Health Technology Assessment 2000; Vol. 4: No. 31

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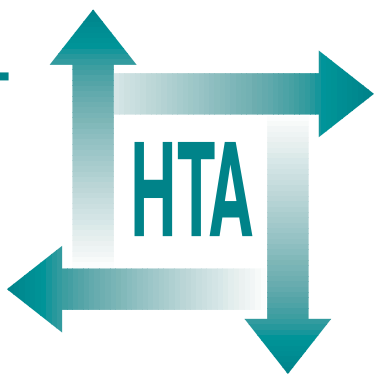
Health Technology Assessment
NHS R&D HTA Programme



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A randomised controlled trial of prehospital intravenous fluid replacement therapy in serious trauma

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Competing interests: none declared.

Published November 2000

This report should be referenced as follows:

Turner J, Nicholl J, Webber L, Cox H, Dixon S, Yates D. A randomised controlled trial of prehospital intravenous fluid replacement therapy in serious trauma. *Health Technol Assess* 2000;**4**(31).

Health Technology Assessment is indexed in *Index Medicus*/MEDLINE and *Excerpta Medica*/EMBASE. Copies of the Executive Summaries are available from the NCCHTA website (see overleaf).

NHS R&D HTA Programme

The NHS R&D Health Technology Assessment (HTA) Programme was set up in 1993 to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS.

Initially, six HTA panels (pharmaceuticals, acute sector, primary and community care, diagnostics and imaging, population screening, methodology) helped to set the research priorities for the HTA Programme. However, during the past few years there have been a number of changes in and around NHS R&D, such as the establishment of the National Institute for Clinical Excellence (NICE) and the creation of three new research programmes: Service Delivery and Organisation (SDO); New and Emerging Applications of Technology (NEAT); and the Methodology Programme.

This has meant that the HTA panels can now focus more explicitly on health technologies ('health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care) rather than settings of care. Therefore the panel structure has been redefined and replaced by three new panels: Pharmaceuticals; Therapeutic Procedures (including devices and operations); and Diagnostic Technologies and Screening.

The HTA Programme will continue to commission both primary and secondary research. The HTA Commissioning Board, supported by the National Coordinating Centre for Health Technology Assessment (NCCHTA), will consider and advise the Programme Director on the best research projects to pursue in order to address the research priorities identified by the three HTA panels.

The research reported in this monograph was funded as project number 93/23/19.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health. The editors wish to emphasise that funding and publication of this research by the NHS should not be taken as implicit support for any recommendations made by the authors.

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The editors and publisher have tried to ensure the accuracy of this report but do not accept liability for damages or losses arising from material published in this report. They would like to thank the referees for their constructive comments on the draft document.

ISSN 1366-5278

Published by Core Research, Alton, on behalf of the NCCHTA.
Printed on acid-free paper in the UK by The Basingstoke Press, Basingstoke.

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Contents

List of abbreviations

A&E	accident and emergency
AIS	Abbreviated Injury Scale
ALS	advanced life support
BASICS	British Association of Immediate Care Scheme
BLS	basic life support
CI	confidence interval
CONSORT	Consolidation of Standards for Reporting Trials
df	degrees of freedom*
EMT	emergency medical technician*
ICD-10	International Statistical Classification of Diseases and Related Health Problems
ISS	Injury Severity Score
MTOS	Major Trauma Outcomes Study*
NS	not significant*
OR	odds ratio*
PAS	patient administration system
PRF	patient report form
RR	relative risk*
RTS	Revised Trauma Score
SBP	systolic blood pressure*
SD	standard deviation*
SE	standard error*
SF-36	Short Form with 36 items
T-RTS	Triage Revised Trauma Score
TS	Trauma Score*

* Used only in tables

Executive summary

Introduction

The initiation of intravenous fluid replacement in injured patients at the accident scene is becoming a routine procedure. It has been assumed that early volume replacement in a bleeding patient will result in the patient arriving at hospital in a better haemodynamic state than if no fluids are given. However, some non-randomised studies of trauma patients and one quasi-randomised study of patients with severe bleeding injuries have begun to cast doubt on this assumption.

In the UK most on-scene fluid therapy is given by ambulance-service paramedics acting in accordance with their protocols. We therefore conducted a pragmatic study to compare the effects of two different fluid protocols, one usually with fluid administration and one usually without, used by paramedics.

Methods

With approval from 16 local research ethics committees, paramedics in two ambulance services were randomly allocated to one of two treatment protocols for the prehospital use of intravenous fluids in adult trauma patients.

- Protocol A: intravenous fluids were administered at the incident scene to all adult trauma patients who under current procedures the paramedic would consider starting on intravenous fluids.
- Protocol B: fluids were withheld until arrival at hospital, unless the time to hospital was likely to be over 1 hour.

Paramedics who had been qualified for at least 1 year were randomised to an initial treatment protocol using a simple random-number generator. Approximately half way through the trial the paramedics were crossed over to the alternative protocol.

Trauma patients aged 16 years or over who died or stayed in hospital for three or more nights and who were attended by a paramedic crew randomised to a treatment protocol were included in the study. Patients with burns, poisoning, asphyxiation, minor uncomplicated skin or skeletal injuries, isolated fractured neck of femur, or who were pregnant were excluded.

Death, complications, general health status (measured using the Short Form with 36 items (SF-36) questionnaire), processes of care and costs were measured up to 6 months post-incident.

Data collection

Characteristics of the incidents, the patients and their injuries, and the crews attending were taken from: ambulance-service dispatch records and patient report forms; hospital accident and emergency (A&E), inpatient and administrative records; and from coroners' records. Death was assessed from hospital and coroners' records at 6 months post-incident, and all survivors identified within 7 months of their accident (n = 878) were sent a follow-up questionnaire, which included the SF-36 health status questionnaire, and asked about use of healthcare services.

Results

In total 1309 patients were entered in the study: 699 (53.4%) were treated by paramedics operating protocol A and 610 (46.6%) were treated by paramedics operating protocol B.

The randomisation worked well and there were no significant differences between treatment groups in incident characteristics, ambulance performance times, or patient or injury characteristics, apart from slightly more moderate or severe head injuries in the protocol A group (25.3% versus 20.3%).

Protocol compliance was poor, with only 31% of protocol A patients receiving prehospital fluids and only 80% of protocol B patients not given fluids. The estimated odds ratio for being given prehospital fluids when treated by protocol A compared to protocol B was 2.09 (95% confidence interval (CI), 1.53 to 2.81).

Mortality
There were 73 deaths within 6 months in the 699 patients in the protocol A group (10.4%), and 60/610 (9.8%) in the protocol B group. Thus the crude odds ratio for deaths when managed by protocol A was 1.07 (95% CI, 0.73 to 1.54).

Excluding 26 patients whose cause of death may not have been trauma related, the odds ratio was 1.04 (95% CI, 0.69 to 1.55). Excluding 17 patients who may have been dead on arrival of the ambulance at the scene the odds ratio was 1.04 (95% CI, 0.70 to 1.53).

Adjustment for age, injury severity and whether the patient was unconscious at the scene did not significantly alter these odds ratios.

Complications
A total of 106 patients were identified from hospital notes as having at least one of eight major complications (adult respiratory distress syndrome, sepsis, acute renal failure, coagulopathy, wound infection, pneumonia, fat embolism or pulmonary embolism). The proportions with recorded complications were similar in the two groups: 60/699 (8.5%) in the protocol A group versus 46/610 (7.5%) in the protocol B group.

Health status
A total of 878 questionnaires were sent to patients, and 559 (64%) usable replies were received. The response rate was similar in the two groups (62.9% versus 64.6%). In all eight dimensions of the SF-36 health status measure patients who had been managed by paramedics operating protocol A reported better average health than did patients in the protocol B group. However, none of the differences were at a level considered clinically important and only for one of the eight dimensions was the difference statistically significant.

Composite outcomes
No significant differences in outcome were found between the two protocol groups in terms of patients who either died or had serious complications, nor for patients who either died or had known poor health.

Subgroups
Subgroups of patients were defined on eight characteristics (ambulance service area, whether a doctor was on scene, paramedic–patient contact time, injury severity, whether taken to theatre for emergency surgery, type of injuries, type of area, and whether the patient was treated before or after protocol cross-over). There was no evidence of any difference in mortality rates or composite outcomes between any subgroups, or between protocols within any subgroup.

Time to A&E department
The analysis suggests that patients given fluids spent 12–13 minutes longer at the accident scene than did patients not given fluids. However, because only one-quarter of patients were given fluids, and the specific protocol used made little difference to this, average on-scene times were largely unaffected by protocols.

Costs
In the prehospital and immediate-care phase (including A&E treatment), the mean costs of the protocol A and protocol B groups were £419 and £416, respectively. This small difference reflects two small and offsetting effects of protocol B: reduced on-scene time ($p = 0.08$) and increased use of blood in the A&E department ($p = 0.03$). There were no other statistically significant differences in costs, with the mean total costs being £2706 and £2678 in the protocol A and protocol B groups, respectively ($p = 0.52$).

Conclusions
This study does not support the idea that protocols recommending fluid administration do harm in blunt trauma patients. Previous studies have shown that, even though the initiation of intravenous fluids by paramedics seems to be associated with an increased risk of death, this may not be remediable by altering fluids protocols. It is possible that either giving fluids early does no harm, or that only one-quarter of patients are given fluids, and thus the specific protocol used makes little difference to this proportion. Ambulance services should therefore concentrate on avoiding unnecessary delays and speeding up transfer to definitive care in hospital rather than concentrate on their fluids protocols.

Recommendations for future research
- The relationship between the time taken by paramedics on scene and outcome in blunt trauma may be the critical issue, and this needs investigation.
- One way of avoiding on-scene delay is to start fluid infusion in the ambulance en route to hospital, but further research into the

advantages and difficulties of this approach is needed.
- Any future research in the UK into the benefits in blunt trauma patients should compare strict no-fluids protocols (as would be operated by technicians) rather than discretionary protocols. Ways of separating out the effect of fluid infusion and on-scene time delays should be sought.
- The fluids issue remains unresolved. It is not just a problem for prehospital care but also for care prior to definitive surgery. Is the giving of intravenous fluids appropriate in A&E departments? Do the same arguments about the time taken to reach theatre or pretheatre resuscitation apply, and if so can a trial to prevent fluid resuscitation in blunt trauma patients prior to arrival in theatre be organised?

Chapter 1
Introduction

The initiation of intravenous fluid replacement in injured patients at the accident scene is rapidly becoming a routine procedure, although there is no clear evidence that this treatment improves patient outcome. The perceived benefits of prehospital fluid therapy are based on the assumption that early volume replacement in the bleeding patient will result in the patient arriving at hospital in a better haemodynamic state. However, there is growing evidence that this assumption is questionable. Arguments against the use of early intravenous fluids centre around two issues. Firstly, that extra time spent on scene initiating fluid therapy leads to a delay in transport to hospital and hence to definitive care, and secondly that the concept that any volume replacement must produce a beneficial effect is flawed.

The first stage of fluid therapy is insertion of an intravenous cannula. Substantial variation has been reported in the time taken to complete this task. One US study found the time taken to establish intravenous access was between 8.6 and 11.5 minutes[1] and another that on-scene time was increased by 13 minutes[2] when this procedure was carried out. In the UK, it has been shown that intravenous cannulation is associated with increased on-scene times.[3,4] Others have found that intravenous placement does not necessarily increase on-scene time[5] and that a cannula can be inserted in less than 90 seconds.[6]

It is also recognised that the speed with which intravenous access can be gained is related to the competence of the practitioner. This is determined by both training and the frequency with which the procedure is carried out. The majority of the reported studies have been carried out in the USA, where training varies between states.[7] This may have some influence on the efficiency with which cannulation takes place. It has also been suggested that paramedics in rural settings may perform the task less competently than their urban counterparts as advanced life support (ALS) skills are used less frequently.[2] However, a comparison of intravenous placement by urban and non-urban paramedics in the USA showed no difference in the time taken to carry out the procedure.[8]

The primary concern about prolongation of on-scene times in urban areas is that this may exceed the time taken to transport the patient to hospital and delay definitive treatment.[1] In this situation it is hard to justify carrying out such a procedure. It has been reported that intravenous cannulae can be successfully placed en route to hospital, thus avoiding any delay in transport.[9] However, even if on-scene times are unaffected by intravenous placement there is no evidence to demonstrate that the administration of intravenous fluids improves patient outcome. At best, mortality in patients who receive prehospital intravenous fluids is the same as those who do not.[10,11] One study of the effects of prehospital intervention in penetrating cardiac wounds found mortality increased in patients who received on-scene ALS treatment including intravenous fluids.[12] Another study conducted over an 8-year period reported a decrease in mortality in one group of patients with open abdominal intravascular trauma, but it is difficult to distinguish the effects of prehospital treatment from other changes that may have occurred over this period.[7] Some studies have used physiological change, most notably the change in systolic blood pressure, as the outcome measure for intravenous fluid therapy. While a change in this parameter has been found, it does not appear to result in a better outcome for the patient.[11] In one study 91% of patients who died unexpectedly had their blood pressure raised during the prehospital phase.[8] Explanations for these findings might be found in the relationships between the types of fluids used, the infusion rates and the physiological processes that accompany circulatory volume loss.

Studies that have attempted to measure the effects of prehospital intravenous fluids have predominantly used crystalloid infusion as recommended by American Advanced Trauma Life Support guidelines.[13] There are several disadvantages to this strategy. Computerised modelling of intravenous fluid therapy has suggested that potential benefits of crystalloid infusion will only occur if there is a bleeding rate of 25–100 ml/min, the rate of fluid infusion is at least equal to the bleeding rate, and if the prehospital time exceeds 30 minutes.[14] In practice, these criteria are unlikely to be met. One study

found that, while the 30 minute criterion was just exceeded, the volumes infused were small, with the most seriously injured patients receiving an average of only 620 ml. Blood loss in these patients could exceed 1500 ml in the 10 minutes it took to establish intravenous fluids.[10] For the seriously injured patient, bleeding at a rate of 50 ml/min, it is almost impossible, in practice, to provide an adequate volume of crystalloids since only one-quarter of infused fluid stays in the vascular system. Thus 200 ml/min would be required to replace volume loss and this cannot be achieved through the small-bore cannulae used by paramedics.[15]

Animal experiments have also shown that aggressive crystalloid infusion in uncontrolled haemorrhage results in increased bleeding and decreased survival.[16] Survival is worst in animals receiving the largest volume of fluid.[17] Although the mechanisms are not fully clear, it is possible that the volumes infused prevent vasoconstriction and clot formation and cause fluid accumulation in the extracellular space. Attention has therefore turned to the usefulness of other types of fluid in the treatment of hypovolaemia.

Hypertonic saline and mixtures of hypertonic saline and colloid have been suggested as suitable fluids for prehospital use. Small volumes of these solutions have been shown to improve survival in animals subjected to controlled haemorrhage.[18] However, their use in uncontrolled haemorrhage, when fluid resuscitation begins whilst bleeding is still occurring, has produced conflicting results in animals[19,20] and inconclusive results in humans.[21]

Overall, there is no convincing evidence that prehospital treatment with intravenous fluid in the non-trapped patient in the urban setting produces any benefits, although there is evidence that crystalloids may be harmful in some situations. If the time to hospital is short, even the most severely injured patients show no increase in mortality if intravenous fluids are witheld.[22] In this instance 'load and go' is the favoured option. At the other extreme, for the severely injured trapped patient in whom prolonged extrication is envisaged, or in very rural areas where transport times are long, prehospital intravenous fluids may have a more important role to play if exsanguination is to be avoided. In these circumstances large volumes of fluid, including blood, may be required under medical direction. For intermediate transport times (15–60 minutes) there may be some advantage to giving mixed fluids, although this is unproven.

Irrespective of whether the patient is being treated at the scene, in an ambulance or in hospital, there is no clear evidence to guide when any fluid therapy should be commenced. It is this question of whether the giving of fluids should be started at the scene or delayed until arrival at hospital which is particularly amenable to a controlled trial within the UK. Paramedic training is standardised through the NHS Training Division, so there are no training differences that may affect a paramedic's ability to provide venous access. Competence is maintained by statutory continuing education. UK paramedics practice independently at the incident scene, so an intravenous fluid protocol can be carried out without having to seek medical permission, as is usually required in the USA. Finally, unlike their counterparts in the USA, paramedics in the UK are not restricted to using crystalloid only in the prehospital phase and, although they do not use hypertonic solutions, they are familiar with administering mixed crystalloid and colloid regimens. The therapeutic value of colloid administration has recently been questioned,[23] and this is discussed more fully later. However, at the start of this study, the administration of colloid in the prehospital phase of care was part of the standard protocol for intravenous fluid infusion in UK ambulance services.

The aim of this study was to examine the effects of the policy of the administration by paramedics of intravenous fluids in the prehospital setting. We conducted a randomised controlled trial of two paramedic treatment protocols. The first protocol involved the use of a combined crystalloid and colloid fluid regimen started as soon as possible. The second protocol involved giving no fluids to injured patients who were not *in extremis* or delayed giving fluids if the prehospital time was long.

Chapter 2
Methods

Overview

Paramedics in two ambulance services were randomly allocated to one of two treatment protocols for the prehospital use of intravenous fluids in adult trauma patients. One protocol required fluid administration to be started at the incident scene and the other for fluids either to be witheld until arrival at hospital or the administration of fluids to be delayed if the time to hospital was likely to be longer than 1 hour after arrival of the ambulance crew at the incident scene. The protocols were used over a 17-month period from May 1996 to September 1997 inclusive.

With some minor exceptions (outlined below), all trauma patients aged 16 years or over attended by a paramedic crew randomised to a treatment protocol and who died or stayed in hospital for three or more nights were included in the study. Surviving patients were followed up 6 months after the incident.

