The development and validation of a prognostic model that assists in the management of blunt chest wall trauma patients.

Battle, Ceri Elisabeth

Swansea University
Prifysgol Abertawe

The development and validation of a prognostic model that assists in the management of blunt chest wall trauma patients

Ceri Elisabeth Battle

Submitted to the University of Wales in fulfilment
of the requirements for the Degree of Doctor of Philosophy

2013

ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

Summary

Introduction: The difficulties in the management of the blunt chest wall trauma patient in the Emergency Department due to the development of late complications are well recognised in the literature. The first aim of this study was to investigate the risk factors for the development of complications following blunt chest wall trauma. Using these risk factors, the second aim was to develop and validate a prognostic model that can be used to assist in the management of this patient group.

Methods: The risk factors for the development of late complications following blunt chest wall trauma were investigated using a number of methodologies. These included a systematic review and meta-analysis, a questionnaire study and a retrospective observational study. Following identification of the risk factors, a prognostic model was developed using multivariable logistic regression. This model was then externally validated in a prospective multi-centre study.

Results: The systematic review, questionnaire study, retrospective study and development study results highlighted that the risk factors for the development of complications following blunt chest wall trauma were an increasing patient age, the existence of chronic lung disease, an increasing number of rib fractures, the use of pre-injury anti-coagulants and a decreasing oxygen saturation level on presentation to the Emergency Department. These risk factors were included in the final model. Results of the validation study indicated an overall model accuracy of 87%, a sensitivity of 75% and a specificity of 97%. A concordance index of 0.96 highlighted an excellent discriminatory ability of the model.

Conclusions: The prognostic model developed in this study demonstrated good predictive capabilities in the derivation sample and excellent discrimination in the validation sample. The model demonstrates clinical usefulness as it includes risk factors not normally considered in the management of blunt chest wall trauma patients in the clinical setting.

Declarations and Statements

DECLARATION

This work has not been previously accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

Signed.....

Date.....6 DEC 13.....

STATEMENT 1

This thesis is the result of my own investigations, except where otherwise stated. Where correction services have been used, the extent and nature of the correction is clearly marked in a footnote.

Other sources are acknowledged by footnotes giving explicit references. A bibliography is appended.

Signed.....

Date.....6 DEC 13.....

STATEMENT 2

I hereby give consent for my thesis, if accepted, to be available for photocopying and for inter-library loan, and for the title and summary to be made available to outside organisations.

Signed.....

Date.....6 DEC 13.....

Contents

Chapter 5

Chapter 6

Acknowledgements

I would like to thank the following people:

- Dr Hayley Hutchings and Professor Adrian Evans (PhD supervisors)

- Simon Lovett (statistician)
- Anne, Sue, Rita and Sarah (Morriston Hospital Library)
- The Welsh Intensive Care Society (main study sponsor)
- Physiotherapy Department at Morriston Hospital (employer and second sponsor)
- Cynthia Davis and the R&D department (ABMU Health Board)

- Dr Jeremy Williams, Dr Sally Jones, Dr Aruni Sen, Dr Jake Hartford-Jones, Dr James Gagg, Dr David Robinson, Professor Fiona Lecky. (Principal Investigators in validation study)

- Lesley Bensted, Sara Biggs, Penny Roberts, Rachel Williams, Julie Tunicliffe, Physiotherapy Team at Musgrove Park Hospital. (Data collectors in validation study)

List of figures **Page no.**

List of tables **Page no.**

Abbreviations and definitions

AIC	Akaike information criteria
AIS	Abbreviated Injury Score
ARDS	Acute respiratory distress syndrome
ATLS	Advanced Trauma Life Support
BMI	Body mass index
CI	Confidence Interval
CPD	Cardio-pulmonary disease
CRD	Centre for reviews and dissemination
CT	Computed tomography
CXR	Chest x-ray
ED	Emergency department
EPV	Events per variable
FN	False negative
FP	False positive
glm	Generalised linear model
HDU	High dependency unit
HLOS	Length of stay in hospital
ILOS	Length of stay on intensive care unit
ICP	Integrated care pathway
ISS	Injury Severity Score
ICU	Intensive care unit
LOS	Length of stay
mfp	Multivariable fractional polynomial
MV	Mechanical ventilation
MVA	Motor vehicle accident
NHS	National Health Service
NIHR	National Institute for Health Research
NISCHR	National Institute for Social Care and Health Research
NPV	Negative predictive value
OR	Odds ratio
p-value	Probability value
PEC	Pre-existing conditions

PEFR	Peak expiratory flow rate
PPV	Positive predictive value
REC	Research ethics committee
RCT	Randomised controlled trial
R&D	Research and development
ROC	Receiver operator characteristic (curve)
RTC	Road traffic collisions
RTS	Revised Trauma Score
TARN	Trauma Audit Research Network
TN	True negative
TP	True positive
VC	Vital capacity

1.0 Introduction

1.1 Demographics and Incidence of blunt chest trauma

In the present day, injury to the chest is reported as the second most common cause of trauma deaths with rib fractures being the most frequent cause of subsequent morbidity after blunt chest trauma. (Shorr et al 1989) Research has highlighted significant morbidity and mortality for the blunt chest trauma patient, with reported mortality ranging between 4-20%. (Brasel et al 2006, Zeigler and Argawal 1994) A number of authors have highlighted however that as blunt chest wall trauma often causes death indirectly, through delayed pulmonary complications, an accurate estimate of mortality is hard to calculate. (Simon et al 2005, Karmakar and Ho 2003) The elderly blunt chest wall trauma patient, with poor respiratory reserve, decreased muscle mass and loss of bone density is recognised as the most vulnerable. (Bergeron et al 2003, Albaugh et al 2000, Alexander et al 2000) Blunt chest wall trauma accounts for over 15% of all trauma patients presenting to the ED in the United Kingdom. (Trauma Audit and Research Network 2010) It has been suggested that the true incidence of bony injury to the chest wall may be underreported, as up to 50% of rib fractures are undetected on chest radiograph. (Davis and Affatato 2006, Banisdhar et al 2002)

The most common mechanisms of injury in the blunt chest wall trauma patients were motor vehicle accident (MVA), fall from a height and pedestrian low velocity fall. (Sharma et al 2008, Bergeron et al 2003) The high incidence of MVA in America may be due to different legislation which only enforces seat belt use in the front of the car, but not for rear seat passengers. Comparable data is not available for different countries with alternative legislation. Bergeron et al (2003) concluded that MVA was significantly more common in the patient aged less than 65 years compared with the low velocity fall which was significantly more common in the patient aged greater than 65 years. (Bergeron et al 2003) With the steady growth in the elderly population due to increased life expectancy, a concurrent increase in elderly trauma rates has been reported. (Sharma et al 2008, Young and Ahmad 1999) The elderly continue to engage in many of the same activities as some of their younger counterparts, therefore subjecting themselves to the same injury risks. Numerous studies however have highlighted that the elderly have a significant risk of

morbidity and mortality, increased admission rate and increased hospital length of stay compared to younger patients with the same traumatic injuries. (Sharma et al 2008, Bergeron et al 2003, Perdue et al 1998, Martin and Teberian 1990)

Blunt chest wall trauma also remains a major source of morbidity and mortality in children with blunt forces accounting for up to 85% of paediatric chest injuries. (Sartorelli and Vane 2004, Peterson et al 1994, Nakayama 1989) In blunt injury mechanisms, chest trauma rarely occurs in isolation as a result of the child's small surface area. (Sartorelli and Vane 2004) It has been further highlighted that chest wall compliance varies greatly. In a child with a very compliant chest wall, the child may have sustained a significant amount of force and resultant injury to the underlying lungs, with no apparent injury to the bony chest wall. Evidently, special attention should be given to the child with blunt chest wall trauma. (Sartorelli and Vane 2004, Peterson et al 1994, Nakayama et al 1989)

1.2 Anatomy of the thorax

The thorax is the region of the body composed of the sternum, the thoracic vertebrae and the ribs and extending from the neck to the diaphragm. The thoracic viscera (organs) including the heart, lungs and many great blood vessels are contained in the thoracic cage. The diaphragm makes up the floor of the thoracic cavity and is pushed upwards into the thorax by the abdominal viscera. The lower half of the thoracic wall therefore surrounds and protects abdominal rather than thoracic organs. (Moore and Dalley 2006)

Humans have 12 pairs of ribs. The first seven pairs are known as true ribs with the following five pairs being described as false ribs, three of these sharing a common cartilaginous connection to the sternum. The first ten pairs are directly attached to the sternum through the costal cartilage, with the eleventh and twelfth pairs of ribs termed floating ribs as they are attached to the vertebrae only. (Moore and Dalley 2006) The costal cartilages prolong the ribs anteriorly and contribute to the flexibility of the thoracic wall. Figure 1.2.1 indicates the basic anatomy of the thorax.

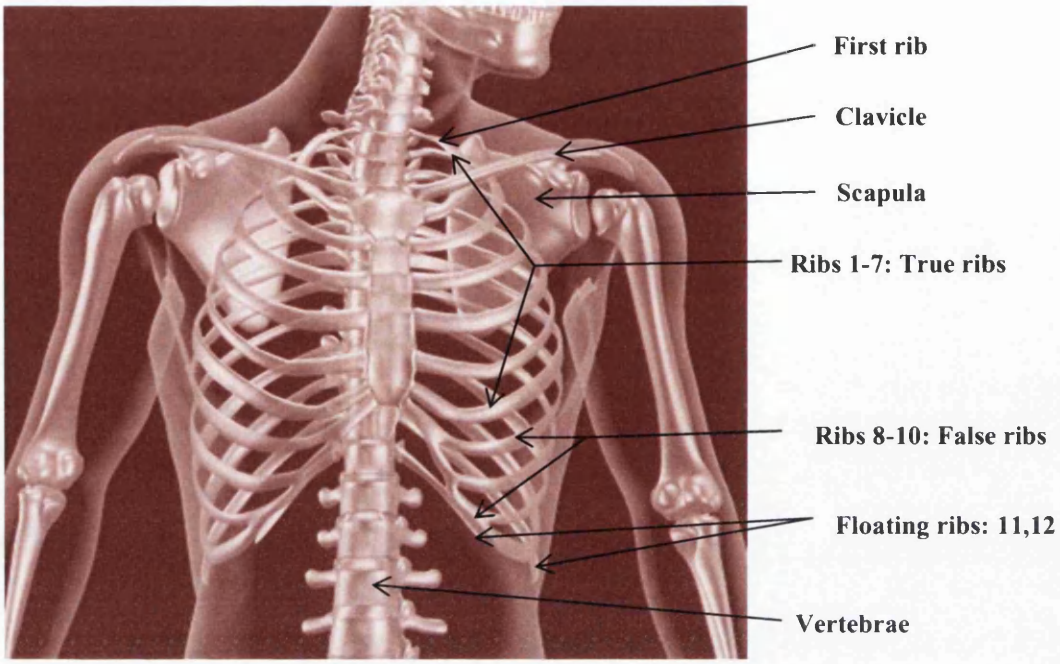


Figure 1.2.1: Basic anatomy of the human thorax. (Pargeter, 2005)

Intercostal spaces separate the ribs from one another and are occupied by the intercostal muscles (innermost, internal and external) and two sets of intercostal blood vessels and nerves. A costal groove runs parallel to the inferior border of the rib which provides protection for the intercostal nerve and vessel. (Moore and Dalley 2006) The nerves and blood vessels travel through the intercostal spaces parallel to the ribs in the costal groove, supplying the three layers of intercostal muscles and the pleura (the lining membranes of the lungs). (Moore and Dalley 2006) In addition, there are 12 pairs of thoracic spinal nerves that supply the thoracic wall. Figure 1.2.2 indicates the course of the intercostal nerve, arteries and veins through the costal groove between the intercostal muscles.

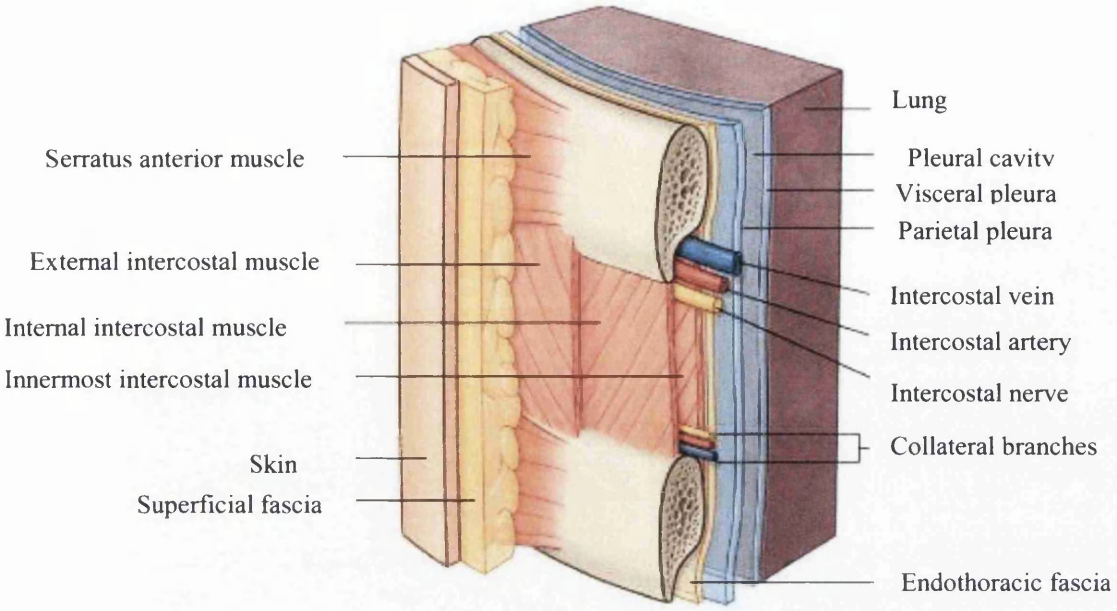


Figure 1.2.2: Intercostal nerves, arteries and veins. (Drake et al 2009, p154)

The thoracic wall surrounds the thoracic cavity which is described as being comprised of three parts. The right and left pulmonary cavities are bilateral compartments which contain the lungs and lining membranes or pleurae. The central mediastinum is the third compartment which completely divides the pulmonary cavities and contains all other thoracic structures. (Moore and Dalley 2006) The pulmonary cavities are completely lined by membranous parietal pleura whilst the outer surface of the lungs is lined by the visceral pleura (See Figure 1.2.2). The pleural cavity lies between the two pleura and is filled with a lubricating pleural fluid.

The pleural fluid has a number of other functions including the maintenance of the surface tension that keeps the outer surface of the lung attached to the inner surface of the thoracic wall. This action prevents collapse of the lung and causes the lung to expand with the thorax on inspiration. The visceral pleura is insensitive to pain as it receives no nerves of general sensation however, the parietal pleura is extremely sensitive and causes severe pain when injured as a result of its rich innervation by the phrenic and costal nerves. (Moore and Dalley 2006)

The lungs are the organs of respiration in which venous blood in the pulmonary capillaries exchanges oxygen and carbon dioxide with each tidal breath. The lungs are separated from each other by the mediastinum (which is responsible for the conduction of air and blood to and from the lungs) to which they are attached by the

lung root. (Moore and Dalley 2006) Air and blood are delivered to each lung by the lung root which consists of the bronchi and associated bronchial blood vessels, pulmonary arteries and veins, pulmonary plexus of nerves and lymphatic vessels. (Moore and Dalley 2006) The mediastinum is the central compartment of the thoracic cavity and contains all the thoracic viscera except the lungs, including primarily the heart, thoracic sections of the great vessels, trachea, oesophagus, thymus and lymph nodes. The mediastinum is a pliable and dynamic structure that is constantly moved by the heart that lies within it and the lungs and diaphragm that surround it. (Moore and Dalley 2006) The position of the heart, great vessels and lungs are shown in Figure 1.2.3.

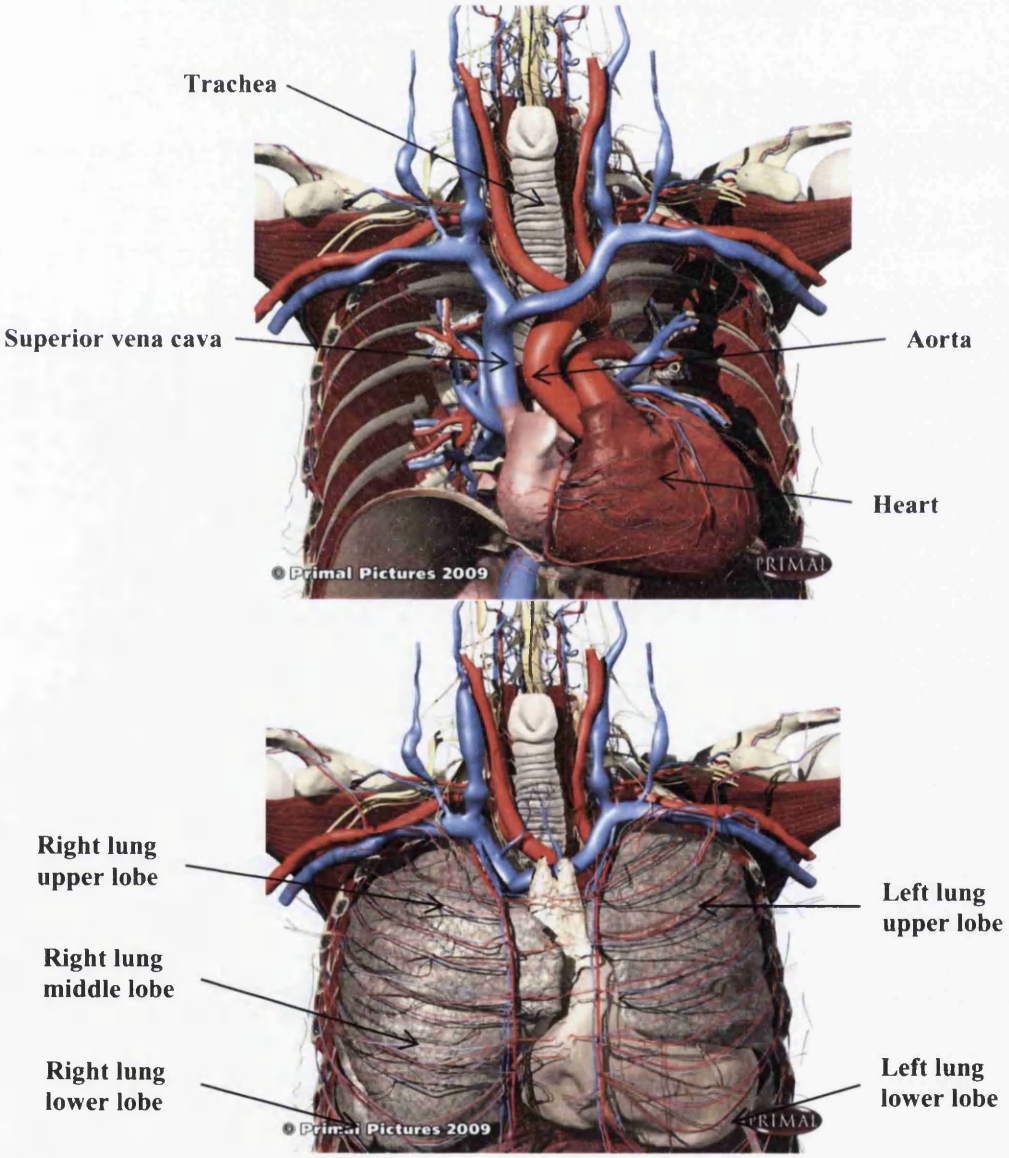


Figure 1.2.3: The position of the heart, great vessels and lungs. (Darzi et al 2009)

1.3 Functional anatomy of the thoracic cage

The true thoracic wall not only includes the thoracic cage, but the muscles, skin, subcutaneous tissue, fascia, intercostal nerves and blood vessels. The domed shape of the thoracic cage provides remarkable rigidity considering the light weight of its component parts. This shape enables the thoracic cage to have a number of functions: (Moore and Dalley 2006)

1) Protection of the thoracic and upper abdominal organs from external forces.
2) Resistance of the internal, sub-atmospheric pressures generated by the elastic recoil of the lungs during respiration.
3) Support for the weight of the upper limbs.
4) Attachment for the muscles of the upper limbs, neck, abdomen, back and respiration.

Even though the shape of the thoracic cage provides rigidity, the shape of the bones and joints allows flexibility allowing it to change shape as required for respiration. The thorax is one of the most dynamic regions of the body. During inspiration the diaphragm and the muscles of the thoracic wall and abdomen work together to expand the thoracic cavity causing the lungs to expand creating negative or sub-atmospheric pressure and drawing air in. Passive recoil due to the elasticity of the lungs and relaxation of the muscles of respiration decreases the volume of the thoracic cavity, compressing the lungs, thus forcing the air to be expelled out of the lungs. (Moore and Dalley 2006)

In addition to respiration, the flexibility of the thoracic cage provides protection. The ribs are curved, flat bones that are remarkably lightweight, yet highly resilient to external forces and resultant fractures. (Moore and Dalley 2006) As with all bones, the ribs have protective, structural and metabolic functions. (Moore and Dalley 2006, Vlessis and Trunkey 1997) It is evident that an injury or fracture to the thoracic wall will potentially damage any of the underlying structures and furthermore, will have a detrimental effect on the protective, structural and metabolic functions of the thoracic cage. (Moore and Dalley 2006, Vlessis and Trunkey 1997)

1.4 Blunt chest trauma

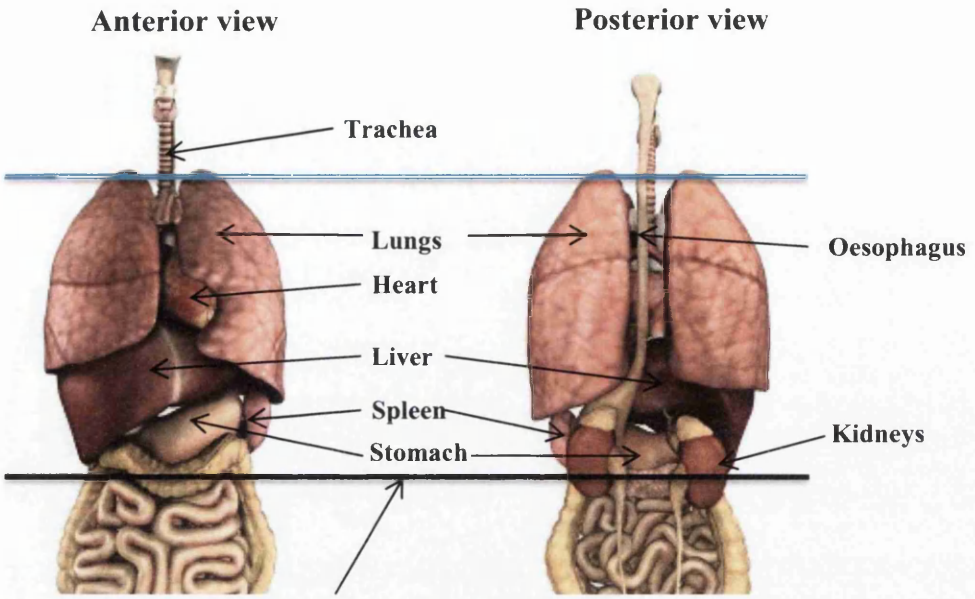
Chest trauma can be defined as injury to the thoracic wall and the underlying structures, including the lungs, pleura, tracheobronchial tree, oesophagus, heart and great vessels. (Kulshrestha et al 2004) Chest trauma can be further categorised as either penetrating or blunt. Penetrating chest trauma can be defined as an opening in the chest wall with resultant trauma to the chest wall and underlying structures and results from incidents such as stab wounds or gunshot injuries. (Limmer et al 2008) Penetrating trauma can lead to damage to all structures of the thoracic cage and cavity, resulting in marked anatomical changes in structure and massive haemorrhage from major blood vessels. (Vlessis and Trunkey 1997)

Penetrating chest trauma frequently leads to serious or fatal injury because of the vital structures such as the heart and great vessels are contained within the chest cavity. (Vlessis and Trunkey 1997) Maintaining normal pressures within the chest cavity and intrapleural space is essential for adequate breathing so disruption to these pressures through a penetrating injury to the chest becomes a potentially life-threatening emergency. (Limmer et al 2008) The patient with penetrating chest trauma therefore often requires immediate surgical intervention. The decision making process regarding patient management is therefore dictated by the patient's associated injuries, necessary surgical intervention and potential pathophysiological course. (Limmer et al 2008, Vlessis and Trunkey 1997)

Blunt chest wall trauma does not involve any opening of the chest wall and can vary in severity from minor bruising or an isolated rib fracture to severe crush injuries on both sides of the thorax leading to potentially fatal respiratory compromise. (Vlessis and Trunkey 1997) Simple chest trauma is characterised as a blunt chest wall injury that results in chest wall bruising with or without rib fractures. (Sanidas et al 2000) In more severe trauma, injury to the underlying lungs and associated pleurae may occur including pulmonary contusion or laceration, or a pneumothorax or haemothorax (all discussed below). Multiple rib fractures will often be associated with an underlying pulmonary contusion or bruising due to the transference of kinetic forces from the ribs to the lungs, which are not always immediately apparent on an initial chest radiograph. (Bastos et al 2008)

The most common forms of blunt chest wall trauma seen in the Emergency Department (ED) are rib fractures. Rib fractures are a sign of more extensive injury with high incidence of mortality from associated injuries to the head, chest, abdomen or long bones. (Barnea et al 2002) Rib fractures are also a reported marker for other associated significant organ injury, both intra and extra thoracic. (Flagel et al 2005, Lee et al 1990) The upper ribs are protected by the bony framework of the upper limbs, including the scapula, humerus and clavicle, in addition to their muscular attachments. Fractures to the first and second ribs, scapula or sternum suggest a magnitude of trauma that places the head, neck, spinal cord, great vessels and lungs at high risk for serious associated trauma. (Vlessis and Trunkey 1997) Damage to the underlying brachial plexus of nerves and subclavian vessels is also commonly reported. (Bergeron et al 2003, Moore and Dalley 2006) Consequently, mortality in this patient group can be high. (Sirmali et al 2003, Vlessis and Trunkey 1997) Sirmali et al (2003) suggested that fracture of the first rib should prompt a thorough examination for other injuries due to the significant amount of force that is required for a fracture indicating major energy transfer and risk for serious damage to underlying vessels.

The middle ribs are the most commonly fractured due to external forces, with the fourth to sixth ribs most frequently involved. (Bergeron et al 2003, Sirmali et al 2003) The weakest section of the rib is anterior to the rib angle but direct force can fracture the rib at any point along its length. The fractured bone end may injure the underlying organs including the lungs and spleen. (Moore and Dalley 2006) Fractures to the lower ribs can lead to rupture of the diaphragm or abdominal injury. (American College of Surgeons 2008, Moore and Dalley 2006, Vlessis and Trunkey 1997) Lee et al 1990 highlighted a relative risk of increased incidence of splenic and hepatic injuries with fractures to ribs ten to twelve. It has been suggested that the younger patient with the more flexible thoracic cage is less likely to sustain rib fractures. However more serious underlying injury may be present without the expected number of rib fractures from the described mechanism of injury. (American College of Surgeons 2008, Vlessis and Trunkey 1997) Figure 1.4 indicates the organs underlying the ribs that can be potentially damaged by trauma to the thoracic wall.



NB: Thick blue line represents the level of the top of the thoracic cage (first rib) and the thick black line represents the level of the bottom of the thoracic cage (12th rib) overlying the viscera.

Figure 1.4: Viscera underlying thoracic wall. (Bucklin, 2005)

1.5 Pain Mechanisms

As a result of the rich neurovascular supply of the thoracic wall and underlying structures, injury to the chest wall also leads to severe pain and most authors agree that pain as a result of blunt chest wall trauma can be more debilitating and harmful than the injury itself. (Sharma et al 2008, Simon et al 2005, Karmakar and Ho 2003) Inflammation and bruising in the thoracic wall will occur as a consequence of a fractured rib. The thoracic wall and parietal pleura are rich in sensory nerves responsible for nociception, thus injury to the chest wall and underlying lung can lead to severe pain. (Moore and Dalley 2006) Rib fracture pain originates at the site of the bone injury and injured adjacent muscle and is often reported by patients to be exacerbated by any movement of the chest wall. (Simon et al 2005, Vlessis and Trunkey 1997) Pain limits the patient's ability to cough and inspire deeply resulting in retained pulmonary secretions, collapse of lung segments (atelectasis) and reduced lung function and lung volumes. (Simon et al 2005) There is no evidence in the literature to suggest that injury to different areas of the thoracic wall produces greater levels of reported pain and one study reported no correlation between the number of fractured ribs and the reported pain levels. (Osinowo et al 2004)

Failure to control the patient's pain, compounded by other direct injuries to the lung, can result in serious, often fatal respiratory complications. (Osinowo et al 2004, Karmakar and Ho 2003) In blunt chest trauma care today, it has been suggested that the cornerstone of conservative management is early and effective pain control, thus allowing aggressive respiratory physiotherapy and early mobilisation. (Karmakar and Ho 2003, Kerr-Valentic 2003, Sirmali 2003) Inpatient blunt chest trauma pain control has been emphasised as a priority therefore and a variety of pain management techniques have been suggested including oral analgesics such as narcotics and non-steroidal anti-inflammatory drugs, intravenous narcotics, epidural analgesia and intercostal nerve blocks. (Simon et al 2005, Karmakar and Ho 2003, Kerr-Valentic et al 2003)

Analgesia following blunt chest wall trauma has been well researched and limited consensus exists regarding the optimal analgesic agents and their most efficacious mode of delivery. Berben et al (2008) emphasize however that the management of pain while the patient is in the ED has received less attention, especially in trauma patients. In their study, 91% of patients reported pain on admission to the ED and 86% of patients reported pain on discharge from the ED. The barriers to effective pain management in the ED were described which include patient anxiety and a lack of knowledge by the ED staff, both problems which could be potentially addressed to improve patient experience in the ED. It was concluded that acute pain in trauma patients is a significant problem and that pain is not treated effectively at any point during the ED experience. (Berben et al 2008)

Inpatient analgesia for blunt chest wall trauma patients has historically been emphasized as a priority. Oral analgesics such as narcotics and non-steroidal anti-inflammatory drugs, intravenous (IV) opioids and a number of invasive techniques such as epidurals and intra-thoracic blocks have been investigated. (Kerr-Valentic et al 2003) The use of a thoracic epidural compared to IV opioids for pain relief in rib fracture patients has been investigated in a number of studies. In a short review by Parris (2007), the benefits of epidural over IV analgesia are reported, but conclusions suggest that further higher quality studies are needed. When compared to IV opioids, thoracic epidurals are reported to decrease the incidence of nosocomial pneumonia and mechanical ventilation days, (Bulger et al 2004) decrease morbidity and

mortality, (Wisner 1990) and also provide superior pain relief when compared to intercostal block. (Hashemzadeh et al 2011) In a meta-analysis investigating the effects of epidural analgesia in rib fracture patients, Carrier et al (2008) reported no differences between epidurals and other analgesic modalities.

The use of the intercostal nerve block and thoracic paravertebral block has also been investigated in blunt chest wall trauma patients. Osinowo et al (2004) reported an increase in patient oxygen saturations and peak expiratory flow rate after intercostal nerve block with 0.5% bupivicane. In another study, Mohta et al (2009) highlighted that a continuous thoracic epidural had equivocal results with a thoracic paravertebral block in patients with unilateral rib fractures. Karmakar and Ho (2003) concluded that there was no preferred technique for pain relief in rib fracture patients and clinicians need an understanding of all analgesic options. More recently Ho et al (2011) concluded that thoracic epidural, thoracic paravertebral block and intercostal nerve block are all the most effective analgesia options for multiple rib fracture patients and each has its own contraindications for use and strengths and weaknesses.

Simon et al (2005) have produced comprehensive guidelines for pain management in blunt chest wall trauma, considering all relevant published studies. They conclude that more research is needed investigating the safety of regional anaesthetic techniques for pain relief. It is important to emphasize that effective pain relief in more severely injured blunt chest trauma patients also has its pitfalls. Karmakar and Ho (2003) emphasised that highly effective pain relief can actually mask subtle signs of delayed splenic rupture and delayed haemothorax, both common entities following multiple rib fractures. It is therefore advised to establish cardiovascular stability, exclude abdominal visceral injury and drain any pneumothorax or haemothorax before using regional anaesthetic technique for pain relief. (Karmakar and Ho 2003) Table 1.5 summarises the advantages and disadvantages of the pain management techniques commonly used in the management of blunt chest wall trauma.

Technique	Advantages	Disadvantages
NSAIDs	Non-invasive, orally administered No systemic side effects	Poor reported analgesic effect in severe pain Risk of stomach / duodenal ulcer Risk of renal dysfunction
Opioids	Easy to administer Effective for severe pain	Risk of respiratory and CNS depression Nausea
Thoracic epidural	Reduced risk of systemic sedation Immediate and substantial effect Minimal local anaesthetic toxicity Not associated with PTX	NSAIDs / opioid supplementation often required Invasive and painful to perform Risk of dural puncture / spinal cord injury Risk of hypotension Risk of motor block making mobilisation difficult Risk of urinary retention
Thoracic paravertebral block	Easier to perform than epidural Immediate and substantial effect No CNS depression Can be used with moderate degree of haemostatic deficiency Can be used in patients with hypovolaemia / hypotension No urinary retention	Risk of PTX Risk of local anaesthetic toxicity Less accuracy of site of analgesic effect than epidural
Intercostal nerve block	Extremely effective No CNS depression	Needs multiple injections as only lasts 4-8 hours depending on analgesic used Risk of local anaesthetic toxicity Risk of PTX Less accuracy of site of analgesic effect than epidural Difficulty with posterior ribs
Intrapleural block	Effective pain relief No CNS depression	Loss of analgesia if chest drain present Presence of blood in intrapleural space dilutes analgesia Direction of catheter unpredictable Site of analgesic effect influenced by gravity
Lidocaine patches	Non-invasive No CNS depression Minimal / no side effects	Poor analgesic effect in moderate to severe pain Limited supporting research
Transcutaneous nerve stimulation	Superior to NSAIDS in minor blunt chest wall injury Non-invasive No CNS depression Minimal / no side effects Patient can self-manage	Poor analgesic effect in moderate to severe pain Limited supporting research

Table 1.5 Advantages and disadvantages of the pain management techniques used in the management of blunt chest wall trauma.

The drawback of many of these interventions is that they cannot be continued for the length of time that the patient with rib fractures has significant pain. (Kerr-Valentic et al 2003) In a study by Kerr-Valentic et al 2003, the on-going pain suffered by rib fracture patients led to significant levels of disability at 30 days when compared to a reference population with chronic illness ($p<0.001$), even though their reported perception of general health was better. This study highlighted that a group of

patients with isolated rib fractures were unable to return to work for an average of 50 days post injury, while patients with a concurrent extra-thoracic injury returned to work on average 40 days later. (Kerr-Valentic et al 2003)

1.6 Pathophysiology of blunt chest trauma

In contrast to penetrating trauma, blunt chest trauma follows a different pathophysiological course. In penetrating trauma, injury to the major blood vessels such as laceration or perforation can often result in dramatic pathophysiological results which lead to an urgent need for early diagnosis and correction if the patient's life is to be salvaged. (American College of Surgeons 2008, Vlessis and Trunkey 1997) With the exception of severe blunt chest trauma leading to major mediastinal injuries, massive haemorrhage from major blood vessels does not occur in simple blunt chest trauma. (Vlessis and Trunkey 1997) Micro-vascular bleeding occurs in blunt chest trauma as a result for example, of damage to the small vessels supplying structures such as the periosteum, lung tissue and pleura. (Moore and Dalley 2006, Vlessis and Trunkey 1997) Direct force applied during blunt trauma also ruptures the cell membranes, allowing the material within the cell known as cytoplasm to leak out, thus causing cell death. (Goepel 2004) In addition, an inadequate supply of oxygen to cells is potentially damaging to cellular function, as seen for example in hypoxaemia as a result of pulmonary contusion or haemothorax. (Goepel 2004)

Metabolic changes have also been described in response to trauma. (Nicholson 2005, Haljamae 1990) The magnitude of the metabolic response is proportional to the injury severity. (Nicholson 2005) Following trauma, the neuroendocrine and inflammatory changes that occur in the body result in substrate mobilisation, muscle protein loss, and sodium and water retention. (Nicholson 2005) The hormonal changes associated with the metabolic response to trauma involve increased secretion of hormones primarily from the pituitary and adrenal glands and the pancreas. Such hormones include growth hormone, catecholamines, cortisol and aldosterone. (Nicholson 2005) Failure of normal feedback mechanisms that control secretion of hormones also occurs. (Nicholson 2005) These metabolic changes that occur have evolved to aid survival following trauma however a number of modulating factors for metabolic changes following trauma have been suggested by Haljamae (1990)

including the patient's nutritional status, complicating medical conditions, age, sedation and pain treatment.

Inflammation is the local physiological response to tissue injury and has some beneficial effects, such as the destruction of invading micro-organisms, thus preventing infection. (Stephenson 2004) Inflammation is classified according to its time course as acute and chronic. Acute inflammation is the initial and usually transient responses of the tissues to an injury. (Stephenson 2004) It has a vascular component in which the blood vessels dilate and an exudative component where the blood vessels leak fluid which is rich in protein. White blood cells called neutrophil polymorphs are recruited to the inflamed tissue to fight off potential infection. (Stephenson 2004) The outcome of the acute inflammatory phase may either be resolution or progression to the chronic phase. Macroscopic appearances of the acute phase include redness due to small blood vessel dilatation, heat due to increased blood flow through the area, swelling resulting from the accumulation of fluid (oedema) as part of fluid exudates and arrival of inflammatory cells to the area, pain due to stretching or distortion of tissues due to oedema, and loss of function due to pain and swelling. (Stephenson 2004)

Chronic inflammation occasionally follows acute inflammation and is defined as chronic not only due to the extended time period of the process, but furthermore due to the differing types of cellular reaction to that seen in acute inflammation. (Stephenson 2004) Chronic inflammation is defined as an inflammatory process in which lymphocytes, plasma cells and macrophages predominate. Abundant and often excessive granulation and scar tissue are formed to the detriment of movement of the body part and function. Chronic inflammation has a relatively insidious onset, a prolonged course and a slow resolution. (Stephenson 2004)

A common injury seen in blunt chest trauma is a rib fracture. (Bastos et al 2008, Bergeron et al 2003) The ribs are flat bones which have a protective function and provide a broad surface for muscular attachment. (Moore and Dalley 2006) All adult bone consists of an outer cortical shell which is compact bone of variable thickness. Within the cortical bone lies medullary or spongy cancellous bone which forms a network of trabeculae (microscopic tissue element in the form of a rod), which

follow the lines of stress within the bone. (Moore and Dalley 2006, Hughes 2004) The dense fibrous membrane covering the surface of bones is known as the periosteum which contains blood vessels and nerves which supply nourishment and sensation to the bone. (Moore and Dalley 2006) The ribs receive a superficial blood supply from the periosteal arterioles which are small vessels which supply the outer layers of cortical bone, in addition to a supply from large nutrient arteries that penetrate directly into the medullary bone. (Moore and Dalley 2006) Blood is drained from bone through veins that accompany the arteries and frequently leaves through foramina near the articular ends of the bones. Lymph vessels are also abundant in the periosteum. (Hughes 2004) The nerve fibres supplying bone accompany the blood vessels into the interior of the bone, many of which are sensory nerves causing pain. As a result of the blood and nerve supply to the bone, external forces causing fracture to the bone will result in both bleeding and pain. (Moore and Dalley 2006, Hughes 2004) Figure 1.6.1 Illustrates the anatomy of adult bone.

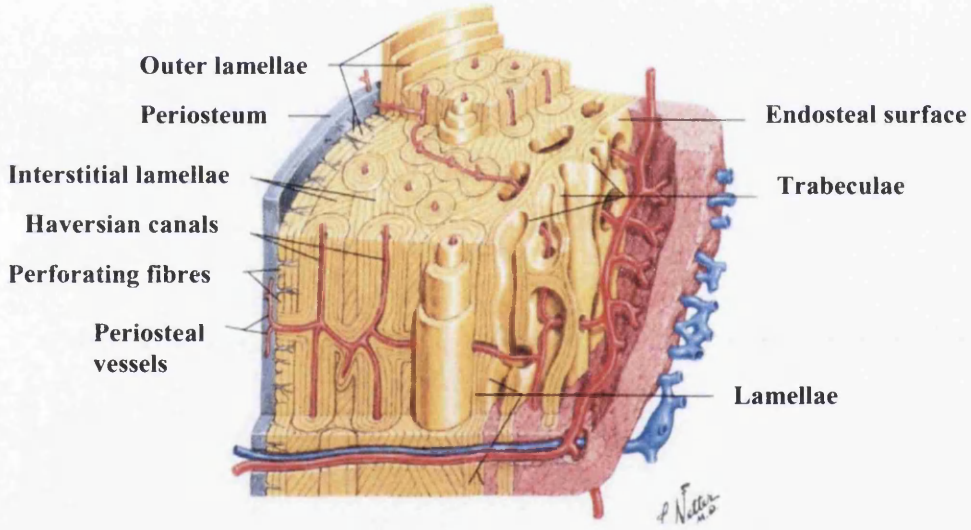


Figure 1.6.1: The anatomy of compact bone (Greene 2006, p17)

It has been suggested that the pathophysiological response of bone to trauma can be divided into two stages; those occurring immediately as a result of the applied force, and the subsequent inflammatory and reparative stages which ultimately lead to union or repair of the bone. (Mars and Spencer 1997) Immediately following fracture of a bone (reactive or inflammatory phase), bleeding will occur adjacent to the fracture site between the bone ends, as a result of the disruption to the blood supply to the periosteum. (Moore and Dalley 2006, Hughes 2004) Within a few days, the

extravascular blood cells will form a blood clot known as a haematoma. All of the blood cells within this clot will degenerate and die, however cells called fibroblasts will survive and replicate. (Hughes 2004) These cells will form granulation tissue, a loose aggregate of cells which are interspersed with blood vessels. This process takes between three to five days. From approximately day four to three weeks, the reparative phase occurs in which the fibroblast cells in the granulation tissue produce a spongy bone callus that bridges the gap between the fractured bone ends. (Hughes 2004) This spongy callus will be transformed into hard woven bone and at between six to twelve weeks the bone ends will be healed and connected by a hard callus. The bone remodelling phase may occur over several years and this is where the hard callus is remodelled where the normal shape and structure of the bone reformed. (Hughes 2004, Mars and Spencer 1997) Figure 1.6.2 Illustrates the stages of fracture healing.

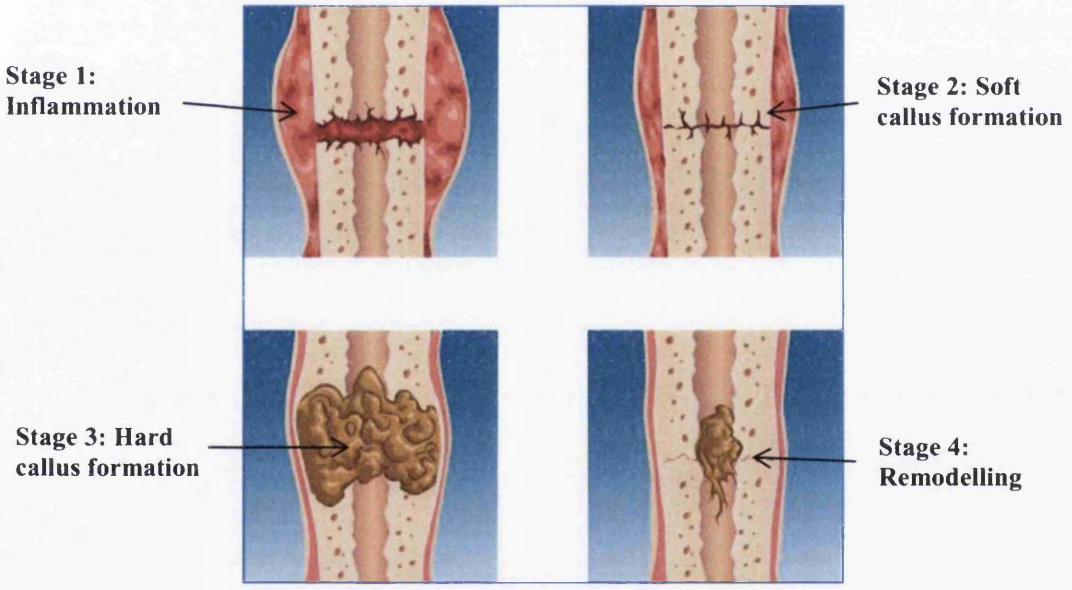


Figure 1.6.2: The stages of fracture healing. (Aral, 2007)

The normal process of respiration requires use of both bony structures and the accessory muscles of the thorax. Following rib fractures however there is a reduction in the efficiency of this dual action, leading to a decrease in normal lung volumes. Pain secondary to blunt chest wall trauma has been reported to inhibit coughing and complete respiration and exacerbates the loss in lung volumes. (Zeigler and Argawal 1994) Progressive collapse of segments of the lung (atelectasis) occurs when respiratory function is limited by pain. (Flagel et al 2005, Zeigler and Argawal 1994)

Consequently, the most common pathophysiologies resulting from blunt chest trauma are atelectasis and pneumonia. (Elmistekawy and Hammad 2007, Stawicki et al 2004)

Atelectasis is defined as the lack of gas exchange within alveoli, due to alveolar collapse. (Hough 2001) It may affect part or all of one lung. It is a condition where the alveoli are deflated. Normal alveoli are kept open by the elastic structure of the lung and the liquid lining of the alveoli called surfactant. (Moore and Dalley 2006) The surfactant counters the natural tendency of the alveoli to collapse. (Moore and Dalley 2006) Atelectasis is caused by a blockage of the bronchi or bronchioles (passages supplying alveoli) or by external pressure on the alveoli. When a bronchus or bronchiole becomes blocked, the air in the alveoli beyond the blockage is absorbed into the bloodstream, causing the alveoli to shrink and collapse. (Hough 2001) The main function of the alveoli is gaseous exchange which involves the absorption of oxygen into the bloodstream from atmospheric air and to expel the carbon dioxide from the blood. (Benditt 2004) In collapsed alveoli, gaseous exchange cannot occur, thus decreasing the volume of oxygen being delivered to the blood. The body compensates by constricting the blood vessels in the affected alveoli and redirecting the blood to the functioning alveoli, thus minimising a ventilation-perfusion mismatch. (Benditt 2004)

Causes of atelectasis include sputum retention, pleural effusion (build up of fluid in pleural space), pneumothorax, haemothorax, shallow breathing and immobility in bed with minimal posture change. (Benditt 2004, Hough 2001) Many of these causes occur as a result of blunt chest trauma, thus highlighting the severity of risk of atelectasis following chest trauma. The area of collapsed lung may become infected because bacteria and white blood cells can build up behind the blockage. Infection or pneumonia is particularly likely if atelectasis persists for several days or more. (Benditt 2004) Figure 1.6.3 Illustrates atelectasis and its effect on the lung.

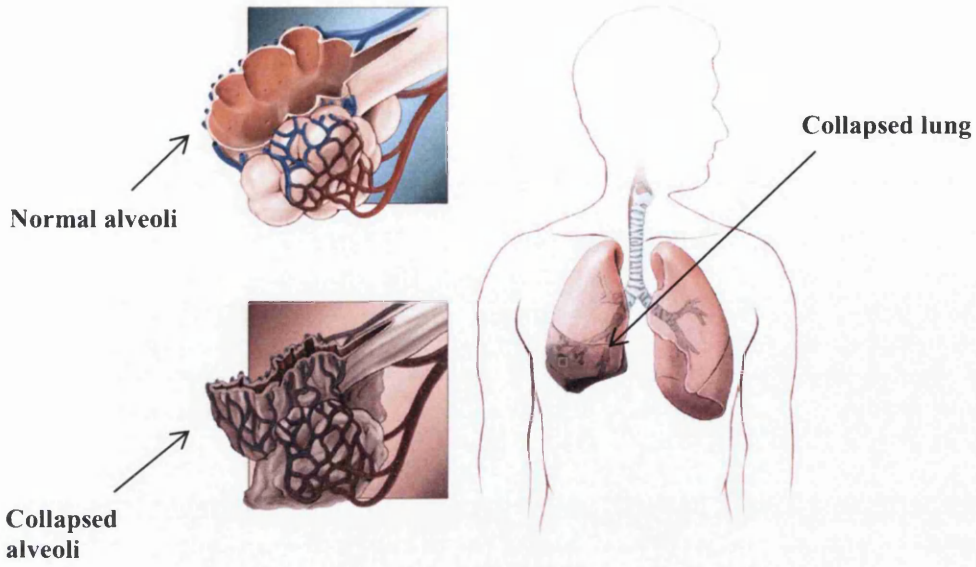


Figure 1.6.3 Atelectasis (National Heart, Lung and Blood Institute, 2011).

Pneumonia is defined as an acute infection of the lung parenchyma that often impairs gaseous exchange and has many different classifications, according to site affected within the lung, microbiological aetiology or how the pneumonia is acquired. (Springhouse 2003) In bacterial pneumonia, an infection initially triggers an inflammatory response and resultant oedema in the alveoli. The capillaries supplying the alveoli become engorged with blood which leads to a breakdown in the alveolocapillary membrane. The alveoli subsequently fill with blood and exudate, causing or worsening atelectasis. (Springhouse 2003) Severe pneumonia in a normal healthy adult can lead to the need for mechanical ventilation as a result of the failure of respiration and gaseous exchange. (Brasel et al 2006, Vlessis and Trunkey 1997) This risk is further compounded in the elderly patient with pre-existing cardio-pulmonary disease with limited physiologic reserve. (Bergeron et al 2003) In debilitated patients, bacterial pneumonia has been reported as the leading cause of death in the United States. (Springhouse 2003) Figure 1.6.1 illustrates pneumonia.

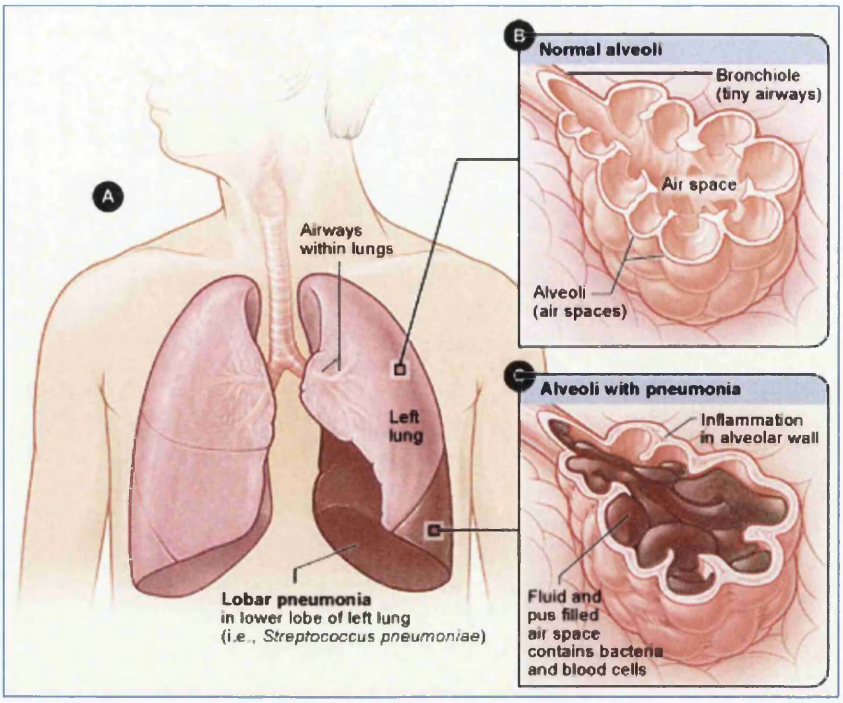


Figure 1.6.4 Left lung pneumonia (National Heart, Lung and Blood Institute, 2011)

High energy blunt chest trauma can result in injury to the underlying lung such as pulmonary contusions or bruising as the associated forces can be transmitted to the lung parenchyma or tissue.(Wanek and Mayberry 2004, Hoff et al 1994) The pulmonary contusion is characterised by capillary disruption resulting in intra-alveolar haemorrhage, oedema and fluid obstruction of the peripheral airways with leukocyte infiltration.(Wanek and Mayberry 2004, Clark et al 1988) Subsequently, the haemorrhagic exudate affects the lung alveoli by inactivating the surfactant, leading to atelectasis or collapse of associated lung segments. (Vlessis and Trunkey 1997) This can lead to hypoxaemia or decreased oxygen levels in arterial blood, which is the most commonly reported consequence of lung contusion. (Wanek and Mayberry 2004, Klein et al 2002, Hoff et al 1994) As a result of extensive parenchymal injury, pulmonary shunting and dead space ventilation can develop. (Mizushima et al 2000) More simply, bleeding and inflammation from the bruising to the chest wall and lung leads to decreased oxygen uptake by the lungs and subsequent reduced delivery of oxygen to the arterial blood. Patients with a pulmonary contusion who present with significant hypoxia (ie <8.6 kPa) should be considered for early intubation and mechanical ventilation, thus requiring Intensive

Care management. (Bastos et al 2008, Wanek and Mayberry 2004, Mizushima et al 2000)

A common injury seen following blunt chest trauma is a pneumothorax which occurs when the integrity of the chest wall is compromised allowing air to enter. (American College of Surgeons 2008) A pneumothorax is defined as an accumulation of air in the pleural cavity that leads to partial or complete collapse of the lung. (Springhouse 2003) The visceral pleura is disrupted which allows communication with the alveolar sacs or bronchi, air therefore escapes from the tracheobronchial tree into the pleural space. (Springhouse 2003, Vlessis and Trunkey 1997) This can be caused by either a penetrating wound, or by a rib fracture which punctures the underlying lung tissue. (Vlessis and Trunkey 1997) When an opening is created between the outside environment and the pleural space, intrathoracic and environmental pressures have a tendency to attempt to equalize, thus interfering with the normal physiology of respiration. (Moore and Dalley 2006) The thorax is normally completely filled by the lung which is held to the inner chest wall by the surface tension between the two pleural membranes. Air in the pleural space will collapse the underlying lung tissue resulting in an alteration in ventilation / perfusion, that is, the blood is perfusing a non-ventilated area of lung. (Springhouse 2003) Figure 1.6.5 indicates a pneumothorax in which the right lung can be seen to have retracted from the chest wall.

