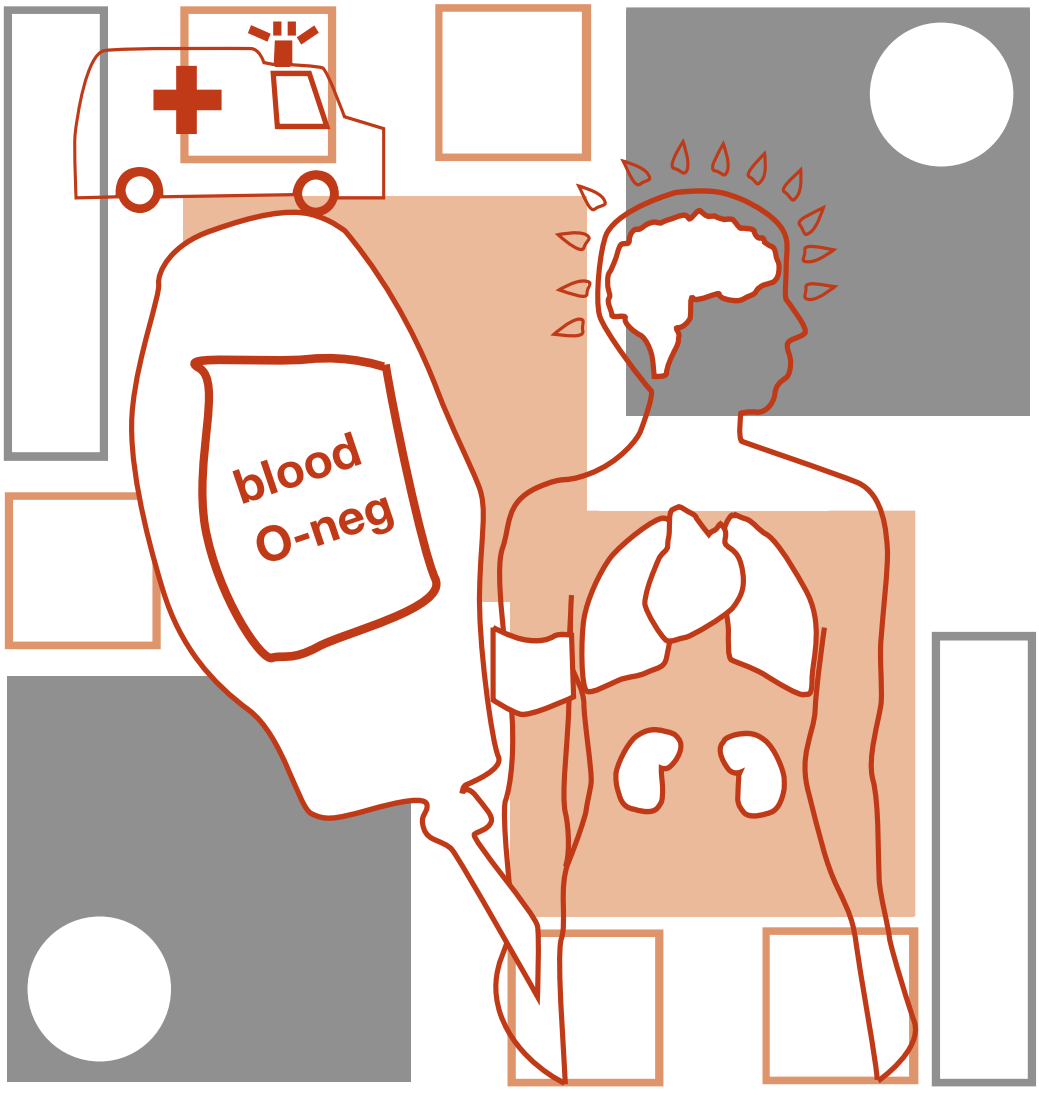
ADULT TRAUMA CLINICAL PRACTICE GUIDELINES

Management of Hypovolaemic Shock in the Trauma Patient

HYPOVOLAEMIC SHOCK GUIDELINE



NSW HEALTH

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January 2007

Important notice!

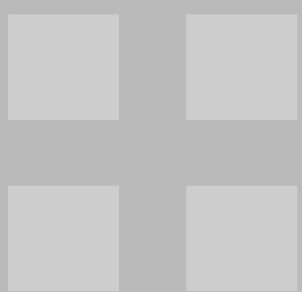
'Management of Hypovolaemic Shock in the Trauma Patient' clinical practice guidelines are aimed at assisting clinicians in informed medical decision-making. They are not intended to replace decision-making. The authors appreciate the heterogeneity of the patient population and the signs and symptoms they may present with and the need to often modify management in light of a patient's co-morbidities.

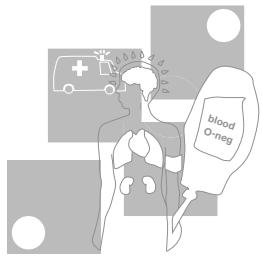
The guidelines are intended to provide a general guide to the management of specified injuries. The guidelines are not a definitive statement on the correct procedures, rather they constitute a general guide to be followed subject to the clinicians judgement in each case.

The information provided is based on the best available information at the time of writing, which is December 2003. These guidelines will therefore be updated every five years and consider new evidence as it becomes available.

These guidelines are intended for use in adults only.

All guidelines regarding pre-hospital care should be read and considered in conjunction with NSW Ambulance Service protocols.





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The Management of Hypovolaemic Shock in the Trauma Patient

If definitive care is not available in your facility make early contact with retrieval services

Primary survey

Includes organising the trauma team, calling the surgeon and notifying the blood bank. Also consider early call to Retrieval Services (AMRS 'formerly MRU' 1800 650 004).

Airway / C-spine	Breathing	Circulation	Disability	Exposure / Environment	Adjuncts
▪ Protect airway, secure if unstable. ▪ Airway adjunct as needed. ▪ Control of c-spine.	▪ Definitive control of airway. ▪ Oxygen. ▪ Bag and mask.	▪ Secure venous access x 2 large bore cannula. ▪ Bloods: – x-match – FBC – EUC's – Creatinine – ABG's – Blood ETOH. ▪ Control external bleeding.	▪ Assess neurological status. ▪ AVPU: – alert – responds to vocal stimuli – responds to painful stimuli – unresponsive.	▪ Undress patient. ▪ Maintain temperature.	▪ X-ray: – chest – pelvis – lateral c-spine.

REMEMBER – BP and HR will not identify all trauma patients who are in shock.
ASSESS – History and perfusion indices – ABG's, base deficit, lactate, Hb and HCT.

SIGNS OF SHOCK? — NO → **Perform Secondary Survey**

YES ↓

Identify the source of haemorrhage

External	Long bones	Chest	Abdomen	Retroperitoneum
▪ Careful visual inspection.	▪ Careful visual inspection.	▪ Chest x-ray.	▪ DPA* and / or FAST**.	▪ Pelvic x-ray.

* Diagnostic Peritoneal Aspiration (DPA). >10mls of frank blood = positive DPA.
** Focused Abdominal Sonography in Trauma (FAST). Free fluid = positive FAST.

Interventions

External	Long bones	Chest	Abdomen	Retroperitoneum
▪ Apply direct pressure. ▪ Suture lacerations.	▪ Splint + / - reduce #.	▪ Chest tube.	▪ Emergency Laparotomy.	▪ Externally stabilise pelvis. ▪ Emergency angiogram.

In the presence of uncontrolled haemorrhage and a delay of greater than 30 minutes to operative haemostasis, infuse small aliquots (100-200mls) of fluid to maintain systolic blood pressure between 80-90mmHg. Use caution in the elderly. Contraindicated in the unconscious patient without a palpable blood pressure. Maintain the systolic blood pressure >90mmHg for those with a traumatic brain injury.

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Summary of guidelines

How do you know when the patient is in hypovolaemic shock?

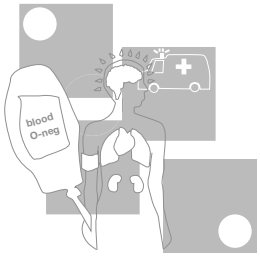
GUIDELINE	LEVEL OF EVIDENCE
Blood pressure and heart rate will not identify all trauma patients who are in shock. Assessment of the trauma patient should include: :: arterial blood gases and assessment of base deficit :: haemoglobin :: lactate :: haematocrit. These tests are only of value when interpreted in a series, therefore should be repeated.	III-2

How do you find the sources of bleeding in a hypotensive trauma patient?

GUIDELINE	LEVEL OF EVIDENCE
When the haemodynamically unstable patient enters the resuscitation room, a primary survey with full exposure takes place. Carefully inspect for external bleeding sources and examine the long bones. If x-ray facilities are available, a supine chest x-ray and pelvic x-ray should be obtained within 10 minutes of arrival. The CXR will identify any large haemothorax. If the pelvic x-ray shows a pelvic fracture, the remaining two sites of significant bleeding are the abdomen and the pelvic retroperitoneum. The options for assessing the abdomen are DPA and / or FAST.	IV

What is the best management of the bleeding patient?

GUIDELINE	LEVEL OF EVIDENCE
:: Establish patent airway. :: Ensure adequate ventilation and oxygenation. :: Secure venous access – large bore cannula x 2. :: Control any external bleeding by applying direct pressure. :: Rapidly identify patients requiring operative haemostasis. :: Establish prompt contact with the major referral hospital and retrieval service.	III-2
In the presence of uncontrolled haemorrhage and a delay of greater than 30 minutes to operative haemostasis, infuse small aliquots of fluid (100-200mls) to maintain systolic blood pressure between 80-90mmHg. Use caution in the elderly. Contraindicated in unconscious patients without a palpable blood pressure and those with traumatic brain injury (see over leaf).	II



Summary of guidelines

What is the best management of the bleeding patient? continued...

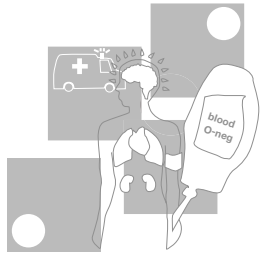
GUIDELINE	LEVEL OF EVIDENCE
In the presence of uncontrolled haemorrhage in the patient with a concurrent traumatic brain injury, prevention of secondary brain injury from hypotension is crucial as a systolic blood pressure <90mmHg is associated with poor outcomes. Infuse small aliquots of fluid (100-200mls) to maintain systolic blood pressure above 90mmHg.	I

If fluid resuscitation is indicated, what type of fluid should be given?

GUIDELINE	LEVEL OF EVIDENCE
:: Early use of blood, if available, remains the optimal resuscitation fluid for the hypovolaemic patient. Use with caution due to numerous complications.	Consensus
:: Where blood is not available or delayed, Compound Sodium Lactate (Hartmanns) is the preferred alternative for the initial resuscitation of the hypovolaemic trauma patient. Caution should be exercised in the trauma patient with liver disease. :: 0.9% Normal Saline is also an acceptable alternative. Large volumes, however may result in metabolic acidosis.	II

What are the endpoints of fluid resuscitation in the trauma patient?

GUIDELINE	LEVEL OF EVIDENCE
Traditional haemodynamic parameters do not adequately quantify the degree of physiological derangement in hypovolaemic trauma patients. If point of care blood gas analysis is available base deficit and lactate levels should be used to identify the magnitude of tissue oxygen debt and the adequacy of resuscitation. These tests are only of value when interpreted in a series, therefore should be repeated. A persistently high or increasing base deficit indicates the presence of ongoing blood loss or inadequate volume replacement.	III-2
In the absence of point of care blood gas analysis capability the restoration of a normal mentation, heart rate, skin perfusion and urine output and maintain ing the systolic blood pressure at 80-90 mmHg serve as the end point of resuscitation.	Consensus



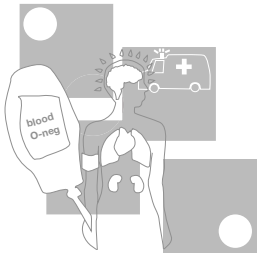
1 Introduction

Despite significant advances in the management of trauma victims, traumatic injury remains the fifth leading cause of death in Australia. A significant number of these deaths are the result of hypovolaemic shock. Acute blood loss following injury leads to a depression of organ and immune function that, if prolonged, progresses to the sequential failure of multiple organ systems.[1]

Timely diagnosis, surgical control of on-going loss and physiologically directed fluid replacement remain the cornerstones of management. In recent years, however, the practice of rapid fluid replacement has been questioned.

Early recognition of hypovolaemic shock is vital for optimal care of the injured patient. Ongoing controversy exists regarding the diagnosis of occult shock and the ideal resuscitation scheme. Advancement in technology and pharmacology has added more treatment options to care for the bleeding patient. This guideline aims to objectively analyse the literature to provide the clinician with evidence-based options. The guidelines will also seek to establish the optimal care of the bleeding patient in the rural setting where resources may be lacking and access to definitive care is delayed.

This guideline has been developed to provide evidence-based recommendations for the management of hypovolaemic shock in the trauma patient.



2 Methods

2.1 Scope of the guideline

This guideline is intended for use by all clinicians who are involved in the initial care of patients with hypovolaemic shock: ambulance officers, emergency nurses, and physicians.

This guideline has been developed to assist clinicians to provide a selective evidence based approach to the management of trauma patients with hypovolaemic shock. It is recognised that this guideline will not suit all clinical situations.