Details about the incidents, patients and attending ambulance crews were recorded. Processes of care, outcomes and costs were assessed and compared between the two treatment groups. Analyses were made on the basis of the protocol to which the attending paramedic was randomised.

The methods used are outlined below in more detail.

Study areas

Two ambulance-service areas were used for the study. These services were chosen to reflect the full range of distances, and hence times, to definitive hospital care that is typical in English counties. Both areas included a mix of urban, suburban and rural environments, with some very rural, sparsely populated areas in area 1 (*Table 1*).

Approval for the study

Approval for the study was sought from the 17 local research ethics committees which covered the hospitals to which the study patients would be taken. Ethical committee approval was granted by 16 of these committees. One ethical committee in area 1 refused to grant approval. We appealed against this decision, provided written justification for the study and attended in person a meeting of the ethics committee to discuss the project in detail. In addition, the two accident and emergency (A&E) consultants at this hospital wrote to the committee stating their support for the trial. However, the committee did not change their decision, giving their reasons for refusal as being a strong objection by one clinician "whose subjective opinion was that patients who had early intravenous fluids did better", and that the study was inappropriate for patients in the particular geographical area around this hospital. This was despite the fact that the ethical committees for all the surrounding areas, some of which had identical geographical characteristics, had all approved the study. As a consequence of this decision, 35 paramedics located at the three ambulance stations that served this area had to be excluded from the study.

Following ethical committee approval, the A&E consultants, medical directors and chief executives of each of the 17 hospitals were contacted by letter to obtain permission for

TABLE 1 *Ambulance service areas included in the study*

	Area 1	Area 2
Population (millions)	2.14 (4.0*)	1.0
Operational area (miles†)	4835	986
Population/mile†	442	1000
Cities and major urban areas	4	1
Ambulance stations	34	11
Major A&E departments used†	9	9

**Peak summer time population*

†Numbers denote A&E departments served. Not all were within the ambulance service operational area. In area 2 there was one major department within the county. The other eight departments were in neighbouring counties and were used as they were the nearest hospital for incidents occurring around the county boundaries. One A&E department was used by both services

access to the A&E department records and inpatient medical records of the patients included in the study. These were followed up by personal visits to the hospitals by the researchers for each area, who established contacts in both the A&E and medical records departments. Access to both computerised records (A&E and patient administration system (PAS)) and medical records was given at all the hospitals. Similarly, access to computerised records and patient report forms (PRFs) was obtained in each of the two ambulance services.

Interventions

The primary interventions were protocols for early, or no or delayed infusion of intravenous fluids to adult trauma patients in the prehospital phase of care. An operational protocol was designed for each of these alternatives:

- Protocol A: intravenous fluids were to be administered following primary patient assessment.
- Protocol B: intravenous fluids were to be withheld for the first hour of prehospital care.

In practice this meant that protocol B patients who arrived at hospital within 1 hour of the ambulance crew's arrival on scene may have received no fluids. If the prehospital time exceeded 1 hour then some patients would receive fluids, but initiation of this intervention would be delayed. Protocols A and B both stated that, within these time constraints, fluids could be given in accordance with the currently operational clinical protocol for paramedics giving fluid infusions. This standard clinical protocol is given in appendix 1.

The protocols were initially designed by the clinical collaborator (DY) and were amended following consultation with the ambulance service Medical Advisory Groups and A&E consultants. The final protocols were approved by the Medical Advisory Groups of each service. The study was also approved by the Trust boards of the two services and the protocols were adopted as paramedic standing orders for the duration of the trial. This safeguarded the legal position of the paramedics where there was a change in practice.

The paramedics in both protocol groups were given a check-list of initial patient assessment and management items and specific instructions for intravenous fluid infusion. The details of the two protocols are given in *Boxes 1* and *2*.

BOX 1 Protocol A

Protocols for intravenous infusion in adult trauma patients

- Complete primary survey of:
  – airway
  – breathing
  – circulation
- Secure airway with cervical spine control
- Ensure adequate breathing
- Give high-flow oxygen via a close-fitting face-mask
- Measure pulse rate
- Measure capillary refill (normally less than 2 seconds)
- Splint obvious fractures and give Entonox® as necessary
- Obtain details of incident and assess forces applied to patient
- Consider possibility of concealed bleeding in chest, abdomen and pelvis

Protocol A

- Measure blood pressure
- Establish an intravenous line (large cannula) with crystalloid to keep line open
- Measure respiratory rate
- Assess Glasgow Coma Scale score
- If any of the indicators given in the current operational protocols for intravenous infusion are present:
  – run through 500 ml crystalloid rapidly
  – start 500 ml Haemaccel® and continue administering according to current procedure up to a limit of 2000 ml of total fluid
  – seek advice on further transfusions over 2000 ml from A&E department
- **Do not delay extraction or transfer to establish this intravenous line or administer intravenous fluids**
- En route to hospital:
  – repeat primary survey
  – measure blood pressure
  – measure respiratory rate
  – assess Glasgow Coma Scale score

In protocol A the crystalloid used in both areas was Hartmann's solution (compound sodium lactate). In protocol B the original instruction was not to set up an intravenous line for the purpose of fluid infusion. An intravenous cannula could be inserted for other reasons, for example the administration of intravenous analgesia. However, at the outset

BOX 2 Protocol B

Protocols for intravenous infusion in adult trauma patients

- Complete primary survey of:
  – airway
  – breathing
  – circulation
- Secure airway with cervical spine control
- Ensure adequate breathing
- Give high-flow oxygen via a close-fitting face-mask
- Measure pulse rate
- Measure capillary refill (normally less than 2 seconds)
- Splint obvious fractures and give Entonox® as necessary
- Obtain details of incident and assess forces applied to patient
- Consider possibility of concealed bleeding in chest, abdomen and pelvis

Protocol B

- Measure blood pressure
- Measure respiratory rate
- Assess Glasgow Coma Scale score
- Repeat primary survey
- Ensure good airway control and maintain high-flow oxygen
- Control pain by use of Entonox® and splints as appropriate
- **Do not set up an intravenous line for the purpose of fluid infusion**
- **If after 45 minutes from arrival at the scene the patient is still at the scene or in transit**
  – and the estimated time to the A&E department is less than 15 minutes, do not start fluids
  – and the estimated time to the A&E department is greater than 15 minutes, administer fluids if necessary in accordance with current operational protocols in your area
  – **Do not delay extraction or transfer to establish this intravenous line or administer intravenous fluids**
- En route to hospital:
  – repeat primary survey
  – measure blood pressure
  – measure respiratory rate
  – assess Glasgow Coma Scale score

of the trial some paramedics and one A&E consultant expressed anxieties that delaying the insertion of a cannula could prove problematic, particularly in patients whose clinical condition suddenly and rapidly deteriorated, following which intravenous access could be difficult. It was therefore agreed that, if the prehospital time was likely to be long, for example if the patient was trapped or if there was a long distance to hospital, then a cannula could be inserted early, as long as this did not delay extrication or transfer of the patient to hospital.

Randomisation

Paramedics

There were two randomisation options: to randomise patients to one of the intravenous fluid protocols at the incident scene, or to randomise paramedics to a treatment protocol. Random allocation of a protocol to patients presented several difficulties. Firstly, there were issues around the requirement to obtain informed consent to randomisation from patients at the incident scene. For some patients, for example those who were unconscious, this would not be possible. For others, even if awake and talking, the process of providing information and requesting consent from an injured person immediately after an accident seemed inappropriate. Furthermore, this process, if carried out properly, would inevitably lead to delays at the scene and would therefore be contrary to the basic prehospital care management principle of transporting the patient to hospital as quickly as possible. It is possible to waive the requirement to obtain informed consent in certain emergency situations and critical patient conditions.[24] However, it was envisaged that the patient group eligible for inclusion in this trial was likely to be sufficiently heterogeneous with respect to injury type and physiological condition at the incident scene that the waiver conditions would not apply in every case. This could lead to difficulties for the attending paramedics, as they would be required to decide whether or not informed consent should be sought.

Secondly, if each patient were randomised to a treatment protocol at the incident scene, paramedics would be required to be familiar with both protocols, and to be constantly changing between the two. The inability to predict in advance the method of management to be used with respect to intravenous fluids could slow down the patient-management process.

Finally, the difficulties in obtaining consent and the lack of consistency in patient management could potentially result in low compliance by the paramedics involved.

Because of these practical difficulties it was decided to randomise each paramedic, rather than patients, to one of the two treatment protocols. The advantage of this approach was that there was no requirement for consent to be obtained prior to giving treatment, as no choice was involved. Treatment was prescribed by the paramedic's standing order for intravenous fluid therapy, which was determined by the protocol to which the attending paramedic had been assigned. In addition, working with just one protocol allowed the paramedic to become familiar with a single method of treatment, and thus to provide consistent and more efficient patient management, and removed the potential delay that could occur if randomised treatment choices had to be made at the incident scene. This process also reduced the obstacles to protocol compliance.

A potential problem with randomising paramedics was possible skill decay in the paramedics randomised to the protocol B if this was assigned for the entire duration of the trial. This could be avoided by swapping the assigned protocol half way through the trial. This both limited the length of time for which paramedics would be restricted in the use of intravenous fluids and ensured that any differences in individual paramedic practice were equally distributed in each treatment group.

A further advantage to this strategy was that, by using both treatment protocols, paramedics would manage patients in both treatment groups and hence remove the possibility that, if there was a substantial difference in patient outcome between the two treatment groups, no paramedic would have treated only patients in the group with the poorest outcome.

Randomisation was stratified by base ambulance station (34 in area 1 and 11 in area 2). For each station a random string of digits equating to protocols A and B was computer generated. Paramedics were listed by station and sequentially assigned a treatment protocol from the random-number string for that station. To ensure that the paramedics involved in the trial had received some operational exposure to the use of intravenous fluids, only paramedics who had been qualified as NHS Training Division paramedics for at least 1 year were included at the start of the study. Additional paramedics were randomised to a treatment protocol during the course of the trial when they had been qualified for 1 year. At the outset a total of 311 paramedics, 237 in area 1 and 74 in area 2 were randomised, with an additional 90 paramedics added during the study (72 in area 1 and 18 in area 2), giving a total of 401 paramedics in all.

Immediate-care doctors

There were four British Association of Immediate Care Schemes (BASICS) operating in the study areas, three in area 1 and one in area 2. At the outset of the study it was intended to exclude any patient attended on scene by a doctor, as a doctor's scope of practice, including the use of intravenous fluids, extends beyond that of paramedics, and the purpose of this study was to examine paramedic practice. However, all four BASICS readily supported the study and did not want to limit the number of patients available for inclusion. One scheme in area 1 was particularly active and requested that the doctors be randomised to the same treatment protocols as the paramedics. As a result, a total of 54 BASICS doctors were also randomised to protocols A or B and they also swapped protocols half way through the trial. However, for the purpose of analysis, the assigned protocol for a case was considered to be the protocol of the attending paramedic unless a BASICS doctor randomised to a protocol was recorded in the paramedic's PRF as being the first on the incident scene, in which case the assigned protocol was that of the doctor.

The other BASICS were less active and doctors were not randomised to protocols, but it was agreed that if a doctor attended an incident where a paramedic randomised to a treatment protocol was also present they would adhere to the protocol of the attending paramedic. Therefore, patients attended by BASICS doctors not randomised to protocols were also included in the study.

Patients treated at the scene by other doctors, for example those who were opportunistically present at the time of an incident or a local general practitioner (GP) in rural areas, were excluded unless it was stated on the PRF that the paramedic protocol had been applied and that the treatment given was consistent with the protocol. In area 1 a large number of GPs who were not part of a BASICS were available for call out to an incident, particularly in rural areas. During the pilot phase

of the trial a number of cases were excluded because attending GPs had administered fluids to patients where initially a no-fluids protocol had been applied by the paramedic at the incident scene. In order to limit the number of exclusions, all these GPs were sent summary information about the trial and a letter requesting that, if they attended an incident where a paramedic randomised to a treatment protocol was also present, where possible the paramedic protocol be followed. In general, this request was adhered to for the remainder of the trial.

Implementation of the treatment protocols

Prior to the start of the trial a number of information sessions were held for paramedics in both areas. Every paramedic eligible for randomisation was written to personally and invited to attend one of the sessions. A total of 12 sessions were held, ten in area 1 and two in area 2. Daytime and evening sessions were held in order to accommodate shift patterns. BASICS doctors and staff from the local A&E departments were also invited to attend.

The sessions were given by the research team (JT, HC, EW) and members of the ambulance-service training departments. They comprised a formal presentation outlining the background to the research, the research problem, the design of the trial, the data to be collected and how the data would be analysed. This was followed by an informal discussion in which any questions the paramedics had could be answered and any anxieties about the study addressed. Paramedics were also given an information pack containing details of the study, a list of the information we would require and reiteration of the importance of completing PRFs as fully as possible, details of patients to be included and excluded from the trial and instructions on when the intravenous fluids protocols should be used. The paramedics were also given the protocol they had been randomised to on a pocket-sized, double-sided laminated card. In area 2 each paramedic was also given a personal identity number and asked to record this on their PRFs. In area 1 paramedics already had an identity number which they were required to record on each PRF they completed. Paramedics who could not attend an information session were sent an information pack and their protocol via their base ambulance station.

The information sessions were held during March and April 1996 and the trial commenced on 1 May 1996. Originally it had been intended to conduct a pilot phase for 2 months followed by a further 12 months of study, but the loss of paramedics from three stations in area 1 because ethical approval was not given meant that it was unlikely our target number of patients could be reached in this time. Consequently, the trial ran for an additional 3 months, giving a total trial period of 17 months from 1 May 1996 to 30 September 1997.

In addition to informing the A&E departments involved, immediately before the start of the trial the local Community Health Councils were sent information about the trial and, at the request of the paramedics, the relevant police and fire services were also sent information and told that they might see differences in patient management at incident scenes. The ambulance staff themselves were reminded of the start of the trial by posters sent to every station.

From 1 May 1996 paramedics randomised to the protocols were required to use these protocols. The instructions for the use of the protocols are given in *Box 3*. The decision about whether or not to initiate the protocol remained that of the individual paramedic. This is in keeping with the standing orders of the NHS Training Division, which specify that intravenous fluids be administered if signs of hypovolaemic shock are present. The standing orders do not provide more specific indicators, for example based on physiological measurements, as these have been shown to be unreliable.[25] Keeping the clinical decision about intravenous fluid treatment (and hence use of the treatment protocol) within the domain of the paramedic therefore reflected current paramedic practice.

The instruction that intravenous fluids could be administered to protocol B patients without a palpable pulse was added after paramedics expressed concern at the information sessions and felt that they would have great difficulty in withholding fluids from a patient who was *in extremis*, particularly if the journey time to hospital was likely to be long. Although it would have been preferable for the protocol to be strictly adhered to for all patients, it was decided that if some provision was not made for this small group of patients there was a much higher risk of non-compliance by the paramedics across all patients if they were not confident and committed to using protocol B.

BOX 3 Instructions for use of intravenous fluid infusion protocols A and B

The protocol should be used in the treatment of any **trauma** patient who, **under current standing procedures, you would consider starting an intravenous infusion on**

The protocols should not be used for patients who:

- are aged under 16 years (or apparently so)
- have sustained burns
- have no cardiac output or absent breathing – **resuscitation protocols take priority**
- are known to be pregnant

If you are operating to protocol B and the patient's condition deteriorates such that there is **no longer a palpable radial pulse** you may start fluids **but only in transit**. Do not delay transfer to start an infusion. **TRANSFER TO HOSPITAL REMAINS THE PRIORITY**

- Only trauma patients are eligible
- All timings in protocol B refer to times **from arrival on scene**
- Resuscitation protocols take priority
- Complete a PRF for every case
- Record if a radial pulse was present or absent
- Record the actual volume of fluid infused by the time you reach the hospital
- Every time you use a protocol record A or B and your personal study number in the PRF comments box

PRF, patient report form

Inclusion and exclusion criteria

The focus of the trial was moderate to severely injured patients who outside of the study may have routinely received intravenous fluids as part of their prehospital management by paramedic ambulance crews. However, it is difficult for the severity of injury to be properly assessed at the scene of an incident, and paramedic crews could apply the intravenous fluids protocol to patients who subsequently were found to have relatively minor injuries. The administration of intravenous fluids in these patients is unlikely to influence outcome and their inclusion would not therefore have been of value to the trial. We therefore used inclusion criteria similar to those used in the UK Trauma Audit and Research Network study (previously the Major Trauma Outcome Study),[26] which excluded patients with minor injuries. Data were collected on all adult trauma patients attended by paramedics randomised to a treatment protocol and who were transported from the incident scene to a hospital or mortuary by ambulance. The following inclusion and exclusion criteria were used to identify appropriate patients.

Inclusion criteria

All adult patients attended by a paramedic crew or BASICS doctor randomised to protocol A or B and who:

- were trauma admissions whose length of stay was three nights or more, unless it was written in the patient's notes that admission was extended for social reasons or non-trauma care (e.g. psychiatric, geriatric, general medical or palliative care)
- were trauma patients who were admitted either to an intensive care unit or to a high dependency area, which was distinctly identified as a separate unit on the hospital's administrative database
- died before arrival at hospital or in hospital, but did not die before the ambulance arrived at the scene, or who had no vital signs on arrival of the crew but who had a transient recovery of vital signs during the prehospital phase of care, when an injury of traumatic origin was stated as a cause of death
- were trauma patients transferred to another hospital for further emergency care whose total length of stay was three nights or more, or who were admitted to an intensive care unit or a high dependency area, or died from their injuries, when an injury of traumatic origin was stated as a cause of death
- all trauma patients who died within 6 months of their incident, irrespective of the above criteria, and whose death certificate listed a cause of death as the trauma sustained in the incident.