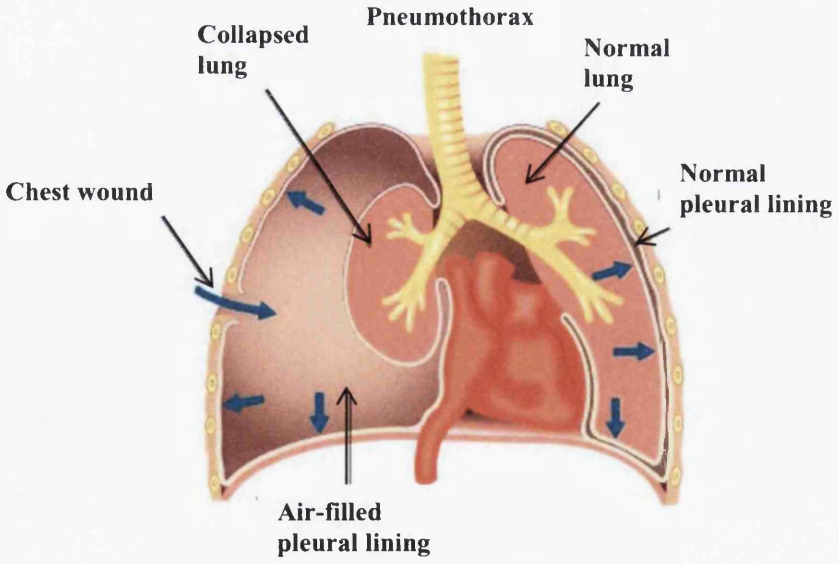


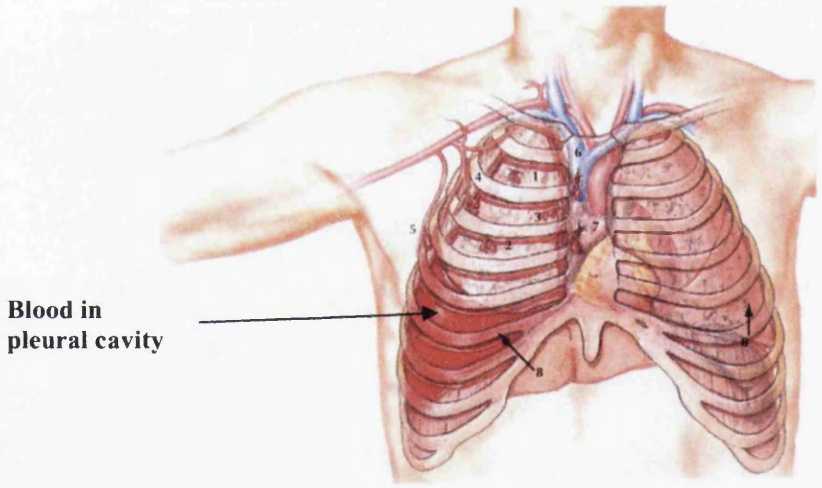
Figure 1.6.5 Pneumothorax. (Biasini, 2011)

Flagel et al (2005) reported that the incidence of pneumothorax increased with increasing number of fractured ribs ($p<0.01$). A small pneumothorax can be treated conservatively if it is not interfering with respiration, where the affected lung is left to re-expand naturally. However, a more significant pneumothorax will require an intercostal chest drain or chest tube which is used to normalise pressures within the thorax thus allowing normal respiration to resume. (Springhouse 2003, Vlessis and Trunkey 1997) Patients with large a pneumothorax may require mechanical ventilation as part of their management. (Flagel et al 2005)

In a study investigating the use of whole body computed tomography (CT) scanning in multi-trauma patients, Sampson et al (2006) reported that of the 96 CT detected pneumothoraces, 36 had not been detected on initial supine chest radiography in the ED. Similarly, a number of studies have concluded that the use of an ultrasound scan for the detection of a traumatic pneumothorax is more sensitive than the supine chest radiograph in the ED. (Wilkerson and Stone 2010, Blaivas et al 2005) This highlights the potential difficulty of managing the simple blunt chest trauma patient in the ED.

A potentially life-threatening type of pneumothorax commonly seen following severe blunt chest trauma is a tension pneumothorax. (Springhouse 2003) In a tension pneumothorax, there is damage to the visceral pleura which causes air to travel from the tracheobronchial tree on each inspiration into the pleural space. This air accumulates intra-pleurally unable to escape back to the tracheobronchial tree on expiration, usually as a consequence of a tissue flap valve, or one-way valve created by the injured pulmonary parenchyma or pleura.(Moore and Dalley 2006, Springhouse 2003) As a result, the pressure becomes higher in the pleural space than in the adjacent lung with each breath, thus pushing against the recoiled lung causing atelectasis and compression of the mediastinum, displacing the heart and great vessels. (American College of Surgeons 2008, Springhouse 2003) If untreated, the compression on the mediastinum by the tension pneumothorax will eventually decrease venous return to the heart, and ultimately the heart and unaffected lung will be compressed with fatal consequences. (Springhouse 2003) A tension pneumothorax is most common in those patients managed with positive pressure ventilation.

A haemothorax is a collection of blood in the pleural space caused by an injury to the chest wall with a laceration of the parietal pleura, or an injury to the lung parenchyma or blood vessels with a concomitant tear of the visceral pleura. (American College of Surgeons 2008, Springhouse 2003) It can be fatal for two reasons. The pleural space can potentially hold between three and four litres of blood. (Moore and Dalley 2006) Blood in the pleural space can result in compression of the underlying lung tissue which can cause collapse and prevent gas exchange in the lungs and cause hypoxaemia. (Vlessis and Trunkey 1997) The haemothorax can also cause death due to blood loss without any blood ever exiting the body. (Vlessis and Trunkey 1997) The treatment for a haemothorax is an intercostal chest drain which allows the blood to drain from the pleura, thus allowing underlying lung tissue to re-expand and reverse hypoxaemia. (American College of Surgeons 2008, Simon et al 1998) Surgery may be required to address the haemorrhage through repair of the bleeding blood vessel. (American College of Surgeons 2008, Vlessis and Trunkey 1997) Figure 1.6.6 illustrates a haemothorax in the right lung.



NB: Accumulation of blood in the pleural cavity transforms this potential space into a real space capable of accommodating a large volume.

Figure 1.6.6 Haemothorax. (Hansen and Lambert, 2005, p328)

A flail chest is relatively rare, but is the most serious of the blunt chest injuries. (Wanek and Mayberry 2004) Reported mortality for flail chest ranges from 10%-20% while morbidity is markedly higher due to often protracted and complicated hospital stays. (Bastos et al 2008, Clark et al 1988) In adults, the likelihood of death

in patients with flail chest increases by 132% per each decade increase in age. (Albaugh et al 2000) A flail chest occurs when a segment of the thoracic cage is separated from the rest of the chest wall and usually occurs when there are at least two fractures per rib, in two or more adjacent ribs. (American College of Surgeons 2008) Large flail segments will involve a much greater proportion of the chest wall and may extend bilaterally or involve the sternum. Pulmonary contusion is the associated injury to the underlying lung tissue. (Bastos et al 2008, Wanek and Mayberry 2004)

The diagnosis of the flail segment is often established through observation of paradoxical movement of the affected segment in the spontaneously breathing patient. Wanek and Mayberry 2004) On inspiration, the flail segment is sucked inwards by the negative intra-thoracic pressure, moving paradoxically to the rest of the thorax. On exhalation, the positive pressure forces the segment outwards. (Moore and Dalley 2006, Wanek and Mayberry 2004) In the non-ventilated patient, the flail segment will lead to a dramatic reduction in tidal volumes and effective coughing, thus placing the patient at risk of atelectasis and pneumonia. (Wanek and Mayberry 2004) Figure 1.6.7 illustrates a flail chest.

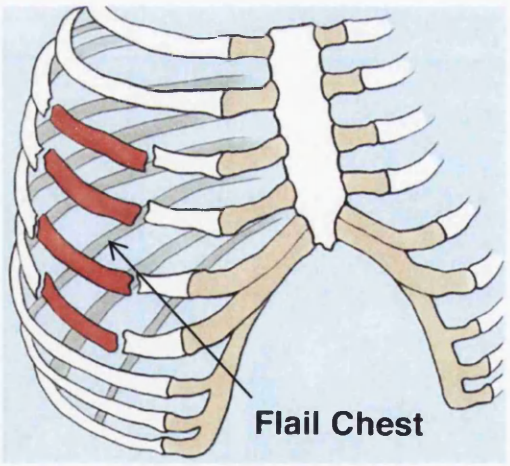


Figure 1.6.7 Flail chest (Mandaria et al 2003, p89)

As a result of the extensive number of bony fractures, the pathophysiological progressions following fracture described earlier are marked. (Vlessis and Trunkey 1997, Clark et al 1988) Total resultant bleeding from the damaged periosteum at all the fracture sites in a flail chest will inevitably be extensive. (Vlessis and Trunkey

1997) Similarly, the alterations seen in respiratory function secondary to fracture pain will be more exaggerated due to the increased number of fracture sites. The presence of a flail chest segment results in severe disruption of normal chest movement and if the injury (normally pulmonary contusion) to the underlying lung is significant, serious hypoxia may result. (Bastos et al 2008, Borman et al 2006, Clark et al 1988) Although chest wall instability leads to paradoxical movement of the chest wall during respiration, this mechanism is not alone in causing hypoxia. (Wanek and Mayberry 2004) Another major contributory factor to a patient's hypoxia is their associated pain and restricted chest wall movement. (Nirula et al 2009) Flail segments are commonly seen in severe chest wall injuries and patients often also present with a pneumothorax or haemothorax. In these cases the disruption of normal mechanics of respiration may be large enough to require mechanical ventilation. (Bastos et al 2008, Borman et al 2006)

1.7 The Elderly

There are a number of patient groups who are considered at risk from morbidity, mortality and increased hospital length of stay following blunt chest trauma and these patients are more likely to require admission to hospital from the ED for closer monitoring and more aggressive intervention in order to prevent the development of the pathologies previously described. (Stawicki et al 2004, Shorr et al 1989) Identification of the high risk blunt chest trauma patient however is a difficult process due to the complex nature of the physiological response to trauma, especially in the elderly population. (Bergeron et al 2003, Barnea et al 2002) The importance of trauma in the management of the elderly patient cannot be over-emphasised. The elderly have been reported to suffer mortality as a result of trauma at a rate three times higher than younger patients and this has been attributed to the complex changes in physiology associated with ageing and medical co-morbidity. (Bulger et al 2000, Damian et al 1996) Management of trauma in the elderly population therefore has been described as an epidemic deserving of deliberative study, with the results of such studies potentially influencing morbidity, mortality and financial expenditure. (Young and Ahmad 1999) The elderly population is rapidly expanding which consequently increases the demand for improvement in trauma care, especially when considering the current climate of government targets and cost reduction within

the NHS. (Taylor et al 2002) The National Service Framework for Older People (2001) stated that there should be early access to the care and advice of a specialist team for each older person admitted to a general acute hospital and that this is particularly important for the emergency admission. (Department of Health 2001)

On admission to the ED, the first stage of assessment of patients of any age is to take a history from the patient which includes establishing the mechanism of injury. (American College of Surgeons 2008) The mechanism of injury will provide valuable information regarding the magnitude and direction of external forces applied to the patient's chest wall and possible concurrent injuries. Diagnosis of the trauma sustained is then considered through the history taken and clinical findings. (American College of Surgeons 2008) Chest radiographs are routinely obtained in the ED after chest trauma however the indications for such radiographs are not well defined. (Davis and Affatato 2006, Banisdhar et al 2002) The chest radiograph will potentially provide information regarding the presence of rib fractures, underlying damage to the lung such as a contusion or a laceration, pneumothorax or haemothorax. (Davis and Affatato 2006) Physical examination of the chest wall will identify any bruising or haematoma, deformity, crepitus, tenderness, unequal breath sounds. (Bokhari et al 2002) This assessment will be the same for the elderly patient however the subsequent clinical reasoning may be very different.

A sound knowledge of anatomy and physiology will assist the Emergency Physician in deciding on appropriate management for the patient. (American College of Surgeons 2008) In the elderly patient however, the anatomy and physiology may be altered as a result of the normal ageing process and their potential presenting signs and symptoms and consequent response to injury may be altered. (Bulger et al 2000, Martin and Teberian 1990) The hormonal and metabolic responses to injury in the elderly patient are reported to differ to those of the younger adult counterpart. (Haljamae 1990) The elderly patient has a marked decrease in the proportion of skeletal muscle to viscera compared with the younger patient and furthermore, the composition of the ageing muscle alters.(Haljamae 1990) The elderly patient will differ in terms of their normal levels, as well as their post injury levels, of blood and tissue metabolites. The cells of the elderly patient will have decreased enzyme concentrations and lower activity levels compared to the younger patient, thus

explaining the age-dependent loss in cellular reserve capacity and the consequential increased vulnerability of the elderly to blunt chest trauma. (Haljamae 1990) This vulnerability in the elderly patient is exacerbated by the potential presence of pre-existing morbidity and poor nutritional status. (Bulger et al 2000, Haljamae 1990)

In the elderly blunt chest trauma patient, it takes significantly less force to fracture ribs than in younger patients. (Bulger et al 2000, Inci et al 1998) The elderly patient may potentially have extensive chest wall injury, for example a large flail segment, but the underlying lung injury may not be as severe as the chest wall injury should suggest. (Clark et al 1988) The elderly population is potentially more vulnerable to chest injury and increased mortality as a result of decreased muscle mass and loss of bone density due to the normal ageing process. (Albaugh et al 2000, Damian et al 1996) Elderly patients with osteoporotic bones and increased chest wall rigidity are more vulnerable to both rib and sternal fractures. (Sharma et al 2008) Damage to the underlying lung is further exacerbated by limited respiratory reserve in the elderly patient. (Sharma et al 2008, Shorr et al 1989) The elderly patient's pathophysiological changes following blunt chest trauma are exaggerated as a result of potential pre-existing disease, decreased cardiopulmonary reserve, impaired metabolic and immunologic responses and often poor nutritional status. (Haljamae 1990) Consequently, phases of inflammation and fracture or soft tissue healing can be protracted in the elderly patient. (Hughes 2004, Damian et al 1996)

Age alone does not account for all the differences between elderly and young patients. (Sharma et al 2008) The pathological course of blunt chest trauma will be influenced by the patient's pre-morbid state. (Alexander et al 2000) Some younger patients have severe physiologic compromise secondary to pre-existing disease and tolerate blunt chest trauma less effectively than a healthy elderly patient. (Sirmali et al 2003) The elderly patient population however suffer from increased number of pre-morbid conditions as a result of the normal ageing process. (Perdue et al 1998, Shorr et al 1989) A number of studies have been undertaken investigating the effect of the patient's pre-morbid state in recovery from trauma, with particular emphasis on cardiopulmonary disease. (Stawicki et al 2004, Alexander et al 2000, Damian et al 1996) In the patient with reduced lung function secondary to pre-existing cardiopulmonary disease, the effects of the blunt chest trauma will further exacerbate

the patient's difficulties with respiration. (Alexander et al 2000) For example, it could be suggested that in a healthy patient following blunt chest trauma, the consequences of the collapse of a segment of lung are minimal, as the patient will use the rest of the healthy lung to compensate, thus reducing ventilation-perfusion mismatch. In the patient with pre-existing lung disease, this compensation may be less effective as the remaining uninjured lung may already be damaged through disease and unable to carry out its normal functions of respiration. This lack of compensation therefore potentially places this patient at increased risk of increased morbidity, mortality and length of hospital stay following blunt chest trauma. (Alexander et al 2000, Damian et al 1996, Morris et al 1990)

Research has further highlighted that elderly patients with blunt chest trauma often suffer later complications than younger patients. (Perdue et al 1998, Simon et al 1998, Shorr et al 1989) A number of researchers have stated that elderly patients should be reviewed 48-72 hours post blunt chest trauma as this is when pulmonary complications frequently appear. (Liman et al 2003, Alexander et al 2000, Shorr et al 1989) It could be concluded therefore that knowledge of the different responses of the elderly patient to blunt chest trauma is imperative if the Emergency Physician is to make appropriate decisions regarding management of this patient group. Researchers suggest that the elderly blunt chest trauma patient with a history of cardiopulmonary disease should be directly admitted to the Intensive Care Unit (ICU) from the ED for close monitoring and aggressive management. (Alexander et al 2000, Shorr et al 1989) The elderly patient often presents with complex needs which exceed the clinical cause of attendance which results in ED staff regularly underestimating the impact of injury on the patient's capacity to cope at home. (Bentley and Meyer 2004)

1.8 Treatment options: Historical Perspective

Chest trauma is not a new problem. Hippocrates' writings in the 5th century contain a case series of trauma reports, including thoracic injuries. He described haemoptysis as a result of fractured ribs and observed an association between pleurisy and empyema with trauma to the chest wall. (Wagner and Slivko 1989, Garrison 1966) Management of blunt chest trauma by stabilising the chest wall with linen was common for centuries (Karmakar and Ho 2003) with reports as early as the Common

Era describing the Roman surgeon Soranus (Common Era 78-117) reporting resection of depressed ribs for the relief of pleuritic pain. (Hurt 1996) The twentieth century witnessed a dramatic evolution in the management of blunt chest trauma, especially in the years since World War II. (Hurt 1996) Prior to 1950, the main belief guiding management options was that morbidity and mortality following blunt chest trauma was due to chest wall instability. (Simon et al 2005, Karmakar and Ho 2003) External stabilisation of the chest wall became the primary management choice for blunt chest trauma, using various mechanical devices including sandbags and traction systems initially, later followed by pins, wires and screws. (Simon et al 2005, Karmakar and Ho 2003)

Following World War II, the concept of internal pneumatic stabilisation was introduced by Avery in 1956, in which positive-pressure mechanical ventilation became the standard treatment of choice for blunt chest trauma. (Karmakar and Ho 2003) Consequently, mortality rates following blunt chest trauma were reported to fall however, through the widespread use of mechanical ventilation, so the incidence of the complications associated with use of mechanical ventilation increased. (Karmakar and Ho 2003, Simon et al 2005) Ventilator-associated pneumonia is a common complication of mechanical ventilation causing high rates of morbidity even today. (Terragni et al 2010) Trinkle et al (1975) completed a study which challenged the common and routine use of mechanical ventilation in the management of blunt chest trauma patients and demonstrated that other effective treatment options included optimal pain control, chest physiotherapy and non-invasive positive-pressure ventilation. Trinkle et al (1975) introduced the concept that instead of focussing treatment on the chest wall defect, treatment should be concentrated on the damage to the underlying lung only.

In the same year, Dittman (1975) completed a study which demonstrated that the use of continuous epidural pain relief negated the need for mechanical ventilation in patients with multiple rib fractures. Since the work of Dittman and Trinkle and his colleagues in 1975, a continuing improved understanding of the pathophysiological effects of blunt chest trauma has led to an increase in the use of conservative management with non-ventilatory strategies of treatment. (Simon et al 2005, Karmakar and Ho 2003) Thus the management of blunt chest trauma today is

focussed primarily on treatment of the underlying lung injury and an optimisation of mechanics through chest physiotherapy and appropriate analgesia. (Simon et al 2005, Karmakar and Ho 2003)

1.9 Management of the Blunt Chest Trauma Patient

Assessment of the blunt chest trauma patient presenting to the ED is often carried out initially by the triage nurse followed by the Emergency Physician. For trauma patients, the Emergency Physician will often follow the assessment principles outlined in the Advanced Trauma Life Support (ATLS) guidelines. (American College of Surgeons 2008) Blunt chest wall trauma can be life-threatening if not diagnosed and treated promptly and appropriately. These life-threatening injuries may include trauma to the head, abdomen, spine or limbs, and furthermore, associated injuries to the thorax such as great vessel rupture, pneumothorax, tracheobronchial or mediastinal injuries. Once life-threatening associated injuries are ruled out then the physician can focus on the blunt chest trauma and decide on appropriate intervention. Research has highlighted that less than 10% of blunt chest trauma requires surgical intervention. (Simon et al 2005)

The ATLS guidelines state that correct triage is essential to the effective running of a trauma centre. They further state that under-triage can produce inadequate initial care and may result in preventable morbidity and mortality. However the perfect triage model does not exist for the trauma patient. (American College of Surgeons 2008) Attempting to summarize the severity of injury in a patient with multiple trauma with a single number is difficult at best. Therefore multiple alternative scoring systems have been proposed, each with its own problems and limitations.

A widely used triage model that was initially developed by Champion et al (1981) is the Revised Trauma Score (RTS) which is a physiological scoring system using the Glasgow Coma Scale, systolic blood pressure and respiratory rate to predict potential mortality in trauma patients. (American College of Surgeons 2008) The RTS is a well-established predictor of mortality in trauma populations however there is a lack of definitive evidence supporting its use as a primary triage tool in the ED and as a predictor of outcomes other than mortality. Difficulty in collecting the components of the RTS is also reported and as a result, data reliability and validity is questionable. For example some trauma patients require immediate mechanical ventilation

therefore assessment of respiratory rate and verbal response for the GCS is not possible. The RTS has been updated by weighting each of the components in order to improve the prediction capacity however a limited number of studies reporting its use exist. In summary, further studies are required to clearly establish the usefulness of the RTS as a triage tool, to further evaluate the weighted version of the RTS, and to determine the ability of the RTS to predict other outcomes such functional status and quality of life. (Gabbe et al 2003)

The original Abbreviated Injury Severity Scale (AIS) was developed in 1969 and was a simple numerical method for grading and comparing injuries by severity. (Copes et al 1998) The AIS is a consensus-derived, anatomically based system of grading injuries on an ordinal scale ranging from 1 (minor injury) to 6 (lethal injury). It can be used for individual anatomical injuries such as chest trauma. The AIS has been continuously improved and updated since its original inception however this continual updating has been criticised. (Palmer and Franklyn 2011) The latest update in 2008 resulted in a significant decrease in the number of patients classified as major trauma and also many original codes are missing. As a result of this continual update, comparison between data coded using different AIS versions may not be possible. (Palmer and Franklyn 2011) The AIS does not reflect the combined effects of multiple injuries however it forms the foundation for the Injury Severity Score (ISS).

Baker et al introduced the ISS in 1974 as a means of summarizing multiple injuries in a single patient. (Baker et al 1974) The ISS is defined as the sum of squares of the highest AIS grade in the 3 most severely injured body regions. Six body regions are defined, as follows: the thorax, abdomen and visceral pelvis, head and neck, face, bony pelvis and extremities, and external structures. One injury per body region only is allowed. The ISS ranges from 1-75, and an ISS of 75 is assigned to anyone with an AIS of 6. (Baker et al 1974) A number of limitations of the ISS have been reported. (Esme et al 2007, Chawda et al 2004) The main limitations are its inability to account for multiple injuries to the same body region and it also limits the total number of contributing injuries to three. As a result, the ISS often omits significant injuries altogether. Another reported limitation is that the ISS weights injuries to each body region equally, disregarding the importance of head injuries in mortality.

(Esme et al 2007) Furthermore the ISS does not take into account physiological parameters, which is reported to impair its ability to predict short-term mortality. (Chawda et al 2004)

Todd et al (2006) developed a multidisciplinary clinical pathway for high-risk trauma patients with four or more rib fractures. They concluded that implementation of a rib fracture multidisciplinary clinical pathway decreased mechanical ventilator-dependent days, lengths of stay, infectious morbidity and mortality. This study however, only included high risk trauma patients over the age of 45 years with 4 or more rib fractures. The patients included had a reported AIS of 4 and an injury severity score of 21, thus reflecting the patients as severely injured trauma patients, although severe head injuries were excluded. (Todd et al 2006) The study group patients were also significantly younger than the control group ($p=0.02$) which may have acted as confounding.

In a study by Easter (2001), a protocol based on a synthesis of existing literature for the management of multi-trauma patients with rib fractures was proposed. The protocol was designed to aid decisions regarding rapid mobilisation, respiratory support and pain management, in order to test the hypothesis that these interventions will decrease the length of patient's stay in intensive care units. (Easter 2001) To date however, the scoring system has not been either tested or validated for any population of multi-trauma patients with rib fractures and the suggested hypothesis not investigated. In a similar recent retrospective study by Pressley et al (2012) a simple scoring system was designed in which chest wall injury patients were assigned a score according to a number of risk factors. The assigned score was used to stratify the patient according to risk of need for mechanical ventilation and prolonged course of care. (Pressley et al 2012) This scoring system has not been prospectively validated and also included patients with traumatic brain injuries. Wutzler et al (2012) developed and validated the Lung Organ Failure Score which was designed for use in patients with multiple injuries including chest trauma. This model is not useful however for patients without multiple trauma. Ahmad et al (2010) investigated whether an ideal scoring system exists for the assessment of severity of chest trauma. They concluded that current medical literature has very few scoring systems that are specific only for chest injuries and that further scoring systems

designed for evaluation of blunt chest trauma are desirable. It could be suggested that as a result of no universally accepted guidelines for the management of simple blunt chest trauma, variation exists in the assessment of the blunt chest trauma patient between physicians. The general assessment principles however should be similar. (Gabram et al 1995)

Assessment of the patient will focus on obtaining a detailed examination of the patient's history such as mechanism and force of injury, past medical conditions, smoking history and age. A physical examination is normally performed in which the physician may palpate the chest wall to assess tender areas and obvious deformation, auscultation with a stethoscope of the patients breathing and flow of air in the lungs, oxygen levels in the patient's blood and the patient's ability to take a deep breath and cough effectively. The use of the chest radiograph is discussed extensively in the literature for this patient group and many physicians will use this as part of their examination in order to rule out any more serious pathologies following blunt chest trauma, including pneumothorax, haemothorax or pulmonary contusions.(Davis and Affatato 2006, Banisdhar et al 2002) A clinical decision will be made by the physician regarding the level of the patient's risk for developing any complications as a result of the blunt chest trauma. This will guide the physician in deciding the level of intervention required in terms of possible discharge home, admission location, surgical intervention or referral source. (Barnea et al 2002)

The management or treatment of the blunt chest trauma patient is focussed on the prevention of the complications previously described, such as alteration in the mechanics of respiration and subsequent hypoxaemia and collapse of lung segments. A number of blunt chest trauma patients therefore can be managed at home with advice and pain relief. The physician must be sure however that late complications are unlikely to occur in these patients. (Barnea et al 2002) Patients at risk of complications will require admission to hospital for pain relief, physiotherapy to assist pulmonary function or even mechanical ventilation and critical care management. (Klein et al 2002, Rashid et al 2000) A key factor in the management and care of the blunt chest trauma patient is concluded to be adequate pain control, thus facilitating early aggressive respiratory care to consequently prevent the development of pulmonary complications. (Bulger et al 2000)

A certain proportion of patients with blunt chest wall trauma will require ventilatory support. Trauma to the thoracic cage can lead to substantial impairment of spontaneous breathing mechanics and this is further amplified by pain. In addition, direct trauma to the underlying lung, through increased vascular permeability of the lung capillaries and extravasation of protein-rich fluid, can also lead to a progressive respiratory failure. (Richter and Ragaller 2011) Research highlights that the presence of pulmonary contusion, with or without flail chest, is usually associated with the need for mechanical ventilation however an optimal ventilator strategy that is applicable to all blunt chest wall trauma patients does not exist. (Richter and Ragaller 2011) The overall management strategy of all modes of ventilation is to support the respiratory system while the chest wall heals and thus prevent complications. (Easter 2001)

If the patient is suitable for early mobilisation, then they should be encouraged to sit up and walk short distances in order to maintain adequate ventilation and perfusion in their lungs. (Easter 2001) Non-invasive ventilation (NIV) should be considered the first choice of treatment in the compliant blunt chest wall trauma patient with poor oxygenation and only in the failure of NIV should intubation and invasive mechanical ventilation be considered. (Richter and Ragaller 2011) The use of NIV has been shown to reduce the need for invasive mechanical ventilation in hypoxaemic blunt chest wall trauma patients. (Hernandez et al 2010) A number of studies have also reported that the use of NIV leads to lower mortality and pulmonary complications rates in blunt chest wall trauma patients, when compared to conventional invasive ventilation. (Gunduz et al 2005, Tanaka et al 2001)

Although it is generally agreed that mechanical ventilation increases the risk of complications such as ventilator associated pneumonia and ventilator induced lung injury, current consensus is that selective use of invasive mechanical ventilation is advisable for blunt chest wall trauma patients with poor gas exchange and respiratory effort. (Simon 2005, Easter 2001) Shackford et al (1976) reported that mechanical ventilation used primarily for the correction of instability of the chest wall resulted in increased mortality rates. Early studies focussed on the use of intermittent mandatory ventilation compared with continuous mandatory ventilation (Pinella 1982) however more recently, the emphasis is on the use of continuous positive airway pressure

ventilation (both invasive and non-invasive) in blunt chest wall trauma patients. (Tanaka et al 2001)

There are a number of newer modes of ventilation although they are still in the experimental stage and not all hospitals currently have the equipment to support their use. (Easter 2001) The use of extra-corporeal membrane oxygenation (ECMO) in traumatic lung injury appears to compare favourably with conventional modes of ventilation in a recent small study by Cordell-Smith et al (2006). Further research is needed investigating the use of ECMO in blunt chest wall trauma. Another mode of ventilation that should be considered in the management of the severe blunt chest wall trauma patient is high-frequency jet ventilation however this also needs further investigation in good quality prospective studies. Single lung ventilation through the use of double lumen endotracheal tubes are also under investigation for use in patients with severe unilateral blunt chest wall trauma. (Richter and Ragaller 2011)

The use of prophylactic antibiotics in patients with blunt chest wall trauma remains controversial. Current research focusses primarily on the use of prophylactic antibiotics in chest trauma patients who require a thoracostomy for a haemopneumothorax. Luchette et al (2000) concluded in their practice guidelines that there were not sufficient good quality studies to support the use of prophylactic antibiotics in chest trauma patients. In a more recent meta-analysis by Sanabria et al (2006) however, the use of prophylactic antibiotics were recommended in patients with isolated blunt chest trauma requiring thoracostomy as a protective measure against the development of post-traumatic empyema and pneumonia. Eren et al (2008) reported that the use of prophylactic antibiotics should be considered in patients with certain risk factors, including prolonged duration of thoracostomy and intensive care length of stay, lung contusion and retained haemothorax.

No consensus exists regarding the use of rib belts in the treatment of fractured ribs. (Kerr-Valentic et al 2003) The rib belt is applied with the top edge of the belt level with the xiphoid process and then tightened to provide optimal pain relief for the patient. In a pilot study investigating the use of rib belts in acute rib fractures, Lazcano et al (1989) concluded that the use of a rib belt contributed little to the improvement of pain severity compared to oral analgesics alone but more importantly, a number of complications occurred in the patients using rib belts.

Although the authors felt the complications were sufficiently clinically significant to warrant advice of caution in the use of rib belts, the complications were not statistically significant and further studies were recommended. In contrast, Quick (1990) reported in his pilot study that a rib belt was used to provide additional pain relief for the patient with fractured ribs, with no compromise to the patient's respiratory function. In an interesting letter to the editor of the Lancet in 1980, Norcross (p 590) anecdotally described the benefits of rib belts and concluded by commenting "...we doctors were responsible for stopping the most useful method of treatment of painful rib fractures". Further good quality studies are needed investigating the use of rib belts as an adjunct to conventional analgesia in blunt chest trauma patients.

Klein et al (2002) highlighted that one of the major controversies regarding chest trauma is the ability to identify the patient who presents with less severe symptoms following blunt chest trauma, but will develop complications such as hypoxaemia, atelectasis or pneumonia within the following 24 to 72 hours. Researchers concur that clinical decompensation or complications can occur up to 7 days after the initial chest injury resulting in potential difficulties for the Emergency Physician in deciding whether or not to admit a patient for further intervention. (Alexander et al 2000, Simon et al 1998, Shorr et al 1989) A key aim identified in the Welsh Assembly Government document Delivering Emergency Care Services 2008 was to empower staff to be confident to make appropriate decisions and to move away from the "admit to decide" to "decide to admit" approach. (Welsh Assembly Government 2008) It has been suggested that identification of risk factors predictive of increased morbidity and mortality in the blunt chest trauma patient would facilitate effective triage in the ED and could potentially regulate the over and under triage frequently reported within trauma systems. (Liman et al 2003, Sanidas et al 2000)

1.10 The role of the ED in the management of the blunt chest wall trauma patient

In a report in 2007, consultants and middle grade doctors from more than one third of ED in hospitals in England highlighted that they were not reaching the government target of 98% of all patients being seen and managed appropriately within 4 hours. (Mayor 2007) ED revisit rates are highest around one week following discharge and

rapidly decrease thereafter. (Moore et al 2007) Research has suggested that approximately one third of revisits are avoidable and common reasons for revisits are reported to be poor patient education regarding the condition and prognosis in the initial consultation and failure to provide appropriate analgesia. (Wilkins and Beckett 1992) Improved patient education may minimise misuse of the ED service resulting in a better standard of care for those patients who need it. Early identification and appropriate referrals for those patients who are at risk of unplanned revisits to the ED could potentially assist in reducing overcrowding and could therefore assist in the achievement of government targets.

One of the primary decisions made by the Emergency Physician regarding the blunt chest wall trauma patient is the appropriate discharge location following ED assessment. Barnea et al 2002 reported that only 10% of patients with isolated blunt chest wall trauma require admission to hospital and can be safely discharged home from the ED. The difficulty in the decision making arises due to the potential for delayed on-set of complications, a common entity in this patient group. (Blecher et al 2008, Simon et al 1998) If the patient is deemed appropriate for inpatient management, deciding what level of care is most appropriate can be complex and a sound knowledge of the risk factors for delayed complications is important. In a study by Blecher et al (2008), a large subgroup of patients admitted to the ward following chest injury subsequently deteriorated and required ICU management.

Blecher et al (2008) investigated the risk factors for failed ward management and reported that risk factors included the need for intercostal drain insertion, multiple fractures, flail chest and increasing injury severity with associated injuries. General consensus exists that the patients who should be considered for ICU management are the elderly patients with three or more rib fractures. (Stawicki et al 2004) Similar consensus exists, that patients with one or two rib fractures may potentially need admission to a ward for observation for 24 hours. (Bergeron et al 2003)

Easter (2001) concluded that if rapid mobilisation, respiratory support and optimal pain management were implemented simultaneously, then Emergency Physicians would be able to define the appropriate level of care needed by multiple rib fracture patients. They therefore advocate the use of a standardised protocol guiding the management of the multiple rib fracture patient, encompassing preventive care,

anticipatory management and emergent crisis care. (Easter 2001) Although a number of hospitals in the UK use locally developed protocols and guidelines (Battle et al 2012), a comprehensive protocol that has been fully validated is yet to be developed for the blunt chest wall trauma patient.

Furthermore, patients discharged home directly from the ED who go on to develop late complications such as morbidity, mortality or lengthy hospital stays can be potential sources of litigation as a result of medical errors and patient dissatisfaction. (Wang et al 2007) Therefore, appropriateness of management in the ED is imperative in the current climate of medico-legal liability and this is a major concern for both physician and the health-care provider.

1.11 The role of ICU in the management of the blunt chest trauma patient.

Research has highlighted that delayed admission to ICU can result in poorer outcomes such as morbidity, mortality, ICU length of stay and total hospital length of stay. (Higgins et al 2003, McQuillan et al 1998) The difficulty in the management of any trauma patient is the early identification of the need for ICU input. This is because patients should be excluded from ICU when either death is inevitable or where the patient will survive without ICU care. Admission to ICU should be restricted to patients likely to benefit as intensive care is often a limited and expensive resource. (Goldhill and Sumner 1998) There may be little that can be done to alter prognosis in ICU once the patient is admitted from the ward at a late stage, due to the fact that by the time the patient is admitted to ICU, the underlying pathology is severe and irreversible. (Goldhill and Sumner 1998) The patient admitted late to ICU also has reported increased mortality (McQuillan et al 1998) and significantly prolonged ICU and total hospital length of stays. (Buist et al 1999) In one study by Higgins et al (2003), it was suggested that because of the amount of money consumed by critical care per year, it was necessary to find additional factors that predict prolonged ICU length of stay in critically ill patients. This study concluded that although mechanical ventilation and presence of infection were found to affect length of stay, the length of ward stay prior to ICU admission was one factor that was more easily controlled and modified.

Early identification of the high risk blunt chest trauma patient could therefore result in improved patient outcome due to earlier admission to ICU, reduced prolonged ward stay prior to ICU admission and a consequent reduction in ICU length of stay. Prolonged hospitalisation has financial implications to the NHS and early recognition of the high risk blunt chest trauma patient through accurate triage is therefore imperative.

1.12 Radiological evaluation of blunt chest trauma.

Despite dubious sensitivity, chest radiographs are widely performed to investigate suspected rib fracture following blunt chest trauma. (Banisdhar et al 2002) Figure 1.12 illustrates a series of chest radiographs highlighting the on-set of pneumonia following blunt chest wall trauma.

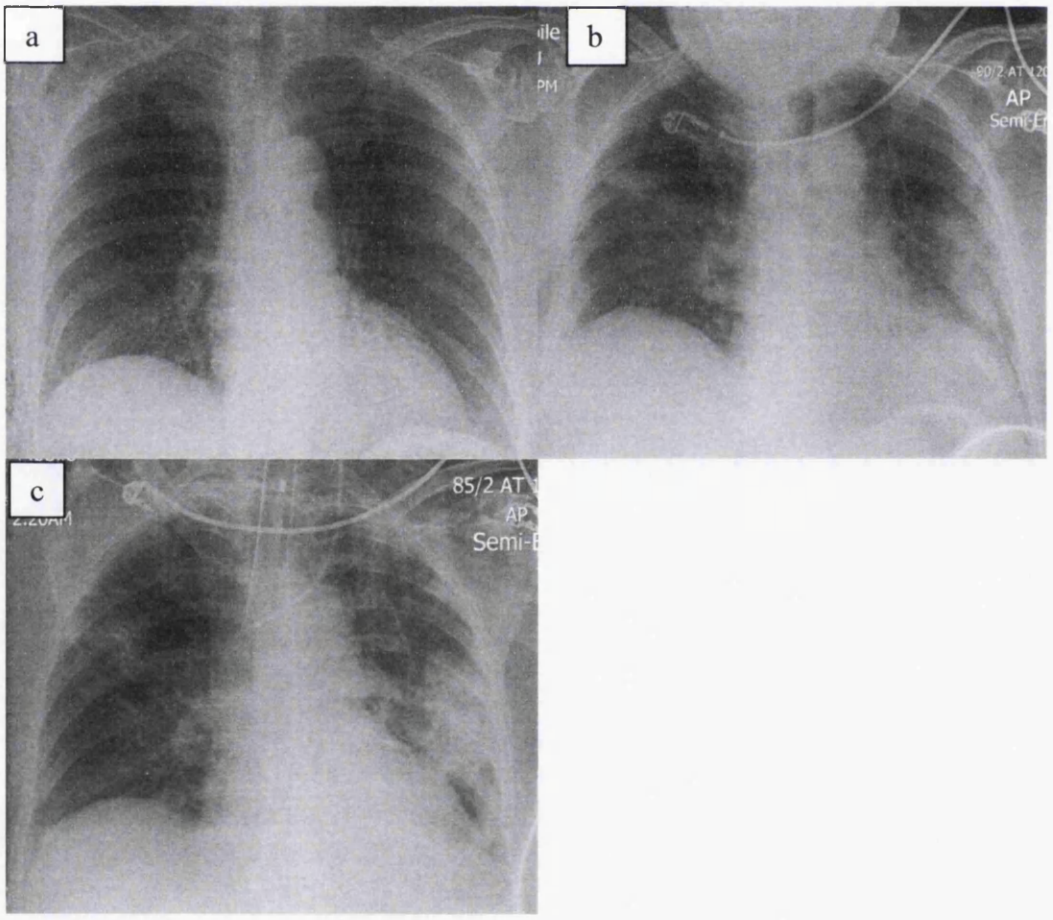


Figure 1.12.1 Series of chest radiographs highlighting the on-set of pneumonia and in a patient with blunt chest wall trauma. CXR a) Right side rib fractures with surgical emphysema on the initial day of presentation to the ED. CXR b) Early

shadowing indicative of pneumonia on the second day following presentation to the ED. CXR c) Bilateral pneumonia with patient now intubated and ventilated by the third day following presentation.

Table 1.12 summarises the strengths and weaknesses of each of the imaging techniques used in the assessment of the blunt chest wall trauma patient.

Imaging technique	Strengths	Weaknesses
Chest x-ray	Cost effective Time effective Good risk factor of morbidity and mortality	Lacks sensitivity in identifying rib fractures and PTX Identification of rib fractures rarely influences management
Computed tomography	High sensitivity for identifying rib fractures, PTX, contusion, major organ / vessel damage.	Expensive Time consuming Iatrogenic radiation exposure
Ultrasonography	Small / Portable Allows rapid examination Clinicians can perform High sensitivity for identifying rib fractures, pleural fluid and PTX	Lacks sensitivity for small collections in pleural space Inaccessible for subscapular injuries Difficulties with obese or patients with large breasts

Table 1.12 Strengths and weaknesses of the imaging techniques used in blunt chest wall trauma assessment

The chest radiograph has been reported to be the most effective method of identifying rib fractures however research has highlighted that between 33% and 50% of rib fractures are missed on the chest radiograph. (Davis and Affatato 2006, Mayberry and Trunkey 1997, Zeigler and Agarwal 1994) Furthermore, it has been established that although rib fractures can be commonly perceived as trivial, if they are left unrecognised and untreated, the resultant morbidity and mortality can be significant. (Banisdhar et al 2002, Zeigler and Agarwal 1994) Computed tomographic (CT) scanning is considered the more accurate imaging modality in severe blunt chest trauma and is reported to be significantly more accurate in the differentiation of chest wall from parenchymal or mediastinal injuries. (Collins 2000) The use of 3D reconstructions of CT scans is now more commonly used to inform decision making regarding surgical fixation of blunt chest wall trauma. (Bottlang et al 2013) Figures 1.12.2 and 1.12.3 illustrate three-dimensional CT reconstructions of blunt chest wall trauma.

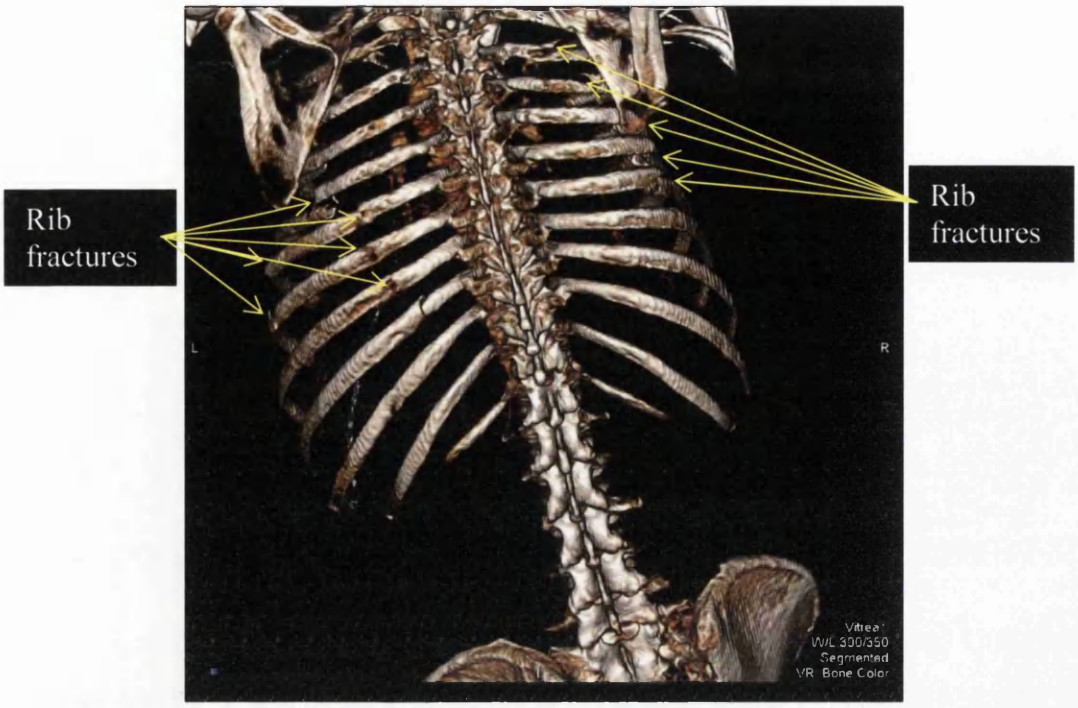


Figure 1.12.2: 3D CT reconstruction of blunt chest wall trauma (posterior).

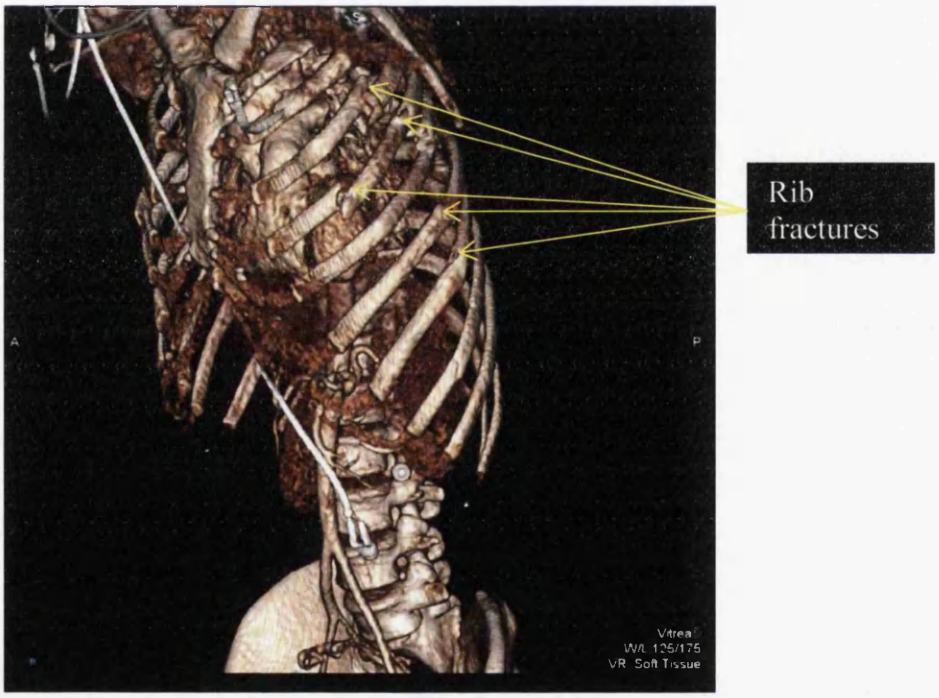


Figure 1.12.3: 3D CT reconstruction of blunt chest wall trauma (lateral).

For the less severely injured blunt chest wall trauma patient, with no immediately life-threatening injuries, the CT scan is considered by most ED physicians as unnecessary, especially when considering iatrogenic radiation exposure, time and

cost implications. (Brink et al 2010) Livingston et al (2008) highlighted that although truncal computed tomographic (CT) scanning has improved the diagnosis and delineation of rib fractures, a more accurate predictor of subsequent pulmonary morbidity and mortality is the screening chest radiograph. They reported that their logistic regression analysis identified only injury severity score and presence of a parenchymal injury on plain CXR as independent predictors of subsequent respiratory failure. In contrast based on previous literature, they also concluded that radiology reports are commonly lacking descriptive information regarding number and fracture location with reliance on these reports leading to subsequent erroneous conclusions. (Livingston et al 2008)

In the current financial climate in the NHS, one method of controlling spiralling medical costs could be the careful evaluation of relatively inexpensive, yet frequent examinations such as the chest radiograph. (Davis and Affatato 2006, Thompson et al 1986) It has been suggested that the results or interpretation of the chest radiograph does not influence the subsequent prescription of medication or the treatment plan instigated by the physician in the ED. (Davis and Affatato 2006) Treatment in this patient group is symptomatic, primarily aimed at the relief of pain and is rarely affected by specific knowledge of number and location of rib fractures. (Thompson et al 1986) Thompson et al (1986) stated that the decisions regarding discharge or admission location should be made on the basis of clinical factors such as age, history and mechanism of injury and stability of the patient, and not on the presence or absence of one or more rib fracture. Therefore, the usefulness of the chest radiograph for this patient group is questionable and a number of authors have suggested that they have no benefit. (Davis and Affatato 2006, Thompson et al 1986) Considerable cost savings may therefore be realised without the routine use of chest radiographs for the blunt chest trauma patient. (Davis and Affatato 2006, Thompson et al 1986)

Chest radiographs obtained solely to detect rib fractures therefore appear rarely warranted. A necessity still exists however to assess pleural or pulmonary complications of blunt chest trauma. A number of researchers have highlighted that the major complications of rib fractures such as pneumothorax, haemothorax, major vascular injuries, pulmonary contusions and flail chest may be life-threatening and

should be assessed with a chest radiograph and treated accordingly. (Livingston et al 2008, Thompson et al 1986) Therefore, it is evident that discrepancy exists in the literature regarding the value and accuracy of the chest radiograph. Researchers have agreed that unrecognised and untreated rib fractures result in increased morbidity and mortality, and therefore that a more specific and sensitive predictive screening model for the blunt chest trauma patient is required. (Livingston et al 2008, Alexander et al 2000)

1.13 Surgical fixation of blunt chest wall trauma

The use of surgical fixation for rib fractures has remained controversial for many years however there has been a recent resurgence in interest as its efficacy is realised. (Bille et al 2013) Simon et al (2005) highlighted that less than 10% of blunt chest trauma require surgical intervention. There are a number of potential indications for surgical repair of rib fractures including flail chest, chest wall deformity, symptomatic non-union and in some severe cases pain caused by moveable rib fractures that is not responding to conventional pain management. (Nirula et al 2009)

Rib fracture surgical repair is technically difficult, primarily due to the shape and structure of the human rib, in particular a thin cortex which tends to fracture obliquely. (Nirula et al 2009) Fixation must also be able to withstand 25,000 breathing cycles per day. (Lafferty et al 2011) Individual ribs do not tolerate stress well and also provide a poor surface for good cortical screw purchase, especially due to their tendency to fracture obliquely. (Lafferty et al 2011) The proximity of the intercostal nerve to the rib often results in iatrogenic damage due to intra-operative manipulation and implant placement and post-thoracotomy pain syndrome is commonly reported. (Laffertty et al 2011, Nirula et al 2009)

Common surgical techniques involve a thoracotomy followed by fixation of the damaged section of chest wall with a variety of stabilisation devices including wires, nails, struts and both metal and absorbable plates. (Nirula et al 2009). Fixation devices that are both rigid and non-rigid systems have been developed and both systems have a number of reported potential disadvantages including stress-shielding (plated bone is protected from normal stress and therefore fails to heal as strongly as non-plated bone), palpable implants and the need for further surgical intervention to

remove loosened or painful implants. (Lafferty et al 2011, Nirula et al 2009) The most commonly used fixation technique involves the use of a generic metal plate which is applied to the anterior surface of the rib and either wired or screwed into place. Contemporary chest wall reconstruction requires intra-operative contouring of generic devices to the complex surface geometry of the ribs. (Mohr et al 2007)

In 2007 using human cadaveric ribs, Mohr and his colleagues established a biometric foundation to generate specialised, anatomically contoured osteosynthesis devices for use in rib fracture fixation. This was the first study in which the characteristic differences in cortex thickness distribution within rib cross-sections over the rib length were described. (Mohr et al 2007) As a result of this study, recent technological advances in rib fracture fixation include the use of titanium devices which are pre-contoured plates designed for specific ribs, which negates the need for bending of the device. (Bille et al 2013) Figure 1.13 highlights the surgical procedure from the crucial preparatory work through to the actual rib stabilisation. (Bottlang et al 2013)

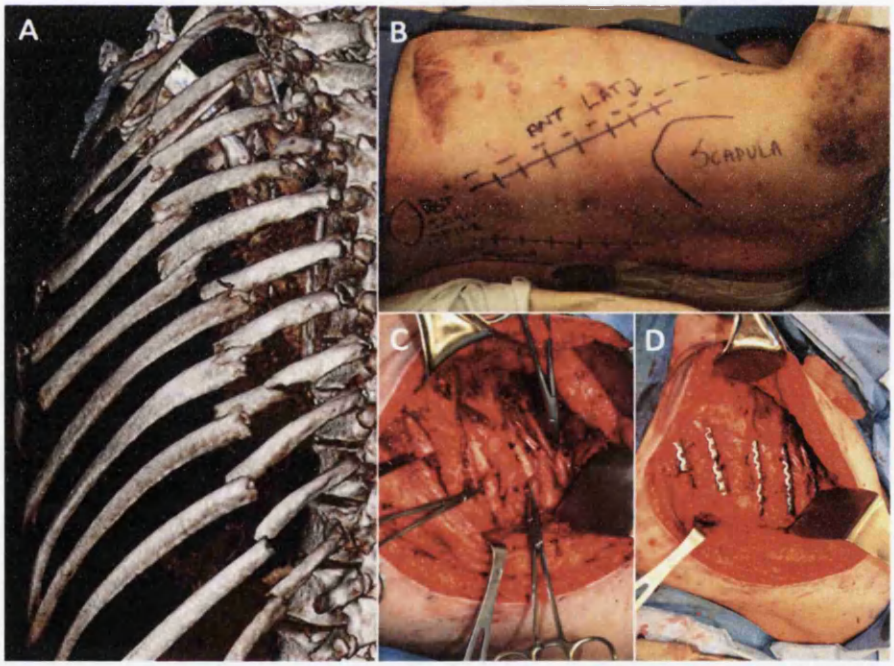


Figure 1.13: Stages of surgical rib fracture stabilisation. Reproduced with permission from Bottlang et al (2013). (A) CT reconstruction is crucial for fracture visualization. (B) Intra-operative planning of left thoracotomy overlying the flail segment with latissimus sparing exposure. (C) Exposure of rib fracture with preservation of periosteum. (D) Surgical stabilization with anatomic plates.