These guidelines are not prescriptive, nor are they rigid procedural paths. The guidelines rely on individual clinicians to decipher the needs of individuals. They aim to provide information on what decisions can be made, rather than dictate what decisions should be made.

2.2 Aims and objectives of the guideline

This guideline aims to summarise the available evidence to allow clinicians to make evidence-based decisions in the diagnosis and management of trauma patients with hypovolaemic shock.

A multidisciplinary team was consulted to aid in the identification of the key clinical dilemmas that faced clinicians when caring for patients with hypovolaemic shock. By identifying the key clinical questions, the guideline should facilitate:

- early diagnosis of hypovolaemic shock
- identification of the source(s) of bleeding
- enhancement of tissue perfusion while minimising ongoing haemorrhage.

The clinician using this guideline can identify:

- when the patient is in hypovolaemic shock
- how to find the sources of bleeding in a hypotensive trauma patient
- what is the best management of the bleeding patient
- over what timeframe a hypovolaemic trauma patient should be fluid resuscitated
- what type of fluids should be used if required
- what the endpoints of fluid resuscitation in the hypovolaemic trauma patient.

2.3 Inclusion and exclusion

Inclusion criteria

Meta-analysis
Randomised control trials
Controlled clinical trials
Case series
Population aged >16 years
Traumatic hypovolaemic shock

Exclusion criteria

Case reports
Paediatric <15 years
Hypovolaemic shock secondary to burns or non-traumatic (sepsis, dehydration)

2.4 Strength of the evidence

2.4.1 Level of evidence

The articles were classified according to their general purpose and study type.

Table 1. Levels of evidence[2-4]

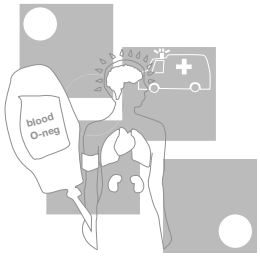
Level I	Evidence obtained from a systematic review of all relevant randomised control trials
Level II	Evidence obtained from at least one properly-designed randomised control trial.
Level III-1	Evidence obtained from well-designed pseudo-randomised controlled trials (alternate allocation or some other method).
Level III-2	Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case-control studies, or interrupted time series with a control group.
Level III-3	Evidence obtained from comparative studies with historical control, two or more single arm studies or interrupted time series without a parallel control group.
Level IV	Evidence obtained from a case-series, either post-test or pre-test / post-test

2.4.2 Quality appraisal

The included articles were appraised according to the NHMRC. The MERGE assessment tool.[5]
The articles were rated for quality on a 4-point scale as follows:

Table 2. Codes for the overall assessment quality of study checklists

Low risk of bias	A	All or most evaluation criteria from the checklist are fulfilled, the conclusions of the study or review are unlikely to alter.
Low-moderate risk of bias	B1	Some evaluation criteria from the checklist are fulfilled. Where evaluation criteria are not fulfilled or are not adequately described, the conclusions of the study or review are thought unlikely to occur.
Moderate – High risk of bias	B2	Some evaluation criteria from the checklist are fulfilled. Where evaluation criteria are not fulfilled conclusions of the study or review are thought likely to alter.
High risk of bias	C	Few or no evaluation criteria fulfilled. Where evaluation criteria are not fulfilled or adequately described, the conclusion of the study or review are thought very likely to alter.



3 How do you know when the patient is in hypovolaemic shock?

GUIDELINE	LEVEL OF EVIDENCE
Blood pressure and heart rate will not identify all trauma patients who are in shock. Assessment of the trauma patient should include: :: arterial blood gases and assessment of base deficit :: haemoglobin :: lactate :: haematocrit. These tests are only of value when interpreted in a series, therefore should be repeated.	III-2

Acute blood loss or the redistribution of blood, plasma, or other body fluid predisposes the injured patient to hypovolaemic shock. Absolute hypovolaemia refers to the actual loss of volume that occurs in the presence of haemorrhage. Relative hypovolaemia refers to the inappropriate redistribution of body fluids such as that that occurs following major burn trauma.[6]

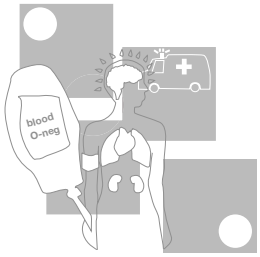
Acute blood loss is a very common problem following traumatic injury. Rapid recognition and restoration of homeostasis is the cornerstone of the initial care of any seriously injured patient. Delay in recognising and quickly treating a state of shock results in a progression from compensated reversible shock to widespread multiple system organ failure to death. Morbidity may be widespread and can include renal failure, brain damage, gut ischaemia, hepatic failure, metabolic derangements, disseminated intravascular coagulation (DIC), systemic inflammatory response syndrome (SIRS), cardiac failure, and death.

The standard physiological classification of acute blood loss has been promulgated through the Advanced Trauma Life Support Course developed by the American College of Surgeons.[7] While a useful theoretical basis for understanding the stages of shock, the physiological changes said to occur as a patient progresses through the four stages are not supported by evidence.

Lechleuthner et al in a study of blunt trauma found that a systolic blood pressure (SBP) <90mmHg will only identify 61% of patients with active haemorrhage (sensitivity 61% and specificity 79%). 3.1% of patients with uncontrolled haemorrhage had undisturbed physiological variables.[8] These findings are supported by others.[9-11] Demetriades examined the incidence and prognostic value of tachycardia and bradycardia in the presence of traumatic hypotension. The incidence of relative bradycardia (SBP <90mmHg and HR <90 minute) was present in 28.9% of hypotensive patients.[11] The results of these studies suggest that commonly monitored variables, in and of themselves, do not accurately reflect or predict the circulating volume of injured patients.[9] The accuracy of circulatory values (HR, BP, urine output and capillary return) in detecting hypovolaemia in trauma patients is hampered by complex neurohormonal mechanisms that can successfully compensate for 15% loss of circulating volume, particularly considering the majority of trauma patients are young, fit males.[9] Confounders such as traumatic brain injury also decreases the sensitivity of SBP and HR to detect hypovolaemic shock.[8]

Detecting hypovolaemic shock in the trauma patient with normal haemodynamics is reliant on history, physical examination and pathology, including, base deficit, lactate, haematocrit and haemoglobin. However, these tests are only of value when interpreted in a series. Initial haemoglobin (Hb) of <=6g/l correlated well with mortality (48.4%) and vital signs. A low level Hb (<8g/l) was found by Knottenbelt, in a review of 1000 trauma patients, to be an indicator of serious ongoing haemorrhage.[12] Lactate and base-deficit have also shown to correlate well with vital signs and mortality.[13,14] The ability and value of haemoglobin, lactate and base-deficit, however, to predict blood loss in haemodynamically stable patients is unknown.

Oman examined the predictive power of haematocrit decrease of >5% as an indicator of ongoing haemorrhage in trauma patients who receive IV fluids. The study found that haematocrit was not useful in identifying patients who were bleeding, but was accurate 97% of the time for identifying those who were not (sensitivity 94%, specificity 43%, PPV 26%, NPV 97%).[15]



4 How do you find the sources of bleeding in a hypotensive trauma patient?

GUIDELINE	LEVEL OF EVIDENCE
When the haemodynamically unstable patient enters the resuscitation room, a primary survey with full exposure takes place. Carefully inspect for external bleeding sources and examine the long bones. If x-ray facilities are available, a supine chest x-ray and pelvic x-ray should be obtained within 10 minutes of arrival. The CXR will identify any large haemothorax. If the pelvic x-ray shows a pelvic fracture, the remaining two sites of significant bleeding are the abdomen and the pelvic retroperitoneum. The options for assessing the abdomen are DPA and / or FAST.	IV

4.1 Probabilities and assessment

In a haemodynamically unstable trauma patient there are five potential sites of major blood loss: externally, long bones, the chest, the abdomen and the retroperitoneum.[7]

4.2 Externally and long bones

Blood loss from fractures and lacerations can result in a significant amount of blood loss. The scalp is a highly vascular region and may be associated with significant blood loss. It is however, extremely difficult to estimate the volume of bleeding from scalp and other lacerations due to blood loss at the scene and en route to the hospital. External blood loss requires careful visual inspection.

Clarke reported that a single long-bone fracture may result in 10-30% loss of total blood volume. Bleeding from long bone fractures is present in approximately 40% of cases and is usually evident from swelling due to haematoma formation. This is usually a contribution, not a major ongoing cause of blood loss.[16-18]

4.3 The chest

Intrathoracic haemorrhage is to be expected in 4-29% of cases[16-19] and can be evaluated on a chest x-ray, which should be performed within 10 minutes of the patients arrival.[20] There are minor limitations to first mobile supine chest x-ray. A small haemothorax can be initially missed in 5% of surviving patients and in up to 18% in non-surviving patients. However, a large haemothorax contributing to haemodynamic instability should not be missed.

4.4 The pelvis

The next part of the decision tree is crucial, trying to decide whether the blood loss is in the abdomen or in the pelvic retroperitoneum or in both. At this point the AP pelvic radiograph should be reviewed. If a pelvic fracture with possible disruption of the pelvic ligaments causing an unstable fracture pattern is seen or suspected, the probability of pelvic arterial bleeding is 52%.

The initial AP pelvic radiograph is the only guide to determine the probability of pelvic bleeding. Disruptions involving only the pubic rami do not vertically or rotationally unstabilise the pelvic ring, but when recognising a fracture of the pubic bone, posterior disruption and probability of arterial bleeding must always be suspected. One must also bear in mind that bilateral inferior/superior pubic ramus fractures (butterfly type fracture from AP compression mechanism), acetabular fractures and even simple ramus fractures in the elderly can lead to arterial bleeding causing hypotension.

4.5 The abdomen

The abdomen is the most difficult to assess in the rural and urban environment. Diagnostic Peritoneal Aspiration (DPA) and Focused Abdominal Sonography in Trauma (FAST) are the preferred diagnostic means to determine if there is intra-abdominal bleeding. Although the availability of FAST is increasing, it is not available in all urban and rural emergency departments. DPA is recommended if an EMST accredited clinician is available. If neither FAST nor DPA can be undertaken, the clinician should examine the other four sources for blood loss, upon exclusion of these it must be assumed that the patient has intraabdominal bleeding until proven otherwise.

Seventy-eight per cent of intraperitoneal injuries result in haemorrhage including; the spleen (22%), the liver (20%), the bladder (15%), the bowel mesentery (10%) and diaphragmatic lesions (4%). Renal haemorrhage is found in 7% of cases. The other 22% are intraperitoneal injuries not associated with bleeding.

4.6 Decision-making

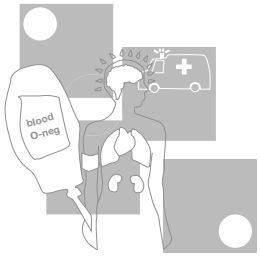
In the face of continuing haemodynamic instability and in the absence of external blood loss, long bone or pelvic fractures or any evidence of bleeding on chest x-ray, immediate laparotomy is warranted.

If an unstable pelvic fracture is seen on x-ray the chance of pelvic arterial bleeding is 52%. The patient should have their pelvis externally stabilised in the resuscitation room. Please refer to the *'Adult Trauma Clinical Practice Guidelines The Management of Haemodynamically Unstable Patients with a Pelvic Fracture'* (which is available from the NSW Institute of Trauma and Injury Management, contact details listed on the inside cover).

4.7 Timeframes

For every three minutes of haemodynamic instability elapsed without haemorrhage control in the emergency department, there is a 1% increase in mortality. Therefore decision making within pre-determined timeframes is crucial. The haemodynamically unstable pelvic fracture patient should leave the resuscitation room within 45 minutes heading for either angiography or laparotomy. Assessment of external bleeding sources and long bone fractures should take place within the first five minutes. The chest x-ray and pelvic x-ray should be performed within 10 minutes of the patients arrival. Assessment of the abdomen with FAST / DPA if possible, should be completed within 30 minutes.

Performance indicators
Assessment of external bleeding sources and long bone fractures should take place within the first five minutes.
The chest x-ray and pelvic x-ray should be performed within 10 minutes (if x-ray facilities are available).
FAST / DPA within 30 minutes.



5 What is the best management of the bleeding patient?

What is the best management of the bleeding patient?

GUIDELINE	LEVEL OF EVIDENCE
:: Establish patent airway. :: Ensure adequate ventilation and oxygenation. :: Secure venous access – large bore cannula x 2. :: Control any external bleeding by applying direct pressure. :: Rapidly identify patients requiring operative haemostasis. :: Establish prompt contact with the major referral hospital and retrieval service.	III-2
In the presence of uncontrolled haemorrhage and a delay of greater than 30 minutes to operative haemostasis, infuse small aliquots of fluid (100-200mls) to maintain systolic blood pressure between 80-90mmHg. Use caution in the elderly. Contraindicated in unconscious patients without a palpable blood pressure and those with traumatic brain injury (see below).	II
In the presence of uncontrolled haemorrhage in the patient with a concurrent traumatic brain injury, prevention of secondary brain injury from hypotension is crucial as a systolic blood pressure <90mmHg is associated with poor outcomes. Infuse small aliquots of fluid (100-200mls) to maintain systolic blood pressure above 90mmHg.	I

Management priorities in the bleeding patient include controlling blood loss, replenishing intravascular volume and sustaining tissue perfusion.[1] When services are needed that exceed available resources, it is of critical importance that early consultation with a trauma specialist and rapid transportation to definitive care occurs.
(Refer to *NSW Department of Health Circular 2002/105 Early Notification of Severe Trauma in Rural NSW*)

5.1 Controlling blood loss

After establishing a patent airway, ensuring adequate ventilatory exchange and oxygenation and securing venous access, the highest priority in the bleeding patient is to control haemorrhage.[21] Because patients may bleed from multiple sites, it is imperative that the attending medical officer establish strategies to address all sources of bleeding. Sources of bleeding may be broadly classified as external or internal.

