

**Strategies to improve the outcome of
pre-hospital cardiac arrest
in Leicestershire.**

Thesis submission for
the degree of MD at the University of Leicester.

By

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**To travel hopefully is a better thing than to arrive.....and
the true success is to labour.**

Robert Louis Stevenson 1881

Acknowledgements

It is difficult to look back over the past 4 years and be certain that I will remember the many individuals who have helped me to complete this thesis. They would certainly not all fit onto one page and I hope they will forgive me if I do not mention them all specifically. They do however, know who they are.

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A Special Tribute.

This thesis is dedicated to my late father,
Bashir Hussain,
who tragically died on April 22nd 1999.

His wisdom, humility, benevolence, good humour and
remarkable vision remain an inspiration to me
and the many others who were lucky enough to have known him.

The Bridge Builder

An old man going a lone highway
Came at the evening cold and grey
To a chasm vast and wide and steep
With waters rolling cold and deep.
The old man crossed in the twilight dim
The sullen stream held no fear for him
But he turned when safe on the other side
And built a bridge to span the tide
Old man, said a fellow pilgrim near
You're wasting your strength with building here
Your journey will end with the ending day
You'll never again cross this way
You've crossed the chasm deep and wide
Why build this bridge at eventide?
The builder lifted his old grey head
Good friend on the path I have come he said
There followeth after me today
A youth whose feet must pass this way
The chasm that was naught to me
To that youth may a pitfall be
He too must cross in the twilight dim
Good friend, I am building this bridge for him.

Anon

Thesis Abstract

Despite the increasing complexity of pre-hospital care systems, the outcome from cardiac arrest (CA) remains extremely poor. The major objective of this thesis was to explore the ways in which outcome could be improved within a defined Emergency Medical Service (EMS) system in the UK. The four studies were designed to investigate certain structures and processes of care involved in achieving a successful outcome.

The first study provides a detailed descriptive account of the incidence, processes of care and outcomes for adults suffering a pre-hospital CA in a defined EMS system with a predominant single tiered ALS response. Results are compared with other relevant work. In the second study, I evaluated the resource implications of additional single paramedic units with a priority dispatch system and their impact on the short term outcome of pre-hospital CA. Prioritised response and introduction of single paramedic units had no significant impact on the number of lives saved from pre-hospital CA. Significantly increased NHS costs were incurred per life year gained. The third study was a double blind placebo controlled trial using empirical intravenous magnesium sulphate as a therapeutic intervention. My hypothesis was that given early in the resuscitation phase for patients in refractory or recurring VF, outcome could be significantly improved. However, the results showed no significant improvement in outcome. Finally, I designed and carried out a study to develop consensus opinion on future design characteristics of EMS systems in the UK using senior expert staff from Ambulance Trusts in the UK. Consensus confirmed the need for multi-tiered systems, fully implemented priority dispatch and increasing use of 'first responders'. Opinion was significantly different from the present EMS model recommended by the Department of Health.

This work has shown that despite a number of strategies to improve the outcome of pre-hospital CA in the Leicestershire EMS, no significant improvement could be produced. A more radical re-configuration of system design is suggested by experts in the field of EMS which could have a more significant impact on outcome. The thesis has also provided robust data which can be used locally in Leicestershire as well as providing avenues for future research.

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Originality of the work.

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Glossary of abbreviations and terminology

ACLS	Advanced cardiac life support
AED	Automated external defibrillator
AHA	American Heart Association
ALS	Advanced life support
AMI	Acute myocardial infarction
ARF	Ambulance report form
BLS	Basic life support
BLS-D	Provider of basic life support and defibrillation
CA	Cardiac arrest
CBD	Criteria based dispatch
CEA	Cost effectiveness analysis
CER	Cost effectiveness ratio
CFR	Certified first responder
CPR	Cardio-pulmonary resuscitation
CI	Confidence interval
DOH	Department of Health
DOT	Department of Transport
DRI	Defibrillatory response interval
EMD	Emergency Medical Dispatch
EMS	Emergency Medical Service
EMT	Emergency medical technician
EMT-D	Emergency medical technician with defibrillation skills
ERC	European Resuscitation Council
GP	General practitioner
ICU	Intensive Care Unit
IQR	Inter quartile range
LAPS	Leicestershire Ambulance and Paramedic Service
MICA	Magnesium In Cardiac Arrest study
OPALS	Ontario Prehospital Advanced Life Support study

PAD	Public access defibrillation
PDS	Priority dispatch system
PEA	Pulseless electrical activity
ROSC	Return of spontaneous circulation
SD	Standard deviation
SSM	System status management
VF	Ventricular fibrillation
VT	Ventricular tachycardia

Chapter 1

Introduction, aims and objectives.

1.1 Introduction

Achieving an optimal outcome for a patient having suffered a pre-hospital cardiac arrest (CA) remains one of the most challenging obstacles in emergency medicine. The discharge alive from hospital of a neurologically intact patient relies upon a number of time critical interventions . The original concept of the 'rescue chain' linking these interventions was described by Professor F.W. Ahnefeld in the early 1960s (Safar 1989). Subsequently, Safar changed the phrase into the 'life support chain' before it gained its present day description and became known as the "Chain of Survival" (Cummins, and others 1991). However, each link in this 'chain' has a weighted effect on outcome depending upon the circumstances of the CA at the time.

The first 'link' is affected to an extent by the play of chance. The presence of a witness to the CA and the geographical location of the patient at the time will strongly influence access to the EMS. Unwitnessed events invariably result in death (Eisenberg, and others 1990). The role of the bystander is therefore critical. He or she must notify the EMS and institute bystander CPR. Efficient emergency communication systems and the rapidity of the EMS response are critical to the success of subsequent interventions and eventual outcome. An essential component of a 'high performance' EMS system is regarded as being its ability to respond to all immediately life threatening calls (category A) within 8 minutes in at least 90% of cases (Stout 1983). At present no system in the UK is able to achieve these results. Factors to consider in attempting to improve on this performance standard include EMS system design, the use of information technology systems, and their management within inevitably tight fiscal constraints (Ryan 1994). There is also marked variation in response times for category A calls between individual systems in the UK. This variation cannot be attributed to geography or population density alone (Audit Commssion). Debate continues as to how systems should be configured in order to improve their

performance standards but with little consensus of opinion (Chief Medical Officer 1997; Glucksman and Cocks 1993; NHS Executive Steering Group 1996).

The provision of bystander CPR constitutes the second essential link in the 'Chain of Survival'. CPR buys time, maintaining some perfusion to the brain and heart until access to a defibrillator and other ALS interventions are possible (Cummins, and others 1985). In the UK most CPR training programmes for the public are funded by charitable organisations. Despite much hard work they have been found to be largely unsuccessful in maintaining the performance of skills required to carry out adequate CPR (Morgan, and others 1996). Some studies have suggested that some form of CPR is better than none at all (Bossaert, and others 1989). Certainly in populations with a high incidence of bystander CPR, outcome is significantly improved (Cummins and Eisenberg 1985). However, most systems world wide report an incidence of bystander CPR which remains static at around 20-30% (Kaye, and others 1995).

Rapid defibrillation for a patient in VF is the third link in the 'chain'. It has been clearly shown to be the most critical intervention in order to achieve an ultimately successful outcome. Essential to success is the ability to minimise the defibrillatory response interval (DRI), the time from receiving the call at the dispatch centre to applying the first defibrillatory shock (Cummins, and others 1991). With the advent of increasingly portable automated external defibrillators (AEDs) and the need to provide a rapid response, this link in the chain is becoming the responsibility of other agencies integrated into the EMS (Bocka 1989).

The fourth link in the 'Chain', advanced life support (ALS) measures, has attracted a great amount of research in pre-hospital medicine and yet debate as to its efficacy continues (Pepe, and others 1994). Evidence from North American systems has suggested that ALS measures produce some additive effect (Pepe, and others 1993; Cummins, and others 1989). However, there is a notable

contrast in outcomes between individual systems (Eisenberg, and others 1990). In addition, weaknesses in study design have compromised the validity of the conclusions that suggest a benefit (Stiell, and others 1998).

Numerous studies have confirmed that patients with non-VF rhythms have a uniformly dismal outcome (Eisenberg, and others 1990; Mullie, and others 1989). Ventricular fibrillation on the otherhand is widely regarded as being a highly salvageable rhythm. Unfortunately, a significant proportion of patients in VF, who do not respond to the three initial defibrillatory shocks will remain in refractory or recurrent VF and die (Herlitz, and others 1997). There is conflicting evidence as to whether ALS measures have any significant effect on eventual outcome in these patients. Many alternative therapeutic manoeuvres have been tried for patients in refractory VF without any proven positive effect (Stiell, and others 1995). There may even be a worse outcome as a result of some of these drug therapies due to their negatively inotropic and pro-rhythmic effects.

Magnesium has been shown to act favourably against intractable ventricular tachycardia and fibrillation as well as a variety of supraventricular arrhythmias (Fazekas, and others 1993). It has been proven to be a simple and safe agent with minimal side effects in a large cohort of patients suffering acute myocardial infarction (Woods, and others 1992). Its lack of negative inotropism as compared to all other anti-arrhythmic agents is particularly notable. For these reasons, magnesium has potential benefit in the treatment of VF, but to date has not been rigorously evaluated.

This thesis has provided the opportunity to study a well defined EMS system with particular regard to its structure and processes of care in order to evaluate strategies that could improve the outcome of pre-hospital CA. Achieving a successful outcome is a very much more complicated challenge and there are many more components than the four links outlined above. Much of the existing knowledge and research for UK systems is derived from the North American

experience of EMS development. I have used this information to identify deficiencies in the knowledge base of British systems and attempted to construct studies which will explore some of these deficiencies. I have chosen to explore those factors that I considered could have either the greatest impact on the outcome of pre-hospital CA or might have a novel role to play.

1.2 Aims of the thesis.

The aims of this thesis are to scientifically :

- Define the demographics and characteristics of pre-hospital cardiac arrest in the Leicestershire EMS system and factors associated with a successful outcome.
- Evaluate the costs of existing processes of care in these patients as well as the cost effectiveness of a priority dispatch system and paramedic 'fast responders' on outcome using pre-hospital CA as the study model.
- Investigate the role of empirical intravenous magnesium as an anti-arrhythmic agent in treating patients with refractory or recurrent ventricular fibrillation.
- Investigate the optimal features of EMS system design in the UK using the Delphi technique to achieve consensus of opinion amongst a group of 'experts'.

1.3 Specific hypotheses to be tested.

- The introduction of a priority dispatch system (PDS) and single paramedic 'fast responders' will produce a significant improvement in response times for immediately life threatening (category A) conditions and be cost effective in improving the outcome of patients suffering pre-hospital CA.
- Empirical intravenous magnesium sulphate will significantly reduce the mortality of patients suffering a pre-hospital CA who remain in refractory or recurrent ventricular fibrillation following defibrillation.
- Senior personnel working in Ambulance Trusts in the UK (the 'experts') would prefer to maintain the current single tiered ALS model of care with a paramedic on every front line ambulance.

1.4 Potential outcome of results and impact on current practice

- The results will allow for a more informed appraisal of the structure, processes of care and impact on outcome of patients suffering pre-hospital CA in a well defined EMS system in the UK.
- An economic evaluation will quantify and compare suggested pre-hospital care models and their possible effect on the outcome of pre-hospital CA. It will provide accurate information which can inform planning for emergency services in the future both within Leicestershire and possibly on a national basis.
- The efficacy of intravenous magnesium in refractory VF for pre-hospital CA is being evaluated in the first randomised controlled trial of its kind. If the hypothesis proves to be correct, it could potentially increase survival and alter the management of refractory VF.
- The Delphi questionnaire will provide a consensus of opinion from senior Ambulance Trust directors on certain optimal design features for EMS systems in the UK.

Chapter 2

**EMS system development and its impact on the
outcome of cardiac arrest.**

2.1 Historical overview

Emergency pre-hospital care dates back to before 1500 BC with descriptions of triage and urgent treatment being described both in the Edwin Smith Papyrus and the Babylonian Code of Hammurabi (Mustalish and Post 1994). Although subsequent tales of battle field surgical care exist throughout history, the exploits of Dominique-Jean Larrey (1766-1842) stand out as the clearest account of a successful military surgeon. He cared for Napoleon's soldiers both on the battlefield as well as developing the technique of rapid transport away to first aid stations and front line hospitals using his 'ambulance volante' – flying ambulances (Brewer 1986).

Subsequent military experiences in the Crimea and American Civil War acted as a catalyst for the development of urban ambulance systems both in the United States and England (Haller 1990). As a result by the 1870s, the Red Cross and St Johns Ambulance Association had been established as voluntary aid organisations. Within five years first aid courses sponsored by St Johns were being taught throughout Great Britain, the United States, Russia, Germany and Australia. In Britain, this enthusiasm for developing pre-hospital care services was related in large measure to the number of injuries sustained in the mines and on the railways. The first proper ambulance service was set up in the City of London in 1906 (Anderson 1978).

The other major stimulus to improving the transport of patients to hospital at this time was the intractable problem of sudden cardiac arrest, usually from drowning. The management of this condition in the pre-hospital setting during this time produced no real success and the event was accepted as being associated with universal mortality.

In 1937 an emergency 999 telephone system was set up initially in London and then Glasgow to improve the speed of response by the ambulance service

(Anderson 1978). Elsewhere, there were reports in the early 1960s that ambulance physicians were providing counter-shock treatment for sudden death victims on the streets of Moscow and Prague with success (Safar and Rosomoff 1964). However, the first objective scientific reports, and turning point in improving outcome from pre-hospital cardiac arrest, occurred in the streets of Belfast (Pantridge and Geddes 1967). A 'portable' battery powered defibrillator (said to weigh approximately 110lbs) was transported in an ambulance staffed by a doctor and nurse to patients with suspected myocardial infarction. They were alerted via the hospital switchboard by the patient's general practitioner. The average response time of this system was 78% of patients being reached within 15 minutes. Over a 15 month period, 312 patients were admitted to hospital, 10 of whom had been successfully defibrillated in the community from VF back into a stable rhythm. Of the 10 patients admitted to hospital, 6 were eventually discharged alive.

2.2 Developments in modern EMS system design.

Following Pantridge and Geddes' work, from 1969 onwards a number of EMS systems in North America radically reconfigured themselves to provide basic and advanced life support to victims of cardiac arrest in the community (Graf, and others 1972; Liberthson, and others 1974). The Seattle Fire Department's 'Medic I' programme were the pioneers of an integrated tiered response consisting of fire officers, technicians and fully trained paramedics (Mayer 1979).

In the UK a number of communities developed 'cardiac' ambulances with specially trained ambulance personnel (White, and others 1973). Some were manned by doctors on the Belfast model and vaunted as mobile coronary care units. In 1974, significant re-organisation occurred in the role of ambulance services. They changed from providing a transport service under the control of the local authorities to providing an increasing emphasis on healthcare directly and came under the auspices of the NHS (Anderson 1978). The Department of

Health and Social Security in reviewing the advanced training of some ambulance services recommended that such schemes were experimental and required further evaluation (Department of Health and Social Security Health service development. 1976). Subsequent work from Nottingham provided evidence that the outcome from pre-hospital cardiac arrest was not improved by having a doctor on the ambulance (Hampton, and others 1977). They recommended that every ambulance should be equipped with a defibrillator and the crew trained to use it (Hampton and Nicholas 1978).

Work from other systems, predominantly from the US, confirmed that ambulance crews were capable of managing patients with pre-hospital cardiac arrest and achieving a good outcome (Eisenberg, and others 1980). Comparisons made to the variability and sub-optimal response within British systems (Redmond 1984) led eventually to the sanctioning of advanced training for ambulance personnel and the introduction of a syllabus for extended training (Ambulance Staff Training Committee 1987). By 1991 further progress had resulted in the recommendation that every frontline ambulance in Great Britain should by 1996 have a paramedic and technician with a defibrillator on board (Department of health 1993). Notably, the Scottish Ambulance Service had elected to train all ambulance technicians in the use of automatic external defibrillators (AEDs) as a first step instead. This training was completed in 1989 and proved to be remarkably successful (Sedgwick, and others 1993). By the end of 1996, there was a single tiered advanced life support (ALS) response to all emergency calls in Great Britain, although some services had still not been able to train an adequate number of paramedic staff.

2.3 Essential components of an EMS system

The primary role of EMS systems has changed radically in the last 30 years. From simply providing a transport facility, EMS systems have evolved to provide ill or injured patients with lifesaving pre-hospital treatment and rapid transport to definitive care centres. However, the exact benefits of a number of these pre-hospital interventions have been questioned (Smith, and others 1985; Anderson, and others 1987). In contrast, others have suggested an expanded role for EMS providers in delivering ever more sophisticated emergency care, non-emergency care and involvement in public health related services to augment the public's 'emergency medical safety net' (Delbridge, and others 1998; Neely, and others 1997). Similar debate has gone on in the UK (Guly, and others 1995; Nicholl, and others 1998; Glucksman and Cocks 1993). Significant emphasis has therefore been placed on the need for having scientifically sound research that will identify what works best in out of hospital care (Spaite, and others 1995). In addition the need for better systems to evaluate the effectiveness and efficiency of EMS systems has been highlighted (Callaham 1997).

The study of patients suffering pre-hospital cardiac arrest has been regarded in the past as an ideal model to study the general quality of care and overall effectiveness of an EMS system (Spaite, and others 1995). The identification of selected health problems to determine overall quality has been termed the 'tracer' concept (Kessner, and others 1973). Tracers should be conditions with a relatively high frequency and have a high potential for the condition to be beneficially affected by medical care. The use of ALS skills in patients suffering severe injury has been another much studied tracer (Reines, and others 1988; Nicholl, and others 1998). As a result, a system's overall effectiveness can be judged on the assumption that producing good outcomes for critically ill patients also improves the quality of care provided for those with other illnesses and more minor injury. This is not necessarily true. However, it has been recognised that as the scope of EMS care expands so the study of conditions or diseases using

non mortality outcome measures need to be better developed. These measures would need to take into account both the frequency of the disease or condition as well as the impact of pre-hospital care on it (National Highway Traffic Safety Administration 1994).

In order to appreciate how these measures can best be evaluated for overall effectiveness and efficiency, it is important to firstly understand the essential components of a modern EMS system. The next section sets out to describe these components and the available evidence that their development is based upon.

2.3.1 Levels of provider

Subsequent to the work of the Belfast group (Pantridge and Geddes 1967), the concept of pre-hospital care providers with varying skills and scope of practice developed initially on an ad hoc basis. In the United States, although the exact composition of the systems varied and no two states defined levels similarly, training standards were set by the Department of Transport (DOT) with a centrally established curriculum (Pointer 1994). Four levels of provider are common in North America at present : first responder, emergency medical technician –ambulance (EMT-A), emergency ambulance technician-intermediate (EMT-I) and the emergency medical technician-paramedic (EMT-P). Table 2.1 below lists the training hours for the four pre-hospital provider levels based on the DOT standards.

Table 2.1 Training hours for pre-hospital providers.

Level	Didactic	Clinical	Internship	TOTAL
First responder	40	Optional	Optional	40
EMT-A	99-104	10	Optional	109-114
EMT-I	36-75	48	48	132-171
EMT-P	212-350	232-250	256-500	700-1100

The classification is however only a broad outline as the scope of practice for each of the above individuals has changed significantly within the various states (Pointer 1994). Certified first responders (CFRs) are defined as non-medical public safety personnel who are often firemen or police and who are literally the first individuals called to the scene. The skills of the first responder have been expanded in certain systems to include not just assessment and BLS but also use of automated external defibrillators (AEDs) and basic airway management in certain circumstances. In a before and after study with police officers using AEDs survival to discharge from hospital was 26% as compared to 3% when defibrillation was performed by EMS personnel (Mosesso, and others 1998). This was attributed to the difference in improved time to defibrillation. The interval from call to defibrillation was 7 minutes for the police officers as compared to 10 minutes for the EMS personnel.

The exact distinction for the different levels of EMT is different for most American EMS systems. In the most basic form, the EMT-A's scope of practice is little more than that of the CFR. At the other end of the spectrum, the American EMT-P or 'paramedic' can provide the most sophisticated level of pre-hospital care available. He or she has a wide scope of practice depending upon the needs of the EMS system and the level of medical oversight and control (Pointer 1994).

In the UK, there are two basic levels of pre-hospital personnel as shown in the table 2.2. The length and quality of training for both EMTs and paramedics is

standardised and comes under the auspices of the NHS Training Authority or the Institute of Healthcare Development (IHCD) as it is now known. Some scope for local variation is allowed and is controlled by the system's Paramedic Steering Committee. The training for an EMT is usually for a period of 8 weeks although an additional cardiac module also teaches defibrillation skills. Subsequent recruitment to a paramedic programme occurs after approximately 2 years. A period of 11 weeks of didactic and clinical training is followed by preceptorship in the field for one year to produce a fully trained paramedic. This training is still significantly shorter than the American model.

Studies from a number of UK systems have suggested that paramedics have no positive effect on the outcome of pre-hospital cardiac arrest as compared to technicians with AEDs (Guly, and others 1995; Rainer, and others 1997; Mann and Guly 1997). In addition, in a study of 3 systems looking at the influence of paramedic skills and protocols on patients suffering severe injury, increased mortality of between 4 and 8 times was identified in those dying from bleeding injuries (Nicholl, and others 1998). Although the authors accepted that there were some limitations to their study, they felt that the results were reliable and generalisable. Future work recommended study of training programmes and protocols.

Table 2.2 Types of pre-hospital provider and training for UK personnel.

Level	Didactic	Clinical	Internship	TOTAL
Technician (EMT)	40	0	80	120 hrs
Paramedic	80	200	160	440 hrs

A number of British systems have begun to employ 'first responders' to certain emergency calls. They have been defined as anyone selected and trained by an ambulance service to provide basic life support and, in the event of a cardiac arrest, to use an AED (NHS Executive Steering Group 1996). The exact role and agencies involved as 'first responders' continues to develop within individual UK systems. At present, six fire services and four police forces are actively involved as first responders in cardiac arrest and have been provided with AEDs (Porter and Allison 1998). A substantial number of others expressed an interest in developing such a role in the future.

2.3.2 Tiers of service

The development of multiple levels of pre-hospital provider has inevitably led to different models of service being created within individual EMS systems.

Although in the U.S. such variation may be due to the geography of a system and the population density, different models exist even when these factors are taken into account.

Braun et al reviewed systems serving 25 mid-sized cities with populations of 400,000 to 900,000, (Braun, and others 1990) and broadly classified them into either one or two tier models. In the one tiered model, an ALS unit responded to and transported all patients who activated the service. The two tiered service was sub-divided into three types. In system A, ALS units responded to all calls but once on scene could turn over a patient to a BLS unit for transport. In system B, ALS units did not respond to all calls, with BLS units being sent for non critical calls. In system C a non-transporting ALS unit was sent with a transporting BLS unit. The majority of EMS systems in the study (64%) were classified as one tiered ALS systems. It is argued that a multi-tiered system is advantageous because it appropriately targets and increases the use of the paramedic skills as well as improving the response time of the system (Curka, and others 1993). It will also reduce the number of paramedics required within a system which is

beneficial both economically and if recruitment is difficult (Giordano and Davidson 1994). This is particularly suitable within urban settings.

Critical to providing a tiered response is the need for an emergency medical dispatch system (EMD) with a high level of safety (Curka, and others 1993). The alternative view suggests that the savings incurred by adopting a tiered structured do not match the flexibility achieved with a single tiered ALS model using optimal productivity and management strategies (Stout 1983). In addition, it is argued that the costs of upgrading from a mixed BLS/ALS response to an all ALS response is minimal with the guarantee that there will be no chance of a failure or misclassification of the dispatch category (Ornato, and others 1990). Notably in a meta-analysis of out-of-hospital cardiac arrest, survival was found to be twice as likely in a two tiered system as opposed to a one tiered system (Nichol, and others 1996).

In the UK, government adopted a uniform single tiered ALS service which has been in place since the end of 1996 (Department of health 1993). This occurred despite evidence to suggest that a multi-tiered service might be more appropriate (Anderson, and others 1987). Other strategies employed by some individual systems have included the development of single paramedic 'fast responders' in cars or on motorcycles. These have been found to improve responses times, turn around availability times and at half the cost of a fully manned ambulance. One disadvantage is that the units do not have the capability to transfer the patient to hospital (Glucksman 1995). These single paramedic units have been recommended as being the most cost effective strategy for future EMS development (NHS Executive Steering Group 1996). Other suggestions include the increased availability of 'first responder' schemes which might include other emergency services.

2.3.3 Emergency Medical Dispatch (EMD)

The concept of structured EMD developed in the US in the late 1970s in response to the tension between demands on the system and the need to provide a time critical response in selected cases. Increased demand was due also because systems were being used as a 'safety net' for a host of other health care events (Judge 1997). In addition, a need was identified to give appropriate advice and instigate immediate lifesaving treatment in certain emergencies prior to the arrival of the EMS as well as sending an appropriately skilled team to attend to the patient's needs. These goals were described as 'sending the right thing to the right person, at the right time, in the right way and doing the right things until help arrives' (Clawson 1981). This dilemma led in 1978 to the identification of the medical dispatcher as the 'weak link' in the chain of survival in the Salt Lake City EMS and the emergence of structured EMD protocols (Clawson 1984). A series of key questions allowed the dispatcher to determine life threatening conditions quickly so that an appropriate response could be instigated. In the mean time, pre-arrival instructions including telephone CPR saved critical minutes and could impact significantly on outcome (Kellermann, and others 1989).

The additional advantage of EMD is to be able to more appropriately target the use of a paramedic's ALS skills hence allowing greater skill retention and producing lower attrition rates. Critical to the success of an EMD system is its ability to operate with a high level of efficiency and effectiveness. This requires an integrated quality assurance programme and active medical involvement (Clawson 1989).

In the UK, two EMD systems have undergone formal preliminary assessment for safety and reliability – the Medical Priority Dispatch System (MPDS) and the Criteria Based Dispatch (CBD) (Nicholl, and others 1996). It is outside the scope of this discussion to review the advantages and disadvantages of the two

systems but both are widely used in the United States. In addition in the UK study, both produced very similar results in terms of identifying high and medium priority categories appropriately and had low levels of under prioritisation. With appropriate quality assurance, only one call in 2200 calls was thought to be potentially seriously under-prioritised. This compares favourably with other mature EMS systems such as Houston, Texas (Curka, and others 1993). When they audited implementation of their EMD programme, they suggested that only five or six patients of over 14,000 dispatches had been under-prioritised and might have benefited from an immediate paramedic presence.

The importance of EMD in the UK has now been recognised and implemented (NHS Executive Steering Group 1996). The potential risks of underprioritising 1 in 2200 cases (Nicholl, and others 1996) were far outweighed by the potential advantages of improving response times especially for those requiring potentially life saving treatments. However, full implementation of EMD has not been accepted by the Government and patients with minor, category C calls (not life threatening or serious) continue to be treated as serious (category B) cases (Audit Commission 1998). This could compromise the ability of an EMD system to impact on the response time and hence the outcome of certain time critical conditions such as cardiac arrest.

2.3.4 Information systems

Mature 'high performance' EMS systems with optimal response times and benchmarking standards for conditions such as pre-hospital cardiac arrest survival are underpinned by having a clear strategy in the field of information technology (Stout 1994). This key element not only helps a command and control structure to use data for operational purposes but is also vital for system evaluation, quality assurance, continuing education and research. In addition, evaluation of broad public health issues and the ability to allocate societal

resources is increasingly dependent on pre-hospital data (Spaite, and others 1995).

The greatest impact of having a developed information system is the ability to integrate the use of computer aided EMD protocols, automated vehicle location systems, digitised data transfer to field units and system status management (SSM) protocols to achieve optimal response times. SSM refers to the plans and procedures which determine where ambulance units should be located when the next call comes in, taking into account historical cyclical patterns of volume and geographic demand rather than the traditional practice of locating ambulances at stations (Stout 1983). Increasingly powerful information systems have allowed computerised system status plans (SSPs) to be developed so that as many as 2,000 SSPs can be integrated into a medium sized urban system for the average 168 hour week (Stout 1994). Implementation of SSM in Kansas City, Missouri improved the monthly response times for emergency calls by between 19-46% over a one year period and resulted in a 90% fractile response time of less than 8 minutes (Ryan 1994). Automated vehicle location systems are an important component of modern SSM. However, in actual practice, only 78% of EMS systems in the U.S. in 1995 had a computerised dispatch system and only 13% had automated vehicle location systems (Cady and Scott 1995). Both are considered essential to a mature SSM.

A number of initiatives in the U.S. have also focused on the need to develop improved techniques for collecting EMS related data and identified data elements that are essential or desirable (Spaite, and others 1995). Barriers to the success of producing a uniform and complete data-set include the separate and disparate locations in which data to describe an EMS event resides. There are also lack of integrated information systems between healthcare providers. The ability to overcome these deficiencies would lead to continuous EMS evaluation and enhance the quality of EMS related research (Delbridge, and others 1998).

In the UK many EMS systems have lacked investment in management information systems. This has compromised their ability to audit working practices and implement effective change (Audit Commission 1998). However, most systems are in the midst of introducing computerised EMD protocols and a number have implemented digital radio communication. Investment into information systems for operational issues, system evaluation and quality assurance was considered essential (Audit Commission 1998). The North Staffordshire Ambulance NHS Trust which pioneered the use of SSM in the UK has produced the best response time performance standards for any system in the years 1995-1998 (Department of health 1999).

2.3.5 Medical control

As the role of EMS systems has changed from one of providing a transport service to one of diagnosing and treating a host of illnesses and injuries, so the involvement of physicians has increased dramatically. In the U.S. such medical involvement or 'control' has been present in some states from as early as 1974. It has developed to a point where EMS systems in most states that provide advanced care have a physician medical director mandated by law. The director provides 'medical accountability and control throughout the planning, implementation and evaluation of the system' and should be actively involved within the pre-hospital care system (American College of Emergency Physicians 1982). The employment of an EMS medical director with a clear strategy for training, certification and monitoring increased the proportion of patients surviving a CA with VF to hospital discharge from 0% to 21% (Pepe and et al 1993). The medical director's role can also include providing direct medical control to providers at the scene for certain selected patients although there has been some debate as to the usefulness of this strategy (Gratton, and others 1991).

The ideal state of medical control was defined as one where 'directors are able to monitor all EMS providers and their activities as well as positively influencing

systems, the care they deliver and applying new developments in clinical research' (Delbridge, and others 1998). In actual practice, even in the U.S. a comprehensive state wide system of medical direction was lacking in 63% of states in 1993 with inconsistencies in training, monitoring and involvement of physicians in EMS activities (Snyder, and others 1995).

In the UK, development of Paramedic Steering Committees in the late 1980s consisted of members of the ambulance service and hospital clinicians. These clinicians supervised paramedic training and gave some clinical input into medical protocols alone. The first full time medical director was appointed to the Scottish Ambulance Service in 1992 (Audit Commission 1998). By 1998, 41% of ambulance services had a medically qualified person serving on the trust board although only 7 of the 17 medical directors were actively involved in the pre-hospital environment (Allison and Cooke 1998). In addition, chief executives of the trusts varied considerably in their views of the role of a medical director. A well defined commitment to the post, right of access to the system's trust board and a clinician with a recognised qualification in pre-hospital care have been recommended as being essential (Audit Commission 1998).