Table 1.13 outlines the fixation devices commonly used in rib fracture surgical repair and their reported potential advantages and disadvantages. (Lafferty et al 2011, Bemelman et al 2010, Nirula et al 2009)

Device	Potential advantages	Potential disadvantages
Generic metal plates	Standard technique used Most cost effective technique	Intra-operative contouring of plates Impingement of intercostal nerve Stress-shielding Screw-loosening
Pre-contoured metal plates	Thin design leading to less stress-shielding Decreased loosening and failure Allow physiologic movement during breathing No intra-operative contouring	Expensive Unproven superiority in research to date
Absorbable plates / polymers	Retain adequate rigidity until healing complete Reduced stress –shielding Reduced need for implant removal Faster healing times Addition of antibiotics to plates	Foreign body reactions Swelling and fluid accumulation Cyst formation Costly compared to standard implants
U-plate and locking screws	Facilitation of minimally invasive techniques Can be used in osteoporotic patients Durable No impingement of intercostal nerve	Reduced fixation length
Intermedullary fixation	Recent advances in titanium pre-contoured intramedullary struts	Risk of wire dislodgement Technically demanding Lack of rotational stability
Judet strut	Bendable plate using tongs to grasp rib without need for screw fixation Facilitation of minimally invasive technique	Impingement of intercostal nerve (although not yet reported)

NSAIDS: non-steroidal anti-inflammatory drugs, PTX: pneumothorax, CNS: central nervous system,

Table 1.13: Fixation devices and reported advantages and disadvantages.

Beneficial outcomes following surgical fixation have been reported in a randomised controlled trial (RCT) by Tanaka et al (2002) such as improved pain, quicker weaning from ventilation and improved lung volumes. In a similar study by Granetzny et al (2005), flail chest patients treated with surgical intervention had a significantly lower rate of pneumonia and significantly fewer ICU days, ventilator days and hospital days than flail chest patients managed conservatively. More recently, Marasco et al (2013) completed a prospective RCT of operative fixation in flail chest. They reported a reduction in ventilator days and ICU length of stay in patients with flail chest managed with surgical fixation. A meta-analysis by Slobogean et al (2013) reported that surgical fixation of flail chest may have

substantial critical care benefits however they conclude that further prospective studies are required before definitive conclusions can be achieved.

A number of retrospective studies which reviewed surgical outcomes in blunt chest wall trauma patients have reported various positive outcomes including fewer total ventilator days, (Nirula et al 2006) lower mortality (Ahmed and Mohyuddin 1995) and decreased narcotic use. (Balci et al 2004) Surgical repair of flail chest was shown to lead to a cost effective means for managing these patients, with the cost effectiveness of $15,259 for surgical repair compared to $16,810 for standard care. (Bhatnagar et al 2012). One prospective single-centred study reported positive outcomes for surgical fixation using titanium plates including decrease in pain and early return to work, (Khandelwal et al 2011) A number of recent studies have reported their experiences and outcomes of using a variety of surgical devices for rib fracture fixation including intramedullary nails, (Helzel at al 2009) hand fracture fixation plates, (Dunlop et al 2010) titanium bars and clips (Barajas et al 2010) and anatomic plates. (Bottlang et al 2013)

One interesting finding in a study by Voggenreiter et al (1998) reported that patients with pulmonary contusions did not benefit from surgical fixation and they therefore suggested that pulmonary contusion can be considered a relative contraindication to surgical fixation. A number of different complications following surgery have been described in the literature including wound infections, empyema, fixation failure or device migration, post-operative chest wall rigidity and pain necessitating removal of fixation devices. (Nirula et al 2009) In order to reduce this complication rate, surgeons advocating chest wall repairs will need to further refine their surgical techniques and adequately train colleagues. (Lafferty et al 2011)

The studies investigating outcomes following these various fixation devices are often of poor quality primarily due to small study samples, no control group and lack of appropriate randomisation and therefore it is not currently possible to accurately compare surgical techniques to modern selective management. (Simon et al 2005) In a survey of American Trauma Surgeons, it was concluded that barriers to surgical repair of rib and sternal fractures include a lack of research investigating optimal techniques and a lack of expertise. (Mayberry et al 2009) It is generally agreed however that surgical fixation is effective for some rib fracture patients, but further

good quality, multi-centred studies are needed investigating the patients most likely to benefit from surgical fixation and the most appropriate repair techniques. (Mayberry et al 2009, Simon et al 2005) The future of rib fracture fixation is the minimally invasive approach using three-dimensional CT scan imaging to identify which injuries are most appropriate for fixation. (Nirula et al 2009)

1.14 Prognostic models: development and validation

The term prognosis refers to the risk of an individual developing a particular outcome over a certain time frame, based on the individual's clinical and non-clinical characteristics. (Moons et al 2009a) Commonly investigated outcomes in medical research include mortality, morbidity, quality of life factors such as pain or disability and resource utilisation factors such as duration of mechanical ventilation, discharge disposition or hospital length of stay. It is well recognised that prognostic research has received limited attention when compared to therapeutic and aetiological research. Prognostic research can either investigate the effect of a single risk factor (such as a biomarker) on a particular outcome, or on multiple variables or a series of risk factors and their effect on an outcome. (Moons et al 2009a) The latter type of study is commonly referred to as multivariable prognostic research and involves the development of a prognostic model that can be used to predict outcomes in a pre-specified patient cohort. (Adams and Leveson 2012)

Prognostic models have a number of uses in the field of medicine and Moons et al (2009a) provide an overview of these uses. Their primary use is to inform the patient about the future course of their illness and to guide the medical team in decisions regarding management of the patient and their illness. A secondary use of prognostic models is the selection of patients for inclusion in therapeutic research. For example a research team may wish to investigate the efficacy of a particular drug on a group of patients who are high risk of developing a certain disease. The high risk patients can be identified for the study through the use of a previously validated prognostic model. A final use of prognostic models is to compare differences in performances between hospitals and a number of models were originally developed and validated for this purpose (Moons et al 2009a)

It is important to emphasise that although similarities exist in the design and analysis of prognostic and aetiological research, the prediction of outcomes is not synonymous with establishing causation. (Moons et al 2009a) For example a tumour marker can predict cancer progression, but the marker will not cause the disease to progress. Another key difference between prognostic and aetiological research is that the calibration and discrimination of multivariable prognostic models is highly pertinent to prognostic research only. (Moons et al 2009a)

The primary objective of a prognostic study is to determine the probability of a pre-specified outcome using different combinations of risk factors in a well-defined patient cohort or study sample. (Wyatt and Altman 1995) The study sample should consist of a cohort of patients who at known to be at risk of developing the outcome under investigation, defined by the presence of a particular condition or disease. (Moons et al 2009a) The most appropriate study design for prognostic research is a cohort study and although a prospective study is considered preferable, retrospective studies are more common in the literature. (Wyatt and Altman 1995) Three key phases in prognostic research have been described by Moons et al (2009a), the development, validation and impact phase.

The development phase in multivariable prognostic research involves the background work required to identify the risk factors that should be included in the prognostic model. (Royston et al 2009) This background work commonly involves the completion of a systematic review of the pertinent literature in order to develop an understanding of the relevant risk factors requiring investigation. The selection of clinically relevant risk factors for inclusion in the prognostic model is one of the most important decisions for the researcher. (Wyatt and Altman 1995) It is also important that the risk factors under investigation are simple for the doctor to obtain reliably and without expending undue resources. (Wyatt and Altman 1995) Other important decisions that must be considered prior to prognostic model development include the methods required to evaluate the quality of the data and the handling of missing data, a strategy for variable selection in the final model, methods for modelling continuous data and measures for evaluation of the model's predictive accuracy. (Royston et al 2009)

Following development of the prognostic model the next phase is the validation of the model. Prognostic models are of limited clinical relevance unless they are shown to work in other samples. (Altman et al 2009) There are a number of well-documented explanations for the poor performance of a prognostic model when applied to other patients. (Wyatt and Altman 1995) These include poor design on the original model for example if the model was over-fitted or an important risk factor was missing, and differences in the setting of patients in the new validation sample compared to the development sample for example differences in patient characteristics or differences in methods of measurements or healthcare systems. (Altman et al 2009)

To validate a model it is necessary to compare observed and predicted event rates for groups of patients (calibration) and to quantify the model's ability to distinguish between patients who will or will not experience the outcome of interest (discrimination). (Royston et al 2009) There are a number of methods used to validate a prognostic model including internal validation, temporal validation and external validation. (Royston et al 2009) External validation provides a true evaluation of the prognostic model's generalizability and this is often necessary before the model is accepted for clinical use by doctors. (Wyatt and Altman 1995)

An accurate and validated prognostic model is of limited clinical benefit if it does not change behaviour. (Moons et al 2009b) The final phase of prognostic research is the impact study. (Moons et al 2009a, Wyatt and Altman 1995) The impact study aims to quantify the effect of using the prognostic model on the clinician's behaviour, patient outcome, or cost effectiveness of care compared with usual care without the model. (Moons et al 2009b) Most clinicians would agree that more evidence beyond validation is required before they will confidently apply a prognostic model to their patients. (Moons et al 2009b) The model therefore needs to be investigated for its effectiveness or impact on clinical practice, for example a study is needed that provides evidence for decreased incidence of morbidity and mortality, or decreased hospital length of stay using the model. (Wyatt and Altman 1995)

1.15 Aims and objectives of study

Blunt chest wall trauma accounts for over 15% of all trauma patients presenting to Emergency Departments in the United Kingdom. (Trauma Audit and Research Network 2011) Research has highlighted significant morbidity and mortality for the blunt chest wall trauma patient, with reported mortality ranging from 4-20%. (Bergeron et al 2003) The patient with severe thoracic injuries will be managed in the Emergency Department by the trauma and various surgical teams and intervention is dictated by the resuscitation protocol of the department. (Blecher et al 2008) Disposition of chest injury patients from the Emergency Department is therefore straightforward when the patient requires immediate surgery or supportive mechanical ventilation. (Blecher et al 2008) When the injury is less severe, or associated injuries are not present, deciding which blunt chest wall trauma patients require a higher level of clinical input can be difficult. Clinical symptoms are not considered an accurate risk factor of outcome following non-life threatening blunt chest wall trauma and furthermore, complications often develop up to 72 hours after the initial injury. (Dubinsky and Low 1997)

The development of risk scores or prognostic models has been introduced in an attempt to improve the provision of trauma care, including blunt chest trauma. (Esme et al 2007) Hippocrates, in his writings included prognosis as a principal concept of medicine. (Garrison 1966) In medicine, prognosis refers to the probability of an individual developing a particular state of health over a specific period of time, based on the clinical and non-clinical profile of the patient. (Moons et al 2009a) As a result of the significant variation in patients' aetiology, presentation and physiological status, a single risk factor rarely provides a reliable estimate of prognosis. (Moons et al 2009a) It has been suggested that using the risk score or prognostic model as a clinical model in the ED can assist in guiding doctors in their treatment decisions, thus expediting health care delivery. (Alexander et al 2000)

Researchers have stated that identification of risk factors predictive of increased morbidity at the time of admission would allow improved triage for patients with blunt chest trauma, (Kulshrestha et al 2004, Barnea et al 2002, Alexander et al 2000) however no 'gold standard' guidelines or universally recognised clinical pathways

exist. (Blecher et al 2008) Although numerous trauma scoring systems exist which are designed to predict prognosis, these scoring systems tend to be complicated and impractical, especially in a non-trauma setting. (Stawicki et al 2004) These scoring systems are also designed for use in the multi-trauma patient and not the isolated blunt chest wall trauma patient.

Pape et al (2000) developed a scoring system for guiding initial clinical decision making in the blunt chest trauma patient with multiple associated injuries however there are currently no evidence-based guidelines to guide patient management in the blunt chest wall trauma population with no associated injuries. Ahmad et al (2010) suggested that a scoring system needs to be designed to evaluate the degree of injury following blunt chest trauma. Methods are required to assist identification of the patient who presents with non-immediate life threatening blunt chest wall trauma, but will develop complications within the following 24 to 72 hours. (Ahmad et al 2010, Dubinsky and Low 1997) Evidence suggests that these patients can deteriorate up to a week after initial presentation to the Emergency Department (Sharma et al 2008, Klein et al 2002) and elderly blunt chest wall trauma patients are particularly at risk of delayed deterioration. (Albaugh et al 2000, Shorr et al 1989) The appropriate management of the blunt chest wall trauma patient with no immediate life threatening injuries has been an area of interest in previous research which has highlighted the difficulty in identifying the high risk patient in this population. (Sanidas et al 2000, Lee et al 1989, Lee et al 1990) Blecher et al (2008) described a group of chest trauma patients who were considered suitable for ward management by the Emergency Department, of which 10% went on to require Intensive Care Unit admission with associated longer lengths of stay and higher rehabilitation requirements. (Blecher 2008)

In summary, the blunt chest wall trauma patient who walks into the emergency department is often more difficult to manage than the patient who has severe immediately life-threatening blunt chest wall trauma. The management of the severely injured patient is dictated by the required life-saving intervention or surgical procedure with the emergency department trauma team following a management protocol such as the ATLS guidelines. The ambulatory patient however may initially present with what is believed to be an innocuous blunt chest wall injury and is

subsequently discharged home from the ED with analgesia and advice. If the patient is elderly, they are sent to a ward where they are given analgesia and physiotherapy. This is the patient who often develops late unexpected complications such as pneumonia and either represents to the ED if they were discharged home initially or if they were already on a ward requires late admission to ICU and possible mechanical ventilation. Morbidity and mortality in this patient group is avoidable with appropriate early management. Identification of the high risk blunt chest wall trauma patient would facilitate the early management required for reducing avoidable morbidity and mortality.

This study has the following aims:

- To investigate the risk factors for the development of complications following blunt chest wall trauma.

- To develop and validate a prognostic model that enables the Emergency Physician to reliably risk stratify the blunt chest wall trauma patient presenting to the ED, on the basis of how the patient should be managed (admission location and referral source).

In order to achieve these aims, the study had the following objectives:

1) To complete a systematic review and meta-analysis where possible of research investigating risk factors affecting outcomes in the blunt chest wall trauma patient.
2) To complete a survey of all major EDs in the UK to assess existing local and national prognostic models to determine current practice.
3) To develop a new prognostic model that risk stratifies the blunt chest wall trauma patient on the basis of identified risk factors in objective 1 and 2.
4) To validate the prognostic model in a prospective, multi-centre study.

It has been highlighted that the first stage in the process of developing a prognostic model is the completion of a systematic review of risk factors for potential inclusion in the model. (Royston et al 2009) For the purpose of this study, we defined blunt chest wall trauma as blunt chest injury resulting in chest wall contusion or rib fractures, with or without non-immediate life-threatening lung injury. This is because

a concurrent life-threatening serious injury such as an injury to the aorta, oesophagus, diaphragm or heart would either dictate the management of the patient through the need for surgical intervention and intensive care management or could potentially affect the patient's prognosis. Patients with minor concurrent injuries are included in the blunt chest trauma population as minor injuries should not dictate management of influence disease progression.

2.0 Risk factors that predict mortality, morbidity and utilisation of resources in patients with blunt chest wall trauma: Systematic review and meta-analysis

2.1 Background

2.1.1 Introduction

The first stage in the design of a prognostic model has been described as the development stage, in which the risk factors or risk factors for inclusion in the model are identified. (Adams and Leveson 2012) Prognostic models however can only be safely used in daily clinical practice if they are developed according to methodological guidelines. (Janssen et al 2010) One strategy that can be used to identify potential risk factors for inclusion is a systematic review and meta-analysis of available literature. (Royston et al 2009)

2.1.2 Outcome measures in trauma research

Risk factors for poor outcomes in the blunt chest wall trauma patient have been investigated previously in the literature and various outcome measures are used including mortality, morbidity and different aspects of resource consumption. When provided, definitions for these outcome measures vary in each study, leading to questionable validity and difficulty in comparison of studies. The use of mortality is the most common outcome measure used when investigating risk factors for blunt chest trauma. Mortality is the most easily quantified outcome for a number of reasons. For example when analysing trauma registries and databases retrospectively, death is a dichotomous variable most easily inputted by the staff involved with the patient and interpreted by the researcher at a later date. (Flagel et al 2005)

Morbidity is another dependent variable investigated however referenced definitions or methods of identifying or diagnosing morbidity are rarely discussed. (Elmistekawy and Hammad 2007, Svennevig et al 1986) Some researchers have been more specific in using pulmonary complications such as pneumonia, pleural effusions, atelectasis and acute respiratory distress syndrome as their definition of morbidity. (Brasel et al 2006, Bergeron et al 2003) The need for mechanical ventilation, admission to a critical care facility and the number of days the patient is

ventilated have been used as outcome measures in studies investigating risk factors for blunt chest trauma. Other studies use "resource consumption" as the outcome measure, which includes ICU and hospital length of stays, upgrade in care and discharge disposition. Discharge disposition refers to the status of the patient on discharge, for example, whether the patient has achieved pre-injury functional levels, discharged location and need for on-going input from a care facility or organisation. It is evident therefore that variation exists in the outcome measures used when investigating risk factors in blunt chest wall trauma patients.

2.1.3 Overview of the quality assessment process of studies.

Quality is a complex concept with numerous alternative definitions in research. The aim of assessing study quality is essentially concerned with establishing the level of accuracy or truthfulness of the results and furthermore whether the reported results are of relevance to the particular patient group of interest. (Centre for Reviews and Dissemination 2009) Quality assessment should consider whether the study is reliable enough to safely guide treatment of a patient group. Methodological weaknesses in a study design can result in bias and consequently can influence the observed effects of the intervention being studied. The potential impact that methodological quality had on the studies' reported results should be considered. Recording the strengths and weaknesses of the included studies in a systematic review or meta-analysis therefore provides the reader with a clear indication of whether the results have been influenced by study design. (Moher et al 2009, Centre for Reviews and Dissemination 2009)

The use of quality scoring in meta-analyses of observational studies however remains controversial. (Stroup et al 2000) It has been stated that even though numerous quality assessment models are available, no single model exists which is suitable for use in all reviews. (Centre for Reviews and Dissemination 2009) The quality assessment model used in this study was adapted from a previously designed criteria list by Duckitt and Harrington (2005). Stroup et al (2000) stated that key components of design, rather than aggregate scores themselves may be important in a quality assessment model. Therefore, a total validity score was not calculated in this study to summarise quality assessment as numerous guidelines have stated that such scores

are unreliable and not recommended. (Centre for Reviews and Dissemination 2009, Higgins and Green 2009)

The first of the key components of design adapted from the list by Duckitt and Harrington (2005) included a quality score representing participation selection. This considered whether the patient group selected for the study was representative of the general blunt chest trauma population or focussed only on one portion of the population. This key component assessed the generalisability of the studies' results to the blunt chest trauma population. For example, the results obtained from a study that only investigates the elderly blunt chest trauma population may not be generalisable to the younger adult blunt chest trauma population due to the potential differences in physiological reserve or incidence of co-morbidities between the two groups which may influence prognosis post-injury.

Comparability of the groups was the second component and assessed whether any significant differences existed in the groups other than the variables under investigation. It is important that the patients selected for the study are allocated to either the experimental or control group appropriately so the groups are as similar as possible. For example, consider a study investigating increased age as a risk factor for mortality in patients with blunt chest trauma. If all the patients in the elderly group had 6 rib fractures, compared to the patients in the younger group who all had 1 rib fracture, reported increased mortality in the elderly group may not be due to age, but the fact that all the elderly patients had a more severe injury, thus compromising the reliability of the reported results. In studies where the authors have either reported no differences in the groups or explicitly reported such differences in the groups and adjusted for them using particular statistical techniques, full marks were awarded in the quality assessment process.

The final component assessed was the studies reproducibility, which considered whether the study authors accurately defined chest trauma through a referenced or explicit definition. In order for a study to be repeated or the results applied to a similar population, the reader must be able to ascertain exactly how each study variable has been defined. For example, a study may be investigating mortality rates in the blunt chest trauma population using multi-trauma patients who have also

sustained blunt chest trauma, compared to another study in which the authors use patients who have sustained isolated blunt chest trauma only. Each study was assessed therefore on whether the authors have provided a referenced definition for the variables under investigation.

In summary, the quality assessment model used in this study offers an individual score for each component of study design of all included studies. The individual scores obtained provide the basis for the discussion of each quality issue thus enabling the reader to make an informed decision regarding reliability and validity of any results obtained through meta-analysis.

Egger et al (2001) have highlighted that meta-analyses of observational studies produce very precise but often spurious results. These authors have recommended that the statistical combination of data should not be a prominent component of systematic reviews and that more is gained through the careful examination of possible sources of heterogeneity between the results from observational studies. Heterogeneity refers to the differences in treatment effect between studies. (Glasziou et al 2001) Analysis of heterogeneity provides an opportunity to investigate why treatment effects may vary across studies causing potential spurious differences in reported results. If there is significant heterogeneity, this suggests that the studies investigated were not estimating a single common treatment effect. In this study, levels of heterogeneity were calculated statistically where possible or discussed for each risk factor and outcome measure investigated.

2.1.4 Aims of systematic review

The aim of this review was to summarise the risk factors for mortality in the blunt chest wall trauma patient in order to assist in the identification of the high risk patient and facilitate decisions regarding the required appropriate level of care. The outcomes used in this study are those most commonly investigated in blunt chest trauma literature. Mortality was the primary outcome measure, with secondary outcome measures including morbidity, number of days the patient requires mechanical ventilation (ventilator days), length of stay in ICU (ILOS), total length of stay in hospital (HLOS) and discharge disposition.

The study focussed on identifying risk factors in patients following simple blunt chest trauma. For the purpose of this study, we defined blunt chest wall trauma as blunt chest injury resulting in chest wall contusion or rib fractures, with or without non-immediate life-threatening lung injury. Studies that included patients who had sustained multi-trauma including a major injury to another body part such as the head, spine, abdomen or long bones (with no reference to blunt chest trauma) were not included in the review as the patient's management and prognosis could be dictated by their other injuries. Furthermore, patients with penetrating chest trauma or those patients with blunt chest trauma who require surgical management were not included in the definition of blunt chest trauma.

2.2 Methods

2.2.1 Search strategy

The first stage of the systematic review followed the guidelines in the NHS Centre for Reviews and Dissemination (CRD) Guidelines (2009) as the identification of the need for the review. There are a number of factors outlined that will determine whether the review is required, including the rationale or motivation for the study and whether a previous or on-going review exists. (CRD 2009, Higgins and Green 2009) The potential difficulties in the management of the blunt chest trauma patient have been outlined, with emphasis on the development of late complications by the patient and the variation in the current literature investigating risk factors that affect patient outcomes. It has been summarised that the clinical symptoms presented by these patients are not a good risk factor of the disease course or prognosis, thus providing further justification for this review. (Barnea et al 2002)

Extensive literature exists that examines systematic reviews of literature and common errors in the methodology used. (Egger et al 2001, Chalmers and Altman 1995) The CRD guidelines (2009) and Cochrane Handbook for Systematic Reviews (Version 5.1.0) (2011) were developed in order to guide authors in writing literature reviews that are systematic, reproducible and minimise any potential bias which could affect the results. Similarly, the PRISMA statement (Moher et al 2007) and MOOSE guidelines (Stroup et al 2000) were developed in order to improve the quality of systematic reviews and meta-analyses. These guidelines were therefore

considered in the methodology for this systematic review. Following justification for the systematic review, the first recommendation in the guidelines is the design of a review protocol that was followed throughout the entire process. The guidelines suggest that the protocol can be altered during the review process as required, but any changes should be recorded and available to the reader, thus enhancing reproducibility of the review.

The guidelines and further literature (Greenhalgh and Peacock 2005, Glasziou et al 2001, Chalmers and Altman 1995) outlined the need for developing a review protocol for undertaking a systematic review of literature of this nature with an emphasis on observational studies. The justification for the focus on observational studies was that studies investigating risk factors are not generally randomised as they relate to inherent human characteristics. Exposing patients to potentially harmful risk factors would therefore be deemed unethical. (Stroup et al 2000)

The first stage in the review protocol is suggested in the CRD guidelines is the setting of the review question, as this will determine the methodology to be designed. Following this, it is recommended that a research team should check whether there are any existing or on-going reviews on the subject to be studied. Therefore, an initial literature search was undertaken using the Database of Abstracts of Reviews of Effects (2008) (DARE) the Cochrane Database of Systematic Reviews (CDSR) (2008), and Medline from 2000 to the end of May 2010. The search terms used were MeSH headings, text words and word variants for chest trauma combined with risk factors and limited to review articles. The initial search as suggested in the CRD guidelines highlighted that no systematic review existed in the literature that investigated the risk factors for blunt chest trauma.

The CRD guidelines (2009) and Cochrane Handbook for Systematic Reviews (2011) recommend a two-step process which involves the use of a review team of a minimum of two people in order to minimise bias and error throughout the review process. Recommendations were followed for the search strategy, including search terms and use of electronic databases. The Cochrane Library, Medline and Embase were selected based on suggestions in the literature as they were reported to be the most commonly used for reviews of healthcare studies. There can however be no

standard agreed for what constitutes an acceptable search in terms of the databases used. (CRD 2009)

Other guidelines for search strategies in systematic reviews have been proposed by Greenhalgh and Peacock (2005). They reported that 51% of sources obtained were identified by pursuing references of studies ('reference tracking' or 'snowballing'). They further stated that another system of identifying relevant studies for inclusion in a systematic review is through the research team's own personal knowledge and personal contacts or academic networks, revealing another 24% of possible relevant studies. (Greenhalgh and Peacock 2005) All the guidelines concurred that in order to minimise publication bias, it is important to include unpublished or on-going research. A number of databases exist which assist in the identification of grey literature and were included in the search strategy. (CRD 2009) Finally, all guidelines for data extraction, quality assessment and data synthesis were considered.

The review team in this study consisted of the primary researcher (CB) and a secondary researcher (KJ). A third researcher (PE) was used where a discussion between the first and second researcher could not resolve differences in opinion regarding studies being investigated. No conflicts of interest for each of the researchers were identified at the outset of the study. An advisory group was formed which consisted of a senior lecturer in health services research, a senior medical librarian, an emergency medicine physician, a senior critical care physiotherapist, a consultant intensivist, a consultant surgeon and a research fellow in critical care. This group was used to seek advice regarding methodology at key stages in the review process.

A review protocol was designed and approved by the review team in order to set out the methods to be used in the review. The review protocol was amended as required during the search, data extraction and analysis stages and discussion regarding the modifications applied to the protocol is included in the methodology. The question investigated by this review was agreed by the research team; 'Risk factors that predict mortality, morbidity and utilisation of resources in blunt chest wall trauma patients'.

In order to address the review question a search filter and electronic search were developed in collaboration with an experienced librarian in systematic reviews. A broad search strategy for potential articles was used in order to include all relevant studies. The search filter was used for a number of databases to identify articles including Medline, Embase Databases and the Cochrane Library from the introduction of the databases until the end of June 2010.

The search term combinations for electronic databases, based on guidance from research (CRD 2009, Greenhalgh and Peacock 2005) and the librarian involved were Medical Subject Heading (MeSH) terms, text words and word variants for chest trauma. These were combined with relevant terms for aetiological factors. Table 2.1 illustrates the key words used in the search. Furthermore, if any new relevant search terms were identified during the database searches or reference tracking and were considered appropriate by the investigators, a new search was completed including the new search term, using the combinations previously described. New terms identified included "wounds, non-penetrating."

Chest trauma	AND	Prognos*
Thora* trauma		Risk factor
Rib fractures		Caus*
Thora* injury		Risk factors
Chest injury		Risk
Wounds, non-penetrating		Outcome

The asterisk indicates where the truncated version of the word was used.

Table 2.1 Keyword combinations used in the literature search.

In order to limit publication bias, the references of all primary studies and review articles were hand-searched in order to identify studies potentially missed in the electronic search. (CRD 2009, Greenhalgh and Peacock 2005) The Annals of Emergency Medicine, The Emergency Medicine Journal, Injury and the Journal of Trauma were hand-searched from the introduction of the journals until the end of May 2010 for relevant studies. The individual journal's on-line archives were searched where available. The College of Emergency Medicine and the authors of

the selected studies were contacted in order to provide expert opinion on further possible studies for inclusion and a deadline for response was set at three months.

All accessible College of Emergency Medicine Conference abstract supplements, European Congress on Emergency Medicine abstracts and International College of Emergency Medicine conference abstracts were also searched. The dates used to search were the years in which the conferences were first held. The National Technical Information Service and Health Management Information Consortium databases include unpublished papers and were therefore searched using broad search terms in order to maximise chance of identifying any grey literature. Search terms included "rib fractures", and combinations of "chest or thoracic or thorax" with "trauma or injury" with no limitations used. Similarly, the OpenSIGLE database was searched. The System for Information on Grey Literature in Europe provides access to SIGLE bibliographical references of reports and other grey literature produced in Europe from 1980 until 2005.

The searches were international and no search limitations were imposed in order to minimise the chance of missing relevant studies and selection bias. Translators were used to assist with identified foreign language studies. No formal definition for chest trauma was used for the study selection process and studies were included if the chest trauma was stated to be blunt or non-penetrating. If it was not clear from the title or abstract whether the study investigated penetrating chest trauma only, then the study was included. CB and KJ analysed each title and abstract independently and then met to discuss any discrepancies. PE was consulted to resolve any discrepancies. For duplicate studies, only the most recent publication was included. Similarly, if a published abstract and full paper of the same work were identified, only the full paper was included. No restrictions were applied on the year of publication, study design, risk factors or outcomes investigated and age of the subjects. The selected studies were obtained and the full paper analysed by the reviewers using the same method. Table 2.2 summarises the inclusion and exclusion criteria applied to the citations identified at each stage of the search process. The sub headings are based on the CRD guidelines (2009).

	Inclusion	Exclusion
Population	Patients presenting to the ED with blunt chest wall trauma(blunt chest injury resulting in chest wall contusion or rib fractures, with or without underlying lung injury)	Studies investigating: a) Patients with penetrating trauma only b) Patients with multi-trauma only and no reference to chest trauma c) Patients with intra-thoracic injuries and no blunt chest wall trauma d) Scoring systems or prognostic models
Outcomes	Studies investigating outcomes in patients with blunt chest trauma including morbidity and mortality, admission to hospital or ICU, HLOS or ILOS, ventilatory support, changes in level of care	Studies investigating management or treatment strategies only
Comparators	Studies allowing estimates of association between risk factor and outcome for blunt chest wall trauma	Studies that fail to provide comparative data on risk factors and outcome.
Study Design	All observational studies, published and unpublished	Descriptive studies with no comparative data such as a narrative review or case studies

Table 2.2 Inclusion and exclusion criteria for studies.

2.2.2 Study quality assessment

The final studies to be included were selected and data extraction of the studies was completed by the reviewers individually, then meeting to resolve discrepancies. The methodological quality of the included studies was evaluated by means of a previously designed criteria list adapted from Duckitt and Harrington (2005) which is outlined in Table 2.3. Individual sub-sections of methodology were allocated a score between 0 – 2 following the descriptions as outlined in Table 3, using the two-step process described for study selection. Studies were not excluded on the basis of quality, but any existing quality issues were highlighted in the discussion. Confounding variables potentially affecting the results of the study were considered separately in the results and discussion. The STROBE checklist was used to further assess the studies quality and issues highlighted were included in the discussion. (Vandenbroucke et al (2007)

Patient selection
Selected cohort was representative of the general blunt chest trauma population (1)
Cohort was a selected group or the selection was not described (0)

Comparability of groups
No differences between the groups was explicitly reported (especially in terms of age, number of rib fractures, pre-existing disease) unless it was one of the variables under investigation, or such differences were adjusted for (2)
Differences in groups were not recorded (1)
Groups differed (0)

Outcomes
Referenced definition of chest trauma (2)
Explicit definition that included explanation of thoracic structures injured or type of injury incurred (1)
Chest trauma not defined (0)

Group size
>100 participants in each group (2)
<100 participants in each group (1)

Cohort design
Prospective cohort design (2)
Retrospective design / use of trauma registry or database (1)

Numbers in brackets are the individual quality scores for each methodology sub-section

Table 2.3 Quality Assessment of non-randomised studies. Adapted from Duckitt and Harrington (2005).

2.2.3 Analysis and presentation of data

Where sufficient data were available in the studies, the odds ratios with 95% confidence intervals were calculated for the risk factors investigated. Statistical analysis was completed using the RevMan software. (The Cochrane Collaboration 2008) The I^2 statistic was calculated for combined studies in order to assess heterogeneity and true effect size. I^2 describes the percentage of total variation across the studies that are due to heterogeneity rather than chance. (Higgins et al 2003) Combined odds ratios were calculated where feasible using Mantel-Haenszel method with a fixed effect model for each outcome measure. (Kirkwood and Sterne 2003) For some of the included studies, the data could not be combined for the risk factors as a result of pronounced differences in study design. Therefore the results are described in a narrative format with the studies' published odds ratios and adjusted odds ratios presented individually where available. Funnel plots were not used as a large number of studies is required in the analysis to allow depiction of the funnel. (Banerjee 2003) (CRD 2009) Discussion of publication bias, heterogeneity and study quality was included in place of funnel plots.

2.3 Results

2.3.1 Search results

A total of 4326 citations were identified from the electronic searches. Following screening of titles and abstracts 4278 studies were excluded using the two-step process. Following this process a total of 48 citations were retrieved for detailed evaluation based on the exclusion criteria above. A further 25 citations were identified through hand-searching and snowballing which were retrieved for detailed evaluation. The contacted authors who responded suggested using the reference lists from their own studies as relevant studies for inclusion. These studies had already been considered through the snowballing process and therefore no further hits were identified. No relevant hits were identified through the searches for grey literature or unpublished studies. Two non-English language studies were identified and translated. Following critical appraisal of the 73 studies identified in the literature search, a total of 44 studies were excluded. A reject log is included in Appendix A which highlights the reasons for exclusion of the studies selected in the initial stages of the search strategy. (Stroup et al 2000) The final number of included studies for discussion in this review was 30 and the selection process and reasons for exclusion are highlighted in the flow diagram in Figure 2.1.

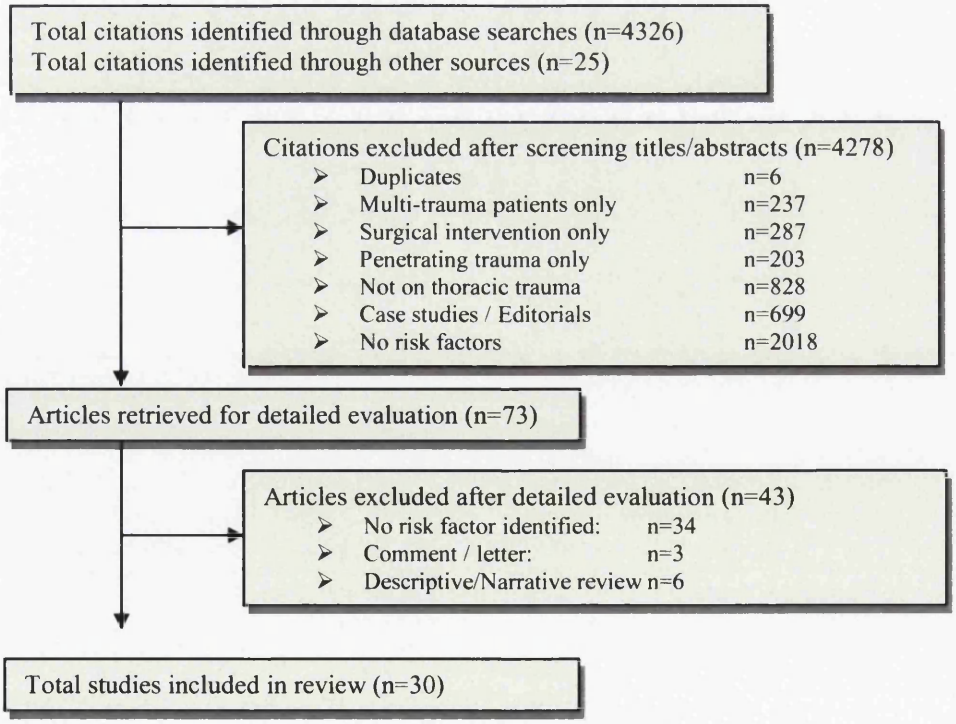


Figure 2.1: Flow diagram of study selection process

Data extraction was completed on the 30 included studies. The studies were grouped according to the risk factor for outcomes in patients with blunt chest trauma. There was some degree of overlap as a number of studies investigated had more than one risk factor. Furthermore, the populations investigated differed. A number of studies investigated risk factors in the elderly, whereas others investigated age as a risk factor itself. Two studies investigated risk factors affecting outcomes in patients with flail chest only and one study assessed pulmonary contusions only. As a result of the differences in study design and inclusion criteria, cross comparison of all the studies was not possible. Table 2.4 outlines a summary of each study investigating the risk factors for mortality in blunt chest wall trauma patients. Risk factors include age (shaded blue), number of rib fractures (shaded pink), presence of pre-existing conditions (shaded green) and the on-set of pneumonia in the recovery phase following the injury (shaded yellow).

OUTCOME MEASURE: MORTALITY

Study	Population	N	Risk factor	Results including reported odds ratios
Albaugh (2000)	Flail chest patients	58	Age	Likelihood of death increase by 132% for each decade of life
Athanassiadi (2004)	Flail chest patients	150	Age	Age had no effect on mortality in flail chest patients
Athanassiadi (2010)	Flail chest patients	250	Age	Age had no effect on mortality in flail chest patients
Bergeron (2003)	Rib fracture patients	405	Age	Adjusted OR of death for rib fracture patients aged 65+years: 5.03 (1.8-13.9, 95% CI)
Brasel (2006)	Rib fracture patients	17,308	Age	Adjusted OR of death for rib fracture patients aged 65-74: 2.7 (1.1-7.1, 95% CI)
Borman (2006)	Flail chest patients	262	Age	OR of death in flail chest patients aged 45-64 years: 1.7 (0.8-3.7). OR death in flail chest patients aged 65 years+:2.1 (1.0-4.6)
Bulger (2000)	Rib fracture patients	464	Age	Rib fracture patients aged 65+yrs had significantly higher mortality than rib fracture patients aged <65 years ($p<0.001$)
Harrington (2010)	Rib fracture patients 50years+	1621	Age	OR of mortality for rib fracture patients aged 50years+: 1148.5 (184.9-7132.6 CI:95%)
Holcomb (2003)	Isolated rib fracture patients	171	Age	No differences in mortality between age groups
Inci (1998)	Blunt chest trauma patients	101	Age	Rib fracture patients aged 60+years had significantly higher mortality rate than adults and children (both $p<0.001$)
Kulshrestha (2004)	Blunt chest trauma patients	1359	Age	OR death with each 1 year increase in age: 1.04 (1.02-1.05, 95% CI)
Lee (1990)	Rib fracture patients	105,493	Age	3+Rib fracture patients aged 65+ years had significantly higher mortality than patients aged <65 years ($p<0.001$)
Lien (2009)	Rib fracture patients18yearspost MVA	18,856	Age	Adjusted OR death in rib fracture patients aged 65-74: 2.21(1.63-2.99, 95% CI)
Liman (2003)	Blunt chest trauma patients	1490	Age	Rib fracture patients aged 60+years had significantly higher mortality ($p<0.001$)
Perna (2010)	Blunt chest trauma patients	500	Age	Blunt chest trauma patients aged 55+ years had a significantly higher rate of mortality ($p<0.05$)
Peterson (1994)	Blunt chest trauma patients	2073	Age	Blunt chest trauma patients aged 60+years had higher mortality (No p-value)
Sharma (2008)	Rib fracture patients	808	Age	Rib fracture patients aged 65+years had significantly higher mortality. ($p<0.05$)
Shorr (1989)	Rib fracture patients	92	Age	Rib fracture patients aged 65+years had significantly higher mortality ($p<0.001$)

Sirmali (2003)	Rib fracture patients	1417	Age	Rib fracture patients aged 60+ years had higher mortality. (no p value)
Stawicki (2004)	RF patients 18years+,	27,855	Age	Rib fracture patients aged 65+years had significantly higher mortality ($p<0.001$)
Svennevig (1986)	Blunt chest trauma patients (12years+ no head injury)	262	Age	Rib fracture patients aged 70+years had significantly higher mortality ($p<0.05$)
Testerman (2006)	Isolated rib fracture patients	307	Age	No differences in mortality between groups
Barnea (2002)	Isolated rib fracture patients aged 65years+	77	Number of rib fractures	Correlation between increasing number of rib fracture and increased mortality ($p=0.006$) in elderly patients
Bergeron (2003)	Rib fracture patients	405	Number of rib fractures	Adjusted OR of death for 3+rib fracture patients: 3.13 (1.3-7.6 CI 95%)
Brasel (2006)	Rib fracture patients	17,308	Number of rib fractures	Adjusted OR of death for 3+rib fractures patients: 1.8 (1.1-3.0 CI 95%)
Bulger (2000)	Rib fracture patients	464	Number of rib fractures	OR death with each additional rib fracture: 1.19
Elmistekawy (2007)	Isolated rib fracture patients aged 60years+	39	Number of rib fractures	No correlation between mortality and number of rib fractures
Flagel (2005)	Rib fracture patients	64,750	Number of rib fractures	Significant increase in mortality with each successive rib fracture ($p<0.02$)
Harrington (2010)	Rib fracture patients 50years+	1621	Number of rib fractures	Patients aged 50+ years with 3 + rib fractures had a significantly higher rate of mortality ($p<0.001$)
Hoff (1994)	Isolated pulmonary contusion	94	Number of rib fractures	No correlation between number of rib fractures and mortality
Holcomb (2003)	Isolated rib fracture patients	171	Number of rib fractures	No correlation between mortality and number of rib fractures
Kulshrestha (2004)	Blunt chest trauma patients	1359	Number of rib fractures	OR death for 5+rib fractures patients: 2.43 (1.31-4.51, 95% CI)
Lee (1990)	Rib fracture patients	105,493	Number of rib fractures	Patients with 3+rib fractures had significantly higher mortality than patients with 1-2rib fractures ($p<0.001$)
Lien (2009)	Rib fracture patients18yearspost MVA	18,856	Number of rib fractures	Adjusted OR death within 24hours for 3+rib fractures patients: 2.44 (0.93-6.41)
Liman (2003)	Blunt chest trauma patients	1490	Number of rib fractures	Patients with 3+rib fractures had significantly higher mortality than patients with 1-2rib fractures ($p<0.001$)
Perna 2010	Blunt chest trauma patients	500	Number of rib fractures	Blunt chest trauma patients with 3+rib fractures and a flail chest had a significantly higher mortality ($p<0.05$)
Sharma (2008)	Rib fracture patients	808	Number of rib fractures	Patients with 3+rib fractures had significantly higher mortality than patients with 1-2 Rib fractures ($p<0.05$)
Sirmali (2003)	Rib fractures patients	1417	Number of rib fractures	Patients with 6+rib fractures had higher mortality than patients with 3-5rib fractures (no p values)
Stawicki (2004)	Rib fracture patients aged 18years+	27,855	Number of rib fractures	correlation between increasing number of Rib fractures and increased mortality (no p values)
Svennevig (1986)	Blunt chest trauma patients aged 12+years no head injury	n=262	Number of rib fractures	Patients with 4+rib fractures had significantly higher mortality than patients with <4 rib fractures ($p<0.05$)
Testerman (2006)	Isolated rib fracture patients	307	Number of rib fractures	No differences in mortality between groups
Alexander (2000)	Isolated rib fracture patients 65years+	62	PEC	Rib fractures patients with cardiopulmonary disease had significantly higher mortality ($p<0.05$)
Barnea (2002)	Isolated rib fracture patients 65years+	77	PEC	Rib fracture patients with congestive heart failure had significantly higher mortality ($p<0.001$)
Bergeron (2003)	Rib fractures patients	405	PEC	Adjusted OR for mortality in rib fracture patients with PEC: 2.98 (1.1-8.3 CI 95%)
Brasel (2006)	Rib fracture patients	17,308	PEC	Adjusted OR for mortality in rib fracture patients with congestive heart failure: 2.62 (1.93-3.55, 95% CI)
Elmistekawy (2007)	Isolated rib fractures patients 60yrs+	39	PEC	Elderly rib fracture patients with chronic lung disease had significantly higher mortality than patients without ($p=0.006$)
Harrington (2010)	Rib fracture patients aged 50years+	1621	PEC	OR mortality in rib fracture patients aged 50years+ with congestive heart failure: 5.7 (1.3-25.0 CI 95%) Lung disease showed no association with mortality
Stawicki (2004)	Rib fracture patients, aged 18+years,	27,855	PEC	Effect of PECs on patient mortality inversely related to number of rib fractures Effect of PECs most pronounced in patients with 4 or less rib fractures
Bergeron (2003)	Rib fracture patients	405	Onset of Pneumonia	Rib fractures patients with pneumonia have OR of mortality 3.80 (1.5-9.7, 95% CI)

Brasel (2006)	Rib fracture patients	17,308	Onset of Pneumonia	Rib fracture patients with pneumonia have OR of mortality 3.5 (2.2-5.7, 95% CI)
Elmistekawy (2007)	Isolated rib fracture patient. 60years+	39	Onset of Pneumonia	Rib fracture patients with pneumonia have a significantly higher rate of mortality (p=0.015)
Harrington (2010)	Rib fracture patients 50years+	1621	Onset of Pneumonia	Rib fracture patients aged 50years+ with pneumonia have a significantly higher rate of mortality (p<0.001)
Svennevig (1986)	Blunt chest trauma patients aged 12 years+ no head injury	262	Onset of Pneumonia	Rib fracture patients with pneumonia have a significantly higher rate of mortality (p<0.05)

OR: odds ratio, **CI**: confidence interval, **MVA**: motor vehicle accident, **PEC**: pre-existing condition,

Table 2.4: Risk factors for mortality in blunt chest wall trauma patients

Table 2.5 outlines a summary of each study investigating the risk factors for morbidity in blunt chest wall trauma patients. Risk factors include age (shaded blue), number of rib fractures (shaded pink) and the presence of pre-existing conditions (shaded green).

OUTCOME MEASURE: MORBIDITY				
Study	**Population**	**N**	**Risk factor**	**Results including reported odds ratios**
Bergeron (2003)	Rib fracture patients	405	Age	Rib fracture patients aged 65+years had significantly higher incidence of pneumonia (p<0.005) OR developing pneumonia in rib fracture patients aged 65+years:1.75 (0.8-3.6,95% CI)
Brasel (2006)	Rib fracture patients	17,308	Age	Adjusted OR for pneumonia in rib fracture patients aged 65+years: 1.3 (0.7-2.2,95% CI)
Bulger (2000)	Rib fracture patients	464.	Age	Rib fracture patients aged 65+ years had significantly higher level of pneumonia (p<0.01)
Inci (1998)	Blunt chest trauma patients	101	Age	Rib fracture patients aged 60+years had higher morbidity (not significant)
Shorr (1989)	Rib fracture patients	92	Age	No difference between age groups for morbidity rates in rib fracture patients
Sirmali (2003)	Rib fracture patients	1417	Age	No difference between age groups for morbidity rates in rib fracture patients (pneumonia not included)
Stawicki (2004)	Rib fracture patients <18years+,	27,855	Age	Rib fracture patients aged 65+years had significantly higher rates of pneumonia. (p<0.05)
Testerman (2006)	Isolated rib fracture patients	307	Age	Rib fracture (4+) patients aged 45+years had higher rates of pneumonia (p<0.05)
Barnea (2002)	Isolated rib fracture patients 65yrs+	77	Number of rib fractures	Correlation between increasing number of rib fractures and increased morbidity (p=0.027) in elderly patients
Bergeron (2003)	Rib fractures patients	405	Number of rib fractures	Adjusted OR of pneumonia for 3+rib fracture patients: 1.60 (0.86-2.98 CI 95%)
Brasel (2006)	Rib fractures patients	17,308	Number of rib fractures	Adjusted OR of pneumonia for 3+rib fracture patients: 3.5 (2.2-5.7, CI 95%)
Bulger (2000)	Rib fractures patients	464.	Number of rib fractures	OR pneumonia with each additional rib fracture: 1.19 (p<0.001)
Elmistekawy (2007)	Isolated Rib fracture patients 60 years+	39	Number of rib fractures	Correlation between number of rib fractures and increased morbidity (p=0.012)
Flagel (2005)	Rib fracture patients	64,750	Number of rib fractures	Significant increase in incidence of pneumonia with each successive Rib fracture (p<0.01)
Holcomb (2003)	Isolated rib fracture patients	171	Number of rib fractures	Patients with 4+rib fractures aged 45+ years had higher morbidity than patients with <4RFs aged <45 years (no p value)
Testerman (2006)	Isolated rib fracture patients	307	Number of rib	Patients with 4+rib fractures aged 45+ years had higher morbidity than patients with <4Rib fractures aged <45 years

			fractures	(p<0.05)
Alexander (2000)	Isolated rib fracture patients 65years+	62	PEC	Rib fracture patients with cardiopulmonary disease had significantly higher rate of morbidity (p<0.05)
Barnea (2002)	Isolated rib fracture patients 65years+	77	PEC	Rib fracture patients with diabetes had significantly higher rate of morbidity (p=0.0095)
Bergeron (2003)	Rib fracture patients	405	PEC	Adjusted OR for incidence of pneumonia in rib fracture patients with PEC: 2.62 (1.2-5.7, 95% CI)
Brasel (2006)	Rib fracture patients	17,308	PEC	Adjusted OR for incidence of pneumonia in rib fracture patients with chronic pulmonary disease: 1.97 (1.62-2.40, 95%CI)
Elmistekawy (2007)	Isolated rib fracture patients 60years+	39	PEC	Rib fracture patients with diabetes (p=0.005) and chronic lung disease (p=0.001) had significantly higher rate of morbidity

OR: odds ratio, **CI:** confidence interval, **PEC:** pre-existing condition

Table 2.5: Risk factors for morbidity in blunt chest wall trauma patients

Table 2.6 outlines a summary of each study investigating the risk factors for prolonged length of stay in blunt chest wall trauma patients. Risk factors include age (shaded blue), number of rib fractures (shaded pink) and the presence of pre-existing conditions (shaded green).

OUTCOME MEASURE: PROLONGED LENGTH OF STAY				
Study	**Population**	**N**	**Risk factor**	**Results including reported odds ratios**
Bergeron (2003)	Rib fracture patients	405	Age	Rib fracture patients aged 65+years had significantly longer (p<0.0001)
Bulger (2000)	Rib fracture patients	464.	Age	Rib fracture patients aged 65+years had significantly longer LOS (p<0.01)
Holcomb (2003)	Isolated rib fracture patients	171	Age	Rib fracture (4+) patients aged 45+years had longer LOS (not significant)
Stawicki (2004)	Rib fracture patients aged18years+	27,855	Age	Rib fracture patients aged 65+years had significantly longer LOS (p=0.001)
Testerman (2006)	Isolated rib fracture patients	307	Age	No differences between age groups
Flagel (2005)	Rib fracture patients	64,750	Number of rib fractures	Correlation between increasing number of rib fractures and increased LOS (p<0.01) up to 7 rib fractures
Sharma (2008)	Rib fractures patients	808	Number of rib fractures	No correlation between number of rib fractures and LOS
Stawicki (2004)	Rib fractures patients 18years+	27,855	Number of rib fractures	Correlation between increasing number of rib fractures and increasing LOS (p<0.001) up to 5 rib fractures
Alexander (2000)	Isolated rib fracture patients 65years+	62	PEC	Rib fracture patients with cardiopulmonary disease has a significantly higher LOS (P<0.05)

OR: odds ratio, **CI:** confidence interval, **LOS:** length of stay, **PEC:** pre-existing conditions

Table 2.6: Risk factors for prolonged length of stay in blunt chest wall trauma patients

Table 2.7 outlines a summary of each study investigating the risk factors for poor discharge disposition in blunt chest wall trauma patients. The only risk factor investigated was age (shaded blue).

OUTCOME MEASURE: DISCHARGE DISPOSITION				
Study	**Population**	**N**	**Risk factor**	**Results including reported odds ratios**
Bulger (2000)	Rib fracture patients	464	Age	Rib fracture patients aged <65years had higher rate of discharge home (not significant)
Sharma (2008)	Rib fracture patients	808	Age	Rib fracture patients aged <65years had higher rate of discharge home (not significant)

Table 2.7: Risk factors for poor discharge disposition in blunt chest wall trauma patients

Table 2.8 outlines a summary of the individual studies that investigated a risk factor or outcome measure not investigated in another study.