5.1.1 Controlling external bleeding

The Australian Resuscitation council advocates the use of direct pressure to gain prompt control of external bleeding.[22] The recommended method involves approximating the wound edges if possible, holding an absorbent dressing firmly over the area with the heel of the hand, and elevating the bleeding part. After bleeding is controlled the absorbent dressing may be secured with a bandage. If bleeding continues through the initial dressing, apply a second dressing over the first and secure with a bandage. Do NOT disturb the dressing once the bleeding has been controlled. Arterial tourniquets are reserved for life-threatening bleeding and when direct pressure to the wound has failed to stop the bleeding or when protruding objects prevent direct pressure.

5.1.2 Controlling internal bleeding

Evidence from numerous studies over the past two decades indicates that immediate and definitive operative haemostasis is the optimal treatment for internal bleeding.[23] To delay leaves the patient susceptible to multi organ dysfunction and other complications. In the rural and remote setting however, immediate operative haemostasis is limited by a lack of surgical presence and or operating facilities at the site, and or lengthy transport times to institutions capable of providing definitive operative haemostasis.

Given these limitations the challenge for the rural and remote physician is to rapidly identify patients who would benefit from early transfer based on available local resources, manage any life-threatening injuries, and establish prompt contact with the major referral centre, and the transport /retrieval service. Prolonged time spent in a local emergency department poses a significant risk of mortality for the internally bleeding patient.[24]

In a prospective analysis of the interhospital transfer of injured patients to a tertiary centre by Martin et al, up to 60% of the time delay pertaining to the transfer of injured patients was related to the time taken to notify the retrieval team.[25] In some cases this accounted for delays in excess of three hours. Numerous other studies have suggested that prompt early contact with the retrieval service and subsequent timely transfer of severely injured patients is associated with increased survival rates.[26-28]

5.2 Repleting intravascular volume

It is generally recognised that a depleted intravascular volume robs the cardiovascular system of the preload required for adequate cardiac output and peripheral oxygen delivery.[29] Inadequate perfusion, even in the absence of overt hypotension can result in a neurohumoral cascade that ultimately leads to sequential organ failure.[30]

Since the early 1900's the conventional approach to restoring intravascular volume and subsequently sustaining tissue perfusion in the bleeding patient has focused on early aggressive fluid replacement with large volumes of crystalloid and or blood products.[31] There is a growing body of evidence, however, that suggests that in the presence of uncontrolled haemorrhage, fluid replacement may result in increased haemorrhage and subsequent greater mortality.[1;31-34] This is thought most likely to be the result of increased blood pressure and the subsequent reversal of vasoconstriction, dislodgement of early thrombus and subsequent secondary haemorrhage, and the dilutional coagulopathy that occurs in the presence of large volumes of fluid.[1]

Bickell et al studied the outcomes of swine that were bled from a 5mm tear in the infrarenal aorta and aggressively resuscitated with lactated ringers solution. Control swine were not resuscitated.[33] A significant elevation of mean arterial pressure (MAP) in the resuscitated swine was observed. One-hundred per cent of resuscitated swine died within 100 minutes. All of the control swine survived. The follow-up interval, however was only two hours. Kowalenko and his associates developed a more severe model of aortic tear and similarly demonstrated that animals aggressively resuscitated with high volumes of crystalloid had significantly lower survival rates than animals under-resuscitated.[35] Data from Capone et al[36], and Stern et al[37] are consistent with the study by Kowalenko.[35]

Several solid organ injury animal models of uncontrolled haemorrhage demonstrate results that also support low volume fluid resuscitation in the presence of uncontrolled haemorrhage[37;38] In Krausz et al[39] study of aggressive resuscitation following moderate splenic injury in rats, untreated controls sustained significantly less haemorrhage volumes than treated animals. Similarly, Solomonov et al[38] study of severe splenic injury in rats demonstrated that animals aggressively resuscitated experienced greater haemorrhage volumes and a significantly lower survival time in comparison to untreated animals.

Findings from the animal models are substantiated by Bickell et al[40] prospective controlled study of patients presenting with a penetrating torso injury and a prehospital systolic blood pressure less than 90mmHg. Patients received either immediate or delayed fluid resuscitation following penetrating torso trauma. The delayed resuscitation group (n = 289) had intravenous access secured, but received no fluid resuscitation until admission to the operating theatre. The immediate resuscitation group (n = 309) were aggressively fluid resuscitated at the scene and during transport. The volume of fluid infused was 2,478mls. Survival to discharge rates was significantly higher in the delayed resuscitation group compared to the immediate resuscitation group (70% versus 62%;

p = 0.04). A number of methodological flaws, however, have led some to question the study. First the causes of death were not well defined. Second, there were a number of protocol violations. Eight per cent of the delayed resuscitation group received fluids prior to operative intervention. Finally there was wide variation in the severity of shock across both groups.[31] Despite these limitations, Bickell's paper has led us to question traditional fluid resuscitation regimes.

A randomised study undertaken by Turner compared early and delayed fluid administration in trauma patients. Significant protocol violation (with only 31% of the fluid group actually receiving fluid) resulted in the inability of this study to find any treatment affect (10.4% mortality early fluid group vs 9.8% mortality in delayed group).[41]

Dutton, in a randomised study evaluated fluid resuscitation titrated to a SBP of 100mmHg or 70mmHg during a period of active haemorrhage on mortality. There was no difference in mortality between the two groups (7% vs 7%).[42] The low pressure group appeared sicker than the higher pressure group (ISS in the conventional-pressure group was 19.65 ± 11.84, compared with 23.64 ± 13.82 in the low-pressure group). This may have had a negative affect on survival in the low pressure group.

Evidence from retrospective studies further supports the concept of delayed resuscitation. Sampalis et al[43] reviewed the outcomes of 217 trauma patients who had received intravenous fluid and compared them with 217 controls who received no fluid. Correction was made for gender, age, mechanism of injury and injury severity score. Patients who received on-site fluid resuscitation had a higher mortality than the control group, particularly when fluid resuscitation was combined with prolonged prehospital times. Another study by Hambly and Dutton[44] compared patients given fluids using a rapid infusion device with historical controls who had undergone standard resuscitation. Patient resuscitated with the rapid infusion device had a higher mortality than those receiving standard resuscitation.

The advocates of early aggressive resuscitation of hypotensive bleeding patients argue that the trauma population is too heterogenous to rely solely on animal studies, and limited clinical trials. It should be noted, however, that a systematic review on the effects of early or large volume intravenous fluid in uncontrolled bleeding by Kwan et al[45] found no evidence to support the conventional practise of early aggressive fluid resuscitation in the presence of uncontrolled haemorrhage.

From this data consensus opinion now recommends a more discriminating approach to the conventional practice of delivering liberal volumes of intravenous fluids to patients with uncontrolled bleeding.[46] The emerging evidence demonstrates that aggressive fluid resuscitation in the bleeding patient leads to additional haemorrhage through soft clot dissolution, hydraulic acceleration of bleeding and dilution of clotting factors. While aggressive fluid resuscitation it is still considered appropriate for unconscious patients with no palpable blood pressure, the latest recommendations are to limit or delay intravenous fluid resuscitation preoperatively in those with uncontrolled haemorrhage, even if they are hypo perfusing, although caution should be used with the elderly.

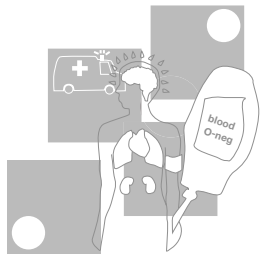
In the presence of uncontrolled haemorrhage in the patient with a concurrent traumatic brain injury, prevention of secondary brain injury from hypotension is crucial as a systolic blood pressure <90mmHg is associated with poor outcomes. Infuse small aliquots of fluid (100-200mls) to maintain systolic blood pressure above 90mmHg.[122]

There is abundant data to suggest that hypotensive or limited resuscitation may be preferable to aggressive fluid resuscitation in the setting of uncontrolled haemorrhage. There is, however, little evidence suggesting the volume of fluid required to maintain vital organ perfusion yet prevent thrombus dislodgment and subsequent secondary haemorrhage and coagulation dilution. At best the literature suggests that small aliquots of fluid (100-200mls) should be given to maintain the patients systolic blood pressure between 80-90mmHg.[47;48]

Performance indicators

- Primary Survey completed.
- Initial stabilisation of life threatening injuries.
- Early transfer to definitive care..
- Fluid administration <600mls/hr.

6 If fluid resuscitation is indicated, what type of fluid should be given?



GUIDELINE	LEVEL OF EVIDENCE
:: Early use of blood, if available, remains the optimal resuscitation fluid for the hypovolaemic patient. Use with caution due to numerous complications.	Consensus
:: Where blood is not available or delayed, Compound Sodium Lactate (Hartmanns)is the preferred alternative for the initial resuscitation of the hypovolaemic trauma patient. Caution should be exercised in the trauma patient with liver disease. :: 0.9% Normal Saline is also an acceptable alternative. Large volumes, however may result in metabolic acidosis.	II

Although a wide variety of options are currently available for fluid resuscitation, most agree tnat the best resuscitation fluid is blood. It provides simultaneous volume expansion and oxygen carrying capacity.[49] However, there are a number of disadvantages to blood as a resuscitation fluid (Table 1, p.7). In addition, issues regarding compatibility, cost and storage requirements make blood and its derivates in the rural setting unlikely options as a permanent solution for the rural physician. This limits the choice in the rural setting to crystalloid and or colloid.

Table 3. Complications of blood transfusions

Complication	Mechanism
Impaired oxygen release from haemoglobin	The ability of red blood cells to store and release oxygen is impaired after storage.[2,3] DPG levels fall rapidly resulting in a shift to the left of oxygen disassociation curve, and subsequent impaired oxygen release.
Dilutional coagulopathy	Stored blood contains all coagulation factors except factors V and VIII. Microvascular bleeding and coagulopathy can occur in the setting of massive transfusion due to decreased levels of Factor V, VIII and fibrinogen and associated increased prothrombin times.
Thrombocytopenia	Dilutional thrombocytopenia is inevitable following massive transfusion as platelet function declines to zero after a few days of storage.
Hypothermia	Cold blood is associated with major coagulation derangements, peripheral vasoconstriction, metabolic acidosis, and impaired immune response.
Citrate toxicity / Hypocalcaemia	Each unit of blood contains approximately 3g of citrate. Citrate toxicity is caused by acutely decreasing serum levels of ionised calcium, which occurs because citrate binds to calcium
Hyperkalaemia	The plasma potassium concentration of stored blood increases during storage and may be over 30mmols/l. The potential for Hyperkalaemia occurs with infusion rates of blood greater than 120ml/min and in patients with severe acidosis.
Acid-base abnormalities	Lactic acid levels in the blood pack give stored blood an acid load of up to 30-40mmols/l. This along with citrate is metabolised rapidly. Citrate in turn is metabolised to bicarbonate, and a profound metabolic alkalosis may result.
Haemolytic transfusion reactions	Reactions that result in destruction of the transfused cells may occur from errors involving ABO incompatibility, or when the recipients antibody coats and immediately destroys the red blood cells.

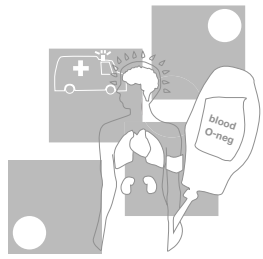
Source: Adapted from Trauma.Org, *Transfusion for Massive Blood Loss,* http://www.trauma.org/resus/massive.html, accessed 27 April 2004

The debate regarding the relative effectiveness of colloids compared to crystalloid continues several decades after it began. Despite numerous publications recommending specific fluids, there is no evidence from randomised control trials that resuscitation with colloids carries a reduced mortality in patients with trauma, burns and following surgery.[50;51] Because colloids are not associated with an increase in survival and they carry a significant cost compared to crystalloids there is no apparent benefit to their use in the initial management of the hypovolaemic patient.[50;51]

A number of recent studies[52-54] have suggested that the administration of hypertonic solutions, in the absence of a head injury, allows for a more rapid stabilisation of macro and micro-haemodynamics. A recent systematic review by Alderson et al,[50] suggests that there is no evidence that hypertonic crystalloid is better than isotonic crystalloid. Due to the clinically different outcomes identified during the review, however, Bunn et al recommends further large-scale trials comparing hypertonic crystalloids with isotonic crystalloids are required to inform practice.

