SURGICAL RIB FRACTURE FIXATION: SYSTEMATIC REVIEW OF EFFECTIVENESS, ASSESSMENT OF CURRENT UK PRACTICE, AND DEVELOPMENT OF A CORE OUTCOME SET

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Abstract

Aim

To synthesise contemporary evidence for rib fracture fixation, and thereby to fill the gaps in the knowledge required to inform a trial and provide recommendations for future study.

Method

A systematic review of systematic reviews and a meta-analysis of primary research were the methods used to examine the effectiveness of rib fracture fixation. Delphi consensus methods were used to survey three international stakeholder groups so as to define a core outcome set and a consensus on indications for and timing of rib fracture fixation. A United Kingdom (UK) survey assessed the provision of rib fracture care and analysis of a UK trauma database assessed the factors that predict rib fixation and the outcomes experienced by rib fracture patients.

Results

The systematic reviews and meta-analysis suggest that rib fracture fixation shortens the duration of mechanical ventilation, reduces critical care and hospital stay as well as overall mortality. UK clinical data suggests that rib fracture fixation improves these outcomes, and that early intervention confers an advantage over late fixation. With regard to which patients receive an intervention; fracture pattern, pulmonary contusion, admission to a major trauma centre, injury severity and age are all important predictors of undergoing surgery. A core outcome set was derived to include 23 outcomes. Consensus was achieved on 20 indications and 7 timings of surgery. Care of rib fracture patients in England and Wales is delivered in a variety of centres with different care protocols, referral pathways, lead specialties and rehabilitation services.

Conclusion

Further evidence is required to assess the effectiveness of rib fracture fixation. A feasibility trial is required to understand more clearly if clinicians have equipoise, patients are willing to be randomised and whether comparative care can be delivered. A trial will need to be stratified for surgical indication and further study is required to define outcome instruments.

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Chapter 1 - Introduction

1.1 Introduction

The enthusiasm of trauma surgeons for surgical fixation of rib fractures has led to a recent upsurge of published literature in this area. This has meant that it has become possible, and indeed essential, to synthesise this evidence base so as to ascertain the safety and efficacy of this intervention.[1] A recent Cochrane review has highlighted that 'There is an urgent need for larger high-quality randomized controlled trials' and that 'because of the small sample sizes [currently on-going trials] are unlikely to resolve the research question'.[2] This thesis represents the preparatory work for undertaking a large randomised control trial.

1.1.1 Chapter summary

This introductory chapter provides a clinical summary of rib fracture injuries, including their biomechanics, injury sequelae and current treatment options. The existing evidence is highlighted, showing the gaps in knowledge that this thesis addresses and the justification for undertaking this research. The aims and specific research questions are then discussed with a summary of the methods used.

1.2 The Injury

A rib fracture is defined as a break in the cortex of one of the horizontal bones of the chest. It occurs most often following a blunt force to the chest, commonly in road traffic accidents,[3] but could occur as a result of a low energy fall.[4] There are multiple definitions ascribed to rib fracture diagnosis and these are often not consistent in the literature. Simple (also described as unifocal or non-segmental) rib fractures occur when the rib is broken in one place within a single bone. When several of these rib fractures occur in adjacent ribs they are termed multiple rib fractures.

The terms bifocal or segmental describe a rib fractured in two separate places (Figure 1). A flail segment, meanwhile, is a specific type of chest injury in which a rib is fractured in more than one place and where this occurs in more than two adjacent ribs, producing a free-floating segment.[5]