VARIOUS OUTCOME MEASURES / RISK FACTORS					
Study	**Population**	**N**	**Risk Factors**	**Outcome measures**	**Results including reported odds ratios**
Bakhos (2006)	Rib fracture patients aged 65years+	38	Vital capacity	LOS	Vital capacity could predict HLOS in elderly rib fracture patients
Hoff (1994)	Isolated pulmonary contusion	94	Pa02/Fi02 ratio	Mortality	Pa02/Fi02 ratio <250 on admission was an independent risk factor of mortality in isolated pulmonary contusion patients
Lee (1989)	Rib fracture patients	3282	Number of rib fracture	Need for transfer trauma centre	Patients with 3+ib fractures required transfer to a trauma centre (positive predictive value = 92.8%)
Reiff (2007)	Blunt chest trauma patients	3649	Body mass index	Need and duration of mechanical ventilation	OR of need for MV in overweight rib fracture patients:1.40 (1.08-1.81, 95% CI) and obese RF patients: 1.53 (1.17-1.99, 95% CI)

OR: odds ratio, **CI:** confidence interval, **HLOS:** length of stay, **MV:** mechanical ventilation

Table 2.8: Individual risk factors / outcome measures with no comparable study

2.3.2 Quality assessment

Using the STROBE checklist (Vandenbroucke 2007) and quality assessment process (Duckitt and Harrington 2005) the quality of the studies selected for this review was considered variable, with only a small number of studies scoring maximum marks on each component. The 30 included studies had comparable data reporting on the risk factors for blunt chest trauma and outcomes. (27 retrospective cohort studies, three prospective cohort study). Ten of the studies had fewer than 100 patients in at least one of the groups studied and two of the studies had no adjustment for confounders. Nineteen studies used a cohort that was representative of the general blunt chest trauma population. Only thirteen of the studies gave referenced definitions for either independent or dependent variables under investigation. Table 2.9 highlights details of the quality of the 30 included studies.

Included study	Selection	Comparability	Outcome	Size	Cohort design	Total score
Albaugh 2000	0	2	1	1	1	5
Alexander 2000	0	1	1	1	1	4
Athanassiadi 2004	0	2	1	1	1	5
Athanassiadi 2010	0	2	1	1	1	5
Bakhos 2006	0	0	1	1	1	3
Barnea 2002	0	1	2	1	1	5
Bergeron 2003	1	2	2	2	2	9
Borman 2006	0	1	2	2	1	6
Brasel 2006	1	2	2	2	1	8
Bulger 2000	1	2	2	2	1	8
Elmistekawy 2007	0	1	1	1	1	4
Flagel 2005	1	2	2	2	1	8
Harrington 2010	0	1	1	2	1	5
Hoff 1994	0	0	2	1	1	4
Holcomb 2003	1	2	2	1	1	7
Inci 1998	1	1	1	2	1	6
Kulshrestha 2004	1	2	2	2	2	9
Lee 1989	1	2	2	2	1	8
Lee 1990	1	2	2	2	1	8
Lien 2009	0	2	2	2	1	7
Liman 2003	1	1	1	2	1	6
Perna 2010	1	2	1	2	2	8
Peterson 1994	1	1	2	1	1	6
Reiff 2007	1	2	1	2	1	7
Sharma 2008	1	2	1	2	1	7
Shorr 1989	1	1	1	1	1	5
Sirmali 2003	1	2	1	2	1	7
Stawicki 2004	1	2	2	2	1	8
Svennevig 1986	1	1	1	2	1	6
Testerman 2006	1	2	1	1	1	6

(Points scored: see protocol adapted from Duckitt and Harrington, 2005, Table 2.3

Table 2.9: Quality assessment of included studies

It is evident from Table 2.9 that the quality of the studies selected for this review was variable. Only the studies by Bergeron et al (2003) and Kulshrestha et al (2004) scored the maximum possible on each variable assessed. A number of other studies scored highly including Brasel et al (2006), Bulger et al (2000), Flagel et al (2005), Lee et al (1989, 1990) and Stawicki et al (2004), only dropping a mark due to the retrospective design of the study. The studies which scored low on quality included Bakhos et al (2006) and Elmistekawy and Hammad (2007) as they used a retrospective study design, a small sample size not representative of the blunt chest trauma population, with no referenced definition for the variables investigated. A number of the studies included attempted to address the effects of confounding in order to evaluate true risk factors affecting outcomes in blunt chest trauma patients.

Table 2.10 outlines the possible confounding variables quoted in each of the studies and the methods employed, if any, by the authors to address this.

Included study	Potential confounders	Methods to address confounding
Albaugh et al 2000	Includes patients with associated injuries and multi trauma	None
Alexander et al 2000	None	All patients with associated injuries excluded
Athanassiadi 2004	Includes patients with associated injuries and surgical intervention	None
Athanassiadi 2010	Includes patients with associated injuries and surgical intervention	None
Bakhos et al 2006	No discussion whether patients had associated injuries	None
Barnea et al 2002	None	All associated injuries excluded
Bergeron et al 2003	Includes patients with associated injuries and multi-trauma	Statistical methods used to adjust for confounders
Borman et al 2006	Includes patients with associated injuries and multi-trauma	None
Brasel et al 2006	Includes patients with associated injuries and multi-trauma	Discussion regarding limitations. Statistical methods used to control for effects of co-morbidity so only age and injury severity investigated as risk factor of mortality
Bulger et al 2000	Includes patients with associated injuries and multi-trauma	None
Elmistekawy 2007	None	Isolated rib fractures only
Flagel et al 2005	Includes patients with associated injuries and multi-trauma	Statistical methods used to adjust for confounders
Harrington 2010	Includes patients with associated injuries and multi-trauma	None
Hoff et al 1994	None	All confounders addressed
Holcomb et al 2003	Excluded patients with no identified rib# but research states rib#s difficult to diagnose	Patients with head and abdominal trauma excluded
Inci et al 1998	No discussion whether patients had associated injuries	None
Kulshrestha et al 2004	Includes patients with associated injuries and multi-trauma	None
Lee et al 1989	Includes patients with associated injuries and multi-trauma	Statistical methods used to adjust for confounders
Lee et al 1990	Includes patients with associated injuries and multi-trauma	Statistical methods used to adjust for confounders
Lien et al 2009	Includes patients with associated injuries and multi-trauma (investigated as a risk factor)	Statistical methods used to adjust for confounders
Liman et al 2003	Surgical intervention included. Patients with associated injuries included (as risk factor)	Statistical methods used to adjust for confounders
Perna 2010	Includes patients with associated injuries and multi-trauma	None
Peterson et al 1994	Includes patients with head injuries.	None
Reiff et al 2007	Patients with penetrating trauma included. No discussion re ventilator weaning protocols	None
Sharma et al 2008	Includes patients with multi-trauma (investigated as a risk factor)	Statistical methods used to adjust for confounders
Shorr et al 1989	Includes patients with associated injuries and multi-trauma	None
Sirmali et al 2003	Includes patients with associated injuries and multi-trauma	None
Stawicki et al 2004	Includes patients with associated injuries and multi-trauma	None
Svennevig et al 1986	Includes patients with associated injuries	None
Testerman 2006	Includes patients with associated injuries or multi-trauma	Excludes serious associated injuries to head and abdomen

Table 2.10 Potential confounders highlighted in the extracted articles and methods (if any) used to address them.

2.3.3 Age as a risk factor for mortality (primary outcome measure)

The age of the patient was a well reported risk factor as illustrated in Tables 2.4 to 2.7 however results differed regarding the actual age at which risk of poor outcomes became significant. Eight studies reported a significant increase in mortality rate in blunt chest wall trauma patients aged 65 years or more compared to blunt chest wall trauma patients less than 65 years old. (Lien et al 2009, Sharma et al 2008, Stawicki et al 2004, Bergeron et al 2003, Brasel et al 2006, Bulger et al 2000, Lee et al 1990, Shorr et al 1989) Similarly, three studies reported a significant increase in mortality rate in blunt chest wall trauma patients aged 60 years or more (Liman et al 2003, Sirmali et al 2003, Inci et al 1998) while Harrington et al (2010) reported increased mortality in blunt chest wall trauma patients aged 50 years or more. In contrast, two studies reported no differences in mortality rates, in which the authors investigated outcomes in blunt chest wall trauma patients using the age of 45 years as the point at which risk was hypothesised to increase. (Testerman 2006, Holcomb et al 2003)

The age of the patient was investigated as a risk factor for mortality in patients who had sustained a flail chest in five studies. Borman et al (2006) reported an odds ratio of 1.7 (0.8-3.7, 95% CI) for mortality in patients aged between 45 and 64 years with a flail chest and an odds ratio of 2.1 (1.0-4.6, 95% CI) in patients aged 65 years or more. Albaugh et al (2000) reported a risk ratio of 2.32 (1.15-4.58, 955 CI) for death with each additional decade of age in patients who have sustained a flail chest. This study concluded that the likelihood of death increased by 132% for each decade of life between the second and eighth decade in patients with a flail chest. Perna and Morera (2010) reported a patient age of 55 years or more to be a risk factor for mortality in flail chest patients. Two studies by the same authors reported no increased risk of mortality in elderly patients with flail chest. (Athanassiadi et al 2010, Athanassiadi et al 2004)

The studies investigating the age of 65 or more years as a risk factor for mortality in patients with blunt chest wall trauma were combined for analysis and are illustrated in Figure 2.2.

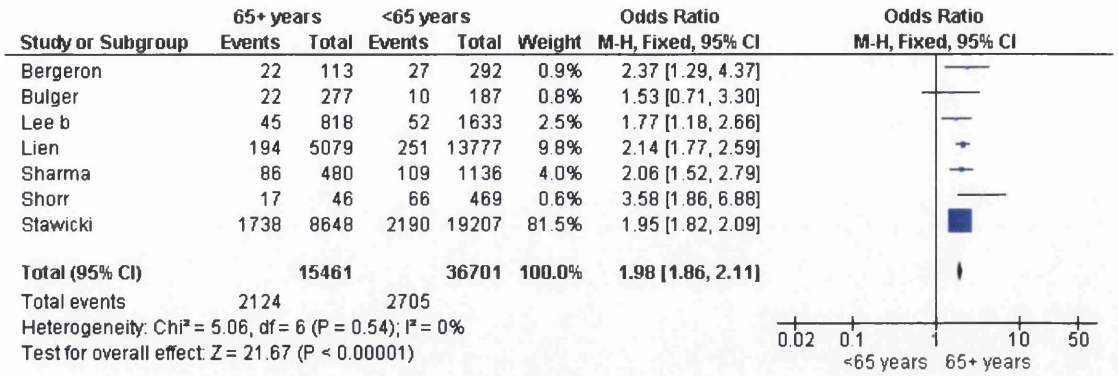


Figure 2.2: Forest plot illustrating the odds of mortality in blunt chest wall trauma patients aged 65 or more years.

Figure 2.2 indicates a combined odds ratio for mortality of 1.98 (1.86-2.11, 95% CI) in blunt chest trauma patients aged 65 or more years. An I^2 statistic of 0% indicates a low level of heterogeneity between the studies for this risk factor and mortality. The result of the test for overall effect, Z=21.67 ($p<0.00001$) suggests that the odds of mortality is significantly greater in blunt chest trauma patients aged 65 or more.

2.3.4 Age as risk factor for morbidity, length of stay and discharge disposition (secondary outcome measures)

Age as a risk factor for morbidity was investigated in eight of the studies, as illustrated in table 2.3.2. (Brasel et al 2006, Testerman 2006, Stawicki et al 2004, Bergeron et al 2003, Sirmali et al 2003, Bulger et al 2000, Inci et al 1998, Shorr et al 1989) Four studies reported that blunt chest wall trauma patients over the age of 65 years were at significant risk of developing pneumonia compared to blunt chest wall trauma patients under the age of 65 years. (Brasel et al 2006, Stawicki et al 2004, Bergeron et al 2003, Bulger et al 2000,) Inci et al (1998) reported that patients 60 or above had an increased risk of developing pneumonia however the results were not statistically significant. Testerman (2006) reported a significantly higher rate of pneumonia in blunt chest trauma patients aged 45 years and above with four or more rib fractures compared to younger patients with the same severity injury. Two studies reported no differences in morbidity rates between elderly and adult blunt chest wall trauma patients. (Sirmali et al 2003, Shorr et al 1989)

The blunt chest wall trauma patient's age was also reported as a risk factor for increased length of hospital stay and is illustrated in table 2.3.4. Three studies reported blunt chest wall trauma patients aged 65 years and above had a significantly longer length of hospital stay than blunt chest wall trauma patients aged less than 65 years. (Stawicki et al 2004, Bergeron et al 2003, Bulger et al 2000 et al) In contrast, Testerman (2006) reported no differences in length of stay in blunt chest wall trauma patients above or below the age of 45 years. Two studies reported that blunt chest wall trauma patients over the age of 65 years were less likely to be discharged home than younger blunt chest wall trauma patients, however the results were not statistically significant. (Sharma et al 2008, Bulger et al 2000) Length of stay may be influenced however by the differences in 'on-going' care (rehabilitation facilities available) between different healthcare systems.

2.3.5 Number of rib fractures as a risk factor for mortality (primary outcome measure)

The number of rib fractures sustained was another risk factor for poor outcomes. Tables 2.4 to 2.8 illustrate the variability that existed across the studies in terms of number of rib fractures in which poor outcomes were considered significant. Eight studies concluded that patients sustaining three or more rib fractures were at significantly increased risk of mortality compared with patients sustaining less than three rib fractures. (Harrington et al 2010, Perna and Morera 2010, Lien et al 2009, Sharma et al 2008, Brasel et al 2006, Bergeron et al 2003, Liman et al 2003) Svennevig et al (1986), Kulshrestha et al (2004) Sirmali et al (2003) reported that four, five and six rib fractures respectively were the crucial numbers of fractures leading to increased risk of mortality. Four studies reported a correlation between an increasing number of rib fractures with increased patient mortality. (Flagel et al 2005, Stawicki et al 2004, Barnea et al 2002, Bulger et al 2000) Three studies reported no differences in mortality rates for any given number of rib fractures. (Elmistekawy and Hammad 2007, Testerman 2006, Holcomb et al 2003)

The studies investigating three or more rib fractures as a risk factor for mortality in blunt chest wall trauma patients were used to calculate combined odds ratios. Figure

2.3 illustrates the results of the combined studies for odds of mortality in patients with three or more rib fractures.

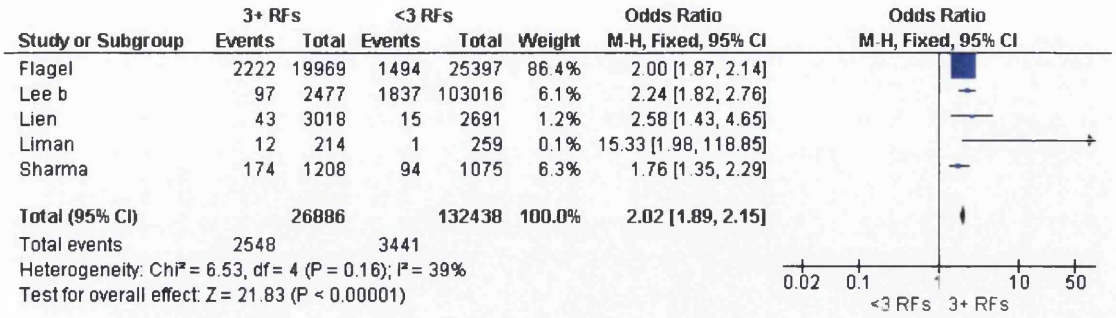


Figure 2.3: Forest plot illustrating the odds of mortality for patients with three or more rib fractures

The combined odds ratio for mortality in patients with three or more rib fractures was 2.02 (1.89-2.15, 95% CI). The I^2 statistic of 39% for this meta-analysis however indicates a moderate level of heterogeneity between the included studies. The Z result of 5.15 ($p<0.00001$) suggests that the overall effect is significant and therefore the odds of death in patients with three or more rib fractures is significantly higher when compared with patients with less than three rib fractures.

2.3.6 Number of rib fractures as a risk factor for morbidity and length of stay (secondary outcome measures)

Table 2.5 highlights the studies in which the number of rib fractures sustained is investigated as a risk factor of morbidity. Two studies reported that patients with three or more rib fractures are at increased risk of developing pneumonia compared to patients with less rib fractures. (Brasel et al 2006, Bergeron et al 2003) Patients with four or more rib fractures were reported to have increased rates of morbidity than patients with three or less rib fractures. (Testerman 2006, Holcomb et al 2003) Three studies demonstrated a significant increase in the incidence of pneumonia with each successive rib fracture sustained. (Elmistekawy and Hammad 2007, Flagel et al 2005, Barnea et al 2002) A correlation between an increasing number of rib fractures and an increased length of hospital stay was reported in two studies. (Flagel et al 2005, Stawicki et al 2004) In contrast however Sharma et al (2008) reported no correlation between number of rib fractures and length of stay.

2.3.7 Presence of pre-existing conditions as a risk factor for mortality (primary outcome measure)

The occurrence of a pre-existing condition or co-morbidity was another risk factor investigated for mortality. (Table 2.4 to 2.7). Bergeron et al (2003) reported an adjusted odds ratio of 2.98 (1.1-8.3 95% CI) for mortality in rib fracture patients with a pre-existing condition. Similarly, Brasel et al (2006) reported an adjusted odds ratio of 2.62 (1.93-3.55, 95% CI) for mortality in rib fracture patients with congestive heart failure. The results of four other studies concurred and highlighted that rib fracture patients who have cardiopulmonary disease are at a significantly increased risk of mortality than patients without cardiopulmonary disease. (Harrington et al 2010, Elmistekawy and Hammad 2007, Barnea et al 2002, Alexander et al 2000)

Meta-analysis of the studies investigating pre-existing conditions as a risk factor for mortality following blunt chest wall trauma was performed and the results are illustrated in Figure 2.4.

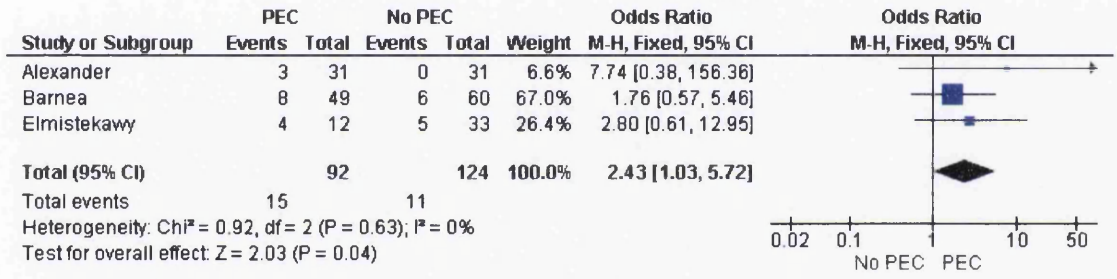


Figure 2.4: Forest plot illustrating the odds of mortality for blunt chest wall trauma patients with pre-existing conditions

A combined odds ratio of 2.43 (1.03-5.72, 95% CI) was calculated in this meta-analysis. Heterogeneity between the three studies was reported to be low, with an I^2 statistic of 0% however it could be suggested that in a meta-analysis with only three studies, this result should be interpreted with caution. This is further evident as the confidence intervals for the calculated odds ratios for each included study are very wide and all include the value 1. The calculated Z statistic for overall effect size of 2.03 (p=0.04) indicates that blunt chest wall trauma patients with pre-existing conditions are at significantly increased risk of mortality.

2.3.8 Presence of pre-existing conditions as a risk factor for morbidity and length of stay (secondary outcome measures)

Bergeron et al (2003) reported an adjusted odds ratio of 2.62 (1.2-5.7, 95% CI) for pneumonia in blunt chest wall trauma patients with pre-existing conditions and similarly, Brasel reported an adjusted odds ratio of 1.97 (1.62-2.40, 95% CI) for pneumonia in patients with chronic pulmonary disease. Diabetes was also reported in two studies to be a risk factor of morbidity in patients sustaining blunt chest wall trauma. (Elmistekawy and Hammad 2007, Brasel et al 2006) The study by Alexander et al (2000) demonstrated a significantly higher rate of morbidity and longer hospital and Intensive Care Unit length of stay in the elderly blunt chest wall trauma group with pre-existing cardiopulmonary disease compared to the elderly group with no pre-existing disease (all $p<0.05$).

Interestingly, the study by Stawicki et al (2004) reported that the effect of pre-existing conditions was most pronounced for patients with less than four rib fractures, suggesting an inverse relationship between variables. The authors concluded that the effect of pre-existing conditions was greatest at intermediate levels of injury, where outcomes or prognosis was less predictable. However, no other study reported similar results.

2.3.9 On-set of pneumonia as a risk factor for mortality (primary outcome measure)

Table 2.4 indicates that in a number of the selected studies, the on-set of pneumonia in the recovery phase following the injury, was reported to be a significant risk factor of death following blunt chest wall trauma. Bergeron et al (2003) reported that blunt chest wall trauma patients with pneumonia had nearly four times the odds of dying when compared with patients without pneumonia. (OR: 3.80; 95% CI, 1.5-9.7) Similar significant results were demonstrated by Brasel et al (2006) who reported an odds ratio of 3.5 (2.2-5.7, 95% CI) for mortality in isolated blunt chest wall trauma patients who develop pneumonia. Three other studies reported a significantly higher mortality rate in rib fracture patients who develop pneumonia. (Harrington et al 2010, Elmistekawy and Hammad 2007, Svennevig et al 1986) Meta-analysis of the studies

investigating the development of pneumonia as a risk factor for mortality following blunt chest wall trauma was performed and the results are illustrated in Figure 2.5.

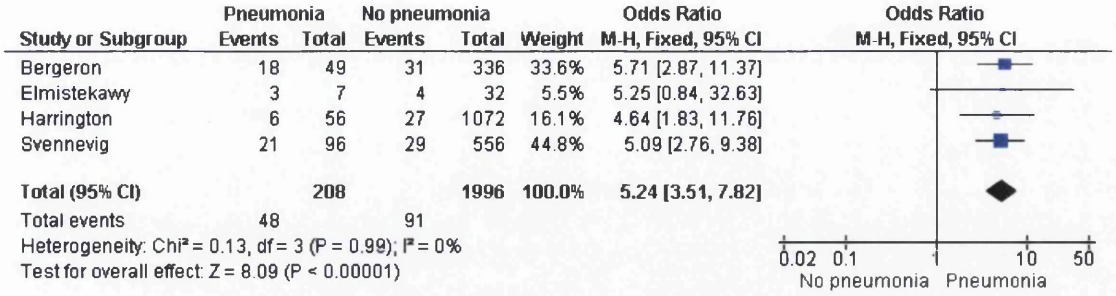


Figure 2.5: Forest plot illustrating the odds of mortality for blunt chest trauma patients who develop pneumonia

A combined odds ratio of 5.24 (3.51-7.82, 95% CI) was calculated in this meta-analysis. Heterogeneity between the three studies was reported to be low, with an I^2 statistic of 0% however it could be suggested that in a meta-analysis with only four studies, this result should be interpreted with caution. The calculated Z statistic of 8.09 ($p<0.00001$) for overall effect size indicates that blunt chest wall trauma patients who develop pneumonia are at significantly increased risk of mortality.

2.3.10 Other risk factors

Other risk factors outlined in Table 2.8 were investigated in single, individual studies which did not allow any cross-comparison between studies. The patient's respiratory function on admission to the ED was investigated in a number of individual studies. One study investigated vital capacity within 48 hours of ED evaluation in a small elderly cohort of blunt chest wall trauma patients (n=38) and suggested that bedside vital capacity (VC) could predict length of stay, but not morbidity or mortality. (Bakhos et al 2006) In another study, decreased oxygen saturations on presentation to the ED were reported to be a risk factor for increased morbidity in patients with isolated rib fractures (p=0.009). (Barnea et al 2002) Similarly, in a study by Hoff et al (1994), a Pa02/Fi02 ratio of less than 250 on admission to the ED was found to be a risk factor for mortality, LOS greater than seven days and pulmonary complications in adults diagnosed with pulmonary contusion on chest radiograph, but not in the general blunt chest wall trauma population.

Body mass index (BMI) was investigated as a risk factor for need for placement on mechanical ventilation and duration of ventilation following blunt chest wall trauma. (Reiff et al 2007) Overweight and obese patients were reported to have increased risk of placement onto mechanical ventilation following blunt chest wall trauma compared to patients with normal BMI (odds ratio of 1.40, 95% CI 1.08-1.81 and odds ratio of 1.53, 95% CI 1.17-1.99 respectively). (Reiff et al 2007)

Svennevig et al (1986) examined the number of blood transfusions required by the blunt chest wall trauma patient as a risk factor for mortality or incidence of pneumonia, sepsis or coagulopathy. They reported that the number of blood transfusions required during acute resuscitation was a risk factor of mortality ($p<0.05$). Barnea et al (2002) reported that the patient's haemoglobin level on admission was not a risk factor of morbidity or mortality in patients with isolated blunt chest wall trauma with no associated injuries.

Three studies investigated the Injury Severity Score (ISS) as a risk factor for the need for placement on ventilation, the number of ventilator days and complications. (Athanassiadi et al 2010, Athanassiadi et al 2004, Albaugh et al 2000) It was reported that the likelihood of death increased by 30% for each unit increase in ISS and furthermore that a high score on the ISS in the elderly may reflect a more lethal condition than similar scores in the younger population. (Albaugh et al 2000) Athanassiadi et al (2004) found that the ISS was a strong risk factor of morbidity and LOS but not mortality in flail chest patients but in a later study in 2010, the same authors found that the ISS was a strong risk factor of mortality in flail chest patients. Similarly, a number of studies reported associated injuries as a risk factor for mortality in blunt chest wall trauma patients however, the deaths were primarily due to associated injuries and not blunt chest wall trauma in these studies. (Borman et al 2006, Brasel et al 2006, Kulshrestha et al 2004, Shorr et al 1989)

In both studies by Lee et al (1989, 1990) the Injury Severity Score (ISS) was used as an outcome measure, investigating whether three or more rib fractures is a useful triage model or risk factor of need for transfer to a trauma centre. They reported that in a group of patients with three or more rib fractures, there was a significant

difference in ISS, mortality and LOS ($p<0.001$) compared with patients with one or two rib fractures.

2.4 Discussion

This systematic review was conducted in order to summarise the risk factors for mortality, morbidity and utilisation of resources in blunt chest wall trauma patients who can normally be safely discharged home from the emergency department, but will develop later complications. Klein et al (2002) stated that controversy remains regarding methods to identify the mild to moderate blunt chest wall trauma group who develop late complications. Studies investigating only severe blunt chest trauma patients, such as intra-thoracic injuries were excluded in order to minimise confounding of this study's results. The population of interest in this study was those patients with blunt chest wall trauma in which the management decision is less straightforward due to a lack of immediate life-threatening injuries requiring either surgical or intensive care management.

To date, no systematic review has been completed on this topic. A total of 30 studies were identified using a search strategy that met the criteria laid down in the PRISMA, MOOSE and CRD guidelines. All identified studies were observational studies using either a retrospective or prospective cohort study design and were published in peer-reviewed journals with the earliest study in 1986 and the most recent in 2010. The studies selected were assessed for their methodological quality which was found to be variable, but rather than exclude studies as a result of methodological issues, it was decided to include all studies and discuss any limitations.

The primary outcome measure investigated in this study was mortality. Increasing age and its predictive value on mortality in trauma has been investigated in the research extensively. Questions still remain regarding the exact age at which risk of mortality increases significantly and whether the increased mortality in the elderly is due to loss of physiologic reserve, or underlying co-morbidities common in the elderly. In this study, results of the meta-analysis suggest that an age of greater than 65 years is a risk factor for mortality in blunt chest wall trauma patients. Results also suggest that pre-morbid conditions especially cardiopulmonary disease and diabetes,

irrespective of age, were risk factors for mortality in blunt chest wall trauma patients with no associated injuries. Meta-analysis results indicate that patients with three or more rib fractures are at increased risk of mortality. A number of other studies investigated four, five and six rib fractures as the point at which increased risk of death occurs resulting in limited possibility for cross-comparison. Increasing number of rib fractures were demonstrated to lead to an increased length of stay and higher levels of morbidity.

Vital capacity and Pa02/Fi02 ratio were also investigated as a risk factor for mortality in blunt chest trauma patients in single poor quality studies however there is insufficient evidence currently in the literature to draw conclusions. A high ISS score was reported to be a risk factor for mortality following blunt chest trauma however this scoring system was designed for use with multi-trauma patients and has not been validated for use in the blunt chest trauma patients.

Mortality as a result of pneumonia in trauma patients remains controversial. Results of the meta-analysis suggest that blunt chest wall trauma patients who develop pneumonia have significantly higher mortality than blunt chest wall trauma patients who don't develop pneumonia. These results were reported in the blunt chest wall trauma patients with no associated injuries, thus reducing the level of confounding in the studies. The results highlight the need for appropriate management of this patient population in order to minimise the on-set on pneumonia in the patient's recovery, including adequate analgesia and pulmonary hygiene.

Meta-analysis of four of the risk factors for mortality following blunt chest trauma was completed. Further meta-analysis was not completed due to substantial heterogeneity and also a number of the studies did not provide sufficient raw data to calculate the odds ratios for inclusion in the meta-analysis. Definitions of the secondary outcome measures investigated especially 'morbidity' and 'discharge disposition' also lacked consistency across the selected studies. Meta-analysis of such studies was consequently considered inappropriate and the studies were discussed individually.

One of the secondary outcome measures investigated in this study was morbidity. Limited consensus existed in the literature regarding all the risk factors for morbidity in blunt chest wall trauma patients and cross comparison is not possible due to the limited use of standardised definitions for 'morbidity' used in the studies. Results suggest however, that elderly blunt chest wall trauma patients are at increased risk of pneumonia. Hospital length of study and discharge disposition was another secondary outcome measure investigated in this study. Variation in the definition of discharge disposition was also evident in the studies resulting in limited potential for cross-comparison however the results demonstrate that that the need for on-going medical care was higher in the elderly group. Results suggest that elderly patients with blunt chest wall trauma have an increased number of ventilator days, hospital and intensive care unit stay compared to their younger counterparts.

Quality assessment of the studies was undertaken. The first component of quality evaluated was study design. Research has suggested that a retrospective study design may lead to reduced reliability compared with a prospective study due to the inability to establish causation. (Brasel et al 2006, Flagel et al 2005) This inability to establish causation when analysing a database retrospectively may have exacerbated the problem of confounding. For example, reported outcomes by the studies in this review such as mortality rate or number of ventilator days may be attributed to associated injuries such as a head injury and not blunt chest wall trauma. In a number of studies in this review, this problem was addressed by attempting to exclude patients with associated injuries, or by adjusting results to account for the confounding effects. A number of the authors concluded that in order to further enhance the reliability of the results in their studies, a prospective study was required. (Reiff et al 2007, Testerman 2006, Holcomb et al 2003, Bulger 2000, Lee et al 1989)

An inability to independently verify any of the diagnoses as all the retrospective data is based on codes could potentially affecting reliability of the studies' results. (Brasel et al 2006) A known limitation of retrospective database analysis is the inability to ascertain the cause of death in the patient cohort. (Flagel et al 2005) In all of the studies identified that used a trauma database for analysis, the exact cause of death may be attributable to causes unrelated to the blunt chest trauma, a limitation which is exacerbated in the studies including patients with associated injuries. It has

therefore been reported that the studies should only comment on associations, and not directly attribute cause and effect. (Brasel et al 2006)

Further limitations of using trauma databases for data collection were outlined in a number of the studies. (Lien et al 2009, Brasel et al 2006, Flagel et al 2005) It has been commented that trauma databases are not specifically designed to identify pre-existing diseases or complications and these are infrequently reported by centres contributing to the databases. (Flagel et al 2005) Co-morbidities, nutritional and functional status of the patients on admission to the ED are rarely reported on trauma databases. (Holcomb et al 2003) Database reporting is always open to bias by the staff involved in their completion. Database generation requires staff to complete data extraction from paper-based medical records, resulting in potential missing or erroneous data. As a result of the lack of uniform criteria and definitions, databases are subject to both selection and information bias. (Flagel et al 2005) The study by Stawicki et al (2004) considered another limitation to database analysis to be the lack of information on living wills and advanced directives. Databases fail to record management strategies used in patient care. Specific therapies used in the management of the blunt chest trauma patients such as chest drains or epidural catheters may have further affected the morbidity and mortality outcomes.

The second component of quality evaluated was outcomes, which referred specifically to the inclusion of fully referenced definitions for each outcome measure. A lack of referenced definitions for both the independent and dependent variables in the studies was highlighted in the quality assessment. It could be suggested therefore that this affected the external validity and reproducibility of the study and furthermore, made cross-comparison of the selected studies questionable. (Glasziou 2001) For example, in the studies investigating risk factors in patients with blunt chest wall trauma, the reader may question whether this included patients with rib fractures, flail segments, pulmonary contusion, pneumothorax, soft tissue injuries or a combination of any of these. Therefore a definition of 'blunt chest wall trauma' was required or clearly defined exclusion criteria when selecting a sample population. (Greenhalgh 2006)

Mortality was commonly used as an outcome measure in the studies however only six of the studies in this review defined mortality within a specific time frame. The time frames specified ranged between 24 hours to 30 days. A number of authors have demonstrated clinical compensation frequently occurs days after the initial chest injury. (Alexander et al 2000, Simon et al 1998, Shorr et al 1989) A pre-specified time frame for mortality would therefore increase both reliability and external validity of the studies. Only the study by Barnea et al (2002) discussed the duration of follow up of the patients included in the study. Sufficient follow up duration is required in order to ensure any reported results are not time dependent and if this is the case, that the authors discuss this in their findings. (Greenhalgh 2006)

Morbidity was another outcome measure used in the studies however in a number of the papers there was no definition of morbidity, time frames or diagnosis criteria. This invariably affects the reliability of the results and reproducibility of the studies. Some studies used the presence of pneumonia to define morbidity, yet provided no explanation regarding how pneumonia was diagnosed. Brasel et al (2006) outlined how even the best existing diagnostic tests for pneumonia are imperfect. Other studies use atelectasis, acute respiratory distress syndrome, pneumothorax or haemothorax to describe morbidity. (Bakhos et al 2006, Barnea et al 2002, Albaugh et al 2000) A number of studies used the 9th Revision of the Clinical Modification of International Classification of Diseases (ICD-9CM) codes to define or categorise the chest trauma suffered by the patient, but again, the codes used differ between the studies. (Lien et al 2009, Brasel et al 2006, Flagel et al 2005, Stawicki et al 2004, Peterson et al 1994, Lee et al 1990)

Other outcome measures included in the studies were related to utilisation of resources. The need for mechanical ventilation, number of ventilator days, Intensive Care Unit and Hospital length of stay and discharge disposition were commonly used as outcome measures however definitions were again inconsistent across studies. The effect of confounding may be substantial when using 'utilisation of resources' as an outcome measure. It is evident that different centres will have different criteria for ICU admission, need for ventilation, weaning protocols and discharge facilities. It could be argued that variability may exist in the studies due to the difference in criteria for admittance to ICU in different hospitals. In some hospitals blunt chest

wall trauma patients may be managed with epidural catheters which are managed on the ICU, in contrast to other hospitals where epidural catheters may be managed in the ward environment. In order for the studies to be reproducible therefore, full definitions and explanations of all independent and dependent variables are required. (Glasziou et al 2001)

Another stage of the quality assessment process of the studies involved determining whether the selected cohort was representative of the general blunt chest trauma population. Most of the studies were considered representative of the blunt chest trauma population, however four studies investigated flail chest only, one investigated pulmonary contusion and one investigated blunt chest trauma secondary to motor vehicle accident. These studies were thought not to be representative of the general blunt chest trauma population, but were included in the study as they provided valuable information on a sub-group of the general blunt chest trauma population. This marked variation between the selected studies in terms of the sample investigated also resulted in a lack of possible cross-comparison and difficulty drawing conclusions.

The size of the groups was also considered in the quality assessment. All studies should have a sample size or power calculation performed prior to the commencement of data collection. The sample size needs to be large enough to detect a true effect if it exists, thus enhancing reliability of the study's results. (Greenhalgh 2006) A number of the studies reported large numbers of patients analysed, but when the patients were placed in sub-groups according to age for example, the sample size was reduced substantially. The studies selected for this review did not discuss power calculations therefore it could be suggested that the results lack the reliability of the studies with larger sample sizes.

Comparability of groups was also examined as part of the quality assessment process. It has been stated that the selection of a comparable control group in an observational study is the most difficult decision facing the authors. (Greenhalgh 2006) The difficulty exists in identifying two exact groups in terms of age, presence of co-morbidity, injury severity and respiratory or functional status on admission with the single difference being only the risk factor under investigation. In a number of the

studies investigated, statistical adjustment for baseline differences in key variables was performed and reported at the analysis stage of the study. These studies explicitly reported any differences in the groups, especially in terms of age, injury severity and co-morbidity, unless it was one of these variables under investigation. In two of the selected studies however no comparison group was used and results were based on statistical analysis which included linear or logistic regression and multivariate analysis of the single cohort studied.

In addition to the components of the quality assessment model, the effects of confounding were considered in the studies. The effect of confounding on the reliability of observational studies has been investigated extensively in the literature. In an article by Smith and Phillips (1992), it was concluded that many of the associations identified in studies are due to confounding, often by factors which are difficult to measure. It was evident that there was a significant level of confounding in the selected studies. As a result of the difficulty in negating the effects of confounding in observational studies, it is important that the results of each individual study are interpreted with caution.

A number of the studies in the review included patients with associated injuries or multi-trauma when studying a cohort of blunt chest trauma patients. It is possible that the patients may have suffered poorer outcomes as a result of a head or abdominal injury which were unrelated to the blunt chest trauma. Similarly, the studies in the review which investigate risk factors affecting outcomes following blunt chest trauma in elderly patients only, it is possible that the authors are immediately introducing confounding as increased age is a proven independent risk factor of mortality, regardless of the other risk factors being investigated. (Sharma et al 2008, Brasel et al 2006, Bergeron et al 2003) For example, poor outcomes could be attributable to increased age and not the number of rib fractures sustained or the patient's respiratory status on admission to the ED.

Further confounding variables were identified in the included studies that investigated length of stay on ICU. None of the included studies discuss whether the length of stay on the High Dependency Unit (HDU) was included in the results. It could be argued that one hospital may use non-invasive ventilation to manage a blunt

chest wall trauma patient in respiratory distress on the ward or HDU in order to minimise the need for ventilation and admission to ICU, whereas another may ventilate a patient early to avoid late complications. Similar confounding was evident in the studies investigating discharge disposition as an outcome measure. Discharge facilities vary from one centre to another, so one centre may have more care in the community which would facilitate earlier discharge, whereas another centre may have to keep patients in hospital until they are fit for discharge home with no extended care.

The development of pneumonia in the recovery phase following the injury (as an outcome measure) is a further potential example of confounding evident in the studies. A number of patients with blunt chest trauma are managed with the use of mechanical ventilation. Mechanical ventilation is a known risk factor for pneumonia, which potentially could be a confounding variable in these studies. (Flagel et al 2005) It is questionable whether various risk factors such as age or number of rib fractures as a cause of pneumonia in patients with blunt chest trauma who require mechanical ventilation as part of their management.

The relationship between the risk factors identified in this review should be examined carefully, as it could be suggested that poor outcomes following blunt chest trauma are rarely caused by one risk factor alone. For example, the elderly patient is more likely to suffer from an increased number of pre-existing conditions than their younger counterparts. (Perdue et al 1998, Morris et al 1990) Age alone therefore may not be the risk factor for increased mortality following blunt chest trauma, but potentially more importantly, the presence of co-morbidity. Physiological reserve becomes reduced with increased age leading to a consequential decrease in the ability to recover from trauma and a reported increase in mortality rates. (Perdue et al 1998) Therefore, the studies that fail to employ methods to adjust for confounding secondary to inter-related risk factors should be read with caution.

2.5 Limitations

Systematic reviews of observational studies remain a contentious issue in research. Identification of potential forms of bias is especially important in observational

studies, which are sensitive to publication bias and confounding. No restrictions were used in an attempt to minimise any possible bias. (CRD 2009) As with all systematic reviews the results of this review are subject to publication bias as research has suggested that often the studies with significant findings are more readily published in peer-reviewed journals than those without. (Greenhalgh and Peacock 2005, Chalmers and Altman 1995) Furthermore, research has highlighted that there is a tendency among authors to only present significant results and omit non-significant findings, thus increasing publication bias. (CRD 2009, Greenhalgh and Peacock 2005) It could be suggested therefore that studies may have investigated the interaction of several risk factors for poor outcomes in blunt chest trauma but published only those that were interesting or statistically significant. The studies with positive results are most likely to be published in English language journals and often more than one journal, resulting in a higher chance of capture in the search process. (Bowers 2008) The search strategy included a number of methods to reduce publication bias as suggested in the CRD guidelines but no unpublished studies investigating risk factors were identified in the search. Publication bias is therefore possible in this review and results should be interpreted with possible bias as a consideration.

2.6 Conclusions

In this systematic review and meta-analysis, the most significant risk factors for increased morbidity, mortality and utilisation of resources in patients sustaining blunt chest wall trauma were a patient age of 65 years or more, three or more rib fractures, the presence of pre-existing disease especially cardiopulmonary disease or diabetes and the development of pneumonia post injury. However, as a result of the variation in outcome measures used, the quality of the studies and lack of referenced definitions of independent variables used in the studies, the results of the selected studies should be interpreted with caution. Further prospective studies are needed in order to fully validate the reported results of the selected studies for this review.

3.0 Expert opinion of the risk factors for morbidity and mortality in blunt chest wall trauma: results of a national postal questionnaire survey of Emergency Departments in the United Kingdom.

3.1 Background

3.1.1 Data collection methods

As the controlled experiment research design is not always appropriate for all types of measurement in scientific research a number of methods have been described for data generation and collection. (Oppenheim 1992) These include the face-to-face interview, telephone surveys and postal questionnaires. (Boyton and Greenhalgh 2004, Streiner and Norman 2008, Oppenheim 1992) Each of these methods has their own unique advantages and disadvantages which need to be considered fully when designing a study aimed at data generation and collection. Health surveys provide important sources of information for evidence-based medicine. In order that the investigator can collect the most accurate data from the respondents, the health survey must be unbiased. Bias may arise from the way the survey is designed, the way individual questions are asked and how the survey is administered or completed. For each of the methods used in health surveys, consideration of the effect of bias is paramount.

Interviews: Face-to-face interviews are one of the most widely used methods of data collection in research and involve a direct meeting between an interviewer and an interviewee. (Oppenheim 1992) Various methods are used in interviews to collect data and one which is frequently utilised is the completion of a structured pre-designed questionnaire and an example of which being the Hospital Anxiety and Depression Scale (Zigmund and Snaith 1983) Face-to-face interviews in which the interviewer is present during the completion of the questionnaire by the respondent have a number of benefits including flexibility in presenting the items and the ability to clarify any misunderstandings related to the questions. The interviewer can be sure who is responding to the questions, in contrast to telephone or mailed questionnaires. In addition, in a face-to-face interview it is more difficult for the responder to omit any items as it might be when completing a postal questionnaire. Interviews however

are significantly more expensive and time consuming to administer than other methods of data collection and consequently sample size may be limited. (Oppenheim 1992)

A long interview may also be viewed as an imposition on the respondent. In order to collect data from a representative sample, often a large team of researchers is required. (Streiner and Norman 2008) The interviewer will have to be trained and instructed in the use of standardised probes in order to ensure sufficient inter-rater reliability. (Oppenheim 1992) The importance of the use of standardised probes is highlighted in the development of the Hamilton Anxiety Rating Scale in which the use of such probes was shown to increase inter-rater reliability. (Bruss et al 1994) The interviewer themselves may also affect responses given and consequently introduce bias and can also subtly lead the respondent into giving the answers they want to hear. (Streiner and Norman 2008) A review of literature identified and categorised 48 different types of bias found in questionnaire research focussing only on bias related to administration and design of the questionnaire and interview techniques. (Choi and Pak 2005) Bias can be caused by the interviewer's subconscious or conscious gathering of selective data. Non-blinding of the interviewer to the study hypothesis can also lead to the same bias. The best way of ensuring this form of bias is addressed is to ensure the interviewer is properly trained. (Choi and Pak 2005)

Telephone surveys: Telephone surveys have similar advantages to the interview and have also been shown to be cheaper to complete. (Streiner and Norman 2008) The sample obtained however is often determined by the time of day the call is made and who is available to respond. Another person may be prompting the respondent in a telephone survey or 'standing in' for the person to whom the interviewer believes they are speaking. (Streiner and Norman 2008) As in the face-to-face interview, the interviewer completing the telephone survey will have to be trained and instructed in the use of standardised probes in order to ensure sufficient inter-rater reliability. (Oppenheim 1992) In the telephone survey, difficulty may arise with questions that require the respondent to choose from various response options, a problem which is not encountered with the postal questionnaire. (Streiner and Norman 2008)

Postal questionnaires: Postal questionnaires are frequently used in medical research as an objective means of collecting information regarding a population's knowledge, beliefs, attitudes and behaviours. (Boynton and Greenhalgh 2004) Postal questionnaires are the cheapest method of collecting data from large populations. (Marshall 2005) Unbiased interpretation of the responses provided in a postal questionnaire is important in order to ensure the study results are valid. The data collection process can be coordinated from one central location even in national or international studies. (Streiner and Norman 2008) The major drawback of postal questionnaires is the difficulty in ensuring a good response rate. Non-response reduces the effective sample size and can introduce bias. (Edwards et al 2002) Respondents may also omit some of the questions or provide incomplete, invalid or illegible responses. In some instances, there may be a delay of up to three months before all the questionnaires are returned. (Streiner and Norman 2008) Methods can be employed to improve the response rate and a number of studies have been published that have investigated methods of achieving high response rates. (Greenhalgh 2006, Sharp et al 2006, Edwards et al 2002)

3.1.2 Response rates

Contacting the participants of the study prior to posting the questionnaire has been shown to increase response rates as did follow up contacts. (Edwards et al 2002). Higher response rates have been reported if a covering letter explaining the aim of the study is included with the questionnaire that is written on the research institution headed paper and looks different from that of a commercial organisation. A stamp-addressed envelope for questionnaire return and the use of first class recorded delivery have been reported to enhance response rate. (Edwards et al 2002) The use of a lottery incentive was reported to significantly improve response rate. (Kalantar and Talley 1999) Similarly, enclosing a pen was shown to significantly increase response rates. (Sharp et al 2006) The inclusion of gifts can introduce bias into the data collection process and arguably introduce potential conflict of interest. The reported influence of the length of the questionnaire on response rates varied between studies. Mond et al (2004) and Kalantar and Talley (1999) reported questionnaire length to have no influence on response rate in contrast to Edwards et al (2002) who reported that shorter questionnaires yield better response rates. The

use of electronic reminders was reported to reduce response time to postal questionnaires but had limited effect on response rate. (Ashby et al 2010). In contrast, a lottery incentive did not improve response rates in a separate study. (Harris et al 2008)

It has been noted that initial response rates are frequently too low to draw any reliable or valid conclusions. (Streiner and Norman 2008, Oppenheim 1992) It has been suggested that a response rate of less than 80% is insufficient to draw reliable conclusions and the British Medical Journal will only accept questionnaire papers for publication if the response rate is greater than 70%. (Greenhalgh 2006) Consequently, some form of follow up contact is required to improve overall response rate. (Streiner and Norman 2008) Some researchers stress however that low response rate should be less of a focus, with more emphasis on controlling bias. (Streiner and Norman 2008, Oppenheim 1992) It may be necessary to investigate whether the reasons for non-response are related to the topic of research. Such confounding variables will introduce bias and will result in conclusions which are lacking reliability and validity. (Oppenheim 1992) Non-response bias has been reported as the most important factor in assessing the effect of a response rate on the validity of a study. (Cummings et al 2001) If no differences are found between non-responders and responders, investigators can be more confident that their reported findings are reliable and valid, even with a lower than acceptable response rate. (Cummings et al 2001) Cummings et al 2001 stated that if the non-responders are similar to the responders, the response rate will not affect generalisability to the study population as responder bias is not present.

3.1.3 Administration of questionnaires

Careful planning of the research design is important when considering the administration of the questionnaire. The aim of quantitative or qualitative sampling is to obtain a representative sample from a population so that the results gained from studying the chosen sample can be generalised back to the larger population. (Marshall 1996) Identifying a sample that is representative of the population under investigation will reduce the risk of recruitment bias. Different sampling techniques have been described and include random, stratified random, opportunity, purposive,

convenience, quota or snowball samples. (Greenhalgh 2006, Marshall 1996) Studies that investigate areas of special expertise or knowledge may use a key informant sample, in which the researcher actively selects the most productive sample to answer the research question. (Marshall 1996) The sample also needs to be sufficiently large in order to detect any differences and to be as representative of the population as possible. (Boyton and Greenhalgh 2004) It is also important that the qualitative researcher provides the reader with explicit information on the research processes used in sampling to ensure a valid study. (Daly and Lumley 2002)

3.1.4 Design and content of questionnaires

The style of questionnaire used has been reported to be an important aspect of the research design and needs careful consideration as it can influence response rate and introduce bias. (Oppenheim 1992) The questionnaire may use open, closed or mixed format questions depending on the research design. (Boyton and Greenhalgh 2004) Open questions provide no options or pre-defined categories and the responder is free to offer any response. Closed ended questions offer the respondent a choice of fixed responses. Closed questions allow the researcher to collect and analyse data quickly, but the range of possible answers is pre-set by the researcher, which may frustrate the respondent and limit the richness of potential answers. The choice of answers in closed questions must be considered carefully in order to avoid the introduction of bias into the answers. (Oppenheim 1992) Free text boxes are advisable with closed ended questions to overcome these issues. Open questions are not followed by any choice of responses and provide richer responses but as a result are more time consuming to collect and complicated to analyse. (Streiner and Norman 2008)

The actual wording of the questions in a questionnaire will depend on the research topic and the information the researcher is attempting to capture. There are a number of basic rules described by Oppenheim (1992) regarding the wording of questions. These include the avoidance of questions that are leading or too lengthy, and questions that contain double negatives, jargon, abbreviations, words with alternative usage or ambiguous words such as 'frequently' and 'regularly'. (Oppenheim 1992)

Similarly, it is important to avoid asking about two separate issues in one question. (Streiner and Norman 2008)

The order that the questions appear on the questionnaire is also considered important. The 'funnel approach' is used frequently which involves using broad questions at the start of the questionnaire then progressively narrowing down the questions to more specific points. (Oppenheim 1992) The choice of question order will be determined however by the research design and the results obtained when piloting the questionnaire. Explicit instructions on how to complete each question are recommended in questionnaire research. (Marshall 2005, Boyton and Greenhalgh 2004) The ultimate aim is to ensure that the questionnaire is standardised, as this will increase its reliability. (Boyton and Greenhalgh 2004) The most appropriate method of checking the wording of the questions is to pilot the questionnaire. (Boyton 2004)

3.1.5 Questionnaire piloting

Research suggests that the use of an existing reliable and valid questionnaire will save both time and resources. (Boyton and Greenhalgh, 2004) If no such questionnaire exists however, the newly designed questionnaire should be piloted prior to completion of the finalised questionnaire by the research sample. (Streiner and Norman 2008, Oppenheim 1992) The pilot study is essential to assess the wording, length and content of the questionnaire and to determine if a redraft if necessary. The respondents in the pilot study can provide feedback about the questionnaire including whether any vital areas relating to the research topic were omitted. The respondents also need to be representative of the population under investigation in the main study. (Greenhalgh 2006) The data gained in the pilot needs to be analysed to ensure usable results can be obtained from the questionnaire. If redrafting is required, it may be necessary to re-pilot the questionnaire a second time. (Marshall 2005)

3.1.6 Reliability and validity

A pilot study can assist in ensuring that questionnaire is reliable and valid. The extent to which results are consistent over time and an accurate representation of the total

population under study is referred to as reliability. Reliability refers to the consistency or repeatability of the measure. (Marshall 2005) Validity refers to the degree to which the instrument truly measures what it intends to measure. (Marshall 2005, Boyton and Greenhalgh 2004) Selection of an appropriate representative sample and sufficient sample size can contribute to the validity of the questionnaire. (Marshall 2005)

3.1.7 Data processing and analysis

Methods have been described in the literature concerning ways of maintaining accuracy of quantitative data during completion of data entry. (Boyton 2004, Oppenheim 1992) Errors in the data entry process such as typing errors or misinterpretation of a respondent's answer may lead to unreliable and invalid results and conclusions. Methods to avoid this include avoiding fatigue and taking regular breaks, working with a colleague, running statistical frequencies on all items and scanning the results for obvious anomalies. (Boyton 2004)

Incomplete data is another difficulty facing the researcher using questionnaires. It may be necessary again to investigate whether the missing data are related to the topic under investigation. How the missing data are accounted for depends on the type of analysis to which the data will be subjected. (Oppenheim 1992) Rejecting all questionnaires with missing data or 'listwise deletion' can decrease the response rate significantly as the entire questionnaire is excluded from analysis. In 'pairwise deletion' the remaining responses on the incomplete questionnaire are included in the analysis. It is important to deal with missing data carefully as listwise deletion can introduce bias. (Oppenheim 1992) Collecting and analysing geographic or demographic data on non-responders is recommended as this will allow the researcher to monitor and modify the research process thus potentially reducing bias. (Oppenheim 1992) Similarly, collecting data on omitted questions will assist the researcher to alter the questionnaire if appropriate or examine reasons for the omitted data. (Boyton 2004)

Analysis of the questionnaire will be dependent on the style of questions used. Recognised statistical tests should be used for analysis of closed-ended questions such as means and standard deviations for descriptive analysis or Chi-squared,

Spearman and Wilcoxon tests for more in-depth analysis. For rating scales or visual scales the use of Pearson, t-test and analysis of variance tests are recommended (Greenhalgh 2006) A recognised method of analysis for qualitative analysis in open-ended questions or free text replies is recommended such as the use of thematic content or discourse analysis. (Boyton 2004)

3.1.8 Guidelines for questionnaire studies

Although clear guidelines exist on the design and reporting of both the randomised controlled trial (CONSORT) and the meta-analysis (PRISMA), an equivalent framework does not exist for the design and reporting of questionnaire research. (Greenhalgh 2006) Methodological errors are common therefore in questionnaire research undertaken by health professionals. It has been suggested that this lack of rigour in questionnaire research inevitably results in poor quality studies with conclusions which are often misleading. (Boyton and Greenhalgh 2004) A series of papers were published in the British Medical Journal (Boyton 2004) which provided guidelines to assist the researcher undertaking questionnaire research. These guidelines provide an overview of methods that should be used to ensure a questionnaire study is reliable and valid, non-discriminatory and contributes to a generalisable evidence base. (Boyton and Greenhalgh 2004)

3.1.9 Ethical considerations

There are a number of ethical considerations when completing questionnaires on NHS patients or staff in the UK. The study must be formally approved and registered with a trust Research and Development department. A university or hospital trust must also obtain ethical approval from an appropriate research ethics committee if appropriate. In some cases, ethical approval is not required for example in a study that is focussed on service evaluation. Researchers must also consider and comply with data protection law. (Boyton and Greenhalgh 2004)

3.1.10 Questionnaires and the physician.

The term physician is used in this context to describe a medical doctor of any grade working in any speciality in primary or secondary care, but not including surgeons.