Wade and colleagues undertook a meta-analysis of randomised trials examining the effects of Hypertonic Saline (HS) and Hypertonic Saline/Dextran (HSD) on survival of trauma patients until discharge or for 30 days. The study found that HS alone does not offer any benefit in terms of 30-day survival over isotonic crystalloids. HSD may improve mortality (OR 1.20 [95% CI 0.94-1.57]). The summary statistics of the available data shows that HS does not provide any benefit over current practices in terms of survival and that HSD may be superior.[55]

The optimal resuscitation fluid for the hypovolaemic trauma patient remains the early use of blood. In the absence of type specific blood, isotonic crystalloids have an established safety record when used appropriately.[42] Isotonic crystalloids produce a relatively predictable increase in cardiac output and are generally distributed throughout the extracellular space. Where blood is not available or delayed, Compound Sodium Lactate (Hartmanns) solution is the preferred alternative for the initial resuscitation of the hypovolaemic patient.[7;56] Compound Sodium Lactate solution contains a bicarbonate precursor that when metabolised helps to correct metabolic acidosis and its attendant detrimental effects.[56] Compound sodium lactate may need to be discontinued in the presence of liver disease. Normal Saline 0.9% is an acceptable alternative, however, large volumes of 0.9% Normal Saline may result in metabolic acidosis.[56]



7 What are the endpoints of fluid resuscitation in the trauma patient?

GUIDELINE	LEVEL OF EVIDENCE
Traditional haemodynamic parameters do not adequately quantify the degree of physiological derangement in hypovolaemic trauma patients. If point of care blood gas analysis is available base deficit and lactate levels should be used to identify the magnitude of tissue oxygen debt and the adequacy of resuscitation. These tests are only of value when interpreted in a series, therefore should be repeated. A persistently high or increasing base deficit indicates the presence of ongoing blood loss or inadequate volume replacement.	III-2
In the absence of point of care blood gas analysis capability the restoration of a normal mentation, heart rate, skin perfusion and urine output and maintain ing the systolic blood pressure at 80-90 mmHg serve as the end point of resuscitation.	Consensus

The challenge of caring for the hypovolaemic trauma patient involves limiting cellular oxygen deficits, anaerobic metabolism and resultant tissue acidosis.[57] Resuscitation is complete when the cellular oxygen deficits have been corrected, tissue acidosis is eliminated and normal aerobic metabolism is restored.[58] Many patients may appear to be adequately resuscitated, but have occult hypoperfusion and ongoing tissue acidosis (compensated shock).[57] Failure to recognise this may result in organ dysfunction and death.

Traditionally it has been assumed that the restoration of a normal mentation, blood pressure, heart rate, skin perfusion and urine output signified the end points of resuscitation.[59] Recent studies[60;61] however, suggest that even after normalising these parameters, up to 85% of severely injured patients have evidence of compensated shock. Compensated shock is defined as the presence of ongoing inadequate tissue perfusion despite the normalisation of heart rate, blood pressure, skin perfusion and urine output.[58] Recognition of compensated shock and its rapid reversal are critical to minimise the risk of multi organ dysfunction or death. Consequently, the traditional end points of fluid resuscitation in the hypovolaemic trauma patient need to be supplemented with global and end organ markers that are sensitive to the symptoms of compensated shock.

Global markers include: lactate levels and base deficit.[54] Arterial pH is not as sensitive as it is buffered by the body's compensatory mechanisms.[54] End organ markers include: monitoring of gut perfusion with gastric tonometry, and direct measures of tissue oxygen tension.

7.1 Base deficit

A recent study by Davis et al[62] found that the initial base deficit was a reliable early indicator of the magnitude of volume deficit. Patients were stratified according to the level of base deficit as mild (base deficit 2 to -5mmol/L), moderate (base deficit -6 to -14) or severe (base deficit < -15). Patients with the more severe base deficit required a greater volume of fluid for resuscitation. Sixty-five per cent of patients with an increasing base deficit had ongoing blood loss. This is consistent with the findings of Canizaro et al[63], and James et al[64].

Kincaid and his associates[65], further found that among trauma patients who normalised their lactate levels, those with persistently higher base deficits had a significantly increased risk of multi-organ dysfunction and death. Patients with persistently higher base deficits also demonstrated impaired oxygen utilisation. In a similar study Rixen et al[13] found that an increase in base deficit between the

time the patient arrived at the hospital to the time of admission to intensive care identified patients who were haemodynamically unstable, had high transfusion requirements, coagulation and metabolic derangements, and an increased risk of death.

It is important to note that base deficit may be confounded by a number of factors. Firstly, approximately 12-16 hours following resuscitation, base deficit may no longer correlate with lactate.[66] Secondly, the administration of bicarbonate may alter the base deficit without correcting the oxygen debt.[57] Underestimation of base deficit may occur in the hypocapnic or hypothermic trauma patient, whereas an elevated base deficit may be present in the presence of excess heparin in the blood. Finally, alcohol intoxication can worsen base deficit for similar levels of injury severity after trauma.

In summary, although base deficit has its limitations, it is apparent that base deficit levels are a useful guide for identifying the magnitude of tissue oxygen debt and the adequacy of resuscitation. A persistently high or increasing base deficit indicates the presence of ongoing blood loss or inadequate volume replacement.[57]

7.2 Lactate levels

Recent evidence suggests that serum lactate levels accurately reflect the degree of circulatory failure and level of oxygen debt in trauma patients.[54] Abramson[67] studied patients with a moderate injury severity score who were resuscitated to supranormal values of O_2 transport. They found that patients who had a normalised serum lactate level within 24 hours had a significantly higher survival rate than those whose lactate levels did not return to normal within 48 hours. Manikis and his associates[68] in a study on the correlation of serial blood lactate levels to organ and mortality after trauma reported similar results. Sauaia et al[69] found that a serum lactate of more than 2.5mmol/L 12 hours post injury accurately predicted the onset of multiple organ failure.

When using lactate levels as an end point to resuscitation it is important to note that as the oxygen debt becomes normalised lactate maybe washed out into the circulation, thus spuriously increasing lactate levels. Nevertheless returning lactate levels to normal, and in particular normalising them in a short time period, has proved to be a useful goal in the resuscitation of trauma patients.[57]

7.3 Gastric pH

The gastrointestinal circulation appears to be exquisitely sensitive to changes in perfusion. Measuring gastric pH has been attributed to detect intestinal hypoxia to determine both the depth of shock and the adequacy of resuscitation. The potential value of detecting intestinal hypoxia is two-fold. Intestinal mucosal hypoxia may be an early warning sign of inadequate global oxygen delivery due to compensatory mechanism which redistribute blood flow away from the gut, especially the splenic bed and intestinal mucosa. The resulting intestinal mucosal hypoxia may itself have deleterious effects, playing a role in the development of multi-organ failure as a result of increased intestinal permeability and translocation of endotoxin and bacteria across the intestinal wall. Thus, correction of low pHi by treatment aimed at correction of mucosal hypoxia should result in an improved outcome.

Ivatury and colleagues compared global oxygen transport indices versus organ-specific gastric mucosal pH as resuscitation endpoints in trauma patients and found a large reduction in mortality in patients resuscitated to achieve a gastric pH >7.3 (mortality 9.1% vs 31.3%, $p = 0.27$).[70] However in a similar study undertaken by the same authors a year later found inconsistent results with survival being higher in the patients randomised to normalisation of gastric ph (90% vs 74.1%, $p = 0.16$) but organ failures also being higher (56.7% vs 29.6%).[71] Both studies, however were underpowered to draw any conclusions. Larger studies are warranted.

7.4 Sublingual capnometry

One study was identified that included trauma patients and evaluated the predictive power of sublingual capnometry for identifying peripheral hypoperfusion. Sublingual CO_2 correlated strongly with haemodynamic parameters and lactate (r_2=0.84, $p<0.01$).[72] The application of this instrument may serve to diagnose and estimate the severity of shock, but does not appear to add any new information that is not readily determined by standard monitoring of heart, blood pressure and lactate.

7.5 Supranormal circulatory values

Shoemaker, Bishop and colleagues have done a number of studies examining and evaluating supranormal circulatory values as resuscitation goals (based on cardiac index, oxygen delivery and oxygen consumption) in severely injured patients.[61;73-75]

A quasi-randomised study compared global oxygen indices as resuscitation goals to resuscitation based on standard variables (HR, BP, U/O, BD, and Lactate). Bishop and colleagues found a lower mortality for patients who were resuscitated to achieve supra-normal circulatory values (18% vs 37%, $p<0.027$) and a lower incidence of organ failures per patient (0.74 +/- 0.28 vs 1.62 +/- 0.28, $p<0.002$).[76] It is notable that predicted and observed mortality between the two groups is different with 81% observed survival vs 84% predicted survival in the intervention group versus 63% observed vs 91% predicted in the control group. The observed mortality is much lower than the predicted mortality in the control group whilst the observed mortality is similar to the predicted mortality for the intervention group. Resuscitation to supranormal circulatory values did not seem to improve survival when compared to predicted survival for this group. It is concerning as to why the observed mortality was 28% more than predicted. In conclusion, this study highlights that failure to achieve normal of supranormal circulatory values is a predictor of a poor outcome, however augmentation of survivor values in reducing mortality is not conclusive from this study.

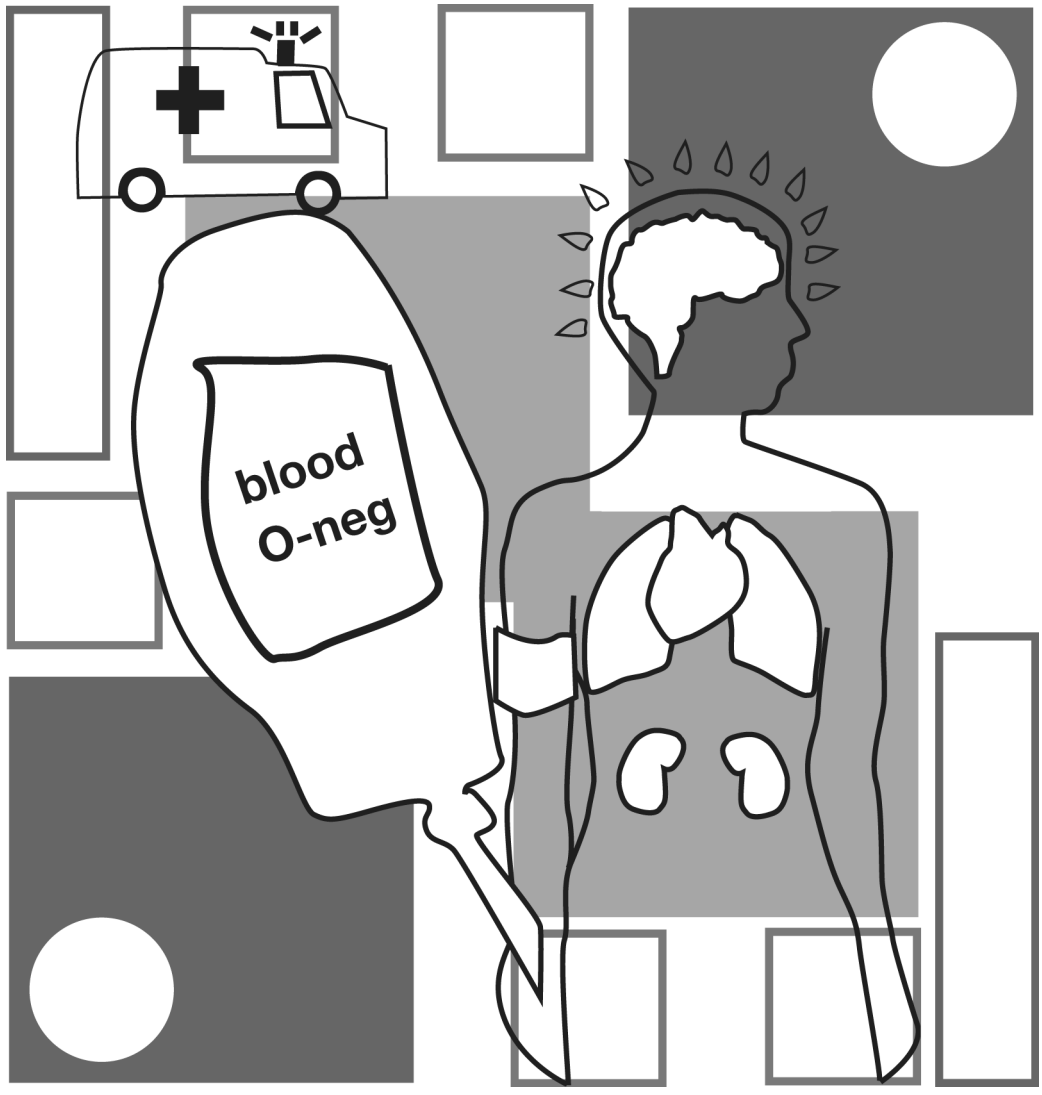
A randomised trial undertaken by Velmahos and colleagues also evaluated the effect early optimisation on the survival of severely injured patients. However no difference in mortality (15% vs 11%), organ failure, sepsis or length of intensive care unit stay was observed between the two groups. The authors conclude that patients who can achieve optimal haemodynamic values are more likely to survive than those who cannot, regardless of resuscitation techniques.[77]

Conclusion

Much controversy exists regarding the optimum end points for resuscitation. What is agreed upon is that vital signs are very poor indicators of the adequacy of resuscitation. In recent times, 'occult hypoperfusion' has dominated the literature on highlighting that current end points of resuscitation are inadequate. This has fuelled the development of Gastric Tonometry, Capnometry and goal directed therapies. Application of these tools in resuscitation of trauma patients has shown them to be powerful predictors of mortality, however the research has failed to consistently demonstrate an improvement in outcomes when used to direct therapy in comparison to standard endpoints such as HR, BP, urine output, lactate and base deficit. There is compelling data for the early recognition of compensated shock.

