 and OR=1.44; 95% CI 0.97 – 2.13 for ED and in-patients respectively).

Similar to Pons *et al.*, this study found a greater association at the four minute exposure level when compared to the eight minute level. Unlike Pons *et al.* the four minute exposure was not statistically significant (Table 7.1).

The adjusted odds of dying given a response time greater than or equal to nine minutes is 0.93 times that of dying given a response time of less than eight minutes. This OR may be as high as 1.21 or as low as 0.72.

The adjusted OR for a nine minute exposure however does not reflect the same pattern of statistical significance or trending to significance as both the eight minute and four minute dichotomous exposures (OR=0.83; 95% CI 0.53 – 1.31 and 1.02; 95% CI 0.73 – 1.41 for ED patients and in-patients respectively).

These findings suggest that a potential signal is present for a four minute dichotomous exposure, but not at the nine minute dichotomous exposure level. Moreover, the association for ED patients and those that subsequently become in-patients may be different at the nine minute dichotomous exposure level compared to both the four and eight minute dichotomous exposure levels.

7.3 Exploratory analysis questions

Findings from the exploratory sub-group analysis suggest that attempting to further restrict the dataset for etiologic purposes to potentially time-sensitive tracer conditions that are readily tracked in the EMS system is challenging. The sample size is small for each sub-group making interpretation of findings difficult due to the presence of random error in the estimate of effect.

Despite these limitations some findings warrant further discussion. Although there were no statistically significant findings for the cardiac arrest, STEMI, and severe trauma subgroups, there was a statistically significant finding in the stroke subgroup. It is beyond the scope of this study to determine the etiologic mechanism that may account for this finding as these data were not available in the dataset. Moreover, controlling for the type of stroke may provide important information. These findings do warrant further investigation to determine if they are spurious.

7.4 Limitations

7.4.1 Selection bias

Selection bias (SB) is defined as error due to systematic differences in characteristics between those who take part in the study and those who do not. For instance those patients who are selected to participate may have a different exposure outcome relationship than those who are theoretically eligible to be included in the study.(26, 59) This type of systematic bias can move effect measures towards or away from null.

There were three theoretically plausible opportunities for the introduction of SB into the study design:

1. During collection of all unit responses in the 2006 calendar year.
2. During inclusion of unit responses for the final sample for linkage.
3. During linkage of prehospital and hospital data.

The first opportunity for SB is unlikely as the Calgary EMS system collects all events that are created. Events are created automatically when a 911 call is received, or when an additional event is needed for a situation in which a 911 call is not received (e.g., an ambulance is flagged down for help, etc.). Anecdotally there are no known situations where an event has gone "missing" from the CAD database. Therefore it is unlikely that a group of events are missing, and if there is a group missing, that this group had a different exposure outcome relationship than those included.

The second opportunity was in the selection of unit responses for the sample for linkage. *A priori* defined criteria were established describing which unit responses would be eligible for inclusion and exclusion (outlined in section 4.1.1 and 4.1.2). One of the inclusion criteria, unit responses resulting in transport to an acute care facility, could theoretically introduce a SB. If for example a patient died on-scene and was not transported, as in the case of a cardiac arrest, then it is plausible that this subset of patients may bias results if the exposure outcome relationship was different compared to those included.

One method to test the extent to which non-transported patients would influence the reported effect estimate is through sensitivity analysis.(26) Those patients that did not receive a resuscitation attempt, in most instances, would not have received a resuscitation attempt regardless of the response time (e.g., patients with injuries incompatible with life, decomposition or line of lividity present, Do Not Resuscitate order, etc.) and so only patients who received a resuscitation attempt and died in the field were included.

There were 171 unit responses in the cardiac arrest sub-group that corresponded to a patient that died in the field. These patients are all Delta and

Echo level unit responses where an unsuccessful resuscitation attempt was made. A total of 131 out of 171 unit responses received a response time of less than eight minutes and 40 out of 171 received a response time of greater than or equal to eight minutes. The OR is largely unchanged for the primary research question when these additional unit responses are included (Table 7.2).