The use of questionnaires for investigating professional behaviour is controversial as some researchers believe that what a physician reports in a questionnaire they do, is not always the same as what they actually do (adjusted response), particularly when they believe that their method of practice is being scrutinised by a researcher. (Boyton and Greenhalgh 2004) In order to collect information regarding physicians' beliefs or expert opinion however, the descriptive survey design is considered by Oppenheim (1992) to be the most appropriate. The questionnaire used in the descriptive survey design is purely fact-finding and descriptive. (Oppenheim 1992) The use of questionnaires to collect information from physicians has been investigated by numerous researchers. (Cummings et al 2001, Kellerman and Herold 2001, Asch et al 1997) Physicians have been reported to have a 14% lower response rate than those of non-physicians. (Asch et al 1997) In published articles, Cummings et al (2001) reported that the average response rate for mailed physician questionnaires was 61% (individual study sample sizes not known) and the average response rate for large sample physician questionnaires (greater than 1000 participants) was 52%. Mailed questionnaires were reported to have better response rates than telephone or personal interview surveys. (Kellerman and Herold 2001)

One study reported that structuring the questionnaire with general questions first can significantly increase response rate in postal questionnaires sent to primary care physicians. (Drummond et al 2008). This study also reported that written pre-contact did not significantly increase response rate. (Drummond et al 2008) In another study investigating mailed physician questionnaire, Jepson et al (2005) found that there was a threshold level of questionnaire length of approximately 1000 words and above this threshold, response rate decreased. These authors also stated that physicians are unlikely to be influenced by monetary incentives. (Jepson et al 2005) In contrast however, one study reported a significantly lower response rate in a promised-incentive group of physicians compared with an up-front incentive group of physicians. (Delnevo et al 2004) In a study by Kellerman and Herold (2001) monetary incentives, the use of stamped addressed return envelopes and shorter questionnaires all increased response rates in physicians. These small monetary incentives such as a book token or lottery ticket do not involve any conflict of interest however this may be a consideration if much larger monetary incentives were introduced. (Streiner and Norman 2008)

3.2 Introduction

There has been a dramatic increase in the number of people attending Emergency Departments (ED). The total number of attendances at all Emergency Departments in England increased from 14,293,307 in 2000-2001 to 20,511,908 in 2009-2010. (Department of Health 2010) In order to risk stratify the blunt chest wall trauma patient, the risk factors for development of complications in the recovery phase need to be identified. Following the identification of the risk factors, a care pathway could be developed which would detail the essential steps of effective management in the care of this patient group and thus decrease unwanted practice variation. (Campbell et al 1998)

The information gained regarding the Emergency Physicians' expert opinion on the risk factors for increased morbidity, mortality and resource consumption in blunt chest wall trauma patients, in conjunction with the results from the systematic review and meta-analysis, could form the basis for a prognostic model for the management of this patient group. The aim of this study therefore was to collect information on Emergency Physicians' beliefs and expert opinion regarding the risk factors for morbidity, mortality and resource consumption in England and Wales. For the purpose of this study, blunt chest wall trauma was defined as blunt chest injury resulting in chest wall contusion or rib fractures, with or without non-immediate life-threatening lung injury.

3.3 Methodology

This study was designed following available guidelines in questionnaire research (Streiner and Norman 2008, Oppenheim 1992) and the guidelines published in a series of papers in the British Medical Journal. (Boyton, 2004) Following a review of the literature, no questionnaire was identified which investigated Emergency Physicians' knowledge and expert opinion regarding the risk factors for any outcomes in blunt chest wall trauma patients. A new questionnaire was therefore designed.

3.3.1 Questionnaire design

The first stage in this process was devising the items for inclusion. It was decided that questions regarding demographic data should be included in order to ensure analysis of non-responders would be possible following data collection. These related to the type and size of the hospital in which the respondent was working when completing their questionnaire, the team to which the patients were referred if admission to hospital was required and what guidelines, if any, were followed in the management of the blunt chest wall trauma patient in the ED. A free text box was also included in order to allow the respondent to provide an answer which was not included in the choice of responses provided. Information regarding the way in which patients with blunt chest wall trauma are managed in their hospital was also requested. This was included in order that some basic conclusions could be drawn regarding current practice on a national level. In order to gain these data, the first three questions were closed-ended questions with a set choice of responses. The final question was open-ended in design, in which the respondent was asked to list all the risk factors they believed contributed to morbidity and mortality when assessing the blunt chest wall trauma patient. This question was open in design in order not to lead the consultant into providing specific responses and to reduce the risk of introducing response bias. All questions included specific instructions on how to complete the question. The questionnaire was printed on headed hospital and university headed paper in size 12 font. (Appendix B)

The questionnaire was designed in order to minimise potential bias. The questions were unambiguous and questions that were complex, double-barrelled or too short were avoided. Technical jargon and vague or uncommon words were also avoided. Questions were designed in such a way that they did not lead the respondents into giving a particular response. The questionnaire was also kept short to avoid response fatigue which can introduce bias. The guidance provided in a study by Choi and Pak (2005) was followed in order to minimise the bias in the questionnaire.
A covering letter was also designed which included an outline of the study, information regarding how long the questionnaire should take to complete, confidentiality and anonymity, clear contact details for further information and details on how to return the questionnaire. (Appendix B) The covering letter also explained that the purpose of the data collection was part of a study being completed by the principal author for an educational degree.

3.3.2 Pilot study

The first draft of the questionnaire and covering letter was distributed to six consultants working in the Emergency Department in Morriston Hospital, South West Wales, United Kingdom. This sample was purposively chosen as it was considered representative of the consultant population to be investigated in the main study. Morriston Hospital is a regional trauma centre in South West Wales with 750 beds and approximately 90,000 presentations to the ED per year and was therefore considered to provide an appropriate sample for the pilot study. A form was also attached which encouraged the consultant to provide feedback regarding the design and content of the covering letter and questionnaire. The feedback suggested that a question should be included that investigated the use of chest radiographs in the assessment of a blunt chest trauma patient. Following discussion of this, it was decided that this information would not provide any further valuable information for this study as the primary aim was to investigate expert opinions of the risk factors for morbidity and mortality in blunt chest wall trauma patients. All feedback regarding design and content of the covering letter and questionnaire was positive and no further refinements were considered necessary.

3.3.3 Study sample

As the aim of the study was to gain expert opinion of the risk factors for morbidity and mortality in blunt chest wall trauma patients presenting to the Emergency Department, a purposive key informant sample was used. A total of 100 major Emergency Departments out of a total of 203 (Unify2 2011) in England and Wales were selected for inclusion in this study in order to generate conclusions that were generalisable nationally from the data. The hospitals were selected to provide a range of district hospitals, teaching hospitals and regional trauma centres and also small, medium and large in size. The size of the hospitals were categorised by number of beds; small (less than 400), medium (400 to 599) and large (600 or more). (Button et al 2011) The hospitals were also selected in order to provide a sample with an even distribution geographically. Walk in Centres or Minor Injury Units were not included as a large number of these are run by a nurse or general practitioner and the study was focussed only on consultants working in the Emergency Departments. Only

consultants were targeted in this study as the purpose of the study was to gain expert opinion. It was considered that only using consultants was the most appropriate way of ensuring that the person completing the questionnaire had sufficient knowledge and experience to be regarded as an expert in Emergency Medicine due to the level of training and expertise required to become a consultant. The consultants were chosen randomly from the British Association of Emergency Medicine Directory for each of the selected hospitals.

3.3.4 Administration and distribution of the questionnaire

The selected consultants were given a reference number which was added to the questionnaire and recorded on the data collection spread sheet as the questionnaires were returned. This method was used to enable follow up contact for non-responders, with the aim of enhancing the response rate. Non-responder analysis was also possible using this method. However, no personal information was stored and all data were anonymised following data inputting and non-responder analysis. All respondents were assured that their responses would remain confidential throughout the study process. The consultants were provided with an explanation of this method of anonymity in the covering letter, allowing them to opt out of completing the questionnaire.

The Emergency Departments in question were contacted by email or telephone prior to sending the postal questionnaire notifying them in advance about the study and confirming that the selected consultant still worked at the hospital and would consider completing the questionnaire. At this stage, email or telephone contact was used in order to reduce cost of postage and save time. Once a suitable contact had been identified, the questionnaires were addressed to the named consultant working in each of the Emergency Departments. The covering letter and a stamp-addressed envelope was included (with return address) for return of the questionnaire. The most appropriate time for sending out the questionnaires was researched and discussed by the authors. No research or guidelines were found investigating timing of administration of questionnaires in physicians, therefore the questionnaires were sent at a time when the consultants would have be experiencing minimal additional

pressures. For example, questionnaires were not sent out during the winter months or when the junior doctors were starting their Emergency Medicine rotation.
A second set of questionnaires were sent out to non-responders after two months. As the researcher was not present when the questionnaires were completed, a self-completion design was used with clear instructions for completion of each question provided to all respondents. The instructions given to each respondent were the exactly the same in order to standardise the questionnaire and its completion.

3.3.5 Data processing

The questionnaire responses were entered onto an Excel spread sheet. Any questionnaires with missing demographic data were included in the study and the remaining responses included in the analysis. The questionnaires in which the respondent failed to suggest any risk factors for morbidity and mortality in blunt chest wall trauma patients were excluded. Data processing was completed by the principal researcher and a 10% validation check was completed. This involved a second researcher taking 10% of the completed questionnaires and assessing whether the data has been inputted accurately on the spread sheet by the principal researcher.

As the final question concerning possible risk factors was open-ended, all the variables suggested by the respondents were listed for inclusion in the data analysis. Prior to statistical analysis, the complete dataset was subject to a series of checking operations such as the 10% validation check and calculation of frequency distributions in order to eliminate some of the more obvious errors that may have potentially occurred during data processing.

3.3.6 Data analysis

Response rates were fully recorded and non-responder analysis was completed to compare the characteristics of the non-responders and the responders. Results were presented descriptively using numbers and percentages. Data analysis was completed using the Microsoft Excel software.

3.3.7 Ethical approval

A letter explaining the purpose and design of the study was sent to the Chairman of the South West Wales Research Ethics Committee. It was confirmed by the chairman that no ethical approval was required for this study.

3.4 Results

A total of 90 out of the 100 physicians who were sampled completed the questionnaires appropriately after three months giving a response rate of 90%. Re-sampling of other consultants from non-responder EDs was not completed due to the high response rate. The flow diagram in Figure 3.1 illustrates the number of respondents at each stage. The total number of attendances at all of the 90 emergency departments included in the sample was 7,914,000 per year.

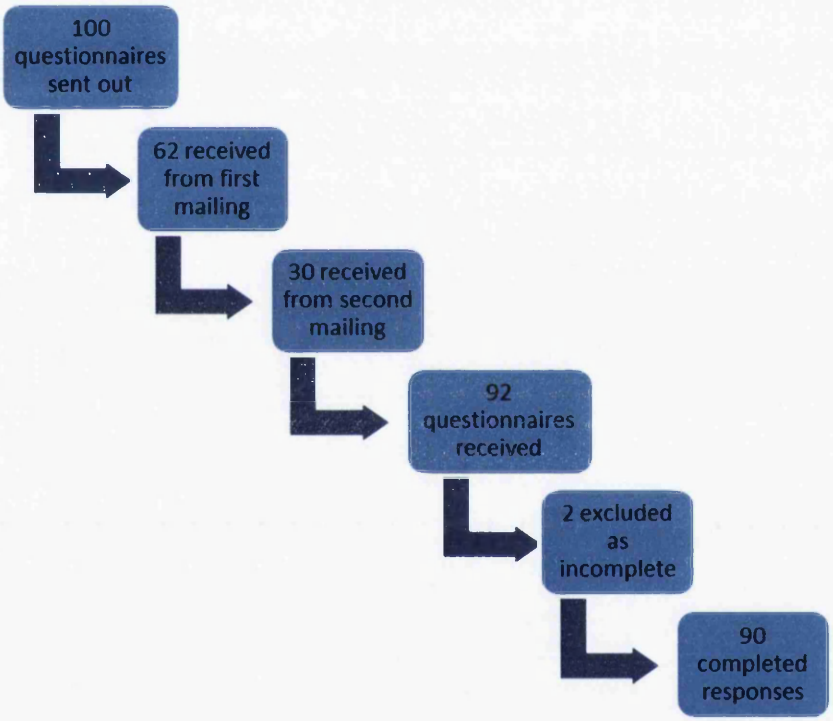


Figure 3.1 Diagram illustrating sample response rate

The non-responder analysis indicated no differences in demographics between the responders and non-responders in terms of location and type of hospital. Table 3.1 highlights the responses to the first three questions. The first section of the table illustrates the type of hospital in which the respondents worked as an Emergency Physician, with 50% of respondents working in a District General Hospital. The team to which the blunt chest wall trauma patient was referred if they need admission to

hospital but not ICU care is listed in the second section of Table 3.1. In 51.1% of the hospitals (n=46), the patients were referred to the care of the general surgical team. The least commonly used team was reported to be the general medical team (n=4, 4.4%). Eleven of the respondents stated that it was the policy in their ED to refer this patient group to more than one team. Table 3.1 highlights the guidelines that are used to assist the physicians working in the ED in the management of the blunt chest wall trauma patient. In 26 (28.9%) of the hospitals, no guidelines are used to assist the Emergency Physician in the management of this patient group.

Type of hospital	**n**	**%**
District General hospital	45	50
Teaching hospital	33	36.7
Regional trauma centre	11	12.2
Field hospital	1	1.1
Team to which patient referred		
General surgical team	46	51.1
Cardiothoracic team	17	18.9
Emergency medicine team	16	17.8
Orthopaedic team	10	11.1
Thoracic team	5	5.6
General medical team	4	4.4
Guidelines used		
Local	43	47.8
None	26	28.9
ATLS	18	20
Regional	4	4.4
Consultant experience	2	2.2
CEM guidelines	1	1.1
Oxford Handbook of EM	1	1.1
Trainee induction lecture	1	1.1

ATLS: Advanced trauma life support. CEM: College of Emergency Medicine. EM: Emergency Medicine
NB: Percentages were calculated by dividing the number of responses to a particular response option by the total number of respondents (n=90)

Table 3.1 Type of hospital (n= number of responses to each question) in which the respondent works as an Emergency Physician

The final question related to the management of the blunt chest wall trauma patients who do not require immediate life-preserving intervention or surgery, but are potentially at high risk of developing late on-set complications. The variables that the respondents believed should be considered risk factors for morbidity and mortality when assessing blunt chest wall trauma patients are listed in Table 3.2. All the

responses that were only suggested by either one or two respondents have been grouped together into the 'other' category.

Risk factor	n=439	%
Age	57	63.3
Chronic lung disease	52	57.8
Past medical history	29	32.2
Mechanism of injury	28	31.1
Number of rib fractures	25	27.8
Associated injuries	25	27.8
Pre-injury anti-coagulant use	18	20
Smoking history	14	15.6
Presence of lung contusion	13	14.4
Cardiovascular disease	13	14.4
Low oxygen saturations	12	13.3
Presence of haemothorax	12	13.3
Presence of pneumothorax	11	12.2
Pain	9	10
Social history	8	8.9
Results of chest radiograph	7	7.8
Changes in arterial blood gases	6	6.7
Vital signs	6	6.7
Long term medications (not specified)	5	5.6
Mobility status	5	5.6
Electrocardiogram results	5	5.6
Respiratory rate	5	5.6
Troponin T results	4	4.4
Presence of flail chest	4	4.4
Site of injury	4	4.4
Presence of fractured sternum	4	4.4
Hypoxia	3	3.3
Response to treatment	3	3.3
Presence of surgical emphysema	3	3.3
Reduced tidal volume	3	3.3
Bone fragility	3	3.3
Blood pressure	3	3.3
Others	40	9.1

NB: Percentages were calculated by dividing the number of responses to a particular response option by the total number of respondents (n=90)
Responses which were only listed n=1 or n=2 were combined into the 'other' category

Table 3.2 The risk factors (n=439 responses) considered contributing to increased morbidity and mortality in blunt chest wall trauma patients

3.5 Discussion

This qualitative study reports on the findings of a questionnaire based study in which experts were asked about the risk factors that they felt contributed to morbidity and mortality in the blunt chest wall trauma patient. Blunt chest wall trauma has been reported as a difficult injury to assess and manage in the ED as up to 50% of rib fractures are missed on chest radiograph (Davis and Affatato 2006) and

complications often occur a number of days after the initial injury and presentation to the ED. (Ahmad et al 2010, Blecher et al 2008) When life-threatening injury is not apparent, the appropriate treatment and follow up care are not well defined and furthermore little consensus exists among Emergency Physicians regarding the management of this patient group. (Dubinsky and Low 1997)

In this study, there was a good representation of the different hospital types in the sample with Emergency Departments of District General Hospitals, Teaching Hospitals and the larger Regional Trauma Centres. The majority of respondents to the questionnaire worked in a District General Hospital in England or Wales with between 25,000 and 120,000 attendances at the ED per year. The type of hospital in which the trauma patient would be most effectively managed is an on-going debate in England and Wales.

The ward based team to which the blunt chest wall trauma patient was referred from the ED varied between hospitals. The results highlighted that the general surgical team is most commonly used to provide care for the blunt chest wall trauma patient who required admission to hospital, but not immediate surgical or ICU intervention. In the Regional Trauma Centre however, only one of the respondents stated that they referred the blunt chest wall trauma patient to the general surgical team with the others all utilising the specialist services available in trauma centre such as thoracics, cardiothoracics and emergency medicine. It is not possible to draw conclusions from this study regarding the most suitable ward based team for the care of the blunt chest wall trauma patient however it could be concluded that inconsistencies are evident in the management of this patient group in England and Wales.

The use of guidelines in general patient care is a contentious issue in the National Health Service. The aim of clinical guidelines is to standardise practice around an appropriate norm, however concerns regarding the use of clinical guidelines include the variable quality of existing guidelines and the risk of inadvertently suppressing innovative or patient centred care. (West and Newton 1997) For the blunt chest wall trauma patient who presents to the ED with immediate life-threatening injuries requiring surgical or intensive care intervention, the Advanced Trauma Life Support (ATLS) guidelines are most commonly used in the UK and 50 countries worldwide.

(American College of Surgeons 2008) No similar national guidelines exist however to assist the Emergency Physician in the management of blunt chest wall trauma patients with non-immediate life threatening injuries, despite evidence that has highlighted the difficulty in identification of the high risk blunt chest wall trauma patient and their consequent morbidity and mortality. (Blecher et al 2008; Dubinsky and Low 1997)The results of our questionnaire study highlighted that at present in England and Wales, the use of guidelines in the management of this patient group was inconsistent. In 28.9% of hospitals, guidelines are not used at all irrespective of the type of hospital providing trauma care.

The risk factors for morbidity and mortality in blunt chest wall trauma patients have been reasonably well researched in the literature to date. In a recent systematic review and meta-analysis the risk factors for mortality following blunt chest wall trauma were outlined. (Battle et al 2012) These included a patient age of 65 years or more, a pre-existing condition, (specifically cardiopulmonary disease or diabetes) the presence of three or more rib fractures and the on-set of pneumonia during the patient's recovery phase. In addition, other risk factors for morbidity, mortality and resource consumption such as vital capacity and obesity have been investigated in single smaller studies. (Reiff et al 2007, Bakhos et al 2006) It could be suggested that consensus exists between the expert opinion gained in this study and previous literature in that the main risk factors for morbidity and mortality in blunt chest wall trauma patients that we identified according to the experts were patient age, past medical history including chronic lung disease and diabetes, and the number of ribs that were fractured. Only a small number of the respondents however suggested that they would consider vital capacity or obesity as risk factors for morbidity and mortality in blunt chest wall trauma patients.

Additional risk factors including the patient's reported pain level, pre-injury anticoagulant use (warfarin, aspirin and clopidogrel were highlighted by the respondents), smoking history, bone fragility and metabolic bone disorders were identified in this study. It is evident however that these risk factors have been inadequately investigated to date in trauma research. Further research into the effect of these risk factors on morbidity and mortality in blunt chest wall trauma patients is required.

This qualitative study outlines current inconsistencies in the management of this patient group in England and Wales. These inconsistencies include the use of guidelines, the team to which the patient is referred on admission to hospital and the consequent differences in clinical care received by the patient. Inconsistency also exists in the expert opinion of the risk factors for morbidity and mortality in blunt chest wall trauma patients and this is highlighted by the low number of respondents who listed the well-known risk factors which are supported by previous research. For example, only 27.8% of respondents suggested the number of ribs fractured was a risk factor for morbidity and mortality however the presence of three or more rib fractures is a well-documented risk factor for increased mortality in blunt chest wall trauma patients.

The systematic review and meta-analysis presented four main risk factors for mortality in blunt chest wall trauma patient, however the results of this study highlight that the Emergency Physicians managing these patients on a day to day basis consider numerous additional risk factors to be influencing outcomes in the blunt chest wall trauma patients. It is evident that this opinion is based on clinical experience as there is no supporting research for these risk factors. It could be suggested that the importance of this qualitative study to the reader is that it not only adds depth to the recent meta-analysis, but also highlights a number of new areas for potential further research into the risk factors for morbidity and mortality in blunt chest wall trauma patients.

3.6 Limitations

A purposive sample was used in order to gain expert opinion of consultants working in the emergency departments in England and Wales. A total of 100 emergency departments were selected as a representative sample of 203 major Emergency Departments in England and Wales. In a purposive sample, selection bias is possible however the aim at the outset of this study was to gather expert opinion. All minor injuries units and walk in centres were excluded from the sample as most of these are general practitioner or emergency nurse practitioner led and the aim of our study was to gain expert opinion from Emergency Physicians. Although the aim of the study was to gain expert opinion, it may have been interesting to investigate whether the

opinions of the GP or Emergency Nurse Practitioner differed from those of the Emergency Physicians.

3.7 Conclusions

The risk factors listed as contributing to morbidity and mortality in the blunt chest wall trauma patient concurred with the current research with an emphasis on patient age, number of rib fractures and pre-existing conditions. The use of pre-injury anti-coagulant therapy or coagulopathy was also highlighted as important however no current research has investigated this. The results of this study have highlighted a number of potential important areas for further research such as the influence of pre-injury anti-coagulant therapy, smoking history, social and mobility status, bone fragility and pain levels on outcomes in blunt chest wall trauma patients. It could also be concluded that there is a moderate degree of inconsistency between the way the blunt chest wall trauma patient in managed in different hospitals in England and Wales. This could be explained by the lack of current national guidelines for this patient group and the inappropriate reliance on the use of ATLS guidelines for the less severely injured patient who is at risk of developing complications a number of days after their initial presentation to the ED.

4.0 The risk factors for the development of complications during the recovery phase following blunt chest wall trauma: a retrospective study.

4.1 Background

4.1.1 Research designs in Emergency Medicine.

Evaluative studies are commonly used in Emergency Medicine research. The aim of the evaluative study is to determine existence and strength of a possible association between an exposure intervention and an outcome. (Clancy 2002) This subsequently allows the reader to determine whether an exposure affects an outcome or not. Two types of evaluative study have been described extensively in the literature including observational studies and experimental studies. (Clancy 2002, Lecky and Driscoll 1998)

4.1.2 Experimental research

The experimental study involves the researcher employing a pre-defined change to a study population and then collecting data on the outcome of that change. There are a number of different types of experimental studies which include the randomised controlled trial (RCT), quasi-RCT, explanatory and pragmatic experimental studies. (Clancy 2002) The RCT is the study design which when appropriate, practical and ethical is considered the gold standard in research. This study design however is not always appropriate for answering certain types of research question. For example, certain research questions could not be answered using a RCT study design as it would not be ethical to remove a treatment which is beneficial to the study population, just for the purposes of research. Similarly, RCTs are rarely large enough to measure accurately an outcome which occurs infrequently or interventions that are designed to prevent rare events. Where the RCT is not appropriate or feasible, the observational study can be considered. (Clancy 2002, Lecky and Driscoll 1998)

4.1.3 Observational research

Observational studies aim to describe a health care situation that relates to populations or groups of patients. In this type of study, there is commonly a focus on

the relationship between two or more independent variables and their influence on a disease process or outcome. (Mann 2003, Lecky and Driscoll 1998) The primary difference between the RCT and the observational study is that in the observational study the study population do not receive an intervention. (Lecky and Driscoll 1998) Observational studies therefore tend to be either descriptive or analytical in design. (Mann 2003) Descriptive studies may use a cross-sectional approach in order to determine the number or percentage of people within the study population who have a particular characteristic of interest at a pre-defined point in time. A longitudinal approach describes the incidence of the characteristic of interest in a study population. (Lecky and Driscoll 1998) Analytical studies however concentrate on a cohort (population groups or individuals) and include cohort and case-control studies which may either be prospective or retrospective in study design. These types of studies investigate disease and the potential associated factors. (Clancy 2002, Mann 2003)

4.1.4 Confounding

There are a number of limitations of observational studies which should be considered. Confounding occurs when an association is found incidentally between two variables due to a failure of the study design. The study therefore must take into account other factors which can be associated with the outcome under investigation. (Lecky and Driscoll 1998) Commonly described confounding variables in emergency medicine observational research include clinical setting, patient age and severity of injury. (Clancy 2002) The aim of making the two study groups as similar as possible with respect to the confounders is more likely to be achieved if confounding is controlled in both the design and analytical phase of a study. In order to overcome the effect of possible confounding variables in the design phase, all relevant variables should be measured and furthermore, all patients in the study population should be followed up for the duration of the study. (Mann 2003) In the analytical phase, statistical techniques are available such as multiple linear and logistic regression which adjusts the analysis for the possibility of confounding variables, thus enhancing internal validity. (Clancy 2002) In contrast to the RCT, the effects of confounders are not diminished with increasing sample size. (Clancy 2002)

4.1.5 Bias

Another pitfall in observational studies is the effect of bias. Bias is the systematic deviation from the truth which results in distortion of the study results, as a result of the way in which the study has been conducted. (Lecky and Driscoll 1998) Over 35 different types of bias have been described by Sackett (1979) however more recent research emphasizes the importance of selection bias, intervention bias, follow-up bias and measurement and information bias. (Clancy 2002, Lecky and Driscoll 1998)

Selection bias occurs when the selected study sample differs systematically from the population with the same condition. (Clancy 2002, Lecky and Driscoll 1998) For example, volunteers to a study may differ from those who refuse to participate and consequently the study group may not be generalizable to the population as a whole. Intervention bias refers to the greater use of treatment procedures on the favoured arm in a trial leading to an over-estimation of the benefit of the intervention. (Clancy 2002) Information bias is another major source of bias in observational studies and results from short-comings in the collection and recording of data. (Lecky and Driscoll 1998) For example if a researcher is aware of the exposure received by a sample, this could influence his assessment of the outcome. Similarly, knowledge of the outcome could influence his assessment of the exposure. (Clancy 2002) Follow up bias occurs when the patients who remain in the study differ from those lost in follow up in terms of personal characteristics and outcome status. (Clancy 2002)

The key principle in overcoming bias in observational studies is to identify all possible areas that could be affected by bias and change the study design accordingly. Bias occurs due to inherent errors in the study design therefore simply increasing the sample size will not reduce bias, only magnify it. (Clancy 2002) Each type of bias needs to be considered and addressed long before the data collection has commenced. As with the RCT, the observational study should collect data systematically and rigorously and if this is achieved, the observational study can prove a practicable method of studying certain research questions which cannot be ethically or feasibly answered using the RCT.

4.1.6 Retrospective studies

This study design uses data that have already been collected for some other purpose than the study itself. A study sample is selected from the population and the investigator examines a pre-determined number of variables that might be relevant to the condition being investigated. The study is performed post-hoc therefore the sample or cohort is 'followed up' retrospectively. With this type of research, the study period may be over many years, however the time to complete the study is only as long as the time it takes to collate and analyse the data. (Mann 2003) There are a number of advantages and disadvantages with this type of cohort study.

4.1.7 Advantages of retrospective cohort studies

A retrospective cohort study is advantageous when the use of the RCT is neither feasible nor ethical due to the nature of the research question. The retrospective study design allows certain research questions to be answered both safely and ethically. A further advantage of the retrospective cohort study is that the cohort allows calculation of the effect of each variable on the probability of the outcome of interest (relative risk). This ensures full and comprehensive study results which in turn enables the reader to make informed decisions about the study. Although bias is a potential problem in retrospective studies, one advantage of this study design is that bias may actually be reduced as the outcome of current interest may not be the original reason the data were collected. (Mann 2003) A more practical advantage of retrospective studies is that they are often cheaper to run as the data have already been collected. (Mann 2003)

4.1.8 Disadvantages of retrospective cohort studies

There are a number of disadvantages to the use of the retrospective cohort study. One of the principal disadvantages is that as the cohort was originally constructed for another purpose it is unlikely that all the required information has been rigorously collected, leading to missing data. (Mann 2003) Recall bias is also a disadvantage of retrospective research as people who have the outcome of interest are more likely to exaggerate or minimise what they now consider risk factors. (Mann 2003) Due to the nature of retrospective cohort studies, two groups will be compared, one of which will have been exposed to the risk factor or intervention of interest and the other will

not. The issue then arises that there is an inability to control for all other factors which may affect the outcome. The principal problem of retrospective studies is therefore that their internal validity may be undermined by previously unrecognised confounding factors. (Clancy 2002)

4.2 Introduction

A number of well-documented risk factors for morbidity and mortality have been identified for blunt chest wall trauma including patient age, pre-existing disease, number of ribs fractured and the on-set of pneumonia during the recovery phase. (Battle et al 2012) Blunt chest wall trauma patients aged 65 years of more have a significantly higher morbidity, mortality and hospital length of stay than those patients aged less than 65 years. (Brasel et al 2006, Bergeron et al 2003) Blunt chest wall trauma patients with cardiopulmonary disease and diabetes have significantly higher rates of morbidity and mortality than patients with no such diseases, (Bergeron et al 2003, Barnea et al 2002, Alexander et al 2000)) while three or more rib fractures has been reported as the "danger number" resulting in significantly higher rates of morbidity, mortality, ventilator days and hospital length of stay. (Brasel et al 2006, Bergeron et al 2003, Barnea et al 2002) The on-set of pneumonia during recovery from blunt chest wall trauma results in significantly higher mortality rates. (Battle et al 2012, Bergeron et al 2003) Other risk factors such as associated injuries, vital capacity, pulmonary contusion, flail chest and body mass index have also been investigated as risk factors for various poor outcomes in blunt chest wall trauma patients.

It is evident that there are numerous risk factors highlighted in the research for various poor outcomes in blunt chest wall trauma patients and furthermore that there are no guidelines available to assist in the management of this patient group, often resulting in discharge from the ED to an inappropriate level of care. (Blecher et al 2008) The aim of this study was to investigate the risk factors for development of complications in the recovery phase following blunt chest wall trauma. Using the results of this study, the aim is to develop and validate a prognostic model that can be used to assist in the management of the blunt chest wall trauma patient in the ED. For the purposes of this study, blunt chest wall trauma was defined as blunt chest injury

resulting in chest wall contusion or rib fractures, with or without non-immediate life-threatening lung injury. (Battle et al 2012)

4.3 Methodology

4.3.1 Setting

A retrospective study design was used in order to examine the medical notes of all blunt chest wall trauma patients who presented to the ED of Morriston Hospital, a large regional trauma centre in South Wales between 2009 and 2010. Morriston hospital has approximately 90,000 presentations to the ED per year and serves a population of 450,000 people. Patients with multi-trauma were excluded to reduce the effect of confounding. This included patients with major organ, head, spinal, abdominal, pelvic or long bone trauma and also patients who required any immediate life-saving intervention.

4.3.2 Sample

For this study it was necessary to include sufficient patients that the unadjusted and adjusted odds ratios and 95% confidence intervals could be presented, for the risk factors for the development of complications following blunt chest wall trauma. Peduzzi et al (1995) suggested that the number of patients needed to ensure sufficient power in a retrospective cohort study is equivalent to ten events per variable (EPV) being investigated. In this study nine variables or risk factors were under investigation therefore a minimum of 90 events (on-set of complications in the recovery phase following blunt chest wall trauma) were required.

4.3.3 Data collection

The ED medical notes of all patients aged 16 years and over presenting to the ED of Morriston Hospital in 2009 and 2010 were examined following the guidelines suggested in a study by Gilbert et al (1996) and data were recorded on a pre-designed database. A validation check was completed in which an additional researcher checked the accuracy of the data input for 10% of all patients, in order to reduce information bias. If a patient's notes had missing or incomplete data for the variables under investigation, they were still included in the database. It was assumed that if a

variable was not documented, that it was either normal or absent. For example, if it was not documented that the patient was a smoker, the patient was considered to be a non-smoker.

The dataset included demographic variables such as age, gender, injury mechanism and whether the patient had a chest radiograph or arterial blood gases taken in the ED. The independent variables were defined a priori and consisted of the risk factors for mortality and morbidity highlighted previously in the literature. These included patient age, pre-existing conditions, number of suspected rib fractures, smoking history, pre-injury anticoagulant use (for the purpose of this study any type and dose of anti-coagulant or anti-platelet medication were included), respiratory rate and oxygen saturation levels. The outcome measure investigated was the development of complications in the recovery phase following blunt chest wall trauma.

To ensure confidentiality, patients' names were not recorded during the data collection period. The dataset was also stored on a hospital encrypted computer (safe-end protector) to ensure data security. The South West Wales Research and Ethics Committee were contacted about the study and confirmation was received from the Chairman that ethical approval was not required. The Caldicott guidelines were adhered to throughout the study process.

4.3.4 Definition of variables

The patient's age, presence of pre-existing conditions including; chronic obstructive pulmonary disease or bronchiectasis, diabetes and cardiovascular disease (all disease affecting the heart or blood vessels), smoking history (current smokers only, ex-smokers classified as non-smokers), pre-injury anti-coagulant use (all anti-coagulant and anti-platelet therapy and any dose were included), respiratory rate and oxygen saturation levels were all identified from the medical notes. The number of rib fractures was determined from the clinical notes however in the cases where the number of rib fractures could not be determined using clinical records, then the X-ray report (IMPAX software) was reviewed by the investigators. The number of rib fractures was dichotomised into two groups for this study; nought to two rib fractures

or three or more rib fractures, due to the results of previous studies. (Battle et al 2012, Lien et al 2009, Sharma et al 2008, Flagel et al 2005)

Patient age of 65 years or more was investigated as the point at which increased risk occurred, due to the results of previous studies. (Battle et al 2012, Lien et al 2009, Sharma et al 2008, Bergeron et al 2003, Bulger et al 2000) Respiratory rate and oxygen saturation levels were analysed as categorical variables in this study so a point at which increased risk was considered to occur was set at more than 20 breaths per minute for respiratory rate (Cretikos et al 2008, Subbe et al 2003) and less than 90% for oxygen saturations. (Jacques et al 2006, Harrison et al 2005)

The development of complications during the recovery phase following blunt chest wall trauma was the composite outcome measure investigated in this study. Data collection for this outcome was completed from the time the patient presented to the ED, through to discharge from hospital. Patients were reported to have developed complications if one or more of the following were documented in the medical notes; in-hospital mortality, morbidity including all pulmonary complications (chest infection, pneumonia, pneumothorax, haemothorax, pleural effusion and empyema), ICU admission, or a prolonged length of stay as defined as a total hospital stay of seven or more days. (Flagel et al 2005, Hoff et al 1994)

4.3.5 Data analysis

Statistical analyses were performed using SPSS Version 16 (Chicago). Subjects' demographics were analysed using descriptive statistics. Descriptive data are presented as numbers and percentages. Univariable analyses were performed for each of the independent variables investigated. Pearson's chi square test or Fisher's exact test was used (where a sample size of less than ten on any of the variables existed) to assess the association between the independent variables (various risk factors) and the dependent variables (outcome). Unadjusted odds ratios and 95% confidence intervals are reported for the outcome based on the univariable analysis.

4.4 Results

During 2009 and 2010, a total of 13,520 trauma patients presented to Morriston Hospital. A total of 174 blunt chest wall trauma patients were identified from the hospital database requiring admission to hospital. Figure 4.1 outlines the number of patients presenting to Morriston Hospital and their reasons for inclusion in the analysis.

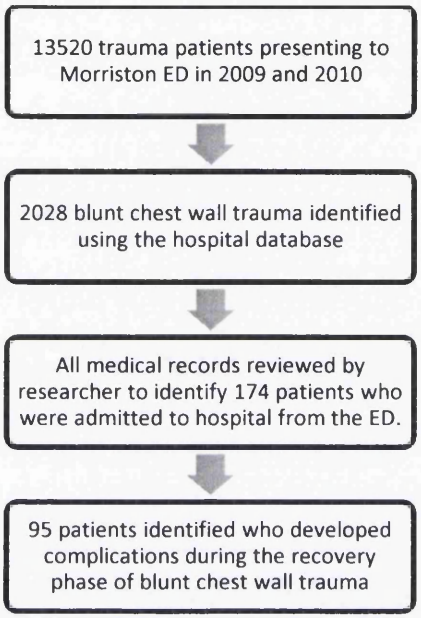


Figure 4.1. Flow diagram of trauma patients presenting to the ED in Morriston Hospital in 2009 and 2010.

Data including demographics, independent and dependent variables were recorded for each of the patients identified for inclusion in this study. With the exception of recoding of two patients' respiratory rates, there were no missing variables in the dataset. Table 4.1 highlights the demographic data for each of the patients (n=174). Patients' age, gender, injury mechanism and need for chest radiograph or arterial blood gases in the ED are presented. The number of different complications (mortality, morbidity, ICU admission and prolonged length of stay), causes of death and respiratory complications are also included in the table.

Patients aged 65 years or more accounted for 68.4% of all admitted patients and 56.9% of patients were male. Falls were the most common injury mechanism (58.1%). A chest radiograph was used as part of the clinical assessment in 98.3% of admitted

patients and arterial blood gases in 48.3% of admitted patients. Further analysis highlighted that of the total number of patients from which arterial blood gases were taken, 81% had sustained three or more rib fractures, 94% were from patients who had sustained a fall and 77% were from patients aged 65 years or more.

	Total patients (n=174)	
	n	%
Age		
65 years or more	119	68%
Under 65 years	55	32%
Gender		
Male	99	57%
Female	75	43%
Injury mechanism		
Fall	148	85%
RTC	13	8%
Sporting injury	6	3%
Assault	6	3%
Strain	1	1%
CXR taken		
Yes	171	98%
No	3	2%
ABGs taken		
Yes	84	48%
No	90	52%
Outcomes		
Mortality	16	9%
Morbidity	66	38%
Total ICU admission	35	20%
ICU admission (direct from the ED)	28	80%
ICU admission (unplanned from ward)	7	20%
Total Prolonged LOS	70	40%
Prolonged LOS (due to on-set of complications)	46	66%
Respiratory complications		
Chest infection / pneumonia	20	11%
Pneumothorax	7	4%
Haemothorax (in pre-injury anticoagulants patients)	12	7%
Haemothorax (in no pre-injury anticoagulants patients)	1	1%
Tube thoracostomy	10	6%
Pleural Effusion	16	9%
Empyema	1	1%
Pathological fracture	2	1%
Need for mechanical ventilation	12	7%
Causes of death (n=16)		
Pneumonia	8	50%
Haemothorax	4	25%
Withdrawal of care	5	31%
Myocardial infarction	2	12%
Lung cancer	1	6%

RTC: Road traffic collision. CXR: chest x-ray. ABGs: Arterial blood gases, LOS: length of stay

Table 4.1: Patient demographics, injury mechanisms, complications and outcomes.

Table 4.2 highlights the results for each risk factor investigated using univariable analysis. The unadjusted odds ratios and their 95% confidence intervals are presented for each risk factor investigated. The risk factors for the development of complications in the recovery phase following blunt chest wall trauma were a patient age of 65 years or more, three or more rib fractures, presence of chronic lung disease

or cardiovascular disease, use of pre-injury anti-coagulants and oxygen saturation

Risk factor (n)	Complications n (%)	p value	Unadjusted OR (95% CI)
65 years or more (n=118)	78 (66%)	0.001	4.4 (2.3-8.9)
Less than 65 years (n=56)	17 (30%)		
Three or more rib fractures (n=117)	79 (68%)	0.001	5.3 (2.7-10.7)
Less than three rib fractures (n=57)	16 (28%)		
Chronic lung disease (n=106)	74 (70%)	0.001	5.2 (2.7-10.0)
No chronic lung disease (n=68)	21 (31%)		
Cardiovascular disease (n=65)	44 (68%)	0.007	2.4 (1.3-4.5)
No cardiovascular disease (n=109)	51 (47%)		
Diabetes mellitus (n=29)	16 (55%)	0.946	1.0 (0.5-2.3)
No diabetes mellitus (n=145)	79 (55%)		
Smoker (n=64)	32 (50%)	0.353	0.7 (0.4-1.4)
Non-smoker (n=110)	63 (57%)		
Pre-injury anticoagulant use (n=71)	53 (75%)	0.001	4.3 (2.2-8.3)
No pre-injury anticoagulant use (n=103)	42 (41%)		
Respiratory rate over 20bpm (n=52)	30 (58%)	0.592	1.2 (0.6-2.3)
Respiratory rate 20bpm or less (n=122)	65 (53%)		
Oxygen saturations 90% or less (n=20)	18 (90%)	0.001	9.0 (2.0-40.1)
Oxygen saturations less than 90% n=154)	77 (50%)		

levels of less than 90%.

OR: Odds ratios, CI: Confidence intervals

Table 4.2: Results of univariable analysis. Risk factors and their outcomes in blunt chest wall trauma.

4.5 Discussion

Blunt chest wall trauma accounts for over 15% of all trauma admissions to the Emergency Departments in the UK. (TARN 2011) As no current guidelines exist for the management of this patient group, recognition of the high risk patient in the ED is not always straightforward due to the nature of the injury and its recovery phase. The severely injured patient who presents to the ED requiring immediate life-preserving intervention will usually be managed using the ATLS guidelines and subsequently, the intensive care team will take over the patient's care. The blunt chest wall trauma patient who walks into the ED with no immediate life-threatening injury will commonly develop complications up to 72 hours or more post injury, which may also prove life-threatening. (Alexander et al 2000, Simon et al 1998) An understanding of the risk factors for development of complications in the recovery phase following blunt chest wall trauma patient could assist in the accurate risk stratification of this patient group in the ED and thus improve outcomes. This study investigated the risk factors for a number of different outcomes in blunt chest wall

trauma patients using a retrospective analysis of the ED medical notes of all patients presenting to a large regional trauma centre in South Wales.

The most common injury mechanism in this study was falls, which as expected was had a higher incidence in the patients aged 65 years or more and concurs with previous studies (Bakhos et al 2006, Barnea et al 2002). Road traffic collision was the most commonly reported injury mechanism in a number of other studies however these studies only selected patients who had confirmed fractured ribs and furthermore included patients with multiple trauma or immediate life-threatening injuries. (Bergeron et al 2003, Brasel 2006) The results of this study highlight that the patients with the more severe injuries were the elderly patients who had sustained the lower impact injury mechanism. These results concur with previous research that has suggested that lower levels of force (low velocity falls) results in more significant trauma in an elderly patient. (Bulger et al 2000) More severe injuries occur as a result of structural changes in bone associated with the ageing process. (Bulger et al 2000) This study's results highlight that low velocity falls in the younger patients very rarely resulted in any rib fractures. Injury mechanisms in the younger patients with more severe injuries were road traffic collisions, sporting injuries or assaults. These are all higher velocity injury mechanisms.

Results highlighted that for the patients who required admission to ICU directly from the ED, the admission criteria included patient age and co-morbidity, severity of injury and need for invasive analgesia. The seven patients with unplanned or delayed ICU admission were admitted to ICU due to on-set of late respiratory complications. Prolonged hospital length of stay was used as a component of the composite outcome measure in this study. Results highlighted that in two thirds of the patients with a prolonged hospital length of stay, this was directly attributable to respiratory complications. Other primary causes of prolonged hospital length of stay included on-going pain control issues and social factors preventing discharge.

Only three patients who were admitted to hospital with blunt chest wall trauma did not have a chest radiograph in the ED. These figures are not reported in other recent similar studies in order to make comparisons however the use of the chest radiograph in the identification of rib fractures remains controversial. (Davis and Affatato 2006)

As a result of the number of rib fractures that have been shown in the research to be missed on chest radiograph, the severity of injury recorded in this study could potentially be underestimated. (Davis and Affatato 2006)

Arterial blood gases were taken in just under half of the patients who were admitted to hospital. The results highlighted that arterial blood gases are most frequently used in assessment of elderly patients who have fallen and sustained three or more rib fractures. This less common use of arterial blood gas analysis may be due its more invasive nature and the greater reliance on the patient's respiratory rate and oxygen saturation levels which is quicker, less expensive and non-invasive to test. The triage nurse can also record the patient's respiratory rate and oxygen saturations in comparison to the arterial blood gas which is more commonly taken by the Emergency Physician. Respiratory rate were recorded almost all (98.9%) patients and oxygen saturations were recorded in all patients (100%). Research has highlighted the accuracy with which respiratory rate can be used to predict respiratory failure and how it is a useful, but commonly neglected vital sign. (Cretikos et al 2008, Subbe et al 2003)

An overall in-hospital mortality rate of 9% was reported in this study which is similar to that reported in other studies with comparable populations. (Brasel et al 2006, Barnea et al 2002, Alexander et al 2000) The most common causes of death in this study included pneumonia, haemothorax and withdrawal of care or palliation. The previous studies reporting higher mortality rates included patients with multiple trauma and immediate life-threatening injuries. Comparison between the studies investigating risk factors for mortality in blunt chest wall trauma is difficult as a result of the varying definitions used for 'mortality', a number of studies failing to define mortality at all. In this study, in-hospital mortality was used as the definition as a result of the difficulty in accurately attributing death to the blunt chest wall trauma following discharge from hospital. All deaths in this study were recorded in patients aged 65 years or more and this concurs with a number of other studies which all report a higher mortality rate in elderly patients. (Battle et al 2012, Brasel et al 2006, Bergeron et al 2003, Bulger et al 2000) The injury mechanism in all the deaths was a fall and with the exception of one, all patients had sustained three or more rib fractures. The morbidity rate in this study (38%) is similar to those reported in other

studies however differences between studies in definitions of dependent variables is commonplace.

The risk factors for the development of complications in the recovery phase following blunt chest wall trauma on univariable analysis were a patient age of 65 years or more, three or more rib fractures, chronic lung disease or cardiovascular disease, the use of pre-injury anti-coagulants and oxygen saturation level in the ED of less than 90%. These findings concur with a number of other studies (Sharma et al 2008, Bergeron et al 2003, Barnea et al 2002, Bulger et al 2000) however the use of pre-injury anticoagulants (any anti-coagulant or anti-platelet medication) as a risk factor has not been investigated previously in the literature for this patient group. One other study reported that low oxygen saturation levels were a risk factor for morbidity following isolated blunt chest trauma which concurs with the findings of this study. (Barnea et al 2002) Low saturations (less than 90%) have also been reported to be associated with death and cardiac arrest in ward patients outside of the critical care areas. (Jacques et al 2006)

An unexpected result of this study in the univariable analysis highlighted that the non-smokers had a higher rate of complications than the smokers, although the results were not statistically significant. There was no significant difference in age or chronic lung disease between the smokers and non-smokers. As patient age or chronic lung disease does not account for the differences between the smokers and non-smokers, this could be an interesting area for further research. Although the negative effects of smoking on the respiratory system are well documented, it is possible that the patients who smoke often have a more effective, secretion-clearing cough than non-smokers. It is also possible that the smokers tend to start mobilising earlier than the non-smokers, as they have a motivation to mobilise to quite reasonable distances from the ward to an area in which smoking is permitted. Early mobilisation is advocated in blunt chest wall trauma studies as a first line treatment in reducing risk of mortality. (Bolliger and Van Eeden 1990) Diabetes mellitus, smoking and respiratory rate were not found to be risk factors on univariable analysis.

The National Institute for Health and Clinical Excellence (NICE) have developed guidelines for patients who have sustained a head injury and this covers those that

are using pre-injury anticoagulants due to the increased risk of bleeding, but no comparable guidelines exist to date for blunt chest wall trauma. (NICE 2007) Patients using pre-injury anti-coagulants could therefore be considered as a higher risk for late complications due to the potential risk of a developing either a haematoma or a haemothorax, both of which may compromise ventilation. In this study, just under a third of patients using pre-injury anticoagulants developed a haemothorax following their injury, with four of these patients dying as a direct result. A previous study highlighted the significant risk of morbidity in patients with late on-set haemothorax. (Simon et al 1998)

The outcome measure used for this study comprised a number of different components; mortality, morbidity, need for ICU admission and prolonged hospital length of stay. This composite outcome measure was used as result of the fairly low incidence of complications that occur in this patient group. It could be suggested that each of the individual components differ in terms of clinical importance and therefore larger scale prospective studies are needed using each of the component measures.

All of the risk factors reported in this study to be significant in contributing to the development of complications in the recovery phase following blunt chest wall trauma are routinely assessed for this patient group in the ED. It is reasonable to suggest therefore that knowledge of the impact of these risk factors could prove valuable in the management and risk stratification of this patient group. Identification of such risk factors may also lead to the development of prognostic models in future research which may assist in the management of this patient group. An interim analysis of the prognostic risk factors identified in this chapter has been published. (Battle et al 2013)

4.6 Limitations

The use of the database to identify the patients for inclusion in this study may have resulted in a degree of selection bias. Errors may have occurred in the collation of the list of patients from the hospital database and similarly by the doctors completing the

coding form in the ED. A further limitation of the retrospective nature of the study is that not all of the medical notes could be successfully located. This may have led to a loss of important data which could have influenced the study's findings. Similarly, as the data were being collected for each of the patients from their ED medical notes, reliance was placed on the information being both accurately and legibly documented. This may have led to some error in data collection and should be considered when interpreting the study results. The most appropriate method of overcoming a number of the study limitations is to complete a prospective study.

Although there were only two missing variables in the dataset, the assumption used that if a variable was not recorded then it was considered normal or absent may have led to a degree of information bias. Furthermore, the time at which the patients' vital signs were recorded in the ED was not commonly documented, so the initial assessment respiratory rate and oxygen saturations were always included in the dataset. These variables may have both improved with analgesia provided in the ED, or worsened over time while waiting in the ED so this should be considered on interpretation of the study results. There may also have been a lack of inter-rater reliability in the identification of the number of rib fractures on chest radiograph and this may have occurred as any doctor in the ED or radiologist may have interpreted the x-ray.

It is important to state that this study excluded patients with multi-trauma so the results are only generalisable to isolated blunt chest wall trauma patients. Also, this study only investigated the outcomes in the patients who were admitted to hospital from the ED. In similar future research it would be interesting to include the outcomes of those patients who have unplanned representations to the ED with late complications following discharge home on initial presentation. Attendance at the General Practitioner with late complications may also be of interest.

4.7 Conclusions

These results concur with the findings reported in other studies but also highlight areas for further research in particular the effect of pre-injury anticoagulant use and oxygen saturations of less than 90% in blunt chest wall trauma outcomes. This study

provides the basis for the development of a new prognostic model for the blunt chest wall trauma patient who does not develop complications until days after the injury and cannot be safely managed using the ATLS guidelines in the ED. Identifying which patient will go on to develop complications at a later stage in the recovery phase of their injury is not always straightforward so knowledge of the risk factors for development of late complications is important to guide clinical decision making.