Performance indicators

Arterial blood gases and lactate measured to assess degree of shock.
Urinary catheter inserted to assess urine output.


blood
O-neg

Evidence Table 1. How do you know when a trauma patient is in hypovolaemic shock?

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Victorino, GP. Battistella, FD. Wisner, DH. 2003[78]	III-2 Diagnostic test	B2	To determine the correlation between tachycardia and hypotension.	Heart rate was not found to be a good predictor of hypotension, but its sensitivity and specificity make it clinically unreliable in diagnosing hypovolaemic hypotension. ***Need to calculate sensitivity and specificity.	Tachycardia was not found to be a reliable indicator of hypotension. However, there are some limitations of this study. Hypotension is a surrogate or late outcome for hypovolaemia. Perhaps the authors should have measured circulating volume and cardiac output to determine the usefulness of tachycardia. As some patients may be hypovolaemic, tachycardic but have a normal blood pressure due to compensatory mechanisms.
Lechleuthner, A. Lefering, R. Ouillon, B. 1994[8]	III-2 Diagnostic test	A	To evaluate systolic blood pressure, capillary refill and trauma score in identifying uncontrolled haemorrhage in patients with blunt trauma.	Systolic blood pressure <90mmHg was the most sensitive parameter, however only identified 50% of blunt trauma patients with uncontrolled haemorrhage. The sensitivity improved to 66% with a SBP<60mmHg. An accompanying traumatic brain injury impaired the ability of SBP to detect uncontrolled haemorrhage.	The sensitivity and specificity of SBP<90mmHg is 61% and 79% respectively. For a SBP<70mmHg the sensitivity drops even lower to 27% but specificity increases to 94%. 3.1% of patients with uncontrolled haemorrhage had undisturbed physiological variables. A SBP<50mmHg, the presence of TBI impairs the detection quality. No parameter is sufficiently predictive to diagnose accurately those patients with uncontrolled haemorrhage. The study was undertaken in patients with trauma scores 1-15.
Shippy, CR. Appel, PL. Shoemaker, WC. 1984[9]	III-2 Diagnostic test	B2	To evaluate the reliability of clinical monitoring to assess blood volume in critically ill patients.	In patients with measured hypovolaemia (~1400mls) there were significant reductions in MAP, HR, and CI. CVP was not significantly reduced. None of the correlation coefficients between blood volume and these commonly measured variables were significant.	The data suggest that the commonly monitored variables, in and of themselves, do not reflect adequately the blood volume status in critically ill patients. Commonly monitored variables provided adequate data needed to begin resuscitation in shock, but there absolute values independently are not a reliable estimation of blood volume status. Clinicians need to be mindful of the complex neurohormonal mechanisms which profoundly effect the circulation in general which could lead clinicians down the garden path of thinking that many patients are fully resuscitated although they may still be hypovolaemic and at risk of developing the sequelae of shock.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Knottenbelt, JD. 1991[12]	III-2 Diagnostic test	B1	To evaluate the importance of a low initial haemoglobin and its correlation with shock.	Initial haemoglobin correlated with vital signs and mortality. In 31 patients with initial Hb levels of less than 8 g/dL, the overall mortality was 48.4%, compared with 2.6% in 969 patients whose initial Hb level was 8 g/dL or more ($p < 0.00001$).	A low Hb level observed soon after injury is usually an indicator of serious ongoing haemorrhage and has important implications for management and prognosis.
Wo, CCJ. Shoemaker, WC. Appel, PL. 1993[10]	III-2	B1	To evaluate the reliability of the vital signs to evaluate circulatory stability as reflected by cardiac index.	In sudden severe hypovolaemic hypotension, the lowest mean arterial pressure (MAP) roughly correlated ($r_2 = .25$) with flow, but there was poor correlation ($r_2 = .0001$) when all pressure and flow values were evaluated.	Authors conclude that blood flow cannot reliably be inferred from arterial pressure and heart rate measurements until extreme hypotension occurs. 75% of the variation in MAP was not explained in this data set by cardiac index.
Bishop, MH. Shoemaker, WC. Apel, PL. 1993[80]	III-2 Observa-tional study	B2	To examine the relationship between circulatory values and mortality and organ failure.	Data not presented.	MAP and heart were poorly correlated with blood loss and the amount of blood transfused. The estimated blood loss was a more reliable means than MAP and HR is estimating the degree of shock. In the cutely injured patient, widely variable catecholamine responses to hypovolaemia, pain, or drugs made MAP and HR unreliable predictors of intravascular volume.
Ardagh, MW. Hodgson, T. 2001[81]	III-2 Diagnostic Test	B2	To evaluate a calculation of pulse rate over pulse pressure as a method of predicting decompensation in patients with compensated haemorrhagic shock in victims of major road trauma. ROPE is calculated by: :: pulse rate :: SBP-DBP.	Sensitivity 55%. Specificity 79%. A ROPE value of greater than 3.0 had a positive predictive value of 53% and a value less than 3.0 had a negative predictive value of 86% for the development of decompensated shock.	ROPE >3.0 is not 100% accurate in identifying those who will or will not decompensate in the emergency department, however it may provide clinicians with a useful tool to increase suspicion of those who may.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Tatevossian, RG. Wo, CCJ. Velmahos, GC. 2000[82]	III-2	B1	To evaluate the usefulness of transcutaneous oxygen and carbon dioxide monitoring in trauma patients for tissue hypoxia and possible shock.	Compared with survivors, patients who died had significantly lower $PtcO_2$ and higher $PtcCO_2$ values beginning with the early stage of resuscitation. Transcutaneous O_2 correlated well with death and morbidity. However little correlation was made with already monitored values such as HR & BP to test whether these values correlated with them.	There is no quantification of values in this study to reflect impending shock or decompensation. Values are correlated with death and morbidity. Unsure of the usefulness of this test as it take ~20 minutes to calibrate machine.
Oman, KS. 1995[15]	III-2	B2	To validate Haematocrit as an indicator of ongoing haemorrhage in trauma patients who receive IV fluids.	The mean haematocrit change was -5.3%; in group 2 (haemorrhage group) the haematocrit change was -8.3%. ($p < 0.05$).	A haematocrit decrease of 5% has a sensitivity of 94%, specificity 43%, PPV 26%, NPV 97%. Meaning that haematocrit changes are not useful in identifying patients who are haemorrhaging, but are accurate 97% of the time in identifying patients who are not.
Rixen, D. Raum, M. Bouillon, B. Lefering, R. 2001[13]	III-2 German Abstract only	N/A	To evaluate the prognostic value of base deficit in trauma patients.	Increasing base deficit was associated with a significant decrease in systolic blood pressure and prothrombin time as well as increases in heart rate, lactate level and mortality ($p < 0.0001$). Mortality increased significantly ($p < 0.0001$) with a worsening of BD from hospital to ICU admission.	Base deficit is an early available important indicator to identify trauma patients with haemodynamic instability, high transfusion requirements, metabolic and coagulatory decompensation, as well as a high probability of death.
Bannon MP. O'Neill CM. Martin M. 1995[14]	III-2 Diagnostic Test	B1	To explore the usefulness of central venous oxygen saturation, arterial base deficit, and lactate concentration in the evaluation in 40 patients with operative truncal injuries.	Preoperative hypotension occurred in 12.5% of these initially stable patients. $S(cv)O_2$ did not significantly correlate with any of the parameters of blood loss and severity of injury examined. However, both base deficit and lactate concentration correlated with transfusion requirements; in addition, base deficit correlated with trauma score, and lactate correlated with peritoneal shed blood volume.	Base deficit and lactate were indicators of ongoing blood loss or inadequate resuscitation. Need to check sensitivity and specificity in full text.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Demetriades, D. Chan, LS. Bhasi, P. Berne, TV. 1998[11]	III-2	B1	To examine the incidence and prognostic significance of tachycardia and relative bradycardia in patients with traumatic hypotension. (Relative bradycardia is defined SBP < or = 90 mm Hg and a HR < or = 90 beats per minute).	The incidence of relative bradycardia in this study was 28.9% of hypotensive patients. Patients with relative bradycardia in the subgroups with ISS >16 significantly better survival than patients with similar injuries presenting with tachycardia.	Relative bradycardia in hypotensive trauma patients is a common haemodynamic finding. Mortality among tachycardic patients was more predictable than among bradycardic patients using commonly used demographic and injury indicators.

Evidence Table 2. How do you find the sources of bleeding in a hypotensive trauma patient?

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Githaiga, JW. Adwok, JA. 2002[83]	III-2 Diagnostic	B1	To determine the accuracy and sensitivity of diagnostic peritoneal lavage in the assessment of intra-abdominal injury using the dipstick method.	DPL using the dipstick method had an accuracy and sensitivity of 93% and specificity of 98%.	Diagnostic peritoneal lavage is a cheap, safe and reliable method for assessment of abdominal trauma.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Kwan, I. Bunn, F. Roberts, I. 2003[45]	I	B2	To assess the effects of early versus delayed, and larger versus smaller volume of fluid administration in trauma patients with bleeding.	Due to their heterogeneity, in terms of types of patients and types of fluids used, we did not attempt to perform a meta-analysis of the studies.	There was no evidence for or against early or larger volume of intravenous fluid administration in uncontrolled haemorrhage. A large, well-conducted RCT is required as the quality of the current evidence is poor.
Bickell, WH. Wall, MJ Jr. Pepe, PE. Martin, RR. 1994[40]	III-1 Quasi randomised trial	B2	598 hypotensive trauma patients with penetrating torso injuries were quasi-randomised (alternate day allocation) to early versus delayed fluid administration.	Mortality was 38% in early fluid administration vs. 30% in delayed. Prothrombin and partial thromboplastin time in early 14.1 and 31.8 seconds and 11.4 and 27.5 seconds in delayed group.	RR of death with early fluid administration is 1.26 (95% CI 1.00-1.58). Intravenous fluid administration should be withheld until definitive surgical management is available as early fluid administration is associated with increased risk of death and prolongation of coagulation cascade. The study however is not conclusive, methods of allocation using quasi-randomised methods is not ideal. A proper randomised trail is needed to draw definite conclusions.
Turner. 2000[41]	II	B2	1,309 hypotensive trauma patients randomised to receive fluids or no fluids.	Early fluid administration mortality 10.4% vs. 9.8% in delayed/no fluid group.	Relative risk for death was 1.06 (95% CI 0.77-1.47). There was significant non-compliance to study protocol with 31% of fluid group receiving fluid and 80% of non fluid group not receiving fluid.
Kaweski, SM. Sis, MJ. Virgilio, RW. 1990[84]	III-2 case control	B2	The outcomes of 6,855 trauma patients were studied retrospectively to evaluate the impact of pre-hospital intravenous fluid on mortality.	Mortality was similar between the two groups.	This study failed to show an influence of fluid administration on survival.
Hambly, PR. Dutton, RP. 1996[44]	III-3 Historical control	B2	To address the impact of rapid infusion devices on patient outcome.	Compared to matched control patients injured to the same extent during the same time period, patients who received fluids via the RIS had a 4.8 times greater chance of dying (95% confidence interval 2.4-7.1). Actual versus expected mortality was also higher than expected mortality (52.9% vs. 61.8%, p <0.001).	This study raises the question of the safety of rapid infusing devices. This anecdotal evidence suggests the need for a prospective randomised trial to determine its true impact. However, in the light of current evidence that suggests small volume hypotensive resuscitation this is unlikely to occur.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Dutton, RP. Mackenzie, CF. Scalea, TM. 2002[42]	II	B2	To evaluate the affect of fluid resuscitation titrated to a lower than normal SBP (100mmHg vs. 70mmHg) during the period of active haemorrhage on survival in trauma patients presenting to the hospital in hemorrhagic shock.	Mortality between the two groups was the same (7% vs. 7%).	Titration of initial fluid therapy to a lower than normal SBP during active haemorrhage did not affect mortality in this study.
Kwan, I. Bunn, F. Roberts, I. 2003[45] I		B2	To assess the effects of early versus delayed, and larger versus smaller volume of fluid administration in trauma patients with bleeding.	Due to their heterogeneity, in terms of types of patients and types of fluids used, we did not attempt to perform a meta-analysis of the studies.	There was no evidence for or against early or larger volume of intravenous fluid administration in uncontrolled haemorrhage. A large, well-conducted RCT is required as the quality of the current evidence is poor.
Bickell, WH. Wall, MJ Jr. Pepe, PE. 1994[40]	II	B2	The purpose of this study was to determine the effects of delaying fluid resuscitation until the time of operative intervention in hypotensive patients with penetrating injuries to the torso.	598 hypotensive trauma patients with penetrating torso injuries were quasi-randomised (alternate day allocation) to early versus delayed fluid administration. Mortality was 38% in early fluid administration vs. 30% in delayed. Prothrombin and partial thromboplastin time in early 14.1 and 31.8 seconds and 11.4 and 27.5 seconds in delayed group.	RR of death with early fluid administration is 1.26 (95% CI 1.00-1.58) Intravenous fluid administration should be withheld until definitive surgical management is available as early fluid administration is associated with increased risk of death and prolongation of coagulation cascade.
Turner. 2000[41]	II	B2	Early fluid administration vs. no fluid.	Early fluid administration mortality 10.4% vs. 9.8% in delayed/no fluid group.	Relative risk for death was 1.06 (95% CI 0.77-1.47). There was hug non-compliance to study protocol with 31% of fluid group receiving fluid and 80% of non fluid group not receiving fluid.
Kaweski, SM. Sise, MJ. Virgilio, RW. 1990[84]	II	B2	The outcomes of 6,855 trauma patients were studied retrospectively to evaluate the impact of pre-hospital intravenous fluid on mortality.	Mortality was similar between the two groups.	This study failed to show an influence of fluid administration on survival.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Blair, SD. Janvrin, SB. McCollum, C. 1986[86]	II	B1	Early versus delayed blood transfusion for patients with gastrointestinal bleeding. Mortality was 8% in the early versus 0% in the late. The early blood transfusion group was 5.4 (95% CI 0.3 to 107.1).	The were nine patients in the transfused group that re-bled compared with only one in the non-transfused group (p <0.01).	The authors conclude that early blood transfusion appears to reverse the hyper coagulable response to haemorrhage thereby encouraging re-bleeding and hence the need for an operation.
Dunham, CM. Belzberg, H. Lyles, R. Weireter, L. 1991[87]	II	C	Rapid infusing device vs. conventional fluid administration	The relative risk for death is 0.80 (95% CI 0.28-2.29). Lactate levels were lower in the RIS group at virtually all times from hours 1 to 24 (4.3/5.3 mM/l, t-value = 3.3, DF = 279, p = 0.001). Post-admission hypothermia was greater in the CFA group at all times during the first 24 h (35.2 / 36.4 degrees C, t-value = 5.6, DF = 250, P = 0.001). The mean partial thromboplastin time was significantly higher in the CFA group (47.3/35.1 s, t-value = 3.1, DF = 279, P = 0.002). The PTT and PT were related to the degree of lactic acidosis (p = 0.0001) and hypothermia (p = 0.001) but not to the amount of FFP given (p = 0.14).	Hypovolaemic trauma patients resuscitated with the RIS less coagulopathy; more rapid resolution of hypoperfusion acidosis; better temperature preservation; and fewer hospital complications than those resuscitated with conventional methods of fluid / blood product administration.
Dutton, RP. Mackenzie, CF. 2002[42]	II	B2	Large vs small fluid resuscitation.	Mortality was 4/55 (7.3%) in the group administered a larger volume and 4/55 (7.3%) in the group administered a smaller volume (1000ml less than in the intervention group). The relative risk for death is 1.00 (95% CI 0.26-3.81).	There was no evidence for or against large volume administration in patients with traumatic hypotension.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Neff, TA. Doelberg, M. Jungheinrich C. 2003[88]	II	B1	To investigate the safety of repetitive large-dose infusion of a novel hydroxyethyl starch solution (6% HES 130/0.4) in cranio-cerebral trauma patients.	There were no differences between groups in mortality, renal function, bleeding complications, and use of blood products. There were also no major differences in coagulation variables.	Previously, the effect of hydroxyethyl starch (HES) types for plasma volume expansion on coagulation and renal function. However, this study suggests that HES 130/0.4 can safely be used in critically ill head trauma patients over several days at doses of up to 70 mL x kg(-1) x d(-1).
Buchman, TG. Menker, JB. Lipsett, PA. 1991[89]	IV	C	To evaluate the effect of rapid infuser on unsuspected survival rates in hypotensive penetrating trauma patients.	There was a statistically significant improvement in clinical flow rates, decrement in resuscitation times and unexpected survival. Statistical summary not presented in paper, unable to determine.	Use of rapid infusion device in this small series of patients is hypothesised by the authors to improved unexpected survival.
Remmers, DE. Wang, P. Cioffi, WG. 1998[90]	Scientific Animal	N/A	To determine whether prolonged (chronic) resuscitation has any beneficial effects on cardiac output and hepatocellular function after trauma-haemorrhage and acute fluid replacement.	Chronic resuscitation with 5 mL/kg/hr restored cardiac output, hepatocellular function, and hepatic microvascular blood flow at 20 hours after haemorrhage. The regimen above also reduced plasma IL-6 levels.	Chronic fluid resuscitation in addition to acute fluid replacement should be routinely used in experimental studies of trauma- haemorrhage.