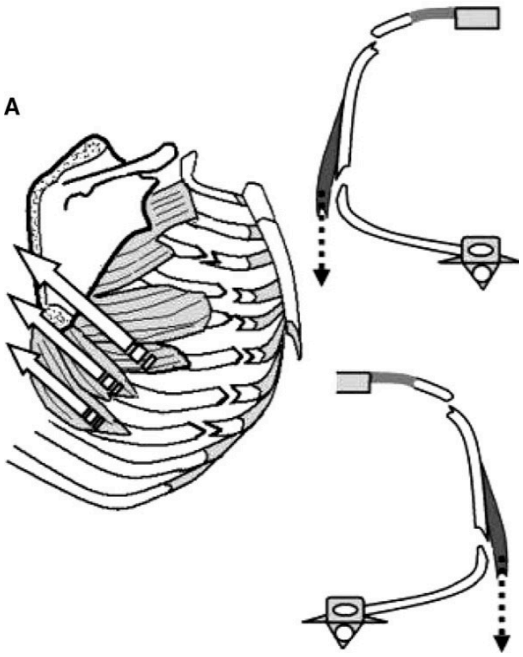


Figure 1 A bifocal rib fracture and deformity created by the serratus anterior muscle pulling on lateral flail segments [6]

A flail chest is a distinctly separate injury from a flail segment. In this definition flail chest is a flail segment that has paradoxical movement. Paradoxical movement describes an alteration in the normal chest wall biomechanics such that the movement of the chest wall occurs in the opposite direction to the movement of the flail segment.[7] Paradoxical movement is possible in both unifocal and bifocal rib fractures but the movement in unifocal rib fractures is hinged at the joint rather than a free floating segment. The injury coined ‘stove in chest’ relates to a complete collapse of the flail segment into the chest cavity.

1.2.1 Normal chest wall biomechanics

In normal inspiration the chest volume increases by way of contraction and downward pull of the diaphragm, as well as contraction of the intercostal muscles that sit in between the ribs.[8] The chest wall is elevated and expanded during inspiration.

Inspiration is an active process requiring activation of muscles to overcome the intrathoracic pressure within the lung. As the chest volume increases the pressure within the lung relative to the air pressure decreases and air is drawn into the lungs. Normal expiration is a passive process in which the weight of the chest wall under gravity increases the intrathoracic pressure together with relaxation of the diaphragm to expel the air out of the lungs. Expiration can also be an active

process, however, in which air can be forced quickly out of the lungs by contraction of the chest wall and abdominal muscles.[9]

1.2.2 Altered chest wall biomechanics after chest wall injury

Rib fractures represent a defect in the chest wall in which abnormal movement can occur. During inspiration, the unrestrained rib fractures are pulled inwards due to the relative negative pressure within the chest. The opposite occurs on expiration. Flail chest in which the ribs move paradoxically provide a mechanical disadvantage as they do not contribute to normal chest wall biomechanics which are essential for ventilation (exchange of air between the lungs and the atmosphere). The effect of this paradoxical movement on the chest wall's ability to ventilate is often underestimated. Not only does the damaged chest wall not contribute to ventilation but it can also cause damage to the underlying lung.[10] The pressure within the chest cavity is such that the lungs and heart can shift from one side of the chest to the other, crossing the midline (Figure 2). The intrathoracic pressure within the chest can cause strain on the opposite lung as well as the injured side and can reduce blood flow back to the heart causing haemodynamic instability. The whole effect reduces the ability of the lungs to take in oxygen, clear secretions and thus increases the patient's work in breathing.