Exclusion criteria

- Poisonings, hangings, drownings and asphyxiations.
- Patients transported to hospital by helicopter.
- Any patient attended at the incident scene by a non-BASICS doctor and where the intravenous fluids protocol of the attending paramedic was recorded as having been overridden by that doctor.
- Patients dead at the scene before the ambulance arrived and who remained without vital signs for the duration of the prehospital phase of care.
- Patients with superficial skin injuries, including simple penetrating injuries.

- Any patient with burns.
- Any patient whose trauma diagnosis on admission was an isolated fractured neck of femur or single pubic rami fracture, whether or not they died.
- Patients whose trauma diagnosis on admission was an isolated simple facial injury, including simple eye injuries.
- Patients whose trauma diagnosis on admission was a simple spinal strain (i.e. acute cervical, thoracic or lumbar sprain with no fracture or dislocation).
- Patients involved in 'major incidents', as defined by each individual ambulance service.
- Any trauma patient aged or apparently aged less than 16 years.
- Any female trauma patient known to be or apparently pregnant.
- Any patient attended by a crew that had only an emergency medical technician or a paramedic qualified for less than 1 year and not randomly allocated to a treatment protocol.
- Trauma patients who were urgently referred by a GP to the ambulance service.

Children under the age of 16 years and pregnant women were not included as the fluid requirements for these patients vary and are more difficult to calculate and hence cannot be met by a standard fluid regimen. In addition, many ambulance services do not, as a matter of policy, cannulate and administer intravenous fluids to children. Similarly, the fluid requirements of burns patients are very different from the requirements of patients whose source of volume depletion is haemorrhagic, and it was the effects of fluid therapy on patients with bleeding injuries that was the focus of this study.

Case identification

Two strategies were employed to maximise the chances of identifying all trauma patients who were attended by a paramedic randomised to a treatment protocol and who met the study inclusion criteria.

Cases were initially identified from the ambulance service computerised activity data. All calls were screened to exclude medical emergencies, maternity cases, stopped calls, interhospital transfers and trauma cases that met the exclusion criteria. These data were cross-referenced with all PRFs for the appropriate months of the study period, to maximise the potential of capturing all relevant cases.

These cases were followed up at hospital using a combination of A&E department registers, resuscitation records, hospital PASs, computer-generated admission lists and A&E department notes to ascertain whether patients met the inclusion criteria. At the same time, all trauma cases brought to hospital by ambulance and admitted were also followed up. In this way patients missed from the ambulance-service records were identified, and vice versa. If no PRF could be located at the ambulance stations, from the A&E department notes or inpatient records, the patient was excluded from the study, since not all the personnel (doctors and paramedics) present at the incident scene could be identified with certainty, and information about vital signs for deciding on inclusions was missing. Approximately 5% ($n = 69$) of patients initially identified in each area were excluded for this reason.

Because patient consent was not requested at the incident scene, patients were informed of the trial after the incident. In the first instance we wrote to the patient's GP notifying them of their patient's inclusion in the study and including an information sheet detailing the study objectives. The GP was asked to inform us if the patient was known to have died or if they believed it was not appropriate to contact a particular patient. If the researchers had not been contacted by the GP within 10 days, the patient was written to directly, informing them of their inclusion in the study and providing an information sheet about the trial. Patients were also advised they would be receiving a health-status questionnaire in approximately 6 months time. At this point patients were given the opportunity to decline to be included in the follow-up study. Six months after their incidents, patients were sent another letter and a questionnaire; a reminder was sent after 2 weeks if the initial questionnaire had not been returned. In all communications the telephone number of the researcher in that area was provided so that patients who had questions or required further information could make direct contact with a member of the research team.

Due to delays in accessing data at certain hospitals, some patients were identified several months after their trauma incident. Those patients identified 6 or 7 months after their incident were sent an inclusion letter and questionnaire simultaneously. Those patients identified later than 7 months after their incident were sent an inclusion letter but not a questionnaire.

Information recorded

Prehospital

Prehospital information was abstracted from the ambulance-service PRF and the computerised activity data. The latter provided details of the date and nature of the incident, and all relevant timings (call, dispatch, arrival at scene, time left scene and arrival at A&E). Grid references for the incident location and the destination hospital were also obtained. Additional incident details were abstracted from the PRFs, including a description of the incident, the mechanism of injury (blunt or penetrating), the length of time for which the patient was trapped (if applicable), the protocol initiator, the paramedic's identity code, and if cardiopulmonary resuscitation had been given by a bystander.

On-scene details were abstracted from the PRF relating to the Triage Revised Trauma Score (T-RTS), when recorded, the condition of the patient, details of interventions and treatments carried out, including the administration of intravenous fluids and adherence to the assigned protocol, and whether a doctor was present. The T-RTS is a measure of physiological derangement calculated from the sum of values between 0 and 4 assigned to each of the Glasgow Coma Scale score, systolic blood pressure and respiratory rate. It ranges from 0, indicating no vital signs, to 12, indicating normal responses.

In hospital

Each case identified from ambulance service records was matched to an A&E department and inpatient record, and each case identified at hospital was matched to an ambulance service incident. The matching criteria used were the name of the patient (where this had been identified in the ambulance records), the date and time of the incident, the time of arrival at the A&E department and the type of incident. Where the researchers had access to manual A&E department registers and the PAS very few cases remained unmatched, and we are confident that by using both ambulance-service and hospital data to identify cases all possible inclusions, including deaths, were identified. Where computerised A&E department registers and computer-generated lists were used, direct matching to all cases was more difficult. We were reliant on the completeness of the hospital computerised lists and the correctness of the coding data used to generate the list. Cases that could not be matched with hospital admissions records were assumed to have been patients with minor injuries who were not admitted, unless the researchers had other information from ambulance records that indicated a more serious incident. The latter cases were followed up further, wherever possible, to exclude the possibility that they might have died or been transferred urgently.

Hospital information was obtained from A&E department records, inpatient notes and the PAS. Information was recorded in five sections: A&E department events, operations, inpatient stay and readmissions, injury descriptions and death details.

A&E department events

The information recorded included the time the patient spent in the A&E department, the first recorded T-RTS, fluid resuscitation (including the volumes infused and the number of units of blood given), estimated blood loss, the condition of the patient on leaving the A&E department, systolic blood pressure, peripheral pulse (present or absent) and destination after discharge from the A&E department. For patients transferred to other hospitals within 6 hours, the time of departure, the hospital transferred to, the reason for transfer and the time of arrival at the second hospital were recorded, if known.

Operations

Details were recorded of operations, including the date, day, number, time and type of operation and the outcome. For patients taken directly to theatre from the A&E department details were abstracted regarding systolic blood pressure and the presence of a pulse before induction and at the end of the procedure, the number of additional intravenous lines, the volume of fluid infused, the number of units of blood given and the estimated total blood loss.

Inpatient stay and readmissions

For patients who stayed in hospital, the date, hospital, ward type, specialty and length of stay were recorded, along with the destination on discharge. When patients were transferred between hospitals or between specialties within the same hospital, each episode was treated as a separate event. Where a patient was subsequently transferred to a hospital outside the study regions, the patient's consultant in the receiving hospital was contacted for details of final discharge date and final diagnosis, in order to complete the injury descriptions. In addition, we recorded whether or not complications that have previously identified as possibly being influenced by intravenous fluid therapy[27] occurred during the inpatient stay.

These complications are:

- adult respiratory distress syndrome
- sepsis syndrome
- acute renal failure
- coagulopathy
- wound infection
- pneumonia
- fat embolism
- pulmonary embolism.

We also recorded whether any of six pre-injury conditions thought to influence outcome following trauma[28] were present. These conditions are:

- hepatic disease
- respiratory disease
- diabetes
- cardiovascular disease
- immunocompromise.

Any readmissions to hospital for reasons directly attributable to the original injury were also recorded, detailing dates of readmission, hospital, specialty and length of stay.

Injury descriptions

A full description of all injuries sustained and their Abbreviated Injury Scale (AIS) codes[29] were made using A&E department records, inpatient notes and post-mortem reports. AIS codes indicate threat to life and range from 1, indicating a minor injury, to 6, indicating a non-survivable injury. Injury mechanism was classified as blunt or penetrating.

The injury descriptions were coded using the AIS90 dictionary[29] and Injury Severity Scores (ISSs) calculated.[30] ISSs are calculated by summing the squares of the AIS scores of the most severe injury in up to three body regions. ISSs range from 1 to 75, the latter indicating the most severe injuries.

The researchers attended several 1-day injury coding training sessions in Sheffield in order to practise and discuss difficulties. These training sessions were designed to ensure, as far as possible, consistency in scoring between the two researchers.

Death details

For all patients who died within 6 months of their incident details were recorded of the date, time and place of death and the causes of death. The cause, or causes, of death were coded according to the International Statistical Classification of Diseases and Related Health Problems (ICD-10).[31]

After discharge

Survivors were sent a postal questionnaire 6 months after their injury to assess their use of health and social services, and their health status and morbidity since their accident. Information was requested about readmissions to hospital, day-case surgery (relating to accident), outpatient visits, GP consultations and visits by other paramedical staff (e.g. district nurse and social worker). Patients were also asked about their health in general, any limitations in carrying out daily activities, the amount of help required from family or voluntary organisations, and the number of work-days lost.

Coroners' records

For trauma deaths, the coroner's records were examined. Details were abstracted of the time, date and cause of death, and a copy of the *post-mortem* report obtained to determine the injuries sustained.

Outcomes assessment

Mortality

Patients who met the study inclusion criteria and who died up to 6 months after their incident were included in the study as deaths. Patients who died up to 6 months after their incident and whose deaths were considered to be non-trauma related were treated as survivors in some analyses. Patients who died more than 6 months after their incident were included in the study as survivors. It is possible that some patients may have died within 6 months without our knowledge (e.g. if they were discharged from hospital and moved out of the area) and their subsequent deaths recorded by coroners elsewhere.

Morbidity assessment

Morbidity in survivors was assessed by postal questionnaire at 6 months after their incidents.

Questionnaire

Previous studies have used several different measures of disability and general morbidity following trauma. In the present study, as in a parallel study of the costs and benefits of paramedic care in trauma patients,[4] the Short Form with 36 items (SF-36) questionnaire was chosen. The SF-36 questionnaire is a proven and reliable instrument for measuring general health status while covering a broad range of disabilities, including physical, mental and social functioning.[32] The 36 questions were extended to 39 in order

to differentiate lower orders of physical function in the older population,[33] and the analysis of the data was performed taking these extra questions into account.

The consequences of trauma are very variable, and so the instrument used to measure it must be able to measure a wide range of disability within each dimension. Some traditional measures of disability, such as the Barthel Index, have focused on more severe forms of disability and have been insensitive to change. The SF-36 questionnaire covers a wide range of health states, generating scores for eight dimensions (physical function, social function, physical role, emotional role, mental health index, energy and vitality, pain index, and general health perceptions). An important advantage of the SF-36 questionnaire is its brevity, taking just 5–10 minutes to complete.

The dimensions were scored according to the questionnaire developer's recommendations, modified for the UK version.[34] Each dimension is scored from 0 to 100, with 100 indicating no disability or evidence of limitations.

As well as the SF-36 questions, patients were asked about their use of health and social services after their incident. Questions included readmission to hospital, day-case surgery (as a result of the accident), outpatient visits, GP consultations, and district nurse and social worker visits. Patients were also asked how limited they were in carrying out daily activities, whether they needed extra help with daily activities from family or friends, and how many days off work they had taken.

Selection of patients for follow-up

All identified survivors included in the study were sent a postal questionnaire 6 months after their incident unless the patient was identified more than 7 months after their trauma incident (usually because of delays in accessing hospital records), or their GP or medical records indicated that a questionnaire would be inappropriate.

Where possible, the questionnaire was completed by the patients themselves at home. If a patient was too ill or disabled to complete the questionnaire themself, the patient's relative or carer was asked to complete the questionnaire on their behalf and this was recorded as completed by proxy. The response rate to the postal questionnaire was 64%.

Economic evaluation

The methods used in the economic evaluation are discussed separately in chapter 4.

Statistical considerations

Sample size

Number of paramedics

Paramedics rather than patients were randomised. Based on an unpublished Medical Care Research Unit 1995 survey of ambulance services we estimated that we needed to randomise 420 paramedics into the study. In a previous study of 466 patients who met similar inclusion criteria and who were attended by London Ambulance Service paramedics there were 77 (17%) deaths,[35] and this mortality rate was assumed in the sample-size calculation. Thus, assuming

- 420 paramedics,
- that the number of patients seen by each paramedic is the same,
- that mortality rates in the two groups would be compared in terms of the distribution of the logits of the observed probabilities of survival of the patients of each paramedic, and
- an intraclass correlation coefficient, measuring the relative variation between and within paramedics in the probability of patients surviving, of 0.1,

in order to have an 80% chance of detecting (as significant at the 5% level) a difference in mortality of 14% versus 20% in the two groups of the trial, 3.77 patients needed to be seen by each paramedic.[36]

A simulation to assess the effect of allowing the number of patients seen by each paramedic to vary according to a Poisson distribution with a mean of 3.8 resulted in a power of 75%. The standard deviation of the between-paramedic probability of survival in this simulation was 0.25.

Analysis

The odds ratio of an outcome in the protocol A (fluids) group compared to the protocol B (no fluids) group was estimated, with 95% confidence intervals (CIs) where appropriate. Even though the intervention was really protocol B, estimates of the effect of giving fluids (or strictly, of protocol A) seem more natural. The effect of protocol B is easily obtained by

simply inverting the reported effect of protocol A (e.g. 1.5 becomes 1/1.5 = 0.67, a 33% reduction in the odds ratio).

Pragmatic analysis

Some patients were given fluids or not given fluids against the protocol that should have been in operation. These 'cross-overs' can cloud any differences between the outcomes of the two groups, and in order to help explain the results of the study it can also be helpful to exclude these patients from the analysis or to analyse the data according to the treatment they actually received. However, these sorts of explanatory analyses cannot usefully be undertaken in this type of study because the intervention actually used was chosen by the paramedic in the light of the expected outcome. Thus to analyse outcome by the intervention used is plainly absurd. Consequently, the main analyses that we made were pragmatic and compared the outcomes in all patients attended by paramedics randomised at the time to protocol A with the outcomes of patients attended by paramedics randomised at the time to protocol B. If the patients were first attended on scene by a BASICS GP who had been randomised to a protocol, then the protocol used in the analysis was the one to which the doctor had been randomised.

Subgroup analyses

A number of potentially important subgroups were identified prior to examining the data, and these subgroups were analysed individually. The subgroups were:

- ambulance service area
- time period (before or after the paramedics crossed over protocols)
- the type of injury sustained by the patient (bleeding injuries, head injuries, both, other)
- transfer time to hospital (< 10 minutes, urban area; > 10 minutes, non-urban area)
- contact time (on-scene + transfer times)
- whether or not there was a doctor at the scene
- injury severity
- whether or not the patient was taken to emergency theatre.

These analyses were undertaken by calculating the crude and adjusted odds ratios for death, or another outcome, in patients managed by paramedics operating protocol B compared with the outcome in other patients. A test for heterogeneity between the subgroups was also undertaken.

Adjustment

Crude estimates of the risk of outcomes in the protocol A group compared to the protocol B group were adjusted for prognostic factors using standard multiple logistic regression. The prognostic factors considered were age, ISS, unconsciousness at the scene, head AIS score, mechanism of injury, type of injury, pre-injury morbidities, type of incident, and whether the patient was trapped during the incident. The association of outcomes with the transfer time to hospital and the giving of fluids at the incident scene were also examined.

The principal outcome was death from any cause within 6 months. This was found to be independently related to age, ISS and consciousness at the incident scene, but with these factors in the model the other prognostic factors contributed little explanatory power. This basic model was therefore used in most of the adjustment models.

Composite outcomes

Combining mortality and morbidity outcomes has always been troublesome for health-outcomes research. Two simple strategies are available. Firstly, to add deaths to the quantitative quality of survival scores as the lowest possible health status (e.g. scoring deaths as 0 in the SF-36). Secondly, when not all survivors have a quantitative score an alternative approach is to identify other adverse outcomes to add to the deaths to give a composite poor outcome.

In the present study the candidates that could be added to the deaths were serious complications (as described above), long admission to an intensive care unit, a long stay in hospital, or a poor SF-36 health outcomes score. The length of stay in hospital and the length of stay in an intensive care unit represent processes of care and are thus not really suitable candidate outcomes. Complications can be viewed as near-misses, and therefore death or complications may be useful indicators of serious events. SF-36 scores are health outcomes, as are deaths, and it might therefore be useful to have a composite 'poor outcome' defined by death or a poor SF-36 score. In the present study poor survival was arbitrarily defined as an SF-36 General Health Perceptions score below the 20th centile of the distribution of scores in this sample. As only about half the survivors were both followed up and responded to the follow-up, two possible analytical approaches could be taken. Either those survivors with

unknown health status could be excluded from the analysis, or the outcome could be defined as 'death or known poor survival'. The latter approach was taken in order not to exclude cases on unknown grounds, but this means that some survivors with poor health will have been included in the good health group and any difference between the groups will have been diminished.

Chapter 3
Results

Sample size

Patients

A total of 1309 patients treated by paramedics who had been randomised to the protocols were entered in the study (854 in area 1 and 455 in area 2) (*Table 2*). A small majority of these patients (699 (53.4%)) were treated by paramedics operating protocol A. Examination of the numbers treated in each time period shows almost equal numbers before the paramedics were crossed over to the alternative protocol and an unexpected imbalance in the second period (424 versus 330).

Paramedics

Most of the imbalance in the number of patients treated by each protocol after the cross-over appears to have been due to a small number of paramedics working out of three busy city stations in area 1 who were recruited late into the study and who were therefore not crossed over. The majority of these paramedics were randomised to protocol A (fluids).

This emphasises the clustered nature of the trial. There were in fact 330 paramedics randomised to the trial who contributed at least one patient. The mean number of patients contributed by each paramedic was 3.97 (compared to an estimate of 3.77 in the protocol) and the median was 3 (*Figure 1*).