The recent implementation of the Government's Clinical Governance strategy to improve the quality of care in the NHS has to some extent solved the thorny issue of how clinicians are involved in EMS systems (Department of health 1998). It mandates that Trusts who are responsible for the running of EMS systems in the UK have nominated lead clinicians actively involved in all critical aspects of the trust's functions through the work of a Clinical Governance Committee. These include responsibility and accountability for quality of clinical care and quality improvement, clear risk management strategies, maintaining continuing professional development as well as identifying and remedying poor performance. In addition there are responsibilities to identify and disseminate evidence based best practice in clinical care. The formation of the British

Ambulance Service Medical Directors group (BASMeD) in 1999, will act as a focus for many of these activities.

2.4 Quality assurance in EMS care.

The ability of patients to receive the highest quality of care is a cornerstone of the Government's strategy for NHS development (Department of health 1997).

Quality is defined as care which is appropriate to the patient's needs, effective, (thus drawing upon best available clinical evidence) and economically efficient (Department of health 1998). An EMS system's ability to reach defined performance standards in terms of their response times to emergency calls is just one component of a quality service (NHS Executive Steering Group 1996).

The need for improvement in quality assurance strategies for EMS systems has been clearly identified (Audit Commission 1998). Many deficiencies in existing programmes were noted. In particular there was a need to strengthen clinical audit and integrate it with health authorities and A&E departments. Further development of clinical risk strategies and better continuing education for staff was also found to be necessary. In one study, 61% of Ambulance training school managers admitted that there was no form of continuing education for their pre-hospital personnel and 70% of these specified the need for closer links with hospital staff and especially their A&E department (Hassan and Bodiwala 1998). Within individual EMS systems, Trust Boards have developed clinical governance committees whose remit is to achieve these goals by using various strategies.

Evaluating the process of assessing quality, even in mature EMS systems, is difficult. Classical measures include structural (input), process and outcome variables. However, because long term patient outcomes may be insensitive to the variation in care provided by the EMS, intermediate outcomes that have a closer temporal relationship to EMS care and greater impact on eventual

outcome are often utilised. Cardiac arrest and trauma have been widely used in the past as 'tracer' conditions as outlined earlier (Shackford, and others 1987; Eisenberg 1987). Evaluation, in the form of comprehensive, medically directed quality assurance programmes has therefore remained poor even in the U.S. with 89% of states failing to achieve adequate defined standards (Snyder, and others 1995). These results paralleled the lack of physician involvement in the system itself as well as lack of direction in protocol design. Lack of resources resulted in almost a half of the states (44%) not having a state-wide data collection system. Only 11% were considered to have an adequate pre-hospital data recording system to capture the minimum data necessary to measure compliance with standards.

2.5 Challenges and solutions to EMS system design.

The demand put on individual EMS systems in the UK in the last decade has compromised their ability to perform their primary function of accessing, treating and transporting patients with time critical illness and injury (NHS Executive Steering Group 1996). It has been estimated that an extra 3,200 lives could be potentially saved from cardiac arrest alone if 90% of category A calls were reached within 8 minutes. Unfortunately, the number of emergency 999 calls has increased annually by between 4.8% and 9.4% since 1992 (Department of health 1997). In 1997-8 ambulance services in England and Wales dealt with 4.4 million emergency and urgent calls (Audit Commission 1998).

2.5.1 Appropriateness.

The appropriateness of emergency ambulance usage by the public has been studied in the UK as well as North America. A review of published studies between 1989 and 1997 identified 10 studies of which 9 estimated the incidence of inappropriate use to be between 30% and 52% (Snooks, and others 1998). This was consistent with the figure of 40% identified by ambulance crews ratings

of emergency calls in London (London Ambulance Service NHS Trust 1997) but was somewhat higher than the 16% quoted by another study of the same system (Palazzo, and others 1998).

Strategies to deal with 'inappropriate' demand can be to either influence the public not to call the emergency services – generally regarded as being ineffectual – or by providing alternatives for the public when they seek assistance through the introduction of strategies such as NHS Direct (Chief Medical Officer 1997). In addition, other strategies include the full implementation of EMD and having a tiered response to an emergency call rather than a fully manned ambulance every time (Audit Commission 1998).

2.5.2 Effectiveness.

The effectiveness of a system is reliant upon being able to evaluate performance and new interventions with robust methodology and clear end points. A review of the literature has revealed that there is a notable lack of information relating to the effectiveness of clinical care procedures carried out in the pre-hospital environment (Callaham 1997). Cardiac arrest however, has been regarded as 'the best outcome evaluation of an EMS systems's performance' (Eisenberg 1987).

The difficulties of quantifying the effectiveness of EMS care in the U.S. were addressed by the National Highway Traffic Safety Administration (NHTSA) in 1994 when they convened a 'Workshop on Methodologies for measuring morbidity outcomes in EMS' (National Highway Traffic Safety Administration 1994). The workshop recommendations included the need for conditions or diseases to be prioritised with research being concentrated on high priority conditions as well as measures for risk adjustment and outcome to be identified for these conditions.

Subsequent work identified experts in the field of EMS who used the six patient outcomes as originally defined by the NHTSA (table 2.3) to determine those conditions with the greatest potential value for the study of effectiveness of EMS care (Maio, and others 1999). They also incorporated a weighting for the frequency of the condition.

Table 2.3: Definition of outcome categories to determine those conditions with the greatest potential value for the study of effectiveness of EMS care.

Term	Definition
Survival	Mortality directly attributable to the condition.
Impaired physiology	Objectively measurable signs of altered physiology
Limit disability	A change in the functional status of the patient in terms of ability to live independently and go about their lives at home, work or recreation.
Alleviate discomfort	Uncomfortable symptoms such as pain, nausea, vertigo or shortness of breath.
Satisfaction	Expectations of patient and family are met by the services provided
Cost-effectiveness	The financial consequences of health care to the patient and society

The weighted rank ordered EMS conditions for children and adults provided the basis for the study of effectiveness of out-of-hospital emergency care. The top quartile for each represented 85% of paediatric transports (minor trauma, major trauma, respiratory distress, airway obstruction, respiratory arrest, cardiac arrest and seizure) and 65% of emergency adult transports (minor trauma, respiratory distress, chest pain, major trauma, airway obstruction, cardiac arrest and respiratory arrest). Importantly, relief of discomfort was identified as the parameter having the greatest potential impact on the majority of the top quartile conditions.

2.5.3 Efficiency.

Critical to a system's ability to provide a service which is appropriate and effective however, is the need to be cost efficient (Stout 1994). Systems in the U.S. can vary by as much as 300% in terms of economic efficiency and these variations are often related to the design of the system itself. These statistics are similar to those in the UK (Audit Commission 1998). Therefore, by necessity, systems have needed to change and optimise their performance. This is likely to continue over the next decade. Some operational factors such as productivity, sickness absence and vehicle maintenance may be amenable to change whereas others such as population density and the geography of the system are not. In addition organisational mergers of Ambulance Trusts have produced larger systems with both financial and non financial benefits. The latter includes the ability to bring together a 'critical mass' of expertise amongst staff, for example in audit and management information systems (Audit Commission 1998).

Formal cost effectiveness analyses of EMS systems have concentrated on patients suffering cardiac arrest or severe injury alone although the need to evaluate other aspects of EMS care has been stressed (Maio, and others 1999). Comparisons with other healthcare interventions such as coronary bypass grafting have suggested that interventions to improve the response time of an EMS system in the UK can be very cost effective per life year gained (NHS Executive Steering Group 1996). However, the authors made it clear that a number of key assumptions had been made and that the results needed to be validated at a local level. Thus far, there have been no economic evaluations from individual systems in the UK using cardiac arrest as a model.

2.6 Economic evaluation of EMS care

The complexity of an EMS system will have a significant impact on the healthcare it aims to provide and the societal expense it incurs. However, it is essential to be able to identify the cost effectiveness of a system, in order to make comparisons and benchmark with other systems. In addition, it can be used to evaluate the impact of strategic change on performance measures and the outcome of certain conditions.

A variety of models can be used to compare systems. 'Cost per response' is a crude measure which does not take into account the geography of the system or the economies of scale which advantage larger systems by minimising overheads (Audit Commission 1998). In 1998 this produced a threefold variation in a costings exercise of UK systems of between £50 - £125 per emergency call response. An alternative technique, employing a non-parametric mathematical programming technique, took into account operational resources to develop an efficiency score. This was based upon percentage of calls dealt with in defined performance times and the cost per journey. A relationship was identified between the efficiency score and the response time. Although it was suggested that the technique could be used in the future as a better measure of overall system performance, it took no account of impact on patient care (Turner 1998).

The ability of systems to meet defined standards of response time is widely regarded as a robust measure of overall performance and can be used as an indirect measure of impact on life threatening conditions. The 90% fractile of 8 minute response to all immediately life threatening calls is regarded as one of the essential components of a 'high performance' system (Stout 1994). However, there is a paucity of formal cost effectiveness evaluations of individual systems and some variation in the results attained. As stated earlier, the two conditions most often studied are major trauma and cardiac arrest.

In evaluating the impact of paramedic skills on major trauma outcomes there have been two methodologically robust studies in the UK. Costs of £213 were incurred by a paramedic crew as opposed to £162 for a technician crew in one study to evaluate the role of paramedics in treating major trauma patients (Knapp, and others 1997). However, in a similar study evaluating 3 other EMS systems, costs of a paramedic callout were between £63-£97 as opposed to a technician crew where they varied between £58-£98 (Nicholl, and others 1998). The variations were attributed to differences between ambulance services.

The treatment of pre-hospital CA has been frequently used as a model to evaluate cost effectiveness. Proponents argue that it is the only intervention that has been clearly demonstrated to save lives in the pre-hospital setting. In 1981 it was suggested that it cost \$42,000 to avert a cardiac death using the King County suburban paramedic program (Urban, and others 1981). In contrast in 1990, it was calculated to be \$8,886 per 'life year' saved in the Tucson, Arizona urban paramedic system (Valenzuela, and others 1990). A Canadian programme of system optimisation using firefighter defibrillation as the main strategy calculated the start-up costs to be \$46,900 per life saved and \$2400 per life saved to maintain the program in 1999 (Stiell, and others 1999). The only work from the UK using the CA model suggested costs per life year gained of between £700 and £2,200 depending upon whether the patient was under or over 70 years of age and collapsed in an urban or rural community (NHS Executive Steering Group 1996). However, this work made a number of key assumptions and used published work from the UK and the US to derive their data. They strongly recommended validation by individual systems.

It seems therefore that economic evaluations can produce markedly varying results. This has been attributed to differences in quality of the sample data and methodology employed. These factors can affect the interpretation and generalisability of the results (Kernick 1998). It is essential therefore to apply rigorous structure to the evaluation in order for the findings to be relevant and

applicable to others (Drummond and Jefferson 1996). Important factors to consider include a detailed account of costs and outcomes, incremental analysis methods, costs and outcomes to be appropriately discounted and a sensitivity analysis to be used to validate the robustness of the model (Laupacis, and others 1992). In addition, although economic evaluations will deal with economics and effectiveness, the introduction of a new technology or strategy was also noted to be influenced by ethics and politics.

2.7 EMS development in the future

Increasing demand and changes to the delivery of health care are impacting significantly on the provision of emergency services and hence the reconfiguration and design of EMS systems both in the UK and North America. A system's primary responsibility is to respond optimally, treat and rapidly transport all life threatening and other emergency conditions. This is compromised by the need and duty to triage, process, care for and transport the vast majority of other patients with more minor complaints to an appropriate facility. New strategies are therefore necessary in order to meet the primary responsibility and cope with increasing number of challenges that EMS systems are being called upon to deal with.

In the US, new models are being developed with multiple decision points available to EMS personnel at each stage of the patient's care pathway from dispatch, on arrival at scene and when treatment and transport are considered necessary (Neely, and others 1997). This model will require a reconfiguration of pre-hospital providers in some systems. Skills will need to reflect the needs of the system and integration with hospital services. Similar changes are suggested as being beneficial and necessary in the UK with a wider range of responses being available to those who call for an ambulance and better multi-agency working (Audit Commission 1998; Chief Medical Officer 1997)

In 1995, the development of a document by major EMS stakeholders in the U.S. provided a clear focus and benchmark for future development of pre-hospital care (Delbridge, and others 1998). A summary of some of its recommendations that are relevant to practice in the UK are provided in table 2.4. The key components are the need to develop systems that are well integrated and have education, research and medical direction at the core of their service. Robust systems of evaluation and improvement are also necessary.

In this chapter, I have reviewed the developments that are occurring and those that are necessary in UK pre-hospital care systems in six key areas. I have compared them predominantly with North American EMS systems for a number of reasons. The systems in North America are similar to those in the UK in terms of the providers of pre-hospital care. A number of different models exist in mainland Europe which employ physicians. Comparison with these systems would be inappropriate. In addition, much of the available evidence on EMS design for urban communities emanates from North America. It is therefore most applicable to UK practice.

**Table 2.4 : Summary of recommendations made by the EMS Agenda
for the Future Steering Committee.**

Integration of health services.

- Expand the role of EMS in public health
- Involve EMS in community health monitoring activities
- Integrate EMS with other health care providers and provider networks

Medical direction

- Formalise relationships between all EMS systems and medical directors
- Identify appropriate resources for EMS medical direction
- Require appropriate credentials for all those who provide on-line medical control
- Develop systems for critical incident stress management

Education systems

- Ensure adequacy of EMS education programs
- Conduct EMS education with medical direction
- Incorporate research, quality improvement and management learning objectives in higher level EMS education
- Establish collaborative relationships between EMS education programs and academic institutions
- Update education core content objectives frequently enough so that they reflect patient EMS health care needs

EMS research

- Allocate specific funding for research
- Develop information systems that provide linkage between various public safety services and other health care providers
- Develop institutional commitments to EMS related research with collaborative relationships between EMS systems, medical schools and other academic institutions

Clinical care

- Subject EMS clinical care to ongoing evaluation to determine its impact on patient outcomes
- Employ new care techniques and technology only after shown to be effective

Information systems

- Adopt uniform data elements and definitions and incorporate them into information systems
- Develop mechanisms to generate and transmit data that are valid, reliable and accurate
- Develop information systems that are able to describe an entire EMS event
- Provide feedback to those who generate the data

Communication systems

- Promulgate, update and optimise standards for EMS dispatching
- Determine the benefits of real time patient data transfer
- Facilitate exploration of potential uses of advancing communications technology by EMS

Public education

- Collaborate with other community resources and agencies to determine public education needs
- Explore new techniques and technologies for implementing public education
- Evaluate public education initiatives

Prevention

- Collaborate with community agencies and health care providers with expertise in illness and injury prevention
- Include the principles of prevention and its role in improving community health as part of EMS education core contents
- Improve the ability of EMS to document injury and illness circumstances

Evaluation

- Develop valid models for EMS evaluations
 - Evaluate EMS effects for multiple medical conditions
 - Determine EMS cost effectiveness
-

Chapter 3

**Impact of the 'Chain of Survival' on outcome –
the evidence.**

3.1 Historical evidence.

The historical basis for modern day resuscitation medicine extends back over 200 hundred years (Safar 1989) although the efforts of Elijah in the Old Testament who, 'blew air into the child three times' are much quoted (Paraskios 1992). Techniques including mouth-to-mouth ventilation, open and closed chest cardiac massage, defibrillation and intubation are all described from the late 1700s onwards (Safar 1989). Dr Charles Kite, produced a document in 1788 which provided probably the first scientific work on the subject (Eisenberg 1994). The epidemiology of the cause of sudden cardiac death in London, drowning in those days, is recorded in detail. In addition, the successful use of a 'protodefibrillator' is described. This machine employed a capacitor, a way to adjust the charge and two electrodes applied to the chest. Unfortunately, techniques during this time were all based upon individual anecdotal reports.

The first significant steps towards improving outcome occurred in the late 1950s. It was scientifically proven that mouth to mouth ventilation and mouth to nose ventilation allowed adequate oxygenation which was superior to that provided by compression of the chest and lifting of the arms (Safar, and others 1958). By 1960 external cardiac massage was shown to provide an effective cardiac output (Kouwenhoven, and others 1960). Soon after, the combination of ventilation and closed cardiac massage formed the cornerstone of basic cardiac life support (BLS) in adults (Safar, and others 1961). Training in BLS was initially recommended only for doctors and allied health professionals because of its complexity and worries regarding the possibility of trauma. This advice was soon reversed (Lind 1961).

Ventricular fibrillation (VF) was first described in experiments on animals in the late nineteenth century. The first report of successful defibrillation was reported in 1947 (Beck, and others 1947). The first case series of 30 patients who had suffered VF during surgery, 20 of whom were defibrillated, resulted in nine

survivors (Milstein and Brock 1954). By 1956 the first effective externally applied defibrillator had been invented (Zoll and et al 1956). Over the next decade ventricular fibrillation became recognised as a common and early complication of acute myocardial infarction. This led to the development of coronary care units where expertise and resuscitation equipment was at hand. However, it was recognised that most patients who suffered an acute coronary event were dying before they reached hospital. The world's first programme to provide emergency cardiac care in the community was the seminal work which launched modern day EMS care for pre-hospital CA (Pantridge and Geddes 1967).

The concept of the 'rescue chain' was first described by Professor F.W. Ahnefeld in the early 1960s (Safar 1989). Subsequent refinement resulted in the 'chain of survival' concept (Cummins, and others 1991). Weakness in any one of the links compromises the ability to achieve a successful outcome. In the rest of this chapter, the evidence base for each of these links is explored and discussed.

3.2 The 'early access' link.

The resuscitation chain is initiated when a medical emergency is recognised and the EMS accessed and activated (Cummins, and others 1991). In sudden cardiac arrest, access time begins at the moment of collapse and encompasses a number of critical events ending with the initiation of emergency treatment by the EMS. Early access is strengthened by public education, a uniform emergency access number, an efficient EMS dispatch system and a rapid EMS responder system.

Educating the public to activate the EMS and perform BLS in the meantime has produced varying results. A population survey in Glamorgan revealed that on encountering someone in cardiac arrest, 65% of subjects would firstly phone for an ambulance. This increased to 73% amongst those who had received no formal training in life support skills (Assar 1995). However, in a more robust

assessment of what the practice of trained BLS responders would be in such circumstances, only 10% of subjects activated the EMS before initiating CPR (Morgan, and others 1996). In another study of actual practice, witnesses to a CA telephoned neighbours, relatives or even their personal physician rather than the EMS (Walters and Glucksman 1989).

Access to emergency services is achieved in developed countries by having a three digit emergency number. In the UK the 999 system provides uniform access to the emergency services. In the US, although the use of 911 as an emergency access number has become widespread, a number of communities are still without the service (Becker and Pepe 1993). 'Enhanced 911' provides dispatchers with automatic electronic displays of information regarding the caller's address and phone number. Other countries have also adopted universal emergency telephone numbers for their systems (03 in Russia, 120 in China, 119 in Japan).

The rapid and efficient dispatch of EMS responders is a vital part of the early access link. Emergency medical dispatch is essential for dispatchers to be able to carry out this function. Two systems have been evaluated in the UK and found to be equally successful (Nicholl, and others 1996). The EMS response itself is either a single tiered ALS or a mixture of two-tiered systems with first responders trained in early defibrillation. These aspects of the 'early access' link have been discussed in chapter 2.3.

3.3 Bystander CPR.

The second link, bystander CPR, is maximally effective when started at the time of patient collapse. In most clinical studies, this link has been reported to have a significant positive effect on survival (Bossart, and others 1989; Ritter, and others 1985). Its value is that it maintains enough blood flow to essential organs such as the brain and heart until more definitive treatment arrives. Early bystander CPR is much less helpful in resuscitation if EMS personnel arrive late, up to 8-12 minutes after the collapse (Mullie, and others 1989). In addition, if rescuers start CPR early, a patient is more likely to be in VF when an EMS unit arrives (Weaver, and others 1986). In King County, investigators observed that 80% of cardiac arrest victims were in VF if they had received early bystander CPR, compared with 68% if they had received delayed CPR (Cummins, and others 1985). In the Belgian Cardio-Pulmonary Cerebral Resuscitation Registry, there was a 42% prevalence of VF in cardiac arrest patients who received bystander CPR, compared with 29% in arrest patients who received delayed CPR (Bossart, and others 1989). Impact on eventual outcome has also been shown to be clearly beneficial if good CPR is administered. In a study of 334 patients in Oslo, Norway, the discharge rate with good bystander CPR was 23% versus 1% with poor CPR and 6% with no CPR (Wik, and others 1994).

Cardiopulmonary resuscitation with chest compressions only (i.e., no assisted ventilation) has been proposed as one simplified technique that may encourage increased bystander CPR. Such a modification makes CPR easier to learn and to master, and it alleviates the fears and concerns associated with mouth-to-mouth contact. Animal studies have established that prompt initiation of chest compressions without assisted ventilation for 8 to 12 min can be as effective as ABC CPR with respect to 24 h survival and neurologic outcome after VF (Berg, and others 1995; Noc, and others 1995). Immediately after an acute fibrillatory cardiac arrest, aortic oxygen and carbon dioxide concentrations do not vary from the prearrest state, because there is no

blood flow and aortic oxygen consumption is minimal. When effective chest compressions are initiated, this oxygenated blood flows from the aorta to the coronary circulation. Importantly, these studies have documented no outcome disadvantage with less than optimal gas exchange from chest compressions alone, particularly when associated with active gasping during CPR.

Hallstrom et al. compared chest compressions alone to chest compressions plus assisted ventilation in the setting of dispatcher-directed telephone-assisted bystander CPR when the dispatchers determined that the bystander or caller did not know CPR (Hallstrom, and others 2000). They instructed nearly 500 bystanders to provide chest compressions alone or chest compressions plus assisted ventilation. Survival to hospital discharge was 10% after chest compressions plus assisted ventilation and 14.5% after chest compressions alone ($p = 0.09$). Chest compressions alone was certainly not worse than chest compressions plus assisted ventilation, and the trend suggests it might be better.

Optimal BLS for asphyxial arrests is quite different. Asphyxia results in progressive oxygen consumption and carbon dioxide and lactate production before cardiac arrest. Therefore, adequate myocardial oxygen delivery during CPR for an asphyxial cardiac arrest requires re-establishment of arterial oxygenation and improvement of pH through adequate gas exchange in the lungs, as well as myocardial perfusion. Chest compressions plus rescue breathing is the treatment of choice for asphyxial arrest. However, laboratory and clinical experience suggests that patients with asphyxial cardiac arrest can sometimes be resuscitated with ventilation alone or compressions alone, despite a history of pulselessness and unresponsiveness (i.e., it is better to do "something" than "nothing") (Berg, and others 1999).

There is also evidence to suggest that the routine provision of approximately 90 seconds of CPR prior to use of an AED is associated with increased survival when the response interval of the EMS is longer than 4 minutes (Cobb, and

others 1999). This study was an observational pre and post-intervention strategy design carried out in a mature EMS. It recruited a total of 1,117 patients suffering out-of-hospital VF. Overall survival to discharge from hospital was significantly greater during the intervention rather than the pre-intervention period (30% vs 24%, $p=0.04$). Although the study had a number of limitations, if the results were to be reproduced in other systems, a significant change in resuscitation guidelines would be required.

The main difficulty lies in developing strategies to teach populations the principles of BLS which they will be able to retain until called upon to use the skill. A variety of approaches have been employed. The most widely advocated is citizen CPR training. A whole range of community based projects have been endorsed and conducted by organisations worldwide since the first major study involving 8,700 children aged 12-14 in Norway in 1960 (Lind 1961). Despite this, doubts remain as to the effectiveness of such strategies due to de-skilling and the lack of enthusiasm for re-training (Berden, and others 1993).

A review of the literature in 1998 identified a number of reasons for poor performance and retention of skills following BLS training programmes (Kaye and Mancini 1998). These included inadequate instruction, inadequate practice time and teaching excessive amounts of unnecessary information. They recommended a more simplified approach with concentration on the psychomotor skill of BLS and a major focus on repetition whilst practising. Others have confirmed that trained instructors are not required in order to learn and retain BLS skills. A peer training model using a CPR flip chart, videotape and a card board manikin was as successful in a group of factory workers as a regular instructor led 4 hour course (Wik, and others 1995). In a study to evaluate a video CPR self instruction model (with a cardboard manikin and video alone), more than twice as many students were rated competent at 2 months as compared to the standard 4 hour teaching (Braslow, and others 1997). A variety of other innovative educational tools including interactive computer video

systems have also been evaluated and shown to be effective (Kaye and Mancini 1998).

Other approaches to early CPR include the concept of targeted CPR training (Pane and Salness 1989). These programmes are for those who have an increased likelihood of having to perform CPR such as the spouses of those who have suffered a myocardial infarction. Unfortunately, they tend to be individuals who are not participants in BLS training programmes. In the UK, the number of programmes using this approach are limited. In Scotland, out of the 45 cardiac rehabilitation programmes on the British Heart Foundation register, only 37% provided any form of training on basic CPR (Richardson and Lie 1998). Actual numbers trained by these programmes was very small.

A final method to achieve early CPR is dispatcher assisted instruction or telephone CPR. This method has been shown to be successful in those who have never received any form of instruction as well as improving the quality of CPR performed by people who have received previous training (Kellermann, and others 1989, Hallstrom, and others 2000). Along with a number of other educational strategies it is reported to have increased the incidence of bystander CPR in King County, US from 30% in 1980 to 60% in 1988 (Cummins, and others 1991).

3.4 Other types of CPR

A number of other methods of performing BLS have also been evaluated with varying success.

Interposed abdominal compression (IAC) CPR was first described in 1976 (Ohomoto, and others 1976). Theoretical advantages of this technique include increased intra-thoracic pressure and aortic compression producing retro-grade aortic flow and hence improving coronary flow. Despite a randomised study of in-

hospital CA which improved survival to discharge significantly (Sack, and others 1992), there has been no other evidence to support this technique.

The invention of the active compression-decompression (ACD) device was based upon the 'thoracic pump' theory of forward flow during external cardiac massage. Investigators reasoned that as changes in the intra-thoracic pressure caused ventricular filling, so active decompression on the upstroke would increase negative intra-thoracic pressure. Thus ventricular filling would improve and this in turn would improve myocardial and cerebral blood flow. The device was successful in animal models and also a small randomised controlled trial (Lurie, and others 1994). A large well powered randomised study subsequently found no significant difference in survival to discharge from hospital using the ACD device as compared to standard CPR (Stiell, and others 1996). In contrast, another large pre-hospital study from a French system did show marked improvement in outcome using the ACD (Plaisance, and others 1999) although a notable number of limitations to the study were suggested (Callahan 1999).

3.5 Early defibrillation.

The goal of defibrillation in CA is to electrically terminate VF or pulseless VT with the hope that an organised perfusing rhythm will follow. Ventricular tachyarrhythmias have been shown to occur in up to 85% of adults suffering primary cardiac arrest out-of-hospital in the first few minutes after collapse (Bayes de Luna, and others 1989). The earliest success of a portable defibrillator was that of the mobile intensive care unit in the streets of Belfast (Pantridge and Geddes 1967). Since that time, numerous other studies have confirmed the critical importance of defibrillation in treating patients with pre-hospital CA. In 1978, researchers from Nottingham suggested that every ambulance should be equipped with a defibrillator and the crew taught how to use it (Hampton and Nicholas 1978).

In the early programmes both in the UK and North America, defibrillation was performed only by paramedics. In most of these studies, the time between collapse and arrival of the paramedics averaged over 12 minutes. These programmes therefore provided what became known as 'late defibrillation' (Cummins, and others 1991). Consequently the survival rates remained relatively poor (Eisenberg, and others 1990). By the early 1980s, researchers had demonstrated that other EMS personnel such as EMTs, who had fewer skills than paramedics, could also use defibrillators just as well and arrive at the scene more rapidly (Eisenberg, and others 1980). Although this provoked some controversy, by the late 1980s there was widespread acceptance of the principle of early defibrillation.

The introduction of automated external defibrillators (AEDs) allowed many more pre-hospital personnel to be able to perform the skill without having to acquire the complex skills of rhythm recognition (Cummins, and others 1987). Time to defibrillation was also decreased by up to a minute with the use of AEDs as compared to standard defibrillators. In the UK, the HeartStart Scotland campaign resulted in every Scottish ambulance EMT crew being taught how to use an AED (EMT-D) by the end of 1988 (Sedgwick, and others 1993). An overall discharge rate of 10% was achieved when 1700 pre-hospital CAs were reviewed in a one year period. There was no data to show the baseline discharge rate prior to the intervention although it was assumed to have been very poor. Almost all of the survivors had required defibrillation during their resuscitation but received no additional ALS skills. In other systems, the comparison between survival rates before and after introduction of EMT-D programmes was marked. In King County, Washington, survival rates for patients in VF increased from 7% to 26% (Eisenberg, and others 1980). Similarly, in rural communities in Iowa, it increased from 3% to 19% (Stults, and others 1984).

Subsequent progress in the U.S. allowed other personnel also to be taught how to use AEDs. The concept of 'first responders' is a term specifically aimed at non

-professionals who have completed a 40 hour course in the use of AEDs. A variety of public safety employees including firemen, police officers, security guards, airline personnel and part-time volunteers have successfully completed the courses (Cummins, and others 1991). In a prospective 3 year before and after study, police officers from seven Pittsburgh communities were equipped with AEDs (Mosesso, and others 1998). The interval from collapse to defibrillation was reduced from 10 minutes when DC shock was applied by the EMS as opposed to 7 minutes when performed by the police ($p = 0.001$). In patients with VF, survival to discharge was higher as compared to the standard EMS response (14% vs 6%), although the results were not statistically significant. Survival to discharge was 26% when police arrived first and provided defibrillation, compared with 3% when defibrillation was provided by EMS personnel.

In a larger study of 21 communities, optimization of an existing EMT led defibrillation programme occurred with firemen being taught to use defibrillators as one of several interventions (Stiell, and others 1999). This resulted in improvement of the 8 minute response time from 76% to 92%. However, in patients suffering a bystander witnessed VF arrest the improvement was only from 10% to 12% ($p = 0.33$). Overall survival to hospital discharge increased from 3.9% to 5.2% ($p = 0.03$).

3.6 Home and community responder defibrillation programs.

Two other techniques have been advocated in order to achieve early defibrillation. These are home defibrillation for high risk patients and early defibrillation by community responders. Although these approaches have been under evaluation for a number of years, their specific effects on community wide survival rates from cardiac arrest remain as yet undetermined in a large study (Jacobs 1986). In a study of 95 survivors of VF, only 63 were eligible for an AED

and only 38 of 47 persons approached agreed to participate (Moore, and others 1987). In a series of 48 high risk patients where the research team trained family members to operate AEDs, five cardiac arrests occurred. The trained home responders used the automated defibrillators four times and achieved a return of circulation in three of the patients (Swenson, and others 1987). In another series of 59 patients who had AEDs installed at their homes, 10 cardiac arrests occurred and the devices were used in six patients (Eisenberg, and others 1989). Only two were subsequently found to be in VF. One patient was successfully resuscitated but survived only a few months with severe residual neurological deficit.