The third opportunity for SB was during the linkage of prehospital to hospital data. There were 776 Delta and Echo level unit responses that could not be linked to the ED data. Of these unit responses 754 had exposure status data available.

Five SB sensitivity scenarios were tested and are presented in Table 7.2. These scenarios would suggest that if the mortality rate in exposed and unexposed were the same as the linked unit responses (i.e., no SB) then it would not change the effect estimate (Scenario 1). If the exposure outcome relationship was different, however, then the effect estimate would change. Scenario 2 and 3 address the situation that would arise if in reality the mortality of the excluded exposed patients were to increase, while the mortality of excluded unexposed patients decreased. Both scenarios resulted in moving the effect measure away from null and to within a statistically significant range (Table 7.2).

On the other hand if the mortality of excluded exposed patients were to decrease while the mortality of excluded unexposed were to increase (scenarios 4 and 5) then there would be no change in the conclusions based purely on statistical significance (Table 7.2).

These scenarios illustrate that the effect estimate in the study may be biased either towards or away from the null depending on the direction of difference in the exposure outcome relationship for the excluded unit responses.

It is unlikely that the exclusion of these unit responses resulted in a biased effect estimate. The rationale for this conclusion is that mortality has to be 0% in the exposed group and greater than double in the unexposed group to move the effect estimate away from null towards a non-statistically significant protective effect (Scenario 5). This scenario is likely unrealistic and would not change the conclusions of the study. If mortality, however, were to increase in the exposed and decrease in the unexposed, the effect estimate would move away from null (scenario 2 and 3). Scenario 2 and 3, although unlikely, would suggest our reported effect estimate is biased towards the null.

Therefore we conclude that SB does not account for the observed association in our primary research question. If there is SB present our reported effect estimate is most likely an underestimate of the true exposure outcome relationship.

Table 7.2: Sensitivity analysis of selection bias.

Scenario	Outcome	Exposure ≥8 min.	Exposure < 8 min.	OR (95% CI)
Crude	Dead	133	375	1.13 (0.91 – 1.39)
	Alive	1732	5520	
Field deaths included	Dead	133+40	375+131	1.08 (0.91 – 1.31)
	Alive	1732	5520	
Scenario 1*	Dead	133+15	375+35	1.13 (0.93 – 1.38)
	Alive	1732+190	5520+514	
Scenario 2†	Dead	133+23	375+18	1.25 (1.03 – 1.53)
	Alive	1732+182	5520+531	
Scenario 3‡	Dead	133+29	375	1.37 (1.13 – 167)
	Alive	1732+176	5520+549	
Scenario 4‖	Dead	133+7	375+53	1.02 (0.83 – 1.25)
	Alive	1732+198	5520+496	
Scenario 5¶	Dead	133	375+70	0.93 (0.75 – 1.14)
	Alive	1732+205	5520+479	

Note: OR=Odds ratio; CI=Confidence interval
*Assumes the same mortality rate as the included unit responses; 7.1% mortality in exposed and 6.4% in unexposed. N.B. there were 205 exposed and 549 unexposed unit responses excluded from the study that had exposure data available.
† Assumes that the mortality rate in exposed is 50% increased (7.1%X1.5=11%) and mortality rate in unexposed is 50% reduced (6.4%/2=3.2%).
‡ Assumes that the mortality rate is double in exposed group (7.1%X2=14.2%) and the mortality is 0% in unexposed.
‖ Assumes that the mortality rate in exposed is 50% reduced (7.1%/2=3.6%) and the mortality in unexposed is 50% increased (6.4%X1.5=9.6).
¶ Assumes that the mortality rate is 0% in exposed group and the mortality is double in the unexposed (6.4%X2=12.8%).