Evidence Table 4. If fluid resuscitation is indicated, what type of fluids should be used?

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Alderson, P. Schierhout, G. Roberts, I. Bunn, F. 2004[50]	I Not specifically trauma patients, but includes studies on trauma patients.	A	To assess the effects on mortality of colloids compared to crystalloids for fluid resuscitation in critically ill patients.	– Colloids compared to crystalloids: RR1.52 (95% confidence interval 1.08 to 2.13). – Hydroxyethylstarch: RR1.16 (0.68 to 1.96). – Modified gelatin: RR0.50 (0.08 to 3.03). – Dextran: RR1.24 (0.94 to 1.65). – Colloids in hypertonic crystalloid compared to isotonic crystalloid: RR0.88 (0.74 to 1.05).	There is no evidence from randomised controlled trials that resuscitation with colloids reduces the risk of death compared to crystalloids in patients with trauma, burns and following surgery. As colloids are not associated with an improvement in survival, and as they are more expensive than crystalloids, it is hard to see how their continued use in these patient types can be justified outside the context of randomised controlled trials.
Wilkes, MM. Navickis, RJ. 2001[91]	I Not specifically trauma patients, but includes studies on trauma patients.	B2	To test the hypothesis that albumin administration is not associated with excess mortality.	Albumin administration did not significantly affect mortality in any category of indications. For all trials, the relative risk for death was 1.11 (95% CI, 0.95 to 1.28).	No effect of albumin on mortality was detected; any such effect may therefore be small. This finding supports the safety of albumin. Authors conclude that overall methodological quality of studies is poor and effects study results. A large well-executed RCT is needed.
Wade, CE. Kramer, GC. Grady, JJ. 1997[55]	I Trauma	B2	To evaluate the effects of Hypertonic Saline and Hypertonic Saline / Dextran on survival until discharge or for 30 days.	HS was not effective in improving survival. HSD resulted in an increase in survival in 7/8 trials. OR 1.20 (95% CI 0.94-1.57)	Hypertonic Saline alone does not offer any benefit in terms of 30-day survival over isotonic crystalloids. Hypertonic Saline with Dextran may improve mortality. The meta-analysis of the available data shows that HS is not different from the standard of care and that HSD may be superior.
Wade, CE. Grady, JJ. Kramer, GC. Younes, RN. 1997[92]	II	B2	To evaluate improvements in survival at 24 hours and discharge after initial treatment with Hypertonic Saline Dextrose in patients who had traumatic brain injury.	HSD resulted in a survival until discharge of 37.9% (39 of 103) vs. 26.9% (32 of 119) with standard of care (p = 0.080). Using logistic regression, adjusting for trial and potential confounding variables, the treatment effect can be summarised by the odds ratio of 2.12 (p = 0.048) for survival until discharge.	Patients who have traumatic brain injuries in the presence of hypotension and receive HSD are about twice as likely to survive as those who receive standard of care.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Mattox, KL. Maningas, PA. Moore, EE. 1991[93]	II	A	To compare 250 mL of HSD versus 250 mL of normal crystalloid solution administered before routine prehospital and emergency centre resuscitation.	There was no difference in survival between the two groups. The HSD group had an improved blood pressure (p = 0.024). Haematocrit, sodium chloride, and osmolality levels were significantly elevated in the emergency centre.	This study showed the safety of HSD, but failed to show any benefit of this solution in reducing mortality. In light of the cost of this solution in comparison to standard therapy, until proven efficacious is not recommended.
Maningas, PA. Mattox, KL. Pepe, PE. Jones, RL. 1989[94]	II	B1	Pilot study to assess the safety of saline-dextran solutions in trauma patients with penetrating injuries and a prehospital systolic blood pressure < 90 mm Hg.	There were no complications associated with the infusion of the hypertonic saline-dextran solution, and execution of the protocol by paramedic personnel was both safe and uniformly successful.	The results of this feasibility study justify the initiation of a larger prospective, randomised clinical trial on the efficacy of this solution in the prehospital setting.
Sloan, EP. Koenigsberg, M. Gens, D. Cipolle, M. 1999[95]	II	B2	To determine if the infusion of up to 1000 mL of diaspirin cross-linked haemoglobin (DCLHb) during the initial hospital resuscitation could reduce 28-day mortality in traumatic hemorrhagic shock patients.	At 28 days, 24 (46%) of the 52 patients infused with DCLHb died, and 8 (17%) of the 46 patients infused with the saline solution died (p = .003). At 48 hours, 20 (38%) of the 52 patients infused with DCLHb died and 7 (15%) of the 46 patients infused with the saline solution died (p = .01).	Mortality was higher for patients treated with DCLHb. DCLHb does not appear to be an effective resuscitation fluid.
Bouwman, DL. Weaver, DW. Vega, J. et al. 1978[96]	II	B1	To study the effects of albumin on serum protein homeostasis in 52 seriously injured patients.	Altered haemostasis and depressed immune response are two possible effects with clinical significance experienced in the albumin-receiving group.	Additional investigation of secondary homeostatic responses are necessary to more completely evaluate the effects of albumin infusion.
Wu, JJ. Huang, MS. Tang, GJ. Kao, WF. 2001[97]	II	B1	To compare the cardiac and haemodynamic responses to a rapid infusion of 1000 ml of modified fluid gelatin (group A) or 1000 ml of lactated Ringer's solution (group B) in emergency room patients suffering from shock.	In both groups the mean arterial blood pressure (MAP), systolic and diastolic pressure, central venous pressure (CVP), and pulmonary artery occlusion pressure (PAOP) increased significantly. The CVP and PAOP increased significantly more in the modified fluid gelatin resuscitation group.	Modified Fluid Gelatin was more effective than LR in increasing BP, MAP and CO immediately after infusion (<15 minutes) (p <0.05). There was no difference in survival between the two groups. Excluded patients that were mechanically ventilated. **This study includes patients with neurogenic shock.**