A number of studies have suggested variable success with the concept of trained members of the lay public being taught to use AEDs as part of first responder protocols. Short reports of success with security personnel at large gatherings, flight crew on aircraft, staff at train stations and remote communities such as oil rig workers and passenger cruise ships have all been reported (Cummins, and others 1991). Estimations of the potential benefits in the wider community have suggested that a significant number of lives might be saved. An evaluation of over 7,000 pre-hospital CA events in the Seattle – King County system over a five year period identified that 1,130 (16%) had occurred in a public setting (Becker and et al 1998). Ten locations categories were identified that had the highest annual incidence of arrests per site. It was estimated that placement of 276 defibrillators at these sites might permit treatment of 27 cardiac arrest events per year and potentially save between 8-32 lives over the 5 years (Becker et al 1998). The exact benefits remain to be identified. Critical to these considerations are the cost effectiveness of introducing public access AEDs and the need to convince decision makers at government level that significant improvement will result (Weisfeldt, and others 1995).

3.7 Technology of AEDs.

AED technology has revolutionised the management of pre-hospital CA. Safe, effective devices have been produced that can be used by a wide variety of trained persons to convert malignant ventricular arrhythmias to a perfusing rhythm. However, due to the technological issues that affect size, weight, cost and ease of use, dissemination of AEDs to many more personnel has been constrained. The limitations of AEDs derive in part from their reliance on delivering high energies and monophasic waveforms. The development of low energy biphasic truncated exponential (BTE) waveforms has been a significant step forward in AED technology. Many of the technological constraints of previous generation AEDs have been overcome, permitting smaller, lighter, easier to use and less costly devices (Poole, and others 1997).

BTE waveforms have been shown unequivocally to be superior to monophasic waveforms for internal defibrillation by reducing energy requirements (Bardy, and others 1989). Low energy BTE waveforms are rapidly replacing high energy mono-phasic waveforms in AEDs. Other advantages include the ability to compensate for individual patient variation in transthoracic shock impedance and the use of lower energies which reduces post-shock cardiac dysfunction.

The safety and efficacy of impedance adjusting BTE waveforms used in AEDs has been validated in the out of hospital setting in 100 patients (Poole, and others 1997). The AED was 100% sensitive and specific in identifying a shockable rhythm. A single biphasic 150 Joule shock converted 39 out of 44 patients out of VF. This new type of AED will have a significant impact on the dissemination and ease of use of defibrillators, thus strengthening this link in the Chain of Survival.

3.8 ALS measures

This last link in the Chain of Survival is probably the most costly in terms of training and consumables used, yet based upon the weakest evidence base for interventions likely to produce a successful outcome. In the US, paramedics provide ALS skills for patients suffering cardiac arrest. They receive between 1,000 to 3,000 hours of classroom training and field instruction allowing them to perform endo-tracheal intubation and administer a variety of intravenous drugs as well as being able to defibrillate. In European EMS systems, these functions are provided by a variety of staff, ranging from ambulance personnel, nurses and doctors providing physician manned mobile coronary care units. Most of these systems provide a multi-tiered response (Cummins, and others 1991). In the UK, a fragmented ALS response was replaced in 1996 with a single tiered ALS response for all emergency calls. Some systems had employed ALS crews since the mid 1970s with varying success (Hampton and Nicholas 1978).

The rationale for providing empirical therapeutic ALS interventions in these circumstances stemmed from the poor outcome of patients suffering pre-hospital CA in the early 1970s. Most patients failed to survive despite the obvious success of defibrillation in a small minority of cases. Researchers and clinicians therefore began to identify other factors that could explain the lack of success. These included abnormalities of oxygenation and ventilation, aspiration of vomitus, lactic acidosis, refractory or persistently recurring VF, asystole and EMD (Pepe 1989). Interventions including endotracheal intubation, oxygen, sodium bicarbonate, adrenaline, lignocaine, atropine and a variety of other adjuncts were empirically and routinely administered in order to correct these abnormalities (Emergency Care Committee 1974). Much of the supportive evidence was derived from animal and small human studies and became accepted practice for the next 25 years.

Although most of these interventions continue to be recommended, few if any meet the rigorous standards of randomised, placebo controlled trials (Cummins, and others 1991). In 1998, the updated European Resuscitation Council (ERC) guidelines were published (Advanced Life Support Working Group of the European Resuscitation Council. 1998). These were derived from advisory statements made by the International Liaison Committee on Resuscitation. Particular emphasis was made on simplifying the guidelines as a response to the educational needs and evolving technology of resuscitation rather than to any important changes in the science (Nolan and Gwinutt 1998).

The next section provides an overview of the existing evidence base for each of these interventions and potential implications for the future.

3.8.1 Airway interventions.

The updated ERC guidelines recommend that the gold standard for airway management in pre-hospital CA is endotracheal intubation (Advanced Life Support Working Group of the European Resuscitation Council. 1998). Alternatives such as the laryngeal mask airway (LMA) and Combitube are recognised as suitable alternatives in certain circumstances. However, it is important to look in more detail at the actual circumstances of the airway intervention in pre-hospital CA rather than the evidence supporting intubation as a gold standard.

Many EMS systems with high survival rates use endotracheal intubation routinely and their respective paramedics have high success rates for performing this intervention (Pepe, and others 1993). Other systems that do not use endotracheal intubation generally have lower survival rates. Other factors confound this seemingly intuitive observation that intubation must therefore be the best form of airway control for achieving high survival rates. These factors might include better response intervals, more intensive training and more

specialised medical direction. Pepe et al also argued that more often a negative correlation is found between intubation and survival (Pepe, and others 1993). Many survivors of pre-hospital CA respond to early defibrillation and awaken quickly because of the short ischaemia time. Intubation is therefore unnecessary in a patient with a strong gag reflex. Survivors will often only have had basic airway manoeuvres such as bag-valve-mask ventilation. It is this confounding variable which is the actual reason for the negative correlation between survival and endotracheal intubation. Only a randomised controlled trial could truly determine the efficacy of the intervention but this would be considered unethical. An alternative study design which may provide some guide as to the role of advanced airway measures in pre-hospital CA is the Ontario Pre-hospital Advanced Life Support phase III study (Stiell, and others 1998). This powered 'before and after' study will quantify the additive effect of introducing ALS skills into an EMS serving a large population.

3.8.2 Pharmacological interventions.

Survival in pre-hospital CA is particularly poor if initial defibrillation is unsuccessful and drug therapy is required. Patients at this stage of the resuscitation procedure have usually suffered significant hypoxic injury. A variety of pharmacological interventions including adrenaline, atropine, a number of anti-arrhythmic agents and sodium bicarbonate have been used in order to improve the survival rates with very limited success (Advanced Life Support Working Group of the European Resuscitation Council. 1998). Much of the original evidence for use of these drugs is derived from animal data and small limited, human studies (Stiell, and others 1995). However, for many of these interventions, subsequent clinical trials have failed to identify any clear association with improved survival. Of greater concern is the potential harm that may result from use of some of these agents.

This section describes the most relevant and robust studies published thus far aimed at clarifying the role of these agents.

3.8.2.1 Use of Pressor Agents

Patients in VF or ventricular tachycardia (VT) who fail defibrillation and those in bradycardic states who fail BLS need immediate therapy to reverse the metabolic effects of ischemia on the myocardium if CPR is to be successful. Basic life support, including ventilation and chest compression, is intended to generate an adequate coronary perfusion pressure to provide improved flow of blood to the myocardium. However, BLS efficacy is limited, and frequently the clinician will need to proceed to therapy with drugs that might increase myocardial blood flow.

The immediate goal of pressor therapy is to increase vasomotor tone and increase coronary perfusion pressure to improve blood flow to the heart and brain, improving the chance of return of spontaneous circulation (ROSC) and preventing continued brain injury.

Alpha-adrenergic receptor agonists, such as phenylephrine, are powerful peripheral vasoconstrictors that redistribute blood to the brain and heart during CPR. Their effect is principally on the arterial side of the circulation, and in laboratory models they increase the rate of ROSC. Beta-adrenergic agents, such as isoprenaline cause significant vasodilation and can worsen coronary perfusion pressure during CPR. They can also increase myocardial oxygen utilization, and thereby exacerbate the metabolic effects of ischemia. When the beta receptor is blocked before administration of epinephrine, a mixed alpha- and beta-receptor agonist, the resulting coronary perfusion pressure is increased.

Stimulation of vasopressin's V1 receptor results in vasoconstriction that is mediated through a secondary messenger system different from that used by

adrenergic agonists. This holds the promise of synergy when vasopressin is combined with a catecholamine. Vasopressin may decrease oxygen utilization by the myocardium, an effect that is theoretically attractive.

Epinephrine (adrenaline) is considered to be the single most useful drug currently available for the treatment of CA (Advanced Life Support Working Group of the European Resuscitation Council. 1998). Its most important mechanism of action during CPR is to increase peripheral vascular resistance through direct α adrenergic activity on arteriolar smooth muscle. It also has β_1 activity which enhances myocardial contractility, although the resulting increase in myocardial oxygen consumption may cause further myocardial dysfunction (Ditchey and Lindenfeldt 1988).

The recommended initial dose of adrenaline is 1mg in adults (0.014mg/kg) in a 70kg person (Advanced Life Support Working Group of the European Resuscitation Council. 1998). Higher doses are recommended (0.1mg/kg) late on in the resuscitation if the 1mg dose fails. A number of animal and human studies have demonstrated improved cerebral perfusion, myocardial blood flow and resuscitation rates in patients given doses of up to 0.2mg/kg (Paradis and et al 1991). Unfortunately, to date, no prospective clinical trials have ever demonstrated a survival advantage of standard dose or even high dose adrenaline in the setting of CA (Brown, and others 1992; Stiell, and others 1992). In the most recent multi-centre study recruiting 3,327 patients a greater proportion of patients suffering pre-hospital CA were admitted to hospital (26.5% versus 23.6%, $p = 0.05$). The outcome to discharge from hospital was paradoxically higher in the survivors receiving the standard dose (2.8%) versus 2.3% in the high dose group ($p = 0.34$) (Gueugniaud, and others 1998).

Recently, there has been considerable interest in the potential utility of vasopressin in the treatment of refractory cardiac arrest. In a series of laboratory and clinical investigations, Lindner et al appear to have demonstrated

significantly better outcomes with vasopressin than with epinephrine (Lindner, and others 1997). There is also the possibility of using vasopressin in combination with adrenergic agonists (Wenzel, and others 1998). Further studies are needed.

3.8.2.2 Atropine.

Atropine acts as a competitive antagonist of acetylcholine at the muscarinic receptor. In the setting of CA, parasympathetic tone is increased as a result of vagal stimulation possibly due to hypoxia and acidosis of the carotid body. The use of atropine is based upon its ability to block the depressant effects of vagally released acetylcholine at the sinus and AV nodes. Limited studies suggest a possible benefit of atropine in bradycardic arrest (Stueven and et al 1984). Another retrospective review of 529 patients suffering in-hospital CA suggested atropine might have some role if given late in the resuscitation (Stiell, and others 1995). No robust studies are available and based upon the available data, a dose of 0.04mg/kg continues to be used in asystole (Advanced Life Support Working Group of the European Resuscitation Council. 1998).

3.8.2.3 Anti-arrhythmic agents.

Evidence supporting any clinical benefit from early administration of antiarrhythmic drugs in cardiac arrest is scarce. In early animal trials, either resuscitation of VF was not improved by the addition of lidocaine (lignocaine), or any benefit was offset by worsened short-term survival attributed to the drugs' adverse circulatory depressant effects. Ironically, lidocaine, procainamide, quinidine, phenytoin and oral and higher doses of intravenous amiodarone (10 mg/kg body weight) have all been observed to increase the defibrillation threshold and, in theory, make it more difficult to resuscitate hearts from VF (Babbs, and others 1979).

Harrison et al published the only case-controlled clinical trial in which shock-refractory victims of out-of-hospital VF were stratified according to those who did and those who did not receive lidocaine. No significant differences were observed in the return of an organized rhythm, admission to the hospital or survival to hospital discharge between the treatment groups (Harrison E, 1981). A retrospective evaluation of antiarrhythmic drug use during a trial of active compression–decompression CPR found that lidocaine and bretylium were independently associated with a lower likelihood of survival to 1 h after cardiac arrest (OTAC Study Group, 1998). Another retrospective study comparing outcomes from a time when ambulances were or were not staffed by personnel who were authorized to give medications found that recipients of lidocaine were more likely to have a return of spontaneous circulation and to be admitted to the hospital. However, no survival benefit was demonstrated (Herlitz, and others 1997). In contrast, in a prospective, randomized trial comparing administration of lidocaine with standard doses of epinephrine in shock-refractory VF, not only was there absence of benefit, but survival actually worsened when such pharmacologic therapies served to delay defibrillation (Weaver, and others 1990).

Bretylium tosylate has been extensively studied and found to be effective both in the laboratory and in clinical trials for the treatment of refractory VF. A randomised controlled trial found no difference between bretylium and placebo for patients in VF (Nowak and et al 1981). In addition, its prolonged onset of action and negative inotropy have also compromised its ability to be regarded as an agent of choice for chemically converting refractory VF (Stiell, and others 1995).

Amiodarone has been increasingly regarded as a potential agent for use in refractory VF. Anecdotal case reports have suggested that it could be a successful agent in such circumstances. In most studies it has been administered only after the failure of other anti-arrhythmic agents to terminate ventricular arrhythmias. However, Kudenchek and colleagues investigated its

role as a first line agent. A randomised pre-hospital study of patients in refractory VF recruited 504 patients (Kudenchuk, and others 1999). An increased proportion of patients receiving amiodarone survived to be admitted to hospital (44% versus 34%, $p = 0.004$). However, there was no difference between the two groups in survival to discharge from hospital. The authors suggested that the study was under powered to detect this important end point.

Other agents that have been studied and used to varying degrees in CA include magnesium sulphate, sodium bicarbonate and calcium chloride. There have been few studies to evaluate the role of magnesium in CA. This subject is discussed in greater detail in the next chapter. The potential harmful effects of the sodium bicarbonate and calcium chloride have been highlighted in recent years and as a result they are used only in specific circumstances (Pepe, and others 1994). It is not appropriate to this review to discuss these agents in any greater detail.

3.9 Summary.

The true impact of ALS skills on the outcome of pre-hospital CA therefore remains uncertain. Classical 'wisdom' is being challenged to quantify the efficacy and effectiveness of these interventions. Designing studies which are ethically viable are probably the biggest hurdles to overcome.

Chapter 4

Magnesium and its role as an anti-arrhythmic agent.

4.1 Introduction

In the past three decades magnesium has become a much studied and potentially important therapeutic agent for a host of medical conditions. Evidence of its usefulness in the acute management of arrhythmias dates back over half a century (Boyd and Scherf 1943). It has also been reported as effective therapy in a wide variety of disease processes including the acute treatment of pre-eclampsia (Watson, and others 1986), severe asthma (Skobeloff, and others 1989) and possibly of use in minimising cerebral injury following acute cerebrovascular events (Muir and Lees 1995).

The majority of research efforts have however been targeted at its role in various aspects of cardiovascular medicine and particularly in the management of acute myocardial infarction (AMI). Better understanding of its function in minimising re-perfusion injury post AMI and as a novel pharmacological agent for arrhythmia management has occurred. This suggests that magnesium could potentially reduce morbidity and mortality in patients with AMI or those with lethal arrhythmias.

In order to understand magnesium's possible role as an anti-arrhythmic agent, it is important to describe its homeostatic control, cellular function, electrophysiological and haemodynamic effects. In addition, it is necessary to discuss its actions on ischaemic myocardium.

4.2 Normal homeostatic mechanisms

Magnesium is the second most abundant intracellular cation in the human body and plays a role in many enzyme systems including a critical function in ATP metabolism. The average adult has a total magnesium store of some 20-25 grammes or 2,000 meq/l (Burch and Giles 1977), 99% of which is located in the

intracellular space. The free intracellular concentration is in the range of 2-6 mEq/L with the highest levels recorded in myocardial muscle cells (Wu, and others 1981). It is normally maintained under tight physiological control, which is not necessarily altered by extracellular supplementation of further magnesium (Ebel and Gunther 1983). This makes the measurement of serum magnesium by clinicians an inaccurate reflection of intracellular magnesium and thus not clinically useful.

Fifty three per cent of the body's distribution of magnesium has been estimated to be located in bone, 27% in muscle, 19% in soft tissue, 0.5% in erythrocytes and 0.3% in serum (Elin 1988). 55% of extracellular magnesium is in a free ionised form with 33% being bound to protein and 12% complexed to anions. Regulation of the body's stores is by hormonal and metabolic effects on renal and gastrointestinal absorption.

Gastrointestinal absorption varies with the amount of magnesium in the diet. It is normally approximately 300 mgs/day. Absorption occurs in both the jejunum and ileum (Agus, and others 1982). There is an inverse relationship in absorption, which varies from 42% with normal diet, to 79% on a low magnesium diet, to 27% on a high magnesium diet. The kidney, however, provides the major site regulating magnesium balance. Approximately 90% of filtered magnesium is reabsorbed by the kidney with 20-30% being reabsorbed in the proximal tubule and 65% in the loop of Henle (Schindler, and others 1996). Renal impairment will lead to hypomagnesaemia due to an increase in the fractional excretion of magnesium, but in a normally functioning renal system the percentage absorption will vary with the load presented to the kidney. A magnesium rich diet will result in diminished tubular absorption and vice-versa (Agus, and others 1989). At a hormonal level, aldosterone directly depresses tubular absorption of magnesium, as does hyperthyroidism (England, and others 1992). Magnesium's interactions with calcium are linked directly to the activity of parathyroid hormone (PTH), with deficiency resulting in impairment of PTH secretion and its action on

bone (McManus, and others 1971).

4.3 Deficiency states and their identification

Hypomagnesaemia may be due to a variety of causes. These can be classified into gastrointestinal, renal, and distributive. The main source of gastrointestinal loss is associated with lower gastrointestinal tract pathology, especially inflammatory bowel disease. Acute renal insufficiency, particularly due to tubular disorders is another potent cause, although a variety of drugs also have an action at this site. The distributive causes such as acute myocardial infarction are mediated by elevated catecholamines (Altura, and others 1984), resulting in an enhancement of lipolysis and a higher level of free fatty acids. Alcohol related diseases are a common source of hypomagnesaemia, but like malnutrition states are associated with multiple mechanisms related to tubular and gastrointestinal dysfunction.

Difficulty arises when trying to diagnose a deficiency state. Serum magnesium levels correlate poorly with intracellular tissue levels (Riggs, and others 1992) and even severe deficiency may be asymptomatic. As a result, levels of lymphocyte and erythrocyte magnesium have been tried in order to provide a more accurate measure of magnesium balance (Elin 1988). Unfortunately no clear correlation has been demonstrated.

Skeletal muscle magnesium levels are a useful assessment of hypomagnesaemia but are invasive, requiring a muscle biopsy. A much more accurate and applicable measure of magnesium is that of free intracellular magnesium using spectroscopy and magnetic resonance imaging (Barbour, and others 1991). However, these remain research tools and have little clinical significance at present. One other method which is relatively accurate in identifying magnesium depletion is 24 hour urine measurement after an

intravenous loading dose. This is reliant on normal renal function (Dyckner 1979).

4.4 Cellular and electrophysiological effects.

The intracellular magnesium concentration is between 0.3 and 0.8 mmol/litre (White and Hartzell 1989). Magnesium's critical function is in the maintenance of the sodium and potassium gradients of the cardiac cell membrane by the Na-K-ATPase enzyme system (Iseri and French 1984). Magnesium has important actions on re-polarising potassium currents and potassium conductance with several characterised by the property of inward rectification, that is, potassium flows inwards more readily than outwards. Intracellular magnesium is a blocker of cardiac potassium channels. Magnesium also acts as an effective physiological calcium blocker by influencing the regulation of transmembrane calcium inflow and calcium channel function (White and Hartzell 1988). In addition, it influences the slow trans-sarcolemmal calcium inflow via L-type calcium channels. It also appears to moderate intracellular sarcoplasmic reticular calcium handling. As a result, potassium ions have a close functional relationship to magnesium and a deficiency state of one ion is often associated with that of the other. Hypo-potassaemia can often only be corrected if magnesium is administered simultaneously with the potassium (Rude 1989).

The electro-physiological effects of variation in the body's magnesium levels is vital in understanding the potential effects in preventing or treating arrhythmias. Difficulty arises in interpreting data given the lack of correlation between serum levels and the predominant intracellular stores. Compounding this, are the effects of disease processes such as ischaemic myocardium, the influence of other drugs and electrolyte disturbances.

Doubling the serum concentration in humans slows conduction through the atrioventricular (AV) node, significantly prolongs sinoatrial conduction time and in

some studies, the AV nodal effective refractory period (Kulick, and others 1988). No effect on the His-Purkinje system or ventricular refractoriness has been identified. In addition, myocardial magnesium depletion enhances sinus automaticity whereas magnesium supplementation has a negative chronotropic effect (Iseri and French 1984).

The ECG changes of hypomagnesaemia (serum level < 0.7 mmols / l) are similar to the characteristics of a potassium deficiency state (ST segment depression, flattening of the T wave, QT/QTU prolongation). However, as these two deficiency states are often associated, it is not known whether these changes are caused by the magnesium deficiency alone (Iseri, and others 1991). It seems certain that magnesium deficiency enhances the excitability of the atrial and ventricular myocardium whereas it is decreased by therapeutically administering magnesium (Tzivoni and Keren 1990).

4.5 Autonomic and haemodynamic effects

An acutely stressful event such as a myocardial infarction will raise catecholamine levels. This in turn causes increased sympathetic tone and lipolysis resulting in high levels of free fatty acids which bind to magnesium ions resulting in magnesium deficiency (Riggs, and others 1992). When given as a supplementary agent, magnesium has been shown to inhibit catecholamine release from the adrenal medulla and to reduce the sensitivity of β adrenergic receptors to catecholamines. It has also been shown to reduce the likelihood of intravenous adrenaline precipitating arrhythmias (Mayer, and others 1984) and to reduce the size of catecholamine induced myocardial damage (Vormann, and others 1983; Vormann, and others 1983).

The haemodynamic effects of intravenous magnesium have been well described in healthy individuals, as well as hypertensive patients and those with ischaemic

heart disease (Mroczek, and others 1977; Rasmussen 1989). The results are summarised in table 4.1 below.

Table 4.1 Haemodynamic effects of intravenous magnesium in healthy individuals.

Parameter	Effect
Mean arterial pressure	Negative or slight
Systemic vascular resistance	Negative or slight
Cardiac index	Negative or slight
Pulmonary artery pressure	no effect
Pulmonary artery wedge pressure	no effect
Coronary vascular resistance	moderate reduction
Oxygen consumption	no effect

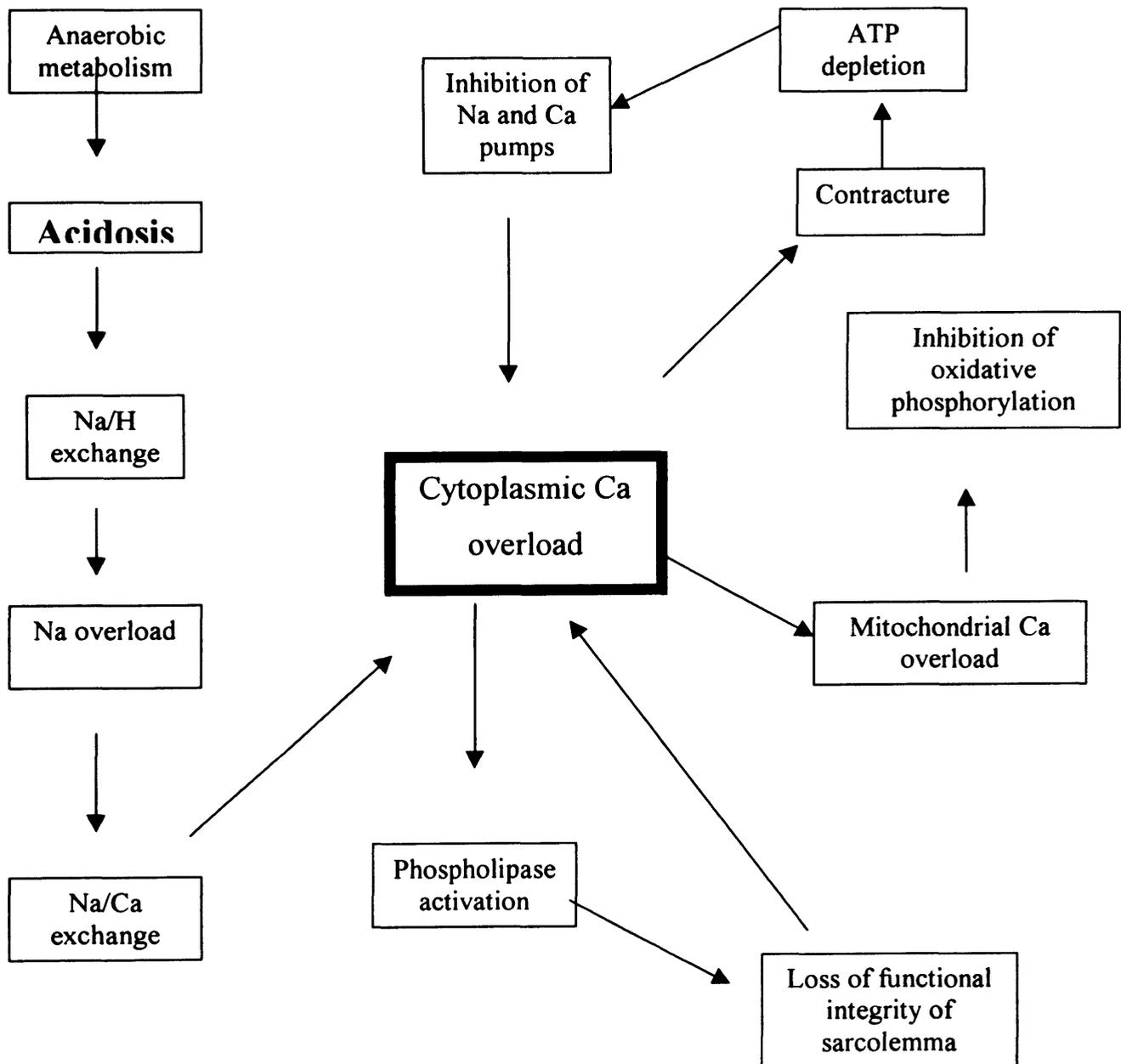
Doses ranging from 8-32 mmols magnesium sulphate over a period of 10-60 minutes will produce cutaneous flushing. This will result in a 50-100% rise in the serum magnesium level. Healthy volunteers will have either no change in arterial blood pressure or a transient fall with a small rise in the heart rate. Hypertensive patients are more likely to have a fall in blood pressure - approximately 10% in one study (Mroczek, and others 1977). Similar results are produced in patients with ischaemic heart disease (Rasmussen, and others 1988). The fall in the blood pressure is negated by the concomitant fall in systemic and pulmonary vascular resistance which result in a rise in the heart rate, cardiac index and stroke volume index. Cardiac contractility itself is little affected. There is some evidence to suggest that small doses may result in a positively inotropic effect (Rasmussen, and others 1988). This is partly due to an increase in cardiac index secondary to afterload reduction (Vigorito, and others 1991).

The underlying mechanism for these haemodynamic effects has been shown to be partly mediated by the effects of prostacyclin secretion (Nadler, and others 1987). There may also be a component related to the inhibition of production of endothelium derived-relaxing factor (EDRF) (Gold, and others 1990). In addition, magnesium competes with calcium to inhibit the contractility of coronary arteries (Altura and Altura 1987). In a clinical setting, patients undergoing rapid atrial pacing had an increased time to angina related to a reduction in coronary vascular resistance, an increase in coronary blood flow at rest and reduced myocardial lactate production (Bergman, and others 1981). These specific vasodilatory actions of magnesium support its use in coronary artery spasm and improving myocardial hypoxia.

4.6 Ischaemic myocardium and magnesium

In order to understand the interplay of magnesium on ischaemic myocardium and its potential benefits, it is worth first reviewing the cellular metabolic changes which occur (figure 4.1). The main factors are intracellular calcium overload and lactate production from anaerobic metabolism resulting in intracellular acidosis (Tani and Neely 1989). In addition, inhibition of the sodium and calcium pumps will increase intracellular concentrations of these cations and produce cell swelling. Thirdly is the depletion of ATP synthesis which occurs following inhibition of oxidative phosphorylation. Intracellular magnesium is mainly bound to ATP and as a result this produces significant cellular hypomagnesaemia. Reperfusion will also exacerbate calcium overload resulting in cell death. Oxygen free radicals and the activation of phospholipases will contribute to loss of sarcolemmal integrity (Woods 1993).

Figure 4.1 : The effects of intracellular calcium overload in ischaemic myocardium



A number of mechanisms have been suggested for magnesium's actions as a cytoprotective agent. These include inhibition of calcium influx across the sarcolemma (White and Hartzell 1988), a reduction of mitochondrial calcium overload and conservation of ATP as magnesium ATP.

There is good evidence that raising serum magnesium will protect ischaemic myocardium. In a perfused rat heart model the extent and speed of recovery of aortic flow (as an indication of myocardial function) were increased, 30 minutes after a 30 minute period of ischaemia at 37 degrees °C, as the magnesium content in the perfusate was increased (Hearse, and others 1978). In addition, reperfusion has been suggested as playing an important role in intracellular magnesium depletion. Increasing extracellular magnesium during reperfusion of the post ischaemic rat heart resulted in a protective effect (Borchgrevink, and others 1989). Assessment parameters included measurement of improvements of intracellular pH, increased coronary flow rates and recovery of pump function.

These in vitro studies have led to a number of clinical studies investigating magnesium's role in acute myocardial infarction. Several have suggested benefit in reducing serious arrhythmias and mortality in the early post infarction period. Meta-analyses of these studies (Horner 1992; Teo, and others 1991) have supported a significant mortality benefit, although two larger studies (LIMIT-2 and ISIS-4) were not included in the meta-analyses.

The LIMIT-2 study was specifically designed and powered to investigate magnesium's role in reducing mortality following myocardial infarction (Woods, and others 1992). The design required magnesium to be administered at the time of initiation of thrombolysis and hence produced a raised serum level of magnesium to be available at the time of reperfusion. The study recruited the required number of 2,000 patients and produced a 24 per cent relative reduction in 28 day mortality with a reduction in the incidence of left ventricular dysfunction

of 25 per cent. This was the largest study of its kind at the time and seemed to provide the first clear evidence of magnesium's beneficial role.

The results in the subsequent publication of ISIS-4 (ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group 1995) were therefore surprising. It showed that magnesium given in the first 24 hours produced no beneficial effect post thrombolysis for acute myocardial infarction. At 35 days follow-up there were 2,216 deaths amongst the 29,011 patients who received magnesium, compared with 2,103 deaths amongst the 29,039 patients who received standard treatments (7.64% -vs- 7.24% : odds ratio 1.06 [1.00 - 1.12] $p = 0.07$). This lack of benefit was seen across all major sub-groups.