The majority of the paramedics (202 (61%)) contributed patients to both groups of the study,

TABLE 2 *Patient numbers by area and time period*

	Protocol A (*n*)	Protocol B (*n*)	All patients (*n*)
All cases	699	610	1309
Area 1	472	382	854
Area 2	227	228	455
Time period before cross-over	275	280	555
Time period after cross-over	424	330	754

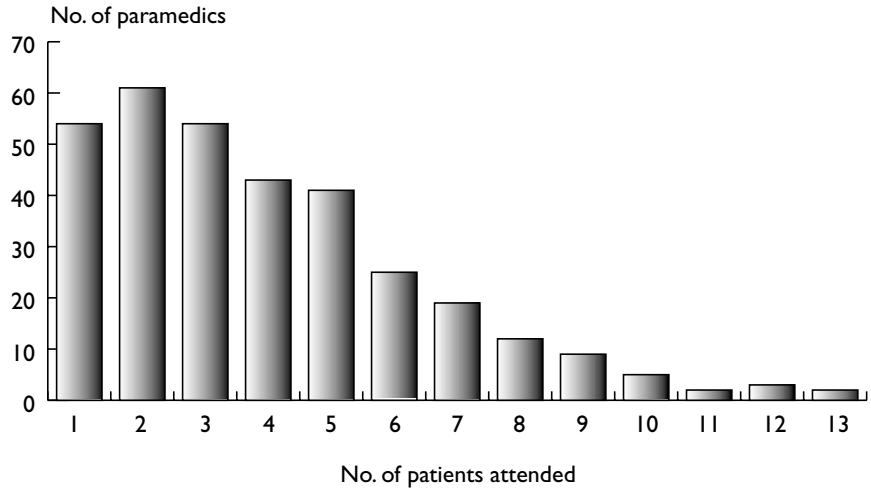

FIGURE 1 *The number of patients attended by each of the 330 paramedics included in the study*

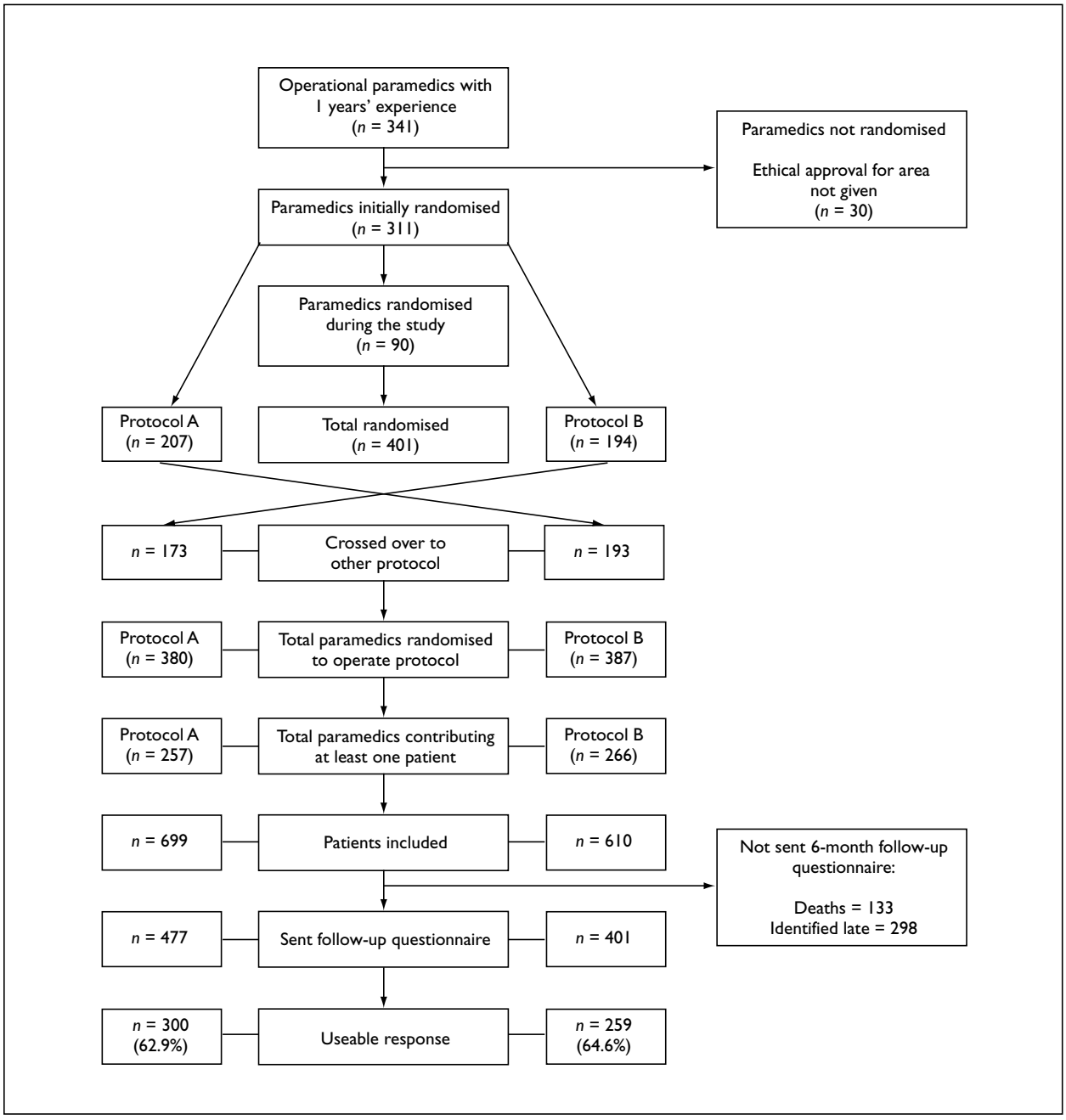

FIGURE 2 *CONSORT diagram of paramedic and patient recruitment*

with similar numbers contributing patients to protocol A only (67 (20%)) as to protocol B (no fluids) only (61 (18%)).

A Consolidation of Standards for Reporting Trials (CONSORT) diagram showing paramedic and patient recruitment is shown in *Figure 2*.

Protocol compliance

Most patients attended by paramedics operating protocol B did not receive any prehospital fluid infusion. However, this was also true for patients attended by paramedics operating protocol A (*Table 3*). Thus, although there was a significantly higher proportion of protocol B patients who did

TABLE 3 *Prehospital fluids by protocol*

Prehospital fluids	Protocol A, *n* (%)	Protocol B, *n* (%)	*p*
Yes	216 (30.9)	123 (20.2)	0.001
No	483 (69.1)	487 (79.8)	

not receive fluids compared to protocol A patients (79.8% versus 69.1%, $p < 0.001$), the difference was small.

One reason why the difference in fluid giving between the protocols was small is that some patients attended by paramedics operating protocol B were allowed to be given fluids by the protocol. These were patients expected to be more than 60 minutes from arrival at hospital or not having a peripheral pulse. A substantial minority of protocol B patients (9.5%) fell into this category (*Table 4*). In a further 6% of cases there was a doctor at the scene and, although there was agreement with some BASICS doctors to follow the paramedic protocol, the assigned protocol may have been overridden.

Compliance with the protocols, as measured by the difference between the two groups in the trial in the proportions of patients actually given prehospital fluid infusions, was reasonable in area 1 (protocol A 35.6% versus protocol B 21.7%, $p < 0.001$), but was poor in area 2 where there was no reliable evidence of any difference between the two trial groups in the rates of giving fluids (protocol A 21.1% versus protocol B 17.5%, $p = 0.33$) (see *Table 4*). In area 2 the rates of fluid infusion in the two groups were similar to one another and to the protocol B group in area 1 (21.1%, 17.5% and 21.7%, respectively, in area 1). This suggests that in area 2 paramedics were reluctant to give fluids even when licensed to do so by protocol A.

Another possible explanation for the fact that fluids were comparatively infrequently given in area 2 under protocol A is that the case mix in area 2 meant that the fluids protocol was rarely applicable (e.g. because patients were only a few minutes from hospital or had less serious injuries). In order to explore the effect of case mix on giving fluids within the two trial groups a logistic regression model for the logarithm of odds ratio of giving prehospital fluids was developed.

Before adjustment for case mix the crude odds ratio of being given fluids when attended by a paramedic using protocol A was +80% higher than when attended by a paramedic using protocol B. There was some weak evidence that this figure differed between areas (+103% in area 1 versus +28% in area 2; $\chi^2_1 = 2.6$, $p = 0.1$) (*Table 5*).

TABLE 5 *Estimated odds ratio for being given fluids when attended by a paramedic operating protocol A compared to a paramedic operating protocol B*

	Estimated OR	95% CI
Crude estimates		
Area 1	2.03	1.48 to 2.78
Area 2	1.28	0.79 to 2.05
Adjusted estimates*		
Area 1	2.33	1.61 to 3.37
Area 2	1.53	0.88 to 2.65

**Adjusted for ISS, age, patient trapped at incident scene, incident type, injury type, doctor on scene and unconsciousness*

TABLE 4 *Protocol compliance*

Protocol	Compliance	Area 1 (*n* = 854) (%)	Area 2 (*n* = 455) (%)	Total (*n* = 1309) (%)
Protocol A				
Complied	Fluids given	35.6	21.1	30.9
	No fluids given:	17.2	18.5	17.6
	no access	–1.7	–2.2	–1.9
	< 10 minutes to hospital	–15.5	–16.3	–15.7
Did not apply protocol A	No fluids given on scene:	47.2	60.3	51.5
	doctor on scene	–7.8	–2.6	–6.2
	other	–39.4	–57.7	–45.3
Protocol B				
Complied	No fluids given	78.3	82.5	79.8
	Fluids given:	9.7	9.3	9.5
	> 60 minutes to hospital	–9.2	–7.5	–8.5
	no peripheral pulse	–0.5	–1.8	–1.0
Did not apply protocol B	Fluids given:	12.0	8.3	10.6
	doctor on scene	–6.5	–4.8	–5.9
	other	–5.5	–3.5	–4.7

After adjustment for case mix the estimated effect of protocol A was increased to +109%. The increase was most pronounced in area 2 (+133% in area 1 versus +53% in area 2; $\chi^2_1 = 1.6$, $p = 0.2$).

In summary, it appears that for a given patient with a given severity and type of injury there was an approximate doubling of the chance of receiving fluids with protocol A. The effect of the protocol was particularly strong in area 1 and was comparatively weak in area 2, where the overall chance of being given fluids was only three-quarters of that in area 1.

Case mix

Comparisons of the patients attended by paramedics randomly allocated to protocol A or B show that the allocation worked well. There were no significant or marginally significant differences in incident characteristics (*Table 6*), ambulance response and performance times (*Table 7*) or patient characteristics (*Table 8*). For injury characteristics there were no differences in the type of injury, the ISS, the first Revised Trauma Score (RTS) recorded at the scene, or whether the patient was unconscious at the scene or had no peripheral pulse (*Table 9*). However, there was some evidence that slightly more protocol A patients who did not receive fluids had a moderate (AIS score of 2 or above) head injury than did protocol A patients who did receive fluids (25.3% versus 20.3%).

On-scene times

The similar on-scene times in the two protocol groups (see *Table 7*) hide the fact that, on average, there was a 12.9 minute difference in the on-scene time of patients who were given prehospital fluids and patients who were not. Giving fluids had a particularly marked impact on on-scene times for patients attended by paramedics operating protocol B (+15.4 minutes) compared to patients attended by paramedics operating protocol A (+11.0 minutes).

Fluids and other prehospital interventions

Type of and place of giving fluids

In both trial groups the patients given fluids were given crystalloids more often than colloids, and although the main difference between the two groups lay in giving crystalloids, colloids were also used more often in the protocol A group than the protocol B group (*Table 10*).

Approximately one-quarter of the patients not given fluids in the prehospital phase went on to receive fluids in the A&E department, and this proportion was virtually the same in both trial groups (127/483 (26.3%) versus 134/487 (27.5%)). Again, these infusions were mostly crystalloid, although colloids and blood were occasionally given.

Because the rate of fluid giving in A&E departments was the same in the two trial

TABLE 6 *Incident characteristics*

Incident characteristic	Protocol A, *n* (%)	Protocol B, *n* (%)	*p*
Type of incident			
Road traffic accident	408 (58.4)	355 (58.2)	
Fall	232 (33.2)	217 (35.6)	
Fire	20 (2.9)	13 (2.1)	0.18
Assault	17 (2.4)	5 (0.8)	
Other	22 (3.1)	20 (3.3)	
Time of day			
Day (08.00–19.59)	482 (69.0)	430 (70.5)	0.55
Night	217 (31.0)	180 (29.5)	
Patient trapped			
Yes	99 (14.2)	88 (14.4)	0.89
No	600 (85.8)	522 (85.6)	
Doctor on scene			
Yes	142 (20.3)	129 (21.1)	0.71
No	557 (79.7)	481 (78.9)	

TABLE 7 *Ambulance response and performance times*

Time interval	Protocol A, mean (SD)	Protocol B, mean (SD)	*p*
Response time (minutes)	12.2 (7.0)	11.7 (6.1)	0.17
Scene time (minutes):			
All cases	26.3 (16.1)	25.4 (15.6)	0.30
Excluding trapped	23.8 (13.4)	23.3 (13.2)	0.48
Transfer time to hospital (minutes)	19.8 (11.9)	19.1 (11.0)	0.34
Ratio scene/transfer	1.88 (1.87)	2.02 (2.98)	0.31
Total patient contact time (on-scene + transfer) (minutes):	45.9 (20.9)	44.2 (19.2)	0.14
0–30	24.0%	25.0%	
30–60	54.9%	57.2%	
> 60	21.0%	17.7%	
Not known (*n*)	42	35	

SD, standard deviation

TABLE 8 *Patient characteristics*

Characteristic	Protocol A, *n* (%)	Protocol B, *n* (%)	*p*
Age (years)			
15–44	395 (57.0)	344 (56.8)	0.89
45–64	169 (24.4)	140 (23.1)	
65–74	65 (9.4)	62 (10.2)	
≥ 75	64 (9.2)	60 (9.9)	
Not known	6	4	
Sex			
Male	450 (64.4)	391 (64.1)	0.92
Female	249 (35.6)	219 (35.9)	
Significant pre-injury morbidity			
Yes	18 (2.6)	17 (2.8)	0.26
No or not known	681 (97.4)	593 (97.2)	

groups, overall the difference in the proportion of patients receiving fluids (or blood) prior to going to theatre or being admitted to hospital was even smaller than the prehospital difference (49.1% versus 42.1%).

Volume of fluids

Of those patients receiving fluids prehospital, approximately half received up to one unit (500 ml) and the other half received over one unit (*Figure 3*). A small proportion of patients received over 1 litre of fluid prehospital.

Other prehospital interventions

There were no significant differences between the two trial groups in other prehospital interventions. Of the 699 patients managed by protocol A, only 16 (2.3%) were successfully intubated at the scene, and this was very similar for protocol B patients (10/610 (1.6%)).

Mortality

Crude mortality

Of the 610 patients included in the protocol B group, 60 (9.8%) died within 6 months of the incident. A similar proportion of protocol A patients died (73/699 (10.4%)). The crude odds ratio for death within 6 months in protocol A patients compared to protocol B patients was 1.07 (95% CI, 0.73 to 1.54) (*Table 11*).

Excluding 26 patients whose cause of death may not have been related to the original trauma, the odds ratio for death in the protocol A group was 1.04 (95% CI, 0.69 to 1.55).