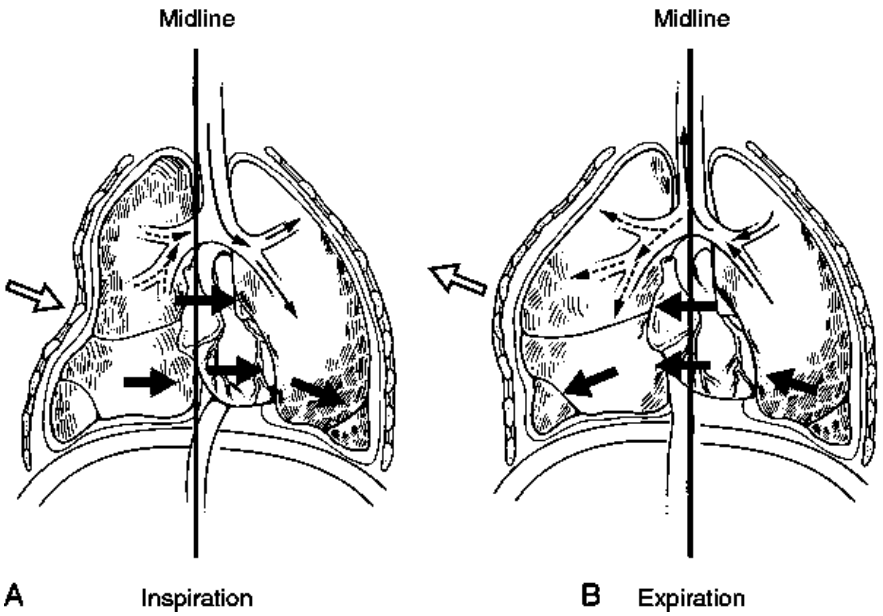


Figure 2 Paradoxical movement of a flail chest showing changes of intrathoracic pressure and midline shift (adapted from Kit et al.[11])

In addition to the forces exerted by the intercostal muscles during breathing, muscles external to the chest wall control the ribs. The serratus anterior muscle attaches long finger-like projections, originating from the scapular, on the superior

1 to 8-9 ribs. The action of this muscle serves to pull the chest wall upwards and outwards. This means that superior-lateral flail segments are pulled upwards and backwards by the serratus anterior muscle since they are unopposed by other muscles and fascia. This in turn increases the chest wall deformity and there is a risk that the segments can be pulled underneath the posterior ribs and injure the underlying lung.

1.2.3 Mechanism of injury and patient demographics

Historically, the typical rib fracture patient was young, sustaining a high-energy blow to the chest. As population life expectancy has increased, however, there has been a surge in fragility-related fractures amongst the elderly following trivial trauma.[4, 12, 13] The Trauma Audit and Research Network (TARN) have routinely collected data on chest trauma within the UK since April 2016,[14] but no data have been published from the chest trauma dataset, and there is little evidence within the UK on the incidence of these injuries. Ziegler et al. in the USA, however, have shown that up to 10% of patients attending with major trauma have associated rib fractures.[15]

1.2.4 Diagnosis and management

Rib fractures are primarily diagnosed using simple radiographs but computerised tomography reconstructive views are often also performed to assist surgical planning.[16] Although radiographic imaging can show the extent of the bony and underlying lung injury, the assessment of paradoxical movement can only be assessed clinically. It is usual for management decisions to be made as part of a multidisciplinary team that may include trauma, orthopaedic or cardiothoracic surgeons, intensive care physicians and rehabilitation consultants.[16] A full assessment of the patient to include other concurrent injuries such as traumatic brain, intrathoracic or long bone fractures should be undertaken at the time of injury. Management decisions should include an assessment of concurrent injuries as well as of chronic medical conditions.[16]

Management options include a range of pain management, ventilator support and surgical options as well as a watchful waiting approach. Often, the treatment is dictated by the severity of the chest injury as well as concurrent injuries and initial response to less invasive treatments (Table 1). Aims of treatment (depending on injury type) may include, in a stepwise manner, pain relief including oral analgesia as well as regional techniques. If the work of breathing is causing the patient to

tire, or gas exchange is ineffectual, assisted mechanical ventilation and invasive ventilation may help pneumatically splint the chest wall and therefore reduce paradoxical movement. Mechanical ventilation although potentially lifesaving is not without risk, however, and can result in trauma to the lungs, infection and ventilator dependence.[17]

Table 1 Classification of interventions for rib fractures

Treatment type	Intervention	Subtype
Conservative treatment	Analgesia	Oral analgesia
		Patient controlled anaesthesia
	Chest physiotherapy	Incentive spirometry
		Postural drainage or suction
	Adjuncts	Adhesive bandages
Analgesic procedures	Local anaesthesia	Intercostal nerve blocks
	Regional anaesthesia	Epidural anaesthesia
		Paravertebral catheters
Ventilation techniques	Non-invasive ventilation	BIPAP
	Invasive ventilation	Endotracheal intubation
		Tracheostomy
Surgical management	External fixation	Towel clip traction (historical)
		Suture traction (historical)
	Internal fixation	Suture or wire wraps
		Strut
		Intramedullary splints
		Plate fixation
		Bioabsorbable materials