The marked variance in the results of these studies has been subject of much debate (Antman 1995; Casscells 1994). A number of differences were noted in both the design and patient characteristics which could explain this variance. Firstly and probably the most critical factor was the timing of the magnesium infusion. In the LIMIT-2 trial, magnesium was administered at a median of three hours following the onset of chest pain. However, in ISIS-4 the design was such that randomisation occurred after thrombolysis had been completed, a mean of 8 hours following the onset of chest pain and in the 30 per cent who did not receive thrombolysis, median time from onset of chest pain was 12 hours. Animal evidence suggests that the effect of magnesium is greatest if given before spontaneous or induced reperfusion (du Toit and Opie 1992; Herzog, and others 1995). In addition, magnesium has anti-platelet effects. Anti-platelet agents are known to be important in accelerating and enhancing thrombolysis (Anderson and Willerson 1993). It may be that magnesium only has a beneficial effect when administered early with the bolus being given before thrombolysis. The dose of magnesium given was similar, although the bolus (8 mmols) was given over 15 minutes in ISIS-4 and over 5 minutes in LIMIT-2. Only 35% of patients in LIMIT-2 received thrombolysis and 69% received thrombolysis in ISIS-4. It may be that the benefit of magnesium is negligible post thrombolysis. In addition, only 66%

of patients in LIMIT-2 compared to 94% in ISIS-4 received aspirin. Magnesium is known to have anti-platelet actions. However, these may have been insignificant in the presence of aspirin at the doses of magnesium used.

The question of magnesium's exact role in the management of acute myocardial infarction remains open to question (Woods and Barnett 1995; Yusuf and Flather 1995). This issue may well be resolved by the large multi-centred study presently being carried out in the United States evaluating magnesium's role in acute myocardial infarction (The MAGIC study). Table 4.2 below summarises magnesium's potential beneficial effects.

Table 4.2 : Potential beneficial effects of magnesium in the setting of acute myocardial ischaemia

- **Cytoprotective agent**
Prevents intracellular depletion of
 Magnesium
 Potassium
 High energy phosphates
Prevents intracellular overload of
 Calcium
 Sodium

- **Vasodilator**
Decreases systemic vascular resistance

- **Increases coronary artery blood flow**
Reduces coronary artery spasm
Decreases coronary vascular resistance

- **Reduces catecholamine secretion**
Reduces damaging effects of catecholamines

- **Anti-platelet agent**
- **Anti-arrhythmic agent**

4.7 Magnesium's anti-arrhythmic properties.

Reports of parenteral magnesium being used to treat arrhythmias date back several decades (Boyd and Scherf 1943). Difficulty arises when attempting to ascertain if magnesium is acting as a primary anti-arrhythmic agent or merely being used to correct an underlying deficiency state. The best indication of a hypomagnesaemic state is by measuring the intracellular concentration but unfortunately this is not possible at present in a clinical setting. This section summarises the available experimental and clinical evidence of magnesium's role in deficiency states as well as situations where it has possible primary anti-arrhythmic activity.

4.7.1 Magnesium deficiency and arrhythmias

Evidence that magnesium deficiency is arrhythmogenic in man is largely limited to case reports (Bigg and Chia 1981; Dyckner and Wester 1982). Unspecified post operative arrhythmias were associated with lower myocardial magnesium concentration in the right atrial appendage of patients undergoing cardiac surgery (Reinhart 1991). Another study of 342 patients admitted with acute myocardial infarction reported that the incidence of ventricular tachycardia and fibrillation was significantly higher in hypo-magnesaemic patients (Dyckner and Wester 1982), although of the hypo-magnesaemic patients who had serious arrhythmias, 30 per cent also had a low serum potassium level.

Others have found no evidence of correlation between magnesium and ventricular arrhythmias. Ralston et al found that patients with heart failure showed no relationship between serum or tissue magnesium and serious ventricular arrhythmias (Ralston, and others 1980). In another study of 215 patients following acute myocardial infarction, no relation between serum or lymphocyte magnesium and tachyarrhythmias was found (Abraham, and others 1986). It seems, therefore, that if hypomagnesaemia causes ventricular

arrhythmias the risk is slight. An exception to this is the case of digoxin toxicity. Hypomagnesaemia is common in digitalised patients (Whang, and others 1985) and magnesium is shown to be very effective in arrhythmias due to digoxin toxicity (Cohen and Kitzes 1983; Iseri and French 1984).

4.7.2 Magnesium as an anti-arrhythmic agent

Arrhythmias occur predominantly as a result of re-entry or automaticity. However, a third mechanism is the presence of after-depolarisations leading to triggered activity. After-depolarisation occurring in the course of repolarisation are designated as early after-depolarisations (EADs). Those occurring after completion of the action potential during phase 4 are defined as delayed after-depolarisations (DADs). Studies have shown that EADs or DADs and the triggered rhythms induced by them are suppressible by magnesium (Cohen and Kitzes 1983; Keren and Tzivoni 1991). The tachycardias ascribed to these phenomena can be eliminated by injection of magnesium in the clinical situation. Clinical trials to assess magnesium's role as an anti-arrhythmic agent have concentrated on its ability to either suppress arrhythmias or as primary treatment for these arrhythmias.

4.7.3 Arrhythmia suppression

4.7.3.1 Arrhythmias in the setting of acute coronary syndromes

There have been a number of studies to investigate magnesium's role in suppressing atrial and ventricular arrhythmias following acute myocardial infarction (Roffe, and others 1994; Roffe, and others 1992). Metanalyses have suggested that magnesium has a beneficial role to play with a reduction in arrhythmias of 49% (Horner 1992; Teo, and others 1991). Unfortunately the studies included have varied markedly in their definition of ventricular arrhythmias, in the duration of monitoring post infusion (24 hours to 1 week) and the type of monitoring employed (ambulatory electrocardiography versus telemetry). Notably the single centre LIMIT-2 study did not show magnesium to have any suppressive anti-arrhythmic action (Woods, and others 1992). In contrast, in ISIS-4 (ISIS-4 (Fourth International Study of Infarct Survival) Collaborative Group 1995) magnesium reduced the incidence of ventricular fibrillation but had no effect on mortality.

4.7.3.2 Arrhythmias post cardiac surgery

The hypo-magnesaemic state of patients post coronary artery bypass surgery has been clearly demonstrated (Holden, and others 1972; Reinhart 1991). Although the serum magnesium did not correlate with the incidence of arrhythmias, right atrial appendage magnesium concentration was shown to be lower in patients with post operative arrhythmias (defined as supraventricular tachycardias, ventricular tachycardia or ventricular fibrillation).

Although there have been a number of randomised studies to investigate magnesium's role following cardiac surgery, these have usually been inadequately powered and produced conflicting results. Hecker et al randomised 76 patients to receive either magnesium sulphate (0.25 mEq/kg during bypass or 0.375 mEq/kg before bypass) or placebo. Magnesium was not shown to affect

spontaneous resumption of cardiac rhythm or produce spontaneous defibrillation (Hecker, and others 1985). In another study, the effect of magnesium on post operative atrial fibrillation was studied in 140 patients randomised to receive either magnesium sulphate (40 mmols/24 hours then 30 mmols/24 hours) or placebo (Parikka, and others 1993). No influence on the incidence of post operative atrial fibrillation was shown. In contrast in 200 patients randomised to receive either magnesium supplementation if serum magnesium was less than 2 mEq/l or monitoring alone, ventricular arrhythmias were less (17% -vs- 34% $p < 0.05$) in the magnesium group (Schweiger, and others 1989). In another well designed study, 100 patients randomised to receive either magnesium chloride (only 2 g intraoperatively) or placebo, the effect of the magnesium was to decrease ventricular arrhythmias and improved cardiac index in the early post operative period (England, and others 1992).

The exact benefit of magnesium supplementation in cardiac surgery remains unanswered although there is strong evidence to show it has a role to play. An adequately powered study with clear end points is required.

4.7.4 Primary antiarrhythmic activities

4.7.4.1 Supraventricular arrhythmias

Magnesium has well defined electrophysiological effects on the atrio-ventricular (AV) node and possible roles in treating supraventricular arrhythmias have been suggested by a number of clinical trials. The first case series in 1946 showed magnesium to successfully terminate SVT in 9 of 13 patients, although 4 developed a transitory AV block (Szekely 1946). Subsequent studies have also mainly been case series, investigating magnesium's role in a variety of supraventricular arrhythmias.

In 10 patients with SVT (4 AV re-entry tachycardias, 6 AV nodal re-entry tachycardias) magnesium terminated 7 of the 10 at a mean of 31 seconds after the infusion (Wesley, and others 1989). In another study of 11 patients with paroxysmal re-entrant SVT, magnesium was shown to increase the tachycardia cycle length by slowing the anterograde limb of the re-entrant circuit. Unfortunately, it was only rarely effective in terminating the tachycardia and did not suppress inducibility or influence the effective refractory period (ERP) of the right atrium, AV node, accessory pathway or the right ventricle (Sager, and others 1990).

Magnesium may modify retrograde conduction in some accessory pathways. Viskin et al showed that paroxysmal junctional tachycardia could be terminated in 5 of the 9 patients following 2 g (8 mmol) magnesium sulphate. Even though adenosine terminated the tachycardia in all of these patients, magnesium was more likely to block conduction in the accessory pathway than adenosine (Viskin, and others 1994).

In a larger randomised study of 57 patients with SVT, 15 (58%) receiving magnesium (5 + 5 mmols followed by 0.04 mmol/min) converted to sinus rhythm within 4 hours. Only 6 (19%) given verapamil (5 + 5 mg followed by 0.1 mg/min) converted within 4 hours ($p < 0.01$) (Gullestad, and others 1993). Iseri et al showed that in multi-focal atrial tachycardia, an arrhythmia associated with respiratory failure and refractory to conventional therapy, 7 of 8 patients converted to sinus rhythm or sinus tachycardia following a bolus of 16 mEq magnesium sulphate followed by 40 to 80 mEq over 5 hours (Iseri, and others 1985). Notably however, 5 of these patients had a serum potassium < 4 mEq/l. Hypokalaemia often accompanies occult hypomagnesaemia. Although magnesium slows conduction through the AV node, there are few reports of a reduction in the ventricular response to atrial fibrillation.

4.7.4.2 Suppression of arrhythmias in patients with heart failure

Evidence of magnesium's ability to suppress non-sustained ventricular ectopy in patients with heart failure is also limited to a number of case series. In 34 patients with heart failure or hypertension, treated with diuretics, potassium infusion had no effect on muscle potassium content or ventricular ectopy. However, magnesium infusion (30 mmols magnesium sulphate) resulted in both an increase in cellular potassium and suppression of ventricular ectopy (Dyckner 1979).

In a six week double-blind cross-over study of 18 patients with chronic heart failure receiving loop diuretics, oral magnesium chloride supplements significantly reduced all forms of ventricular ectopy (Bashir, and others 1991). Serum magnesium failed to rise (as was predicted) and serum potassium rose but did not reach statistical significance. Magnesium is a necessary activator of the Na-K-ATPase pump and these findings suggest that magnesium may have a role for regulating intracellular potassium.

4.7.4.3 Magnesium's role in treating ventricular tachycardia

A number of case reports and case series have identified a role for magnesium in treating ventricular tachycardia (Levine, and others 1982; Tzivoni, and others 1988). However, in many of these reports the patients were apparently hypokalaemic, hypomagnesaemic or both and in most instances the rhythm being treated was a specific type of polymorphic ventricular tachycardia (torsades de pointes). The evidence for a role in monomorphic ventricular tachycardia is less clear.

Torsades de Pointes is an uncommon polymorphic ventricular arrhythmia occurring in the setting of congenital or acquired QT prolongation. It is also a side effect of drugs known to prolong the QT interval, for example, Class I and III anti-

arrhythmic agents, tricyclic anti-depressants and phenothiazines. Magnesium deficiency has been associated with both QT prolongation and polymorphic ventricular tachycardia. Animal studies have shown that low magnesium causes prolongation of the action potential and QT interval in the presence of hypocalcaemia (Surawicz 1989). However, this has not been confirmed in the clinical setting. Nor is it clear that exogenous magnesium reduces the QT interval (Rogiers, and others 1989), although case reports have attributed the long QT syndrome and associated torsades de pointes to hypomagnesaemia (Ramee, and others 1985).

The inter-relationship of early and delayed after depolarisations (EADs and DADs) with arrhythmia generation have been previously described, particularly with the development of 'torsades'. In dogs given cesium to induce EADs, intravenous magnesium reduced QT interval prolongation, although not back to normal (Bailie, and others 1988). There are a small number of case series to support the use of magnesium in treating torsades. In one clinical study, 12 consecutive patients with polymorphic ventricular tachycardia in the setting of QT prolongation were treated with magnesium (Tzivoni, and others 1988). In 9 of these patients, 8 mmols magnesium sulphate abolished the arrhythmia within 1-5 minutes and in another 3 patients a second bolus was successful. Eight of these patients were hypokalaemic and 8 were receiving Type I anti-arrhythmic agents. In another series of 6 patients treated with an infusion of 50 mgs/minute magnesium sulphate, termination of the arrhythmia occurred within 30 minutes in all patients (Perticone, and others 1986). This effect was stated to be independent of the initiating cause and the serum magnesium. On this evidence alone, magnesium has become commonly used as the first line treatment for torsades de pointes.

Investigation in the clinical setting for magnesium's role in treating stable monomorphic ventricular tachycardia is equally scant. Five of 11 patients treated with 8 mmols magnesium sulphate given over 1 minute converted to sinus

rhythm. Two others responded after another 12 mmols and 2 did not respond (Allen, and others 1989).

4.7.5 Magnesium' role in cardiac arrest

Magnesium's possible role in treating ventricular arrhythmias (Ramee, and others 1985; Tzivoni, and others 1988), stimulated interest in its potential as an adjunct in the resuscitation of patients from cardiopulmonary arrest. In a study to investigate serum magnesium levels during cardiac arrest, 8 (36%) of 22 patients were noted to be hypermagnesaemic and 5 (23%) were hypomagnesaemic (Cannon, and others 1987). None of these patients survived to discharge. Four of the 9 patients with normal levels however did survive. Unfortunately, this data provides very little useful information, because intracellular magnesium, which is the important determinant in arrhythmia generation, correlates poorly with serum magnesium.

Two case reports suggested that empirical treatment with intravenous magnesium could convert patients in refractory VF to a stable rhythm and ultimate successful discharge from hospital (Craddock, and others 1991; Tobey, and others 1992). These reports were followed by a study in an animal model (Brown, and others 1993). This showed no improvement in outcome although aortic diastolic and coronary perfusion pressures were decreased with the addition of intravenous magnesium sulphate to standard ACLS protocols, the effects lasting for approximately 20 minutes. Unfortunately, the dose in this swine model, was 0.14 g/kg (equivalent to 10 g in a 75 kg man) - significantly greater than any of the doses given in humans.

The various actions of magnesium in dilating coronary arteries, suppressing automaticity and inhibiting calcium influx into myocytes has been well described and suggests that magnesium supplementation is cardio-protective. However, the exact mechanism by which it might have a beneficial effect in a cardiac arrest

situation remains to be elucidated. The American Heart Association(AHA) and Resuscitation Council (UK) Guidelines for Advanced Cardiac Life Support have both suggested magnesium supplementation for refractory ventricular fibrillation and tachycardia (Advanced Life Support Working Group of the European Resuscitation Council. 1998; Cummins, and others 1991). The guidelines were based on the various case reports and case series summarised previously.

Thus far, there have been three randomised studies to investigate the role of magnesium in cardiac arrest (Fatovich, and others 1997; Miller, and others 1995; Thel, and others 1997). They are summarised in table 4.3. Each one differed notably in terms of the patient population, entry criteria and the dose of magnesium used as the intervention drug. These differences make it impossible to perform any useful metanalysis. In addition, all three studies recruited patients with any cardiac arrest rhythm including asystole and electromechanical disassociation (EMD), as well as ventricular fibrillation or pulseless ventricular tachycardia. These inclusion criteria differ from the guidelines for magnesium usage as recommended by the AHA and Resuscitation Council (UK). Patients with asystole and EMD as their initial rhythm are far less likely to survive, especially in the pre-hospital environment. Nor is there any plausible hypothesis for giving the drug in such situations.

Another important limitation to at least two of the studies included the trial drug being given late in the resuscitation procedure (Fatovich, and others 1997; Miller, and others 1995). No difference in eventual outcome was attained in either study. In the most recent trial, although the study drug was given early in the resuscitation attempt, no difference in return of spontaneous circulation (ROSC) or outcome to discharge from hospital was shown (Thel, and others 1997). However, in that study, 35% of patients were recruited from the Intensive Care Unit. In addition, a significant proportion had malignant disorders as their primary diagnosis and overall 55% were later assigned do-not-resuscitate status. Although magnesium was shown to have no beneficial effect on the ROSC or

discharge from hospital there was a surprising and significant ($p = 0.04$) improvement in the neurological status of the survivors who had received magnesium as opposed to the placebo. In all, eleven patients (69%) receiving magnesium as opposed to 6 (35%) receiving placebo were at home and self caring at discharge.

SPECIAL NOTE

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Table 4.3 : Randomised studies to investigate the role of intravenous magnesium sulphate in adult patients suffering a CA.

	Miller et al – 1995	Fatovich et al –1997	Thel et al - 1997
Setting and Population	In hospital (on CCU and Medical Wards only)	In hospital (pre-hospital cardiac arrest patients, but the study drug given only in the Emergency department	In hospital (Intensive Care and Medical wards only)
Number of Patients	62	77	156
Inclusion criteria	Any rhythm associated with cardiopulmonary collapse	Any rhythm associated with cardiopulmonary collapse	Any rhythm associated with cardio pulmonary collapse
Number of Patients with Pulseless VT	6	26	78
Randomisation	Open label randomisation	Double-blind placebo controlled	Double-blind placebo controlled
Dose of drug used	5g IV bolus followed by second 5g IV bolus after 5 minutes if necessary	5g IV bolus	2 g IV bolus and 8g (32 mmol) over 24 hours if successful
Time from collapse to being given study drug	Unknown (Protocol stated only to be given after at least 5 minutes duration of ACLS- did not specify at what stage)	Unknown (Collapse to arrival in the Emergency department was a mean of 33 minutes (range 5-64 minutes). Study drug was the first therapeutic intervention	A mean of 11 minutes (range 8-16 minutes)
Outcome - Return of spontaneous circulation (magnesium -vs- placebo)	10 (35%) -vs- 7 (21%) (p = 0.21)	7 (23%) -vs- 8 (22%)	41 (54%) -vs- 48 (60%) (p = 0.44)
Discharge alive from hospital (magnesium -vs- placebo)	1 (5.2%) -vs- 1 (4.5%)	1 (2.2%) -vs- 0	16 (21%) -vs- 17 (21%) (p = 0.98)

4.8 Magnesium's possible cerebral protective effect

The potential cerebro-protective effect of magnesium has been attributed to the role magnesium might play in regulating cerebral vascular tone (White, and others 1983). Calcium channel antagonists (including magnesium) may also abort the increased concentration of intraneuronal calcium after CA, hence preventing resultant neurological deterioration. Another potential mechanism is the magnesium ion blocking the ion channel of the N-methyl-D-aspartate (NMDA) receptor causing a non competitive NMDA blockade (Harrison and Simmonds 1985). The NMDA blocking properties may be the mechanism by which it works as an anticonvulsant in preeclampsia (Sibai 1990).

In the clinical setting, magnesium's potential for cerebral protection has been investigated in patients with middle cerebral artery stroke (Muir and Lees 1995). A non-significant decrease in the number of early deaths in the magnesium treated group was identified ($p = 0.06$). At three months 30% of the magnesium treated group and 40% of the placebo group had died, this was also not significant ($p = 0.42$).

In an observational case series, a trend towards improved neurological status in patients treated with calcium channel blockers or magnesium after out of hospital cardiac arrest was identified (Schwartz 1985). Six of 18 patients who received a calcium channel antagonist or magnesium after successful resuscitation had complete neurological recovery, compared with none of the 11 patients in the control group.

4.9 Summary

In summary, magnesium is an important therapeutic agent in cardiovascular medicine. Studies have confirmed its critical role at a cellular level in the electrophysiology of the myocardium. It probably has a significant part to play in improving the outcome of patients who have suffered an acute myocardial infarction. There is also some evidence to suggest that it has a role to play as an anti-arrhythmic agent in certain circumstances. A robust study design is required to elucidate its possible role as an anti-arrhythmic agent for the treatment of VF in pre-hospital CA.

Chapter 5

Characteristics and outcomes of patients suffering pre-hospital cardiac arrest within the Leicestershire EMS system.

5.1 Abstract

Study objectives: This study was designed to provide a detailed descriptive account of the incidence, processes of care and outcomes for adults suffering a pre-hospital CA in a defined EMS system.

Methods: An observational cohort study of adult patients suffering pre-hospital CA between 1st January 1995 and 31st March 1998 in the Leicestershire Ambulance and Paramedic Service. Data was collected prospectively onto a dedicated database in order to conform to the Utstein template for uniform reporting. It was analysed using univariate and multivariate techniques. The main outcome measure was survival to hospital discharge.

Results : During the study period, 1024 eligible patients were treated and entered onto the database. Of these, 83 (8.1%) had suffered a CA in the presence of the EMS and were analysed separately. Survival rates were greatest in those patients who suffered a CA in the presence of the EMS, with overall survival to discharge being 13.2% versus 4.3% if the arrest occurred prior to their arrival. In those patients who had suffered a witnessed VF arrest prior to the arrival of the EMS, the discharge rate from hospital alive was 10.2%. Logistic regression modelling controlled for potential confounding variables and considered five co-variates that were most likely to contribute to survival. The only factor which was clearly associated with better survival was the presence of a witness at the time of the collapse (OR 4.10, C.I. 1.71,9.82). Younger age (<60 years) (OR 1.52, C.I. 0.84, 2.73), CPR initiated by bystanders (OR 1.46, C.I. 0.81, 2.62) and a response time <8 minutes (OR 1.44, C.I. 0.76, 2.73) all had a trend towards statistical significance. There was no association between the type of crew attending the patient and ultimate survival in this model (OR 0.91, C.I. 0.47,1.75).

Conclusion : This study has defined the characteristics and outcome statistics of pre-hospital CA in a system with a predominant single tiered ALS response. The results confirm that outcome is poor and provide a robust baseline for future strategies.

5.2 Introduction.

Studies from EMS systems world-wide show that the outcome of patients suffering a pre-hospital CA remains poor in most communities (Eisenberg, and others 1990). In 1993, the Department of Health recommended that by 1995 every frontline ambulance in England and Wales should be staffed with at least one paramedic and have a defibrillator on board (Department of health 1993). Evidence at that time, suggested that ALS skills (Eisenberg, and others 1990) and especially defibrillation, had a major part to play in improving the outcome of adults suffering a pre-hospital CA. In Scotland, implementation of the programme differed with ambulance technicians initially being taught to use automated external defibrillators(AEDs) (Sedgwick, and others 1993). Subsequently, paramedic training was also started and led to the availability of pre-hospital ALS skills for all emergency calls in the UK by 1996.

A number of EMS systems in the UK have reported on their experiences of managing pre-hospital CA and the impact of introducing of paramedics (Guly, and others 1995; Rainer, and others 1997; Mann and Guly 1997). Thus far, all have shown that outcomes are no different for patients being managed by paramedics as opposed to technicians with AEDs (EMT-Ds). However, despite relatively similar response times, incidence of bystander CPR, access to defibrillation and other ALS skills, the results have varied considerably between systems, with outcome to discharge from hospital ranging from 5-11%. The reasons for these variations are unclear although conformity to uniform reporting of data has been cited (Valenzuela, and others 1992; Eisenberg and Cummins 1999).

The objective of this study is to describe the incidence, processes of care and resulting outcomes for adults suffering a pre-hospital CA in a defined EMS system between 1995 and 1998. The study also acts as a demographic baseline for this thesis.

5.3 Methods

Study design

This was a prospective, observational study of the basic demographics, processes of care and outcomes for adult patients suffering a pre-hospital CA in the county of Leicestershire. The study period was from January 1st 1995 to March 31st 1998. The data collection form and dedicated cardiac arrest database had been designed and validated in a previous study (Hassan, and others 1996). It adhered to the Utstein data set (Cummins, and others 1991). The study was carried out with the permission of the Leicestershire Ethics Committee.

The EMS system

The Leicestershire Ambulance and Paramedic Service (LAPS) was a single self governing emergency ambulance service during the time of the study period. From the beginning of 1995, a minimum standard in the LAPS system was for all crews to be able to operate AEDs. In some circumstances, ambulances were manned by EMTs alone. During 1995, the system achieved the government target for training and recruitment of an adequate number of paramedic personnel to allow a single tiered ALS response to all emergency calls. Paramedic training adhered to the standards set by the National Health Service Training Authority (Ambulance Staff Training Committee 1987). These skills included intravenous cannulation, tracheal intubation and administration of intravenous drugs used in ALS. Manual defibrillators were provided for paramedic ALS ambulances.

In 1997 the LAPS introduced a system of prioritised dispatch for all emergency calls (NHS Executive Steering Group 1996). In addition, there was an increase in the number of personnel and unit hours during the study period. These changes and their impact are described in chapter 6. Additional support for the LAPS in rural areas was provided by general practitioners (GPs) with equipment including

defibrillators. However, in most cases these GPs responded predominantly to patients suffering serious injury and not primarily to cardiac emergencies.

Study population

Case definitions followed the Utstein style guidelines for reporting of cardiac arrest data (Cummins, and others 1991). All adult patients (age > 16 years) suffering a CA and attended by the LAPS were considered for inclusion in the study. Patients with obvious non-cardiac causes such as drug overdose, trauma or drowning were excluded from further analysis. Cardiac arrests occurring in the presence of the EMS were included in the initial analysis but sub-classified according to the Utstein guidelines.

Setting

The county of Leicestershire has a population of approximately 930,000 and covers an area of 2,550km². The Leicester Royal Infirmary NHS Trust is an 1100 bed university teaching hospital with the only 24 hour A&E facility in the county which accepted emergency calls. Fifty five patients were identified by the database to have been treated by the LAPS at the edges of the county and were transported to one of seven other hospitals outside the county boundaries. These were not followed up or included in the study.

Outcome measures and data.

The primary outcome variable for the study was survival which was defined as discharge from hospital alive. This was verified by reviewing the in-hospital patient notes. In cases where the in-hospital notes were missing, the patient's GP was contacted. Secondary end points included a return of spontaneous circulation (ROSC), admission to hospital and admission to a high dependency area or ward from the A&E department. General outcome and neurological function were assessed using the Glasgow-Pittsburgh cerebral performance categories (Cummins, and others 1991).

Study data were collected from the ambulance report forms (ARFs), notes in the A&E department, a dedicated cardiac arrest data form and in-hospital notes. The initial rhythm was taken from data recorded on the ARFs. It was checked against event rhythm strips where they were available. Operational times for dispatch and response were retrieved from manual input of data onto the ARFs for most of the study period. However, from April 1997 this process became automated from a central command and control system.

Data analysis

The demographic, clinical and EMS response characteristics of patients who survived to discharge from hospital were compared with those of non-survivors by means of the χ^2 and Student's t Test where appropriate. Significant predictors of survival to hospital discharge were determined using multivariate stepwise logistic regression analyses. Variables considered included : the age group of the patient (younger or older than 60 years of age), whether the CA was witnessed, whether bystander CPR occurred, a response time (greater or less than 8 minutes) and the type of personnel who attended. All data was analysed using SPSS for Windows 7.0.

The initial rhythm of VF was not included because of its clear association with several other predictors of the model. This approach is similar to that of others (Cummins, and others 1985; Wilcox-Gok 1991). VF is regarded as a 'path' variable – occurring along the causal pathway to survival and regarded as a dependent rather than independent variable in a logistic regression model. The other variables in the model which were predictive of survival to varying degrees are modifiable whereas initial rhythm is not.

5.4 Results

Table 5.1 describes the characteristics of the 1024 adult patients who suffered a pre-hospital CA between January 1st 1995 and March 31st 1998. The results are sub-classified into patients who died in the community or A&E, those who developed a stable ROSC but died in hospital and finally those who were ultimately discharged from hospital alive. The age of the overall study population ranged from 16 to 101 years.

The overall proportion of witnessed arrests were 63.1%, with a significantly greater proportion of ultimate survivors having suffered a witnessed arrest (86.8% of survivors versus 60% in those who did not achieve a stable ROSC, $p = 0.0001$). Bystander CPR ($p = 0.006$) and the location of the arrest ($p = 0.012$) were also significant factors influencing survival. 43.4% of the survivors received some form of bystander CPR versus 33.5% who did not achieve a stable ROSC. Fourteen of the 53 (26.4%) survivors suffered an arrest in the ambulance or at least in the presence of the EMS.

Survivors to discharge from hospital were almost exclusively those who had developed ventricular fibrillation as their initial rhythm as shown in table 5.2 ($p = 0.012$). Survival rates were greatest in those patients who suffered a CA in the presence of the EMS, with 14 of the 83 patients (13.2%) being discharged alive. This compared to 39 survivors out of a total of 941 (4.3%) if the arrest occurred prior to the arrival of the EMS. However, in patients who had suffered a witnessed VF arrest prior to the arrival of the EMS, the discharge rate from hospital alive was 10.2%.

Table 5.3 describes the influence of the response time (time from receipt of the call to arrival at the scene) and the type of response on eventual outcome. A response time of less than 8 minutes was more commonly found in ultimate survivors although this did not reach statistical significance ($p = 0.17$). The type

of response, a paramedic led unit versus an EMT crew, was not associated with increased survival ($p = 0.32$), although there were a greater proportion of survivors to ITU in the paramedic led group (11.4% versus 8.2%). Only 14.3% of patients were documented as being treated by an EMT crew during the study period. Most of these were in 1995 and the early part of 1996 prior to full implementation of Government policy.

Table 5.4 describes the use of individual ALS skills in those patients who suffered CA prior to the arrival of the EMS. At least 21 of the 39 survivors (54%) responded to between 1 and 3 defibrillatory attempts. In those patients who were defibrillated more than 3 times, the ultimate mortality was almost 95%. In terms of airway interventions, 27 of the 39 survivors (69%) required oxygenation using a bag-valve–mask technique alone. Twelve out of the 39 survivors (31%) had successful endotracheal intubation performed. These results are unsurprising as most ultimate survivors are those that respond to rapid defibrillation and do not require advanced airway manoeuvres such as intubation. It is not possible with this study design to identify if endotracheal intubation was associated with a successful outcome in patients who did not respond to rapid defibrillation. Anti-arrhythmic drug therapy was recorded as being used in only a small proportion of patients in the study. Only 7 of 40 patients (17.5%) given lignocaine ultimately survived to discharge from hospital.

During the study period, out of 941 patients who had suffered a pre-hospital CA prior to the arrival of the EMS, 117 (12.7%) were admitted to hospital with a stable ROSC (table 5.5). Survivors spent a median of 2 days on the ITU or CCU and 11 days in hospital. This was similar for the 83 patients who suffered a CA in the presence of the EMS, 14 of whom were ultimately discharged from hospital.