TABLE 9 *Injury characteristics*

Characteristic	Protocol A, *n* (%)	Protocol B, *n* (%)	*p*
Type of injury			0.73
Penetrating	12 (1.7)	12 (2.0)	
Blunt:			
abdomen and thorax	258 (36.9)	211 (34.6)	
limb fractures	255 (36.5)	223 (36.6)	
head injury only	79 (11.3)	66 (10.8)	
other	95 (13.6)	98 (16.1)	
Injury Severity Score (ISS)			0.58
0–8	245 (35.1)	226 (37.0)	
9–15	280 (40.1)	247 (40.5)	
16–24	88 (12.6)	68 (11.1)	
25–40	68 (9.7)	60 (9.8)	
41–75	18 (2.6)	9 (1.5)	
Head injury AIS score			0.02
None	516 (73.8)	474 (77.7)	
1	6 (0.9)	12 (2.0)	
2	44 (6.3)	21 (3.4)	
3	59 (8.4)	34 (5.6)	
4	49 (7.0)	42 (6.9)	
5	25 (3.6)	27 (4.4)	
On-scene T-RTS			0.85
0–7	7 (1.7)	5 (1.4)	
8, 9	21 (5.0)	18 (5.1)	
10, 11	59 (14.1)	43 (12.1)	
12	330 (79.1)	289 (81.4)	
Missing	282	255	
Unconcious at scene			0.42
Yes	149 (21.3)	119 (19.5)	
Not indicated	550 (78.7)	491 (80.5)	
Peripheral pulse at scene			0.82
No	9 (1.3)	7 (1.1)	
Not indicated	690 (98.7)	603 (98.9)	

AIS, Abbreviated Injury Scale; T-RTS, Triage Revised Trauma Score

TABLE 10 *Time of giving intravenous fluids*

	Protocol A (*n* = 699), *n* (%)	Protocol B (*n* = 610), *n* (%)
Prehospital fluids	216 (30.9)	123 (20.2)
Crystalloid	216 (30.9)	90 (14.8)
Colloids	102 (14.6)	66 (10.8)
No prehospital fluids	483 (69.1)	487 (79.8)
Fluids in A&E:	127 (18.2)	134 (22.0)
crystalloid	109	113
colloid	44	55
blood	24	46
No fluids in A&E	356 (50.9)	353 (57.9)
Fluids pretheatre		
Yes:	343 (49.1)	257 (42.1)
crystalloid	316 (45.2)	224 (36.7)
colloid	165 (23.6)	133 (21.8)
blood	661 (9.4)	71 (11.6)
No	356 (50.9)	353 (57.9)

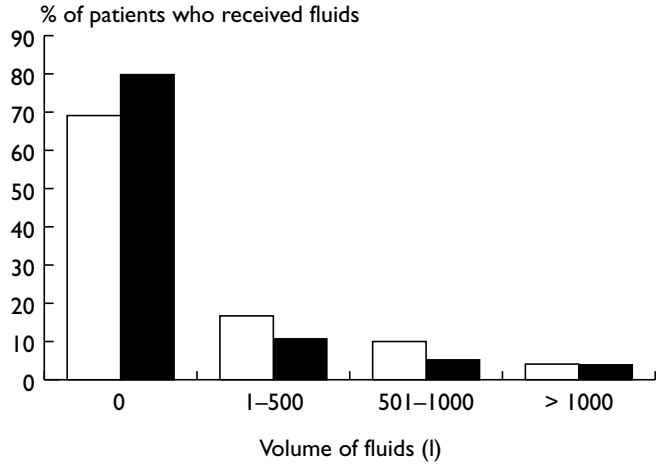

FIGURE 3 *Volume of fluid given prehospital (□, protocol A, ■, protocol B)*

TABLE 11 *Deaths of patients within 6 months of their incident*

	Protocol A (*n* = 699), *n* (%)	Protocol B (*n* = 610), *n* (%)	OR (95% CI) for death with fluids	
			Crude*	Adjusted†
All causes	73 (10.4)	60 (9.8)	1.07 (0.73 to 1.54)	0.93 (0.58 to 1.49)
Trauma-related causes only	58 (8.5)	49 (8.2)	1.04 (0.69 to 1.55)	0.86 (0.50 to 1.49)
Excluding early deaths‡	63 (9.1)	53 (8.8)	1.04 (0.70 to 1.53)	0.97 (0.60 to 1.59)
Excluding late deaths§	41 (6.1)	38 (6.5)	0.95 (0.58 to 1.49)	0.74 (0.40 to 1.38)
Excluding early or late deaths	31 (4.7)	31 (5.3)	0.88 (0.50 to 1.45)	0.75 (0.38 to 1.48)

* *For 11 patients data for age or the ISS were missing, and these patients were omitted from these calculations*
† *Adjusted for the ISS, age and whether the patient was unconscious at the incident scene*
‡ *Deaths possibly occurring before the arrival of the ambulance at the scene*
§ *Deaths occurring 3 days or more after the incident*

Excluding 17 patients who had no pulse and an RTS of 0 at the incident scene, and who may therefore have been dead before the ambulance arrived, the odds ratio for death in the protocol A group was also 1.04 (95% CI, 0.70 to 1.53).

Excluding 54 later deaths occurring 3 days or more after the incident, the odds ratio for death in the protocol A group was 0.95 (95% CI, 0.58 to 1.49). Excluding both early and late deaths the estimated odds ratio was 0.88 (95% CI, 0.50 to 1.45).

Adjusted mortality

The association between 11 characteristics of the incidents, the patients, their injuries and their mortality were examined (*Table 12*). The time from leaving the scene to arrival at hospital (transfer time) was included in this analysis but the on-scene time was not because length of time at the scene may be a consequence of operating different fluid protocols. Nearly all these characteristics showed some association with outcome. However, after taking age and the ISS into account, only unconsciousness at the scene and the head injury AIS score showed any significant association with death. With unconsciousness at the scene included in the analysis, the head AIS score no longer showed any residual association. Although none of these three factors (age, ISS and unconsciousness) showed any significant difference in distribution between the two protocol groups, the estimated effects of protocol A on

TABLE 12 *Association between the characteristics of incidents, patients, their injuries and mortality*

Characteristic	Crude			Adjusted*			Adjusted†		
	χ^2	df	*p*	χ^2	df	*p*	χ^2	df	*p*
Age	70.4	3	< 0.001						
ISS	225.2	4	< 0.001						
Unconscious at scene	97.1	1	< 0.001	18.3	1	< 0.001			
Head AIS score	153.4	5	< 0.001	9.3	5	0.09	5.4	5	NS
Mechanism of injury	2.5	1	NS	1.6	1	NS	1.8	1	NS
Type of injury	129.9	3	< 0.001	5.0	3	NS	2.6	3	NS
Preconditions	12.6	1	< 0.001	1.2	1	NS	1.2	1	NS
Type of incident	4.7	4	NS	2.3	4	NS	3.4	4	NS
Trapped	4.4	1	0.04	0.9	1	NS	0.7	1	NS
Transfer time	5.5	1	0.02	0.7	1	NS	0.7	1	NS
Fluids on scene	6.7	1	0.01	0.1	1	NS	0.0	1	NS

AIS, Abbreviated Injury Scale; df, degrees of freedom; NS, not significant (p > 0.1)

**Adjusted for age and the ISS*

†Adjusted for age, the ISS, and consciousness at the scene

mortality was remodelled adjusting for the influence of these factors. These adjustments made little difference to the results, and no significant association between the two protocol groups and mortality was found (see *Table 11*).

Subgroup analyses

Subgroups of patients defined on eight different characteristics were examined to see whether there was any evidence that the protocol had had an effect in any particular group of patients.

In fact there was no reliable evidence of any heterogeneity in the trial results between any of the subgroups (*Table 13*). In other words, with regard to total mortality there was no evidence in this trial that the effect of the fluid protocol differed between any subgroups of patients. This included patients with bleeding injuries (defined as injuries to the abdomen or thorax, penetrating injuries, or severe or multiple fractures) and patients with head injuries, and patients with both types of injuries. For these three subgroups, after adjusting for age, ISS and consciousness at the scene the estimated odds ratios were all nearly 1.0 (1.0, 0.94 and 0.87, respectively).

For patients with severe bleeding injuries (those with an ISS ≥ 16), the estimated relative risk of death in the fluids group was 1.19 (49/140 (35.0%) versus 28/95 (29.5%)). Although not significant in this small subgroup (95% CI, 0.69 to 2.04) this risk is very similar to the significantly increased relative risk of 1.13 found by Bickell and co-workers[27] in patients with severe penetrating injuries of the torso.

Other outcomes

Change in Triage Revised Trauma Score

The T-RTS is a summary measure of physiological derangement scored from 0, indicating no vital signs (pulse, respiration or consciousness), to 12, indicating normal signs. It can be scored at the incident scene to aid triage decisions and also in hospital emergency departments to assist management decisions. Comparison of the first recorded on-scene T-RTS and the first in-hospital T-RTS indicates the extent to which the physiological responses of the patient have deteriorated or improved in the prehospital phase. To this extent it is an outcome measure of prehospital performance.

There were a total of 509 patients with valid T-RTS recordings both on scene and in hospital, 218 in the protocol B group and 291 in the protocol A group. For most of these patients the T-RTS stayed the same (79.8%), with 7.7% deteriorating and 12.6% improving. The distribution of change was

TABLE 13 *The odds ratios for of death from any cause*

Characteristic	Subgroup	OR (95% CI) for death with fluids		$p^{\dagger}$
		Crude	Adjusted*	
Area	Area 1	1.42 (0.86 to 2.34)	1.26 (0.66 to 2.39)	0.25
	Area 2	0.77 (0.44 to 1.36)	0.71 (0.34 to 1.48)	
Doctor on scene	Yes	1.45 (0.70 to 3.02)	0.98 (0.38 to 2.52)	0.98
	No	0.96 (0.62 to 1.47)	0.91 (0.53 to 1.58)	
Contact time (minutes)	< 15	0.60 (0.12 to 3.03)	0.30 (0.03 to 2.78)	
	15–60	1.10 (0.71 to 1.72)	0.98 (0.56 to 1.72)	0.73
	> 60	1.23 (0.50 to 2.98)	0.97 (0.31 to 3.00)	
	Missing	0.82 (0.18 to 3.64)	1.40 (0.20 to 9.68)	
Taken to theatre	Yes	0.79 (0.33 to 1.88)	0.62 (0.19 to 2.07)	0.47
	No	1.13 (0.75 to 1.70)	1.00 (0.60 to 1.68)	
Injury Severity Score (ISS)	0–8	0.39 (0.10 to 1.53)	0.41 (0.10 to 1.62)	
	9–15	1.13 (0.49 to 2.58)	1.16 (0.48 to 2.80)	0.54
	16–24	1.15 (0.45 to 2.93)	0.91 (0.31 to 2.66)	
	≥ 25	1.04 (0.53 to 2.01)	1.24 (0.59 to 2.58)	
Type of injuries‡	'Bleeding injury'	0.99 (0.54 to 1.79)	1.0 (0.51 to 1.96)	
	Head injury	0.53 (0.21 to 1.31)	0.94 (0.31 to 2.84)	0.45
	Both	1.12 (0.55 to 2.25)	0.87 (0.35 to 2.19)	
Period	Before cross-over	1.12 (0.65 to 1.95)	1.13 (0.56 to 2.27)	0.40
	After cross-over	1.01 (0.61 to 1.68)	0.77 (0.40 to 1.47)	
Type of area	Urban	0.99 (0.46 to 2.12)	1.07 (0.40 to 2.86)	0.95
	Not urban	1.15 (0.73 to 1.80)	0.90 (0.51 to 1.59)	

* *Adjusted for age, the ISS, preconditions and whether conscious at the scene*
† *p-value for heterogeneity between subgroups*
‡ *Other types of injury had too few deaths (2/193) to estimate the ORs*

the same in the two protocol groups (*Figure 4*), with no evidence of any difference in the proportions deteriorating (7.9% versus 7.3%; $p = 0.81$). Adjusting for severity of head injury, mechanism of injury and transfer time to hospital, the estimated odds ratio of deterioration in the T-RTS in the protocol A group relative to the protocol B group was 1.15 (95% CI, 0.56 to 2.35) (*Table 14*).

Complications

A total of 106 patients were recorded in their hospital notes as sustaining at least one of eight major complications (adult respiratory distress syndrome, sepsis, acute renal failure, coagulopathy, wound infection, pneumonia, fat embolism or pulmonary embolism). The proportions with recorded complications were similar in the two groups (46/610 (7.5%) in the protocol B group and 60/699 (8.5%) in the protocol A group). After adjusting for age, ISS and consciousness at the scene, the estimated odds ratio for a complication in patients managed by protocol A relative to those managed by protocol B was 1.15 (95% CI, 0.75 to 1.77) (see *Table 14*).

Admission to intensive care

One-fifth of the study patients were admitted to intensive care, 113 (18.5%) of those managed by protocol B and 148 (21.2%) of those managed by protocol A. Adjusting for age, ISS, consciousness at the scene and type of injury, the estimated odds ratio for admission to intensive care in patients managed by protocol A relative to those managed by protocol B was 1.18 (95% CI, 0.82 to 1.69). For both groups of patients the average length of stay in intensive care was about 1 week, and after adjustment for age, ISS and consciousness at the scene there was no evidence of any difference between the groups (estimated effect of fluids –1.2 days, $p = 0.25$) (*Table 15*).

Length of stay in hospital

The average length of stay in hospital during the 6 months after the incident was over 2 weeks in both patient groups (see *Table 15*) and there was

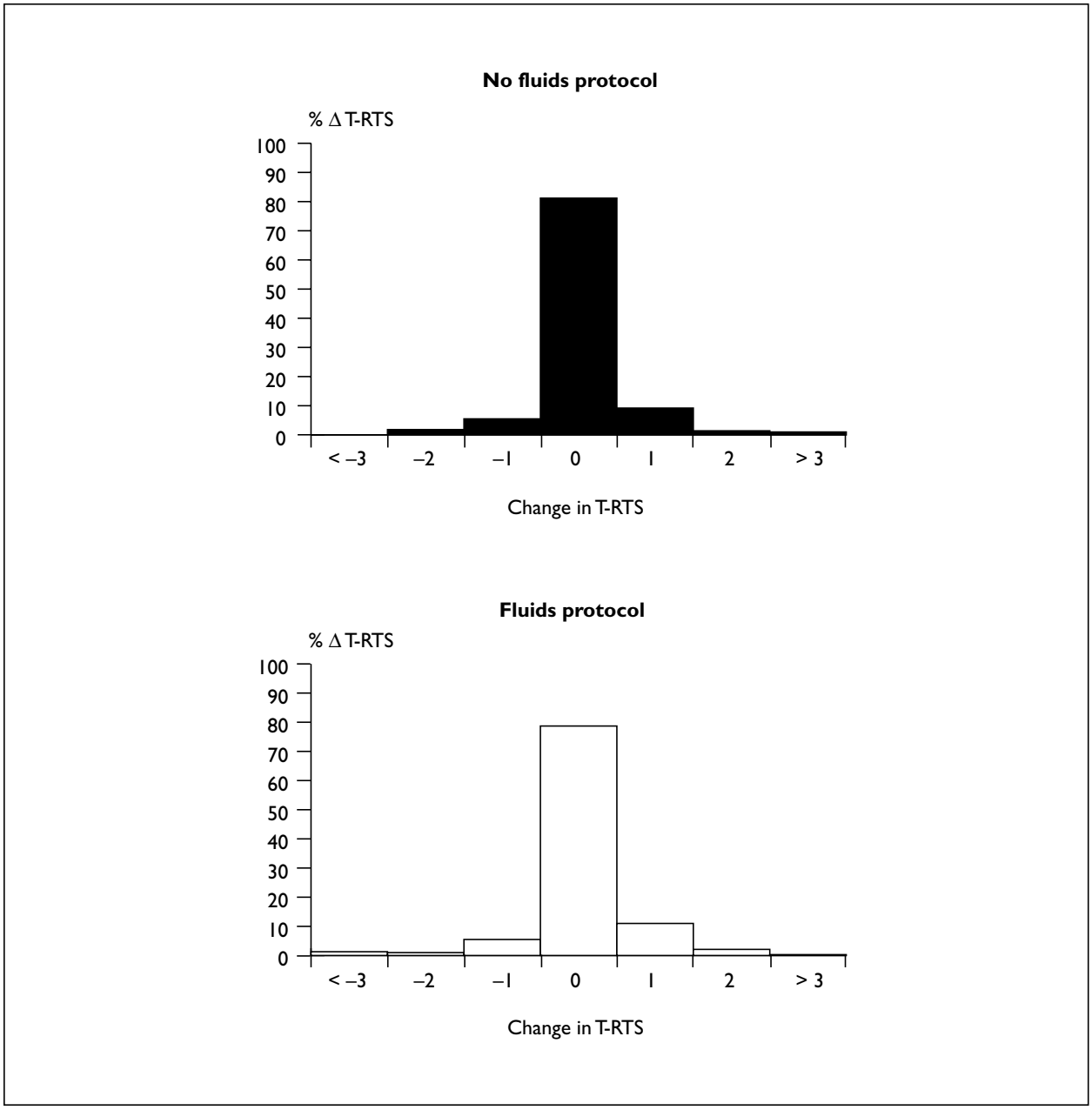

FIGURE 4 *Change in the T-RTS between the incident scene and the hospital*

TABLE 14 *Odds ratios for other adverse outcomes*

Outcome	**Protocol A, *r/n* (%)**	**Protocol B, *r/n* (%)**	**Adjusted OR (95% CI) for adverse outcome with fluids protocol A**
Deterioration in T-RTS	23/291 (7.9)	16/218 (7.3)	1.15 (0.56 to 2.35)
Complications	60/699 (8.5)	46/610 (7.5)	1.15 (0.75 to 1.77)
Admission to intensive care unit	148/699 (21.2)	113/610 (18.5)	1.18 (0.82 to 1.69)

r/n = *number of patients with the outcome/number of patients in whom it was measured; T-RTS, Triage Revised Trauma Score*

TABLE 15 *Other outcomes at 6 months post-incident*

	Protocol A (*n* = 699), mean (SD)	Protocol B (*n* = 610), mean (SD)	Adjusted estimated OR for fluids,* mean (SE)	*p**
Length of stay in intensive care (nights)	6.4 (7.3)	7.7 (8.8)	–1.2 (1.0)	0.25
Total length of stay in hospital (nights)	16.9 (21.1)	16.6 (21.3)	–0.1 (0.84)	0.91
Dimensions of SF-36				
Physical functioning	53.4 (31.1)	56.3 (30.5)	–4.2 (2.6)	0.10
Social functioning:	59.2 (32.2)	62.9 (32.4)	–3.4 (2.8)	0.24
role – physical	35.4 (41.1)	39.2 (42.6)	–3.7 (3.6)	0.30
role – emotional	58.1 (44.2)	64.0 (42.9)	–4.7 (3.8)	0.25
Mental health	62.9 (22.6)	68.3 (20.2)	–4.5 (1.8)	0.02
Energy/vitality	48.3 (22.7)	49.2 (22.2)	–0.56 (1.9)	0.77
Pain	56.0 (27.1)	57.0 (26.4)	–0.25 (2.3)	0.91
General health	61.2 (22.6)	63.0 (23.9)	–1.9 (2.0)	0.37

SF-36, Short Form with 36 items

**Calculated using paramedic re-randomisation tests with the difference in means as the test statistic, and adjusting for age, the ISS and unconsciousness at the scene*

no evidence that protocol B had any effect on the length of stay.

Health status

Questionnaires were sent to 878 patients. The other 431 patients were excluded from the morbidity follow-up because of death or identification for inclusion in the study more than 6 months after the incident in which they were injured. Only 64% ($n = 559$) of the patients sent a questionnaire replied. Respondents were similar to non-respondents in terms of their injury severity ($p = 0.27$) but, as is usual with postal surveys, non-respondents were younger ($p = 0.01$) and a higher proportion were male ($p < 0.001$). However, the response rates were very similar in the two trial groups (64.6% versus 62.9%; $p = 0.60$) (*Table 16*).