Alternatively, if severe chest wall deformity and paradoxical movement is causing respiratory failure, restoration of the chest wall biomechanics with either external or internal surgical fixation may be used. External fixation techniques used in the 20th century, such as suture or towel clip traction are no longer employed since more sophisticated internal fixation devices have been developed and there was no evidence base for their use. The internal surgical options include:

- Intramedullary splints fixation is an often minimally invasive technique in which a smooth wire is passed inside the bone bridging the fracture site.
- Strut fixation is a metal plate or bar that sits over the fracture. It has extending prongs that wrap above and below the rib securing either side of the rib fracture.
- Suture or wire wraps encircle the whole rib and are often used in combination with struts to enhance fixation. Although sutures and steel wire

are non-absorbable, the newer Inion OTPS™ wraps (a mix of L-lactide, D,L-lactide and trimethylene carbonate) are absorbable.

- Plate fixation appears to be the modern implant of choice. These metallic rib fracture plates have not been tested within a randomised control trial (RCT), however, and not synthesised as part of a systematic review. There have, however, been several systematic reviews that have incorporated RCTs of other fixation techniques such as intramedullary wiring, wraps, struts and absorbable plates.[18-20]

1.2.5 UK Trauma Care

As a model of care, Trauma Networks and Major Trauma Centres (MTC) have revolutionised the treatment and survival of patients with major trauma. [21] The recognition that rib fractures and flail chest injuries are still associated with high mortality, despite improved care in other aspects of trauma has reinvigorated this as a priority topic.[22] Prior to the major trauma centre model, rib fractures were not treated in dedicated trauma hospitals and often by non-experts in chest trauma. This is still thought to occur regularly, especially when the rib fractures are isolated injuries and thus do not trigger a referral to a major trauma centre. [23] There is still a variety of specialties undertaking rib fracture care and there is no consensus as to which specialty should be leading this care. It can be found that in one trauma unit patients are looked after by an Accident and Emergency (A+E) physician; while in others any of Trauma and orthopaedic surgeons (T&O), cardiothoracic surgeons (CT) or general surgery, intensivists or respiratory physicians may be leading the care. The knock-on effect of having multiple specialties involved in rib fracture care is that no one specialty has taken a lead in research or in the training of its members. The British Orthopaedic Association standards for Trauma (BOAST) National guidance on the delivery of chest wall injury was introduced as framework to help deliver high standards of care in response to the diverse nature of care pathways that preceded it. The guidance describes how trauma services should be delivered and recommends standards that are auitable[16]. The development of the trauma networks in the UK, and specifically the Trauma Audit and Research Network (TARN), has led to a standardised set of data being routinely collected on blunt chest trauma that can be used for both research and audit.[14]

1.2.6 Evidence to support surgical fixation

The innovation and development of new interventional therapies are essential to healthcare improvement. Interventional therapies should follow the recommendations of the IDEAL framework[24] from their conception to adoption in standard clinical practice and beyond. This continuous evaluation is essential; to identify the proof of concept and safety profile in the early stages through to long-term outcomes in the future. Surgical rib fracture fixation is an established and safe procedure as described by an evidence synthesis by the National Institute for Clinical Excellence (NICE) in 2010.[25] Despite its proven safety profile, however, the efficacy of surgical fixation over non-operative treatments, and the refining of indications and outcome measurement, are still undetermined.

The most prominent evidence to date is a Cochrane review conducted by Cataneo et al.[2] that included three small randomised control trials (RCT). This evidence synthesis also included a meta-analysis of outcomes showing that the primary outcome was mortality. Meta-analysis of the mortality outcome, however, did not show surgical fixation to have a benefit over and above non-surgical management (RR 0.56, 95%CI 0.13 to 2.42, I^2 = 0%, P value = 0.70). Secondary outcomes, including chest wall deformity (RR 0.13, 95% CI 0.03 to 0.67, I^2 = 0%, P value = 0.75) and pneumonia (RR 0.36, 95%CI 0.15 to 0.85, I^2 = 66%, P value = 0.05) showed surgical fixation to have some benefit compared to non-operative patients when these results were combined in the meta-analysis, however. Other secondary outcomes such as length of hospital stay, length of ICU stay and length of mechanical ventilation could not be meta-analysed due to the differences in reporting and incomplete reporting. The conclusions of the Cochrane review suggest that there is some evidence to support efficacy but, to date, these are the only known RCTs, and the quality of the trials was generally poor, with only small numbers of patients. There is, therefore, an urgent need for larger high-quality randomised controlled trials.