The odds ratios of those factors likely to be independently associated with survival are shown in table 5.6. The logistic regression analysis controlled for potential confounding variables and considered five co-variates that were most

likely to contribute to survival. The only factor which was clearly associated with better survival was the presence of a witness at the time of the collapse. Younger age (less than 60 years), CPR initiated by bystanders, and a response time less than 8 minutes did not reach statistical significance. There was no association between the type of crew attending the patient and ultimate survival in this model.

5.5 Discussion.

Principal findings

This study reports on the largest prospective series of patients suffering pre-hospital CA in a single EMS system from the UK. The data has confirmed that a witnessed CA was four times more likely to be associated with survival. The majority of events occurred at home with only a small proportion taking place in a public building or the work place. Other factors including an age less than 60 at the time of the CA, presence of bystander CPR and a response time of less than 8 minutes were not clearly associated with survival in the multivariate analysis. There was no association at all between the grade of the crew attending the patient and an ultimately successful outcome. The overall discharge rate from hospital alive for patients who suffered a CA prior to the arrival of the EMS was 4.3%. More than twice as many patients were discharged if their initial rhythm was VF and the CA was witnessed (10.2%). Patients were three times more likely to survive (13.2%) if the arrest occurred in the presence of the EMS. They were also less likely to be discharged with neurological impairment.

Relevance to other studies.

This study has defined the characteristics and outcome statistics of pre-hospital CA in a system with a predominant single tiered ALS response. The results confirm that the outcome is poor with only 4.3% of patients who suffered CA prior to the arrival of the EMS being discharged alive.

How do these figures compare to those of other systems in the world?

Unfortunately, despite the development of the Utstein criteria for uniform reporting of outcome following pre-hospital CA, results vary markedly (Eisenberg, and others 1990; Herlitz, and others 1999; Cummins, and others 1991). The EMS systems in Seattle and King County in the US are widely regarded as amongst the most sophisticated and mature in the world. They have the highest

reported survival world-wide with rates varying from 17% to 34% for all pre-hospital CA and witnessed VF arrest respectively (Weaver, and others 1986; Weaver, and others 1988; Eisenberg, and others 1984). The systems employed a tiered structure of EMT-Ds and paramedics. Response times for the first tier (EMTs) were 3-4 minutes with paramedics responding in 7-9 minutes.

Elsewhere in the United States outcomes have been disappointing, especially in large cities. In New York, a two tier BLS-D and ALS system obtained an overall survival to discharge of 1.4% (Lombardi, and others 1994). Thirty-two percent of victims received bystander CPR and the median response time in the system was 9.9 minutes. In Chicago, a one-tier ALS system obtained an overall survival of 1.8% (Becker, and others 1993) with a median response interval of 6 minutes and 21% incidence of bystander CPR.

On mainland Europe, a comparison of 5 EMS systems predominantly from Scandinavia reported that 15-23% of patients suffering pre-hospital CA were discharged from hospital alive (Herlitz, and others 1999). Most of these systems had at least two or three tiered responses with a combination of EMTs, paramedics and even doctors in some cases. However, the authors suggested that variations in terminology and small sample sizes might have compromised the accuracy of their results.

In the UK the largest series of published data on pre-hospital CA has come from the Scottish Ambulance Service covering a population of over 5 million people in the whole of Scotland (Sedgwick, and others 1993). In the EMT-D Heartstart Scotland campaign, 10% of patients survived to discharge from hospital. The median response time from receipt of call to arrival at scene was reported as being 7 minutes in this study. The authors admitted however that there was likely to have been under reporting of CA which would have affected the survival calculations.

The largest and most robust study of pre-hospital CA to date has been the work of the Ontario study group in Canada (Stiell, and others 1998). However, their results are markedly different to those reported above, although study populations are similar. Phase I of the OPALS study recruited 5,335 patients from 21 communities over a 3 year period, in a system where ambulance crews were only equipped with AEDs and had no ALS skills (Stiell, and others 1999). Overall survival was 3.9%. It was 8.8% in patients where the initial rhythm was VF/VT. The mean interval from call received to arrival at scene in this system was 6.7 minutes with 76% of patients being reached within 8 minutes. In the phase II study, optimization of the defibrillation programme occurred with the deployment of AEDs to fire crews as well as a number of other interventions (Stiell, and others 1999). Response time was improved, with 92% of patients being reached within 8 minutes. Overall survival increased to 5.2%. A phase III study is presently on-going and aims to quantify the additional benefits of ALS skills in certain groups of critically ill patients such as those suffering CA (Stiell, and others 1998). The results of the OPALS phase I study are similar to those achieved by the Leicestershire EMS even though the structure of the two systems is notably different.

Strengths and limitations

This study has a number of strengths which support its generalisability to other similar sized systems in the UK. The study was based upon a large sample size within a well defined semi-rural EMS system. The study was well designed, targetting and solving deficiencies in data collection which had been identified in a previous pilot project in the same system (Hassan, and others 1996). Data collection was prospective and rigorously controlled. Pre-hospital and in-patient data were collected on standardised record keeping systems.

A number of limitations also merit discussion. The data on response time intervals and pre-hospital interventions were reliant on recording made by the EMS personnel. An automated system for recording the response times and

scene times did not come into operation until the beginning of 1997. It was not possible however to record the time from arrival at scene to the time of the first defibrillatory shock in any of the cases. The importance of accurate time recording in EMS care has been highlighted (Cordell, and others 1994). New technology is improving this deficiency in pre-hospital care research (Spaite, and others 1995). Similarly, recognition and recording of the initial rhythm was reliant upon the pre-hospital care personnel. The quality assurance of recognising and correctly treating rhythms of patients in CA was reliant upon the training and re-certification carried out by the LAPS during the study period (Ambulance Staff Training Committee 1987).

The question of what influence paramedic care might have played in improving the outcome of pre-hospital CA was not an objective of this study. The study design would not have allowed robust conclusions on this question to be drawn. It would not have been possible to distinguish clearly between the impact of other ALS skills apart from defibrillation on outcome. However, in the multi-variate analysis, no association between improved survival and the type of pre-hospital personnel attending the patient was found. These results are in keeping with other UK studies, although they also suffered from similar limitations in terms of study design (Guly, and others 1995; Mann and Guly 1997). The incremental benefit of ALS skills for pre-hospital CA will probably be best quantified by the OPALS phase III study which has been specifically designed to answer this question (Stiell, and others 1998).

Finally, despite rigorous efforts to maintain good data quality, there was a certain amount of missing data, which varied between 8-15% depending upon the parameter being measured. The breakdown in the results shows that this missing data did not significantly influence analysis of outcome.

Implications of the study results

Using a robust study design, this study has described the characteristics and survival rates for pre-hospital CA in a UK system. The data are consistent with that of other well designed studies such as the OPALS group (Stiell, and others 1999). Survival rates are extremely poor.

The study has also acted as a baseline for future strategies and research into a number of areas related to pre-hospital CA in Leicestershire. Further improvements in BLS training for the public are necessary. The impact of these programmes can be better assessed using this data as a baseline. Minimising the time to defibrillation in the future may occur through the use of AEDs by non-EMS personnel in certain locations. Information has been provided for possible strategies to locate these AEDs in the community, although unfortunately most events occur at home. The most important task therefore, is to identify those strategies that will provide the most cost effective improvement in EMS response times. This will minimise the time from collapse to delivery of the first defibrillatory shock.

Tables and figures

Table 5.1 : Characteristics of the overall study population suffering a pre-hospital CA.

	All groups of patients	Patients certified dead at scene or in A&E	Patients who survived to ITU/CCU or ward only	Survived to discharge from hospital alive	P value
Number of patients, n (%)	1024	838 (81.8)	133(13)	53(5.2)	
Mean (SD) age in years	65.4 (19.1)	65.6 (19.6)	65.6 (17.1)	62.1 (15.2)	0.43
Male sex (%)	711 (69.4)	585 (70)	87 (65.9)	39 (73.6)	0.51
Recorded witnessed arrests¹ n (%)	646 (63.1)	503 (60)	97 (72.9)	46 (86.8)	0.0001
Recorded bystander CPR², n (%)	361 (35.2)	281(33.5)	53 (39.8)	23 (43.4)	0.006
Location of CPA					0.012
Home	559 (54.6)	465 (83.1)	71 (12.7)	23 (4.1)	
In ambulance or EMS presence	83 (8.1)	56 (71.7)	13 (15.9)	14 (13.2)	
Public place e.g. street	112 (10.9)	95 (84.8)	12 (10.7)	5 (4.5)	
Public building	99 (9.6)	88 (88.9)	9 (10.0)	2 (2.0)	
Work	42 (4.1)	37 (88.1)	3 (7.1)	2 (4.7)	
GP	10 (1.0)	9 (1.1)	0	1 (10)	
Community hospital	11 (1.1)	6 (54.6)	4 (36.4)	1 (9)	
Other/not recorded	108 (10.5)	85 (78.7)	18 (16.7)	5 (5.9)	

¹Unrecorded data : n = 179

²Unrecorded data : n = 170

Table 5.2 : Initial rhythms of patients suffering pre-hospital CA.

	All groups of patients	Patients certified dead at scene or in A&E	Patients who survived to ITU/CCU or ward only	Survived to discharge from hospital alive	P value
Recorded initial rhythm in patients who collapsed prior to arrival of the EMS : n (%)	941	785 (83)	117 (12.7)	39 (4.3)	0.012
Ventricular fibrillation or tachycardia (VF/VT)	383 (40.7)	300 (78.3)	47 (12.3)	36 (9.4)	
Pulseless electrical activity	131 (13.9)	105 (80.2)	26 (19.8)	0	
Asystole	300 (31.9)	276 (92)	24 (8)	0	
Respiratory arrest	22 (2.4)	16 (72.7)	5 (22.7)	1 (4.6)	
Not recorded	105 (11.1)	88 (83.8)	15 (14.3)	2 (1.9)	
Recorded initial rhythm in patients who collapsed in the presence of the EMS : n (%)	83	56 (71.7)	13 (15.9)	14 (13.2)	0.001
Ventricular fibrillation or tachycardia (VF/VT)	29 (34.9)	13 (44.8)	4 (13.7)	12 (41.4)	
Pulseless electrical activity	24 (28.9)	21 (87.5)	3 (12.5)	0	
Asystole	16 (19.3)	13 (81.3)	3 (18.7)	0	
Respiratory arrest	7 (8.4)	5 (71.4)	2 (28.6)	0	
Not recorded	7 (8.4)	4 (57.1)	1 (14.3)	2 (28.4)	

Table 5.3: LAPS response to patients in CA, excluding those who collapsed in the presence of the EMS.

	All groups of patients	Patients certified dead at scene or in A&E	Patients who survived to ITU/CCU or ward only	Survived to discharge from hospital alive	P value
Number of patients : n	941	785	117	39	
Recorded time intervals : n (%)	883	739	105	39	
Response time ≤ 8 minutes (%)	590 (66.8)	492 (65.6)	68 (64.8)	30 (76.9)	0.17
Mean response time in minutes (Standard deviation, SD)	7.6 (4.4)	7.6 (4.4)	7.7 (4.6)	6.6 (3.5)	
Median response time in minutes (Inter quartile range, IQR)	7 (6)	7 (6)	7 (5)	6(6)	
Median total pre-hospital time in minutes (IQR)	51.2 (26.2)	51.7 (27.9)	49.4 (17.8)	49 (17.4)	
Type of response.					0.32
Paramedic response alone	632 (67.1)	530 (83.8)	72 (11.4)	30 (4.8)	
EMT response alone	135 (14.3)	118 (87.4)	11 (8.2)	6 (4.4)	
Dual EMS response	81 (8.6)	70 (86.4)	9 (11.1)	2 (2.5)	
Type of response unknown	93 (9.8)	77 (82.8)	15 (16.1)	1 (1.1)	

Table 5.4 : Use of ALS skills by pre-hospital personnel, excluding those who collapsed in the presence of the EMS.

	All groups of patients	Patients certified dead at scene or in A&E	Patients who survived to ITU/CCU or ward only	Survived to discharge from hospital alive	P value
Number of patients : n	941	785	117	39	
Response to defibrillation.					0.001
Number of defibrillatory attempts:					
0-3	221 (23.4)	165 (74.7)	35 (15.9)	21 (9.5)	
4-6	105 (11.2)	86 (81.9)	14 (13.3)	5 (4.8)	
7-9	59 (6.3)	52 (88.1)	6 (10.2)	1 (1.7)	
10-12	40 (4.3)	32 (80.0)	5 (12.5)	3 (7.5)	
>12	28 (3.0)	25 (89.3)	2 (7.1)	1 (3.6)	
None or not recorded	465 (51.9)	402 (86.5)	53 (11.9)	8 (1.6)	
Advanced airway interventions					0.001
Intubation performed (%)	544 (57.8)	459 (84.4)	73 (13.4)	12 (2.2)	
Bag –valve –mask technique only	374 (39.7)	303 (81.1)	44 (11.8)	27 (7.2)	
None or not recorded	23 (2.5)	23 (100)	0	0	
Use of anti-arrhythmic drugs given during resuscitation.					
Lignocaine given	40 (8.9)	25 (62.5)	8 (17.5)	7 (17.5)	
None or not recorded	901 (95.7)	760 (84.4)	109 (12.1)	32 (3.6)	

Table 5.5 : Impact and outcomes of patients successfully resuscitated to a stable ROSC and admitted to hospital.

	Patients who collapsed prior to arrival of the EMS (n = 941)	Patients who collapsed in the presence of the EMS (n = 83)
Number of patients achieving a stable ROSC and admitted to ITU/CCU or ward (%of total group)	117 (12.7)	27 (29.3)
Total number of patients discharged alive from hospital (% of total group)	39 (4.3)	14 (13.2)
Number of patients discharged from hospital neurologically intact – GOS 1. (% of survivors in the group)	28 (71.8)	12 (85.7)
Number of patients discharged from hospital with neurological impairment – GOS >1. (% of survivors in the group)	11 (28.2)	2 (14.3)
Median number of days spent on the ITU/CCU for all admitted patients (IQR, range)	1 (0-2.5, 0-12)	2 (1-4.75, 0-12)
Median number of days spent on ITU/CCU for survivors to discharge (IQR, range)	2 (2-4, 1-12)	2 (1-4, 1-10)
Median number of days spent on ward for survivors to discharge from hospital (IQR, range)	11 (8-17, 5-187)	9 (6-16, 5-30)

Table 5.6 : Results of logistic regression and analysis of factors associated with survival in patients who collapsed prior to the arrival of the EMS.

	Estimate(β)	p	Odds Ratio	95% CI
Intercept	-4.45			
Age <60 years	0.418	0.16	1.52	0.84, 2.73
Witnessed CA	1.411	0.001	4.10	1.71, 9.82
Bystander CPR	0.379	0.20	1.46	0.81, 2.62
Response time <8 mins	0.364	0.26	1.44	0.76, 2.73
Grade of crew	-0.098	0.77	0.91	0.47, 1.75

Chapter 6

A cost effectiveness analysis of single paramedic 'fast responder' units and Criteria Based Dispatch on the outcome of pre-hospital cardiac arrest?

6.1 Abstract

Objective : To evaluate the resource implications of a tiered advanced life support (ALS) response and criteria based dispatch (CBD) system on the short term outcome of pre-hospital cardiac arrest (CA).

Design : A cost effectiveness analysis based upon a 'before and after' Emergency Medical Services (EMS) model design. The costings included both pre-hospital and in-hospital costs but did not take into account costs associated with rehabilitation or subsequent long term care.

Setting : An EMS system serving a population of 930,000 with an Accident & Emergency (A&E) facility based geographically in the centre of the system.

Subjects and intervention: All adults (age >16) suffering non- traumatic pre-hospital CA in 1995 (prior to the interventions – model I) and 1997 (after the introduction of single first responder units and a CBD system – model II) were eligible for inclusion to the study.

Main outcome measure : Cost effectiveness based upon survival to discharge from hospital.

Results : 278 patients suffered a pre-hospital CA in 1995 of which 51 were resuscitated to a stable return of spontaneous circulation (ROSC) and there were 15 survivors to discharge from hospital. This compared with 326 patients in 1997 treated in the system with 56 patients having a stable ROSC and 13 survivors to discharge from hospital. Proportionately however, there was no difference in the number of patients with a stable ROSC on the Intensive Care Unit (ICU) between the two models (model I 18.3% versus model II 17.1%, $p=0.78$). There was also no significant difference in the number discharged from hospital alive (model I 5.4% versus model II 4.0%, $p=0.41$). The estimated additional costs associated with model II resulted in a predicted increase of £34,091 per life year gained (LYG) if call volume was taken into account and calculations were made for costs attributable to CA alone.

Conclusion : Prioritised response (CBD) and introduction of tiered ALS care had no significant impact on the number of lives saved from pre-hospital CA. Significantly increased NHS costs were incurred per life year gained.

6.2 Introduction

Significant change in the organisation and sophistication of pre-hospital care has occurred over the past 10 years (Audit Commission 1998). The government's strategy to deliver a single tiered ALS response for all emergency calls has been carried out (Department of health 1993). A number of studies have suggested that the outcome following a CA is no different if a paramedic with ALS skills attends as opposed to a technician crew with an AED (Guly, and others 1995; Rainer, and others 1997; Mann and Guly 1997). The validity of these conclusions has been questioned because of study design. In addition, the response time or 'defibrillation response interval' (DRI) in all of these systems has been poor. The DRI has been further compromised by the increasing demand for emergency services (Department of Health 1999).

In order to improve on poor response times for time critical illness, priority dispatch systems (PDS) have been introduced into UK practice (NHS Executive Steering Group 1996). Other recommendations included the introduction of single paramedic 'fast responders'. These have been particularly successful in some systems (Glucksman 1995).

At present, there are no data to show what impact the introduction of PDS and changes such as single 'fast responders' have had on patients with immediately life threatening (category A) conditions (Nicholl, and others 1996). The greatest benefit should be in those suffering a CA. It was suggested that these additional changes would help to attain new long term performance standards for category A calls of an 8 minute response in 90% of cases (NHS Executive Steering Group 1996). It is estimated that this might lead to the saving of an extra 3200 lives in England and Wales alone and would be an extremely cost effective intervention as compared to other healthcare strategies in the NHS (NHS Executive Steering Group 1996). Although the use of outcome from pre-hospital CA has been recognised as a robust model for assessing the cost effectiveness of EMS

systems (Maio, and others 1999), the Steering Group relied heavily on a number of key assumptions and predictions. They strongly recommended that validation occur within individual systems.

This study is the first in the UK to compare the cost effectiveness of two models of EMS system design. It has used real outcome data of patients suffering pre-hospital CA as a primary measure of effectiveness.

The primary objective was to assess the impact of changes in EMS structure on response times and on the eventual outcome in patients suffering CA. Secondly, a model based upon national recommendations (NHS Executive Steering Group 1996) to meet the long term target of a 90% fractile of 8 minute response for category A patients was developed (model III). This was tested for its potential cost effectiveness.

6.3 Methods.

6.3.1 Study design.

The study was primarily a prospective, single group observational study over two time periods. In addition, the economic evaluation was a cross sectional , cost effectiveness analysis comparing two actual and one hypothetical model of pre-hospital care design using pre-hospital CA as a measure of outcome.

6.3.2 Setting.

The Leicestershire Ambulance and Paramedic Service (LAPS) provide pre-hospital care to approximately 900,000 people in the county of Leicestershire. Critically ill patients are predominantly taken to the Accident and Emergency (A&E) department at the Leicester Royal Infirmary, a 1,100-bedded university teaching hospital. A small number of patients are transferred to other hospitals outside the county. These were not included in the analysis.

6.3.3 Subjects

All adult patients with confirmed CA, treated by the LAPS and delivered to the LRI were eligible for entry into the study. Exclusion criteria consisted of age less than 16 years, and mechanism of cardiac arrest being related to trauma, hanging or drowning. The two study periods were January 1st 1995 to December 31st 1995 and April 1st 1997 to March 31st 1998.

6.3.4 Interventions.

Model I : In 1995 the LAPS was approaching the government target of having a single tiered ALS pre-hospital system with a paramedic and technician on every frontline ambulance (Department of health 1993). There were however still a number of technician only units with at least 2 ALS units for every technician only unit. The 45 ambulance units dealt with all emergency calls and urgent calls from GPs and provided 2560 unit hours of cover per week (one unit hour was defined as an ambulance unit being on duty for one hour).

Criteria Based Despatch (CBD) was not in place at this time. All emergency calls were responded to on a 'first come first served' basis. However, 'ad hoc' priority triage was carried out by the staff in the Dispatch centre.

Model II : By the beginning of 1997 the system had been reconfigured with the addition of two other types (tiers) of response unit in addition to the 45 ambulance units. These consisted of 5 single paramedic 'first responder' units (FRU-P) in cars (Ford Mondeos), which did not have a transport capability and 7 Delta Units (DU). The DUs were ambulances manned by crew with basic training only who dealt with and transported GP urgent calls requiring basic first aid skills only to hospital. They did not have AEDs on board. The system provided a total of 2742 unit hours of cover per week .

The safety of priority dispatch systems in the UK was evaluated and reported on in 1996 (Nicholl, and others 1996). CBD was one of the two systems successfully evaluated and was introduced into the LAPS system in April 1997. It was due to be run in 'shadow' form for the first 6 months for quality assurance purposes. However, it was effectively operational from April due to the significant increase in demand for emergency services.

Model III:

This hypothetical model predicted the number of additional units required to achieve a 90% response for category A calls. It used the analysis and modelling of data by Operational Research in Health (ORH), an independent company commissioned by the Department of Health (DoH). The Chief Executive of the LAPS was also involved in this exercise (NHS Executive Steering Group 1996). The results were derived from modelling of an urban and rural system as well as a survey of 11 systems carried out by the ORH. The modelling concentrated

predominantly on the number of additional single paramedic responder units that would need to be added to model II to achieve the performance standard.

As a pilot for this expansion, another tier of response was added to the LAPS in April 1998 which worked predominantly in the urban community within the city of Leicester. This tier consisted of 8 Central Response Units manned often by single paramedics (CRU-P) using Renault Megane 'people carriers'. These vehicles could be used to transport certain Category B (urgent but not immediately life threatening) or C patients (non urgent) to hospital without having to resort to the more expensive response of a fully manned ambulance unit. They provided an average of an extra 192 unit hours/week.

The modelling revealed that in addition to the above, an extra 60 staff were required. This would allow 2 extra two man ambulance units on the road 24hrs/day (15 paramedics and 15 technicians) providing an extra 336 unit hours/week. The other staff (30 paramedics) would be used to staff 5 single paramedic 'first responder' units with a transport capability (Meganes), between 0800-0200 for each day of the week. This would provide an extra 630 unit hours /week. (personal communication : Mr Terry Porter, Chief Executive LAPS). This would increase the cover to a total of 3900 unit hours per week.

6.3.5 Key assumptions.

In order to identify and reflect costs for the hypothetical model III as well as compare model I with model II more accurately, a number of key assumptions have been made. The number of pre-hospital CAs have been standardised to the number in model II. In addition, the proportion of patients admitted to the ICU/CCU have been hypothesised to be 17.5%, the average of the two previous models.

The response time for model III has been predicted by a method used previously in a meta-analysis of pre-hospital CA and is derived from a convenience sample of North American EMS systems. It takes into account the increase in call volume (Nichol, and others 1996a). Response times for models I and II were also predicted (table 6.7) to compare with the actual mean response times (table 6.4).

Mean expected response time (minutes)

= 0.00039 (area) + 0.00019(annual call volume) – 0.00002(unit hours per year).

(Area of Leicestershire EMS = 2550km²)

A similar model using the same meta-analytical data has been used to predict the expected survival rates for all three models in a one tier system with the expected improvement in response times and incidence of bystander CPR (Nichol, and others 1996a). With an overall incidence of 25% bystander CPR and a mean response time interval of 5.7 minutes, they produced a fitted survival of 5.2%. A one minute decrease in the mean response time interval was associated with an absolute increase in survival of 0.4% in a one tier system. It was assumed that a one minute increase would be associated with a similar 0.4% decrease in survival. In addition, they modelled for survival based upon the incidence of bystander CPR at 25%. A 5% increment of this parameter was associated with an absolute increase in survival of 0.1%.

The number of life years gained (LYG) for each model have been calculated on an assumption of the sample size for model II with survivors' ages being distributed in the same proportions as the age distribution observed in the pooled 1995 and 1997 data. These proportions have been applied to life expectancy tables for patients with pre-existing coronary heart disease (CHD) in a similar fashion to the only other UK economic evaluation which used CA as a model (NHS Executive Steering Group 1996).

Cost effectiveness ratios (CERs) have been calculated using two costing strategies (table 6.5). In the first, all EMS costs were included, similar to the methodology applied previously (NHS Executive Steering Group 1996). The second technique used actual data to reflect more accurately the time spent by the EMS in managing patients with pre-hospital CA.

6.3.6 Data analysis

Data on pre-hospital interventions by LAPS, in-hospital care and outcome was prospectively entered onto a database. The data points were checked and validated (TBH).

Medians and inter-quartile ranges were calculated for all non-parametric data. A χ^2 test was used to analyse all dichotomous or categorical data. Cost effectiveness analyses were carried out to examine the incremental improvements in costs and outcome of moving from model I to model II.

6.3.7 Outcome measures.

The primary outcome measure chosen for this study was the number of LYG for patients discharged from hospital alive following CA. The LYG were calculated from age specific life expectancy tables for patients with coronary heart disease (CHD). A cost effectiveness ratio (CER) was calculated for each model by dividing the incremental costs in each model by the number of LYG. Other measures were: 1) The number of patients admitted to the ICU with a stable return of spontaneous circulation (ROSC). 2) The neurological status of the survivors at discharge from hospital which was extracted from information in the hospital notes.

The patient's general practitioner was contacted if the notes were not located. Neurological and overall status at discharge from hospital alive was measured using the Glasgow Pittsburgh scores for cerebral and overall performance (Cummins, and others 1991).

6.4 Results

6.4.1 Cost determination.

The evaluation was conducted from the viewpoint of the NHS. It included direct costs to the NHS in the pre-hospital and in-hospital settings only. The sources for the pre-hospital costings was the LAPS itself. In-hospital costs were derived predominantly from unit costs quoted by the Finance Department at the Leicester Royal Infirmary NHS Trust. Further costs of care and follow-up of the survivors in the community (in particular rehabilitation and long term care) were not determined in this analysis. System components were costed for the 1997 fiscal year. Operational costs were not depreciated but initial cost of any equipment were over the anticipated life span of the equipment, incorporating a 6% discount rate and assuming zero resale value.

Pre-hospital costs were separated into service costs, personnel training and re-certification costs for each of the three models (see table 6.1). A top-down methodology was employed to calculate the total pre-hospital costs of an EMS system for each model. Staff costs were taken as the mid point of the pay ranges with NHS superannuation and National Insurance contributions added.

The cost per unit hour was calculated using the total costs per year divided by the total number of unit hours provided by each model per year (table 6.1). Fixed costs for the Dispatch centre and ambulance stations were generic to all models and were therefore excluded. None of the models had additional cost implications for any of these elements.

6.4.2 Cost model for pre-hospital cardiac arrest.

Existing data on models of estimating the costs attributable to pre-hospital CA are imprecise. This makes resulting comparisons with the potential benefits - that is, number of lives saved, also very approximate (NHS Executive Steering Group 1996). Cost effectiveness analyses in this field have tended to estimate

the overall costings of an individual system and related these to the number of lives saved or life years gained.

Similarly, the cost per ambulance response is too crude an estimate for a pre-hospital CA. Such a call may occupy a single and or two person unit in prolonged resuscitation and significantly exceed the 56 minutes that a typical call takes before the unit is available again (Audit Commission 1998). If one uses this model to measure the effectiveness of a system it is important not only to calculate the costs involved in achieving a certain level of response within that system, but also the time and costs that are attributable to managing this particular emergency. Therefore, in addition to the overall top down system costs per unit hour a formula was developed to gain a more accurate estimate of the costs incurred by the EMS in treating patients with CA in each model.

The cost per minute of EMS (CPM-EMS) time was calculated from the overall annual costing of the EMS system (table 6.2). The average turnaround time of a unit after arrival at the A&E department to being available again was not available from the database. It was therefore estimated from a sample of 100 pre-hospital CA events where information was available from LAPS. It was found to be 29 minutes. This figure was added to the average time that the unit was active and gave a total CA (TCA) time for each unit.

The total pre-hospital costs attributable to CA was therefore calculated by (CPM-EMS x TCA). From the database it was estimated that a second unit was called in 5% of calls in both models I and II. This was included in the calculation.

6.4.3 In-hospital component costs.

The in-hospital costs were divided into A&E costs, ICU costs and ward costs (table 6.3). The costs for the ICU and ward were daily average unit costs defined by the Leicester Royal Infirmary NHS Trust Finance Department. These were calculated for each patient who survived to hospital admission in models I and II.

A sensitivity analysis was carried out for model III. The A&E costs were estimated by taking the annual costs of resuscitation drugs, equipment including defibrillators and nursing staff costs. This latter cost was calculated by estimating the number of nurses, the average length of time they were involved in a resuscitation attempt for pre-hospital CA and their seniority to derive the number of whole time equivalents involved during each of the study periods. Notably, estimates for the costs of medical staff were not included in the A&E calculation as they were also not available from the daily unit costs provided by the Finance department.

6.4.4 Patient outcomes

Using the model I configuration, a total of 278 patients were recruited into the study between January 1995 and December 1995. Between April 1997 and March 1998, 326 patients were enrolled under model II, incorporating CBD and the paramedic 'fast responders' as the intervention strategy. No significant differences were identified in the basic demographics of the two study populations apart from age (table 6.4).

There were also no significant differences in the response times ($p = 0.46$) and interventions performed by the pre-hospital personnel in the two models (table 6.5) or the proportion of cases in which a dual response was triggered. There was however a notable increase of 16% in the number of emergency calls dealt with by the LAPS over the two time periods. This compared to the 7.1% increase in unit hours as a result of the changed EMS configuration.

The outcome of the patients surviving to achieve a stable ROSC and those discharged from hospital alive were no different between the groups (table 6.6). Fifteen patients were discharged alive in 1995 and 13 in 1997. Both study groups spent similar amounts of time on the ICU or CCU occupying a total of 112 days in 1995 and 134 days in 1997. The data for time spent on the general wards was

skewed by three individuals. In 1995 one patient stayed 91 days contributing to a total time spent by all patients of 346 days whereas two patients in 1997/8 each stayed a total of 58 and 188 days respectively in the total of 499 days. All three had suffered significant cerebral injury at the time of their CA.

At discharge from hospital, review of the hospital notes or contact with the patient's general practitioner revealed that the overall neurological status of the survivors was good. Ten of the 15 patients in 1995 achieved level 1 out of 5 on the Cerebral Performance Category score (Cummins, and others 1991). This compared with 10 of 13 who achieved level 1 in 1997/8. This result was not statistically significant ($p = 0.41$).

In the modelling of outcome data, the number and percentage of actual survivors to discharge approximated to the predicted calculations for models I and II (table 6.7). Using the same formula, a small incremental rise in the number of survivors was predicted for model III on the assumption that this model would meet the 90% fractile of 8 minutes for category A calls.