TABLE 16 *Response rates to the 6-month follow-up questionnaire*

	Protocol A, *n* (%)	Protocol B, *n* (%)
Full response	266 (55.8)	230 (57.4)
Partial response	20 (4.2)	15 (3.7)
Proxy response	14 (2.9)	14 (3.5)
Refused	6 (1.3)	1 (0.2)
No reply	161 (33.8)	130 (32.4)
Returned undelivered	10 (2.1)	11 (2.7)
All sent	477 (100.0)	401 (100.0)
Not sent	222	209
All	699	610

In all eight dimensions of the SF-36 health status measure, patients who had been managed by paramedics operating protocol A reported better health than did patients managed by protocol B (see *Table 15* and *Figure 5*). However, none of the estimated differences was greater than five points (which value is usually taken as indicating a clinically significant difference), and the difference was statistically significant for only one of the eight dimensions (mental health).

It seems unlikely, therefore, that protocol B had any effect on the health status of survivors.

Composite outcomes

Death or complications

A total of 215 patients died or had potentially serious complications recorded: 119 (17.0%) of these were managed by paramedics operating protocol A, and 96 (15.7%) by paramedics operating protocol B. Adjustment for age, ISS and unconsciousness at the scene did not alter the non-significant difference in risk of death or complications (*Table 17*). Furthermore, analysis within subgroups defined on eight characteristics

failed to find any reliable evidence of heterogeneity between subgroups, or any significant effect of protocol B within a subgroup (*Table 18*).

Death or known poor survival

A total of 222 patients died or responded to the follow-up questionnaire at 6 months and reported poor general health as indicated by a general health perceptions score below the 20th centile (< 40 points). These comprised 16.3% of the patients managed by protocol A and 17.7% of those managed by protocol B.

Adjustment for age, ISS and unconsciousness at the scene showed no reliable evidence of a difference in risk between the interventions (see *Table 17*). Furthermore, there was no evidence of a difference between subgroups or of any difference between protocols within subgroups (*Table 19*).

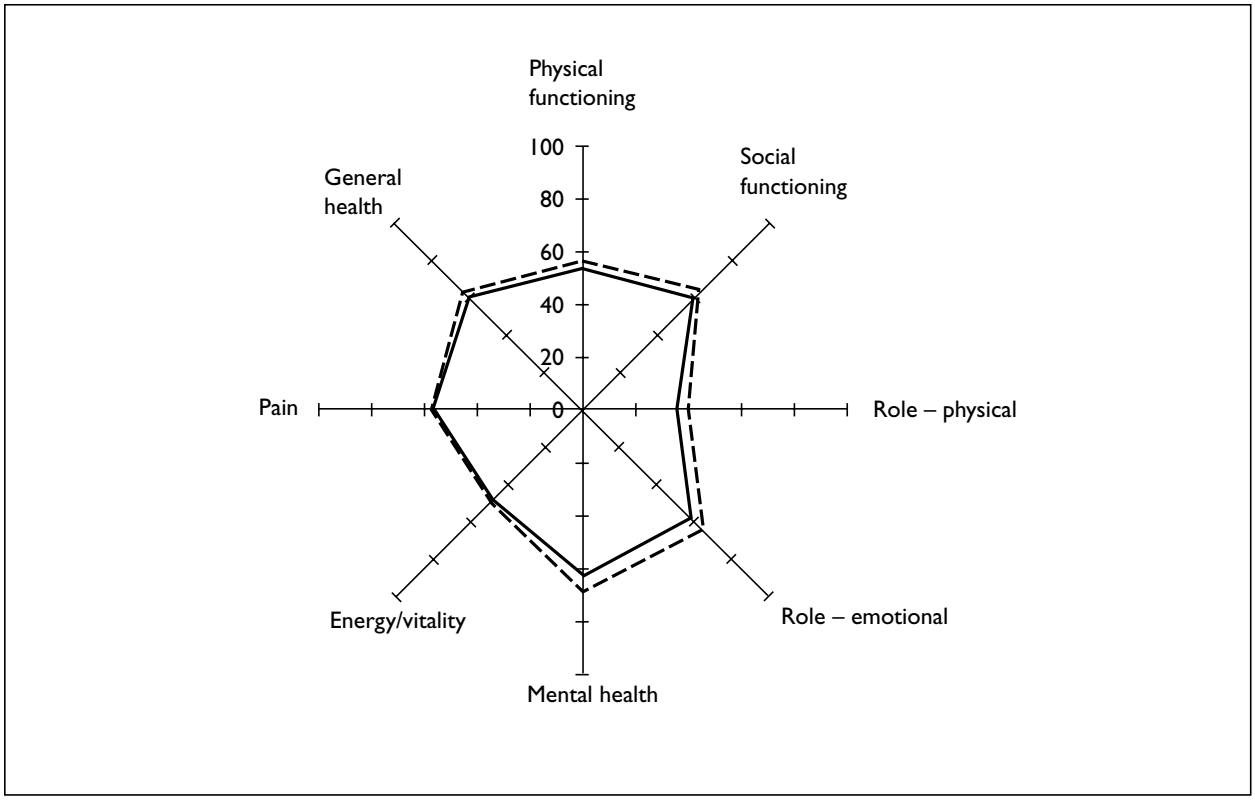

FIGURE 5 *SF-36 scores at 6 months after injury (——, protocol A; – – –, protocol B)*

TABLE 17 *Composite outcomes*

	Protocol A (*n* = 699), *n* (%)	**Protocol B (*n* = 610), *n* (%)**	**Adjusted OR (95% CI) for death with fluids***	***p*†**
All deaths	73 (10.4)	60 (9.8)	0.93 (0.58 to 1.49)	0.78
Death or complications	119 (17.0)	96 (15.7)	1.02 (0.71 to 1.47)	0.93
Death or known poor survival‡	114 (16.3)	108 (17.7)	0.81 (0.58 to 1.13)	0.20

* *Adjusted for the ISS, age and whether unconscious at the scene*
† *Calculated using re-randomisation tests, which allow for clustering of patients within paramedics*
‡ *Poor survival was defined as an SF-36 general health perceptions score below the 20th centile (40.0 points), and was only assessed in patients who responded to the follow-up*

TABLE 18 *The odds ratios for death or complications*

Characteristic	Subgroup	OR (95% CI) for death with fluids		$p^{\dagger}$
		Crude	Adjusted*	
Area	Area 1	1.35 (0.94 to 1.95)	1.22 (0.78 to 1.91)	0.12
	Area 2	0.69 (0.40 to 1.21)	0.65 (0.33 to 1.27)	
Doctor on scene	Yes	1.81 (1.01 to 3.25)	1.47 (0.72 to 3.02)	0.23
	No	0.94 (0.66 to 1.35)	0.89 (0.58 to 1.28)	
Contact time (minutes)	< 15	0.38 (0.08 to 1.78)	0.18 (0.02 to 1.39)	0.25
	15–60	1.28 (0.89 to 1.84)	1.20 (0.77 to 1.86)	
	> 60	1.10 (0.54 to 2.23)	0.77 (0.33 to 1.87)	
	Missing	0.54 (0.15 to 1.93)	0.81 (0.16 to 4.06)	
Taken to theatre	Yes	0.76 (0.40 to 1.43)	0.67 (0.30 to 1.51)	0.23
	No	1.25 (0.88 to 1.77)	1.15 (0.76 to 1.75)	
Injury Severity Score (ISS)	0–8	0.93 (0.37 to 2.30)	0.95 (0.38 to 2.38)	0.20
	9–15	0.99 (0.55 to 1.79)	0.98 (0.53 to 1.80)	
	16–24	0.95 (0.47 to 1.92)	0.87 (0.41 to 1.85)	
	≥ 25	1.37 (0.69 to 2.70)	1.57 (0.77 to 3.19)	
Type of injuries‡	'Bleeding injury'	1.01 (0.65 to 1.56)	0.99 (0.62 to 1.60)	0.82
	Head injury	1.52 (0.76 to 2.99)	1.35 (0.58 to 3.17)	
	Both	0.48 (0.29 to 1.07)	0.78 (0.31 to 1.97)	
Period	Before cross-over	1.33 (0.86 to 2.06)	1.38 (0.81 to 2.35)	0.12
	After cross-over	0.98 (0.64 to 1.50)	0.77 (0.46 to 1.29)	
Type of area	Urban	1.12 (0.61 to 2.07)	1.23 (0.57 to 2.63)	0.80
	Not urban	1.20 (0.83 to 1.73)	0.98 (0.63 to 1.52)	

* *Adjusted for age, the ISS, preconditions, and whether conscious at the scene*
† *p-value for heterogeneity between subgroups*
‡ *'Other' types of injury had too few deaths or complications (5/193) to estimate the ORs reliably*

TABLE 19 *The odds ratios for death or known poor survival at 6 months*

Characteristic	Subgroup	OR (95% CI) for death with fluids		$p^{\dagger}$
		Crude	Adjusted*	
Area	Area 1	1.07 (0.72 to 1.58)	0.92 (0.59 to 1.43)	0.48
	Area 2	0.74 (0.46 to 1.18)	0.73 (0.43 to 1.24)	
Doctor on scene	Yes	1.54 (0.84 to 2.81)	1.21 (0.60 to 2.42)	0.18
	No	0.76 (0.54 to 1.07)	0.71 (0.49 to 1.05)	
Contact time (minutes)	< 15	0.67 (0.15 to 2.93)	0.49 (0.08 to 2.86)	
	15–60	0.79 (0.55 to 1.13)	0.68 (0.45 to 1.02)	0.29
	> 60	1.35 (0.69 to 2.65)	1.23 (0.57 to 2.65)	
	Missing	1.14 (0.35 to 3.74)	1.83 (0.47 to 7.14)	
Taken to theatre	Yes	0.73 (0.36 to 1.46)	0.58 (0.25 to 1.35)	0.40
	No	1.95 (0.68 to 1.31)	0.86 (0.60 to 1.25)	
Injury Severity Score (ISS)	0–8	0.71 (0.37 to 1.36)	0.72 (0.37 to 1.41)	
	9–15	0.90 (0.53 to 1.51)	0.89 (0.52 to 1.54)	0.96
	16–24	0.95 (0.42 to 2.18)	0.83 (0.35 to 1.99)	
	≥ 25	0.83 (0.43 to 1.62)	0.90 (0.45 to 1.80)	
Type of injuries	'Bleeding injury'	0.79 (0.53 to 1.19)	0.79 (0.52 to 1.23)	
	Head injury	0.48 (0.21 to 1.08)	0.69 (0.28 to 1.71)	0.48
	Both	0.88 (0.44 to 1.74)	0.61 (0.27 to 1.39)	
	Other	1.91 (0.53 to 6.88)	1.93 (0.53 to 7.03)	
Period	Before cross-over	0.91 (0.58 to 1.42)	0.85 (0.51 to 1.41)	0.90
	After cross-over	0.89 (0.60 to 1.32)	0.76 (0.49 to 1.20)	
Type of area	Urban	0.78 (0.40 to 1.49)	0.72 (0.34 to 1.53)	0.90
	Not urban	0.95 (0.67 to 1.35)	0.81 (0.55 to 1.21)	

* *Adjusted for age, the ISS, preconditions and whether conscious at the scene*
† p-*value for heterogeneity between subgroups*

Chapter 4

Economic evaluation

Aim

The aim of economic evaluation is to quantify the incremental costs and benefits of intervention(s) and, using this information, to draw conclusions about the relative efficiency of the intervention(s). In the context of the present trial, the incremental benefits were measured as any reduced mortality and/or morbidity of trauma victims treated according to one of the two protocols governing the use of intravenous infusion by paramedics. This chapter focuses on the incremental costs of the two interventions. The economic evaluation takes a societal perspective, and estimates long-term costs.

Methods

Costing can be seen as a four-stage process. Firstly, potential cost differences between the interventions need to be identified. Secondly, the resources used need to be measured in those aspects of care where potential differences may exist. Thirdly, actual resource use differences are valued. Finally, differences in costs are calculated and interpreted.

Different intravenous protocols could have far-reaching effects both within the ambulance service and on the broader health service if there were significant effects on mortality and morbidity. The potential effects on the ambulance service include extra consumables (e.g. cannulae, giving sets and fluids) and time (e.g. additional on-scene time). Both these components represent opportunity costs, since money spent on consumables and additional time spent treating patients could both be used for other beneficial purposes. Potential effects on the broader health service (e.g. admissions to an intensive care unit, length of stay and primary and community care use) are also possible, although only likely if the interventions differ significantly in terms of their outcomes.

The use of the study protocols for the use of intravenous fluids in serious trauma has no training consequences for paramedics. Regardless of how fluids are used within this patient group, intravenous cannulation and intravenous fluids will continue to be used in other patient groups. Consequently, intravenous skills and training will be unaltered, as will be the costs associated with them.

The resources that were identified as potentially varying between protocols, and the sources of data for the measurement and valuation of these resources, are listed in *Table 20*. The main data sources were routine information systems and a 6-month follow-up of patients via a postal questionnaire. Unit costs were taken from routinely available data.

This simple approach for the collection of resource-use data and unit costs was seen as sufficient for several reasons. In terms of ambulance costs, the routine sources that record the use of fluids are of high quality in this study, and therefore a separate study to explore the issue in greater detail was not required. The unit costs for ambulance-service time are crude; however, any potential improvement in their accuracy gained through more detailed work would be greatly outweighed by the variability of the unit costs across Ambulance Trusts (which range from £63.61 to £202.12 per journey (1995–96 prices, NHS Executive 1997[39])). Thus any uncertainty regarding the policy impact on ambulance-service costs will be dominated by the variation in costs across the country.

With regard to inpatient costs, previous studies (by the Medical Care Research Unit) have undertaken more detailed costing exercises of inpatient treatment of trauma patients. These studies showed that robust results can be produced by using just the length of inpatient stay split simply between ward stay and intensive care unit stay.[40–42]

The data collected can be used to produce individual patient costs using the formula given in *Box 4*. All costs given here are in 1997–98 prices, as these are the most recent for which all unit costs are available. All costs fall within 1 year of treatment, and so were not discounted.

TABLE 20 *Measurement and valuation of resources used as a consequence of operating the infusion protocols*

Resource	Measure	Source of data	Valuation
Ambulance service			
Consumables, etc.	Number and type	Ambulance-service PRFs	East Anglian Ambulance NHS Trust
Length of call-out*	Minutes		Minute of emergency call-out time†
A&E department			
Consumables, etc.	Number and type	A&E department records	East Anglian Ambulance NHS Trust
Blood	Units		National Blood Service
Time with patient	Attendance		Cost per attendance (Trust Financial Return TFR2E)
Inpatient departments (including readmissions)			
Ward stay	Length of stay	PAS	Cost per day
Intensive care unit stay	Length of stay		Cost per day‡
Ambulatory care			
Outpatient attendances	Number	Patient questionnaire	Cost per attendance‡
Physiotherapy attendances	Number		
Other hospital attendances	Number		
Primary, community and social service care			
GP contacts	Number and type	Patient questionnaire	Cost per contact§
Other contacts	Number		
Indirect costs**			
Patient time††	Included within the SF-36	None	None
Friction costs‡‡	Days off work	None	None

PAS, patient administration system; PRF, patient report form

**For the purposes of this economic evaluation length of call-out was defined as the time between the call being passed to the ambulance and the time of arrival at the A&E department*

†*Based on 3 months of call-out times and annual emergency costs (Trust Financial Return TFR6)*

‡*Region average*

§*Netten and co-workers*[37]

***Indirect costs are sometimes referred to as production costs*

††*The Washington Panel*[38] *established methodological guidelines for economic evaluation. They recommend that patient time spent sick (i.e. morbidity time) should be measured solely as an outcome. In the present study, morbidity time was measured within the SF-36*

‡‡*Friction costs are costs to society due to lost production. The importance of such costs is highly debated, and is not considered in detail in this evaluation*

BOX 4 Formula for calculating individual patient costs

Cost of patient i =

(length of call-out for patient i × cost per minute of ambulance time) +

(bags of fluids used by patient i × cost per bag) +

(length of hospital stay of patient i × cost per patient day in each specialty) +

(number of outpatient attendances by patient i × cost per attendance) +

(number of GP contacts by patient i × cost per contact) +

(number of other contacts by patient i × cost per contact)

Although the use of protocols A (fluids) and B (no fluids) was randomised across paramedics, an analysis of variance was undertaken in order to remove any remaining systematic differences between the two groups in terms of important prognostic factors. The model used was the same as that used in the majority of the preceding analyses of mortality and morbidity, and used age, injury severity and patient consciousness at the scene as covariates.

Results

Overall, there were few differences between the two study groups. It was therefore decided to

TABLE 21 *Intravenous fluids use*

Fluid volumes (500 ml bags)	No fluids*				Fluids*				$p^{\dagger}$
	n	Mean	Median	SD	*n*	Mean	Median	SD	
Total colloid (patients receiving colloid)	128	2.5	2.0	2.1	155	2.2	2.0	2.1	0.27
Total crystalloid (patients receiving crystalloid)	218	3.1	2.0	2.4	305	2.7	2.0	2.7	0.08
Total colloid (all patients)	603	0.5	0.0	1.4	685	0.5	0.0	1.4	0.37
Total crystalloid (all patients)	603	1.1	0.0	2.1	685	1.2	0.0	1.9	0.70

**Unadjusted for covariates*
†Adjusted using analysis of variance for the ISS, age and consciousness at the scene

TABLE 22 *Non-fluid resources use*

Resource	No fluids*				Fluids*				$p^{\dagger}$
	n	Mean	Median	SD	*n*	Mean	Median	SD	
Ambulance call-out time (minutes)	566	55.6	55.0	21.4	644	58.0	55.0	23.2	0.08
Inpatient-days‡	606	16.0	9.0	21.2	692	16.3	0.0	21.0	0.96
Intensive care unit days	606	1.4	0.0	4.8	692	1.3	0.0	4.2	0.43
Ambulatory care contacts§	262	11.1	7.0	13.1	300	10.1	5.5	11.5	0.18
Primary and community care contacts**	262	6.5	3.0	10.6	302	5.8	3.0	8.7	0.36

**Unadjusted for covariates*
†Adjusted using analysis of variance for the ISS, age and consciousness at the scene
‡Includes intensive care unit days
§Includes day cases, outpatient attendances, physiotherapy and other hospital attendances
***Includes GP surgery contacts, GP home visits and other community and social care contacts*

undertake a more simple costing of treatment than was originally envisaged. Differences in resource use were estimated for all major resource-use groups; however, costs were only estimated for a reduced list of these groups. In the immediate and prehospital phase of treatment, only ambulance call-out costs and fluid costs were included in the analysis. Admission costs were estimated on two specialty groupings (intensive care unit and 'other') and no costs were estimated for patients following discharge from hospital.