Randomised control trials are often called the ‘gold standard’ of evidence-based medicine since they reduce the human bias of selection and the risk of prejudice entailed in the non-blinded assessment of treatment outcomes. The double blinded, placebo-controlled trial would be the hypothetical ‘platinum standard’, but are not practicably obtainable in surgical trials without the significant ethical disparity of performing sham surgery. Since surgery is considered a complex intervention there are multiple considerations when undertaking trial work.

Operator expertise, volume of caseload at a unit, the availability of equipment and the deliverance of other interventions should all be considered when evaluating outcomes.[26] The delivery and content of the intervention needs to as standardised as possible and should be described in enough detail to be replicated. This is at the heart of 'Medical Research Council' (MRC) guidance for developing and evaluating complex interventions.[27]

Since a safety profile of surgical fixation has been established further work is required to assess its efficacy and effectiveness. It is not currently understood whether the indications for surgery in the previous trials are aligned to current practice, and whether outcomes are sufficient to measure a clinically important difference in treatment for patients. Further explanatory work is therefore required before undertaking a more pragmatic trial to establish if the findings are reproducible and generalisable to the UK as a whole.

Several questions need to be addressed when preparing for an RCT (Table 2). These question are discussed by Blencowe et al. in their article describing the issues to consider when designing randomised controlled trials of surgical interventions.[26]

Table 2 Interventions in randomised controlled trials in surgery: issues to consider during trial design, derived from Blencowe et al.[26]

Number	Question
1	Does the RCT involve a surgical intervention?
2	What is/are the surgical intervention(s) under evaluation?
3	What is/are the concomitant intervention(s) accompanying surgery?
4	What will influence standardisation of the interventions?
	a. What is the overall study design?
	b. What type of comparator is in the RCT?
	c. In what stage of development is/are the surgical intervention(s)?
5	How will the intervention(s) be standardised in the RCT?
6	How will delivery of the intervention(s) be monitored in the RCT (fidelity)?
7	Who will deliver the intervention(s) (operator expertise)?
8	Where will the intervention(s) be delivered (context)?

These issues need to be considered before a randomised control trial is undertaken. Evidence to support the justification of a trial and how a trial would be

conducted needs careful exploration. As per the REWARD initiative, research needs to be valuable and efficient, therefore the design of a trial must withstand the scrutiny of funders and patients, be worthwhile and developed with an evidence base. Ultimately, a trial has to be deliverable, therefore understanding the patient pathway, the comparators, the operator expertise and where the intervention can be delivered are all crucial.

1.3 Thesis Aims

The thesis aims to inform the design and delivery of a future randomised control trial of internal rib fracture fixation.

The specific research questions include:

- What is the current evidence for the effectiveness of rib fracture fixation?
- What is the current evidence for the indications and timing of rib fracture fixation?
- In England and Wales, what patient and injury factors predict rib fracture fixation?
- What are the relationships between patient factors, injury type, treatment decisions and outcome in rib fracture patients?
- What are the indications for rib fracture fixation and at what time following injury should surgery be undertaken in an effectiveness trial?
- What outcomes should be measured in a rib fracture fixation effectiveness trial?
- Is a randomised controlled trial feasible with the current provision of rib fracture care in the UK?

There are four different streams of work involved to answer the research questions: A systematic review, a Delphi consensus of indications and outcomes, a survey of current practice and a statistical analysis of the TARN chest wall injury dataset.