6.4.5 Cost effectiveness analysis.

Table 6.8 describes the cost effectiveness of each model using a cost strategy of either including all EMS costs or only those attributable to pre-hospital CA. The predicted CER for model II using these costing strategies is £34,091 to £199,624. However, the model III predictions suggest that if a relatively modest rise in the number of LYG could be achieved, a more cost effective strategy could be produced.

6.4.6 Sensitivity analysis.

The main area of uncertainty for the results related to the hypothetical model III. A simplified sensitivity analysis was carried out for this model. Outcome and the

number of life years gained were varied by 10%. In addition, a 10% variation in the costs per case of pre-hospital and in-hospital care was also included. The resulting incremental CER for model III using the methodology of costs attributable to CA varied from £1,184 to £6,187. This was still considered to be favourable and robust as compared to the results in model II.

6.5 Discussion.

Principal findings.

The study has quantified the cost effectiveness of pre-hospital CA within a well defined EMS system. It has shown that there was no significant improvement in the number of lives saved and potential LYG between model I in 1995 and model II in 1997/8 following the introduction of CBD and addition of 5 paramedic 'fast responder' units. On the basis of this analysis, these changes were not cost effective interventions if pre-hospital CA alone was used as the evaluation model.

In the theoretical model III, the number of extra single paramedic 'fast responders' to achieve the 90% fractile 8 minute response time was calculated from the ORH modelling and the available LAPS data. The results suggest that although the number of extra LYG would be comparatively small, the strategy could be relatively cost effective. However, this would depend upon the costing methodology employed. For example, if costs were calculated for the cardiac arrest model alone, a potential CER of £1,575 would be very cost effective as compared to other strategies (NHS Executive Steering Group 1996). The inclusion of all EMS costs on the otherhand, would make the CER of £63,031 per LYG seem relatively expensive. In this case, using CA alone for assessing impact would also seem unrealistic and the value of other interventions would need to be considered.

Evidence to support further reconfiguration.

There is strong evidence that for patients in VF, minimising the time from receipt of a call to the time of the first defibrillatory shock will increase the number of lives saved (Eisenberg, and others 1990). The 90% fractile 8 minute response time is held as an achievable gold standard for EMS systems. However, the potential number of survivors may well plateau much earlier at 5 or 6 minutes from collapse to defibrillation (De Maio, and others 1999). Various strategies have therefore been employed in order to try and improve response time performance.

A meta-analysis of systems world-wide has suggested that multi-tiered systems produced better outcome for patients suffering CA (Nichol, and others 1996a). Some systems have used other emergency services such as the police with AEDs to act as first responders and achieved success (Mosesso, and others 1998). In North America, fire fighters are often used to provide a dual response and have achieved good outcomes using AEDs (Braun, and others 1990). Public access defibrillation may also be of some benefit although its cost effectiveness has yet to be evaluated (Becker and et al 1998).

Implications for current practice.

In the UK, it was hoped that the introduction of PDS and paramedic 'fast responders' would improve response times and hence improve outcome for immediately life threatening conditions (NHS Executive Steering Group 1996). In this study, no improvement occurred after instituting these interventions. However, it is likely that substantial extra resources as well as innovative approaches of service delivery will be required to optimise the system to meet the long term 90% fractile 8 minute performance standard.

Attempting to improve response times by increasing the number of single paramedic 'fast responders' alone may not be the most cost effective strategy. When the same technique of costing was employed as was used by the NHS Steering Group, the CERs were markedly different with £63,000 per LYG in this study as opposed to £700-£2,200 (NHS Executive Steering Group 1996). There are a number of reasons for this. Many more assumptions were made both for the costing as well as the likely beneficial outcome in the analysis by the Steering Group. The main difference was the assumption of a rate discharge alive from hospital for patients suffering pre-hospital CA of 11% if the system response was improved to the 90% 8 minute standard. This was probably an over optimistic estimate of improvement. For example, in the OPALS Phase II study, a 33% improvement from 3.9% to 5.2% ($p = 0.03$) discharge alive occurred when firefighters were taught to use AEDs (Stiell, and others 1999). This reflected an additional 21 lives saved each year. It was estimated that it had cost \$46,900 per life saved in establishing the rapid defibrillation programme.

Notably, when a more accurate costing methodology was applied as outlined in the methodology of this study, the CER of £1,575 per LYG for model III seems much more attractive to healthcare policymakers (Department of health 1994). In practice, this only saves an extra 2-3 lives per year in a system caring for almost a million people.

It is likely that the results in this study are probably generalisable to many other EMS systems in the UK. The county of Leicestershire serves a significant urban and rural population with an average incidence of coronary artery disease. In order to radically improve response times for those time critical conditions such as VF, the challenges will be similar for many other systems. A significant increase in the number of paramedic 'fast responders' might be viewed as an expensive strategy but could have a positive effect on other critically ill and injured patients. Alternatively, 'first responder' schemes involving the police or fire services integrated into an EMS system might be an alternative. A number of

UK systems already provide some form of integrated response with the fire service and police, although these tend to be rural communities (Porter and Allison 1998). Evidence suggests that this could be an alternative or additional cost effective strategy. A decision analysis model comparing a standard North American EMS with a police or lay person public access defibrillation (PAD) programme found that the strategy could still be deemed cost efficient (Nichol, and others 1998). Nichol and colleagues estimated that a standard EMS had a median cost of \$5900 per CA patient and yielded a median of 0.25 quality adjusted life years. PAD by the lay responders had a median incremental cost of \$44,000 per additional quality adjusted life year, whereas for the police this was \$27,200. They recommended that the effectiveness and cost effectiveness of PAD could only be properly assessed in a randomised controlled trial.

Limitations.

There are six main areas of uncertainty to be taken into account in this study. Firstly, the 16% increase in emergency calls between the two time periods is likely to have contributed to the failure to improve the response time. This was especially relevant as the unit hours in model II were only increased by 7% with the advent of the single paramedic 'fast responders'. Overall in the UK, the number of emergency journeys carried out by EMS systems increased for 7 successive years up to 1997-98. Notably, they were approximately 50% higher in 1997-98 as compared to 1987-88 without the same proportionate increase in unit hours (Department of health 1999).

However, the calculation used to predict the response time of model III (Nichol, and others 1996a) allowed similar models to be fitted for I and II. Parameter estimates taken into account included the additional unit hours, the call volume and the geographical area of the EMS. The predicted response times were found to be comparable to the actual mean response times for these first two models. This suggests that the predicted response time for model III is likely to be a robust estimate.

With respect to the processes, the CBD was officially being operated in 'shadow' form for the first six months in model II. However, due to the marked increase in demand, the LAPS received permission from the Leicestershire Health Authority to use CBD and prioritise calls from the beginning of the study period in April 1997. Unfortunately, the system was not fully implemented due to government policy. All serious and non life-threatening (category B and C) conditions were treated as emergencies (NHS Executive Steering Group 1996). It has been suggested that this should change, with category C patients having separate performance standards in order for further improvement in the response time of category A patients to occur (Audit Commission 1998). The true effect of CBD may not therefore have been established in this study. Other methods such as system status management (Stout 1983) can be used to produce more efficient management of manpower resources and further reduce response times (Ryan 1994). These components were also not in place in the Leicestershire system at the time of study but could produce additional efficiencies in the future, some at minimal cost.

The hypothetical model III assumed only certain response configurations such as single paramedic 'fast responders' or paramedic led ambulance units, as recommended by the Operational Research in Health (ORH) modelling (NHS Executive Steering Group 1996). This relied upon data from urban and rural systems but may not have been entirely applicable to the Leicestershire system. In practice, the LAPS began to implement a programme of 8 single paramedic 'fast responder' units in 1998. However, these units also had a transport capability for certain category B and C patients using Renault Megane 'people carriers'. This strategy provided the additional benefit of only costing half the price of a fully manned ambulance. Although these additional benefits and associated costs were not considered in the original model as proposed by the ORH, they have been taken into account in this study.

The costing exercise for both the pre-hospital and in-hospital components had a number of limitations. In the pre-hospital phase, unit costs were broken down predominantly by a top-down methodology. Although this was not as precise as a bottom-up approach, it was the most feasible strategy for this study. In addition, a calculation to define the costs attributable to CA was developed. This was a more accurate measure of the impact of CA on the EMS as compared to the cost effectiveness exercise carried out by the NHS Executive Steering Group which used overall incremental system costs (NHS Executive Steering Group 1996). The in-hospital costs were calculated from average time spent in the A&E department and number of days spent on high dependency areas such as the ICU and CCU as well as the actual number of days spent on the wards. This type of costing of in-hospital care has limitations in terms of quantifying the exact contributions of various personnel. In particular, costing of medical time in the A&E department was not possible. However, this approach is more accurate and relevant to CA as compared to other evaluations to date (NHS Executive Steering Group 1996; Valenzuela, and others 1990; Nichol, and others 1996b). In addition, the study design did not take into account the ongoing costs of rehabilitation in the community, particularly for those patients who were discharged with neurological compromise.

Missing data may have contributed to some patients not being entered into the study, either because those at the edges of the county were taken to hospitals outside Leicestershire or ambulance report forms were missing. This was minimised by the prospective design strategy and applied predominantly to patients who were certified dead by general practitioners prior to arrival in hospital. Patients admitted to hospital were invariably tracked to well defined end points. The overall pre-hospital costs for treating CA were not significant as compared to the in-hospital treatment costs and therefore unlikely to affect the overall economic evaluation.

Finally, the measurable benefits in this study are specific to patients suffering a pre-hospital CA within the existing system (with a 65-70% eight minute response time). The impact of the system in managing other critically ill and injured patients has not been evaluated.

Conclusions.

This study has shown that prioritised response (CBD) and introduction of 5 single paramedic 'fast responder' units had no significant impact on the number of lives saved from pre-hospital CA in Leicestershire. Increased NHS costs were incurred per life year gained.

Substantial additional resources would be required to improve the response time performance using a single tiered all - ALS strategy. The number of lives saved and life years gained might only be increased by a small amount, but may be viewed as being relatively cost effective. Other less expensive but effective strategies also need to be considered.

Table and figures

Table 6.1 : Annual EMS system service and training costs.

Resource and structure	Costs		
	Model I	Model II	Model III
EMS system service costs	£	£	£
Pre-hospital personnel staff costs	3,607,038	3,668,280	4,880,712
Emergency vehicles	324,730	385,574	427,230
Operating costs of vehicles	342,000	412,700	455,900
Emergency drugs	21,500	24,500	25,625
Consumables	30,500	35,500	36,570
Defibrillators	29,989	29,989	36,825
Command and control staff costs	410,000	442,000	442,000
Training and implementation of CBD		641	641
Chapter 1 EMS personnel training and recertification costs			
Paramedics	31,705	36,554	53,339
Technicians	19,400	13,600	16,600
Basic crew	-	-	-
Total cost	4,816,862	5,041,338	6,365,248
Incremental costs		224,476	1,548,386
Total unit hours per year	133,120	142,584	202,800
Incremental unit hours per year	-	9,464	69,680
Cost per unit hour (£)	36	35	31

Table 6.2 : Annual EMS costs attributable to pre-hospital CA

	Model I	Model II	Model III
Total pre-hospital costs	£ 4,816,862	£5,041,338	£6,365,248
Pre-hospital costs / unit minute	£ 0.60	£0.59	£0.52
Minutes of response for CA	2,289	2,859	2,340
Minutes of transport and turnaround	20,173	26,263	27,229
Total	22,462	29,122	29,569
Pre-hospital costs attributable to CA/ yr	£ 15,800	£17,038	£14,898

Table 6.3 : In-hospital costs attributable to pre-hospital CA

Costings	Model I	Model II	Model III
A&E costs	£ 13,875	£14,985	£ 14,379
ITU/CCU costs	£ 87,360	£ 112,560	£ 117,275
Ward costs	£ 46,686	£ 69,192	£72,710
Total in-hospital costs attributable to pre-hospital CA/yr.	£ 285,305	£ 330,043	£366,167

Table 6.4: Characteristics of the study population.

	Model I (n = 278)	Model II (n = 326)	p value
Mean age (95% C.I.)	68.3 (66.1-70.4)	65.8 (63.6-67.6)	0.01
Male sex (%)	197 (70.9)	234 (71.8)	0.80
Recorded lay bystander CPR (%) (n = 222 (I) and 297 (II))	83 (37)	105 (35)	0.34
Recorded witnessed arrest (%) n = 241 (I) and 292 (II)	155 (64)	205 (69)	0.49
Recorded initial rhythm (%) : n = 269 (I) and 311 (II)			0.17
VF	132 (49.1)	126 (40.5)	
Pulseless electrical activity	30 (11.3)	48 (15.4)	
Asystole	107 (39.6)	137 (44.1)	

Table 6.5: EMS system response for models I and II.

	Model I	Model II	P value
Recorded time intervals	n = 271	n = 317	
Response time ≤ 8 minutes (%)	195 (72.0)	206 (65.2)	0.46
Mean response time in minutes (SD)	7.21 (4.81)	7.84 (4.27)	
Median response time in minutes (IQR)	7.0 (5.0)	6.0 (5.0)	
Median total pre-hospital time in minutes (IQR)	44.0 (26)	53 (31)	0.93
Dual EMS response	14 (5.2)	10(4.9)	
Defibrillation performed (%). n = 265 (I) and 313 (II)	153 (57.7)	168 (53.7)	0.39
Intubation performed (%) n = 262 (I) and 306 (II)	185 (70.6)	225 (73.5)	0.47

Table 6.6 : Survival of patients during the study phases.

	Model I n = 278	Model II n = 326	p value
Number of patients achieving a stable ROSC and admitted to ITU/CCU or ward (%)	51 (18.3)	56 (17.1)	0.78
Mean number of days spent on the ITU/CCU for all admitted patients (95% C.I.)	2.2 (1.7 – 2.7)	2.4 (1.7 – 3.1)	0.24
Number of patients discharged alive from hospital (%)	15 (5.4)	13 (4.0)	0.41
Mean number of days spent on ITU/CCU for survivors to discharge (95% C.I.)	3.5 (2.5-4.6)	4.6 (1.8 – 7.5)	0.20
Mean number of days spent on ward for survivors to discharge from hospital (95% C.I.)	18.5 (7.1–30.0)	27.8 (5.3-58)	0.33

Table 6.7 : Predicted and actual outcome data for models I, II and III.

	Model I	Model II	Model III
Predicted mean response time (mins)	8.21	8.02	6.82
% bystander CPR	37	35	35(assumed)
% survival to discharge –predicted.	4.44	4.47	4.95
% survival to discharge – actual	5.3	3.9	
Number of survivors -predicted	14.4	14.6	16.1
Number of survivors - actual	15	13	

Table 6.8 : Cost effectiveness of each model using a costing strategy of either including all EMS costs or only those attributable to pre-hospital CA for predicted survival.

	Model 1	Model 2	Model 3
Total EMS costs (£)	4,816,862	5,041,338	6,365,248
EMS costs attributable to CA alone	15800	17038	14,898
Total in- hospital costs	285305	330043	366167
EMS and in-hospital costs attributable to CA alone	301105	347081	381065
Total EMS costs and in-hospital costs	5,102,167	5,371,381	6,731,415
Total incremental costs attributable to CA		45976	33984
Total incremental costs inclusive of total EMS costs		269,214	1,360,034
Total life years saved or gained (LYG) – predicted	199.6	200.9	222.5
Incremental benefits (LYG)		1.3	21.6
Cost Effectiveness Ratio (CER) for incremental costs attributable to CA (£/LYG)		34,091	1,575
CER inclusive of total EMS costs (£/LYG)		199,624	63,031

Chapter 7

A randomised controlled trial to investigate the efficacy of intravenous magnesium sulphate for refractory ventricular fibrillation.

7.1 Abstract.

Background: Ventricular fibrillation (VF) remains the commonest and most salvageable rhythm in patients suffering a cardio-pulmonary arrest (CA). However, outcome remains poor if there is no response to initial defibrillation. Some evidence suggests that intravenous magnesium may prove to be an effective anti-arrhythmic agent in such circumstances.

Study hypothesis: Intravenous magnesium sulphate given early in the resuscitation phase for patients in refractory VF (VF after 3 DC shocks) or recurring VF will significantly improve their outcome, defined as a return of spontaneous circulation (ROSC) and discharge from hospital alive.

Design: A randomised, double blind, placebo controlled trial. Pre-defined primary and secondary endpoints were ROSC at the scene or A&E and discharge from hospital alive respectively.

Setting, participants and intervention: Patients in CA with refractory or recurrent VF treated in the pre-hospital phase by the county EMS and/or in the A&E department of the LRI. One hundred and five patients with refractory VF were recruited over a 15 month period and randomised to receive either 2-4 grammes of magnesium sulphate or placebo intravenously.

Results: Fifty two patients received magnesium treatment and 53 received placebo. The two groups were matched for most parameters including age, sex, response time for arrival at scene and airway interventions. There were no significant differences between magnesium and placebo for ROSC at the scene or A&E (17% vs 13%) χ^2 test, $p= 0.56$, and alive to discharge from hospital (4% vs 2%) χ^2 test, $p= 0.55$. After adjustment for potential confounding variables (age, witnessed arrest, bystander CPR and system response time), the odds ratio (95% confidence intervals) for ROSC in patients treated with magnesium as compared with placebo was 1.69 (0.54, 5.30).

Conclusion: Intravenous magnesium given early in patients suffering CA with refractory or recurrent VF did not significantly improve the proportion with a ROSC or who were discharged from hospital alive.

7.2 Introduction.

VF is the most salvageable rhythm in patients suffering a pre-hospital CA (Larsen, and others 1993). Early defibrillation is the best treatment, but its success is dependent upon whether the arrest was witnessed, if bystander CPR took place prior to defibrillation and most importantly, the time from collapse to applying the first shock (Cummins, and others 1991).

There is conflicting evidence about the role of ALS measures other than defibrillation (Pepe, and others 1994). Debate surrounds the additional benefit in terms of outcome in patients who do not respond to the first cycle of three defibrillatory shocks (Herlitz, and others 1997). Anti-arrhythmic agents such as lignocaine and bretylium are recommended for use at this late stage in the resuscitation algorithm although no convincing evidence exists that they are efficacious in treating VF (Stiell, and others 1995). These agents have significant negative inotropic actions as well as some pro-rhythmic effects and this potentially negates any benefit gained from their anti-arrhythmic role. A novel therapeutic approach in the management of refractory or recurrent VF is therefore required.

Magnesium has been shown to act favourably against a number of ventricular arrhythmias including intractable tachycardia and fibrillation as well as a variety of supraventricular arrhythmias (Iseri, and others 1989). It has also been proven to be a simple and safe agent with minimal side effects in a large cohort of patients suffering acute myocardial infarction in whom it is thought to minimise reperfusion injury (Woods, and others 1992). It does not cause negative inotropism as compared to other anti-arrhythmic agents. In addition, its ability to suppress automaticity and inhibit calcium flux into myocytes may be cardioprotective (Woods 1991).

Magnesium's role as a primary anti-arrhythmic agent remains poorly studied. A

number of case reports have suggested a beneficial outcome in treating patients with prolonged refractory VF (Craddock, and others 1991; Tobey, and others 1992). Three randomised studies have been published to date, all suggesting no beneficial outcome (Fatovich, and others 1997; Miller, and others 1995; Theil, and others 1997). However, each study suffered from significant limitations, making the conclusions drawn open to question and leaving magnesium's exact role as an anti-arrhythmic agent unanswered (Hassan and Barnett 1998).

The aim of this study was to assess the efficacy of empirical magnesium treatment as compared to placebo in patients suffering refractory or recurrent ventricular fibrillation during CA. Return of spontaneous circulation and discharge from hospital alive were used as the primary and secondary endpoints respectively.

7.3 Methods

Study design.

This study was a randomised, placebo controlled, double blinded trial. It was approved by the Leicestershire Ethics Committee. The committee accepted that informed consent was not possible as the patients were in a life threatening situation for which existing treatment protocols had been shown to have no significantly beneficial effect.

Study setting and population

The LAPS provided pre-hospital care to approximately 900,000 people in the county of Leicestershire during the study period. Critically ill patients were predominantly taken to the Accident and Emergency (A&E) department at the Leicester Royal Infirmary, a 1,100-bedded university teaching hospital. A small number of patients were transferred to other hospitals at the edges of the county.

All adult patients (age greater than 18) with confirmed pre-hospital CA treated by the LAPS or in CA on arrival in the A&E department at the Leicester Royal Infirmary were eligible for entry into the study. Inclusion into the study protocol required the patient to have either ventricular fibrillation resistant to three defibrillatory shocks (refractory VF) or a second episode of VF during a resuscitation cycle for nonVF treatment. Exclusion criteria were age less than 18 years and mechanism of cardiac arrest being related to trauma, hanging or drowning.

Study protocol

Cardiac arrest was defined as per the ERC guidelines (European Resuscitation Council 1992). All patients were treated according to these guidelines by the paramedics in LAPS and senior staff in the A&E department. The study intervention consisted of either magnesium sulphate (2grammes or 8mmoles) repeated with a further 2 grammes if the patient remained in VF after 6 defibrillatory shocks, or a matched normal saline placebo. All other therapeutic interventions adhered to the ERC guidelines. The study algorithm is set out in appendix 1.

Each patient treatment pack consisted of two pre-filled syringes marked with identical randomisation labels and three spare randomisation labels for the documentation. Codes for the study were kept by the pharmacy department at the Leicester Royal Infirmary and the statistician (CJ). The randomisation schedule was produced from a computer generated list using block randomisation with block sizes of 6. The packs were distributed to each of the 11 ambulance stations in Leicestershire and also to the A&E department.

Primary and secondary outcome measures

The predefined primary outcome measure was a stable ROSC. This was defined as one being present on arrival in the A&E department or on discharge from the Resuscitation Room if the patient had suffered a CA in the A&E department. Secondary outcome measures included admission to the Intensive Care Unit (ICU), duration of stay on the ICU, duration of stay in hospital, neurological outcome as measured by the Glasgow-Pittsburgh Outcome Score and discharge from hospital alive.

Study size

Previous work from the same pre-hospital care system had shown that the mortality in patients with refractory VF was 100% (Hassan, and others 1996). This was consistent with other studies suggesting a mortality in excess of 80% in the same group of patients (Herlitz, and others 1997). The trial was designed to detect an improvement of 15% in the primary endpoint. We estimated that a total of 50 patients per arm of the study would have over 80% power to detect this difference with a 5% level of significance.

Data collection and statistical analysis

There was no facility for prospectively recording the timing of therapeutic interventions. These were therefore noted retrospectively by the EMS personnel. In the A&E department all interventions were documented by a member of the resuscitation team. For the purposes of the study, serum magnesium levels were measured in the A&E department if the patient had suffered a pre-hospital CA. The data collection adhered to the Utstein template for patients suffering a pre-hospital CA (Cummins, and others 1991).

All patients suffering a pre-hospital CA during the study period, regardless of inclusion in the study, were entered onto a dedicated Microsoft Access database by an audit assistant based in the A&E department. Accuracy of the data entry was confirmed by review of each patient record by one of the study investigators (TBH). All follow up data from in-hospital notes was collected and inputted onto the database by TBH.

Analysis was performed on an intention to treat basis. Dichotomous variables were analysed using the χ^2 test. Analysis for identifying significant differences of survival to discharge from hospital alive was carried out using the Mann Whitney U Test. Multivariate logistic regression modelling was used to analyse the primary and secondary end points. The co-variables in the analysis were : age, whether the CA was witnessed or not, presence of bystander CPR, a shorter response time, treatment with the magnesium or not and the amount of magnesium received.

7.4 Results

During the study period from December 1996 to March 1998, a total of 356 patients suffered a pre-hospital CA. A further 27 suffered a CA soon after arrival in the A&E department and were also eligible for entry into the study. Of these patients, 108 met the protocol requirements and were recruited.

Three patients were excluded from analysis due to the randomisation labels being lost prior to arrival at the hospital. It was therefore impossible to ascertain whether the patient had received magnesium or placebo. In all three patients, there was no return of spontaneous circulation (ROSC) at the scene and all were certified dead in the resuscitation room. The trial profile (figure 7.1) describes the outcomes of the remaining 105 patients all of whom were followed up to death or discharge alive from hospital. The study population consisted of 52 patients who received magnesium and 53 who received placebo.

The demographics of the study population are described in table 7.1. The baseline characteristics were generally well matched although there was a greater incidence of the cardiac arrest occurring at home in the magnesium group (65% versus 39%, $p = 0.004$). There was also a greater proportion of professional CPR in the placebo group as compared to the magnesium group (17% versus 36%, $p = 0.032$). Although professional CPR was arbitrarily defined, it was generally consistent with the CA occurring in the presence of the ambulance crew or the patient's general practitioner (GP). The median response time for the LAPS in both study groups was 8 minutes, the arrival time recorded being that for arrival at the scene and not arrival at the patient's side. Overall, the majority of patients entered into the study had VF as an initial and persisting rhythm (77/105). A smaller group (28/105) had non-VF rhythms initially which interchanged with VF on at least 2 occasions after therapy was commenced. They were recruited per the study protocol as being patients with recurrent VF.

Of the 105 patients entered, 16 (15%) achieved a ROSC. Fifteen patients had refractory VF as their initial rhythm (table 7.2). Most patients who were admitted to hospital had a witnessed CA (84%). All 3 of the survivors to discharge from hospital alive had collapsed in front of the EMS. There were no significant differences between those patients who died soon after the CA either at the scene or in A&E versus those admitted to ICU in terms of the response times, number of defibrillatory shocks and the amount of adrenaline given.

Eight patients received lignocaine therapy as an adjunct to treatment for refractory VF after 9 DC shocks. This was in keeping with the study protocol. The only protocol deviation was one patient who was given lignocaine with adrenaline and the study drug after the third DC shock. He had received placebo and went on to be discharged from hospital neurologically intact. In patients who had a stable ROSC in the A&E department, the mean serum magnesium level was 1.35mmol/L in those given magnesium and 0.89mmol/L in the placebo group.

No significant differences were identified between the magnesium and placebo groups in the proportion of patients who died at the scene or in A&E versus those who achieved a stable ROSC with admission to the ICU (χ^2 test: $p = 0.56$). However, two of the 3 survivors had received magnesium. Similarly there were no significant differences in survival to discharge from hospital alive between the two groups (Mann Whitney U Test, $p=0.99$). All three patients discharged from hospital alive were alert, orientated, self caring and independent in activities of daily living. On the Glasgow Pittsburgh Outcome score ratings they each had an Overall Performance Score and Cerebral Performance Score of 1.

In order to account for potential differences in confounding variables between the groups, a logistic regression model was fitted with ROSC as the dependent variables. Confounding variables included the age, the arrest being witnessed, presence of bystander CPR, the response time of the system, whether magnesium was given and the amount given (2 or 4 grammes) (table 7.3). There

were no definite univariate predictors of a return of spontaneous circulation. However, the response time had a statistical trend towards significance ($p = 0.10$). Regression analysis was not possible using the discharge alive from hospital as the dependent variable due to the relative lack of number of survivors. Using multivariate logistic regression the odds ratios (95% confidence intervals) for ROSC in patients treated with magnesium as compared with placebo was 1.69 (0.54, 5.30).

7.5 Discussion

Principal findings.

Coronary artery disease is the leading cause of pre-hospital sudden death in the UK (Sedgwick, and others 1993). Approximately 25% of patients with acute myocardial infarction will die in the pre-hospital phase and up to 84% of these will have a ventricular arrhythmia as their initial arrest rhythm (Bayes de Luna, and others 1989). In excess of 80% of patients with refractory or recurrent VF who do not respond successfully to the first cycle of three defibrillatory shocks will die (Herlitz, and others 1997).

This study was specifically designed to evaluate the primary role of intravenous magnesium sulphate as an adjunct to defibrillation in treating refractory or recurrent VF. It was performed in the difficult and challenging environment of pre-hospital care medicine and is the first study of its kind to be reported. No significant improvement was shown for stable ROSC or discharge from hospital alive for a group of patients with recurrent or refractory VF treated with magnesium as compared to a group treated with placebo.

Existing evidence

Laboratory studies suggest that magnesium has a number of cellular actions which could result in acute suppression or treatment of arrhythmias. These include, suppression of automaticity in partially depolarised cells, inhibition of calcium flux, suppression of early and late after-depolarisations and interactions with potassium to stabilise cell membranes (Fazekas, and others 1993). The exact mechanism particularly in circumstances where there is a co-existing loss of cardiac output, remains unknown (Theil, and others 1997).

Clinical evidence of magnesium's role in preventing serious arrhythmias is predominantly restricted to patients having suffered an acute myocardial infarction. A meta-analysis of randomised trials of patients with AMI found a reduction of ventricular arrhythmias by 49% in those treated with magnesium (Horner 1992). This was supported by the ISIS-4 study which showed a reduction in the incidence of VF post infarction (ISIS-4 1991). In contrast, the largest single centre study to specifically evaluate the role of magnesium did not show any evidence of suppressive anti-arrhythmic action (Roffe, and others 1992).

In the setting of CA, there have been three randomised studies, all of which failed to identify an improvement in outcome (Fatovich, and others 1997; Miller, and others 1995; Thel, and others 1997). However, each trial suffered from a number of methodological limitations. In the first, with 62 patients being recruited, a trend towards improved ROSC and survival to hospital discharge was found (Miller, and others 1995). However, the trial drugs were not blinded, given late in the resuscitation phase and 42 patients were excluded from the study for a variety of reasons. In an Australian study of pre-hospital CA patients, no difference in outcome was identified with only one survivor to discharge from hospital alive (Fatovich, and others 1997). Unfortunately, the study was carried out in an EMS system with no pre-hospital ALS. As a result, the intervention was not given until after arrival in the Emergency Department, an average of some 30 minutes after the collapse.

Thel et al recruited patients who had suffered an in-hospital CA and had not necessarily been admitted with a primary cardiac event (Thel, and others 1997). Thirty five per cent were from the ICU. A significant proportion had malignant disorders as their primary diagnosis and 55% of those who regained a stable ROSC were later assigned do-not-resuscitate status. However, although the study did not show magnesium to have any beneficial effect on the ROSC or discharge from hospital there was a surprising and significant improvement in the neurological status of the survivors who had received magnesium as opposed to

the placebo ($p = 0.04$). This potential cerebro-protective effect has been attributed to the role magnesium possibly plays in regulating cerebral vascular tone and its action as a calcium channel blocker preventing increase in the concentration of intraneuronal calcium during cerebral hypoperfusion (White, and others 1983). It also possesses N-methyl-D-aspartate (NMDA) antagonist properties which have been used to treat pre-eclampsia and imply broader clinical applications as a neuro-protective agent. An observational clinical study which showed that a greater proportion of patients suffering CA who had received magnesium or calcium channel blockers were more likely to be neurologically intact (Schwartz 1985). In our study there were no differences in the GCS of patients on the ICU who had received magnesium or placebo. All three patients who survived to hospital discharge were neurologically intact. Quality of life was not chosen as a secondary end point.