Resource use

A greater proportion of patients were given colloid and crystalloid fluids in the protocol A group than in the protocol B group (23.6% versus 21.8% and 45.2% versus 36.7%, respectively) but a slightly smaller proportion were given blood in the A&E department (9.4% versus 11.6%). For those patients receiving fluids, the protocol A group used fewer bags of fluids (*Table 21*); however, when looking across all patients, there were no significant differences between the two groups.

The mean ambulance call-out time was 2.3 minutes longer in the protocol A group after adjusting for covariates (95% CI, –0.3 to 4.8). The median call-out times in the two groups were identical at 55 minutes (*Table 22*). As such there is weak evidence that protocol A lengthened the call-out times across all patients. There were no statistically significant differences in any of the other categories of resource use.

Costs

Costs were estimated for the total use of fluids across prehospital and A&E care (*Table 23*), using unit costs for Haemaccel (colloid), Hartmann's solution (crystalloid) and blood. The mean cost

TABLE 23 *Intravenous fluids costs (£, 1997–98 prices)*

Fluid	No fluids*				Fluids*				$p^{\dagger}$
	n	Mean	Median	SD	*n*	Mean	Median	SD	
Colloid‡	603	2.0	0.0	5.3	685	1.9	0.0	5.0	0.37
Crystalloid§	603	0.9	0.0	1.7	685	1.0	0.0	1.6	0.70
Blood**	595	32.6	0.0	151.2	679	19.9	0.0	87.6	0.03
Total	594	35.4	0.0	153.7	679	22.8	0.0	90.9	0.03

**Unadjusted for covariates*
†Adjusted using analysis of variance for the ISS, age and consciousness at the scene
‡Haemaccell
§Hartmann's solution
***The cost of a unit of blood during the study was around £40; however, it is currently £78.88 (1999–2000 prices) due to the requirement for all blood to go through leucodepletion (Source: National Blood Service). The current price has been used in the analysis (deflated by the Health Service Cost Index for the year 1998–99 and, in the absence of that, the GDP estimated deflator for the year 1999–2000). No distinction has been made between cross-matched and O-negative blood, with the unit cost representing unmatched blood. Cross-matching costs £6.26 at 1997–98 prices*[43]

of fluid use was £14.85 greater in the protocol B group after adjusting for covariates (95% CI, 1.76 to 27.95).

The increased costs of fluids (including blood) in the protocol B group were offset by reduced call-out time and costs. This resulted in the protocol A group being £2.80 more expensive than the protocol B group (95% CI, –19.6 to 22.7) when viewed across the whole of prehospital and immediate care (*Table 24*). Inpatient costs were also similar, and total costs to discharge were £28 higher in the protocol A group (95% CI, –482.2 to 954.2). The costs profiles of the two groups were broadly similar (*Figure 6*).

The variability in costs was investigated through one-way sensitivity analysis (*Table 25*). The bounds on the ambulance costs were informed by the variation in costs across all Ambulance Trusts in England (NHS Executive 1997).[39] The cost per emergency patient journey in the Leicestershire Ambulance Service is around two standard deviations below the national average (or, alternatively, 50% of the national mean). The baseline cost per minute, which was estimated from the Leicestershire data, was treated as a lower limit of the geographical variation in costs, with costs re-estimated using twice and three times the baseline unit cost. The hospital daily rates were mean estimates based on costs from across the two study regions, and so lower and upper limits were produced by using the mean figure, plus or minus two standard deviations. Considering all analyses, costs were consistently higher in the protocol A group,

TABLE 24 *Summary of the NHS costs (£, 1997–98 prices)*

Cost	Protocol B*				Protocol A*				$p^{\dagger}$
	n	Mean	Median	SD	*n*	Mean	Median	SD	
Pre-hospital and immediate care costs*	559	416.0	384.4	208.8	632	418.8	384.4	171.9	0.89
Inpatient costs†	606	2386.3	0.0	7342.9	692	2319.4	0.0	6736.8	0.42‡
Total costs	559	2678.0	414.7	7315.1	632	2706.2	426.8	6876.3	0.52§

** Includes ambulance costs, fluid costs and A&E costs*
† Includes intensive care unit and ward costs
‡ p-value on log-transformed inpatient costs (plus 10) is 0.53
§ p-value on log-transformed total costs is 0.64

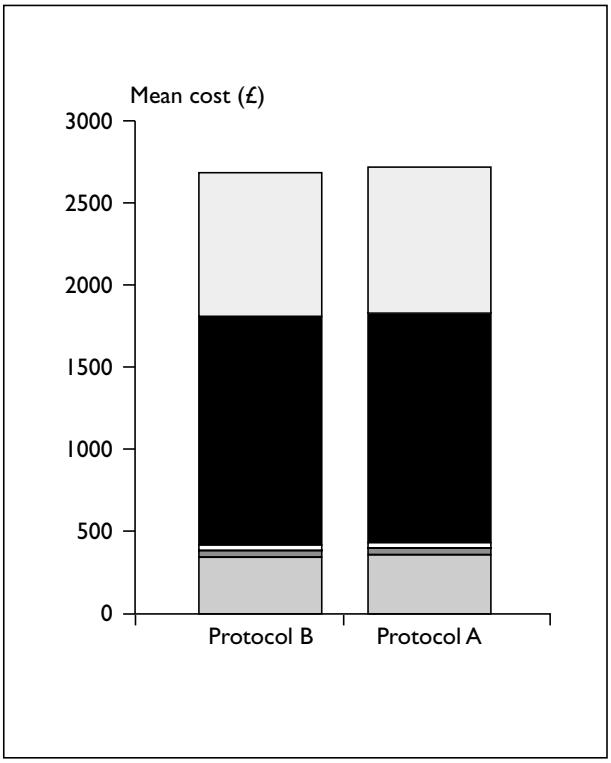

FIGURE 6 *Summary of patient costs (□, ward; ■, intensive care unit; □, A&E department; ■, fluids; ■, ambulance)*

by between £19 and £56. None of these differences were statistically significant.

A subgroup analysis was undertaken to look at costs in different patient groups (*Table 26*). No statistically significant differences were found.

Discussion

The economic analysis did not provide patient costs covering all aspects of care in the 6 months following the incidents. In the prehospital and immediate-care phase, only intravenous fluids and blood were costed separately from an average unit cost covering the ambulance call-out and an average cost of an A&E attendance. Other consumables were not included because they contribute very little to the cost of care and there are a lot of missing data. In a previous study with an identical patient population, the mean cost of consumables used by ambulance crews was £2.25 per patient.[4]

Hospital costs were estimated using daily rates for two specialty groups: intensive care unit and

TABLE 25 *Sensitivity analysis (£, 1997–98 prices)*

		Mean cost		
	Unit cost	**No fluids**	**Fluids**	**Difference**
Baseline		2678.0	2706.2	28.2
Ambulance costs	12.12	3014.8	3057.0	42.2
Cost per minute (baseline £6.06)	18.18	3351.7	3407.8	56.1
Intensive care unit costs	417.00	1849.1	1867.8	18.7
Cost per day (baseline £1057)	1697.00	3506.9	3544.7	37.8
Ward costs	127.00	2357.8	2382.6	24.8
Cost per day (baseline £198)	269.00	2998.2	3029.9	31.7

TABLE 26 *Total costs of patient subgroups (£, 1997–98 prices)*

Fluid	**Protocol B***				**Protocol A***				***p*†**
	n	**Mean**	**Median**	**SD**	***n***	**Mean**	**Median**	**SD**	
Bleeding injury	358	1,777.8	406.4	6,050.3	399	1,716.2	413.1	4,521.6	0.50*
Head injury	58	7,680.4	1,874.4	10,528.4	70	5,414.4	496.5	10,424.1	0.55†
Both injuries	50	7,581.5	1,002.3	11,985.1	79	7,613.8	1,440.7	11,807.3	0.97‡
Other injury	93	386.8	366.2	137.4	84	536.8	365.0	1,225.7	0.32§

* *p-value for log-transformed total costs is 0.69*
† *p-value for log-transformed total costs is 0.36*
‡ *p-value for log-transformed total costs is 0.44*
§ *p-value for log-transformed total costs is 0.60*

'other specialties'. While more complex analysis is possible, this was not thought necessary given the lack of clinical differences between the two trial groups. The main cost driver in the inpatient phase is the use of intensive care unit facilities, and once this has been taken into account very little would be added to the analysis by using more finely divided specialty costs.

The costs following discharge from hospital were not calculated because the analysis of resource use, combined with an interpretation of the clinical and outcome data, indicated that there were no real differences between the two trial groups. Post-discharge resource use was analysed using two broad groups of services: ambulatory care contacts and primary care contacts. It is possible that these broad groups mask different mixes of resource use between the study groups, but this is not thought plausible as there were no significant physiological or clinical effects that could precipitate differences in resource use. It is possible for a difference in resource use to occur in the event of no physiological difference if knowledge of the patient's fluid infusion affected the clinician's management decisions. This may partly explain the greater use of blood in the A&E department in the protocol B group. However, this greater use of blood is unlikely to occur following discharge from the A&E department, and certainly not following discharge from hospital.

Sensitivity analysis was undertaken on the three largest components of cost. The principal aim of the sensitivity analysis was to investigate the effect of the geographical variation in unit costs. One-way sensitivity analysis was used, basing the upper and lower bounds on figures that were roughly plus or minus two standard deviations from the mean value of national ambulance costs and regional hospital costs. Costs were consistently higher in the protocol A group, with the excess cost ranging from £19 to £56 per patient. Analysis of the costs of four patient subgroups showed no statistically significant differences in cost.

Chapter 5

Discussion and conclusions

The present study of 1309 patients, of whom 133 died and a further 82 had serious complications, failed to find any difference between patients whose attending paramedic was randomised to a conventional fluids protocol or to a restrictive prehospital fluids protocol. This 'negative' finding was the same for all the outcomes assessed (including processes of care, deaths, quality of survival and composite outcomes) and was also true for several subgroups of patients. Better SF-36 scores on all eight dimensions of quality of life were observed in the protocol A group than in the protocol B group, but these differences were neither clinically nor statistically significant. Overall, the overwhelming impression was that these protocols failed to have any clinically or statistically important impact.

Previous literature

Numerous studies on the use of intravenous fluids in trauma have been published. Much of the reported evidence both on the volume and the type of fluids infused is based on animal experiments. There are fewer human studies, and of these the majority have assessed the impact of intravenous fluids as part of an ALS 'package' of trauma care rather than as a single intervention. Some are simple descriptive studies that measured on-scene times and outcome for cohorts of patients who received ALS. Two studies concluded that prehospital interventions including intravenous fluid administration are advantageous in that they change haemodynamic status in the prehospital phase[44] and can be accomplished within the same on-scene time frame as a 'scoop and run' protocol.[45] Conversely, Smith and co-workers[1] found that in all cases the transport time to hospital was less than the time taken to establish intravenous access, and Dalton[46] reported that, in an urban area, 98% of patients given prehospital intravenous fluids were infused for less than 30 minutes. Both these studies therefore suggest that, because of the potential delays to definitive care and the small volumes of fluid infused, any benefit to patients of the prehospital administration of fluids is questionable.

The primary purpose of the present study was to compare the effects on mortality of a policy of giving prehospital intravenous fluids and one of not giving them to trauma patients. Nine previous studies have been identified that have attempted to measure differences in mortality for patients given prehospital intravenous fluids compared to patients who received no fluids (*Table 27*). Five of these studies compared ALS care (including the administration of intravenous fluids) with basic life support (BLS) care. These studies produced conflicting results. One study used historical controls to assess the effect of introducing ALS care to patients with abdominal vascular trauma.[7] Survival in the ALS group was better than the BLS group (34.4% versus 29.2%). However, this improvement could have been the result of the uncontrolled effects of other changes in medical care over the same time period. Two other studies[5,11] compared change in physiological status and mortality in contemporary cohorts of trauma patients with both blunt and penetrating injuries. One found an improvement in Trauma Score with ALS care, primarily as a result of increased systolic blood pressure, and that this change was also associated with increased survival, although this could not be directly attributed to the type of ambulance crew.[5] The other study also found ALS care to be associated with an increase in systolic blood pressure, but found no difference in survival between patients who received ALS and those who received BLS after adjusting for age, ISS, RTS and mechanism of injury.[11] One further study[12] measured physiological and survival outcomes for patients with penetrating thoracic injuries who were either stabilised in the field (ALS care) or transported immediately to hospital. Transport included means other than by ambulance (e.g. police or private vehicle). No difference in clinical status was found between the groups, and survival was significantly better in the immediate transport group after adjusting for injury type.

All these studies are severely limited in their ability to shed light on the effect of intravenous fluid administration. Firstly, none of the studies was randomised and possible differences in case mix, which could result from targeting ALS crews to specific types of patients, cannot be

TABLE 27 *Literature relating to the use of intravenous fluids in trauma patients*

Study	Type of patients	Comparison groups	Type of study	Outcome measures	Findings
Aprahamian, 1983,[7] Milwaukee, USA	Major open intra-abdominal trauma	EMT-attended patients (first 8 years) (*n* = 64) vs paramedic-attended patients (*n* = 48)	Historical controls	Deaths in hospital	BLS, 22/64 (34.4%); ALS, 14/48 (29.2%) RR of death for paramedics 0.85 (95% CI, 0.45 to 1.95)
Jacobs, 1984,[5] Boston, USA	Severely injured trauma patients	ALS (*n* = 80) vs BLS (*n* = 98)	Contemporary cohorts	Change in TS Death adjusted for TS + ΔTS	Shows that ΔTS affects outcome and that ΔTS is affected by crew status. But the model of outcome as a function of (TS, ΔTS, crew status, scene time) failed to find a relationship with crew status
Cayten, 1993,[11] New York City, USA	Trauma patients, aged ≥ 13 years; length of stay ≥ 48 hours, ISS ≥ 10	ALS (*n* = 434) vs BLS (*n* = 347)	Contemporary cohorts	Death before discharge Change in SBP	BLS, 51/347 (14.7%); ALS = 74/434 (17.1%) OR = 1.19 RR = 1.16 RR adjusted for age, RTS, ISS, mechanism of injury = 0.98 Change in SBP significantly greater in ALS group for both blunt and penetrating injuries
Ivatury, 1987,[12] New York City, USA	Penetrating thoracic injuries	Stabilisation (*n* = 51) vs immediate transport (*n* = 49)	Contemporary cohorts	Survival to discharge Δ change in TS and PI	Stabilisation, 1/51; immediate transport, 9149 No change is TS or PI for stabilisation group More immediate transport patients arrived at hospital with signs of life
Rainer, 1997,[47] Scotland	MTOS criteria, excluding trapped patients	ALS (*n* = 247) vs BLS (*n* = 843)	Contemporary cohorts	Death in hospital	ALS, 10/247 (4.0%); BLS, 26/843 (3.1%) Crude OR = 1.33 RR = 1.31
Nicholl, 1998,[4] England	MTOS criteria, excluding patients when a doctor was on scene	ALS (*n* = 1440) vs BLS (*n* = 605)	Contemporary cohorts	Death within 6 months of incident	ALS, 86/1440 (6.0%); BLS, 28/605 (4.6%) Crude OR = 1.31 RR = 1.29 Adjusted RR = 1.67

continued

TABLE 27 contd *Literature relating to the use of intravenous fluids in trauma patients*

Study	Type of patients	Comparison groups	Type of study	Outcome measures	Findings
Kaweski, 1990,[10] San Diego County, USA	All trauma patients	Prehospital intravenous fluids given (*n* = 3839) vs prehospital intravenous fluids not given (*n* = 3016)	Contemporary cohorts?	Death in hospital	ISS < 25: 0.7% fluids; 0.5% no fluids ISS 25–50: 23% fluids; 22% no fluids ISS > 50: 90% fluids; 86% no fluids Hypotension associated with significantly higher mortality rate but not influenced by administration of prehospital fluids
Sampalis, 1997,[48] Montreal, Canada	Severely injured patients with a prehospital index score > 3 and alive at hospital	Prehospital intravenous fluids given (*n* = 217) vs prehospital intravenous fluids not given (*n* = 217)	Case control trial	Death within 7 days of admission	Fluids, 23%; no fluids, 6% OR adjusted for age, sex, ISS, mechanism and prehospital time = 2.3 OR prehospital time 0–30 minutes = 1.05 OR prehospital time 30–60 minutes = 3.38 OR prehospital time > 60 minutes = 3.4
Bickell, 1994,[27] Houston, USA	Hypotensive patients aged ≥ 16 years with penetrating torso injuries	Immediate (prehospital fluids) (*n* = 309) vs delayed fluids (*n* = 289)	Randomised controlled trial	Death before discharge In-hospital complications Length of stay in hospital	Immediate fluids, 30%; delayed fluids, 38% (*p* = 0.04) No difference after adjustment for prehospital time Significantly longer length of stay in immediate fluids group Fewer complications in delayed fluids group

ALS, advanced life support; BLS, basic life support; EMT, emergency medical technician; ISS, Injury Severity Score; MTOS, Major Trauma Outcome Study; PI, Physiological Index; SBP, systolic blood pressure; TS, Trauma Score

discounted. Secondly, the effects of intravenous fluid administration cannot be distinguished from other ALS interventions. This is further complicated by the fact that in all these studies pneumatic anti-shock garment suits were also used to control bleeding in some patients, either alone or in conjunction with intravenous fluids. As a result, the measured changes in haemodynamic status are not the result of intravenous fluids alone. Finally, the use of physiological change as an outcome measure can be interpreted in different ways. Jacobs and co-workers[5] and Aprahamian and co-workers[7] both viewed an increase in systolic blood pressure as a positive outcome, which contributed to better survival. Conversely, Cayten and co-workers[11] found no association between increased systolic blood pressure and improved survival; in fact for some patients with penetrating injuries survival in the ALS group was poorer than that expected using Major Trauma Outcome Study standards. The findings of this study were interpreted as supporting the evidence from animal experiments that increasing systolic blood pressure, and hence potentially increasing rather than limiting bleeding, may have a detrimental effect on patient outcome.