7.4.2 Misclassification bias

Measurement bias has been defined as "systematic error arising from inaccurate measurement…of subjects on study variables".(67) This type of bias is further described as misclassification bias (MB) when referring to studies with categorized exposure or outcome measures. MB can be further delineated into non-differential and differential forms; both forms can bias an effect estimate away from the truth.(26, 59, 67)

Non-differential misclassification bias (NDMB) occurs when the misclassification does not depend on levels of another variable.(26, 59, 68) This type of misclassification generally biases the estimate towards null, but not in all situations.(26, 59, 69-71)

Some authors would suggest that misclassification is likely present in all observational studies to some degree.(26, 72) There are three proposed theoretical sources of misclassification bias in this study:

1. Inadequate data cleaning in multiple unit responses.
2. Operator error in time stamping.
3. Holdbacks from scene.

The first source of bias would occur if in the data cleaning phase of this study the response time of the fastest unit to the scene was not imposed on the other units that may subsequently respond to the scene.(15) If the individual response time of subsequently responding units were used, this would always result in an overestimate of the response time compared to the first unit on-scene. Clinically this is problematic as in most situations (but not all), the first unit on-scene will deliver the critical prehospital intervention, not the subsequently arriving unit. This study ensured that the fastest response time for each event was used and applied to all other unit responses to the same event through rigorous manual review of the data.

The second source of error would likely result in both a misclassification of exposed and unexposed. Moreover, it would not depend on the mortality status of the patient and so would be NDMB. Although difficult to predict, anecdotal evidence would suggest that this source of misclassification bias may cancel itself out. EMS crews, for example, may timestamp themselves as on-scene even though they are not on-scene, especially if they have made a mistake in locating the event address, which will result in a prolonged response interval. Alternatively, crews may forget to activate the arrived scene time stamp, but remember while in the patient access or on-scene intervals and activate the time stamp late. Anecdotally both scenarios are equally plausible and no known data exists describing this phenomenon in Calgary EMS.

The third source of misclassification bias is holdback situations. Holdbacks occur when the EMD determines that it is unsafe for the EMS crew to enter the scene, perhaps due to a violent patient or other uncontrolled hazard. In this scenario, the EMS crew "holds back" from the scene until it is safe to enter. Calgary EMS crews tend to activate the arrived scene time stamp when they arrive at the holdback location. This will always result in the response time being an underestimate of the true response time to the actual scene of the emergency. It stands to reason that this type of misclassification bias will only affect unexposed unit responses, as exposed unit responses will not become unexposed from holdbacks; but unexposed unit responses are likely to be in reality exposed from the difference in time spent at the holdback location.

The frequency and magnitude of this bias is unknown in the Calgary EMS system. To that end a sensitivity analysis is provided in Table 7.3 with two plausible scenarios. The first assumes that 2% of all unexposed unit responses are in reality exposed, the second scenario assumes that 5% of all unexposed unit responses are in reality exposed. Anecdotal evidence would suggest that the frequency of holdbacks would not exceed 2% of the number of unexposed unit responses, but a 5% scenario is included as an extreme example.

Both scenarios would suggest that there is a bias away from null as a result of this misclassification. In the most extreme scenario of a 5% unexposed unit response misclassification, there is no change in the conclusions drawn from the study effect estimate. We therefore propose that this type of bias does not change the conclusion of the primary research question.

Table 7.3: Sensitivity analysis of misclassification bias.

Scenario	Outcome	Exposure ≥8 min.	Exposure < 8 min.	OR (95% CI)
Crude	Dead	133	375	1.13 (0.91 – 1.39)
	Alive	1732	5520	
Scenario 1*	Dead	133+8	375-8	1.13 (0.92 – 1.38)
	Alive	1732+10	5520-10	
Scenario 2†	Dead	133+19	375-19	1.11 (0.91 – 1.36)
	Alive	1732+276	5520-276	

Note: OR=Odds ratio; CI=Confidence interval
*Assumes that 2% of unexposed unit responses are in reality exposed.
† Assumes that 5% of unexposed unit responses are in reality exposed.