This study was designed to test the benefit of empirical intravenous magnesium given at an early stage in the resuscitation process. Unlike previous studies, only patients who were defined by the study protocol as being in refractory or recurrent VF were recruited. Patients suffering a pre-hospital CA with asystole or pulseless electrical activity (PEA) as their initial rhythms have a mortality approaching 100% in most EMS systems (Eisenberg, and others 1990). Inclusion of these patients into a study is likely to produce a dilution of the beneficial effect of the agent being tested as most will be unsalvageable. In addition, there is no mechanistic or clinical evidence for giving magnesium in such circumstances. Of the 28 patients who had an initial arrest rhythm other than VF but who developed VF on at least two occasions during the resuscitation process, there was only one who achieved a stable ROSC. He was admitted to the ICU where he subsequently died. In contrast, 15 of the 16 patients who achieved a stable ROSC to be admitted to the ICU, had VF as their initial rhythm.

Multivariate modelling did not identify any factor that significantly contributed to survival, although the shorter response time showed a trend towards a stable

ROSC ($p = 0.10$). Nine of these 16 patients had received at least 2 grammes of magnesium at an early stage in their resuscitation. After multivariate adjustment of all other factors, magnesium did not have a beneficial effect on the ROSC.

Reliability.

This failure to identify any beneficial outcome could be due to magnesium truly having no effect. It is also possible that a type II error occurred. From previous work within the same EMS system and available literature on the effects of magnesium in reducing ventricular arrhythmias, the study was designed to detect an improvement of 15% in the primary endpoint. However, in the study, the observed ROSC rates were 17% and 13% in the magnesium and placebo groups respectively. Assuming this to be true, it would require in excess of 1500 patients with refractory or recurrent VF to be recruited to prove magnesium to have a small effect of 5%.

A second potential limitation is that the dose of magnesium given during CA may have been inadequate. Previous studies have used dose regimens from 8mmoles(2 grammes) (Theil, and others 1997) to 20 mmoles as a bolus (Fatovich, and others 1997). Although it has been shown that 8mmoles will increase the serum concentration two-fold, this is not the case in CA especially if the drug is being given via a peripheral intravenous line. A higher bolus dose of magnesium may however cause side effects. In a dog model (Brown, and others 1993), high dose magnesium of 0.14g/kg (equivalent to 40mmoles in a 75kg male) produced a reduction in the aortic diastolic and coronary perfusion pressures. This dosing regimen was probably too high to be clinically applicable. We chose to use 8mmoles as a bolus with a second similar dose if the patient remained in VF after 6 defibrillatory shocks. Serum measurements of magnesium in patients with a stable ROSC post cardiac arrest in the A&E department and given magnesium, had mean levels of 1.35mmol/L compared with placebo. Future studies may need to give consideration to a higher dosing regime.

Pre-hospital CA is a difficult field in which to carry out randomised studies. Individual factors such as the incidence of bystander CPR, the response time to the first defibrillatory shock, protocol violations and even the aggressiveness of care provided in hospital both within the A&E department and particularly on the ICU can have major influences (Theil, and others 1997). These factors can have a marked effect particularly if the study population is small. They cannot always be controlled for by a single EMS study even if it is robustly designed. For example we chose to include only patients with refractory or recurrent VF, a well recognised group in whom ALS interventions are more likely to have a beneficial effect. The one patient in the placebo group who survived to hospital discharge was a significant protocol violation in that he received lignocaine at the same time as the trial drug after the third defibrillatory shock. This may have been the main contributory factor to his survival.

A multi-centre trial would address a number of these issues and enhance the internal validity of the trial although recruiting from different EMS systems would carry other significant problems. This study took place in a system with average response times and incidence of bystander CPR compared to others in the UK. The response time is obviously critical to success in pre-hospital CA. A high performance EMS with faster response times, approaching 8 minutes in 90% of cases is likely to produce more survivors. There are also likely to be an increase in the proportion that might benefit from other therapeutic interventions. Response time could have been a significant factor in magnesium's seeming lack of efficacy in treating refractory VF in this study population.

Conclusion and future work.

This study has shown that for patients in CA with refractory or recurrent VF, empirical intravenous magnesium did not increase the proportion of patients with a stable ROSC or the number who were discharged home. A smaller beneficial effect cannot be excluded, but would require a much larger study group.

Future work on magnesium's possible role as a primary anti-arrhythmic agent in pre-hospital CA should be carried out in high performance systems. The dose of magnesium to give in these circumstances also merits further investigation.

Figure 7.1 : Trial profile for the MICA study.

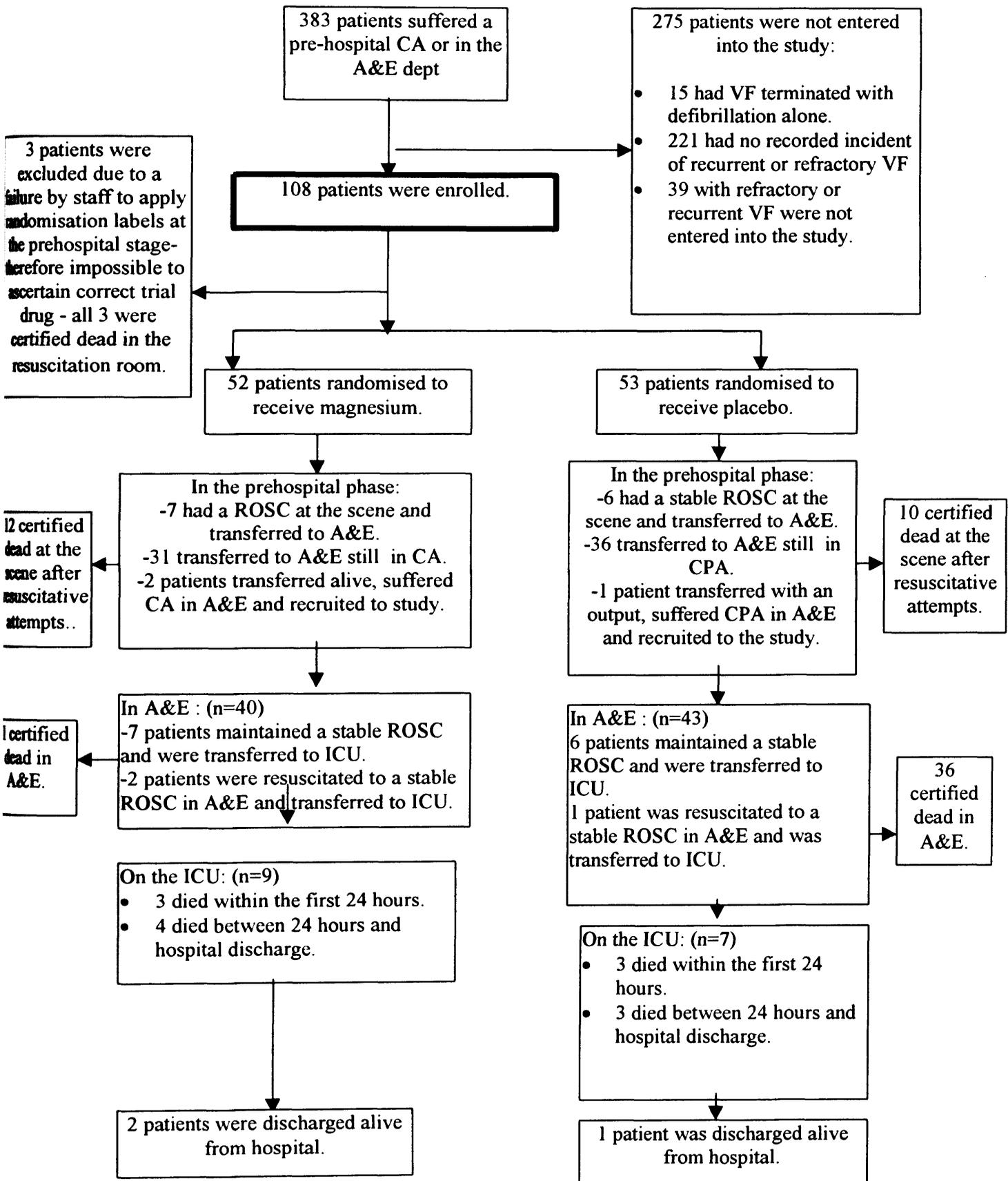


Table 7.1 : Demographic data for the MICA study.

	Magnesium	Placebo
N	52	53
Male (%)	37 (71%)	37(70%)
Median age in years (IQR)	65 (15)	67 (12)
Site of CPA		
At home	34(65%)	21(39%)
In public place	11(21%)	16(30%)
At work	3(6%)	6(11%)
In ambulance	3(6%)	6(11%)
In A&E	1(2%)	2(4%)
At GP surgery	0	2(4%)
Witnessed arrest (%)	42/47 (93%)	43/49 (88%)
Unrecorded data	5/52 (10%)	4/53 (8%)
Bystander CPR (%)		
Professional CPR ¹	9/48 (19%)	19/49 (39%)
Lay CPR ²	13/48 (28%)	10/49 (20%)
No CPR	26/48 (54%)	20/49 (41%)
Unrecorded data	4/52 (8%)	4/53 (7%)
Median response time interval in minutes (range)	8 (1-25)	8 (1-18)
Initial rhythm		
VF	38 (73%)	39 (74%)
EMD	11 (21%)	12 (23%)
Asystole	3 (6%)	2 (4%)

¹CPR given by medical, nursing, paramedical or trained first aid responders

²CPR given by the lay public

Table 7.2 : Characteristics of patient subgroups.

	Died at the scene or in A&E	Died on ICU	Alive to discharge
N	89	13	3
Initial rhythm (%)			
VF	62 (70%)	12 (92%)	0
EMD	22 (24%)	1 (8%)	0
Asystole	5 (6%)	0	0
Witnessed CA	71/91 (78%)	11/13 (84%)	3/3 (100%)
Bystander CPR (%)			
Professional CPR	22 (25%)	3 (23%)	3 (100%)
Lay person CPR	22 (25%)	1 (8%)	0
No CPR	40 (44%)	6 (46%)	0
Unrecorded data	5 (6%)	3 (23%)	0
Median response time in minutes (range)	9.5 (2-20)	8 (1-14)	10 (7-12)
Median number of defibrillatory shocks (range)	5 (2-17)	3 (1-12)	8 (4-9)
Median amount of adrenaline given in mg (range)	5 (2-10)	3 (1-8)	3 (1-8)
Proportion of patients given lignocaine	7/82 (9%)	1/12 (8%)	1/3 (33%)
GCS on admission to ICU.	-	3	3
Number of days on ICU :Median (range)	-	2 (1-6)	1(1-2)
Number of days in hospital:Median(range)	-	2 (2-6)	6(6-8)

Table 7.3 : Logistic regression analysis of possible factors contributing to the primary endpoint : (ROSC at the scene or in A&E).

	Odds ratio (95% C.I.)	P
Age		0.56
An increase of 1 year.	1.01 (0.97 – 1.07)	
Witnessed arrest		0.87
Witnessed	1.00	
Unwitnessed	0.56 (0.06 - 4.97)	
Unknown	0.93 (0.09 – 9.77)	
Bystander CPR		0.23
Good	1.00	
Poor/none	0.48 (0.14 – 1.61)	
Unknown	0.56 (0.23 – 1.72)	
Response time		0.10
An increase of 1 minute.	0.89 (0.77 – 1.02)	
Received magnesium		0.37
Placebo	1.00	
Magnesium	1.69 (0.54 – 5.30)	
Amount of magnesium given		0.51
2 grammes (8 mmols)	1.00	
4 grammes (16 mmols)	1.74 (0.37 – 8.14)	
Placebo	0.77 (0.19 – 3.11)	

Chapter 8

**A Delphi study to develop consensus on the future
design of EMS systems in the UK.**

8.1 Abstract

Objective : To develop consensus opinion on future design characteristics of EMS systems in the UK, taking into account increasing demand and the Department of Health's long term target of a 90% fractile for 8 minute response time to category A (immediately life threatening) emergency calls.

Design : A Delphi questionnaire design with two rounds to gain a consensus of opinion. Investigation of four aspects of EMS design is reported - type of response to a priority based dispatch category, transportation options, enhancement of paramedic skills and structure of a first responder system.

Subjects : Chief Executives, Directors of Operations and Medical Directors of Ambulance Trusts in the United Kingdom (UK).

Outcome measures : Likert scales (0-9) to score opinion on a series of statements with achievement of inter - round consistency. A median score of 0-4 was classified as disagreement and 6-9 as agreement.

Results : A 67% response to the first questionnaire and with iteration, 52% response to the second questionnaire was attained. A tiered response (paramedics, technicians and basic life support first responders) with technicians responding to selected category A and B calls and all category C calls [median score (MS) 7.5, interquartile range (IQR) 4], was recommended. Inter unit handover of selected calls to maintain paramedic availability (MS 7.5, IQR 3.75) and enhancement of paramedic skills (MS 7.0 , IQR 4.0) was also proposed. Finally the development of a first responder system fully integrated into the EMS (MS 8.0, IQR 2.75) involving other agencies including the police force, fire service and trained members of the local community was agreed.

Conclusions : Senior expert staff from Ambulance Trusts in the UK achieved consensus on certain design characteristics of EMS systems. These are significantly different from the present EMS model.

8.2 Introduction

In the UK, despite increasing sophistication in the care given by pre-hospital care providers, EMS systems continue to under perform in terms of response times, quality assurance and cost effectiveness related to desired outcome (NHS Exec, Audit Commission). The design of a system is critical to each of these markers of performance (Stout 1994).

Unfortunately, there are no validated tools for the overall evaluation of EMS systems. Rather, performance and outcome for selected conditions are used as indicative markers. Measurement of the outcome from pre-hospital CA is regarded as a robust tool or 'tracer' for the evaluation of a system's performance and overall quality (Maio, and others 1999). A tracer is a condition which is important, measurable, has a relatively high frequency and great potential to be affected by medical care (Kessner, and others 1973). Major trauma is another commonly used tracer in EMS systems (Reines, and others 1988).

Critical to success for both of these conditions is prioritisation of emergency calls, dispatch of an appropriate unit or units, minimisation of response time, provision of appropriate treatment at the scene and timely transfer to definitive care. Measurement and optimisation of the tracer is hopefully then indirectly reflected in similar high quality care being given for a number of other life threatening pathologies (Maio, and others 1999). However, there is considerable debate as to how the outcome of pre-hospital CA, for example, can be improved in the most cost efficient manner.

A number of changes in the processes of care within a system might make it more efficient and effective. For example, the implementation of priority dispatch systems (PDS) should improve response times, especially for life threatening conditions (NHS Executive Steering Group 1996). This has however yet to be proven. To date, the ability to respond rapidly has been compromised by the

continuing annual rise in the number of emergency calls (Department of health 1999).

Another component in the process of care is the type of response to send to an emergency call. The single tiered ALS system currently in place in the UK offers simplicity and safety because every emergency call receives the benefit of a paramedic attendance. This prevents the likelihood of under-triage by the PDS. However, a number of UK studies have shown that apart from defibrillation, which can be provided by technicians with AEDs, there is no beneficial effect on outcome using other ALS skills in pre-hospital CA (Guly, and others 1995; Mann and Guly 1997). In addition, analysis of the workload of EMS staff has shown that less than one tenth of emergency calls require paramedic skills (Walters and Glucksman 1989).

In the United States (US) paramedic training is on average 4-5 times longer. The single tiered ALS configuration in some of these systems it has been argued, is costly and uses highly trained personnel unnecessarily (Giordano and Davidson 1994). Multi-tiered systems with mature PDS are perceived to use resources more efficiently. In contrast, in the UK, further redesign to the single tiered ALS response has been thought necessary. Recommendations have included a maintenance of the single tier, with expansion of the number of single paramedic 'fast responders'. The development of first responder schemes has also been suggested (NHS Executive Steering Group 1996). However, there are no robust studies to support these changes in system design or evidence to suggest that they are representative of the views of experts in the UK.

The main objective of this study was to identify what UK experts in the field of EMS believed to be the optimal design of systems for the future. They were asked to take into account, resource constraints, the continuing rise in demand for EMS and the need to improve the outcome of certain tracer conditions such as CA.

8.3 Methods

Study design

In order to gain maximal input and a consensus of opinion amongst a group of experts in EMS systems, a Delphi study design was used. Due to the nature of the study, ethical approval for the study was not considered to be necessary.

Delphi methodology.

The Delphi method is a means to determine the extent to which consensus exists amongst a group of people (Rowe, and others 1991) . Consensus takes place in a series of 'rounds'. The first round involves obtaining the opinions of selected experts about a particular issue. In subsequent rounds the same experts are asked to rate the extent of their agreement or disagreement with a series of statements describing the opinions expressed in the first round. Responses are analysed for the degree of consensus achieved. Failure to reach consensus can result in further rounds.

To reduce the number of rounds and hence maximise the return rate of the questionnaires, in the first round, the topics most relevant to future EMS system design were derived from a review of the literature (Delbridge, and others 1998). A pilot study using only senior directors from the Leicestershire Ambulance and Paramedic Service (LAPS) was carried out. This same group were also interviewed individually to further refine the questionnaire. Appropriate changes were made to the questionnaire design, but the results were not included in the main study.

Subjects

In order to gain expert consensus opinion and gauge the national view, all Chief Executives, Directors of Operations and Medical Directors of Ambulance Trusts in the UK were chosen as 'Delphi experts'. A total of 91 individuals were invited to enter into the study from the 42 existing Ambulance Trusts in June 1998.

Chapter 1 Questionnaire design

The 'Delphi experts' were each sent a questionnaire which was divided into two main sections (see appendix 2a). In addition they were sent a copy of a paper outlining the Delphi technique and methodology for their interest and to enhance the quality and rigour of the study (Jones and Hunter 1995). This questionnaire constituted the first round in the study. The first section asked respondents to answer questions which described the existing components of their EMS system. The second section aimed to gauge their opinion on how systems should be developed in the future. Respondents were asked to indicate their level of agreement with each statement on a scale from 0 to 9 (0 indicating total disagreement and 9 indicating total agreement).

Results were collated and a second questionnaire sent to those who had responded to the first (appendix 2b). This second questionnaire was similar to the first but it also showed the initial responses of all the other participants. In addition, the individual's rating for each of the previous round was shown. The purpose of this was to offer the respondents an opportunity to amend their ratings in view of the expressed attitude of their colleagues.

Definition of agreement/disagreement.

Clear prior categorisation of median scores was developed to define disagreement (MS 0-4) and agreement (MS 6-9) with statements in the questionnaire.

Statistical analysis.

Agreement between the first and second scores was measured by calculating the difference in opinion obtained after subtracting the second score from the first for each statement of each respondent, the median change of opinion score (MCOS). The MCOS, inter-quartile range(IQR) and the minimum and maximum differences (range) were calculated for the difference of opinion.

Following good agreement between the first and second questionnaires, median scores (MS) and interquartile ranges (IQR) for each of the statements to the second questionnaire alone were calculated.

8.4 Results :

After the first round, replies were received from 56 of the 91 directors and Chief Executives. Five respondents sent joint responses from their Trusts and one medical director replied but refused to enter into the study. A response rate of 56 out of 85 (66%) was therefore achieved. This represented 37 of the 42 Ambulance Trusts in the UK in operation in August 1998. Table 8.1 describes the basic demographics of each of these systems.

Of note, apart from the small systems serving populations of less than 200,000, the number of emergency calls per thousand population per available unit at peak times was reported to vary considerably from 0.23 to 3.0. Twenty one systems (57%) reported that they operated some form of additional paramedic 'fast responder' service. Only 6 systems (16%) reported an integrated 'first responder' scheme.

Thirty three of the 37 systems (89%) had some form of computer aided dispatch system in place or were in the process of installing one. Similarly, 78% had some form of Emergency Medical Dispatch or were about to install one. Automatic Vehicle Location systems (AVLS) which provides a continually updated report on ambulance location and status, were reported by 10 systems (27%) although 3 others (8%) reported that they were in the process of installing one. Ten systems (27%) reported that they had some form of System Status Management (SSM) package although 8 others (22%) were installing one.

A second questionnaire was sent to the 56 who responded to the first one. From this second round 29 replies (52%) were received. The results of the second

questionnaire are shown in table 8.2. Only slight changes occurred between the two rounds of the Delphi study as shown by the MCOS. The indicators that achieved greatest agreement (highest median scores) increased in the level of agreement and of consensus while the level of disagreement increased for the indicators with the lowest scores in the first questionnaire.

The results of the second questionnaire were divided in to four main categories (table 8.3). A tiered response (paramedics, technicians and basic life support first responders) with technicians responding to selected category A and B calls and all category C calls [MS 8.0, IQR 3.0) was proposed by the panel. The need for an automatic dual unit response for patients assumed to have a CA was also suggested (MS 7.0, IQR 3.5). Inter unit handover of selected calls to maintain paramedic availability (MS 8.0, IQR 2.0) and enhancement of paramedic skills was proposed for certain circumstances. The development of a first responder system fully integrated into the EMS involving other agencies including the police force, fire service and trained members of the local community was agreed (MS 9.0 IQR 2.0).

8.5 Discussion

Principal findings

This study has shown that senior expert staff from Ambulance Trusts in the UK achieved consensus on certain aspects of EMS system design for the future. A tiered response, with paramedics and technicians being dispatched selectively to category A, B and C calls is recommended with a dual response for patients with assumed CA. In addition, they concluded that an active first responder scheme should be developed which is fully integrated into the EMS system. They also suggested that the composition of staff could include members of the police and fire services as well as trained members of the local community. Finally, the expansion of advanced skills for paramedics in certain circumstances was supported.

However, these proposals differ from the present single tiered all ALS model (Department of health 1993). In addition, they also vary from recommendations made by the NHS Executive to attain performance standards of 8 minutes in 90% of calls for all immediately life threatening conditions (NHS Executive Steering Group 1996).

Evidence to support the consensus of opinion

This is the first study to investigate the potential design of EMS systems in the future using the Delphi technique. The need for structural change is obvious. There has been an ever-increasing demand on EMS systems in the UK in the past decade. The number of emergency 999 calls having increased annually by between 4.8% and 9.4% since 1992 (Department of health 1997). This has resulted in a need to be more effective, efficient and appropriate for the response provided to an emergency call (Delbridge, and others 1998; Audit Commission 1998).

PDS systems have been formally introduced into UK practice allowing prioritisation of calls and more appropriate care to be targeted to the needs of the patient (NHS Executive Steering Group 1996). However, debate continues around the most appropriate and cost effective response type given that a substantial proportion of calls do not require paramedic advanced life support (ALS) skills (Glucksman and Cocks 1993; Kuehl, and others 1984; Braun, and others 1990). There is evidence to suggest that a tiered service will increase flexibility within a system and produce better average response times. A review of the EMS systems of 25 mid-sized cities in the United States found that the average response time for two tiered systems was 5.9 minutes versus 7.0 minutes for one tiered systems ($p < 0.05$) (Braun, and others 1990). In addition in a meta-analysis of 41 EMS systems, a rate of discharge for patients suffering pre-hospital CA was 5.2% in 1-tiered systems and 10.5% in 2-tiered systems (Nichol, and others 1996). Evidence also suggests that systems able to provide a dual response for CA will have a much greater percentage discharge from hospital (Eisenberg, and others 1990).

The role of other agencies as first responders in certain groups of patients, especially with possible CA, is still very much in its infancy in the UK. In 1998, six fire services (11%) and four police forces (14%) were involved to some extent as 'first responders' in responding to patients with presumed cardiac arrest (Porter and Allison 1998). This role was predominantly in rural areas but also included central London. In contrast, a survey of EMS systems in 200 American cities, the fire service provided cross trained /dual role personnel for emergency care in 67 systems (33%). Non-transport advanced life support was also provided by fire department based EMS in another 35 cities (17%) (Cady and Scott 1995). An integrated first response with other emergency services has been shown to improve the outcome of patients suffering CA from 3% to 26% (Mosesso, and others 1998). This study has identified that only 16% of systems have some form of integrated 'first responder' system.

Outcome of patients suffering pre-hospital CA is critically related to the defibrillation response interval (DRI). The DRI is classified as 'call received by dispatch' to 'arrival at scene by responder with defibrillator'. The aim of EMS systems in U.S. thus far has been to achieve and maintain a target in 8 minutes or less for at least 90% of cases (Ryan 1994). In the UK this target is regarded as a long term performance standard to be attained (NHS Executive Steering Group 1996). However evidence from a prospective cohort study in Canada of 9,267 adult victims of pre-hospital CA suggests that there is a steep drop off in the first 4 minutes of the survival curve and the slope gradually tails off after 6 minutes (De Maio, and others 1999). They suggested that EMS systems will need to develop novel strategies to further optimise their 90th percentile DRI significantly below 8 minutes.

The role of ALS skills may change in the future from being targeted at management of CA to other issues such as pre-hospital diagnosis of acute myocardial infarction and thrombolysis as well as definitive airway management in the head injured patient (Delbridge, and others 1998). The experts in this study supported the concept of possible expansion of skills for paramedic staff in certain circumstances in the future.

Implications

Alongside the implementation of PDS, existing proposals recommend an expansion of single paramedic 'fast responders' and some development of 'first responder' schemes to meet the 90th fractile 8 minute target. These proposals are at variance with the views of senior experienced personnel as shown in this study. They suggest more cost effective alternatives which would be likely to produce a similar or improved impact on outcome in certain groups of patients.

The exact benefits of PDS, tiered services and the additive role of paramedic ALS skills in managing these patients remains to be properly defined in a prospective study.

Limitations

The Delphi technique was chosen in order to develop a consensus of opinion. The process is known to have a number of strengths which include anonymity, controlled feedback and a statistical group response (Pill 1971). Others have argued that the method forces consensus and is weakened by the inability of the 'experts' to discuss the issues (Rowe, and others 1991).

Anonymity is important as a means of avoiding dominance, and was secured in the study by using a questionnaire. Good agreement between rounds is adjudged to be representative of consensus. Statistical group response ensures that each opinion is represented in those who contribute to the final questionnaire. Although the responses of only 29 of the original 85 entered into the study were taken into account in the final analysis, the high level of agreement between the two questionnaires suggests that this was a representative group. However, it is possible that this may not have been an entirely representative group.

Another weakness in the Delphi technique is its failure to stipulate at what level consensus is deemed to have been reached. Investigators therefore arbitrarily define it. Median scores were chosen for each statement having developed clear prior categorisation of the scores to define agreement and disagreement (Rowe, and others 1991).

In addition, the results of such a study can be sensitive to the number and selection of the participants. Selecting a particular group of Delphi 'experts' presents a number of conceptual problems in defining who has an interest in the issue under investigation and who can provide a relevant and informed opinion on the matter. We chose to use senior executives and directors from Ambulance Trusts because they were a clearly identifiable group, had the greatest experience and expertise of EMS system design in the UK and were likely to be

instrumental in instigating change within their respective systems. However, it must be accepted that this group may be biased towards a particular strategy. The notable lack of dedicated medical directors within EMS systems in the UK at present prevented any representative opinion by them (Allison and Cooke 1998).

Conclusion

This study has quantified the opinion of senior directors of EMS systems in the UK. They suggest that the optimal system would be for a tiered service, better integrated into other emergency services and with a dual response to certain category A emergency calls. Certain circumstances would require the development of additional ALS skills. The results from this study can be used to stimulate further debate amongst policymakers.

Evidence suggests the need for innovative and progressive strategies to significantly reduce the EMS response time for immediately life threatening conditions in order to improve their outcome. Failure to adopt such strategies will result in the continuing dismal outcomes for time critical conditions like pre-hospital CA.

Table 8.1 Characteristics of EMS systems in the study.

EMS system	Population served (peak)	Area covered	Emergency calls per year/1,000 population.	Emergency calls per year/ 1,000 population/ available unit at peak times	Number of fast response units (Motorcycle or car)	Number of 'first responder' units
Bedfordshire & Hertfordshire	1,500,000	710,000	45	1.02	2 (C)	0
Royal Berkshire	1,000,000	312,000	31	1.48	0	3
Cumbria	500,000	1,683,000	38	1.73	2 (C) and 3 (M)	1
Derbyshire	1,000,000	1,680,000	60	2.00	6 (C) and 3 (M)	0
Dorset	1,200,000	655,000	37	1.39	1 (C)	1
Durham	600,000	603,000	60	3.0	0	0
East Anglian	3,000,000	3,200,000	32	0.46	0	0
Essex	1,500,000	908,000	97	2.16	5(C) and 4 (M)	5
Gloucestershire	500,000	732,000	46	1.59	0	0
Guemsey	100,000	400	35	8.75	1 (C)	0
Hereford and Worcester	750,000	970,000	39	1.68	0	0
Humberside	600,000	2500sqkm	68	2.28	0	0
Isle of Man	73,000	227sqmile	41	10.2	2 (C) and 2(M)	0
Isle of Wight	123,000	38,000	53	7.5	1 (C)	0
Jersey	120,000	29,000	58	19	1 (C)	0
Lancashire	1,500,000	736,000	64	1.5	1(C)	0
Leicestershire	1,000,000	630,000	43	2.20	5 (C)	0

EMS system	Population served)	Area covered	Emergency calls per year/1,000 population.	Emergency calls per year/ 1,000 population/ available unit at peak times	Number of fast response units (Motorcycle or car)	Number of 'first responder' units
London	7,000,000	390,000	93	0.41	10 (M)	0
Manchester	2,700,000	266,000	129	1.58	0	0
Mid Glamorgan	540,000	252,000	79	2.21	0	0
Northern Ireland	1,600,000	3,500,000	39	0.78	0	0
Northumbria	1,500,000	1,380,000	67	1.35	2(C) and 3(M)	0
North Yorkshire	732,000	260,000	46	1.86	0	0
Nottinghamshire	1,000,000	543,000	58	1.75	0	0
Chapter 1 Oxford shire	600,000	590,000	40	2.8	0	0
Scottish Amb Service	5,120,000	19,500,000	96	0.23	2 (M)	0
Shropshire	420,000	863,000	47	1.59	11 (C)	0
South Yorkshire	1,600,000	385,000	46	1.25	0	0
Staffordshire	1,200,000	670,000	40	0.99	22 (C)	0
Surrey	1,400,000	700sq mil	64	1.74	0	0
Sussex	1,500,000	935,000	83	1.85	2 (M)	0
Two Shires	1,300,000	1,200,000	36	0.93	0	0
Warwickshire	500,000	489,000	46	1.76	6 (C)	0
Welsh Amb Service	2,921,000	20,800 sq- km	48	0.30	18 (C) and 2(M)	14 (C)
West Country	2,000,000	3,390,000	75	0.78	4 (M)	20
West Midlands	3,250,000	265,600	92	1.28	10(C) and 10(M)	0
Wiltshire	589,000	909,000	53	2.5	1 (M)	0

Table 8.2 Description of the change in opinion score from the first to the second questionnaire for each statement.

	Median change of opinion score (MCOS)	Inter-quartile range (IQR) for change of opinion score	Range (Minimum to maximum change in score)
Dispatch criteria			
Paramedic (ALS) unit sent to all calls	0	0.5	-9 to 0
ALS unit to all category A and B calls only	0	0	-2 to 8
ALS unit to all category A and selected category B calls	0	0	-1 to 7
Technicians with automated external defibrillator (T-AED) unit to selected category A and B calls and all C calls.	0	0	-1 to 4
A first responder unit (with BLS skills only) can be sent to selected category C calls.	0	0	-1 to 7
A first responder unit to all category C calls	0	0.5	-5 to 1
An assumed or confirmed cardiac arrest should receive an automatic additional response from other units.	0	0.5	-2 to 9
Transportation criteria			
After assessment by an ALS unit, certain category B patients can be handed over to a T-AED unit for transportation to hospital	0	0	-1 to 1
After assessment by an ALS unit , certain category B and all category C patients can be handed over to a T-AED unit or first responder unit for transportation to hospital.	0	0.5	-2 to 6

Table 8.2 continued.