More recently, two UK studies comparing contemporary cohorts of ALS and BLS patients[4,47] have also shown increased mortality with ALS care. Rainer and co-workers[47] reported a crude relative risk associated with ALS care of 1.31, while Nicholl and co-workers[4] found a relative risk of 1.67 after adjusting for ISS, head injury AIS score, age, mechanism of injury and whether or not the patient had been trapped. While, as in the earlier studies, the effects of intravenous fluids cannot be disassociated from other ALS interventions, both these studies showed a significant increase in on-scene times when intravenous fluids were administered, suggesting that a delay on scene may be a contributory factor to the increased mortality in ALS patients.

The remaining studies have attempted to isolate more specifically the effects of prehospital intravenous fluid administration. Kaweski and co-workers[10] conducted a retrospective study of 6855 trauma patients and compared outcomes in patients who received prehospital intravenous fluids with those who did not. Mortality was compared between similar groups based on the ISS and systolic blood pressure measured at the scene, although mortality rates were not adjusted for risk factors. There was no difference in mortality between the fluid and no-fluid groups for any of the ISS or systolic blood pressure defined study groups. The mean prehospital time was the same for the fluid and no-fluid groups and, in patients who did receive fluids, there was no difference in the volumes of fluid infused in survivors compared to those patients that died. In a similar study, Sampalis and co-workers[48] also compared mortality after hospital admission in a retrospective sample of patients who received prehospital intravenous fluids compared to patients matched by prehospital index score who received no fluids. After adjusting for age, sex, ISS and total prehospital time the use of prehospital intravenous fluids was associated with a significant increase in the risk of mortality (odds ratio 2.3). In addition, analysis by prehospital time showed the mortality risk associated with prehospital intravenous fluids to increase as the prehospital time increased.

The predominant problem with both the above studies is that, being non-randomised retrospective studies, selection effects cannot be accounted for. In both cases the process by which paramedics made a decision about when to commence intravenous fluid administration and when not to is not known. As a result, there may be systematic biases in case mix. It is possible, for example, that prehospital fluids were started because of a perceived risk of death rather than that death resulted from giving fluids. Sampalis and co-workers[48] acknowledged that, despite adjustment for ISS, there were differences in injury type between the two groups, with more head, chest and abdominal injuries present in the group that received fluids. These differences may in themselves have produced different outcomes. Such differences could have also been present in the groups studied by Kaweski and co-workers.[10]

Clearly the most robust test of the effects of either giving intravenous fluids prehospital or withholding them is to randomise to treatment protocols. To date only one other study, by Bickell and co-workers,[27] has addressed this question using a quasi-randomised controlled trial design. In this prospective study patients with penetrating injuries to the torso injured on even-numbered days of the month were assigned to receive immediate intravenous fluids (in the prehospital phase) and those injured on odd-numbered days were assigned to a treatment protocol where intravenous fluids were delayed until the patient reached the operating theatre. Survival was significantly different between the immediate-fluids (62%) and delayed-fluids (70%) groups, and this difference did not change after adjustment for prehospital and in-hospital time periods. No adjustment was made in the analysis for other factors, but the two groups were well matched for age, sex, ISS and mechanism of injury. In addition, the immediate-fluids group had a significantly longer length of stay in hospital and there was a trend towards more complications in this group.

The study by Bickell and co-workers[27] is the most definitive evidence to date of the impact of prehospital intravenous fluids, although it has not been without criticism. As in the present study, there was some protocol violation, with 8% of the delayed-fluids group receiving fluids before surgical intervention. It has also been suggested that, in a group of rapidly exsanguinating patients such as this, some patients in the delayed-fluids group who died before reaching the operating theatre may have survived if given fluids earlier.[5] However, it could equally be argued that the early deaths in patients given fluids could have been prevented if fluids had been delayed. The study was also, as the authors acknowledged, limited in its generalisability. The evidence produced relates to a group of patients with very specific injuries and cannot be extrapolated to other groups (e.g. blunt injuries). Furthermore, the times from the

incident to definitive operative care were very short, and it is unlikely that this time interval could be reproduced in rural areas or indeed in many other urban areas. Nevertheless, the results provide an important contribution to the debate and support the general principle of the possible detrimental effects of early fluid resuscitation in patients with severely bleeding injuries. The results of the present study, in which there was a non-statistically significant increased risk of death with giving fluids in a group of patients with severe bleeding injuries (+19%), is consistent with those reported by Bickell and co-workers.[27]

Reliability

The only conclusion that can be drawn from the present study is that it provides no evidence that a no-fluids protocol makes a difference to patient outcomes. We cannot conclude that it provides evidence that such a protocol makes no difference, only that we could find no evidence that it does. The former conclusion could only be drawn if the results were completely reliable (i.e. free from bias and as precise as necessary).

Bias

The trial was randomised and individual patients were not required to give consent to enter the trial, so the most well-known source of bias in randomised controlled trials (patient preference bias)[49] cannot be present. On the other hand, only 330/400 paramedics attended any patients included in the trial. Plainly if, for example, there was an interaction between effect (or effect size) and paramedic attendance at incidents involving eligible trauma patients, then the trial is open to some degree of bias. However, it is unlikely that there could be any such interaction.

Secondly, no-one was blinded in the trial, and it could be imagined that this could lead to some bias, at least in analysis or outcome assessment. In pragmatic trials the blinding of patients and therapists may be inappropriate anyway, and 'hard' outcomes such as mortality are objective and not subject to the influence of personal assessments. Analysis bias is potentially present (although the analyst (JN) started with the prejudice that a beneficial effect of the no-fluids protocol would be found, and the failure to find any evidence of such a difference was unexpected).

Precision

With regard to precision, it is conventional to carry out a *post hoc* power calculation to provide some evidence of the capacity of the trial to a reject the null hypothesis when it is false. Although it has been argued that such calculations are meaningless when done *post hoc*,[50] the prospective power of a trial of this size ($n_1 = 699$, $n_2 = 610$) to reject the null hypothesis when the outcome rates are as found in the protocol A (fluids) group (10.4% for mortality, and 17.0% for mortality or complications) and various other rates in the experimental protocol B (no fluids) group are shown in *Figure 7*.

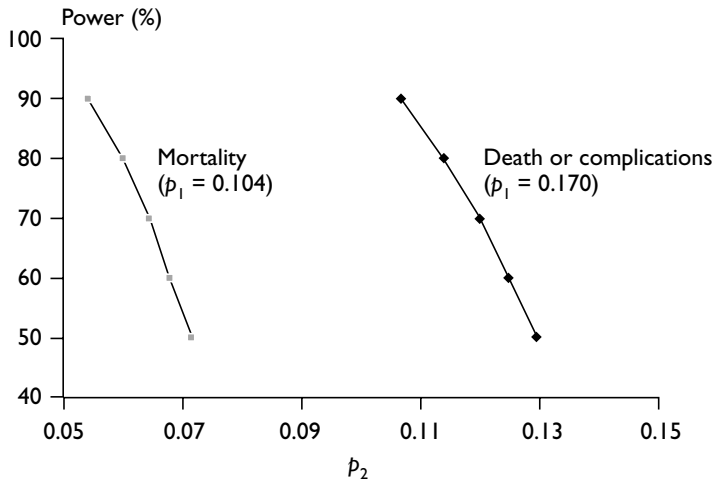

FIGURE 7 Post hoc *power of the study*

It can be seen that the power to detect the effect size targeted in the protocol (relative risk for mortality 0.7, i.e. 7.2% versus 10.4%) was only 50%. For the composite outcome of death or serious complications the power was approximately 72%.

The comparatively low powers are also reflected in the wide CIs for the estimated effect of protocol A (odds ratio 0.93 (95% CI, 0.58 to 1.49), for death; odds ratio 1.02 (95% CI, 0.71, 1.47), for death or complications). However, the key observation is that these point estimates are close to 1.0, and the chance of detecting effects of the size of these observed estimates as significant are small even in very large trials.

Generalisability

The study was carried out across two ambulance service areas representing urban, rural and semi-rural areas. However, neither ambulance service included one of the large metropolitan English conurbations, and it therefore remains possible that it is only in these sorts of areas, where previous studies have shown the intervention by paramedics to be associated with increased mortality and Bickell and co-workers[27] found a significant effect in the USA, that operating a fluids or no-fluids protocol affects outcomes. However, our subgroup analysis found no difference in effect between urban incidents less than 10 minutes and non-urban incidents more than 10 minutes transfer time to the A&E department, and no difference between protocols in the urban incidents (11.8% mortality versus 11.9%) (see chapter 3). We therefore believe that the findings as such are generalisable to other ambulance-service areas.

Only 330/400 paramedics contributed at least one patient to the trial, but there is no record of any non-contributory paramedic attending any patients with sufficiently severe trauma to be included in the study. A total of 69 patients were excluded from the study because the paramedic failed to complete an incident scene PRF, which would have enabled us to identify who was at the scene and who treated the patient. However, only four of these patients were identified in coroners', A&E department or hospital records as having died, and this cannot have introduced any significant bias (internal or external).

Interpretation

The results of the present trial are inconclusive. The trial provides no evidence that conventional prehospital fluids protocols are doing any harm, and some evidence that they are not doing any substantial harm. What can we make of this and what are the possible explanations?

Giving fluids does no harm in blunt trauma

One possible explanation is that fluids do no harm, at least in blunt trauma. Although the weight of evidence from animal models, penetrating injury trials and blunt trauma cohort studies suggests that prehospital fluids may be harmful, the possibility remains that they are not.

The harm of giving fluids is unmeasurably small

Fluids could do harm, but their effect is so small as to be negligible and not measurable in any practical trial. This could arise because:

- Paramedics operating standard protocols in the UK give such small amounts of prehospital fluid that these amounts do not do any non-negligible harm.
- Fluids are given in A&E departments anyway, so that prehospital protocols which determine what happens in the period from 10 to 60 minutes post-incident are irrelevant compared to what happens in the A&E department from 60 to 240 minutes pretheatre.
- It is only colloids that are harmful,[23] and most ambulance services are rapidly moving to crystalloid-only infusion. In the ambulance services studied in the present trial, there was no evidence of how patterns are changing, but a substantial proportion of patients (about 12%) were still given colloid infusions prehospital.

The numbers of patients who could be harmed is negligible

This could be because:

- There are very few patients in whom the protocols used make any difference to whether or not they are given fluids. This would certainly seem to have been the case in the present trial since, although the no-fluid protocol approximately halved the chance of being given fluids, this reduction was from 31% of patients to 17% of patients.

This leaves very few patients who could have been affected.

- There are few blunt trauma patients with the types of bleeding injuries in whom prehospital fluids could be adversely critical. This seems to be a likely contributory factor to the inconclusive evidence from this trial, since only 5% of patients have penetrating injuries and only 50% in total have injuries where bleeding (shock, exsanguination, etc.) is the main cause of potential problems.
- Few patients with injuries in whom fluids are potentially critical are injured in circumstances where this potential is realised. For example, it could be the case that the problem with giving fluids is the result of extra time spent at the incident scene, in which case only patients in whom an extra 10–15 minutes delay in reaching hospital was critical could be affected.

When the possibility that few patients could be affected by fluids is combined with the fact that there are few patients in whom the protocol makes a difference to whether fluids are given at all, it is likely that even if giving fluids (or the delay caused by giving fluids) is harmful fewer than 1/10 patients is likely to be adversely affectable by a fluids protocol. Since only a proportion of those in whom fluids are potentially critical will actually suffer, the proportion affected is likely to be very small.

Only a marginal effect on the time on scene was detected

It is possible that the critical issue is on-scene time.[51] In the present study the mean time on scene was very similar in the two protocol groups. However, this was not because giving fluids did not affect the time spent on scene. The analysis suggests that patients given fluids spent 13 minutes longer on scene than patients not given fluids. However, because only a small additional proportion of patients were given fluids in the protocol A group, and because on-scene times were especially long in patients given fluids in the protocol B group, there was little difference in the average on-scene times between the trial groups.

Conclusions and future research

Despite the lack of conclusive results, some clinical, practical and scientific conclusions can be reached.

- Although intervention by paramedics does seem to be associated with an increase in the mortality rate of serious blunt trauma patients, this may not be remediable by altering fluid protocols. Even if the giving of fluids is the main contributing cause of the increased mortality associated with intervention by paramedics, clinically acceptable protocols only change the proportion of patients being given fluids from 31% to 20% (as opposed to 31% to 0% for paramedics and technicians, respectively).
- There is no evidence from the UK that fluids protocols are doing significant harm in blunt trauma patients. Therefore, it would be appropriate for ambulance-service operators to concentrate on avoiding unnecessary delays at the incident scene and speeding up transfer to definitive care in hospital, rather than concentrate on their fluid protocols. One possibility is for fluids resuscitation to be started in the ambulance en route to hospital rather than at the incident scene. However, further research in the UK into the benefits of and any problems with this approach to avoiding delays and giving fluids early would be necessary.
- Future research in the UK into the benefits of fluids to blunt trauma patients should compare strict no-fluids protocols (as would be operated by technicians) rather than discretionary protocols. Only crystalloids should be permitted in the fluids protocols, and ways of separating out the effect of fluid infusion and on-scene time delays should be sought.
- Finally, the fluids issue remains unresolved. It is not just a problem for prehospital care but also for care prior to definitive surgery. Is the administration of fluids appropriate in A&E departments? Do the same arguments apply to pretheatre resuscitation as to prehospital resuscitation, including questions about avoiding unnecessary delays to theatre, and if so could a trial to compare fluid resuscitation prior to arrival in theatre with delayed giving of fluids in blunt trauma patients be organised?

Acknowledgements

This study was commissioned by the NHS R&D HTA programme. The authors are indebted to the HTA referees for their perseverance in reading this report and the quality of their comments. The views expressed in this report are those of the authors, who are responsible for any errors.

The authors would like to thank the NHS R&D Trust Boards' Medical Advisory Groups, and the staff of the two ambulance services, particularly the training departments for their help in implementing the trial. We are particularly grateful to the paramedics who were randomised to protocols for their cooperation, without which the trail could not have been completed.

The authors would also like to thank the Consultants and staff of the A&E departments, medical records departments and hospitals in the two areas for their help and cooperation. We would also like to thank the project steering group (Mr D Quinton, Mr K Porter, Mr P Henry and Mr M Gregory) and our colleagues Brigette Colwell, Jenny Hall and Wendy Montgomery for clerical and administrative support.

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Appendix 1

Standard NHS Training Division Criteria for prehospital fluid infusion by paramedics

The following are the NHS Training Division Indications for Infusion, taken from the NHSTD Ambulance Service Paramedic Training Manual, Section 3, Unit 3, Fluid Administration.

Neurogenic shock

Definition: A result of massive vasodilation and pooling of blood in the peripheral vessels to such a degree that adequate perfusion cannot be maintained.

These patients may need intravenous lines and fluid infusion to maintain their systolic pressure.

If bradycardia is a problem, consider using atropine in the recommended dose. Remember bradycardia may be the result of pre-existing heart disease or drug therapy.

Septic shock

Definition: A condition of shock resulting from a severe bacterial infection.

Hypovolaemia must be treated but monitor the patient closely for signs of cardiac failure: the response to fluid may be unpredictable if the myocardium has been injured by circulating toxins.

Anaphylactic shock

Definition: An exaggerated allergic reaction with severe bronchospasm and vascular collapse which may prove rapidly fatal.

Treatment should include:

- Reducing the stimulus by use of a venous torniquet and cold packs.
- Administration of oxygen.
- Administration of fluid at the appropriate rate and, where collapse is severe, the injection of 0.5–1 ml of adrenaline 1:1000 by the subcutaneous or intramuscular (IM) route.

You can administer salbutamol if bronchospasm is a problem. Where local standing procedures allow, consider cricothyrotomy if the airway is compromised.

Hypovolaemic shock

Definition: Resulting from an abnormally decreased volume of blood or fluids in the body.

Stage 1

For the first stage of haemorrhage, insert a single wide-bore intravenous cannula into a visible or palpable accessible upper limb vein. Maintain cannula patency with a slow-running infusion of normal saline or other crystalloid.

Stages 2 to 4

Assess the patient's condition continuously to detect further deterioration. You may need to infuse fluid more rapidly. In more severe cases you may need to establish two wide-bore cannulae with intravenous lines in two separate limbs. Infuse fluid at the appropriate rate to maintain blood pressure at a satisfactory level. Routinely administer oxygen at a high concentration.

For patients with severe head injuries and who are showing signs of hypovolaemic shock, you will need to replace the volume deficit adequately before you can properly assess the severity of the injury. Correct the hypotension by infusing suitable volumes of crystalloid or colloid fluid, and by administering oxygen.

If transfusing when head injuries are present, be aware of the possibility of fluid overload. Continual monitoring is essential. Assume that hypovolaemic shock in head injured patients is due to injury elsewhere in the body.

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We look forward to hearing from you.

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ISSN 1366-5278