7.4.3 Confounding

The definition of confounding is the intermixing of effects between the exposure, outcome, and a third extraneous variable that may cause a distortion of the effect estimate.(59) A confounding variable is one that is associated with the exposure, associated with the outcome independent of the exposure, not an intermediate step in the causal pathway between exposure and disease, and present in different proportions between exposed and unexposed.(59)

Confounding can bias an effect estimate towards or away from null, and in extreme cases change the direction of the relationship.(26)

To that end, both stratified and logistic modelling techniques were used to assess the exposure outcome relationship while controlling for important potential confounders. The list of potential confounders was created through careful consideration of potential covariates in this exposure outcome relationship, availability of data, and reviewing previous studies on this topic. The methods used to stratify and model to control for the important effects of confounding corresponded to contemporary thinking on this issue.(26, 60)

One previous study examining this relationship has attempted to control for the confounding effect of patient severity, age, sex, scene interval, and transport interval. We have included the same confounders, except we omitted our variable that we had planned to use to assess severity. Our rationale for not including CTAS in the stratified or multivariable model is because we considered it to be an intermediate step in the causal pathway.

CTAS is created when the paramedic reports to the triage nurse upon arrival at the ED. Therefore CTAS measures patient severity, but not before they have been exposed to ambulance response time and other medical treatments. This intermediate step is an issue as rapidity of response may dictate CTAS level. A complete airway obstruction, for example, that received a rapid response by EMS may be triaged at a CTAS 2 level if the paramedics were successful in removing the obstruction, the response time was short, and the patient is clinically stable. Conversely, if the response time was long, the patient may have gone into cardiac arrest prior to the arrival of paramedics, which would certainly mean that the patient would be rated as a CTAS 1 if transported.

A convenience sample was used for this study consisting of all patients that received a Delta or Echo level unit response. The rationale for using this criterion was to identify patients at the time of the 911 call that could have benefited from a rapid EMS response. In addition, MPDS determinant is often used as a criterion for defining which group of patients will be eligible to receive which response time standard. Hence EMS system planning is often centred on responding quickly to the group of patients pertaining to the most critical MPDS determinant.

It is likely that there were patients included in the sample that were not in a critical life-threatening situation, and during the same time period patients who were in a critical life-threatening situation that did not receive a Delta or Echo level response and hence not included in the sample. This will occur as the determination of MPDS level is based on 911 caller information and the MPDS system itself does not have perfect sensitivity and specificity for identifying patients in a critical life-threatening situation. In addition to clinical severity, there can be Delta or Echo level responses for a variety of clinical conditions. A proportion of these clinical conditions may be amenable to timely application of a prehospital intervention, timely application of a hospital intervention, timely application of both a prehospital and hospital intervention, or neither.

The largest shortcoming of this study design may be the definition of response time. This study defined response time as the time from 911 call to arrival at scene. As has been previously explained this response interval is at best a proxy measure for the more clinically important response interval of time from injury or disease onset to time of application of a critical prehospital intervention.(22, 29) Numerous delays can be incurred outside of this response time definition that can dramatically increase time to intervention, but leave response time seemingly unaffected.

This phenomenon was demonstrated in a study by Karch *et al*. who observed the relationship between response time and time of defibrillation using closed circuit television cameras in casinos. Response time to casino events was the same for survivors and non-survivors, but the interval between arrival on-scene and administration of a defibrillatory shock was significantly longer in the non-survivors.(34)

This shortcoming in the measurement of response time at Calgary EMS is problematic as additional unmeasured time factors may influence survival, but are not accounted for in this analysis. If these unmeasured time variables are greater in those that died compared to those that lived, which would seem both biologically and clinically plausible, then this would logically result in more exposed dead patients. In other words, if we were to measure the clinically important response time of disease injury onset to critical intervention then we would logically have more exposed dead patients in our study. This is because any response time close to 8 minutes in our present definition would certainly be over 8 minutes time if patient access and initial assessment intervals were added. The result would be a larger effect estimate relative to the reported estimate in this study. Therefore changing the definition of exposure to include both patient access and initial assessment intervals may lead to a stronger relationship between exposure and outcome in this study. This alteration in study design, although preferable, may not be feasible because many of the patients responded to by Calgary EMS, have unwitnessed arrests, injuries, etc. and therefore unknown elapsed time prior to the 911 call.