5.0 Development of the prognostic model

5.1 Background

5.1.1 Prognosis and prognostic research

In medicine, prognosis commonly relates to the risk of an individual developing a particular state of health or outcome. These outcomes may be specific events such as death or hospital admission, or they may be quantities, such as pain or quality of life. (Moons at el 2009a, Royston et al 2009) Prognosis is commonly determined by numerous variables such as patient age, sex, family history, signs and symptoms and other specific test results. (Wyatt and Altman 1995) As a result of the variability in patients, a single risk factor or variable rarely gives an adequate estimate of prognosis. (Moons et al 2009a) Prognostic studies therefore need to use a multivariable approach in order to accurately determine the important risk factors of a pre-determined outcome. (Royston et al 2009) Once the researcher has identified the risk factors, a prognostic model or risk score can then be developed. The main objective therefore of a prognostic study is to determine the probability of the pre-determined outcome with different combinations of the identified risk factors, within a well-defined population. (Moons et al 2009a) From this population a study sample should be selected that includes people at risk of developing the outcome of interest. (Moons et al 2009a)

The most appropriate study design used in prognostic research is a cohort study. (Royston et al 2009) Although current literature is dominated by retrospective studies, the prospective study design is preferable as it facilitates the optimal measurement of risk factors and outcomes. (Moons et al 2009a, Royston et al 2009) The selection of risk factor variables can be obtained from a variety of sources including patient demographics such as age or sex, clinical history, physical characteristics, disease characteristics or test results. Research methodologists concur that the risk factors should be clearly defined, standardised and reproducible thus enhancing the validity and application of the study results to clinical practice. (Moons et al 2009a, Royston et al 2009) It is important that the risk factors are measureable using methods that are both time and cost effective and applicable to daily practice. A number of risk factors that are described in prognostic research require subjective interpretation of a test

result, for example a chest radiograph. In this instance there is a risk of investigating the predictive ability of the observer rather than the risk factor itself. (Moons et al 2009a)

The choice of outcomes investigated in prognostic research should be dictated by factors that are relevant to the patient such as occurrence of death, complications, disease remission, pain or treatment response. (Wyatt and Altman 1995) The time period over which the outcome is investigated and the methods of measurement should also be clearly and accurately defined. In order to control and prevent bias, the outcomes should be measured without knowledge of the risk factors being investigated, especially when measurement of the outcome requires observer interpretation. (Moons et al 2009a) Similarly, it may be necessary to ensure blinding when assessing outcomes other than mortality. Prior knowledge of the risk factors might influence assessment of the outcomes in prognostic research and thus introduce bias into the study. (Moons et al 2009a)

Only a limited number of prognostic models or risk scores are available for use in medicine. (Wyatt and Altman 1995, Moon et al 2009a) This may be explained by the lack of validation studies available for these models so the clinician is uncertain as to their accuracy. (Wyatt and Altman 1995) It has also been stated that prognostic models are frequently too complex for use in routine clinical practice. (Moons et al 2009a) It is important to emphasize however that the prognostic model is not meant to replace role of the doctor, rather assist the doctor in their decision-making through the provision of an objective estimate of the probability of outcome. The model should therefore be supplementary to the entire patient assessment. (Moons et al 2009a, Wyatt and Altman 1995)

There are no specific guidelines currently available for use in development or validation study design. A recent systematic review of reporting and methods in clinical prediction research by Bouwmeester et al (2012) outlined a number of factors that should be addressed in model development and validation studies. Figure 5.1 highlights these factors, all of which were followed in the design of the development and validation studies.

Methodological factors	Considerations for study design
Study Design	Type of prediction study (eg model development); participant sampling or selection method (eg cohort, case-control approach)
Participants	Participant recruitment; follow up; inclusion and exclusion criteria; setting (eg primary or secondary care)
Candidate Risk factors	Clear definition to ensure reproducibility; coding of risk factor values; assessment blinded for outcome
Outcome	Clear definition to ensure reproducibility; type of outcome; assessment blinded for risk factors
Statistical power	Effective sample size; (eg number of outcome events compared to number of candidate risk factors)
Selection of risk factors	Selection of risk factors prior to statistical analysis and with statistical analysis; use of variable selection strategies (eg backward elimination); criterion for risk factor inclusion (eg $p<0.05$)
Handling of missing values	Reporting of missing values per risk factor; or number or percentage of participants with missing values; reporting of procedures for dealing with missing values
Presentation of results	Reporting of univariable and multivariable risk factor-outcome effects; reporting of full or final model
Model performance measures and validation	Type of predictive performance measures reported (eg c-statistic and calibration); type of validation (eg internal or external)

Figure 5.1 Overview of methodological factors important in the design of prediction studies (Bouwmeester et al 2012)

5.1.2 Development of a prognostic model

There are a number of phases in multivariable prognostic research, the first of which is the development study. (Adams and Leveson 2012) The goal of this phase of such research is to construct an accurate and discriminating prognostic model from multiple variables. (Royston et al 2009) There are many techniques that can be used to develop a multivariate model but general consensus exists that they should be developed and evaluated by statisticians working in close collaboration with doctors. (Wyatt and Altman 1995) Royston et al (2009) outline a number of issues that affect the model and consequently the conclusion of the research. The first of these relates to the selection of clinically relevant candidate risk factors or risk factors for possible inclusion in the model. For example, it should be simple for the doctor to reliably collect all the required patient data with no increase in resource expenditure. All clinically relevant data should have been tested for inclusion in the model but

without the use of arbitrary thresholds for continuous variables such as patient age, heart rate or tumour size. (Wyatt and Altman 1995) A number of studies measure more risk factors than can realistically be used in a model and therefore pruning is often required. (Royston et al 2009)

The second issue that affects the model is the data quality and judging what to do with missing values. (Royston et al 2009) Measurements of the risk factors and outcomes should be comparable across clinicians and study centres. Risk factors with known considerable measurement error should be excluded as they will dilute their prognostic information. (Royston et al 2009) Missing data should be handled carefully. Consideration as to the cause of the missing data is needed as missing data are seldom completely random. Statistical methods such as multiple imputation are available to handle data sets with missing values. (Royston et al 2009)

A further issue concerning model development is data handling decisions. New variables may need to be created in the model-design process for example combining diastolic and systolic blood pressure to give mean arterial blood pressure. Newly created variables should also be tested for reliability and validity to ensure the model-building process is accurate. (Royston et al 2009) A number of researchers have also emphasised in recent research the importance of not dichotomising continuous variables in analysis since much more predictive information is retained. (Dupont 2010, Royston et al 2009, Sauerbrei et al 2006) It is considered unwise to assume linearity as it can lead to misinterpretation of the risk factor's influence and result in inaccurate predictions in new patients. A number of statistical techniques have been described in the literature to overcome this problem. (Dupont 2010)
The best method of selecting variables for inclusion in a prognostic model continues to lack consensus in the literature. There are two main strategies used for selection each with their own strengths and weaknesses; the full model approach and the backward elimination approach. (Royston et al 2009, Steyerberg 2009) In the full model approach all the candidate risk factors are included in the model. The advantages with this model are the lack of over-fitting and selection bias. (Steyerberg 2009) It is often impractical however to include all candidate risk factors in the model.

The backward elimination approach starts with all the candidate risk factors and a nominal significance level is pre-defined. The variables are removed from the model using a sequence of hypothesis tests until the model is complete with only significant risk factors. The chosen significance levels will determine the number of risk factors left in the model. This method however is known to produce selection bias and over-fitting, meaning the model is too closely adapted to the data. (Royston et al 2009, Steyerberg 2009) As a result of over-fitting prediction in an independent sample is often poor. Risk factors with very small p values however are much less prone to selection bias and over-fitting than weak risk factors with p values close to the nominal significance level. It is common to see a few strong risk factors and several weaker ones in prognostic data sets. (Royston et al 2009)

5.1.3 Sensitivity and specificity

Ideally, a reliable model would demonstrate both high sensitivity and high specificity. As a general rule however, sensitivity and specificity are mutually exclusive, as one rises, the other falls. (Adams and Leveson 2012) Sensitivity refers to the accuracy of a diagnostic test in correctly identifying people who have the disease under investigation. (Loong 2003) When calculating sensitivity therefore we are only concerned with this group of people, those with the disease. In a population of 100 people for example, if 30 people have the disease and the test correctly identified 24 people as having the disease, then the sensitivity of the test is 24/30 = 80%. (Loong 2003) Specificity on the other hand, is concerned with how accurate the test is at identifying those patients who are well, or disease free. For example in our population of 100 people, a test which identifies 56 out of 70 well people would have a specificity of 56/70 = 80%. (Loong 2003) The ideal model therefore would correctly identify as high a percentage as possible of the patients who will develop the disease or other outcome under investigation (sensitivity), while excluding all the patients who will not develop the outcome under investigation (specificity). (Adams and Leveson 2012)

The positive predictive value (PPV) of a test refers to the chance that the positive test results is correct and is therefore concerned with all the positive test results. In a population of 100 people for example, if 24 out of 38 positive test results are correct,

then the PPV would be 24/38 = 63%. (Loong 2003) The negative predictive value is only concerned with the negative results, so if 56 out of 62 negative results are correct (population 100 patients) then the NPV would be 56/62 = 90%. (Loong 2003) One important consideration concerning predictive values is that they will change if the prevalence of the disease changes. If the disease prevalence falls, then the test sensitivity and specificity will remain the same, but the PPV will fall and the NPV will rise. (Loong 2003) A low disease prevalence means that the person being tested is unlikely to develop the disease and based on this fact alone, a negative predictive test result is likely to be correct.

Since both sensitivity and specificity are important to the development of predictive models, the ROC curve is used to visualise the trade-off between the sensitivity and specificity and express the overall accuracy of the model. (Adams and Leveson 2012) Sensitivity is plotted on the y axis and 1-specificity is plotted on the x axis to develop a ROC curve. The closer a point is on the ROC curve graph to the top left corner, then the higher the area under the curve and the more accurate the predictive factor. Conversely, a ROC curve representing a 45 degree diagonal denotes an area under the graph of 50% and a test results which is no better than chance. (Adams and Leveson 2012) The decision regarding the optimal sensitivity and specificity for the model (taken from the ROC curve) is entirely arbitrary and depends of a number of important clinical factors such as the severity of the outcome and the potential consequences of a false negative value (such as missing a person who will develop the disease) or a false positive (such as admitting a patient who will not develop the disease leading to inefficient use of resources). (Adams and Leveson 2012)

5.1.4 Model performance assessment

Assessing the performance of a prognostic model is the final stage in the development process. The performance of a logistic regression model may be assessed in terms of calibration and discrimination. (Royston et al 2009, Chan 2004) Calibration of the model is investigated by plotting the observed proportions of events against the predicted risks for groups defined by ranges of individual predicted risks. (Royston et al 2009) The most common approach used to assess calibration using this method is to use 10 risk groups of equal size taken from the

development sample. (Chan 2004) If the observed proportions of events and predicted probabilities agree over the entire range of probabilities, then the plot shows a 45 degree line and the slope equals one. This plot is often accompanied by the Hosmer-Lemeshow test although researchers agree that this test has limited ability in assessing poor calibration. The model's performance is not guaranteed when the model is validated on an independent sample. (Royston et al 2009, Chan 2004) The potential causes of poor performance on an independent sample include differences in the actual study patients; for example the validation study hospital may serve a different socio-economic group, or have a higher percentage of elderly patients in their catchment area than the development study hospital. Other causes of poor performance may relate to the data collectors themselves; for example the validation hospital may use a different local guideline for the management of a patient group compared to the development hospital. (Royston et al 2009)

The discrimination of the prognostic model is often assessed using the area under the receiver operator curve (ROC) or the equivalent *c* (concordance) index. (Royston et al 2009, Chan 2004) A value of 0.5 means that the model is useless for prediction and is equivalent to tossing a coin. A value nearer to one however means that the higher probabilities will be assigned to the subjects with the outcome of interest compared to subjects without the outcome. The *c* index for a prognostic model is typically between 0.6 and 0.85 although is often higher in diagnostic research. (Royston et al 2009, Chan 2004)

5.1.5 Challenges in using prognostic models.

A number of challenges exist using statistical modelling for prediction in medicine including model uncertainty and limited sample size. Model uncertainty exists as the researcher does not usually fully pre-specify a model before it is fitted to a data set. (Steyerberg 2009) When the structure of the prognostic model is based on findings in the data bias may occur and the uncertainty of the model is often underestimated. Statistical methods are now available which allow the researcher to assess model uncertainty. These techniques include 'bootstrapping' which is a statistical resampling procedure that can be used in many aspects of model development and validation. (Steyerberg 2009)

A sufficient sample size is important in the design of a prognostic model. The sample size in a study is determined by the number of events or outcomes and is therefore commonly much smaller than is indicated by the total number of subjects in a study. For example in a study investigating a particular procedure with a complication rate of 0.1%, a sample size of 10,000 subjects will only yield 10 events. (Steyerberg 2009) In small sample studies model uncertainty may be large, resulting in unreliable data and an inability to derive reliable risk factors. Large sample size studies therefore facilitate many aspects of prediction research. In multivariable prognostic statistical modelling, a large sample size facilitates the selection of risk factors using simple automatic procedures such as stepwise methods and more reliable testing of model assumptions. If a large sample size is not possible as is commonly the case in medical research, the researcher is required to make much stronger modelling assumptions. It has been stated that with smaller sample size studies, the researcher should only aim to address relatively simple questions while more complex questions can be addressed by larger sample size studies. (Steyerberg 2009)

5.1.6 Dichotomising continuous variables

In clinical practice it is considered helpful to be able to categorise an individual as having or not having an attribute, for example being obese or having high blood pressure. This categorisation usually depends on a certain value or cut-point of a continuous variable. (Altman and Royston 2006) Categorisation or dichotomisation is also commonly seen in clinical research however categorisation of continuous variables in unnecessary for statistical analysis and has been shown to have a number of drawbacks. (Royston et al 2009) This technique is used as it allows a binary split and comparison of two groups, above and below a median value. This provides us with a value that represents the difference between two groups and a confidence interval.

Dichotomising leads to several problems including the loss of information which leads to a reduction in the statistical power to detect a relationship between a variable and outcome. (Altman and Royston, 2006) Subjects who are close to, but on opposite sides of the cut point are characterised as being very different when in fact they are

very similar. Inherent problems exist in all methods used to decide at what point or value the cut-point should be. (Altman and Royston, 2006) If the researcher is using regression analysis to adjust for the effect of a confounding variable, dichotomising continuous variables in the analysis will increase the risk that a substantial proportion of the confounding remains. (Altman and Royston 2006) Instead of dichotomising continuous variables therefore, research methodologists concur that they should remain continuous. (Royston et al 2009, Steyerberg 2009, Sauerbrei et al 2006)

5.1.7 Multivariable fractional polynomial analysis.

The aim in the final model-building process is to include only the variables that influence the outcome but for continuous variables, the functional form (for example linear or step function) must be determined. (Sauerbrei et al 2006) A number of different methods for analysing continuous variables in multivariable logistic regression have been suggested in the literature, including the use of fractional polynomials. (Steyerberg 2009, Royston and Sauerbrei 2008, Sauerbrei et al 2006) Fractional polynomials have been recently advocated to model continuous risk factors due to the inherent uncertainty over linearity between continuous variables and an outcome (Steyerberg 2009) Fractional polynomials models therefore are useful when the researcher would like to preserve the continuous nature of the variables in a regression model, but suspects that some or all of the relationships may be non-linear. (Sauerbrei et al 2006) If the researcher is concerned therefore that linear regression would not truly represent the relationship between the risk factor variable and the outcome, the use of a log transformation using a technique such as fractional polynomials should be employed. (Altman and Royston 2006)

5.1.8 Model-building using multivariable fractional polynomial analysis.

The R program (a free software program for statistical computing) contains a number of statistical packages including the *mfp* (multivariable fractional polynomial) function. The *mfp* package is a collection of R functions targeted at the use of fractional polynomials for modelling the influence of continuous variables on the outcome in regression models, as introduced by Royston & Altman (1994) and further modified by Sauerbrei & Royston (1999). The regression model combines

backward elimination with a systematic search for a suitable fractional polynomial transformation using an adaptive algorithm to represent the influence of each continuous variable on the outcome. (Sauerbrei et al 2006) At each step of a `back-fitting' algorithm, *mfp* constructs a fractional polynomial transformation for each continuous variable while fixing the current functional forms of the other variables in the model. The algorithm terminates when no further variable is excluded and the functional forms of the continuous variables do not change anymore. (Sauerbrei et al 2006) In summary, depending on the selected *p* value associated with the best fractional polynomial transformation, one or more risk factors may be excluded from the final model and for some of the continuous variables, a transformation may be selected. (Sauerbrei et al 2006) Figure 5.2 illustrates the process of model building using backward elimination and the likelihood ratio test.

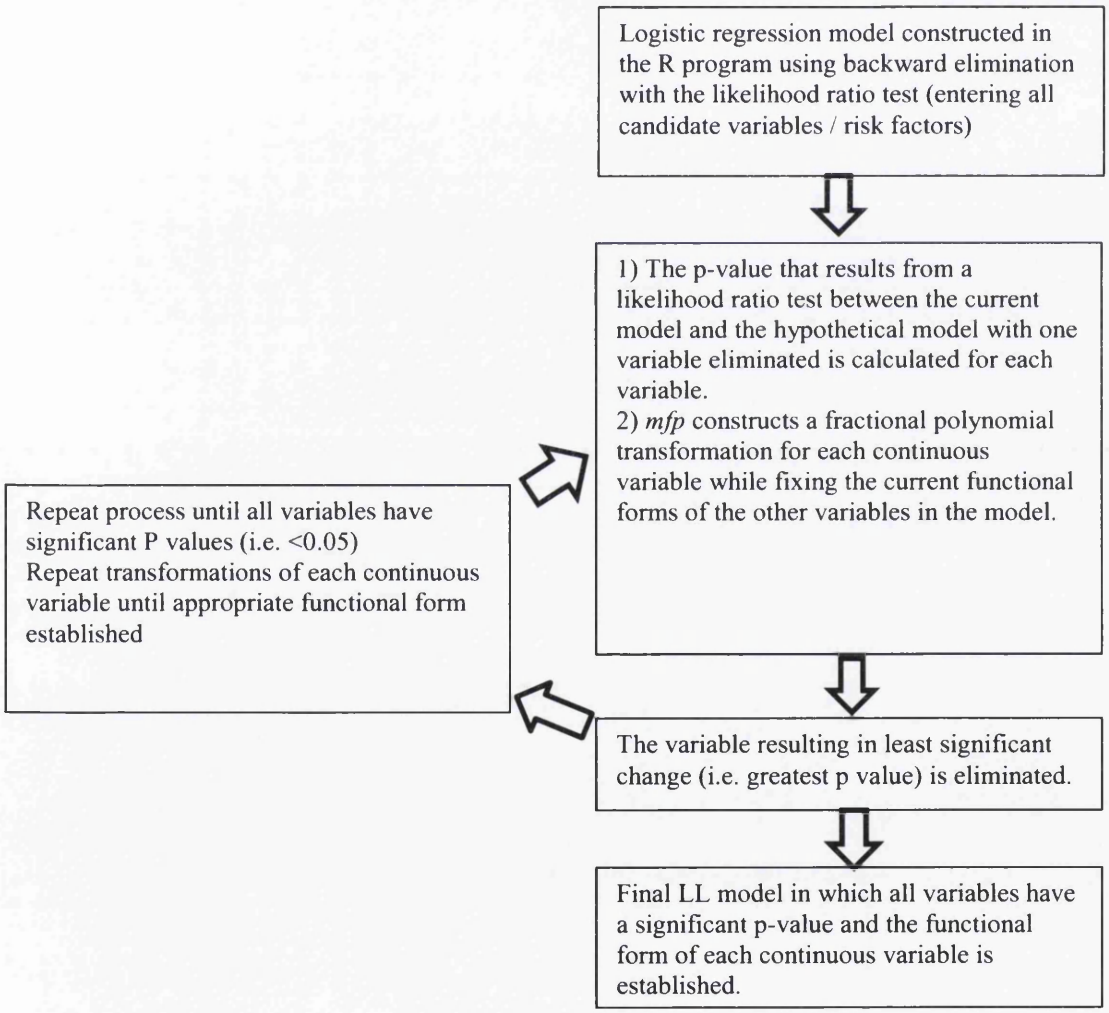


Figure 5.2 Stages of the model-building process using backward elimination and the likelihood ratio rest.

5.2 Methodology

5.2.1 Building a prognostic model for blunt chest wall trauma patients.

The same inclusion criteria were used as described in chapter 4 (which analysed patients from 2009 to 2010) but the sampling time frame was extended in order to recruit more patients. Therefore all patients presenting to the ED at Morriston Hospital between 2009 and 2011 with blunt chest wall trauma were included in the study. Patients with immediate life-threatening injuries and those requiring immediate life-preserving interventions were excluded from the study. Data were collected retrospectively from the patient's ED notes (if discharged home from the ED) or medical notes (if admitted to hospital) for these patients including demographics, candidate risk factors (risk factors for inclusion in model-building process) and a number of outcomes including mortality, any pulmonary morbidity, length of stay and need for ICU admission. The choice of candidate risk factors was based on the results of the background research to this study; a systematic review and meta-analysis and a questionnaire study. (Battle et al 2012, Battle et al 2011)

The complete set of candidate risk factors recorded were patient age, number of rib fractures sustained, presence of chronic lung disease, diabetes or cardiovascular disease, pre-injury anticoagulant use, smoking status, oxygen saturation levels and respiratory rate on initial assessment in the ED. Peduzzi et al (1995) suggested that the number of patients needed to ensure sufficient power in a retrospective cohort study is equivalent to ten events per variable (EPV) being investigated. In this study we set out to investigate nine variables or risk factors therefore a minimum of 90 events (on-set of complications in the recovery phase following blunt chest wall trauma) were required.

5.2.2 Preliminary decisions regarding the model building process

Based on the guidelines outlined in Royston et al (2009), a number of preliminary decisions were made prior to building the model. This process was used in an attempt to pre-specify the model (rather than fit the model to the dataset), thus reducing the risk of selection bias and over-fitting. The following decisions were made:

1) Nine candidate risk factors were selected for inclusion in the model which had been highlighted as prognostic in the background research.

2) As a result of the low incidence of the individual complications in the blunt chest wall trauma cohort, the decision made was to combine the outcomes into a composite outcome labelled 'the development of complications during the recovery phase following blunt chest wall trauma'.

3) Patients were only followed up during their hospital admission as it was considered beyond the scope of this retrospective study to follow up any primary care provision.

4) No candidate risk factors were eliminated on the basis of missing data as there were only two missing values for the entire dataset. Imputation of the variable mean was used to replace the missing variables.

5) Continuous variables were not dichotomised during the model building process therefore patient age, number of rib fractures, oxygen saturation levels and respiratory rate were initially assessed for linearity using scaling transformation.

6) The significant risk factors in the model were selected using backward elimination with the Akaike information criterion (AIC) and the Likelihood ratio at a significance level of 0.05 and these were then compared to a full model using all candidate risk factors.

7) For each model it was decided to assess discrimination and calibration. The *c* index and receiver operating curves were therefore calculated to assess discrimination and the Hosmer-Lemeshow test used to assess calibration. Overall model accuracy was measured using the Nagelkerke R Squared statistic.

5.2.3 Statistical analysis

Baseline characteristics were compared between the validation sample and the original development sample using Fisher's Exact test for categorical variables and Mann-Whitney U test (as not normally distributed) for the continuous variables. The SPSS statistical package (version 20, Chicago) and the R Program (version 2.14.1) were both used for the statistical analysis and model building in this study. (Sauerbrei et al 2006) The use of fractional polynomials within a logistic regression model required the *mfp* (multivariable fractional polynomials) package within the R program. The *mfp* package utilises the RA2 algorithm which is a closed test

procedure outlined by Ambler and Royston (2001) and Sauerbrei and Royston (2006). The *mfp* function applied a scaling transformation to each continuous variable to ensure that no non-positive values are encountered and to reduce the range of values. This process ensured that the correct functional form of each continuous variable was achieved and that linearity was not incorrectly assumed. Multivariable logistic regression with backward elimination was used and results analysed using the Akaike Information Criterion and Likelihood ratio tests. A full model with no elimination was also presented to allow comparisons between all three model results.

To assess the model's discriminatory power to predict an event, the area under the ROC curve (*c* index) was calculated for the validation sample and then compared to the development sample. To assess the accuracy of the model in predicting an event, the sensitivity, specificity, positive predictive value, negative predictive value and odds ratios with 95% confidence intervals were calculated. The Hosmer-Lemeshow test was calculated to assess model calibration. For all analysis, a two-tailed p-value of less than 0.05 was used to define statistical significance.

5.2.4 Ethical approval

The South West Wales Research Ethics Committee confirmed that ethical approval was not required in this study.

5.3 Results

Between 2009 and 2011 a total of 274 patients were admitted to hospital from the Emergency Department of a large regional trauma centre in South Wales (Morriston Hospital) with a primary diagnosis of blunt chest wall trauma. A total of 161 patients developed complications therefore the target sample size of 90 events was achieved. On analysis, only two patients (<0.5%) had missing data (both respiratory rate). As a result of this very small number of missing data, it was decided that a complex imputation calculation was not required and the mean of all the patients' respiratory rates was calculated and used in place of the missing data. (Bouwmeester et al 2012) The baseline characteristics of the patients included in the study are outlined in Table 5.1. The significant risk factors ($p<0.001$) and their unadjusted odds ratios and 95% confidence intervals are illustrated. Table 5.1 highlights that in the univariable

analysis, the significant risk factors for the development of complications in the recovery phase following blunt chest wall trauma include the patient's age, number of rib fractures, chronic lung disease, cardiovascular disease, pre-injury anticoagulant use and oxygen saturations levels.

	Total n=274	No complications n=113 (41%)	Complications n=161 (59%)	p-value	Unadjusted OR (CI 95%)
Age	66 ± 17	57 ± 21	73 ± 17	p<0.001*	
Number of rib fractures	3 ± 2	2 ± 1	3 ± 2	p<0.001*	
Chronic lung disease	154 (56%)	38 (34%)	116 (72%)	p<0.001*	5.1 (3.0-8.6)
Cardiovascular disease	116 (42%)	34 (30%)	82 (51%)	p<0.001*	2.4 (1.5-4.0)
Smoker	92 (34%)	43 (38%)	49 (30%)	p>0.05	1.4 (0.8-2.3)
Pre-injury anticoagulants	117 (43%)	28 (25%)	89 (55%)	p<0.001*	3.8 (2.2-6.4)
Oxygen saturations	94 ± 4	95 ± 3	93 ± 5	p<0.001*	
Respiratory rate	20 ± 5	19 ± 4	20 ± 5	p>0.05	

*significant p-value, n: number (%), mean ± SD using Mann Whitney U test, OR: odds ratio, CI: confidence interval using Fisher's Exact test.

Table 5.1 Baseline characteristics of patients in the development study

Using the results obtained in the retrospective observational study conducted at Morriston Hospital, a prognostic model for use in the blunt chest wall trauma population was developed. The first stage of the analysis involved creating the initial logistic regression model using the RA2 algorithm within the *mfp* function. Using the algorithm, all variables entered into the analysis remained as linear terms. The algorithm also determined that fractional polynomial models did not provide a significantly better fit than the linear models for any of the continuous variables in the context of the multivariable model. Given that no fractional polynomials were present in the complete model as determined by the *mfp* function, a straightforward generalised linear model (*glm*) could be used for the final model building process.

In order to evaluate which type of model was the most accurate in predicting development of complications in the recovery phase following blunt chest wall trauma, three different models were built for comparison. On analysis using the AIC, respiratory rate was the first variable eliminated as it resulted in the greatest reduction in the AIC value. Respiratory rate was also the first variable to be

eliminated using the Likelihood ratio test as it had the greatest p value over the chosen significance level of 0.05. Subsequent elimination steps were similarly performed in the analysis on the reduced models until the removal of any variable resulted in an increased AIC value (in AIC elimination) or until no variable had a p-value above the chosen significance level (in Likelihood ratio test).

Implementation of backward elimination using AIC values resulted in a final model based on the risk factors age, oxygen saturations, number of rib fractures, presence of chronic lung disease and pre-injury anti-coagulant use. If a Likelihood ratio test was used with a 0.15 significance level then the same model results. If a 0.05 significance level was chosen then oxygen saturation levels were also eliminated. For the purpose of performance assessment, the full model, the reduced AIC model and the Likelihood ratio model with a 0.05 significance level used.

Table 5.1 shows the results of the coefficients in a logistic regression model for the full model and the two reduced models selected by backward elimination using the AIC and Likelihood ratio test at 5% significance. The positive regression coefficients indicate an increased risk of developing complications during the recovery phase following blunt chest wall trauma. Oxygen saturation levels had a significant *p*-value even though the regression coefficient was negative. For oxygen saturations the negative coefficient indicates that the lower the oxygen saturation level, the greater the risk for developing complications. Intuitively this result appears correct as the patient with oxygen saturation levels of 70% is at greater risk of complications than the patient with oxygen saturation levels of 98%. The other variables with negative regression coefficients all had non-significant *p*-values and were therefore considered not to influence the outcome.

Risk factor	Full model	AIC	Likelihood Ratio (alpha=0.05)
Age	0.02(0.01)	0.02(0.01)	0.02(0.01)
Oxygen saturation levels	-0.07(0.05)	-0.07(0.04)	-
Number of rib fractures	0.41(0.10)	0.42(0.10)	0.45(0.10)
Respiratory rate	0.01(0.04)	-	-
Chronic lung disease	0.82(0.32)	0.79(0.32)	0.85(0.31)
Cardiovascular disease	-0.13(0.41)	-	-
Diabetes mellitus	-0.34(0.43)	-	-
Smoker	-0.19(0.33)	-	-
Anti-coagulant use pre-injury	0.74(0.40)	0.64(0.33)	0.65(0.33)
Intercept	4.81(4.79)	3.72(4.15)	-2.67(0.57)
***C* index**	0.81	0.80	0.80

Binary variables coded 0 for no, 1 for yes

Linear effects of continuous risk factors previously calculated

Adjusted positive regression beta coefficients (standard error)

Table 5.2 Beta coefficients and standard error values for selected risk factors of development of complications in the recovery phase following blunt chest wall trauma.

The coefficients in the logistic regression models in each case can be converted to odds ratios by taking the anti-log of each coefficient. Table 5.2 shows the odds ratios for each of the risk factor variables using the AIC and Likelihood ratio models. Using the AIC model for example it is evident that the odds of a patient of a given age developing complications are 1.0 times higher than a patient who is one year younger. Similarly, the odds of developing complications increases 1.5 times for each successive rib fracture sustained and a patient using pre-injury anti-coagulants has 1.9 times the odds of developing complications than a patient not using anti-coagulants.

Risk factor	Odds ratios (CI) from the AIC model	Odds ratios (CI) from the Likelihood ratio
Age	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Oxygen saturation levels	0.9 (0.9-1.0)	-
Number of rib fractures	1.5 (1.3-1.9)	1.6 (1.3-1.9)
Chronic lung disease	2.2 (1.2-4.1)	2.3 (1.3-4.3)
Anti-coagulant use pre-injury	1.9 (1.0-3.7)	1.9 (1.0-3.7)

CI: confidence intervals (95%), AIC: Akaike Information Criterion.

Table 5.3 Adjusted odds ratios (confidence intervals) of developing complications in the recovery phase following blunt chest wall trauma using the AIC and Likelihood ratio models

The *c* index and Hosmer-Lemeshow goodness of fit statistic were calculated in order to test the predictive capabilities of the final models. The discrimination of each model was tested using the *c* index (area under the receiver operator curve). Table 5.3 highlights the *c* index for each model. If the *c* index is interpreted as the probability that a patient who experiences complications will have been assigned a higher probability than a patient who does not experience complications, then the model with the larger *c* index can generally be considered as having greater predictive capacity. It is evident from the table that eliminating risk factor variables has had a very limited effect on the *c* index. This result indicates that a small number of variables have a strong predictive capability and therefore supports the use of a model with a smaller number of variables.

Model	*c* index
Full model	0.81
AIC	0.80
Likelihood ratio (5% significance)	0.80

Table 5.4 The *c* index for each of the models

The graph in Figure 5.3 shows the receiver operator curves for each model. Using this graph it is possible to assess the sensitivity and specificity of each model. The optimal sensitivity and specificity is obtained from the nearest point to the left upper corner of the box (marked by the arrow). Thus the optimal sensitivity for the models equals approximately 76% and specificity equals approximately (1- 0.23) 77%.

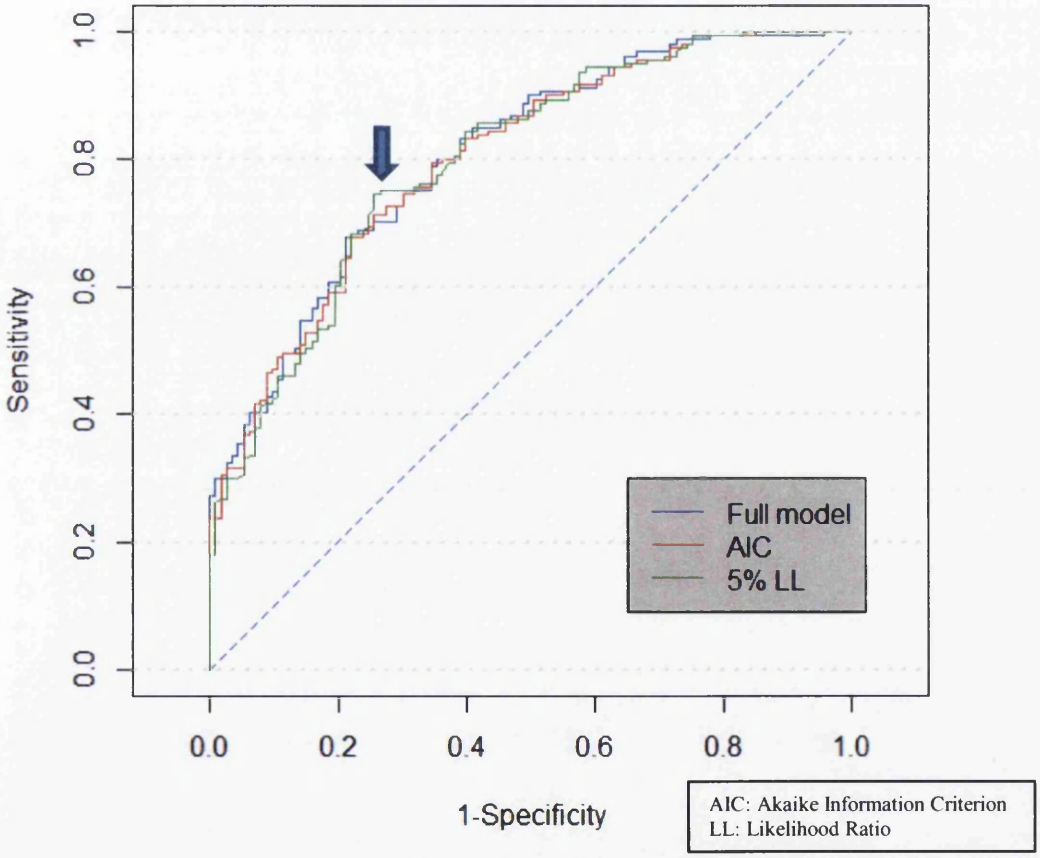


Figure 5.3 Receiver operator characteristic (ROC) curves for the three multivariable models of development of complications in blunt chest wall trauma.

Model accuracy and discrimination can be assessed statistically using the designated function within in the analysis. For example, the following values were assigned using the Likelihood Ratio test: true positives (TP) = 133, false positives (FP) = 44, false negatives (FN) = 28, true negatives (TN) = 69. From these values we can calculate the model's sensitivity (TP/(TP+FN) = 83%, specificity (TN/(FP+TN) = 61%, PPV (TP/(TP+FP) = 75% and NPV (TN/(FN+TN) = 71%. It can be concluded that using the Likelihood Ratio test a total of 75% of patients will be correctly identified as developing complications in the recovery phase following blunt chest wall trauma. The Nagelkerke R Square statistic was 0.351 for the Likelihood Ratio Model indicating reasonable model accuracy.

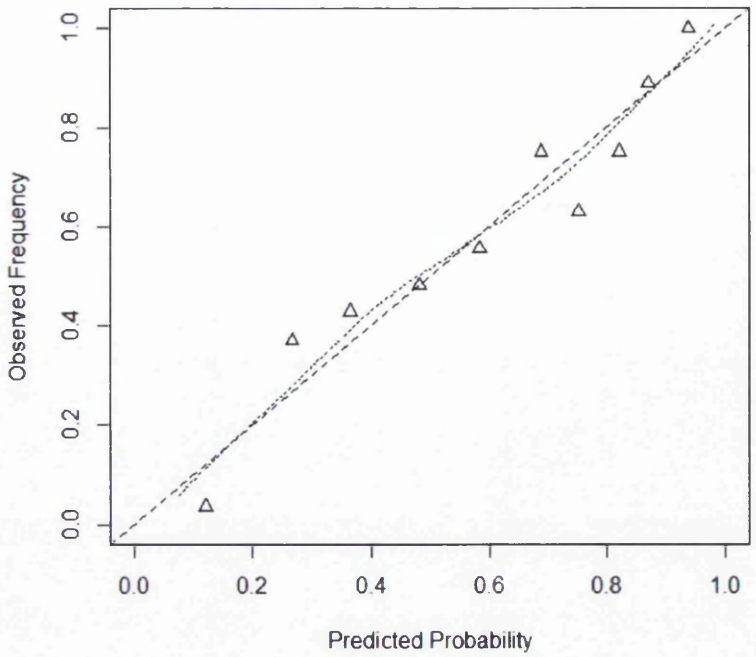
Table 5.4 shows the results of the Hosmer-Lemeshow test for each model. The full model and the AIC model produce large p-values indicating that they produce a good approximation of the data and are all well calibrated. The Likelihood ratio model produced a smaller p-value and this may therefore be attributed to worse fit when compared to the other two models.

Model	H-L statistic (chi-square value)	p-value
Full model	8.95	0.35
AIC Model	9.22	0.32
Likelihood ratio model (5% significance)	12.9	0.11

NB: H-L statistic: Hosmer-Lemeshow statistic.

Table 5.5 Hosmer-Lemeshow results for each model.

A graphical visualisation can be created by plotting the expected proportions against the observed proportions for each of the 10 samples created in the Hosmer-Lemeshow test. In a perfect fitting model a 45 degree line would be expected and anything close to this indicates a good model for this particular dataset. Figure 5.4 illustrates this graphical visualisation for the AIC model and shows a good model fit. It is important to highlight however that good model performance on the existing dataset (development sample) is not necessarily indicative of good predictive performance on a new dataset.



Δ: *Risk of outcome in 10ths of patients with similar predicted probabilities*
Dotted line: *Relationship between observed frequency and predicted probability of development of complications*
Dashed line: *Ideal relationship between observed and predicted frequency of outcome in model with perfect calibration*

Figure 5.4 Graphical representation of Hosmer-Lemeshow test

It is possible to predict a new blunt chest wall trauma patient's probability of developing complications using the logistic model. The diagram in Figure 5.5 represents a black box in which the risk factors can be inserted and an output will be obtained which will be a number between 0 and 1. This output will denote the probability of the new patient developing complications.

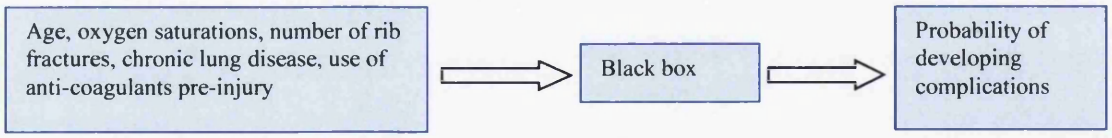


Figure 5.5 The logistic regression prediction model.

Inside the black box the equation for calculating the probability of developing complications can be found, which is given by:

Probability (developing complications) = $\frac{1}{1 + e^{-z}}$ (where e denotes the exponential function)

z = the intercept (beta coefficient of the constant in the model) + beta coefficient for age x actual age of patient + beta coefficient for number of rib fractures x actual number of rib fractures + beta coefficient for chronic lung disease x 1 (1 if present and 0 if absent) and so on for the rest of the risk factors. The beta coefficients are shown in Table 5.2.

For example using the AIC model, the probability can be calculated of a blunt chest wall trauma patient developing complications who is 80 years old, who has oxygen saturations of 88%, with three rib fractures and has chronic lung disease by the following:

$z = 3.72 + (0.02 \times 80) + (-0.07 \times 88) + (0.42 \times 3) + (0.79 \times 1) + (0.64 \times 0) = 1.21$

$1 \setminus (\exp^{-z} + 1)$ = probability of **0.77**; and it is therefore very likely that this blunt chest wall trauma patient will develop complications.

In a second example with a 45 year old patient with oxygen saturation of 98 % and one rib fracture, the probability can be calculated using the AIC model using the following equation:

$Z = 3.72 + (0.02 \times 45) + (-0.07 \times 98) + (0.42 \times 1) = -1.82$

$1 \setminus (\exp^{-z} + 1)$ = probability of **0.14**; and it is very unlikely therefore that this patient will develop complications.

5.4 Discussion

Using the dataset derived from the retrospective study, three logistic regression models have been developed. The use of multivariable fractional polynomials found that the continuous variables age, number of rib fractures, oxygen saturation levels and respiratory rate remained as linear terms. The algorithm used determined that a fractional polynomial model did not provide better fit or effect the estimates of coefficients and their corresponding *p*-values than the linear models for any of the continuous variables in the context of the multivariable model. It was therefore possible to use a straightforward generalised linear model for the analysis.

The full model, AIC model and Likelihood ratio model highlighted the regression coefficients indicating an increased risk of developing complications during the recovery phase following blunt chest wall trauma. These significant risk factors included increasing age, an increase in number of rib fractures sustained, presence of chronic lung disease and the use of pre-injury anti-coagulants. A further risk factor of decreasing oxygen saturation levels was found to be significant on the full and AIC model but not the Likelihood ratio model using a 5% significance level. By inputting the regression coefficients into the equation generated by the model, it is possible to predict in a blunt chest wall trauma patient the probability of developing complications. Using the results of the sensitivity and specificity analysis, it is also possible to state the level of confidence of the prediction.

Odds ratios and their confidence intervals for each of the significant risk factors were presented for both the AIC and Likelihood ratio model. Chronic lung disease and the use of pre-injury anti-coagulants had the highest odds for all of the positive risk factors. The use of pre-injury anti-coagulants has not been previously reported in the literature as a risk factor for poor outcomes in blunt chest wall trauma patients, therefore further research and validation in prospective studies is needed. The use of oxygen saturations as a risk factor of development of complications has also received limited attention in previous research and further studies would therefore be beneficial.

The predictive capabilities of the models were assessed and results demonstrated that there was minimal difference between the discrimination results for the three models as measured by the c index. All three models were shown to have good predictive capability. The calibration results indicated that the full model and AIC model provided a greater approximation of the data and demonstrated a good fit. The results for the Likelihood ratio model indicated a smaller p-value and it is possible that this could be attributed to worse fit. The graph in Figure 2 illustrates the apparent internal validity of the AIC regression model. It is of more interest however to study the validity of the model, that is the performance on an underlying population, or external validity, that is the performance on a different population. The next stage of the study therefore is the validation phase, in which the final model will be externally validated in a different patient cohort and by different investigators.

6.0 A new prognostic model to assist in the management of blunt chest wall trauma patients: a prospective, multi-centred validation study.

6.1 Introduction

A prognostic model is a complex model that combines two or more items of patient data in order to predict clinical outcomes. (Wyatt and Altman 1995) There are numerous prognostic models available for use by clinicians however few of them are actually used in practice. One of the reasons reported for their lack of use is that clinicians believe that no prognostic model derived from one patient cohort can be generalised to a different patient cohort. (Wyatt and Altman 1995) In order to prove the efficacy of a new prognostic model, it is not sufficient to demonstrate that it predicts outcome in the initial development dataset. (Altman et al 2009)

Evidence that the model performs accurately in other patient groups is paramount to its widespread adoption and implementation in clinical practice. (Adams and Leveson 2012) The concept of validating a prognostic model is generally agreed to mean establishing that it works satisfactorily for patients other than those used to develop the model. (Altman and Royston 2000) A validation study is therefore important as there is no guarantee that the prognostic model developed in the previous chapter will work in a new cohort of blunt chest wall trauma patients and researchers commonly report a reduction in accuracy in the validation cohort. (Adams and Leveson 2012, Altman et al 2009)

6.1.1 Poor performance of a prognostic model in validation studies

Altman et al (2009) and Toll et al (2005) outlined a number of reasons for the potential poor performance of a new prognostic model in a validation study. They suggested that over-fitting of the original model could contribute to poor performance in a validation study. This would occur for example, if too many risk factors were investigated compared to an insufficient number of events or outcomes. (Peduzzi et al 1995) The absence of an important risk factor from the original model leading to a systematic deviation of the probabilities (either too high or too low) or simply inherent deficiencies in the design of the original model may also contribute to poor performance on a new dataset. (Altman et al 2009, Vergouwe et al 2005)

Differences in the development and validation samples are summarised by Toll et al (2005). They state that the first possible difference arises from the definitions of the variables under investigation and their measurement methods. All risk factors and outcomes need to be clearly defined in the development model if it is to be generalizable to other populations. (Toll et al 2005) Secondly, there may be significant differences in the patients' characteristics in the development and validation sample and measures should therefore be taken to ensure that this difference is addressed. (Toll et al 2005) For example the researcher may need to clearly define the age of the patients to be recruited in a study in which age is considered a risk factor. The final potential difference may be that there are fewer patients in the validation study than the development study however this effect can be reduced by ensuring there are 100 events and 100 non-events in the validation sample. (Toll et al 2005, Vergouwe et al 2005) All of these potential difficulties should be considered in the analysis of results derived from a validation study for a new prognostic model.

6.1.2 Design of a validation study

An example of validation in its simplest form would be to split the development dataset randomly into two sections, the first used to develop the model and the second used to validate the model. (Altman et al 2009) This method is commonly referred to as internal validation and tends to produce optimistic results due to the similarity between the two groups. (Vergouwe et al 2005) Vergouwe et al 2005 suggested that if the dataset was split in order that the early treated patients were in the development group and the more recently treated patients were in the validation group, then this would be considered temporal validation. This type of validation is considered superior to internal validation due to the prospective evaluation of the model, independent of the original data and development process. (Altman et al 2009) Neither internal nor temporal validation however examines the generalisability of the model, or the external validity. In order for generalisability to be assessed, it is necessary to collect new data from an appropriate patient cohort, in a different location to where the development dataset was obtained. (Altman et al 2009)

External validation is the most rigorous form of model validity assessment. (Bouwmeester et al 2012) The fundamental design issues of external validation studies have received limited attention in prognostic research. (Altman et al 2009) In guidelines by Vergouwe et al (2005) a minimum sample size of 100 events and 100 non-events was recommended for an external validation study. Steyerberg et al (2004) concurred that guidelines for calculation of appropriate sample size in external validation studies are lacking but also emphasized that a large sample size in a validation study is irrelevant if the sample size in the development study was too small. Sample selection had also been largely ignored in prognostic research. (Altman et al 2009, Altman and Royston 2000) In a recent systematic review of clinical prediction research, the importance of reporting all aspects of sample selection was emphasized, including patient recruitment, inclusion and exclusion criteria, patient characteristics, follow up, refusal to participate rates and clinical setting. (Bouwmeester et al 2012) This review was summarised in the development study and the suggestions for methodological design issues and reporting of results are again followed in this study.

To investigate external validity it is necessary to use the logistic regression equation developed in the prognostic model (that is both the selected variables and their coefficients) to predict outcomes for the patients in the validation cohort and then compare these predictions with the patients' actual outcomes. (Altman et al 2009) Since the unbiased estimate of the model accuracy is the main aim of validation, the same risk factors and their coefficients should be assessed in the validation study as were generated in the development study. The model should not be modified by adding or deleting variables as this would invalidate the assessment of fit. (Miller et al 1991) There are a number of methods of updating the model described in prognostic research however these are used after the validation model has demonstrated poor accuracy. (Toll et al 2008, Steyerberg et al 2004)

General consensus exists in the literature regarding the use of calibration and discrimination in the evaluation of the model. (Bouwmeester et al 2012, Altman et al 2009, Toll et al 2008) Calibration can be assessed by plotting the observed proportions of events against the predicted probabilities for groups that are defined by specific ranges of predicted risk. (Altman et al 2009) In addition to this graph, the

Hosmer-Lemeshow test statistic can be used although the result of this statistic should be interpreted with caution as it has less power to assess calibration in the validation study compared to the development study. (Altman et al 2009, Vergouwe et al 2005) As in the development study, discrimination can be summarised using the c index. (Altman et al 2009, Toll et al 2008)

It is the calibration and discrimination results which allow the researcher to evaluate whether the performance on the validated model matches or comes close to the performance in the sample on which it was developed. Even if the performance is inferior to that of the development model, the model may still be useful in clinical practice. (Altman et al 2009) To be considered clinically useful, a risk score needs to be accurate with good calibration and discrimination capabilities, clinically credible and externally validated. (Altman et al 2009) If a validation model has poor predictive capabilities the original dataset should not be rejected as commonly occurs in predictive research, but model updating should be considered. (Janssen et al 2008, Toll et al 2008)

6.1.3 Updating of validation models to improve performance in new patients

The performance of prognostic models needs to be tested in new patients (external validation) before it can be confidently used by clinicians. The predictive performance of models is often poorer in the validation sample than the development sample. Rather than reject the original model and its dataset and develop a new one, the original model can be adjusted and updated. The main advantage of using adjustment techniques is that the updated model is based on combined data from the original and validation dataset, thus enhancing both stability and generalisability (Moons et al 2009b) A number of statistical techniques have been described to adjust the model. (Janssen et al 2008, Toll et al 2008, Steyerberg et al 2004)

In general, when the discrimination of the validation model is sufficient, recalibration techniques alone can improve the model's calibration. If discrimination is also poor, then revision techniques are required. These techniques vary in extensiveness, with the easiest method a simple change in the model intercept (leaving the beta-coefficients for each variable unchanged) to more complicated adjustments where the

beta-coefficients derived in the original model are all re-estimated and combined with those from the validation model. (Janssen et al 2008) It was concluded in the study by Janssen et al (2008) that as long as discrimination results are good, then simple recalibration methods were are effective as techniques used to re-estimate all beta-coefficients.

The simplest method of recalibration described by Steyerberg et al (2004) and Janssen et al (2008) is to update or adjust only the calibration intercept from the validation model. This can be achieved by calculating a correction factor which is added to the intercept of the original development model, which results in a new intercept. The correction factor is calculated using an equation based on the mean predicted risk and the observed outcome frequency in the validation dataset. (Janssen et al 2008) The extent to which this process of model validation and adjustment has to be pursued prior to clinical application of the final model, will depend on the clinical setting in which the model is to be used. Guidelines or general rules are not yet available to guide the researcher attempting to develop and validate such a prognostic model. (Moons et al 2009b)

6.1.4 Validation study aims

The first aim of this study was to validate the development model in a new cohort of blunt chest wall trauma patients and assess the model's predictive capabilities. The second aim was to transform the beta-coefficients for each risk factor in the validated model into a simple prognostic model for use in clinical practice. This model would allow the clinician to enter an individual patient's risk factor data, which would result in the respective probability of outcome. This prognostic model was also assessed for accuracy using the same technique of comparison of predicted and observed outcomes.

6.2 Methodology

6.2.1 Study design

The aim of the study was to validate the prognostic model therefore a data collection form was designed that included all necessary risk factors and outcomes previously

investigated in the model development study. The data collection form can be found in Appendix C. A multi-centred prospective study design was used in order to validate the prognostic model previously developed in the model-building phase.

6.2.2 Study setting

A total of eight hospitals were purposively selected to participate in the study, however Frenchay Hospital in Bristol withdrew from participation due to a lack of study funding. The hospitals were selected in order to achieve an even geographical spread in England and Wales, a variety of type of hospital (district general hospitals, teaching hospitals and regional trauma centres) and size of hospital, thus enhancing generalizability of the model. The hospitals that participated in the study are listed in 6.1.

Hospital and location	Type of hospital	ED attendances per year
Royal Gwent Hospital Aneurin Bevan Health Board Newport, South East Wales	District General Hospital	80,000
West Wales (Glangwili) General Hospital Hywel Dda Health Board Carmarthen, South West Wales	District General Hospital	39,000
Ysbyty Gwynedd Betsi Cadwaladr University Health Board Bangor, North West Wales	University teaching hospital	50,000
Wrexham Maelor Hospital Betsi Cadwaladr University Health Board Wrexham, North East Wales	University teaching hospital	72,000
Musgrove Park Hospital Taunton and Somerset Foundation Trust Taunton, South West England	District General Hospital	55,000
Bradford Royal Hospital Bradford Teaching Hospitals NHS Foundation Trust. Bradford, North England	University teaching hospital	120,000
Salford Royal Hospital Salford Royal NHS Foundation Trust Salford, Central England	Regional trauma centre	85,000

Table 6.1: Details of the hospitals participating in validation study

6.2.3 Sample size

The total number of patients required in this validation study was 200, which included a total of 100 events (patient developing complications) and 100 non-events (patients with no complications) as suggested in the study by Vergouwe et al (2005).

The data collection period of six months and the total number of participating hospitals were selected in order to achieve this sample size.

6.2.4 Data collection

Each of the hospitals agreed to complete data collection for a period of six months, the ED doctors completing the risk factors section of the form and a respiratory physiotherapist completing the outcomes section if the patient was admitted to hospital. The form was completed for every blunt chest wall trauma patient attending the ED, regardless of whether the patient was admitted to hospital or discharged home from the ED. Patients excluded from the study included those with immediate life-threatening injuries, those unable to give consent or those less than 18 years of age. Written consent was gained on initial contact with the patient in the ED and the patient was also provided with the Participant Information Sheet and a Study Withdrawal Letter. (See Appendix C for a copy of the documentation used) The Study Withdrawal Letter allowed the patient to withdraw their consent up to seven days after initial data collection as the Research Ethics Committee considered that the patient may not make a fully informed decision within the time period waiting in the ED and while in pain from their chest trauma.

The dataset included demographic variables such as age, gender, injury mechanism and whether the patient had previously attended the ED with the same injury and the current re-attendance was unplanned. The independent variables were defined a priori based on the prognostic model and were patient age, pre-existing conditions, number of suspected rib fractures, smoking history, pre-injury anticoagulant use, respiratory rate and oxygen saturation levels. The individual doctors and physiotherapists participating in the study were unaware of which of the risk factors and outcomes being collected would be included in the analysis. This allowed a degree of blinding in data collection.