	Median change of opinion score (MCOS)	Inter-quartile range (IQR) for change of opinion score	Range (Minimum to maximum change in score)
Development of advanced skills for paramedics			
A number of paramedics within a system should have additional skills to perform endotracheal intubation using anaesthetic agents	0	0.5	-1 to 5
Paramedics should be taught to carry out and interpret 12 lead ECGs for patients with chest pain	0	0	-1 to 3
Paramedics should be taught to carry out thrombolysis for patients with confirmed acute myocardial infarction on a 12 lead ECG.	0	1.5	-1 to 5
Development of a first responder system.			
A first responder system should be trained and fully integrated into an EMS system.	0	2.0	-2 to 9
Should be employed solely by the ambulance service	0	1.0	-1 to 3
Should be made up partly of members of the voluntary services	0	0	-5 to 3
Should include members of the police service with automated external defibrillators(AEDs)	0	0	-2 to 4
Should include members of the Fire Service with AEDs	0	0	-2 to 3
Should include trained members of the local community	0	0	-1 to 4

Chapter 1 Table 8.3 Final opinions of respondents to the second questionnaire.

	Median score (MS)	Interquartile range (IQR)
Dispatch criteria		
Paramedic (ALS) unit sent to all calls	0	1
ALS unit to all category A and B calls only	4	4.5
ALS unit to all category A and selected category B calls	9	2
Technicians with automated external defibrillator (T-AED) unit to selected category A and B calls and all C calls.	8	3
A first responder unit (with BLS skills only) can be sent to selected category C calls.	4	3
A first responder unit to all category C calls	0	3
An assumed or confirmed cardiac arrest should receive an automatic additional response from other units.	7	3.5
Transportation criteria		
After assessment by an ALS unit, certain category B patients can be handed over to a T-AED unit for transportation to hospital	8	2
After assessment by an ALS unit , certain category B and all category C patients can be handed over to a T-AED unit or first responder unit for transportation to hospital.	8	2

Table 8.3 continued.

	Median score (MS)	Interquartile range (IQR)
Development of advanced skills for paramedics		
A number of paramedics within a system should have additional skills to perform endotracheal intubation using anaesthetic agents.	7	4
Paramedics should be taught to carry out and interpret 12 lead ECGs for patients with chest pain.	9	4
Paramedics should be taught to carry out thrombolysis for patients with confirmed acute myocardial infarction on a 12 lead ECG.	7	4
Development of a first responder system.		
A first responder system should be trained and fully integrated into an EMS system.	9	2
Should be employed solely by the ambulance service	1	7
Should be made up partly of members of the voluntary services	5	3.5
Should include members of the police service with automated external defibrillators(AEDs)	6	4
Should include members of the Fire Service with AEDs	6	4.5
Should include trained members of the local community	8	4

Chapter 9
Final discussion and conclusions

9.1 Final discussion and conclusions.

Improving the outcome of pre-hospital CA is a critical component of EMS system function. Health authorities responsible for purchasing EMS care must have clearly defined goals and policies for improving the poor outcome of patients suffering a CA in the community (Audit Commission 1998).

Government strategy thus far has been to implement a limited form of priority dispatch (NHS Executive Steering Group 1996). Recommendations were also made for expansion of single paramedic 'fast responders' numbers as well as development of first responder schemes in certain circumstances. Until now, there has been little or no evidence from individual EMS systems in the UK to support or refute these strategies.

In this thesis, a number of these key areas have been explored. Factors considered have included those that had the greatest impact on the outcome of pre-hospital CA, such as improving the response time of the system and hence the time to the first defibrillatory shock. In addition, I investigated an intervention (empirical intravenous magnesium treatment), for which there was some evidence to suggest a possible role in the treatment of refractory VF.

In my first study, rigorous data collection resulted in a representative demographic data set. This characterised the processes of care involved in managing pre-hospital CA. Data on the location of events, interventions in the pre-hospital and in-hospital settings and the outcome to death or discharge from hospital alive were defined. Sixty three per-cent of cardiac arrests were witnessed events. Some form of bystander CPR occurred in 35.2%. Only 15.7% took place in a public building, the work place or a primary care facility. The EMS was only able to arrive at the location of a CA within 8 minutes in 67% of cases. Overall survival was poor, with only 4.3% of patients being discharged home alive. Three times as many patients were discharged if the arrest occurred in the presence of the EMS. This information is important in

developing and assessing health policy initiatives in Leicestershire aimed at improving outcome in these critically ill patients.

The second study explored two sub-sets of this study population. It investigated the effect on outcome and cost effectiveness of introducing a limited priority dispatch system (CBD) with single paramedic 'fast responders' into the Leicestershire EMS. Unfortunately, response times did not improve following these interventions. In fact the proportion of calls where the EMS arrived within 8 minutes to patients who had suffered a CA fell from 72% to 65.2%. Outcome to discharge from hospital was also slightly worse, but was not significantly different. A cost effectiveness analysis showed that irrespective of how costs were calculated, the post intervention model was still significantly more expensive than the suggestions made by the NHS Executive Steering Group (NHS Executive Steering Group 1996). A third hypothetical model which considered further expansion of ALS units was modelled and calculated to be relatively more cost effective. This would still require a substantial amount of additional investment to potentially save an extra two lives per year in Leicestershire. A significant barrier to improvement in the performance of the EMS system was the very significant rise in demand for emergency services of a 16% increase between the two study periods.

Advanced life support interventions apart from defibrillation have not been clearly proven to have a beneficial effect in pre-hospital CA. However, anecdotal reports and a number of case series have suggested that magnesium might be beneficial in improving the outcome of patients who suffered from refractory or recurrent VF during their CA. A randomised powered study to investigate the role of magnesium in CA, the first of its kind in the pre-hospital setting, was specifically designed to investigate this question. Unfortunately no clear benefit was shown although a number of limitations complicated the interpretation of the results and a smaller benefit could not be excluded.

From the results of these studies it is clear that increasing workload combined with limited resources, produced little improvement in response times and no

increase in the proportion of patients discharged alive from hospital. An intervention such as magnesium might have shown some benefit if given earlier, that is, in a system with a significantly faster response time. An alternative strategy might be to change EMS system design in order to improve performance and produce a significant effect on response time.

The last study in this thesis therefore sought to achieve consensus on EMS system design for the future, taking into account the factors considered above. The Delphi technique was chosen in order to gain agreement between senior directors of EMS systems in the UK. The results suggested that the 'Delphi experts' had a different view of EMS design from the present single tiered all ALS model espoused by the Department of Health. They suggested that the optimal system would be for a tiered service with EMT-Ds responding to category B and C calls. Better integration into other emergency services was recommended, with a dual response to specified category A emergency calls. Specific circumstances would require the development of additional ALS skills for paramedic staff. It is important to appreciate however, that such recommendations and consensus statements must be evaluated and validated using rigorous methodology prior to widespread dissemination.

Cost effective strategies in the future will need to take all of these factors into account. Most community CA events occur in the home. EMS systems in the UK must therefore improve their performance standards in order to minimise the DRI. They must not only meet but also exceed the 90% 8 minute standard set for these critically ill patients. A 90% 6 minute performance standard must be made into an achievable goal. Radical changes to system design and better integration with other public services will be required for this to occur. With the advent of bi-phasic defibrillator technology and increasingly portable machines, wide spread public access defibrillation linked to BLS teaching could also play a significant role in improving outcome.

9.2 Recommendations

The findings in this thesis therefore lead to a number of recommendations that are generalisable not only to policy makers responsible for EMS care in Leicestershire but also to relevant governmental agencies in the UK.

Significant strategic reconfiguration is required not only to cope with the increasing demand for EMS care, but also to radically improve the response time of systems.

- Priority dispatch systems should be fully implemented with alternative responses and performance standards being developed for category C calls.
- The single tiered ALS response should be modified to a multi-tiered structure with paramedics being targeted to category A and certain category B calls only. Technicians equipped with AEDs and extended skills are capable of dealing with certain category B and all category C calls.
- Other members of the emergency services, such as police and fire should be integrated into the EMS as certified first responders equipped with AEDs.

If implemented fully, this re-organisation would significantly improve the defibrillatory response interval and lead to an increased number of lives being saved in the pre-hospital setting. It would also be a more cost effective strategy as compared to the present single tiered ALS system.

9.3 Future areas for research.

Like any research this thesis has raised as many questions as it has answered. Researchers in the future may wish to;

- Investigate the impact on response times and secondly on time critical illnesses such as pre-hospital cardiac arrest, once priority based despatch systems have been fully implemented in the UK.
- Investigate the benefits of an integrated first responder EMS system on the outcome of patients suffering pre-hospital cardiac arrest.
- Investigate the dose of magnesium in pre-hospital cardiac arrest further, especially within high performance EMS systems. If some benefit is identified direct comparison with amiodarone in a randomised control trial may be considered appropriate especially as magnesium is less negatively inotropic and has potential free radical scavenging activity for cerebral and myocardial salvage.
- Investigate the effects of a multi-tiered EMS system on other time critical conditions managed by pre-hospital care personnel apart from medical causes of cardiac arrest.

9.4 Final thoughts.

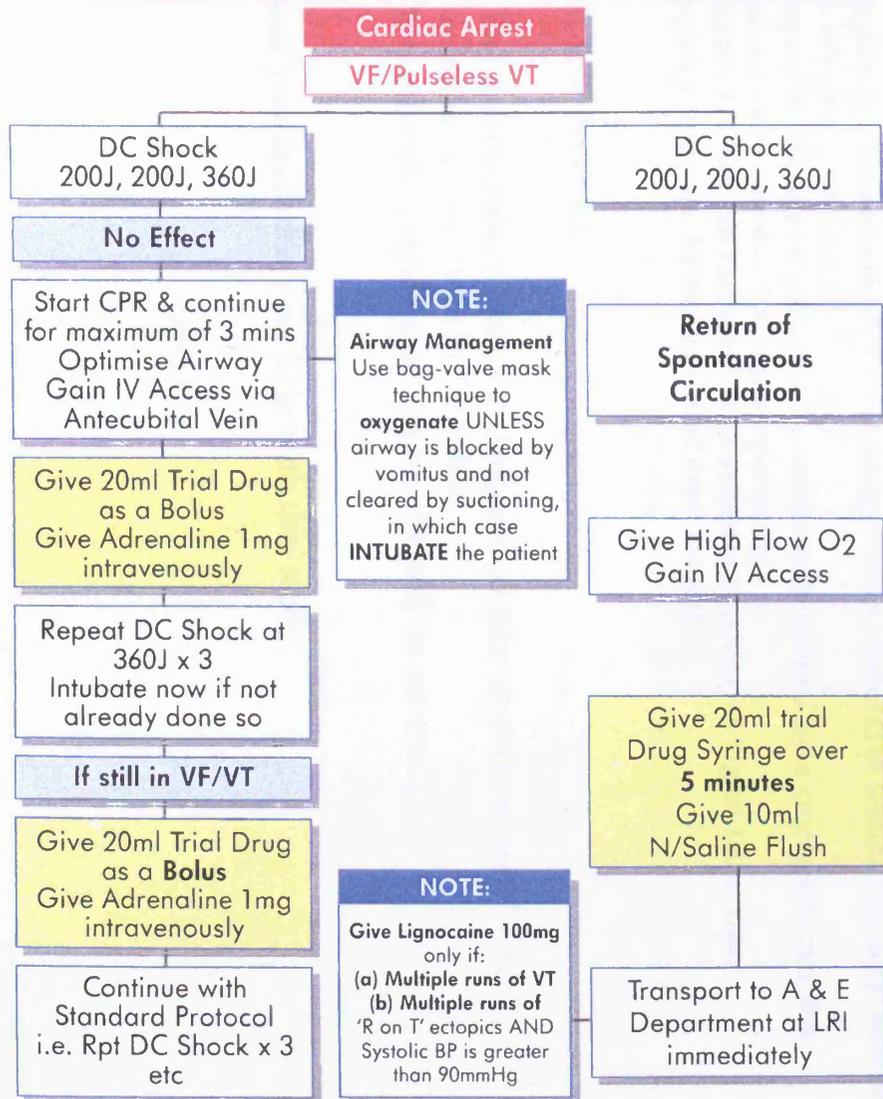
Suffering a pre-hospital CA in the UK is at present, in most circumstances a sudden and devastating event. Adherence and optimisation of a number of basic principles – the links in the Chain of Survival concept – can avert disaster and lead to a good quality of life for survivors.

Strategies exist to strengthen the weaknesses in this 'chain'. They must be implemented in order to improve outcome. This thesis has also identified other areas that need to be explored in the future. Until then, cardiac arrest in the community will remain a challenge that medicine cannot adequately meet.

Appendices

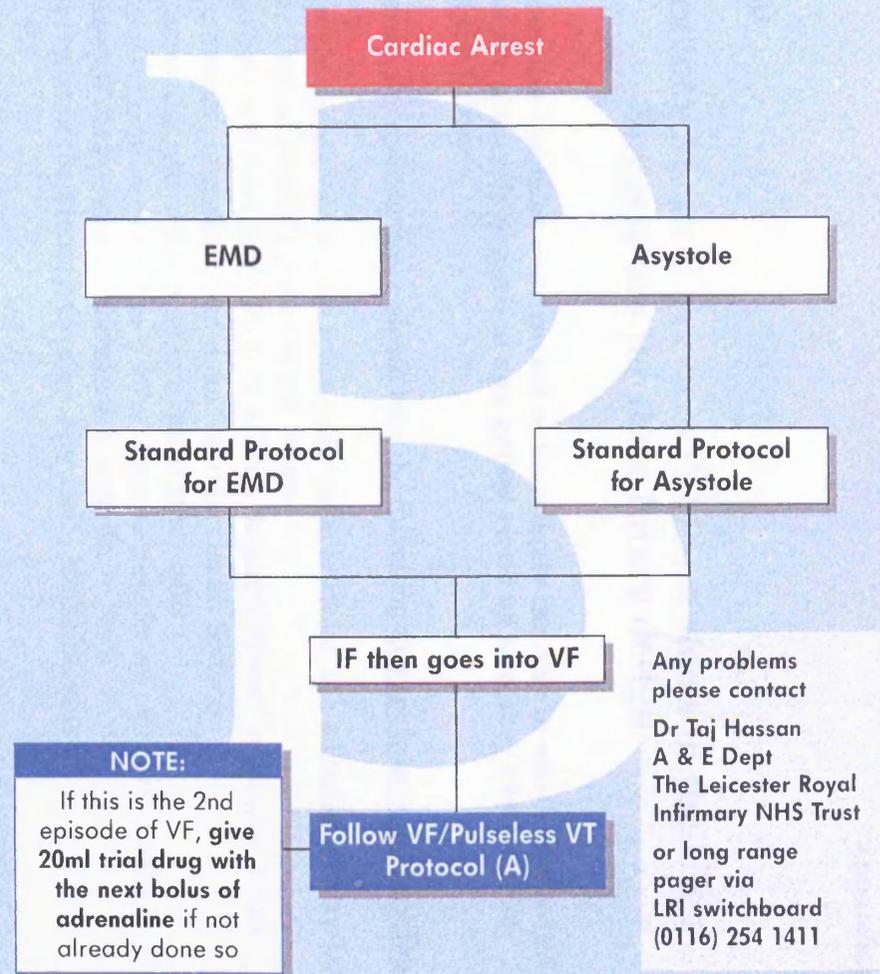
Magnesium in Cardiac Arrest Study (M.I.C.A.)

Standing Procedure (A) Management of VF/Pulseless VT in Cardiac Arrest



Please remember to:
 (a) staple a copy of the defib summary read out to the blue copy of the AS11
 (b) Put the MICA patient No. label onto each copy of the AS11

Standing Procedure (B) Management of EMD or Asystole



Please remember to:
 (a) staple a copy of the defib summary read out to the blue copy of the AS11
 (b) Put the MICA patient No. label onto each copy of the AS11

Appendix 2a.

**Emergency Medical Services (EMS) systems in the UK :
Suggestions for their future design.**

This questionnaire has been constructed to investigate the way in which pre-hospital care systems are presently organised and gather views on how they can be better designed in the future.

When answering the questionnaire please take the following **factors into consideration:**

- the present single tier system (paramedic on every front line ambulance) may not be the Dept of Health's policy in the future.
- all systems will have some form of priority despatch system in the near future
- the economic constraints within the National Health Service.
- the continuing rise in the number of emergency calls
- the long term strategy to have a 90% response time for all category A calls
(Review of Ambulance Performance Standards,
Final report of the Steering Group - July 1996. *NHS Executive*)

You will be familiar with the following definitions (from the same report.) :

Category A : Immediate life threatening (victims of illness or trauma who may benefit from life saving help within minutes).

Category B : Serious (patients with conditions benefiting from emergency care that requires a more conventional degree of urgency).

Category C : Not life threatening or serious (requiring an urgent rather than emergency response, by ambulance or other means)

PLEASE NOTE:

- The questionnaire has been designed to take approximately 10-12 minutes of your time to complete.
- It is entirely confidential and results will be anonymised.

Thank you again for your help with this study.

Emergency Medical Service (EMS) systems in the UK :
Suggestions for their future design.

(A) Demographics of your system.

(Data on population and area covered is already available)

- 1) Number of emergency patient journeys carried out by your service / year (approx).....
- 2) Number of paramedics in your service :.....
- 3) Number of technicians in your service:
- 4) What is the **minimum and maximum number of units per day** (including paramedic fast response units) that you have available covering your region during a normal week?
 Maximum..... **Minimum (0100-0700hrs)**

5) Number of paramedic 'fast response units' in total :
 Please specify number of : Car Motorcycle.....

6) What is your system's response to a patient with assumed cardiac arrest:
 Single paramedic unit responds
 Second paramedic unit sent as standard practice (as soon as available)
 Other (please specify.....)

7) Do you have a **first responder*** scheme integrated into your system:
 Yes No

If yes, how many units do you have:.....

*Please note : A **first responder** is defined as anyone who has been selected and trained by your ambulance service to provide basic life support and received additional training, but whose training is not equivalent to a technician.

Please define the capabilities of your first responder below:

- Possesses basic life support skills only Yes No
- Travels with an advisory external defibrillator(AED) Yes No
- What mode of transport does the first responder have:

 Car Other Please specify.....

Please define other training that the first responder receives :

.....

(B) Information Technology (IT) Systems in your Trust.

Please specify which systems are :

Installed and functioning (I & F) <input type="checkbox"/>	Process of installation (P of I) <input type="checkbox"/>
Not installed (N I) <input type="checkbox"/>	

a) Computer aided dispatch: I & F P of I N I
 If yes,- please specify the system in use:

b) Criteria Based Dispatch or I & F P of I N I
 Advanced Medical Priority
 Dispatch System

c) Automatic Vehicle Location System: I & F P of I N I

d) System Status management
 (Defined as: deployment of units based upon historic
 patterns of demand using computer modelling):
 I & F P of I N I

e) Please describe any other IT systems that you regard as important and you would wish to have
 if resources allowed

(C) EMS design for the future.

The following series of statements are designed to gauge your opinion of particular aspects of
 EMS system design. Please indicate your choice by putting a **circle around a number to show
 the extent** to which you either disagree or agree with each of the statements.

For example, if you **totally disagree circle 0**, if you **totally agree circle 9**, or your opinion may
 be somewhere in between.

e.g. Totally disagree 0 1 2 3 4 5 6 **7** 8 9 Totally agree

Dispatch criteria:

1) A paramedic (ALS) unit should be sent to all calls received by the dispatch centre.
 Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

2) The paramedic (ALS) unit should be sent to all category A calls and all category B calls only.
 Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

3) The ALS unit should be sent to all category A and selected category B calls (identified by the
 dispatch centre).
 Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

4) Technicians with an advisory external defibrillator (T-AED)) unit can be sent to selected
 category A and B calls (identified by the dispatch centre) and all category C calls.
 Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

5) A first responder unit can be sent to **selected** category C calls.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

6) A first responder unit can be sent to **all** category C calls.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

7) An assumed or confirmed cardiac arrest should receive an automatic additional response from other units in the vicinity-either ALS or technicians.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

8) The optimal number of staff to attend a pre-hospital cardiac arrest is:

2 [] 3[] 4[] 5[] 6 []

Development of advanced skills for paramedics.

1) A small cadre of paramedic ‘practitioners’ with additional skills (eg. able to use anaesthetic agents for endotracheal intubation in head injured patients or others with a compromised airway but a gag reflex) should be developed as a part of the system.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

2) Paramedics should be taught to carry out and interpret 12 lead ECGs for patients with chest pain in the prehospital setting.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

3) Paramedics should be taught to carry out thrombolysis for patients with confirmed acute myocardial infarction on a 12 lead ECG.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

Transportation criteria.

1) If after assessment by a paramedic unit, ALS skills are not required, certain Category B patients can be handed over to an T-AED unit for transportation to hospital.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

2) If after assessment by a paramedic unit, ALS skills are not required, certain Category B patients and all Category C patients can be handed over to a non-Paramedic (an T-AED unit or first responder unit) for transportation to hospital or other health care facility.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

Development of a first responder system.

1) A first responder system should be trained and fully integrated into an EMS system.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

2) Members of a first responder system should be employed solely by the Ambulance service.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

3) A first responder system should be made up partly of members of the voluntary services.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

4) A first responder system should include members of the police service with Advisory External Defibrillators (AEDs).

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

5) A first responder system should include members of the Fire Service with AEDs.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

6) A first responder should include appropriately trained members of the local community.

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

Please indicate who you think would be appropriate?

Overall system design.

1) What do you consider to be the best EMS system overall (taking into account the considerations outlined earlier on the cover page) :

Please tick one of the two choices below.

The **existing single-tiered** advanced life support system (paramedic on every front line ambulance) with additional paramedic fast response units (vehicle or motorcycle).

A **tiered system** with two or more of the following: **(Please tick two or more)**

(i) ALS paramedic units and a number of additional 'fast response' paramedic units .

(ii) Technician units with advisory external defibrillators (T-AED)

(iii) 'First responder' units with AEDs.

Any other general comments:

Thank you very much for your help. Please return this questionnaire in the enclosed SAE to Dr Taj Hassan, Dept of A&E Medicine, Leicester Royal Infirmary, Leicester LE1 5WW . Please indicate if you would like further information and details of the study results.

Yes, please send me further details :

No thank you:

Questionnaire Number:.....

(For collection purposes only)

(2nd Questionnaire : sent to respondent number 12.)

Appendix 2b

**Emergency Medical Service (EMS) systems in the UK :
Suggestions for their future design – Questionnaire 2.**

- The following series of statements are designed to gauge your opinion of particular aspects of EMS system design.
- The asterisk (*) indicates the number you selected to indicate the extent to which you agreed or disagreed with the statement in response to the previous questionnaire. Each of the numbers below the scale represents the percentage of those who responded to the first questionnaire and who selected that particular value.
- We would be grateful if you would read through the questionnaire and consider whether in the light of your colleagues' assessments, you would like to alter your response.
- Please indicate the extent to which you either disagree or agree with each of the statements by putting a circle around the appropriate number. If your choice remains unchanged please circle the same number you selected on the previous questionnaire.
- NOTE : If you wish to add comments to justify your position, please feel free to do so in the column beside the relevant question.

Remember, the asterisk(*) signifies your previous answer. You may now choose the same level of agreement with the statement OR, in view of your colleagues' opinion, you may change it to reflect some level of consensus and agreement. The scoring is the same - if you totally disagree you will circle 0, if you totally agree you will circle 9, or your opinion may be somewhere in between.

For example:	*																								
	<table border="0" style="width: 100%; border-collapse: collapse;"> <tr> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">Totally disagree</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">0</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">1</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">2</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">3</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">4</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">5</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">6</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">7</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">8</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">9</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">Totally agree</td> </tr> <tr> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">% response in each group</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">1</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">2</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">7</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">8</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">9</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">9</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">10</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">16</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">18</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">20</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;"></td> </tr> </table>	Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree	% response in each group	1	2	7	8	9	9	10	16	18	20	
Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree														
% response in each group	1	2	7	8	9	9	10	16	18	20															

Dispatch criteria:

1) A paramedic (ALS) unit should be sent to all calls received by the dispatch centre.

	*																								
	<table border="0" style="width: 100%; border-collapse: collapse;"> <tr> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">Totally disagree</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">0</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">1</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">2</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">3</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">4</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">5</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">6</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">7</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">8</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">9</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">Totally agree</td> </tr> <tr> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">% response in each group</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">56</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">12</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">12</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">4</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">2</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">2</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">0</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">2</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">6</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">4</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;"></td> </tr> </table>	Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree	% response in each group	56	12	12	4	2	2	0	2	6	4	
Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree														
% response in each group	56	12	12	4	2	2	0	2	6	4															

2) The paramedic (ALS) unit should be sent to all category A calls and all category B calls only.

	*																								
	<table border="0" style="width: 100%; border-collapse: collapse;"> <tr> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">Totally disagree</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">0</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">1</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">2</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">3</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">4</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">5</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">6</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">7</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">8</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">9</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">Totally agree</td> </tr> <tr> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">% response in each group</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">14</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">4</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">10</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">16</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">12</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">12</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">2</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">18</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">6</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;">6</td> <td style="border-top: 1px solid black; border-bottom: 1px solid black;"></td> </tr> </table>	Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree	% response in each group	14	4	10	16	12	12	2	18	6	6	
Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree														
% response in each group	14	4	10	16	12	12	2	18	6	6															

3) The ALS unit should be sent to **all** category A and **selected** category B calls (identified by the dispatch centre).

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group **4 - 2 - 2 - 2 - 2 - 4 - 4 - 10 - 16 - 54**

4) Technicians with an advisory external defibrillator (T-AED) unit can be sent to **selected** category A and B calls (identified by the dispatch centre) and **all** category C calls.

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group **6 - 2 - 2 - 2 - 4 - 12 - 8 - 14 - 16 - 34**

5) A first responder unit can be sent to **selected** category C calls. (PLEASE SPECIFY WHAT CONSTITUTES A FIRST RESPONDER IN YOUR SYSTEM:)

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group **24 - 2 - 4 - 6 - 4 - 4 - 6 - 10 - 18 - 22**

6) A first responder unit can be sent to **all** category C calls.

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group **38 - 6 - 16 - 4 - 2 - 10 - 2 - 8 - 2 - 12**

7) An assumed or confirmed cardiac arrest should receive an automatic additional response from other units in the vicinity-either ALS or technicians.

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group **6 - 4 - 2 - 6 - 2 - 8 - 4 - 16 - 8 - 44**

8) The optimal number of staff to attend a pre-hospital cardiac arrest is:

*

	2 []	3 []	4 []	5 []	6 []
% response in each group	20	54	26	-	-

Development of advanced skills for paramedics.

1) A small cadre of paramedic ‘practitioners’ with additional skills (eg. able to use anaesthetic agents for endotracheal intubation in head injured patients or others with a compromised airway but a gag reflex) should be developed as a part of the system.

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group 4 - 2 - 6 -4 - 2 -12-4- 16-18-34

2) Paramedics should be taught to carry out and interpret 12 lead ECGs for patients with chest pain in the prehospital setting.

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group 2- 0- 6 -8 - 4 - 2- 8- 12-10-48

3) Paramedics should be taught to carry out thrombolysis for patients with confirmed acute myocardial infarction on a 12 lead ECG.

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group 6 - 0 - 4 - 8 - 2- 10-4 -14-16-36

Transportation criteria.

1) If after assessment by a paramedic unit, ALS skills are not required, certain Category B patients can be handed over to an T-AED unit for transportation to hospital.

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group 6 - 2 - 4 -6 - 2 -4 - 6 -18-20-32

2) If after assessment by a paramedic unit, ALS skills are not required, certain Category B patients and all Category C patients can be handed over to a non-Paramedic (an T-AED unit or first responder unit) for transportation to hospital or other health care facility.

*

Totally disagree	0	1	2	3	4	5	6	7	8	9	Totally agree
------------------	---	---	---	---	---	---	---	---	---	---	---------------

% response in each group 6 - 4 - 4 -4 - 0-10 -8- 18-18-28

Development of a first responder system.

1) A first responder system should be trained and fully integrated into an EMS system.

*

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

% response in each group 0 - 0 - 0 - 2 - 4 - 6 - 14 - 18 - 6 - 50

2) Members of a first responder system should be employed solely by the Ambulance service.

Left blank by you

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

% response in each group 28 - 6 - 12 - 6 - 6 - 8 - 4 - 10 - 8 - 10

3) A first responder system should be made up partly of members of the voluntary services.

*

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

% response in each group 6 - 6 - 6 - 10 - 6 - 24 - 14 - 6 - 2 - 20

4) A first responder system should include members of the police service with Advisory External Defibrillators (AEDs).

*

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

% response in each group 6 - 2 - 12 - 4 - 2 - 18 - 12 - 10 - 10 - 24

5) A first responder system should include members of the Fire Service with AEDs.

*

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

% response in each group 6 - 4 - 10 - 6 - 8 - 24 - 4 - 10 - 10 - 18

6) A first responder should include appropriately trained members of the local community.

*

Totally disagree 0 1 2 3 4 5 6 7 8 9 Totally agree

% response in each group 2 - 2 - 6 - 4 - 8 - 18 - 6 - 10 - 12 - 32

Overall system design.

1) What do you consider to be the best EMS system overall (taking into account the considerations outlined earlier on the cover page) :

Please tick one of the two choices below.

The existing single-tiered advanced life support system (paramedic on every front line ambulance) with additional paramedic fast response units (vehicle or motorcycle).
(% response to previous questionnaire = 22%)

* A tiered system with two or more of the following:
(i) ALS paramedic units and a number of additional ‘fast response’ paramedic units.
(ii) Technician units with advisory external defibrillators (T-AED)
(iii) ‘First responder’ units with AEDs.
(% response to previous questionnaire = 78%)

Any other general comments:
.....
.....

Thank you very much for your help. Please return this questionnaire in the enclosed SAE to Dr Taj Hassan, Dept of A&E Medicine, Leicester Royal Infirmary, Leicester LE1 5WW . Please indicate if you would like details of the final results and conclusions.

Yes, please send me the final results and conclusions:
No thank you:

Questionnaire Number: ... 12...
(For collection purposes only)

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Publications and presentations from this thesis.

Hassan TB. Characteristics and outcomes of patients suffering pre-hospital cardiac arrest within the Leicestershire EMS system.

Submission to *Resuscitation*.

Hassan TB, Jagger C, Barnett DB. A randomised controlled trial to investigate the efficacy of intravenous magnesium sulphate for refractory ventricular fibrillation.

Submission to *Emergency Medicine Journal*.

Hassan TB, Wailoo A, Barnett DB.

Can single 'first responder' units and priority based dispatch produce a significant impact on the outcome of pre-hospital cardio-pulmonary arrest – a cost effectiveness analysis.

Submission to *Heart*

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Emergency Medical Services (EMS) systems in the UK : Achieving consensus on their future design.

Submission to *Emergency Medicine Journal*.

Abstracts.

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