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Wade, CE. Grady, JJ. Kramer, GC. 2003[98]	II	A	To assess whether the administration of hypertonic saline dextran (HSD) was detrimental when administered to patients who were hypotensive because of penetrating injuries to the torso.	82.5% treated with HSD survived vs. 75.5% patients who received normal saline. The difference in survival rates between groups was not statistically significant (p = 0.189). For the patients with truncal injuries that did not receive surgery, there was no significant difference (p = 0.09) between fluid treatments in survival until discharge. For patients treated with HSD, 77.8% survived 24 hours whereas, of those receiving SOC, 91.9% survived until discharge. For penetrating truncal injuries that required surgery, there was a statistically significant effect (p = 0.01) of treatment on overall survival until discharge. Of the 84 patients treated with HSD, 84.5% survived, whereas survival was 67.1% in the 73 patients receiving SOC.	The increase in bleeding and mortality associated with the infusion of HSD resulted in animal studies was not found in this study. Authors hypothesis that this is because the rate of infusion and timing of infusion after injury was different in this study perhaps highlighting the timing of the initiation of fluid infusion and the rate may influence outcome. The results of this study suggest that the administration of hypertonic saline is not detrimental to patients with penetrating truncal wounds despite the increase in SBP. There is some evidence to suggest that HSD improves mortality to hospital discharge. Consider prehospital and ED staff ability to identify early hose requiring OT.
Mauritz, W. Schimetta, W. Oberreither, S. Polz, W. 2002[99]	IV Prospective Case series	B2	To determine the safety of hypertonic hyper oncotic solutions for prehospital small-volume resuscitation.	There were small increases in serum sodium and chloride (7 and 12 mmol/l, medians; p <0.001). On arrival oxygen saturation and systolic and diastolic blood pressure had increased (5%, 30 and 20 mmHg, respectively), whereas heart rate had dropped by 15 b.p.m. (medians; p <0.001). 5% of patients experienced mild side effects (heat sensations, vomiting)	Hypertonic hyper oncotic solutions were found to be safe and effective in this series of patients. However with no comparison group the affects of this intervention are not conclusive.
Shatney, CH. Deepika, K. Militello, PR. 1983[100]	II	B1	To evaluate 6% hetastarch (HES) v 5% plasma protein fraction (PPF) as the colloid component of intravenous (IV) fluid resuscitation in 32 patients with multisystem trauma and/or hemorrhagic shock.	No intergroup differences were noted in indexes of hepatic, pulmonary, or renal function or in the incidence of infection. The frequency of other complications, including bleeding diatheses, and mortality were identical in the two groups.	Results of this pilot study suggest that, compared with PPF, HES in large volumes is a safe, effective colloid solution in the resuscitation of patients with multisystem trauma and / or hemorrhagic shock. Cost of colloids greater than crystalloids, is there any benefit.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Vassar, MJ. Perry, CA. Gannaway, WL. 1991[101]	II	B1	7.5% NaCl/Dextran (HTS) vs. Lactated Ringers (LR) solution for fluid resuscitation in hypotensive trauma patients.	Survival at hospital discharge was 64% vs. 59% for HTS and LR respectively. The rate of survival to hospital discharge **for** the **patients** with severe head injuries was 32% **for** the **HTS** group vs. 16% **for** the **LR** solution group. (this did not reach statistical significance).	Hypertonic saline/Dextran was shown to decrease mortality at hospital discharge in this study; RR18.3 (95% CI 0.60-1.30).
Vassar, MJ. Fischer, RP. O'Brien, PE. Bachulis, BL. 1993[102]	II	B1	To evaluate the use of 250 mL of a 7.5% sodium chloride solution, both with and without added dextran 70, for the prehospital resuscitation of hypotensive trauma patients.	Change in systolic blood pressure on arrival in the emergency department was significantly higher in the hypertonic saline solution group than that in the lactated Ringer's solution group (34 plus or minus 46 vs. 11 plus or minus 49 mm Hg, p <.03). There was no difference in survival between the groups. RR097 (0.68-1.37).	Prehospital infusion of 250 mL of 7.5% sodium chloride is associated with an increase in blood pressure. However no statistically significant difference was noted between the groups.
Vassar, MJ. Perry, CA. Holcroft, JW. 1993[52]	II	B1	To evaluate the contribution of the dextran component in resuscitation of hypotensive trauma patients.	There was no difference in mortality between the groups. RR1.42 (0.77-2.6)	The addition of a colloid, in the form of 6% dextran 70, did not offer any additional benefit, at least in this setting of rapid urban transport.
Tranbaugh, RF. Lewis, FR. 1983[103]	III-2	Scientific	To evaluate the effects of crystalloid fluid resuscitation on lung water (pulmonary oedema).	Extra-vascular lung water remained in the normal range of 7.0 +/- 1.0 ml/kg during the first five hospital days for all patients despite profound decrease in PCOP (less than 15mm Hg).	Crystalloid resuscitation clearly is not harmful to the lung and it is equally as effective as colloid resuscitation. Crystalloid is markedly less expensive than colloid and, given the greater cost of colloid without evident benefit.
Holcroft, JW. Vassar, MJ. Perry, CA. 1989[104]	II	A	To evaluate the effects of a hypertonic 7.5% NaCl / 6% Dextran 70 (HSD) solution in the resuscitation of patients in the emergency room.	There was no difference in mortality between the two groups, or in the physiological variable that were measured.	Hypertonic solution was safe to use, but the data presented in this study show no affect on mortality on bleeding trauma patients.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Johnson, JL. Moore, EE. Offner, PJ. Haenel, JB. 1998[105]	II	B2	To test the vasoconstriction following administration of tetrameric haemoglobins in trauma patients.	There was no difference in any of the measured haemodynamic parameters between patients resuscitated with polymerized haemoglobin versus blood.	Polymerised haemoglobin given in large doses to injured patients lacks the vasoconstrictive effects reported in the use of other haemoglobin-based blood substitutes. This supports the continued investigation of polymerised haemoglobin in injured patients requiring urgent transfusion.
Kerner, T. Ahlers, O. Veit, S. Riou, B. 2003[106]	II (European 'On-Scene' multicentre study)	B2	To test the hypothesis that the early administration of an oxygen carrier may reduce the occurrence of organ failures and improve survival. (10% diaspirin cross-linked haemoglobin (DCLHb) vs. standard IVF.)	Organ failures and survival rates until day five and day 28 showed no significant differences.	The early application of an oxygen carrier (DCLHb) to **patients with severe hemorrhagic shock** following **trauma** had no significant effect on the occurrence of organ failure or on 5- and 28-day survival in this abbreviated trial. (This study was stopped after interim analysis, sponsors expressed some concern on the long-term effects of this drug.)
Johnson, JL. Moore, EE. Offner, PJ. 2001[107]	II	B1	To compare the impact of RBC or Blood substitutes on neutrophil activity. (Packed red blood cells have the potential to exacerbate early post injury hyper inflammation and multiple organ failure through priming of circulating neutrophils [PMNs]).	Polyheme did not result in the aggravation of circulating neutrophils in contrast to PRBC.	The use of a blood substitute in the early post injury period avoids PMN priming and may thereby provide an avenue to decrease the incidence or severity of post injury multiple organ failure.
Hirshberg, A. Dugas, M. Banez, EI. 2003[108]	Scientific/ Computer simulation	C	To calculate the changes in prothrombin time (PT), fibrinogen, and platelets with bleeding.	Prolongation of PT is the sentinel event of dilutional coagulopathy and occurs early in the operation. The key to preventing coagulopathy is plasma infusion before PT becomes subhemostatic. The optimal replacement ratios were 2:3 for plasma and 8:10 for platelets.	Existing protocols underestimate the dilution of clotting factors in severely bleeding patients.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Gould, SA. Moore, EE. Hoyt, DB. 1998[109]	II	B1	To compare directly the therapeutic benefit of PolyHeme with that of allogeneic red blood cells (RBCs) in the treatment of acute blood loss.	There was no difference in total [Hb] between the groups before infusion (10.4 +/- 2.3 g/dL control vs. 9.4 +/- 1.9 g/dL experimental). At end-infusion the experimental RBC [Hb] fell to 5.8 +/- 2.8 g/dL vs. 10.6 +/- 1.8 g/dL ($p < 0.05$) in the control.	PolyHeme is safe in acute blood loss, maintains total [Hb] in lieu of red cells despite the marked fall in RBC [Hb], and reduces the use of allogeneic blood. PolyHeme appears to be a clinically useful blood substitute.
Gould, SA. Moore, EE. Moore, FA. 1997[110]	II	B1	To assess the therapeutic benefit of Poly SFH-P in acute blood loss in 39 injured patients.	Poly SFH-P maintained total [Hb], despite the marked fall in red cell [Hb] due to blood loss. The utilisation of O2 (extraction ratio) was 27 +/- 16% from the red cells and 37 +/- 13% from the Poly SFH-P. Twenty-three patients (59%) avoided allogeneic transfusions during the first 24 hours after blood loss.	Human polymerised haemoglobin effectively loads and unloads O_2 and maintains total haemoglobin in lieu of red cells after acute blood loss, thereby reducing allogeneic transfusions.
Younes, RN. Aun, F. Accioly, CQ. 1992[54]	II	A	To compare the immediate haemodynamic effects of a bolus infusion of 7.5% NaCl or 7.5% NaCl plus 6% dextran 70 (both 2400 mOsm/L) in severe hypovolaemia.	Mortality was similar between the groups. Hypertonic solutions acted faster in restoring blood pressure than isotonic solutions. Greater volume was required for isotonic solutions to achieve the same BP.	Whilst the safety of hypertonic solutions is supported by this study, hypertonic solutions did not prove to be of any benefit in reducing mortality.
Knudson, MM. Lee, S. Erickson, V. 2003[111]	II Animal Study	N/A	Small-volume resuscitation with HBOC-201 (Biopure) vs. lactated Ringer's (LR) solution vs hypertonic saline dextran (HSD) in haemorrhagic shock.	There were no significant differences in measured liver or muscle PO_2 values after resuscitation with any of the three solutions. The cardiac output was increased from shock values in all three animal groups with resuscitation, but was significantly higher in the, animals resuscitated with HSD. Similarly, MAP was increased by all solutions during resuscitation, but remained significantly below baseline except in the group of animals receiving HBOC-201 ($p < 0.01$).	HBOC-201 is significantly more effective than HSD and LR solution in restoring MAP and systolic blood pressure to normal values although its ability to restore tissue oxygenation is no different from conventional fluid therapies.

Evidence Table 5. What are the endpoints of fluid resuscitation in the trauma patient?