6.2.5 Definition of events

The demographic data collected were patient gender, age and injury mechanism. The risk factors collected by the Emergency physicians on initial assessment of the patient in the ED were age, number of rib fractures, presence of chronic lung disease

or cardiovascular disease, use of pre-injury anticoagulants, current smoking status, oxygen saturations and respiratory rate. The studies' Principal Investigators were instructed on the exact definition of variables to be collected, in order to enhance the reliability of the study results. All blunt chest wall trauma patients aged 18 years or more were included in the study. The only exclusion criteria were patients who refused or were unable to consent to participation and those who presented with immediate life-threatening injuries. It was specified that the number of rib fractures could be either clinically suspected or confirmed with imaging. Patients were to be categorised as either a smoker or a non-smoker. The non-smokers category would include ex-smokers. The clinicians completing the data collection were asked to state whether the patient had either chronic lung disease or cardiovascular disease and these variables were not narrowed down to specific diseases. The oxygen saturation levels and respiratory rates were to be taken on initial assessment in the ED.

The development of complications during the recovery phase following blunt chest wall trauma was the composite outcome measure collected in this study. Data collection for this outcome was completed from the time the patient presented to the ED, through to discharge from hospital. Patients were not followed up if discharged directly home from the ED due to a lack of time and resources. Patients were reported to have developed complications if one or more of the following were evident: in-hospital mortality, morbidity including all pulmonary complications (chest infection, pneumonia, pneumothorax, haemothorax, pleural effusion and empyema), ICU admission, or a prolonged length of stay as defined as a total hospital stay of seven or more days. (Flagel et al 2005, Hoff et al 1994)

6.2.6 Data input

On completion of the data collection, all forms were anonymised (including removal of the attached consent form and patient's identifying details) and returned to the study's chief investigator. All data were transferred onto an EXCEL spread sheet. A validation check was completed in which an additional researcher checked the accuracy of the data input for 10% of all patients, in order to reduce information bias. If a patient's notes had missing or incomplete data for the variables under

investigation, they were still included in the database. The dataset was stored on a hospital encrypted computer (safe-end protector) to ensure data security.

6.2.7 Statistical analysis

Baseline characteristics were compared between the validation sample and the original development sample using Fisher's Exact test for categorical variables and Mann-Whitney U test (as not normally distributed) for the continuous variables. This univariable analysis for each of the individual risk factors provided unadjusted odds ratios and 95% confidence intervals. Statistical significance was set at $p<0.05$. The final prognostic model developed using the Akaike Information Criterion in the previous chapter included the patient's age, number of rib fractures, chronic lung disease, the use of anticoagulants and oxygen saturation levels. In order to validate the prognostic model from the development study, a number of statistical techniques were applied to the data collected in the participating hospitals in the validation study.

Exclusion of participants with missing data not only leads to loss of statistical power, but also potentially to biased results. (Bouwmeester et al 2012) Due to the small percentages of missing data in the validation study, a simple imputation method was used. Imputation of the mean was used in this study, in which the mean of the observed values for that variable replaced the missing data.

The beta-coefficients of the significant risk factors (Table 5.2) from the development sample were used in the statistical analysis of the validation study to compare observed and predicted outcomes. More specifically, the final equation that resulted from the logistic regression analysis in the development study was applied to each individual patient in order to give a predicted probability for that patient. This was then compared to the actual observed outcome for that patient. The Akaike Information Criterion model from the development study was selected for external validation as this was the final model with the higher levels of accuracy and predictive capabilities (when compared to the full model and the Likelihood Ratio model).

To assess the validation model's discriminatory power to predict an event, the area under the ROC curve (*c* index) was calculated for the validation sample. Calibration was assessed by plotting the observed proportions of events against the predicted probabilities. In addition to this graph the Hosmer-Lemeshow test was calculated to assess model calibration. Both discrimination and calibration results were then compared to the development sample. To assess the accuracy of the validation model in predicting an event, the sensitivity, specificity, positive predictive value, negative predictive value and overall accuracy (calculated using [TP+TN] / [TP+FP+FN+TN]) were calculated and also compared to the development sample. Adjusted odds ratios with 95% confidence intervals were calculated. For all analysis, a two-tailed p-value of less than 0.05 was used to define statistical significance. The SPSS statistical package (version 20, Chicago) and the R Program (version 2.14.1) were both used for statistical analysis.

Re-calibration was completed in order to update the validation model and improve its predictive capabilities. The calibration intercept of the original development model was adjusted (leaving the calibration slope and all beta-coefficients the same) by calculating a correction factor based on the mean predicted risk and observed outcome frequency in the validation dataset. The correction factor was then added to the intercept of the original development model, which resulted in a new intercept. The correction factor was calculated using the formula described by Janssen et al (2008):

Correction factor = 1n (OOF / 1-OOF / MPR / 1-MPR).
(where OOF: observed outcome frequency and MPR: mean predicted risk)

The next stage of statistical analysis was to transform the final logistic regression equation from the model into a simplified prognostic model that could be easily applied in the clinical setting. In order to achieve this aim, the beta coefficients of each of the risk factors were multiplied by a factor (in this case 6.2) so that the smallest coefficient was transformed into an integer value close to one. This procedure preserves the approximate relative importance or 'weight' of each factor. (Wutzler et al 2011) For the continuous variables, this value was then multiplied by the interval size that it was to be categorised in the final model. For example, the beta

coefficient for age was 0.0162. If this value was multiplied by the factor 6.2, then for each additional year of age, the risk score would increase by 0.1. In order to make the final prognostic model more user-friendly, age was categorised into ten year intervals. The value of 0.1 was therefore multiplied by 10 (number of years in each group) resulting in a risk score of one for each additional decade, thus a thirty year old patient would score three and a sixty year old would score six and so on.

Each individual risk factor then had a specific score, which when added to the other risk factors for that patient, resulted in an overall final risk score. The prognostic model was applied to each individual patient who participated in the validation study and their final risk score was compared to their actual observed outcome. Through the analysis of the number of patients with specific final risk scores compared to observed complication rates, it was also possible to estimate the specific risk scores that equated to the development of complications following blunt chest wall trauma and those patients who may benefit from ICU management. Sensitivity, specificity, positive and negative predictive values were calculated for these specific scores or cut-off values.

The final stage of analysis was to calculate the probability of the development of complications following blunt chest wall trauma for each of the final risk scores. By entering the patient values of the risk factors into the final model, the clinician would be able to obtain the probability of developing complications through the corresponding final risk score. The individual patient's final overall risk score was compared to their probability of developing complications initially calculated using the final logistic regression equation. The individual final risk scores were categorised into groups (0-10, 11-15, 16-20, 21-25, 26-30 and ≥ 31) and the mean and standard deviation of all the corresponding probabilities were calculated for each group. For example, for every patient with a final risk score of 0-10, the mean and standard deviation of all of their corresponding probabilities were calculated. This mean was then used as the probability value for developing complications for that category (0-10) of final risk scores. The clinician using the prognostic model for a patient with blunt chest wall trauma would therefore be able to calculate the final risk score which would correspond to that patient's probability of developing complications.

6.2.8 Ethical approval

This study was granted ethics approval by the South West Wales Research Ethics Committee. Global research and development (R&D) approval was granted by the National Institute for Social Care and Health Research (NISCHR) Research Ethics Service for the NHS hospitals in Wales. The same global R&D approval was not granted by the English NHS equivalent, the National Institute for Health Research (NIHR) due to a lack of study funding. Consequently, each individual hospitals R&D department had to provide their own approval for the study, without the global approval. Each individual participating hospital's R&D department granted approval for this study.

6.3 Results

In the six month data collection period, a total of 237 blunt chest wall trauma patients were recruited to the validation study across the seven participating hospitals. Table 6.2 indicates the numbers of patients recruited from each participating hospital and their complication rate.

Hospital	Number of patients recruited	Complication rate
Royal Gwent Hospital	35	40%
West Wales (Glangwili) General Hospital	16	47%
Ysbyty Gwynedd	36	46%
Wrexham Maelor Hospital	28	43%
Musgrove Park Hospital	68	39%
Bradford Royal Hospital	54	40%
Salford Royal Hospital	0	N/A

Table 6.2 Number of patients recruited and complication rate at each participating centre

A total of 152 (64%) of the patients were male and the most common injury mechanisms were fall (72%), road traffic accident (14%), sporting injury (9%) and assault (3%). There were missing data in less than 2% of respiratory rates and oxygen saturation levels. No other observations were missing from the entire dataset.

Table 6.3 illustrates the baseline characteristics and risk factors investigated for the patients in the validation sample compared to the development sample. The results indicate significant differences in all baseline characteristics except the number of smokers and the patients' respiratory rate on initial assessment in the ED.

	Development sample n (%) / median (IQR)	Validation sample n (%) / median (IQR)	p-value
Total patients	274	237	
No of events	161 (59%)	103 (43%)	p<0.001*
Age	69 (28.0)	57 (34.0)	p<0.001*
Number of rib fractures	3 (3.0)	1 (3.0)	p<0.001*
Oxygen saturations	95 (5.0)	97 (4.5)	p<0.001*
Respiratory rate	18 (6.0)	18 (6.0)	p=0.062
Chronic lung disease	154 (56%)	49 (21%)	p<0.001*
Cardiovascular disease	116 (42%)	53 (22%)	p<0.001*
Smoker	92 (34%)	67 (28%)	p=0.213
Pre-injury anticoagulants	117 (43%)	47 (20%)	p<0.001*

Number and percentages, median (interquartile), *significant difference in p-value

Table 6.3 Comparison between baseline characteristics / risk factors of patients in the development and validation samples

Table 6.4 illustrates the results of the univariable analysis. The table highlights the differences in each of the risk factors between the patients who developed complications in the recovery phase, and those who did not. Unadjusted odds ratios and the 95% confidence intervals are included for each of the categorical variables.

	All patients n=237	No complications n=134	Development of complications n=103	p-value	Unadjusted odds ratios (95% CI)
Age	55 ± 21	47 ± 18	68 ± 17	p<0.001*	
Number of rib fractures	2 ± 2	1 ± 1	3 ± 2	p<0.001*	
Chronic lung disease	49 (21%)	13 (10%)	36 (35%)	p<0.001*	5.0 (2.5-10.1)
Pre-injury anticoagulants	47 (20%)	6 (4%)	41 (40%)	p<0.001*	14.1 (5.7-35)
Oxygen saturations	96 ± 4	98 ± 2	93 ± 5	p<0.001*	

*Number and percentages, means and SD, CI: confidence intervals, *significant difference in p-value*

Table 6.4 Results of the univariable analysis: unadjusted odds ratios for the risk factors for the development of complications following blunt chest wall trauma

The accuracy of the validation model (measured by sensitivity, specificity and positive and negative predictive values) is illustrated in Table 6.5. The results are

compared to the accuracy of the development model, as previously demonstrated in the model development study. The Nagelkerke R square result highlights excellent overall model accuracy.

	Development model	Validation model
Nagelkerke R square	35%	77%
Sensitivity	83%	75%
Specificity	61%	97%
Positive predictive value	75%	95%
Negative predictive value	71%	83%
Overall accuracy	74%	87%

Table 6.5 Accuracy of the validation model compared with the development model

The model's predictive capabilities were assessed using the area under the ROC curve. Figure 6.1 illustrates the ROC curve for the validation model, with a c-index of 0.96 (compared to a c-index of 0.80 in the development model) suggesting excellent discriminatory power of the model to predict development of complications following blunt chest wall trauma.

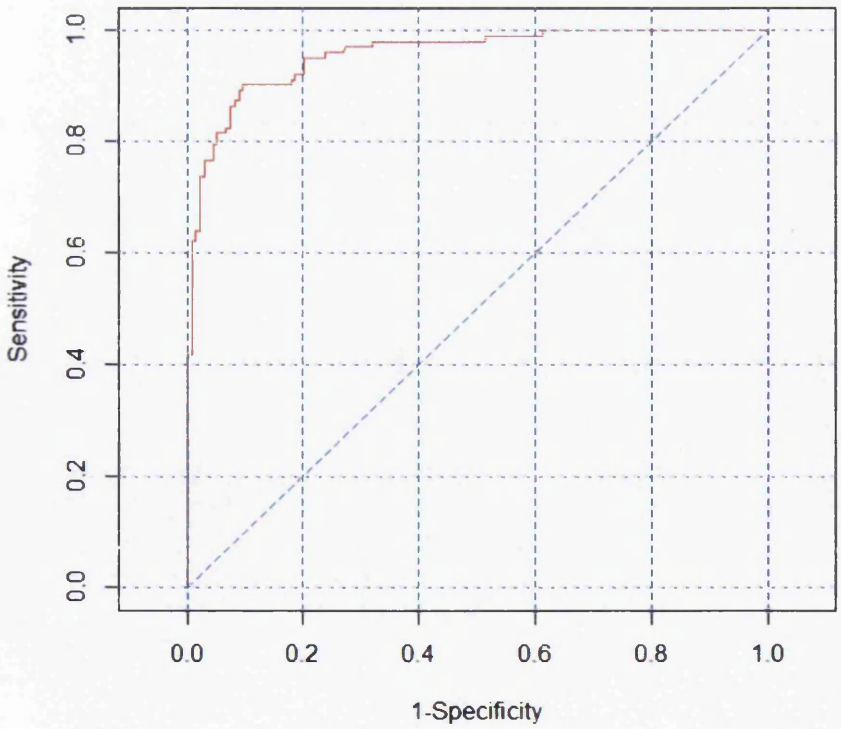
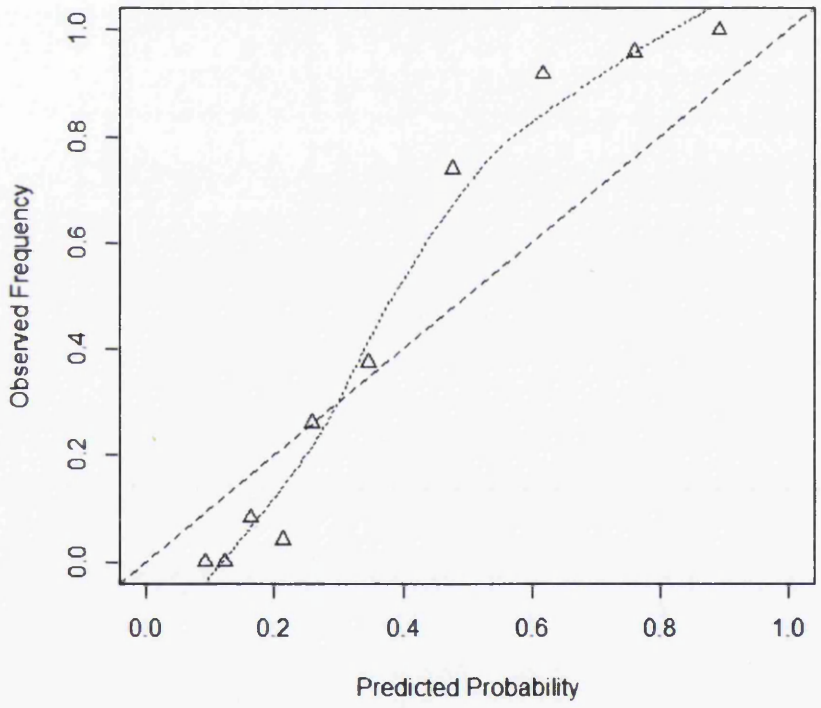


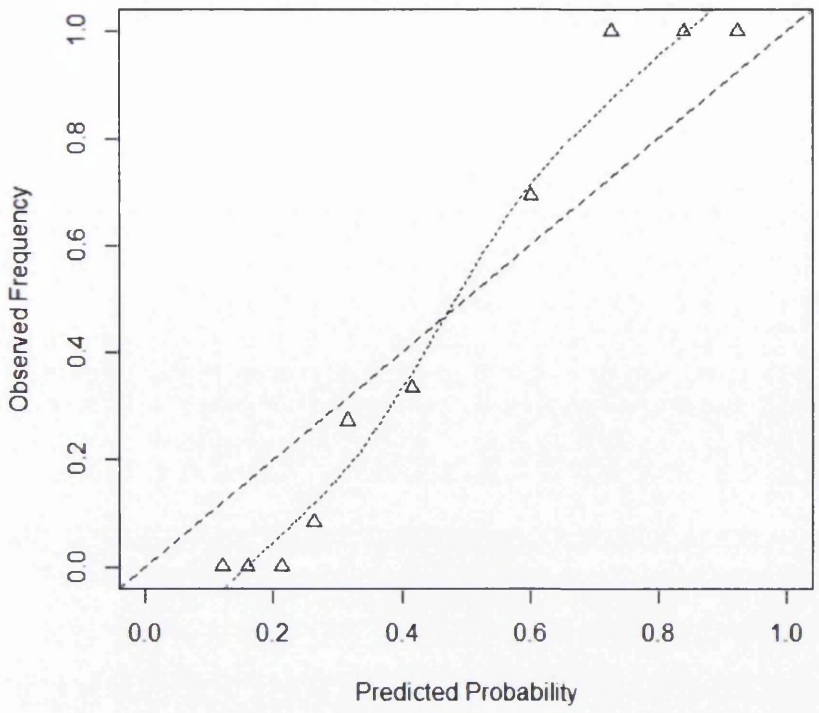
Figure 6.1 ROC curve for validation model

The validation model's calibration is illustrated in the observed versus predicted outcomes graph in Figure 6.2a. As expected, the results of Hosmer Lemeshow test indicate poorer model validation model calibration (compared with the development model) with a chi square value of 33 (p value < 0.001). In order to adjust the validation model to improve the calibration, the slope intercept derived from the development model was adjusted (from 3.72 to 3.97) using a correction factor to correspond with the lower complication rate in the validation sample. This adjustment resulted in improvements in overall accuracy (Nagelkerke R-squared value of 82%), discrimination (c index of 0.97) and calibration (Hosmer-Lemeshow Chi square value of 19.9 and p<0.01) Figure 6.2b illustrates the updated model's observed versus predicted outcomes graph.



Δ: *Risk of outcome in 10ths of patients with similar predicted probabilities*
Dotted line: *Relationship between observed frequency and predicted probability of development of complications*
Dashed line: *Ideal relationship between observed and predicted frequency of outcome in model with perfect calibration*

Figure 6.2a External validation model's calibration, observed versus predicted outcomes



Δ: *Risk of outcome in 10ths of patients with similar predicted probabilities*
Dotted line: *Relationship between observed frequency and predicted probability of development of complications*
Dashed line: *Ideal relationship between observed and predicted frequency of outcome in model with perfect calibration*

Figure 6.2b Updated external validation model's calibration, observed versus predicted outcomes

In order to transform the beta-coefficient of each risk factor into an equivalent accurately weighted risk integer score, each beta-coefficient was multiplied by the factor 6.2. Table 6.6 illustrates the risk factors and their corresponding score for the blunt chest wall trauma prognostic model.

	Beta-coefficient	Risk score
Age	0.0162	1 (per additional 10 year intervals)
Number of rib fractures	0.418	3 (per additional rib fracture)
Chronic lung disease	0.789	5
Pre-injury anticoagulant use	0.637	4
Oxygen saturation levels	-0.0651	2 (per decrease in 5% oxygen saturations)

Table 6.6 Risk factor scores as transformed from the beta-coefficients

Using the scores illustrated in Table 6.7, the patient data can be entered into the model in order to calculate the overall final risk score. For example if a 62 year old patient with a history of chronic lung disease sustains three rib fractures and has oxygen saturations of 88% on presentation to the ED, the final risk score would be 6 (age) + 9 (rib fractures) + 5 (chronic lung disease) + 4 (oxygen saturations) = 24.

	Patient data	Corresponding risk score
Age	10-19	1
	20-29	2
	30-39	3
	40-49	4
	50-59	5
	60-69	6
	70-79	7
	80-89	8
	90-99	9
	100-109	10
Number of rib fractures	0	0
	1	3
	2	6
	3	9
	4	12
	5	15
	6	18
	7	21
	8	24
	9	27
	10	30
Pre-injury anticoagulants	No	0
	Yes	4
Chronic lung disease	No	0
	Yes	5
Oxygen saturation levels	100-95%	0
	90-94%	2
	85-89%	4
	80-84%	6
	75-79%	8
	70-74%	10

NB: Each risk score is added together to give a total risk score.

Table 6.7 Risk factor values and corresponding risk scores

Using the results of the validation study it was possible to identify the most accurate score (the best sensitivity and specificity) for directing management decisions such as discharge home or admission location. If a final total risk score of ≥ 12 was selected as a cut-off point at which the blunt chest wall trauma patient was considered at risk of developing complications, then the number of patients in the validation study who would have been correctly managed (admitted to hospital who subsequently developed complications) was 90%. The number of patients who would have therefore been incorrectly managed (not admitted to hospital but subsequently developed complications) would have been 10%. Similarly the number of patients who would have been admitted but would not have developed complications would have been 13%, but 87% would have been correctly discharged directly from the ED (and not developed complications).

If a final risk score of ≥ 27 was selected as a cut-off point at which the blunt chest wall trauma patient was considered at high enough risk to require ICU admission, then the number of patients in the validation study who would have been correctly managed (scored ≥ 27 and the observed outcome was ICU admission) was 83%. The number of patients who were therefore incorrectly managed (admitted to ICU in the observed outcome, but scored less than 27) was 17%. The number of patients who were not admitted to ICU in the observed outcome and also correctly scored less than 27 was 97% but the number of patients who would have been incorrectly managed (scored ≥ 27 but were not admitted to ICU in the observed outcome) would have been 3%.

Table 6.8 illustrates the sensitivity, specificity, PPV, NPV and overall accuracy of each cut off value. (change table list at start of thesis)

	Cut off value of ≥ 12 (Development of complications)	Cut off value of ≥ 27 (ICU admission)
Sensitivity	90%	83%
Specificity	87%	97%
Positive predictive value	84%	77%
Negative predictive value	92%	98%
Overall accuracy	88%	96%

Table 6.8 Accuracy results for cut-off values for development of complications and ICU admission

Table 6.9 illustrates the final risk scores and their corresponding probability of developing complications following blunt chest wall trauma. Using these results for example, it is possible to estimate that a patient who scores 12 has a 29% (±8) probability of developing complications compared to a patient with a final risk score of 36 who has an 88% (±7) probability of developing complications. If these probabilities are combined with the cut-off values described above a cut-off risk score of ≥ 12 triggering admission to hospital from the ED would have a corresponding estimated probability of 29% of developing complications. Similarly, the cut-off value triggering ICU admission of ≥ 27 would have an estimated corresponding probability of 80% of developing complications.

Final risk score	Probability Mean ± SD
0-10	**13% ± 6**
11-15	29% ± 8
16-20	**52% ± 8**
21-25	70% ± 6
26-30	**80% ± 6**
31+	88% ± 7

SD: standard deviation

Table 6.9 Final risk scores and corresponding probability of developing complications following blunt chest wall trauma

Figure 6.3 illustrates the final prognostic model for use in the clinical setting.

Swansea Blunt Chest Wall Trauma Score

NB: Circle the score for each risk factor in the table and total all scores

	Patient data	Corresponding risk score
Age	10-19	1
	20-29	2
	30-39	3
	40-49	4
	50-59	5
	60-69	6
	70-79	7
	80-89	8
	90-99	9
	100-109	10
Number of rib fractures	0	0
	1	3
	2	6
	3	9
	4	12
	5	15
	6	18
	7	21
	8	24
	9	27
	10	30
Pre-injury anticoagulants	No	0
	Yes	4
Chronic lung disease	No	0
	Yes	5
Oxygen saturation levels	100-95%	0
	90-94%	2
	85-89%	4
	80-84%	6
	75-79%	8
	70-74%	10

Total Score _____

Risk score	Probability of complications
0-10	13%
11-15	29%
16-20	52%
21-25	70%
26-30	80%
31+	88%

Total Score 0-11:	Consider discharge home with advice leaflet and analgesia
Total Score 12-26:	Consider admission to a ward for observation, analgesia and physiotherapy
Total Score ≥27:	Consider ICU management

Figure 6.3: Swansea Blunt Chest Wall Trauma Score

6.4 Discussion

The aim of this multi-centred prospective study was to validate the prognostic model developed in the previous study. The centres that participated in the study provided a good representation of different types and sizes of hospital, with blunt chest wall trauma patients from various geographical locations in England and Wales, thus enhancing the external validity of the study. The significant differences highlighted in the baseline characteristics of the development and validation samples illustrates the differences in the patients investigated and also the inherent differences in the measurement of the variables by the participating investigators. This suggests that the prognostic model may be valid for use in a high percentage of Emergency Department managing blunt chest wall trauma patients in England and Wales.

There are a number of possible explanations for the baseline differences in characteristics between the development and validation samples. One hospital trust may have a different process for dealing with trauma than another trust. For example, if a hospital has an associated minor injuries unit, that unit would manage the less severe injuries, thus skewing the patient baseline characteristics for that hospital. The participating hospitals also serve different populations which invariably may have inherent variances in baseline characteristics, such as a lower socio-economic population with a higher percentage of people who smoke and suffer with smoking related illness. Another explanation for baseline differences could be the actual measurement of the characteristics, for example in one hospital the triage nurse may take the initial recording of oxygen saturation levels, compared to a different hospital in which the assessing doctor records the levels at a later stage in the ED admission when the patient has been receiving supplementary oxygen.

In addition to the differences in baseline characteristics, there was a significantly lower rate of complications in the validation sample than the development sample. This could be explained by management protocol of blunt chest trauma patient in the different hospitals. For example, in Morriston Hospital where the original model was developed, patients are routinely admitted to ICU if they need invasive analgesia such as an epidural, as this is where epidural patients are currently managed. As a result of the on-going studies investigating risk factors in blunt chest wall trauma

patients in Morriston Hospital, the patients considered high risk of developing complications by the Emergency Physicians are also referred to the ICU team early to avoid delayed admission and subsequent prolonged length of stay. As ICU admission was one of the complications included in the composite outcome measure used in this study, both of these factors may have influenced the increased rate of recorded complications in the development cohort compared to the validation cohort

In order to quantify the number of rib fractures sustained by the patient, a chest radiograph or CT scan and its subjective interpretation is required. Due to the inherent difficulties in identification of rib fractures on chest radiograph (Davis and Affatato 2006), the clinician is advised to record the number of rib fractures on imaging or suspected clinically following physical examination of the patient. This subjective interpretation of number of rib fractures may have influenced the final model's accuracy however the use of clinical suspicion through physical examination of the patient (and the final risk score) could potentially negate the need for the routine use of chest radiographs. Considerable cost-savings in the NHS through decreased use of relatively inexpensive but frequent examinations such as the chest radiographs have been proposed in recent research. (Davis and Affatato 2006)

The results of the validation study support the findings of the development study. Patient age, number of rib fractures, chronic lung disease, pre-injury anticoagulants and oxygen saturation levels were the significant risk factors for development of complications following blunt chest wall trauma. Patient age, number of rib fractures and chronic lung disease have been reported as significant risk factors for poor outcomes in a number of recent studies and possible explanations for these factors have been previously discussed. (Battle et al 2012, Brasel et al 2006, Bergeron et al 2003) Pre-injury anticoagulant use and oxygen saturation levels have only been reported as risk factors for the development for complications following blunt chest wall trauma in a previous study by Battle et al (2012) and therefore further research into these risk factors would be beneficial.

The predictive capabilities (sensitivity, specificity, positive and negative predictive values) of the validation model were better than those of the development model with excellent overall model accuracy as reflected by the Nagelkerke R Square statistic.

These results demonstrate the clinical usefulness of the model. The model's discrimination was excellent suggesting that the clinician can confidently assess whether the patient with the higher risk prediction using the model will develop complications following blunt chest wall trauma, compared to the patients with low risk predictions who will not develop complications. As expected, the validation model demonstrated poor calibration and numerous authors have offered explanations for this result in a validation sample. (Altman et al 2009, Toll et al 2005) It could be suggested that the most obvious reason for the excellent discrimination but poor calibration was the significantly lower rates of the development of complications in the validation sample.

As a result of the calibration and discrimination results, the decision was made to update the validation model. Recent research describes how common practice is simply to reject an original prognostic model due to the decreased predictive performance in the validation sample. A new prognostic model is then developed and as a consequence the original dataset is neglected. Clinicians are then faced with numerous possible prognostic models, very few of which have been externally validated for use in new samples. For example there are over 60 models in use for prediction of outcomes in breast cancer and over 25 models for predicting outcomes in neurological trauma. (Moons et al 2009b) Research now suggests that the model should be adjusted in order to improve its performance on the new population and this adjusted model is then based on both the original and validation data, further strengthening its stability and generalisability. (Moons et al 2009b)

The model in this validation study was therefore updated using a simple method known as re-calibration which was described by Steyerberg et al (2004) and Janssen et al (2008). By simply adjusting the intercept using a correction factor for the original model, the poor calibration can be improved. (Toll et al 2008) As expected in this type of validation study, calibration remained poorer in the updated model compared to the development model so the results should be interpreted with caution.

The results of this study have demonstrated that risk can be easily and accurately stratified from simple demographic and clinical variables on initial assessment of the blunt chest wall trauma patient in the ED. The risk factors are all currently routinely

measured in the ED and don't require expensive, time-consuming or complicated technology to investigate. This is one of the most important factors in the success of prognostic model development according to previous research. (Moons et al 2009a, Wyatt and Altman 1995) The clinician would simply collect routine data, total the scores for each risk factor, then obtain the corresponding probability of the development of complications. A more accurate decision can be made by the clinician regarding whether the patient is safe for discharge home directly from the ED, or whether they require admission to hospital. Not only could this reduce the development of complications in blunt chest wall trauma patients through close observation and early aggressive prophylactic treatment in the admitted patient, but also reduce unnecessary admissions of patients unlikely to develop complications.

The overall results of this study suggest that the final validation model could be safely and effectively used in the clinical setting in England and Wales for assisting in the management of blunt chest wall trauma patients. This is the first prognostic model that has been developed and externally validated in a prospective multi-centre study for use with blunt chest wall trauma patients. The model can be used with the less severely injured patient who on presentation to the ED is not suffering any overt signs of respiratory distress, but will potentially go on to develop severe life-threatening pulmonary complications. As a result of the prognostic model, the difficult decision facing the Emergency physician as to whether the blunt chest wall trauma patient will go on to develop complications in the next two or more days, may become easier to predict. Research has demonstrated that careful observation and early aggressive therapy can limit these complications therefore identification of the high risk patient is imperative for optimal management. (Easter 2001) It is inevitable however that the final decision regarding patient management must be individualised and many factors that cannot be translated into a statistical model must be considered. The overall purpose of the prognostic model is simply to guide clinical decision-making, not replace it.

This study has a number of strengths and limitations. External validation using a prospective multi-centre trial is considered the most robust validation technique ensuring generalisability of the study's results. (Moons et al 2009b) Current methodological recommendations for clinical prediction research, as outlined by

Bouwmeester et al (2012) have been followed in the design and completion of the prognostic model for use with blunt chest wall trauma patients. These recommendations included sample size and selection, clear definitions of risk factors and outcomes under investigation, handling of missing data, reporting of both univariable and multivariable results and calculation of model performance measures. The final model was also re-calibrated as recommended by recent research. (Janssen et al 2008) As a result, the reliability and applicability of the model is sufficient that the model could be safely and effectively used in the clinical setting. The external validation results also confirm the model's clinical usefulness in blunt chest wall trauma management throughout England and Wales.

One of the limitations of this study was the loss of patients to follow up. Due to limited resources, it was not considered feasible to investigate the patients' follow up once they had left hospital care. Any use of primary care for complications which developed following hospital discharge would not been included in the study results. The data collection was not fully blinded as recommended by Bouwmeester et al (2012) however the clinicians collecting the data in the validation study were blinded to which of the risk factors and outcomes were being used in the final analysis.

Another limitation of the validation study concerns the timing of the data collection. For example, the patient's oxygen saturation levels may have varied according to the time in which they were recorded. If the data were collected before analgesia was given in the ED, then the results may have been worse than if the patient had received analgesia and could breathe more easily. The final limitation in the validation study was the poor calibration in the final model. A number of authors have highlighted that the Hosmer-Lemeshow statistic can often prove inaccurate in external validation of a prognostic model and that calibration will decrease compared with the original model. (Altman et al 2009, Vergouwe et al 2005)
As a result of these limitations, the results of this study should be considered with caution.

7.0 Conclusions

7.1 Summary

The difficulties experienced by the Emergency Physician in managing blunt chest wall trauma have been outlined throughout this series of studies. The primary cause of these management difficulties is the inability to predict which patients will develop complications in the following 48 to 72 hours. This group of patients account for over 15% of all trauma admissions to Emergency Departments in the United Kingdom and also has a mortality rate ranging between 4 to 20%, which highlights the significance and extent of this problem. Clinical symptoms on presentation to the ED are not considered an accurate risk factor of outcome following non-life threatening blunt chest wall trauma.

Disposition of blunt chest injury patients from the Emergency Department is straightforward when the patient requires immediate surgery or supportive mechanical ventilation but if the injury is less severe, or associated injuries are not present, deciding which blunt chest wall trauma patients require a higher level of clinical input can be difficult. A prognostic model could assist in guiding doctors in their treatment decisions however no current model exists to assist in the management of this patient group. Identification of the high risk blunt chest wall trauma patient would facilitate the early management required for reducing avoidable morbidity and mortality.

The first aim of this series of studies was to identify the risk factors that contribute the development of complications in blunt chest wall trauma patients. In order to achieve this aim, a comprehensive systematic review and meta-analysis of the literature was completed. The results of this study highlighted a number of risk factors for morbidity and mortality in blunt chest wall trauma including patient age, the number of rib fractures, presence of pre-existing disease and the development of pneumonia. The second study used a questionnaire methodology and was completed to gain background knowledge regarding the risk factors for the development of complications following blunt chest wall trauma. A sample of Emergency Physicians was approached to complete a questionnaire in order to gain expert opinion of the risk factors. A 90% response rate was achieved in which additional risk factors were

highlighted (not identified in the systematic review and meta-analysis) including oxygen saturation levels, respiratory rate, smoking history and the use of pre-injury anticoagulants.

The third study was completed in order to further investigate the risk factors and also to commence the data collection required to develop the prognostic model. This was a retrospective study in which demographic, risk factor and outcome data was collected from patients who had presented to the ED at Morriston Hospital between 2009 and 2010. Using multivariable logistic regression analysis the risk factors for the development of complications in blunt chest wall trauma patients were three or more rib fractures, chronic lung disease, pre-injury anticoagulant use and oxygen saturation levels of $\leq 90\%$. Age was not demonstrated to be a risk factor in the retrospective study but this could have been explained by the dichotomisation of the variable into two groups, 18 to 64 years and 65 years or more. A cut-off age of greater than 65 years may have been a significant risk factor so age was still included in the later analysis.

The next aim of the thesis was to develop the prognostic model using the knowledge of the significant risk factors gained in the first three studies. In order to develop the model, an additional year of patients' data was collected. The final dataset included all patients who had presented to the ED in Morriston Hospital with blunt chest wall trauma between 2009 and 2011. Using multivariable logistic regression analysis and fractional polynomials to assess linearity of continuous variables, a prognostic model was developed. The significant risk factors in the final model included patient age, number of rib fractures, chronic lung disease, pre-injury anticoagulant use and oxygen saturation levels. The final model demonstrated good predictive capabilities for both discrimination and calibration.

The final aim was to externally validate this model in a sample of patients from different hospitals in England and Wales. A total of seven hospitals agreed to participate in the validation study and as a result sufficient patient data was collected during a six month data collection period. In order to validate the model, the observed outcomes were compared to the predicted probabilities (calculated using the beta-coefficients from the development model). As a result of the significantly

lower rate of complications in the validation sample, it was necessary to re-calibrate the original model by simply using a new intercept, while keeping the original beta-coefficients. The results of this analysis indicated that the validation model had excellent discrimination, but poorer calibration than the development model.

The next stage of the analysis was to transform the logistic regression equation in the validation model into a simple prognostic model that could be used in the clinical setting. By simply entering the individual patient's data and totalling the scores allocated to each risk factor, the clinician would then know the estimated probability of that patient developing complications following blunt chest wall trauma. Cut-off values were also suggested at which the patient should be discharged home, admitted to the ward from the ED, or admitted to ICU. Sensitivity and specificity values for these cut-off values were demonstrated to be very good and therefore safe to use in the clinical setting.

7.2 Strengths and weaknesses

This series of studies had a number of strengths and weaknesses. The series of studies followed specific guidelines by Moons and his colleagues published in the BMJ in 2009. The guidelines were developed in order to improve the quality of prognostic research and prognostic model development and validation. The first three studies provided extensive background knowledge of possible risk factors for inclusion in the prognostic model, thus reducing the chance of an important risk factor being omitted. The model was tested for external validity which is considered the most robust method of assessing validity and generalisability. Guidelines regarding advanced statistical techniques were followed, such as the use of fractional polynomials to avoid dichotomising continuous variables and the use of re-calibration of the final model to improve its predictive capabilities.

A number of weaknesses of the individual studies were discussed at the end of each chapter. The main overall weakness of the studies was the inability to follow up the patients once they were discharged from hospital, in order to assess later stage complications or use of primary health care. The other possible limitation is the use of a composite outcome measure as this may have resulted in a degree of confounding. The composite outcome measure was used due to the low rate of

mortality in this patient population, which would have resulted in unachievable sample sizes in each of the studies. This may have biased the studies' results and therefore the results should be interpreted with caution.

7.3 Recommendations for further research

There are a number of recommendations for further research which are beyond the scope of this thesis. The next stage would be the completion of an impact study. The aim of the impact study is to evaluate the model's influence on clinical practice. In contrast to the development and validation studies, the most appropriate study design for an impact study would be a randomised controlled trial, so a control group would be required. A number of possible outcome measures could be investigated including quality of life, cost effectiveness of care or changes in clinician practice or behaviour. Statistical analysis would involve comparison of the control and intervention group, rather than any model performance measures.

Another suggestion for further research would be to complete a study which examines the effectiveness and validity of the model in different settings to that which it was originally developed and validated, for example primary care or a minor injuries unit. The model could potentially prove a useful triage model for decision making regarding referral from primary care or a minor injuries unit to the ED of the regional trauma centre.

The final area of interest that has been generated by this series of studies is the influence of smoking on outcomes following blunt chest wall trauma. In contrast to previous research, this series of studies demonstrated that smoking was protective for patients, rather than a risk factor for poor outcomes. A number of potential reasons for this finding were suggested and these need further investigation. Whether this finding is reproducible in further controlled studies needs further investigation as resources such as antibiotic therapy and physiotherapy are often directed more at the smokers than the non-smokers.

7.4 Summary points

- The risk factors in the final prognostic model for use in the management of blunt chest wall trauma are increasing age, increasing number of rib fractures, chronic lung disease, decreasing levels of oxygen saturations in initial assessment in the Emergency Department and the use of pre-injury anticoagulants.

- The prognostic model provides the clinician with probabilities of risk of the development of complications following blunt chest wall trauma. This knowledge can assist the clinician in decision making regarding whether the patient can be safely discharged home directly from the ED, or whether they need admission to a ward or ICU.

- Following external validation, the prognostic model is considered safe and effective for use in all blunt chest wall trauma patients presenting to the Emergency Departments in England and Wales.

- The model demonstrates clinical usefulness as it includes risk factors which are not normally considered in the management of the blunt chest wall trauma patient in the clinical setting. High levels of overall accuracy, sensitivity and specificity were demonstrated for the final model.

- Further research is needed investigating the clinical impact of the prognostic model.

Appendix A

Reject Log: Studies not included in systematic review and meta-analysis.

Investigator(s) and year	Risk factor(s) investigated	Study design	Results	Reason for exclusion
Allen et al 1985	None	Retrospective cohort Descriptive	More blunt injuries in children and elderly than adults. Increased mortality in elderly chest trauma patients	No specific risk factors for poor outcome following BCT
Allen et al 1997	Age,	Retrospective cohort	No difference between adults and children in terms of recovery from pulmonary contusion	No specific risk factors for poor outcome following BCT
Antonelli et al 1994	AIS, presence of RFs, pulmonary contusion, PTX,HTX, mechanical ventilation	Prospective cohort	Main risk factors for developing early onset pneumonia post multi-trauma are thoraco-abdominal trauma. Leads to 10 fold increase in risk	No specific risk factors for poor outcome following BCT
Bamvita et al 2007	Age, gender, pre-existing conditions, mechanism and injury severity	Retrospective cohort	Age, body area injured, pre-existing conditions are significant risk factors of death after blunt trauma	No specific risk factors for poor outcome following BCT
Bassett el al 1968	None	Descriptive retrospective cohort	Study describes incidence, management and outcomes of patients with chest trauma in cohort	No specific risk factors for poor outcome following BCT
Bastos 2008	None	Descriptive	Studies describes flail chest and pulm contusion - management	No specific risk factors for poor outcome
Benson et al 2005	Age, weight, hip t score, smoking, maternal history of hip #, prior # after age 50	Retrospective cohort	Study investigates risk factors of osteoporotic RFs, rather than risk factors of poor outcome following RFs	No specific risk factors for poor outcome following BCT
Clark et al 1988	Pulmonary contusion and flail chest	Retrospective cohort	Combination of both pulmonary contusion and flail chest associated with mortality rate 2 times that of either injury alone	No specific risk factors for poor outcome following BCT
Cocanour 2006	None	Editorial	None	Comment / Letter
Cohn 1997	None	Review	Respiratory distress common after lung injury	No specific risk factors for poor outcome
Cormier 2008	Body mass index, age	Retrospective cohort	BMI and age are both risk factors of sustaining thoracic trauma following a frontal impact MVA	No specific risk factors for poor outcome following BCT
Culliane and Morris 1999	None	Descriptive	None relevant	Descriptive study only
Demetriades et al 2001	Age	Retrospective cohort	Elderly trauma patients should reach trauma team activation status more easily because of their increased age	No specific risk factors for poor outcome following BCT
Dubinsky 1997	None	Prospective cohort	CXRs are of no value in non-life threatening blunt chest trauma	No specific risk factors for poor outcomes
Easter 2001	None	Lit review	Rapid mobilisation, pain management and respiratory support key in BCT management	No specific risk factors for poor outcomes following BCT
Freedland et al 1990	Extent and mechanism of injuries, shock and vital signs on admission, blood transfusion	Retrospective cohort	Extent of associated injuries and ISS≥31, blood transfusions predict outcome in blunt trauma patients	No specific risk factors for poor outcome following BCT
Freixinet 2008	No of RF, age, extent of lung injury	Prospective cohort	Age not an indicator of severity of injury	No outcome measure – looks at severity
Galan et al 1992	None	Descriptive	None relevant	No specific risk factors for poor outcome following BCT
Grossman et al 2002	Pre-existing conditions, age	Retrospective cohort	Hepatic disease, renal disease and cancer have greatest impact on mortality in multi-trauma patients. Odds of dying in multi-trauma geriatric patients increases by 6.8% per year	No specific risk factors for poor outcome following BCT
Hanak et al 2005	Cough	Retrospective	Chronic cough, decreased bone	No specific risk factors

		cohort	density and being female leads to increased risk of cough induced rib fracture	for poor outcome following BCT
James and Moore 1983	None	Retrospective cohort	Patients more likely to require ventilator support will be elderly MVA patients with high ISS, flail chest and pre-existing conditions	No specific risk factors for poor outcome following BCT
Johnson et al 1986	ISS, shock, IV fluid administration, blood transfusion, PaO2/FiO2 ratio, vital signs on admission	Retrospective cohort	PaO2/FiO2 ratio on admission is a good risk factor of extent pulmonary injury. Degree of head injury determines mortality	No specific risk factors for poor outcome following BCT.
Jones 1989	None	Audit	None relevant, all relates to management of chest trauma	No specific risk factors for poor outcome following BCT
Kara et al 2003	None	Prospective cohort	Ultrasonography is a useful model for showing rib fractures missed on CXR	No specific risk factors for poor outcome following BCT
Kerr-Valentic et al 2003	Pain	Prospective case series	Investigates pain management of chest trauma	No specific risk factors for poor outcome following BCT
Kollmorgen 1994	Age, ISS, GCS, PaO2/FiO2 ratio	Retrospective cohort	Outcome dependent on severity of lung parenchymal injury	Unable to interpret results at all
Lu et al 2008	Subcutaneous emphysema	Retrospective cohort	Blunt chest trauma patients with subcutaneous emphysema are at increased risk of delayed pneumothorax	No specific risk factors for poor outcome following BCT
Margolis et al 2000	Body sixe measurements	Prospective cohort	Total weight of patient is risk factor of risk of pelvis, hip and rib#	No specific risk factors for poor outcome following BCT
Maull 2006	None	Editorial	None	Comment / Letter
Mayo et al 1993	Sex, disorientated and ambulatory, age, use of vitamin supplements	Case control	Increased risk of falls in elderly females who are ambulatory, disorientated and using vitamin supplements	No specific risk factors for poor outcome following BCT
McGwin et al 2004	ISS, age, pre-existing conditions	Retrospective cohort	Older patients with pre-existing conditions who present with minor injuries should be considered to have higher relative risk of dying	No specific risk factors for poor outcome following BCT
Miller 2007	None	Descriptive	Use of VATS improves diagnosis and management of BCT pts	No specific risk factors investigated
Milzman et al 1992	Pre-existing conditions	Prospective cohort	PEC are independent risk factors of mortality in multi-trauma patients	No specific risk factors for poor outcome following BCT
Morris et al 1990	Pre-existing conditions	Case control	Pre-existing conditions are risk factors of mortality in multi-trauma patients	No specific risk factors for poor outcome following BCT
Palvanen at el 1998 and 2004 studies	Increased age	Retrospective cohort	Since 1970, no and incidence of RFs in elderly Finns has increased	No specific risk factors for poor outcome following BCT
Perdue et al 1998	Age, pre-existing conditions	Retrospective cohort	ISS, RTS, PECS, age are risk factors of mortality in elderly multi-trauma patients	No specific risk factors for poor outcome following BCT
Quaday 1995	None	Editorial	None	Comment / Letter
Rashid et al 2000	None	Retrospective cohort	Describes extra-pleural haematoma injury course	No specific risk factors for poor outcome following BCT
Reilly et al 1993	Chest trauma in children	Descriptive	None	Descriptive study only
Sanidas et al 2000	Age, sex, time of arrival at ED, no of days after injury, ISS, injury mechanism	Case series	No statistically proven association but a detailed clinical examination and CXR can identify which patients can be managed in primary care	No specific risk factors for poor outcome following BCT
Sariego 1993	Trauma score and ISS	Retrospective review	TS or ISS not accurate risk factors of outcome following BCT	Investigates scoring systems predictive value
Sartorelli at el 2004	None	Literature review	Increased morbidity and mortality in children with chest injuries	No specific risk factors for poor outcome following BCT
Schulpen et al 1986	Associated injuries	Retrospective cohort	Head injuries and multi-organ failure are main causes of death in	No specific risk factors for poor outcome

			patients with chest trauma	following BCT
Senor 204	Need for MV, surgery, pulm contusion	Prospective cohort	Presence of high PEEP, MV, surgery etc indicate severe injury	Only pts included from ICU
Simon et al 1998	None	Retrospective cohort	Delayed haemothorax is a unique entity which is seen patient improving	No specific risk factors for poor outcome following BCT
Sharma et al 2005	RFs causing delayed haemothorax	Retrospective cohort	Delayed haemothorax after RFs rare but should be considered as early intervention needed for good outcomes	No specific risk factors for poor outcome following BCT
Sharma at el 2007	Age	Retrospective cohort	Increased age leads to increased mortality in elderly compared to adults in multi-trauma patients	No specific risk factors for poor outcome following BCT
Tadros et al 2007	Scapula fractures	Prospective cohort	Associated injuries common in patients with scapula fractures	No specific risk factors for poor outcome following BCT
Ullman 2003	None	Lit review	ED management of blunt chest trauma	No specific risk factors for poor outcome following BCT
Vermeulen and Konstantinidis 2005	Delayed complications following simple blunt chest trauma	Case series	Simple blunt chest trauma should not be assumed to be benign, good management is still needed	No specific risk factors for poor outcomes following BCT
Victorino et al 2003	None	Literature review	None	No specific risk factors for poor outcome following BCT
Walker at el 1985	Shock, blunt injury, splenectomy, antibiotic use, GCS in ED	Retrospective cohort	Increased risk of infection after multi-trauma	No specific risk factors for poor outcome following BCT
Wanek 2004	Elderly and patients with limited pulmonary reserve	Descriptive / Review	Elderly and pts with limited pulmonary reserve most at risk from flail / pulmonary contusion	Descriptive study only
Wisner 1990	Age Use of epidural in pain management	Retrospective cohort	Epidural use had positive effect on outcome of elderly patients with rib fractures	No specific risk factors for poor outcome following BCT
Young and Ahmad 1999	None	Descriptive	Trauma in the elderly as a new epidemic	Descriptive study only
Zeigler and Agarwal	Number of RFs	Retrospective cohort	Rib fractures are a marker of injury severity in multi-trauma patients	No specific risk factors for poor outcome following BCT

RFs: rib fractures, BCT: blunt chest trauma, BMI: body mass index, PTX: pneumothorax, HTX: haemothorax, ED: emergency department, GCS: Glasgow coma scale, ISS: injury severity score, CXR: chest x-ray, RTS: revised trauma scale, PECS: pre-existing conditions, #: fracture, MVA: motor vehicle accident, IV: intravenous

Appendix B

Questionnaire and covering letter used in questionnaire study

Date

Dear

I am a senior physiotherapist in Morriston Hospital working in Emergency Medicine and Critical Care. I am currently completing a PhD in the School of Medicine at Swansea University with Professor Adrian Evans and Dr Hayley Hutchings. We are completing a study investigating the risk factors for morbidity and mortality in simple blunt chest wall trauma patients. As there are no current national guidelines available to guide the management of this patient group, we are developing a prognostic model for the management of the blunt chest wall trauma patient.
We are identifying consultants working in Emergency Medicine in England and Wales to provide their expert knowledge due to their experience and expertise in assessing and treating this patient group.

We would appreciate it if you could complete this short questionnaire and return in the stamp-addressed envelope provided. All responses will be confidential and will be anonymised following the data inputting process. The responses obtained will be used to assist us develop these guidelines. A contact email address is included at the end of the questionnaire for any queries or further information that is required.

Thank you for your time and assistance.

Yours faithfully

Ceri Battle

Blunt chest wall trauma questionnaire.

(Blunt chest wall trauma is defined as blunt chest injury resulting in chest wall contusion or rib fractures, with or without non-immediate life-threatening lung injury).

Please tick the appropriate box and complete the spaces provided.

1) **Please specify the type of hospital in which you work and the number of A&E attendances per year**

   i. District General Hospital ☐ Number of A&E attendances per year_____
   ii. Teaching hospital ☐ Number of A&E attendances per year_____
   iii. Regional trauma centre ☐ Number of A&E attendances per year_____

2) **To which team is the blunt chest wall trauma patient referred if the patient requires admission but not ICU care?**

   i. Orthopaedic ☐
   ii. Cardiothoracic ☐
   iii. General surgical ☐
   iv. Other ☐ Please specify_____

3) **What guidelines do you use to assist trainees in the management of blunt chest wall trauma patients with no immediate life-threatening injuries?**

   i. None ☐
   ii. Local guidelines ☐
   iii. Regional guidelines ☐
   iv. National guidelines ☐ Please specify_____
   v. Other ☐ Please specify_____

4) **There are no current guidelines for the management of the blunt chest wall trauma patient. What in your opinion should be considered risk factors (in addition to the trauma sustained) for morbidity and mortality when assessing the blunt chest wall trauma patient?**_____

_____
_____
_____
_____
_____
_____

Thank you for your time in completing the questionnaire. Please return in the stamped addressed envelope provided. For further information or any queries regarding the questionnaire or this study, please contact Ceri.Battle@wales.nhs.uk

NB: Questionnaire font size is reduced to fit the thesis margins

Appendix C

Documentation used in multi-centred validation study:

- Data collection form
- Participant Information Sheet
- Consent letter
- Study withdrawal letter

Remove this corner once form completed (including outcomes section)

Blunt chest wall trauma study

Only complete this form on initial assessment of blunt chest wall trauma patients with no injuries requiring immediate life-saving intervention.

Patient variables (complete questions 1-12 on initial assessment): *(Please circle/fill in blanks)*

1) Is this an unplanned representation to the ED for the same injury: no yes

2) Gender: Male Female

3) Injury mechanism: Fall RTC Sport Assault Other (*specify*)_____

4) Patient age:_____

5) Number of suspected rib fractures:___fractures *(either evident on CXR or suspected clinically)*

6) Chronic lung disease no yes *(any chronic lung disease)*

7) Cardiovascular disease: no yes *(any disease of the heart or vessels)*

8) Current smoker: no yes *(smoker at time of injury)*

9) Pre-injury anticoagulant use: no yes *(any dose of any anticoagulant/antiplatelet)*

10) Oxygen saturations on room air:_____% *(on initial assessment in department)*

11) Respiratory rate: _____bpm *(on initial assessment in department)*

12) Outcome: Discharged Admitted to ward *(specify)*___ Admitted to ICU / HDU

****NB: ON COMPLETION OF ABOVE SECTION PLEASE PLACE FORM IN ALLOCATED FILE****

Patient outcome (complete on hospital discharge): *(Please circle or fill in the blanks)*

ICU admission no yes *(any stage during hospital stay)*

Mortality no yes *(in-hospital mortality)*

Morbidity no yes *(**any** pulmonary complications and interventions)*
Specify: _____

HDU / ICU length of stay: _____days *(combine HDU and ICU days)*

Ward length of stay: _____days *(excluding ICU length of stay)*

Mechanical ventilation: _____days

On completion of the form: please remove top right corner with patient identifiable data immediately and securely store until the end of the data collection period. A member of the research team will collect the forms at the end of the study period.

Patient Information Sheet

Study title: Risk factors in blunt chest wall trauma: a validation study

You are being invited to take part in a research study because you have come to the Emergency Department with an injury to your chest wall. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the information carefully. We will discuss the content of this Patient Information Sheet with you when you see the doctor about your injury.