7.4.4 Power

Power can be defined as the probability of rejecting the null hypothesis when it is false.(58) Power is dependent on sample size, variability of the observations, significance level, and smallest effect of interest.(58) The *a priori* power calculation was based on all emergency responses by Calgary EMS for one calendar year. This was estimated to be 36,000 unit responses. This sample size would have yielded greater than 95% power to detect a 1% difference in mortality between exposed and unexposed patients.

Upon careful reflection, however, it was decided to restrict this study to only critical time-dependent emergencies as defined by the MPDS system. Therefore after data cleaning and linkage there were 7,943 unit responses.

This sample size has resulted in an acceptable level of precision as evidenced by narrow confidence intervals for the primary and secondary research questions. This sample size, however, was problematic for the exploratory analysis, where effect estimate confidence intervals were wide and limitations in the number of covariates that could be considered due to sample size issues were encountered.

It is proposed that effect estimates for the exploratory analysis should be interpreted with caution due to the imprecision caused by sample size issues. Future studies interrogating this exposure outcome relationship should note that restriction of the study sample to clinical subgroups resulted in very small sample sizes and greater than one calendar year of data is needed. Moreover, in the primary and secondary research questions, there were very few patients that received a response time greater than or equal to eight minutes that died between the ages of 18 to 39 years.

7.5 Conclusions

We conclude that for the majority of adult patients receiving a delta or echo level unit response transported by The City of Calgary EMS, a response time of eight minutes was not statistically associated with decreased all-cause mortality. In a subset analysis of patients from this sample that were subsequently admitted to hospital, a response time of less than 8 minutes was statistically associated with decreased mortality. Further subset analyses did not demonstrate a statistically significant association with overall mortality using dichotomous cut points at 4 or 9 minute intervals.

In final exploratory analyses, an eight minute response time was statistically associated with decreased overall mortality in the stroke sub-group, but not in the cardiac arrest, STEMI, or severe trauma sub-groups.

7.6 Response time standards policy: Implications and future direction

7.6.1 Perspective

It is important to emphasize that this study explored the association of EMS response time and mortality from only one perspective – the clinical perspective. Other perspectives are important to this relationship, such as social, environmental, risk, *et cetera*. Examining response time from only the clinical perspective may suggest that an 8 minute response time is not necessary. However, from a societal perspective, citizens that pay taxes to support this service may not consider a longer response time acceptable. Likewise, EMS personnel who are trained to respond to emergencies (with a sociological perspective that an emergency equates with rapid response) may not accept that a slow response for all calls is appropriate.

7.6.2 Implications and future direction

This study has a number of 'firsts' for outcomes research on the provision of Emergency Medical Services, this study: 1) explicitly assessed the association between response time and mortality in an urban Canadian EMS setting, 2) restricted the analysis to the most critical and life-threatening events identified in the EMS system at the point of the 911 call, 3) examined the outcome of patients collectively, and stratified by emergency department and in-hospital phases of treatment, 4) included quantitative assessments of potential systematic bias, and 5) incorporated a stratified analysis to examine the time mortality association in clinical sub-groups pertaining to conditions considered to have a 'time-mortality' association.

This study, however, must be interpreted in light of its one-dimensional perspective and inclusion criteria. It does not consider the economic and social costs to changing response time standards in relation to lives saved. Moreover, this study does not interrogate the exposure outcome relationship in the paediatric population. It also focuses solely on mortality and not morbidity outcome measures. Some examples of potential morbidity measures include hospital length of stay, ICU admission rates, and neurological/functional outcomes. It also takes a pragmatic approach that includes all events designated as critical life-threatening at the time of the 911 call, not an etiologic approach that identifies the patients that would benefit most from a rapid EMS response.