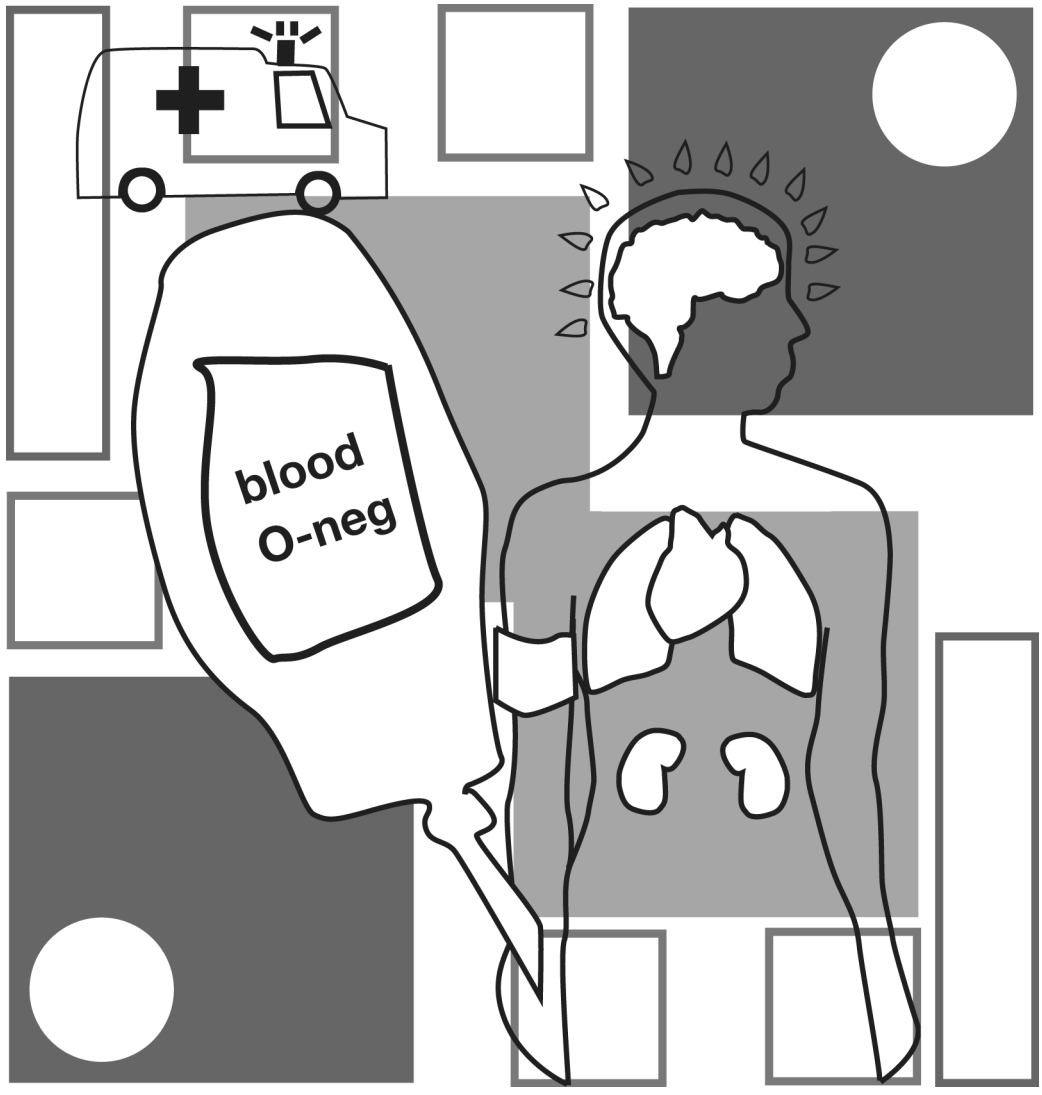
Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Bishop, MH. Shoemaker, WC. Appel, PL. 1995[76]	III-I	B1	To test prospectively supranormal values of cardiac index (CI), oxygen delivery index (DO_2I), and oxygen consumption index (VO_2I) as resuscitation goals to improve outcome in severely traumatised patients. Supranormal values to achieved using volume loading to PCWP 18mmHg and then dobutamine infusion.	Mortality in supranormal values group 18% vs. 37% in normal circulatory values ($p < 0.027$). Organ failure 074+/-0.28 vs. 1.62 +/- 0.28 ($p < 0.002$) in supranormal and normal circulatory groups respectively.	Resuscitation to supranormal circulatory values decreased mortality and organ failure in this study.
Durham, RM. Neunaber, K. Mazuski, JE. 1996[112]	II	B1	To evaluate the efficacy of Oxygen consumption (VO_2I) and delivery (DO_2I) indices as endpoints of resuscitation in 58 critically ill patients.	Mortality was not different between the groups even with exclusion of the group 1 patients who failed to meet VO_2I/DO_2I goals ($p = 0.66$). OF occurred in 18 of 27 (67%) in group 1 and in 22 of 30 (73%) in group 2 ($p = 0.58$). Length of ventilator support, intensive care unit stay, and hospital stay were not different between groups.	No difference was found in the incidence of or death in patients resuscitated based on oxygen transport parameters compared to conventional parameters. Authors suggest that oxygen-based parameters are more useful as predictors of outcome than as endpoints for resuscitation.
Dutton, RP. Mackenzie, CF. Scalea, TM. 2002[42]	II	B2	To evaluate the efficacy of fluid resuscitation titrated to a lower than normal SBP during the period of active haemorrhage on survival in trauma patients.	Duration of active haemorrhage (2.97 +/- 1.75 hours vs. 2.57 +/- 1.46 hours, $p = 0.20$) was not different between groups. Mortality between the groups was the same. (7.3% vs. 7.3%).	Titration of initial fluid therapy to a lower than normal SBP (<70mmHg) during active haemorrhage did not affect mortality in this study.
Ivatury, RR. Simon, RJ. Islam, S. 1996[113]	II	B2	Global oxygen transport indices versus organ-specific gastric mucosal pH in trauma patients.	There was no significant difference in mortality between those who resuscitation goal was optimising oxygen delivery vs optimisation of gastric pH (74.1% vs 90%, $p = 0.16$).	Survival was similar between the two groups.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Fleming, A. Bishop, M. Shoemaker, W. Appel, P. 1992[114]	III-2	B1	To evaluate the early post injury attainment of supranormal values of cardiac index (> = 4.52 L/min), oxygen delivery (> = 670 mL/min), and oxygen consumption (> = 166 mL/min) on outcome in traumatised patients with an estimated blood loss of 2000 mL or more.	Mortality was 24% vs. 44% in protocol and control respectively. The protocol patients had fewer mean organ failures per patient (0.76 +/- 1.21 vs. 1.59 +/- 1.60), shorter stays in the intensive care unit (5 +/ -3 vs 12 +/- 12), and fewer mean days requiring ventilation (4 +/- 3 vs 11 +/- 10) than did the control patients (P<.05 for each).	This non-randomised study displayed attaining supranormal circulatory values improves survival and decreases morbidity in the severely traumatised patient.
Velmahos, GC. Demetriades, D. 2000[77]	II Trauma	B2	To evaluate the effect of early optimisation in the survival of severely injured patients.	There was no difference in rates of death (15% optimal vs 11% control), organ failure, sepsis, or the length of intensive care unit or hospital stay between the two groups.	Severely injured patients who can achieve optimal haemodynamic values are more likely to survive than those who cannot, regardless of the resuscitation technique. In this study, attempts at early optimisation did not improve the outcome of the examined subgroup of severely injured patients.
Shoemaker, WC. Fleming, AW. 1986[79]	III-2 Trauma	B2	To compare outcomes in trauma patients who had resuscitation aimed at improving circulatory values and chemistry vs. those aimed at optimising 'physiologic patterns'.	Could not determine results. Data was not presented clearly.	–
Bishop, MH. Shoemaker, WC. Appel, PL. 1993[80]	III-2	B2	To describe the temporal patterns of haemodynamics and oxygen transport in survivors and nonsurvivors of severe trauma in relation to time delays, mortality, and morbidity.	During the first 24 hours, the mean values of CI (4.52 +/- 1.45 vs 3.8 +/- 1.20l/min/m^2; p<0.05), DO_2 (670 +/- 230 vs 540+/- 200ml/min/m^2; p<0.01) and VO_2 (166 +/- 48 vs 134 +/- 47ml/min/m^2; p<0.01) of the 60 survivors were significantly higher than the 30 non-survivors. Patients who achieved survivor values in less than 24 hours had a mortality of12% vs 54% for those who did not reach survivor values at all or took longer than 24 hours.	Reaching survivor values (or supranormal circulatory values) within 24 hours of injury may greatly improve survival as demonstrated in this observational study.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Waxman, K. Annas, C. Daughters, K. Tominaga, GT. 1994[115]	III-2 Diagnostic test	B1	To test the hypothesis that change in tissue PO_2 in response to an increased inspired O_2 challenge may be related to the state of cellular oxygenation, and hence the adequacy of resuscitation. (Tissue PO_2 is measured through a probe inserted in the deltoid muscle).	Patients were determined to have inadequate resuscitation if a rise in tissue PO_2 did not occur with an increase in inspired oxygen. Nine trauma patients did not exhibit an increase in tissue PO_2. Fluid resuscitation corrected these findings in 5/9. Four patients did not respond after repeated fluid administration.	The usefulness of this test is not demonstrated conclusively in this article. There is insufficient data supplied to determine if there is an absolute tissue oxygen cut off. Further work is needed before this tool can be routinely incorporated in clinical practice.
Davis, JW. Shackford, SR. Mackersie, RC. 1988[62]	IV	B2	To evaluate Base Deficit (BD) as an index for fluid resuscitation in the injured patients.	A retrospective review of 209 charts revealed as Base Deficit became more negative MAP decreased significantly and the volume of fluid required for resuscitation increased with increasing severity of BD group. ($p < 0.001$) A BD that became more negative with resuscitation was associated with ongoing haemorrhage in 65%. ($p < 0.002$). Increasing Base Deficit was associated with decreasing MAP, and decreasing Trauma Score ($p < 0.001$ for both).	This study indicates that base deficit may be a reliable indicator of the relative magnitude of volume deficit. BD may be a useful guide to volume replacement in the resuscitation of trauma patients.
Husain, FA. Martin, MJ. Mullenix, PS. 2003[116]	III-2	B1	To determine whether lactate levels and base deficits in critically ill surgical intensive care unit (SICU) patients correlate and whether either measure is a significant indicator of mortality and morbidity.	Initial and 24-hour lactate level was significantly elevated in nonsurvivors versus survivors ($p = 0.002$). Initial base deficit was not significantly different; 24-hour base deficit did achieve statistical significance ($p = 0.02$). Mortality if lactate normalised within 24 hours was 10%, compared with 24% for >48 hours and 67% if lactate failed to normalise.	Elevated initial and 24-hour lactate levels are significantly correlated with mortality and appear to be superior to corresponding base deficit levels. Lactate clearance time may be used to predict mortality and is associated with outcome at discharge. Initial base deficit was a poor predictor of mortality but did correlate with lactate levels in trauma nonsurvivors.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Weil, MH. Nakagawa, Y. Wanchun, T. Sato, Y. 1999[117]	III-2	B2	To clinically validate sublingual PCO_2 for diagnosing shock in patients with circulatory disarrangement.	Sublingual CO_2 correlated strongly with arterial blood lactate and mean arterial pressure. Increases in $PslCO_2$ correlated with increases in arterial blood lactate (r = 084, p<0.001). When $PslCO_2$ exceeded a threshold 70mmHg its positive predictive value of circulatory shock was 1.0. When it was <70mmHg its predicted survival was 0.93.	The validity of elevated Sublingual PCO_2 as a marker of shock is shown in this study. However absolute values of $PslCO_2$ are not determined. There still remains an overlap of readings in patients who did and did not have clinical shock. Larger trials are warranted as this technique may prove to be a useful, simple and non-invasive technique for quantifying perfusion in trauma patients. The study needs to incorporate patients with and without clinical signs of shock to determine if sublingual CO_2 is a more accurate marker of shock that readily measured variables such as HR, BP and urine output. One of the problems with determining the clinical utility of sublingual CO_2 is that there is no 'gold standard' with which to compare.
Kirton, OC. Windsor, J. 1998[118]	III-2	B1	To compare gastric pH and oxygen variables in survivors and non-survivors of trauma in a ICU.	Sensitivity of gastric pH <7.32 in predicting mortality was 83% and specificity 61%. In predicting multi-organ failure 86% sensitivity and specificity 66%. The risk of death with a pHi <7.32 4.5 (p<0.01) and risk of MOF 5.4 (p<0.01). The risk of death associated with an abnormal lactate at 24 hours was 3.0. The risk of MOF was 3.6.	A gastric pH<7.32 and lactate >2.3mmol at 24 hours is associated with high mortality rates and incidence of multi-organ failure.
Roumen, RM. Vreugde, JP. 1994[119]	IV	B1	To examine the posttraumatic gastric pH in 15 multiply injured trauma patients.	No correlation between gastric pH and shock, ISS, lactic acidosis, or APACHE II scores on admission were found. 25% of patients with a pHi <7.32 died. All patients with normal pHi survived.	Gastric pH may be useful in identifying patients with splanchic malperfusion that is not identified by routine monitoring.

Author & year	Level of evidence	Quality	Study question / population	Results	Conclusion
Ivatury, RR. Simon, RJ. 1995[70]	II	B2	To compare gastric mucosal pH and global oxygen variables (DO_2I / VO_2I) as indicators of adequate resuscitation in trauma patients.	Mortality was 9.1% for patients in normalization of gastric pH (`7.30) compared to 31.3% (p = 0.27).	The control group in this study was sicker than the intervention group as indicated by initial lactate (5.2+/- 3.4 vs 8.3+/-5.7) and base deficit (7.0 +/-3.9 vs 11.7 +/- 8.3), although ISS was similar between the two groups (24.4 vs 24.3). Gastric pH may be an important marker to assess the adequacy of resuscitation. Failure to normalise ph in this study was associated with high organ failure and death. However, the ability to manipulate pHi through oxygen indices and inotropes has yet to be demonstrated. The results do not reach statistical significance but this may be due to small study numbers. A larger study is warranted to validate the results of this study.
Chang, MC. Cheatham, ML. 1994[120]	III-2	B1	To assess the correlation between gastric pH and other markers of haemodynamic status and mortality in critically.	There was poor correlation between gastric pH and global markers of haemodynamic function and oxygen transport variables. PH that did not correct itself within 24 hours was associated with a higher mortality (50% vs 0%, p = 0.03) and organ failure (2.6 organs / patient vs 0.62 organs / patient).	Gastric pH supplements information provided by standard haemodynamic variables and maybe useful is identifying patients at risk of multi-organ failure and death. Treatment implications are not identified by this study.
Heyworth, J. 1992[121]	IV	B1	To evaluate the use of conjunctival oxygen tension monitor ($PCJO_2$) during the early assessment of injured patients.	A $PCJO_2$ less than 45mmHg was associated with hypovolaemia, reduced cardiac output and chest injury.	The usefulness of $PCJO_2$ as a monitoring tool for occult hypoperfusion is not demonstrated in this article.
Weil, MH. Nakagawa, Y. 1999[117]	III-2	B2	To investigate the predictive value of sublingual capnometry ($P(SL)CO_2$) as an early indicator of systemic perfusion failure in 46 patients with acute life-threatening illnesses or injury.	$P(SL)O_2$ >70mmHg had a positive predictive value of 1.00 for the presence of clinical signs of shock.	Sublingual capnometry correlates with signs of shock. This study does not show that $PSLCO_2$ would add any information that is not already routinely collected through standard circulatory monitoring.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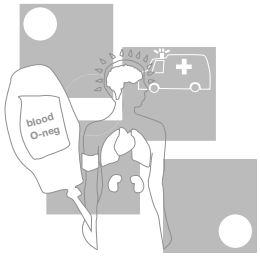


Search strategy for the identification of studies

The following search terms were used in Medline

1 Shock/

2 1 and hypovol?emi$.mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]

3 hypovol?emic shock.mp.

4 shock, hemorrhagic/

5 exp Hemorrhage/

6. (hemorrhag$ or haemorrhag$).mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]

7 Hypotension/

8 low blood pressure.mp.

9 or/2-8

10 "Wounds and Injuries"/

11 trauma.mp.

12 or/10-11

13 exp resuscitation/

14 Fluid Therapy/

15 fluid resuscitation$.mp.

16 blood transfusion/ or exp blood component transfusion/

17 exp Blood Substitutes/

18 blood expand$.mp.

19 exp colloids/

20 crystalloids.mp.

21 (volume expansion or volume expand$ or blood expansion or blood expand$).mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]

22 exp Monitoring, Physiologic/

23 Time Factors/

24 endpoint determination/

25 (endpoint$ or end point$).mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]

26 (or/2-4) and 12 and di.fs.

27 (or/5-6) and (or/7-8) and 12 and et.fs.

28 (or/5-6) and (th.fs. or manage$.mp.) and (rural$ or remote$ or non?urban$).mp. [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]

29 (or/13-16) and 9 and 12 and 23

30 (or/13-16) and 9 and 12 and (or/17-21)

31 (or/13-16) and 12 and (or/24-25)

32 9 and 12 and 22

33 or/26-32

34 9 and 12 and (dt,th.fs. or manage$.mp.) [mp=title, abstract, subject headings, drug trade name, original title, device manufacturer, drug manufacturer name]

35 limit 35 to english language

36 33 or 36

37 limit 37 to human

The following search terms were used in Embase-

1 Hypovolemic Shock/

2 Hemorrhagic Shock/

3 ((hypovol?emic or hemorrhagic or haemorrhagic) adj shock).mp. [mp=title, abstract, cas registry/ec number word, mesh subject heading]

4 exp Bleeding/

5 (hemorrhag$ or haemorrhag$).mp. [mp=title, abstract, cas registry/ec number word, mesh subject heading]

6 hypotension/ or hemorrhagic hypotension/

7 low blood pressure.mp.

8 or/1-7

9 Injury/

10 trauma.mp.

11 or/9-10

12 resuscitation/

13 exp fluid therapy/

14 fluid resuscitation.mp.

15 exp blood transfusion/

16 Blood Substitute/

17 (volume expansion or volume expand$ or blood expansion or blood expand$).mp. [mp=title, abstract, cas registry/ec number word, mesh subject heading]

18 exp colloid/

19 crystalloid/

20 exp monitoring/ or hemodynamic monitoring/ or patient monitoring/

21 (time or timing).mp.

22 (endpoint$ or end point$).mp. [mp=title, abstract, cas registry/ec number word, mesh subject heading]

23 (or/1-3) and 11 and di.fs.

24 (or/4-5) and (or/6-7) and 11 and et.fs.

25 (or/4-5) and (th.fs. or manage$.mp.) and (rural$ or remote$ or non?urban$).mp. [mp=title, abstract, cas registry/ec number word, mesh subject heading]

26 (or/12-15) and 8 and 11 and 21

27 (or/12-15) and 8 and 11 and (or/16-19)

28 (or/12-15) and 11 and 22

29 8 and 11 and 20

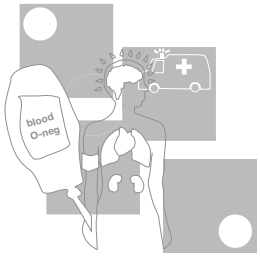
30 or/23-29

31 8 and 11 and (dt,th.fs. or manage$.mp.) [mp=title, abstract, cas registry/ec number word, mesh subject heading]

32 limit 31 to (english language)

33 30 or 32

34 limit 33 to human



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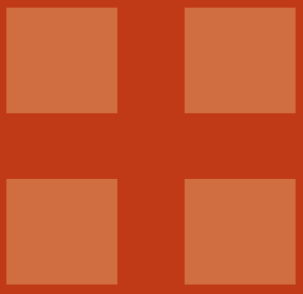

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