1.3.1 Evidence for the effectiveness of rib fracture fixation

Systematic reviews based on randomised control trial evidence are considered to provide the highest level of evidence, as described by both the Scottish Intercollegiate Guidance Network (SIGN)[28] and the Oxford Levels of Evidence.[29] In

the Lancet series “Increasing value, reducing waste”, it is recommended that trials should not be funded unless there is evidence from systematic reviews to show that they are required.[30] Three randomised control trials[18-20] are well known within the literature base and are quoted within a review and meta-analysis undertaken by the Cochrane collaborative.[2] The RCTs and subsequent meta-analysis have shown the superiority of surgical fixation compared to non-operative treatment for outcomes including pneumonia, chest deformity and tracheostomy rates, with no difference in mortality. This evidence is based on a small population of 123 patients, however, and the review[2] declares that no firm conclusions can be made regarding the effectiveness of surgical rib fracture fixation and that therefore further evidence is required.

Several trials were due to complete following this review and therefore a new synthesis is required to clarify whether further trial work is still required and thus to ensure that research effort is not wasted.[31] The first part of the thesis is therefore dedicated to the synthesis of the current evidence base. The initial aim had been to synthesise primary evidence for effectiveness, however in preparing for this I become aware of a number of systematic reviews that had several differing conclusions and therefore decided to review this evidence first. This was a logical next step as a review of reviews allows several reviews to be compared and contrasted to identify if further research evidence is required. Synthesis of systematic review evidence is a relatively new concept and definitive guidance on methodology is not fully developed. The Cochrane Group have developed their guidance of what they term an ‘overview of reviews’,[32] whereas Smith et al.[33] describe this type of synthesis as a systematic review of reviews. This methodology for such reviews of reviews, however, focusses on the effectiveness of interventions and is not designed to capture other key information such as indications for surgical intervention, the timing of surgery and outcome measures.

Based on the gaps identified in the review of reviews a further review of the primary literature was warranted. This was to supplement the evidence for the timing of and indications for fixation, as well as to explore the effectiveness of fixation for a broader range of outcomes. The systematic review also encompassed information gathering on the outcomes used in effectiveness trials that forms the basis of a consensus questionnaire. The synthesis of primary research followed the Centre for Reviews and Dissemination guidance[34] developed at the University of York.

Within this framework the specific objectives were:

- To synthesise the systematic review evidence for the effectiveness of rib fracture fixation
- To identify and synthesise the primary evidence for the effectiveness of internal surgical rib fracture fixation
- To evaluate the primary evidence base in respect to the indications for and timing of surgical rib fracture fixation
- To identify the outcomes measured following surgical rib fracture fixation.

1.3.2 What is the relationship between patient factors, injury type, treatment decisions and outcome?

To develop a recommendation for the design of an RCT, it is necessary to understand the current prevalence and types of injury in order to determine how a trial can be delivered. Accordingly, the patient demographic, the incidence and type of injuries as well as treatments used and outcomes attained will together provide evidence for what is currently achieved in the UK. The eventual RCT design will need to be in line with current practice and should be based on the knowledge derived from national databases with respect to the numbers currently operated on as well as what surgical and anaesthetic techniques that are currently employed.

The Chest Wall Trauma screening was introduced to the Trauma Research Audit Network (TARN) dataset in April 2016 and has gathered data for over 17000 patients in thirteen months.[14] The screening was introduced as there has been a lack of an evidenced-based standard model of care. Despite systematic review evidence,[2] the uptake of this treatment is not consistent throughout the UK. The aim of the analysis of the collected screening data conducted in this thesis is to improve the knowledge of the current patient population, the treatment they receive and to map the patient journey from ambulance to discharge and to better understand what factors determine outcomes. Understanding these factors will affect trial design and will identify potential confounding factors that may need to be considered at randomisation level (cluster randomisation or stratification) or as an a priori statistical analysis. Descriptive statistics, correlation and regression analyses will be used to further explore the relationships and differences of patients presenting with chest wall injuries in respect to their treatment pathway and finally their outcome. Very few studies have explored large scale trauma

databases in this detail. The size and completeness of the database means that a thorough analysis of its data is expected to contribute significant findings to the current evidence base.