What is the purpose of the study?
There is research that suggests that there are a number of risk factors for longer hospital stays and greater chance of chest infection in patients who have injured their chest wall. Our study aims to collect information from patients with blunt chest wall injuries (age, medication history, long term chest illness, injury severity, oxygen levels and respiratory rate) and then to record the patient's outcome (for example; whether the patient was admitted to hospital, how long they stayed, whether they had a chest infection and so on). The aim of this study is to determine if we can predict those patients who have injured their chest wall who may need closer attention. This study is part of an educational postgraduate degree. It is part of the PhD which is being completed by Lead Researcher Ceri Battle.

The information we take from you about your chest injury we would always routinely collect in order to assess your injury. We just want your permission to write it down on separate form in order that the research team can analyse the information at a later date.

Why have I been asked to participate?
You have been asked to help us as you have come to us with a blunt chest injury. We will hopefully have about 200 people like you in our study.

What will I need to do?
If you are happy to help us then all you need to do is sign a consent form to say that you are happy for us to write your information down and analyse it as part of the study.

What are the risks and benefits?
There are no known risks associated with this study. Your treatment will not be changed in any way. There are no direct benefits for you, but the results of this study may help us treat patients like you in the future.

What happens to me once my information is collected?
Your care will be exactly the same as if we were not collecting the information.

What happens if I don't want to participate?
You may decline to participate in the study and will be free to withdraw from the study at any time without fear or prejudice. You will still be offered the normal opportunities for treatment available for patients should you need any medical treatment in the future. If you change your mind within the next seven days and want to withdraw from the study, please send the attached form to Ceri Battle (Physiotherapy Dept, Morriston Hospital, Swansea, SA6 6NL). Your details will then be removed from the study.

Confidentiality

Once the information is collected and you have gone home, (and the 7 days have passed in which you can withdraw from the study – see attached withdrawal letter), your name and address will be removed from the information sheet so it is absolutely confidential and anonymous. The information we have collected about you will be stored by the Lead Researcher Ceri Battle who is writing up the study in Swansea where the research team are based, but all your information will be made anonymous and all ethical and legal practice followed to ensure this. It will not be accessible to anyone other than the people in the study team. During the study period, all information sheets will be stored in the same way as medical records and will be kept locked in a filing cabinet. All records will be destroyed as part of the hospitals confidential waste five years following the study. Results of the study may be presented in seminars, teaching sessions and journals but no personal details of anyone participating in the study will be disclosed.

Request for more information
You are encouraged to discuss any concerns you have with the researcher at any time on the contact details below. We are happy to go through all your results with you if you are interested.

Who is organising the research and who has reviewed this study?
The research is being organised by the clinicians who work for the ABMU Health Board and is sponsored by Swansea University. This study has been reviewed by the South West Wales Research Ethics Committee.

What if there is a problem?
If you have a concern about any aspect of this study you should speak to the researcher who will do her best to answer your questions – Ceri Battle on 01792 703124. If you remain unhappy and wish to complain formally, you can do so through the NHS Complaints Procedure. Details can be obtained from switchboard at Bradford Royal Infirmary on (01274) 542200.

Contact details if you need to receive independent advice regarding the study:
Mrs Karen James – Team Lead Respiratory Physiotherapist
ABMU Health Board. Morriston Hospital. 01792 703124

Researchers' details

Miss Ceri Battle	Clinical Specialist Physiotherapist, ABMU Health Board (01792 703124)
Dr Hayley Hutchings	Senior Lecturer and Researcher in Health Sciences
Professor Adrian Evans	Professor of Emergency Medicine and Haemostasis

Bradford Teaching Hospitals NHS

NHS Foundation Trust

Risk factors in blunt chest wall trauma: a validation study

CONSENT FORM

Please initial each box

1. I confirm that I have read and understood the information sheet (Version 3: 28/06/2012) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐

3. I understand that relevant sections of my medical notes and data collected during this study may be looked at by individuals from Bradford Teaching Hospitals and regulatory authorities, where it is relevant to my taking part in the study. I give permission for these individuals to have access to my records. ☐

4. I agree to take part in the above study. ☐

Name of participant:_____

Signature of participant:_____Date:_____

Name of person taking consent:_____

Signature of person taking consent:_____Date:_____

Once complete: attach to the data collection form and file in the dedicated study consent sheet file. Please remove consent form before sending data collection form to research team in Swansea.

Research Team

Miss Ceri Battle	Clinical Specialist Physiotherapist, ABMU Health Board
Dr Hayley Hutchings	Senior Lecturer and researcher in Health Sciences
Prof Adrian Evans	Professor of Emergency Medicine and Haemostasis

Physiotherapy Dept
Morriston Hospital
Morriston
Swansea
SA6 6NL

Dear Sir / Madam

During your recent visit to the Emergency Department in Ysbyty Gwynedd Hospital you agreed that you were happy for your information to be used in a study we are completing. All the information regarding the study is in the Participant Information Sheet, however if you require further information please contact the Lead Researcher Ceri Battle on 01792 703124.

If you have changed your mind about allowing us to use your information, please could you complete the slip below and return it to Ceri Battle within 7 days (Physiotherapy Dept, Morriston Hospital, Morriston, Swansea, SA6 6NL) who will make the necessary arrangements to remove all your information from the study. Withdrawal from the study will not affect your treatment in any way.

Yours faithfully

Ceri Battle

Please tear off this slip and return to Ceri Battle at the above address within 7 days.

Name: _____
Date of birth: _____
Hospital attended: _____

Appendix D

Study publications (attached as additional files in electronic copy)

Battle CE, Hutchings H, Evans PA. Risk factors that predict mortality in patients with blunt chest wall trauma: A systematic review and meta-analysis. *Injury.* 2012;43:8-17.

Battle CE, Hutchings H, Evans PA. Expert opinion of the risk factors for morbidity and mortality in blunt chest wall trauma: Results of a national postal questionnaire survey in the United Kingdom. *Injury*. 2013;44(1):56-59.

Battle CE, Hutchings H, James K, Evans PA. The risk factors for the development of complications during the recovery phase following blunt chest wall trauma: a retrospective study. *Injury*. In press. http://dx.doi.org/10.1016/j.injury.2012.05.019

Battle CE, Hutchings H, Evans PA. Blunt chest wall trauma: A review. *Trauma.* 2013: In press. DOI: 10.1177/1460408613488480

Glossary

Anticoagulant	Drug that prevents coagulation / clotting of the blood
Atelectasis	Collapse of a segment of a lung tissue
Confounding	When a variable has an unintentional effect on the dependent variable
Contusion	Bruising with micro-vessel haemorrhage or bleeding
Flail chest	Occurs when a segment the thoracic cage is separated from the rest of the chest wall and usually occurs when there are at least two fractures per rib, in at least two ribs.
Haemothorax	A collection of blood in the pleural space
Hypoxia	Low oxygen levels delivered to the cells and tissues of the body
Hypoxaemia	Low oxygen levels in the arterial blood
Mediastinum	The anatomic region containing all principle tissue and organs of the chest located between (but not including) the lungs
Meta-analysis	A quantitative statistical analysis of several separate but similar studies in order to test the pooled data for statistical significance
Oxygen saturations	Relative measure of the amount of oxygen carried in the blood
Pneumothorax	Occurs when the integrity of the chest wall is compromised allowing air to enter the pleural space
Pneumonia	Inflammation of the lung tissue that normally occurs as a result of an infection
Thoracic cage	Bony cartilaginous structure surrounding the thoracic cavity / chest, consisting of ribs, thoracic vertebrae, sternum and costal cartilages
Thorax	Part of the human body between the neck and the diaphragm
Tracheobronchial	Relating to the trachea and bronchus

References

Adams ST, Leveson SH. Clinical prediction rules. *BMJ* 2012;344:d8312 doi: 10.1136/bmj.d8312 (Published 16 January 2012)

Ahmad. MA, Sante ED, Giannoudis PV. Assessment of severity of chest trauma: is there an ideal scoring system? *Injury*. 2010;41:981-983.

Ahmed Z, Mohyuddin Z. Management of flail chest injury: internal fixation versus endotracheal intubation and ventilation. *J Thorac Cardiovasc Surg*. 1995;110:1676-1680.

Albaugh G, Kann B, Puc M, Vemulapalli P, Marra S, Ross S. Age-adjusted outcomes in traumatic flail chest injuries in the elderly. *Am Surg*. 2000;66(10):978-981.

Alexander JQ, Gutierrez CJ, Mariano MC, Laan TV, Gaspard DJ, Carpenter CL. Blunt chest trauma in the elderly: How cardiopulmonary disease effects outcome. *Am Surg*. 2000;66(9):855-857.

Altman D, Royston P. The cost of dichotomising continuous variables. *BMJ*. 2006;332:1080.

Altman D, Royston P. What do we mean by validating prognostic model? *Statist Med*. 2000;19:453-473.

Altman DG, Vergouwe Y, Royston P, Moons KGM. Prognosis and prognostic research: validating a prognostic model. *BMJ*. 2009;338:1432-1435.

Ambler G, Royston P. Fractional polynomial model selection procedures: investigation of type I error rate. *J Statist. Simulation Comput*. 2001;69:89-108.

American College of Surgeons. *ATLS: Advanced Trauma Life Support Program for Doctors* (8th ed). Chicago: American College of Surgeons. 2008.

American College of Surgeons. Advanced trauma life support, 8th edition, the evidence for change. *Jtrauma.* 2008;64:1638-50.

Aral O. 2007. Illustration of bone fracture healing process. Available from http://www.123rf.com/photo_7200140_illustration-of-bone-fracture-healing-process.html (accessed 26th September 2012)

Asch DA, Jedrziewski K, Christakis NA. Response rates to mail surveys published in medical journals. *J Clin Epidemiol.* 1997; 50:1129-1136.

Ashby R, Turner G, Cross B, Mitchell N. Torgerson D. A randomised trial of electronic reminders showed a reduction in the time to respond to postal questionnaires. *J Clin Epidemiol.* 2011;64(2):208-12.

Athanassiadi K, Gerazounis M, Theakos N. Management of 150 flail chest injuries: analysis of risk factors affecting outcomes. *Europ J of Cardio-thoracic Surg.* 2004;26: 373-376.

Athanassiadi K, Theakos N, Kalantzi N, Gerazounis M. Prognostic factors in flail chest patients. *Europ J of Cardio-thoracic Surg.* 2010: doi:10.1016/j.ejcts.2010.02.034.

Baker SP, O'Neill B, Haddon W. The injury severity score: A method for describing patients with multiple injuries and evaluating emergency care. *Jtrauma.* 1974;14:187-196.

Bakhos C, O'Connor J, Kyriakides T, Abou-Nukta F, Bonadies J. Vital capacity as a risk factor of outocmes in elderly patients with rib fractures. *Jtrauma* 2006;61(1):131-134.

Balci AE, Eren S, Cakir O, Eren MN. Open fixation in flail chest: review of 64 patients. *Asian Cardiovasc Thorac Ann.* 2004;12:11-15.

Banerjee A. 2003. *Medical statistics made clear: an introduction to basic concepts.* London: Royal Society of Medical Press Ltd.

Banisdhar BJ, Lagares-Garcia J, Miller SI. Clinical rib fractures: Are follow up chest x-rays a waste of resources? *Am Surg* 2002;68:449-453.

Barajas PM, Otero MD, Sanchez-Gracian CD, Gomez ML, Novella AT, Del Prado JC, Ruiloba SL, Duran ML. Surgical fixation of rib fractures with clips and titanium bars (STRATOS System). *Cirugia Espanola.* 2010;88(3):180-186.

Barnea Y, Kashtan H, Skornick Y, Werbin N. Isolated rib fractures in elderly patients: mortality and morbidity. *Can J Surg* 2002;45(1):43-46.

Bastos R, Calhoon JH, Baisden CE. Flail chest and pulmonary contusion. *Seminars in Thoracic and Cardiovascular Surgery* 2008;20:39-45.

Battle CE, Hutchings H, Evans PA. Blunt chest wall trauma: a review. *Trauma.* 2013, in press. DOI/:10.1177/1460408613488480tra.sagepub.com

Battle CE, Hutchings H, Evans PA. Risk factors that predict mortality in patients with blunt chest wall trauma: A systematic review and meta-analysis. *Injury.* 2012;43:8-17.

Battle CE, Hutchings H, Evans PA. Expert opinion of the risk factors for morbidity and mortality in blunt chest wall trauma: Results of a national postal questionnaire survey in the United Kingdom. *Injury.* 2013;44(1):56-59.

Battle CE, Hutchings H, James K, Evans PA. The risk factors for the development of complications during the recovery phase following blunt chest wall trauma: a retrospective study. In press. http://dx.doi.org/10.1016/j.injury.2012.05.019

Battle CE, Hutchings H, Evans PA. Outcomes in older blunt chest wall trauma patients: a retrospective study. *Crit Care.* 2012;16(suppl):P453(doi:10.1186/cc11060)

Battle C, Hutchings H, Evans PA. Blunt chest wall trauma and outcomes in patients with chronic lung disease: a retrospective study. (Trauma Care International Conference 2012). *Trauma*. 2012;14:359-368.

Battle CE, Hutchings H, Lovett S, Evans P. Risk factors for the development of complications following blunt chest trauma: a new prognostic model. *Crit Care*. 2013;17(Suppl 2): P292 (19th March 2013)

Battle C, James K, Evans P. A scoring system for chest trauma patients. Royal College of Surgeons Edinburgh: Audit Symposia 2009. Available from: *http://www.rcsed.ac.uk/sit/953/DesktopDefault.aspx?tabid=953*

Battle CE, James K, Hepburn D, Frost B, Caplin S, Brown T. An evidence-based guideline for the safe triage of chest wall injuries: a pilot study. *British J of Surg*. 2008;95(S3):178.

Bemelman M, Poeze M, Blokhuis TJ, Leenen LPH. Historic overview of treatment techniques for rib fractures and flail chest. *Eur J Trauma Emerg Surg*. 2010;36:407-415.

Benditt JO. *Atelectasis, lung and airway disorders. Merck Manual Home Edition.* Merck Manuals Online Medical Library. August 2004. (accessed June 13, 2010).

Bentley J, Meyer J. Repeat attendance by older people at accident and emergency departments. *Journal of Advance Nursing*. 2004;48(2):149-156.

Berben SA, Meijs T, van Dongen R, van Vugt A, Vloet L, Groot J, van Achterberg. Pain prevalence and pain relief in trauma patients in the Accident and Emergency Department. *Injury*. 2008;39:578-585.

Bergeron E, Lavoie A, Clas D, Moore L, Ratte S, Tetreault S, Lemaire J, Martin M. Elderly trauma patients with rib fractures are at greater risk of death and pneumonia. *Jtrauma*. 2003;54(3):478-485.

Bhatnagar A, Mayberry J, Nirula R. Rib fracture fixation for flail chest: what is the benefit? *J Am Coll Surg.* 2012;215:201-205.

Biasini R. 2011. Pneumothorax. Available from http://www.123rf.com/photo_15327350_pneumothorax.html (accessed 26th September 2012)

Bille A, Okiror L, Routledge T. Left flank injury – rib fractures and possible splenic puncture: thoracic approach. *Injury Extra.* 2013;**44**:29-31.

Blaivas M, Lyon M, Duggal S. A prospective comparison of supine chest radiography and bedside ultrasound for the diagnosis of traumatic pneumothorax. *Acad Emerg Med.* 2005;12:844-849.

Blecher GE, Mitra B, Cameron PA, Fitzgerald M. Failed emergency department disposition to the ward of patients with thoracic injury. *Injury.* 2008;39:586-591.

Bokhari F, Brakenridge S, Nagy K, Roberts R, Smith R, Joseph K, An G, Wiley D, Barrett J. Prospective evaluation of the sensitivity of physical examination in chest trauma . *Jtrauma.* 2002;53(6):1135-1138.

Bolliger CT, Van Eeden SF. Treatment of multiple rib fractures. Randomised controlled trial comparing ventilator with non-ventilatory management. *Chest.* 1990;97:943-948.

Borman JB, Aharonson-Daniel L, Savitsky B, Peleg K. Unilateral flail chest is seldom a lethal injury. *Emerg Med J.* 2006;23(12):903-905.

Bottlang M, Long WB, Phelan D, Fielder D, Madey SM. Surgical stabilisation of flail chest injuries with MatrixRIB implants: a prospective observational study. Injury. 2013;44:232-238.

Bouwmeester W, Zuithoff NPA, Mallett S, Geerlings MI, Vergouwe Y, et al. (2012) Reporting and Methods in Clinical Prediction Research: A Systematic Review. PLoS Med 9(5): e1001221. doi:10.1371/journal.pmed.1001221

Bowers, D. 2008. *Medical statistics from scratch: an introduction for health professionals.* Chichester: John Wiley and Sons, Ltd.

Boyton PM. Administering, analysing and reporting your questionnaire. *BMJ.* 2004; 328:1371-1375.

Boyton PM, Greenhalgh T. Selecting, designing and developing your questionnaire. *BMJ.* 2004;328:1312-1315.

Brasel KJ, Guse CE, Layde P, Weigelt JA. Rib fractures: Relationship with pneumonia and mortality. *Crit Care Med.* 2006;34(6):1642-1646.

British Association of Emergency Medicine. BAEM directory. London: Available from: http://www.baemdirectory.com. Accessed on 2nd August 2011.

Bruss GS, Gruenberg AM, Goldstein RD, Barber JP. Hamilton anxiety rating scale interview guide: joint interview and test re-test methods for inter-rater reliability. *Psychiatry Research.* 1994;53:191-202.

Bucklin L. 2005. 3D Render depicting the internal organs of the human body. Available from http://www.123rf.com/photo_8758641_3d-render-depicting-the-internal-organs-of-the-human-body.html (accessed 26th September 2012)

Buist MD, Jarmolowski E, Burton PR, Bernard SA, Waxman BP, Anderson J. Recognising clinical instability in hospital patients before cardiac arrest or unplanned admission to intensive care. *Med J Aust.* 1999;171(1):22-25.

Bulger EM, Arneson MA, Mock CN, Jurkovich GJ. Rib fractures in the elderly. *Jtrauma.* 2000;48(6):1040-1046.

Bulger EM, Edwards T, Klotz P, Jurkovich GJ. Epidural analgesia improves outcome after multiple rib fractures. *Surgery.* 2004;136:426-430.

Button LA, Roberts SE, Evans PE, Goldacre MJ, Akbari A, Dsilva R, Macey S, Williams JG. Hospitalised incidence and case fatality for upper gastrointestinal bleeding from 1999 to 2007. *Aliment Pharmacol Ther.* 2011;33:64-76.

Campbell H, Hotchkiss R, Bradshaw N, Porteous M. Integrated Care Pathways. *BMJ.* 1998;316:133-137.

Carrier FM, Turgeon AF, Nicole PC, Trepanier CA, Fergusson DA, Thauvette D, Lessard MR. Effect of epidural analgesia in patients with traumatic rib fractures: a systematic review and meta-analysis. *Can J Anesth.* 2009;56:230-242.

Chalmers I, Altman D. 1995. *Systematic Reviews.* London: BMJ Publishing Group.

Champion HR, Saco WJ, Carnazzo AJ, Copes W, Fouty WJ. Trauma Score. *Crit Care Med.* 1981;9:672-676.

Chawda MN, Hildebrand F, Pape HC, Giannoudis PV. Predicting outcome after multiple trauma: which scoring system? *Injury.* 2004;24:347-358.

Choi BC, Pak AW. A catalogue of biases in questionnaires. *Preventing chronic disease. Public health research, practice and policy.* 2005;2:1-13.

Clancy MJ. Overview of research designs. *Emerg Med J.* 2002;19:546-549.

Clark GC, Schecter WP, Trunkey DD. Variables affecting outcomes in blunt chest trauma: flail chest vs pulmonary contusion. *Jtrauma* 1988;28(3):298-304.

Centre for Reviews and Dissemination. 2009. *Systematic Reviews: CRD's guidance for undertaking reviews in healthcare.* York: University of York.

Centre for Reviews and Dissemination. "DARE (Database of abstracts of reviews of effects)." *www.crd.york.ac.uk/crdweb/.* York: Centre for Reviews and Dissemination, University of York. 9 Sep 2008.

Chan YH. Biostatistics 202: Logistic regression analysis. *Singapore Med J.* 2004;45:149-153.

Cochrane Collaboration. Review Manager (RevMan) *Computer Program. Version 5.0.* Copenhagen: The Nordic Cochrane Centre, 2008.

Cochrane Collaboration. Cochrane Handbook for Systematic Review of Interventions. Version 5.1.0. Updated March 2011. Available from http://www.cochrane.org/training/cochrane-handbook. Accessed on 15th September 2011.

Cochrane Library: Cochrane Library of Systematic Reviews, Issue 2, 2008. *www3.interscience.wiley.com/cgi-bin/mrwhome/106568753/HOME.* Edited by Chichester: Wiley.

Copes WS, Champion HR, Sacco WJ. The Injury Severity Score revisited. *JTrauma.* 1988;28(1):67-77.

Cordell-Smith JA, Roberts N, Peek GJ, Firmin RK. Traumatic lung injury treated by extracorporeal membrane oxygenation (ECMO) *Injury*. 2006;37:29–32.

Cretikos M, Bellomo R, Hillman K, Chen J, Finfer S, Flabouris A. Respiratory rate: the neglected vital sign. *Medical Journal of Australia*. 2008;188:657-659.

Cummings SM, Savitz LA, Konrad TR. Reported response rates to mailed physician questionnaire. *Health Services Research*. 2001;35:1347-1355.

Daly J, Lumley J. Bias in qualitative research designs. *Australian and New Zealand Journal of Public Health*. 2002;26:299-301

Damian J, McMahon C, Schwab W, Kauder D. Comorbidity and the elderly trauma patient. *World J Surg.* 1996;20(8):1113-1120.

Darzi A, Lennard S, Rosin D, Purkayastha S, Hamouda A. 2009. *Interactive thorax and abdomen.* DVD-ROM. London: Primal Pictures Limited.

Davis S, Affatato A. Blunt chest trauma: utility of radiological evaluation and effect on treatment patterns. *Am J Em Med.* 2006;24:482-486.

Delnevo CD, Abatemarco DJ, Steinberg MB. Physician response rates to a mail survey by specialty and timing of incentive. *Am J Prev Med.* 2004;26:234-236.

Department of Health. *National service framework for older people.* 2001

Department of Health. *Attendances at A&E departments in England from 1987-1988 to 2009-2010.* Source: DOH form KH09 QMAE. Last modified 12 November 2010. Available from http://www.dh.gov.uk/en/publicationsandstatistics/Statistics/Performancedataandstatistics/AccidentandEmergency/DH_116933

Dittman M, Ferstl A, Wolff G. Epidural analgesia for the treatment of multiple rib fractures. *Europ J Intensive Care Med.* 1975;1:71-75

Drake RL, Vogl VW, Mitchell AWM. 2009. *Gray's Atlas for students.*2nd Edition. (2009). Philadelphia: Churchill Livingston Elsevier.

Drummond FJ, Sharp L, Carsin AE, Kelleher T, Comber H. Questionnaire order significantly increased response to a postal survey sent to primary care physicians. *J Clin Epidemiol.* 2008;61:177-185.

Dubinsky I, Low A. Non-life-threatening blunt chest trauma: appropriate investigation and treatment. *Am J Emerg Med.* 1997:15;240-243.

Duckitt K, Harrington D. Risk factors for pre-eclampsia at antenatal booking: a systematic review of controlled studies. *BMJ.* 2005;330:549-550.

Dunlop RL, Tiong W, Veerasingam D, Kelly JL. Novel use of hand fracture fixation plates in the surgical stabilisation of flail chest. *Journal of Plastic, Reconstructive and Aesthetic Surgery.* 2010;63:e51-e53.

Dupont WD. Review of multivariable model-building: A pragmatic approach to regression analysis based on fractional polynomials for modelling continuous variables. *Stata Journal.* 2010;10:297-302

Easter A. Management of patients with multiple rib fractures. *Am J Crit Care.* 2001;10(5):320-327.

Edwards P, Roberts I, Clarke M, DiGuiseppi C, Pratap S, Wentz R, Kwan I. Increasing response rates to postal questionnaires: a systematic review. *BMJ.* 2002;324:1183-1192.

Egger M, Davey-Smith G, Schneider M. 2001. Systematic reviews of observational studies. In *Systematic reviews in health care: meta-analysis in context*, by Davey-Smith G, Altman D Egger M, 211-227. London: BMJ Publishing Group.

Elmistekawy EM, Hammad AM. Isolated rib fractures in geriatric patients. *Ann Thorac Med.* 2007;2:166-168.

Eren S, Esme H, Sehitogullari A, Durkan A. The risk factors and management of posttraumatic empyema in trauma patients. *Injury.* 2008;39:44-49.

Esme H, Solak O, Yurumez Y, Yavuz Y, Terzi Y, Sezer M, Kucuker H. The prognostic importance of trauma scoring systems for blunt thoracic trauma. *Thorac Cardiov Surg.* 2007;55:190-195.

Flagel BT, Luchette FA, Reed RL, Esposito TJ, Davis KA, Santaniello JM. Half-a-dozen rib fractures: the breakpoint for mortality. *Surgery.*2005;138(4):717-725.

Gabbe BJ, Cameron PA, Finch CF. Is the Revised Trauma Score still useful? *ANZ J Surg.* 2003;73:944-8.

Gabram S, Schwartz RJ, Jacobs L, Lawrence D, Murphy M, Morrow JS, Hopkins JS, Knauft RF. Clinical management of blunt trauma patients with unilateral rib fractures: A randomised trial. *World Journal of Surgery.* 1995;19:388-393.

Garrison D. 1966. *History of medicine.* Philadelphia: WB Saunders Company.

Gilbert EH, Lowenstein ER, Koziol-McLain J, Barta DC, Steiner J. Chart reviews in emergency medicine: where are the methods? *Ann Emerg Med.* 1996;27:305-308.

Glasziou P, Irwig l, Bain C, Colditz G. 2001. *Systematic reviews in health care: a practical guide.* Cambridge: Cambridge Univeristy Press.

Goepel JR. 2004. Responses to cellular injury. In *General and systemic pathology*, by Underwood JCE, 101-124. Edinburgh: Churchill Livingston.

Goldhill DR, Sumner A. Outcome of intensive care patients in a group of British intensive care units. *Crit Care Med.* 1998;26(8):1337-1345.

Granetzny A, Abd El-Aal M, Emam E, ShalabyA, Boseila A. Surgical versus conservative treatment of flail chest. Evaluation of pulmonary status. *Interact Cardiovasc Thorac Surg.* 2005;4:583-587.

Greene WB. 2006. *Netter's Orthopaedics.* Philadelphia: Elsevier. Illustration.

Greenhalgh T. 2006. *How to read a paper: the basics of evidence-based medicine.* 3rd Edition. London: Blackwell Publishing Ltd: BMJ Books.

Greenhalgh T, Peacock. Effectiveness and efficency of search methods in systematic reviews of complex evidence: audit of primary sources. *BMJ.* 2005;331:1064-1065.

Gunduz M, Unlugenc H, Ozalevli M et al. A comparative study of continuous positive airway pressure and intermittent positive pressure ventilation in patients with flail chest. *Emerg Med J.* 2005;22:325-329.

Haljamae H. 1990. Metabolic consequences of trauma. In *Surgical pathophysiology*, by Risberg B Aasen AO, 47-67. London: Harwood Academic Publishers.

Hansen JT, Lambert DR. 2005. *Netter's Clinical Anatomy*. New Jersey: Icon Learning Systems. Illustration.

Harrell FE, Lee KL, Mark DB. Tutorial in biostatistics. Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Statist Med.* 1996;15:361-387.

Harrington DT, Phillips B, Machan J, Zacharias N, Velmahos GC, Rosenblatt M, Winston E, Patterson L, et al Factors associated with survival following blunt chest trauma in older patients. Results from a large regional trauma cooperative. *Arch Surg.* 2010;145(5):432-437.

Harris IA, Khoo OK, Young JM, Solomon MJ, Rae H. Lottery incentives did not improve response rate to a mailed survey: a randomised controlled trial. *J Clin Epidemiol.* 2008;61:609-610.

Harrison GA, Jacques TC, Kilborn G, et al. The prevalence of recordings of the signs of critical conditions and emergency responses in hospital wards — the SOCCER study. *Resuscitation* 2005; 65:149-157.

Hashemzadeh S, Hashemzadah K, Hosseinzadeh H, Maleki RA, Golzari S. Comparison of thoracic epidural and intercostal block to improve ventilation parameters and reduce pain in patinets with multiple rib fractures. *Journal of Cardiovascular and Thoracic Research.* 2011;**3**:87-91.

Helzel I, Long W, Fitzpatrick D, Madey S, Bottlang M. Evaluation of intramedullry rib splints for less-invasive stabilisation of rib fractures. *Injury.* 2009;40:1104-1110.

Hernandez G, Fernandez R, Lopez-Reina P, Cuena R, Pedrosa A, Ortiz R et al. Non-invasive ventilation reduces in chest trauma related hypoxaemia: a randomised clinical trial. *Chest.* 2010;137:74-80.

Higgins JP, Thompson SG, Deeks JJ, Altman D. Measuring inconsistency in meta-analysis. *BMJ.* 2003;327:557-560.

Higgins TL, McGee WT, Steingrub JS, Rapoport J, Lemeshow S, Teres D. Early indicators of prolonged intensive care stay: impact of illness severity, physician staffing and pre-intensive care unit length of stay. *Crit Care Med.* 2003;31(1):45-51.

Hoff SJ, Shotts SD, Eddy VA, Morris JA. Outcome of isolated pulmonary contusion in blunt trauma patients. *Am Surg.* 1994;60:138-142.

Ho A, Karmakar M, Critchley L. Acute pain management of patients with multiple fractured ribs: a focus on regional techniques. *Curr Opin Crit Care.* 2011;17:323-327.

Holcomb JB, McMullin NR, Kozar RA, Lygas MH, Moore FA. Morbidity from rib fractures increases after age 45. *J Am Coll Surg.* 2003;196:549-555.

Hough A. 2001. *Physiotherapy in respiratory care (3rd Edition). A problem solving approach.* Cheltenham: Nelson-Thornes.

Hughes DE. 2004. Osteoarticular and connective tissue. In *General and systemic pathology*, by Underwood JCE. Edinburgh: Churchill Livingstone.

Hurt R. 1996. The management of fractured ribs and wounds of the chest. In *The history of cardiothoracic surgery from early times*, 231-265. New York: Parthenon.

Inci I, Ozcelik C, Nizam O, Eren N. Thoracic trauma in the elderly. *Europ J Emerg Med.* 1998;5(4):445-450.

Jacques TC, Harrison GA, McLaws ML, Kilburn G. Signs of critical conditions and emergency responses (SOCCER): a model for predicting adverse events in the inpatient setting. *Resuscitation*. 2006;69:175-183.

Janssen KJM, Kalkman CJ, Grobbee DE, Bonsel GJ, Vergouwe Y. The risk of severe postoperative pain: modification and validation of a clinical prediction rule. *Anesth Analg*. 2008;107:1330-1339.

Janssen KJM, Moons KGM, Harrell FE. Prediction rules must be developed according to methodological guidelines. (Letter to editor) *Am Coll Physicians*. 2010:263.

Janssen KJM, Moons KGM, Kalkman CJ, Grobbee DE, Vergouwe Y. Updating methods improved the performance of a clinical prediction model in new patients. *J Clin Epidemiol*. 2008;61:76-86.

Jepson C, Asch DA, Hershey JC, Ubel PA. In a mailed physician survey, questionnaire length had a threshold effect on response rate. *J Clin Epidemiol*. 2005;58:103-105.

Kalantar JS, Talley NJ. The effects of lottery incentive and length of questionnaire on health survey response rates: a randomised study. *J Clin Epidemiol*. 1999;52:1117-1122.

Karmakar MK, Ho AH. Acute pain management in patients with multiple fractured ribs. *Jtrauma*. 2003;54(3):615-625.

Karmy-Jones R, Jurkovich GJ. Blunt chest trauma. *Current Problems in Surgery*. 2004;41(3):223-380.

Kellerman SC, Herold J. Physician response to surveys: a review of the literature. *Am J Prev Med*. 2001;20:61-67.

Kerr-Valentic MA, Arthur M, Mullins RJ, Pearson TE, Mayberry JC. Rib fracture pain and disability: can we do better? *Jtrauma.* 2003;54:1058-1064.

Khandelwal G, Mathur RK, Shukla S, Maheshwari A. A prospective single centre study to assess the impact of surgical stabilisation in patients with rib fracture. *Int J Surg.* 2011;9:478-481.

Kirkwood BR, Sterne JA. 2003. *Essential Medical Statistics. Second edition.* Oxford: Blackwell Publishing company.

Klein Y, Cohn SM, Proctor KG. Lung contusion: pathophysiology and management. *Current Opinion in Anaesthesiology.* 2002;15:65-68.

Kulshrestha P, Munshi I, Wait R. Profile of chest trauma in a level 1 trauma centre. *Jtrauma.* 2004;57(3):576-581.

Lafferty PM, Anavian J, Will RE, Cole PA. Operative treatment of chest wall injuries: indications, technique and outcomes. *J Bone Joint Surg Am.* 2011;**93**:97-110.

Lazcano A, Dougherty JM, Kruger M. Use of rib belts in acute rib fractures. *Am J Emerg Med.* 1989;7:97-100.

Lecky FE, Driscoll PA. The clinical relevance of observational research. *J Accid Emerg Med.* 1998;15:142-146.

Lee RB, Bass SM, Morris JA, McKenzie EJ. Three or more rib fractures an an indicator for transfer to a Level 1 trauma centre: a population- based study. *Jtrauma.* 1990;30(6):689-694.

Lee RB, Morris JA, Parker RS. Presence of three of more rib fractures as an indicator of need for interhospital transfer. *Jtrauma.* 1989;29(6):795-800.

Lien Y, Chen C, Lin H. Risk factors for 24-hour mortality after traumatic rib fractures owing to motor vehicle accidents: a nationwide population-based study. *Ann Thorac Surg.* 2009;88:1124-1130.

Liman ST, Kuzucu A, Tastepe AI, Ulasan GN, Topcu S. Chest injury due to blunt chest trauma. *Europ J Cardiothorac Surg.* 2003;23(3):374-378.

Limmer DD, Mistovich JJ, Krost WS. *http://www.emsresponder.com/print/EMS-Magazine/Penetrating-Chest-Trauma.* August 2008. (accessed February 24, 2010).

Livingston DH, Shogan B, John P, Lavery RF. CT diagnosis of rib fractures and the prediction of acute respiratory failure. *Jtrauma.* 2008;64(4):905-911.

Loong TW. Understanding sensitivity and specificity with the right side of the brain. *BMJ.* 2003;327:716-719.

Luchette FA, Barrie PS, Oswanski MF. Practice management guidelines for prophylactic antibiotic use in chest tube for traumatic haemopneumothorax: the EAST practice management guidelines work group eastern association for trauma. *J Trauma.* 2000;48:753-757.

Mandaria DP, Newton EJ, Demetriades D. 2003. *Color Atlas of Emergency Trauma.* University Press: Cambridge. Illustration

Mann CJ. Observational research methods. Research design II: cohort, cross-sectional and case-control studies. *Emerg Med J.* 2003;20:54-60.

Marasco SF, Davies AR, Cooper J, Varma D, Bennett V, Nevill R, Lee G, Bailey M, Fitzgerald M. Prospective randomised controlled trial of operative rib fixation in traumatic flail chest. J Am Coll Surg. 2013; In press. http://dx.doi.org/10.1016/j.jamcollsurg.2012.12.024

Mars M, Spencer RF. 1997. Penetrating injury of bones. In *Scientific foundations of trauma*, by Dudley HA, Gann DS, Little RA, Maynard RL Cooper GJ, 63-73. Oxford: Butterworth-Heinemann.

Marshall G. The purpose, design and administration of a questionnaire for data collection. *Radiography*. 2005;11:131-136

Marshall MN. Sampling for qualitative research. *Family Practice*. 1996;13:522-525.

Martin RE, Teberian GT. Multiple trauma and the elderly patient. *Emerg Care Elderly*. 1990;8(2):411-420.

Mayberry JC, Ham B, Schipper PH, Ellis TJ and Mullins RJ. Surveyed opinion of American Trauma, orthopaedic and thoracic surgeons on rib fracture and sternal repair. *JTrauma*. 2009;66:875-879.

Mayberry JC, Trunkey DD. The fractured rib in chest wall trauma. *Chest Surg Clin North Am.* 1997;7:239-261.

Mayor, S. Lack of beds leads to missed government targets. *BMJ.* 2007;334:111.

McQuillan P, Pilkington S, Allan A, Taylor B, Short A, Morgan G, Neilson M, Barret D, Smith G. Confidential inquiry into quality of care before admission to intensive care. *BMJ.* 1998;316:1853-1858.

Miller M, Hui S, Tierney WM. Validation techniques for logistic regression models. *Statist Med.* 1991;10:1213-1226.

Mizushima Y, Hiraide A, Shimazu T, Yoshioka T, Sugimoto H. Changes in contused lung volume and oxygenation in patients with parenchymal injury after blunt chest trauma. *Am J Emerg Med.* 2000;18:385-389.

Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *PloS Med* 6(7): e1000097. Doi:10.1371/journal.pmed.1000097. 2009

Mohr M, Abrams E, Engel C, Long W, Bottlang M. Geometry of human ribs pertinent to orthopaedic chest-wall reconstruction. *Journal of Biomechanics*. 2007;40:1310-1317.

Mohta M, Verma P, Saxena AK, Sethi AK, Tyagi A, Girotra G. Prospective randomised comparison of continuous thoracic epidural and thoracic paravertebral infusion in patients with unilateral multiple fractured ribs – a pilot study. *J Trauma*. 2009;66:1096-1101.

Mond JM, Rodgers B, Hay PJ, Owen C, Beumont PJV. Mode of delivery, but not questionnaire length, affected response in an epidemiological study of eating-disordered behaviour. *J Clin Epidemiol*. 2004;57:1167-1171.

b) Moons KGM, Altman DG, Vergouwe Y, Royston P. Prognosis and prognostic research: application and impact of prognostic models in clinical practice. *BMJ*. 2009;338:1487-1490.

a) Moons KGM, Royston P, Vergouwe Y, Grobbee DE, Altman DG. Research methods and reporting. Prognosis and prognostic research: what, why and how? *BMJ*. 2009:338;1317-1320.

Moore G, Gerdtz M, Manias E, Hepworth G, Dent A. Socio-demographic and clinical characteristics or re-presentation to an inner-city emergency department: implications for service delivery. *BMC Public Health* 7 (2007): 320. Publishing Group.

Moore KL, Dalley AF. 2006. *Clinically oriented anatomy: 5th Edition.* Philidelphia: Lippincott Williams and Wilkins.

Morris JA, MacKenzie EJ, Edelstein SL. The effect of pre-existing conditions on mortality in trauma patients. *JAMA*. 1990;263:1942-1946.

Nakayama DK, Ramenofsky ML, Row MI. Chest injuries in childhood. *Annals of Surgery.* 1989;210:770-775.

National Heart, Lung and Blood Institute. 2011. Atelectasis. Available from http://www.nhlbi.nih.gov/health/health-topics/topics/atl/ (Accessed 28th September 2012)

National Heart, Lung and Blood Institute. 2011. Left lung pneumonia. Available from http://www.nhlbi.nih.gov/health/health-topics/topics/pnu/causes.html (Accessed 28th September 2012)

National Institute for Health and Clinical Excellence. Head injury: triage, assessment, investigation and early management of head injury in infants, children and adults. *NICE Clinical Guideline 56.* 2007. National collaborating centre for acute care.

Nicholson, G. Hormonal and metabolic responses to trauma. *Anaesthesia and intensive care medicine.* 2005;6(9):313-314.

Nirula R, Allen B Layman R, Falimirski ME, Somberg LB. Rib fracture stabilisation in patients sustaining blunt chest injury. *Am Surg.* 2006;72:307-309.

Nirula R, Diaz JJ, Trunkey DD, Mayberry JC. Rib fracture repair: indications, technical issues, and future directions. *World Journal of Surgery.*2009;33:14-22.

Norcross K. Strapping up the broken rib. *Lancet.* 1980;8168:589-590.

Oppenheim AN. 1992. *Questionnaire design, interviewing and attitude measurement.* New Edition. London: Continuum.

Osinowo OA, Zahrani M, Softah A. Effect of intercostal nerve block with 0.5% bupivacaine on peak expiratory flow rate and arterial oxygen saturation in rib fractures. *Jtrauma.* 2004;56(2):345-347.

Palmer CS, Franklyn M. Assessment of the effects and limitations of the 1998 to 2008 Abbreviated Injury Scale map using a large population based dataset. *Scand J Trauma Resusc Emerg Med.* 2011;19:1. Doi:10.1186/1757-7241-19-1.

Pape HC, Remmers D, Rice J, Ebisch M, Krettek C, Tscherne H. Appraisal of early evaluation of blunt chest trauma: development of a standardised scoring system for initial clinical decision making. *Jtrauma.* 2000;49:496-504.

Pargeter, K. 2005. 3D Render of a skeleton showing a close up of the rib cage. Available from: http://www.123rf.com/photo_7825439_3d-render-of-a-skeleton-showing-close-up-of-the-rib-cage.html. (accessed 26th September 2012)

Parris R. Epidural analgesia versus systemic intravenous opioid analgesia in the management of blunt thoracic trauma. *Emerg Med J.* 2007;24:848-849.

Peduzzi P, Concato J, Feinstein AR, Holford TR. The importance of events per independent variable in proportional hazards regression analysis. *J Clin Epidemiol.* 1995;48:1503-1510.

Perdue MD, Watts DD, Kaufmann CR, Trask AL. Differences in mortality between elderly and younger adult trauma patients: Geriatric status increases the risk of delayed death. *Jtrauma.* 1998;45(4):805-810.

Perna V, Morera R. Prognostic factors in chest trauma: a prospective study of 500 patients. *Cirugia Espanola.* 2010:87;165-170.

Peterson RJ, Tepas JJ, Edwards FH, Kissoon N, Pieper P, Ceithaml EL. Pediatric and adult thoracic trauma: age-related impact on presentation and outcome. *Ann Thorac Surg.* 1994;58(1):14-18.

Pinella JC. Acute respiratory failure in severe blunt chest trauma. *J Trauma.* 1982;22:221-225.

Pressley CM, Fry WR, Philp AS, Berry SD, Smith RS. Predicting outcomes of patients with chest wall injury. *Am J Surg*. 2012;204:910-914.

Quick G. A randomised clinical trial of rib belts for simple fractures. *Am J Emerg Med.* 1990;8:277-281.

Rashid MA, Wikstrom T, Ortenwall P. Nomenclature, classification and significance of traumatic extrapleural haematoma. *Jtrauma.* 2000;49:286-290.

Reiff DA, Hipp G, McGwin G, Modjarrad K, MacLennan PA, Rue LW. Body mass index affects the need for and the duration of mechanical ventilation after thoracic trauma. *Jtrauma.* 2007;62(6):1432-1435.

Richter T, Ragaller M. Ventilation in chest trauma. *J Emerg Trauma Shock* 2011;4:251-9.

Royston P, Altman D. Regression using fractional polynomials of continuous covariates: parsimonious parametric modelling. *Appl Statist.* 1994;43:429-467.

Royston P, Moons KGM, Altman DG, Vergouwe Y. Research methods and reporting. Prognosis and prognostic research: developing a prognostic model. *BMJ.* 2009;338:1373-1377.

Royston P, Sauerbrei W. 2008. *Multivariable model-building. A pragmatic approach to regression analysis based on fractional polynomials for modelling continuous variable*s. Wiley: Chichester.

Sackett DL. Bias in analytical research. *J Chron Dis*. 1979;32:51-63

Sampson MA, Colquhoun KBM, Hennessy NL. Computed tomography whole body imaging in multi-trauma: seven years experience. *Clinical Radiology.* 2006;61(4):365-369.

Sanabria A, Valdivieso E, Gomez G, Echeverry G. Prophylactic Antibiotics in chest trauma: a meta-analysis of high quality studies. *World J Surg*. 2006;30:1843-1847.

Sanidas E, Kafetzakis A, Valassiadou K, Kassotakis G, Mihalakis J, Drositis J, Chalkiadakis G, Tsiftsis D. Management of simple thoracic injuries at a Level 1 trauma centre: can primary health care systems take over? *Injury.* 2000;31:669-676.

Sartorelli KH, Vane DW. The diagnosis and management of children with blunt chest injury of the chest . *Seminars in Pediatric Surgery.* 2004;13(2):98-105.

Sauerbrei W. The use of resampling methods to simplify regression models in medical statistics. *Appl Statist.* 1999;48:313-329.

Sauerbrei W, Meier-Hirmer C, Benner A, Royston P. Multivariable regression model building by using fractional polynomials: description of SAS, STATA and R programs. *Computational Statistics and Data Analysis.* 2006;50:3464-3485.

Sauerbrei W, Royston P. Building multivariate prognostic and diagnostic models: transformation of the risk factors by using fractional polynomials. *Journal of the Royal Statistical Society.* 1999;162:77-94.

Shackford SR, Smith DE, Zarins CK et al. The management of flail chest. *Am J Surg.* 1976;132;759-762.

Sharma OP, Oswanski MF, Jolly S, Lauer SK, Dressel R, Stombaugh HA. Perils of rib fractures. *Am Surg.* 2008;74(4):310-314.

Sharp L, Cochran C, Cotton SC, Gray NM, Gallagher ME. Enclosing a pen with a postal questionnaire can significantly increase the response rate. *J Clin Epidemiol.* 2006;59:747-754.

Shorr R, Rodriguez A, Indeck M, Crittenden MD, Hartunian S, Cowley A. Blunt chest trauma in the elderly. *Jtrauma.* 1989;29(2):234-237.

Simon BJ, Chu Q, Emhoff TA, Timothy A, Fiallo V, Lee K. Delayed haemothorax after blunt thoracic trauma: an uncommon entity with significant morbidity. *Jtrauma.* 1998;45:673-676.

Simon BJ, Cushman J, Barraco R, Lane V, Luchette FA, Miglietta M, Roccaforte DJ, Spector R. Pain management guidelines for blunt thoracic trauma. *Jtrauma.* 2005;59(5):1256-1267.

Sirmali M, Turut H, Topcu S, Gulhan E, Yazici U, Kaya S, Tastepe I. A comprehensive analysis of traumatic rib fractures: morbidity, mortality and management. *Europ J Cardiothorac Surg.* 2003;24(1):133-138.

Slobogean GP, MacPherson CA, Sun T, Pelletier M, Hameed SM. Surgical fixation vs non-operative management of flail chest: a meta-analysis. *J Am Coll Surg.* 2013;216:302-311.

Smith GD, Phillips AN. Confounding in epidemiological studies: why "independent" effects may not be all they seem. *BMJ.* 1992;305:757-759.

Springhouse, PA, ed. 2003. *Critical Care Challenges. Disorders, Treatments and Procedures.* London: Lippincott, Williams and Wilkins.

Stawicki SP, Grossman MD, Hoey BA, Miller DL, Reed JF. Rib fractures in the elderly: A marker of injury severity. *J Am Geriatr Soc.* 2004;52:805-808.

Stephenson TJ. Inflammation. 2004. In *General and systemic pathology*, by Underwood JCE, 201-222. Edinburgh: Churchill Livingstone.

Steyerberg EW. 2009. *Clinical prediction models: a practical approach to development, validation and updating.* New York: Springer.

Steyerberg EW, Borsboom GJ, Houwelingen HC, Eijkemans MJ, Habbema JD. Validation and updating of predictive logistic regression models: a study on sample size and shrinkage. *Statist Med.* 2004;23:2567-2586.

Streiner DL, Norman GR. 2008. *Health measurement scales: a practical guide to their development and use.* Fourth edition. Oxford: University Press.

Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Moher D, Becker BJ, Sipe TA, Thacker SB. Meta-analysis of observational studies in epidemiology. *JAMA.* 2000;283(15):2008-2012.

Subbe CP, Davies RG, Williams E, et al. Effect of introducing the Modified Early Warning score on clinical outcomes, cardio-pulmonary arrests and intensive care utilisation in acute medical admissions. *Anaesthesia* 2003;58:797-802.

Svennevig JL, Bugge-Asperheim B, Vaage GJ, Pillgram-Larsen J, Fjeld NB, Birkeland S. Prognostic factors in blunt chest trauma. Analysis of 652 cases. *Annales Chirurgiae et Gynaecologiae.* 1986;75(1):8-14.

System for Information on Grey Literature in Europe. Open SIGLE. Available from http://www.opengrey.eu.

Tanaka H, Tajimi K, Endoh Y et al. Pneumatic stabilisation for flail chest injury: an eleven year study. *Surg Today.* 2001;31:12-17.

Tanaka H, Yukioka T, Yamaguti Y. Surgical stabilization or internal pneumatic stabilization? A prospective randomised study of management of severe flail chest patient. *J Trauma.* 2002;52:727-732.

Taylor M, Tracy J, Meyer W, Pasquale M, Napolitano LM. Trauma in the elderly: intensive care unit resource and outcome. *Jtrauma.* 2002;53(3):407-414.

Terragni PP, Antonelli M, Fumagalli R. Early versus late tracheotomy for prevention of pneumonia in mechanically ventilated adult ICU patients. *JAMA.* 2010;303:1483-1489.

Testerman GM. Adverse outcomes in younger rib fracture patients. *South Med J.* 2006;99(4):335-339.

Thompson BM, Finger W, Tonsfeldt D, Aprahamian C, Troliano P, Hendley G. Rib radiographs for trauma: Useful or wasteful? *Ann Em Med.* 1986;15(3):261-265.

Todd SR, McNally MM, Holcomb JB, Kozar RA, Kao LS, Gonzalez EA, Cocanour CS, Vercruysse GA, Lygas MH, Brasseaux BK, Moore FA. A multidisciplinary clinical pathway decreases rib fracture-associated infectious morbidity and mortality in the high risk trauma patient. *Am J Surg.* 2006;192:801-811.

Toll DB, Janssen KJM, Vergouwe Y, Moons KGM. Validation, updating and impact of clinical prediction rules: a review. *J Clin Epidemiol.* 2008;61:1085-1094.

Trauma Audit and Research Network. Number of blunt chest trauma admissions to UK emergency departments in 2010. *TARN* 2011. (kindly provided by Tom Jenks at TARN)

Trinkle JK, Richardson JD, Franz JL, Grover FL, Arom KV, Holstrom FM. Management of flail chest without mechanical ventilation. *Annals of Thoracic Surgery.* 1975;19:355-363.

Unify2: Quarterly monitoring of Accident and Emergency. Number of emergency departments in England. *Knowledge and Intelligence.* 2011 (kindly provided by Paul Steele at Unify2)

Vandenbroucke JP, von Elm E, Altman DG et al. Strengthening the reporting of observational studies in epidemiology (STROBE). *Ann Intern Med.* 2007;138:W1-W12.

Vergouwe Y, Royston P, Moons KGM, Altman DG. Development and validation of a prediction model with missing risk factor data: a practical approach. *J Clin Epidemiol.* 2010;63:205-214.

Vergouwe Y, Steyerberg EW, Eijkemans MJC, Habbema DF. Substantial effective sample sizes were required for external validation studies of predictive logistic regression models. *J Clin Epidemiol.* 2005;58:475-483.

Vlessis AA, Trunkey DD. 1997. Non-penetrating injury of the thorax. In *Scientific foundations of trauma* , by Dudley HAF, Gann DS, Little RA, Maynard RL Cooper GJ, 127-144. Oxford: Butterworth-Heinemann.

Vottenreiter G, Neudeck F, Aufmkolk M, Obertacke U, Schmit-Neuerburg KP. Operative chest wall stabilisation in flail chest – outcomes of patients with or without pulmonary contusion. *J Am Coll Surg.* 1998;187:130-138.

Wagner RB, Slivko B. Highlights of the history of non-penetrating chest trauma. *Surg Clin North Am.* 1989;69:1-14.

Wanek S, Mayberry JC. Blunt thoracic trauma: flail chest, pulmonary contusion, and blast injury. *Critical Care Clinics.* 2004;20:71-81.

Wang H, Chew G, Kung CT, Chung KJ, Lee WH. The use of the Charlson Comorbidity Index for patients revisiting the emergency department within 72 hours. *Chang Gung Med Journal.* 2007;30:437-444.

Welsh Assembly Government. 2008. *Delivering emergency care services: an integrated approach to delivering unscheduled care in Wales.*

West E, Newton J. Clinical guidelines: an ambitious national strategy. *BMJ.* 1997;315:324.

Wilkerson G, Stone MB. Sensitivity of bedside ultrasound and supine anteroposterior chest radiographs for the identification of pneumothorax after blunt trauma. *Acad Emerg Med.* 2010;17:11-17.

Wilkins PS, Beckett MW. Audit of unexpected returns to an accident and emergency department. *Arch Em Med.* 1992;9(4):352-356.

Wisner DH. A stepwise logistic regression analysis of factors affecting morbidity and mortality after thoracic trauma: effect of epidural analgesia. *J Trauma.* 1990;30:799-805.

Wutzler S, Wafaisade A, Maegele M, Laurer H, Geiger EV, Walcher F, Barker J, Lefering R, Marzi I. Lung organ failure score (LOFS): Probability of severe pulmonary organ failure after multiple injuries including chest trauma. *Injury.* 2012;43(9):1507-1512.

Wyatt JC, Altman DG. Prognostic models: clinically useful or quickly forgotten? *BMJ.* 1995;311:1539.

Young L, Ahmad H. Trauma in the elderly: a new epidemic? *Aust NZ J Surg.* 1999;69:584-600.

Zeigler DW, Agarwal NN. The morbidity and mortality of rib fractures. *Jtrauma.* 1994;37:975-979.

Zigmund AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand.* 1983;67:361-70