A truly evidence-based response time standard must incorporate multiple perspectives and outcome measures to create a policy that balances need with expectation and cost.

When these study results are placed in the context of previous knowledge in this area, several recommendations can be made. These recommendations are summarized in Appendix A.

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APPENDIX A: SPECIFIC RECOMMENDATIONS TO ALBERTA HEALTH SERVICES EMERGENCY MEDICAL SERVICES

No.	Recommendation	Rationale: Thesis	Rationale: Other studies	Future Direction
1	Retain the present response time standard of 8 minutes *pro tempore*	The adjusted OR for mortality approaches significance for both the 8 and 4 minute exposure levels. This is not the case for 9 minutes. We conclude that the response time standard should not be increased from 8 minutes. This is especially true for the in-patient population.	Other studies support the notion that the shorter the response time the lower the mortality.(7, 16, 29, 34, 61) There is, however, not universal agreement on the optimal response time.	From a clinical perspective it is challenging to create a universal response time standard that is relevant for all clinical conditions. It stands to reason that condition specific response time standards should be created for known tracer conditions in the EMS system. These standards can then be assessed in light of operational data to determine their cost-effectiveness. These data should be subsequently combined with other perspectives, outcome measures, and paediatric studies to create a universal evidence-based standard.
2	Change the definition of response time to include patient access interval	There are theoretical issues relating to bias and confounding arising from the presently accepted response time definition.	Several studies have identified that in cardiac arrest situations response time by emergency vehicles is not as good a measure when compared to more clinically important measures such as collapse to defibrillation.(25, 34) Although time of collapse would be challenging to collect, patient access interval for all patients would be relatively easier.	Future research should assess the extent of patient access intervals in Calgary EMS. Further studies should be conducted to determine the association of response time including patient access interval on clinical outcomes.

No.	Recommendation	Rationale		Future Direction
		Thesis	Other studies	
3	Identify time sensitive tracer conditions and create condition specific response time standards	The OR trended to significance for both the 8 and 4 minute exposure levels. Cardiac arrest studies in other jurisdictions suggest that the optimal response time should be less than 8 minutes. This illustrates the condition specific nature of this exposure outcome relationship.	The EMS literature would support the notion of using tracer conditions.(73) Epidemiologic literature would support the notion that any observational study should focus on a single etiologic relationship and not multiple relationships.(74)	A literature review and survey of paramedics, managers, and medical directors could inform a short list of potential tracer conditions. The association of response time and mortality associated with these conditions should be assessed and disease specific response time criteria created.
4	Improve data quality	A tremendous amount of data cleaning was required to create a dataset where each line of data pertained to one patient and one unit response. Moreover the quality of the data was poor in terms of missing data and illogical data.	Some authors have suggested moving to "third generation" time recording devices to improve the validity and reliability of the present system.(3, 14) These devices automatically record time points, as opposed to relying on manual entry by paramedics.	Resources could be allocated into improving the present data system pertaining to response times. Specifically the quality of data entering the system and the format of the data exiting the system should be improved to facilitate timely analysis and reporting.

No.	Recommendation	Rationale		Future Direction
		Thesis	Other studies	
5	Link 2004 to 2008 EMS data with hospital outcome data using the thesis linkage process	A 94% linkage rate was achieved between prehospital and hospital data. This simplistic strategy can be utilized on all data up to the switch to electronic patient care records, which occurred at the end of the 2008 calendar year.	There have been numerous recommendations for the study of patient outcomes in EMS.(73)	A new linkage strategy should be created for 2008 data and beyond. A process should be created to obtain outcome data in a prospective fashion. These data are integral to the timely creation of performance metrics and assessing the effectiveness of programs.