1.3.3 What are the indications and timing for surgical management of rib fractures?

A clear and measurable consensus of indications for surgery is not currently agreed upon. Quantification or clarification of these indications is often not discussed within study reports and appears to be largely a subjective assessment from the clinical team rather than an indication based on research evidence. If an RCT is to be undertaken, a consensus on the specific indications should be quantified so as to ensure that the treatment decisions are arrived at equally between recruiting sites. Since the consensus will inform the eligibility criteria for the trial it is hoped that clinicians are more likely to 'buy in' to the trial and recruit to it if it is closely aligned to current practice.

I intend to address this gap in the knowledge base by conducting a systematic review to gather descriptions of current indications. This will inform a basis for a Delphi consensus group in which experts will rate the importance of indications for and the timing of surgical rib fracture fixation in several online questionnaire rounds.

1.3.4 What is the current care provision for rib fracture patients in the UK?

In preparation for further research into the area of rib fixation for both flail and non-flail chest injuries it is necessary to understand referral pathways of patients who may require rib fixation. Understanding which specialties look after these patients is important to identify those who would be likely to participate in research in the future. Understanding the provision of specialist physiotherapy, occupational therapy and rehabilitation consultants is necessary to know whether the UK has the infrastructure to deliver comparable care in potential recruitment sites. A survey of the care currently provided in Trauma units and Major Trauma Centres in England and Wales will provide useful evidence as to what kind of trial is able to be delivered in the UK.

1.3.5 What outcome measures should be measured in patients in a rib fracture fixation trial?

A consensus on outcome measures appears to be the biggest gap within our knowledge base. An RCT trial design requires a primary outcome and secondary outcomes to be defined a priori to reduce bias. Primary outcomes are also used as the basis to power the study and derive the sample size. A lack of a core outcome set has resulted in multiple trials and cohort studies measuring a multitude of outcomes, meaning that outcomes not comparable within a synthesis and making meta-analysis difficult. Trials and studies of rib fracture patients have been growing in popularity over the last decade but the number of trials remains small. The effect of not collating comparable data reduces the number of studies that can be included with a synthesis and therefore reduces the strength of the evidence derived from a systematic review or meta-analysis. This means that developing a consensus in respect to outcomes is a specific priority in rib fracture research. Furthermore, the Core Outcome Measures in Effectiveness Trials (COMET) group has not reported on their database that a specific outcome set is currently in use or in development for rib fracture research.

A systematic review will be undertaken to identify what outcomes are currently measured and to inform the first round of a Delphi consensus process. The COMET group have used the Delphi approach for preparing outcome sets for trials for effectiveness.[35] This would bring together clinical and allied health professionals with patients and public involvement to help inform on the relevant outcomes. Through the subsequent rounds of questionnaire and analysis a smaller and more unified set of outcomes could be achieved.

1.3.6 Recommendations for trial

Clinical questions are often proposed as a standard PICOS format in which the Patient, Intervention, Comparator and Outcomes are clearly stated in order to provide consistency(Figure 3). Both the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT) and Consolidated Standards of Reporting Trials (CONSORT) statements on RCTs have a derivation of the PICOS within their guidance. The structure of the discussion in this thesis is centred on the PICOS style so as to give a structured narrative of recommendations for further trial work, focusing on study design and deliverability within the UK.

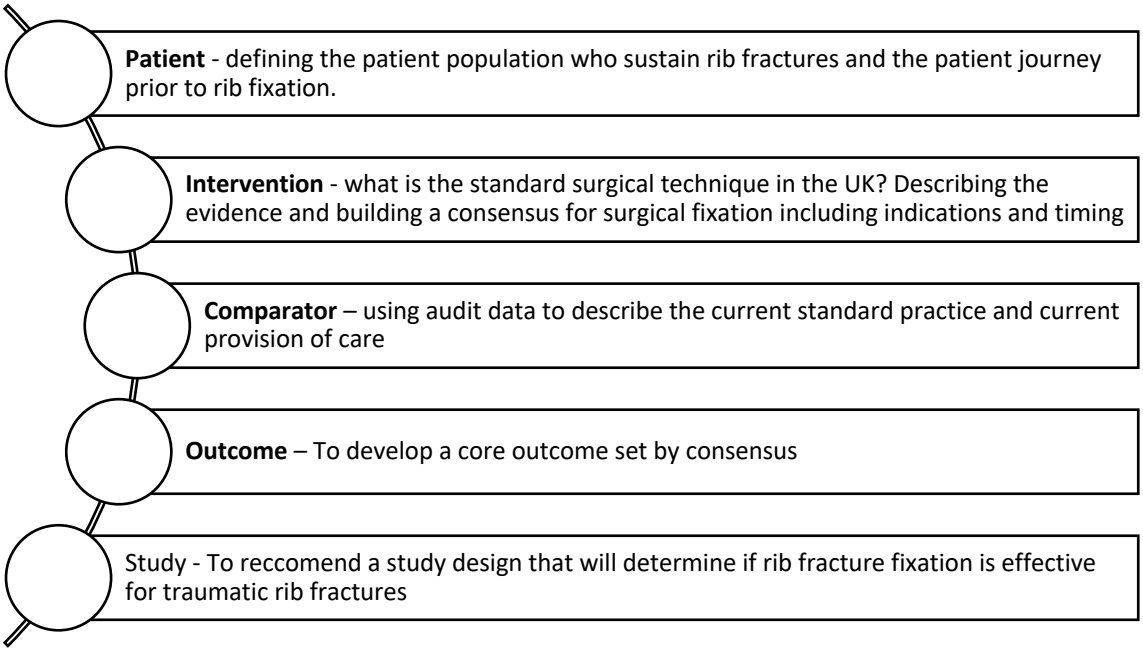


Figure 3 The PICO questions defining recommendations for RCTs

Combined with the new Medical Research Council guidance on developing and evaluating complex interventions, the thesis will provide recommendations for trial design, indications for surgical fixation and determine how the intervention will be delivered and evaluated. The target population for this proposed trial is patients from the UK. Surgical rib fixation has not been evaluated within the UK and this has indeed been set as a priority by the National Institute for Health Research within the UK. It is unknown whether the results from a differently funded healthcare system would be comparable to the UK model of trauma care.

Chapter 2 - A Review of the Current Synthesis of Evidence for the Effectiveness of Internal Fixation of Flail Chest and Multiple Unifocal Rib Fractures

2.1 Introduction

To assess effectiveness of surgical rib fixation a review of the primary literature was planned. On the basis that The Lancet's REduce research Waste And Reward Diligence (REWARD) initiative promotes that research should add value, a search of Cochrane and Medline was completed in the initial stages of preparing for this review to look for similar work already concluded or ongoing. It was found that several systematic reviews have been published but that these were of varying quality and synthesised different primary papers.[2, 36, 37] This implied that the most logical next step in evidence synthesis was to pursue a systematic review of systematic reviews,[33] and the originally planned review of the primary literature was accordingly paused to allow this to take place.

A review of reviews allows multiple review results to be compared and contrasted, alongside an assessment of their quality. When faced with reviews with opposing results a full assessment of the risk of bias, quality and relevance of the reviews would take place before assigning any conclusions, therefore. A systematic review is the gold standard approach to synthesising evidence as it follows a strict predetermined protocol to reduce bias in identifying, extracting and synthesising evidence.[32] A systematic review of reviews follows these same principles to provide transparent approaches to evidence synthesis.

2.1.1 Research Question

What is the current evidence base for the effectiveness of rib fracture fixation?

2.1.2 Objectives

The specific objectives for this review of reviews were to:

- Evaluate the clinical effectiveness of internal surgical fixation of rib fractures
- Explore similarities and differences between existing reviews
- Identify gaps in the evidence and assess the potential value of future research
- Make recommendations for further research

2.2 Method

The review was undertaken systematically using the methods described by the Centre for Reviews and Dissemination.[34] The protocol was developed and published on the PROSPERO register. Pre-publishing the protocol gave transparency to the research plan and was intended to reduce bias in the publication of findings.[38] The PROSPERO entry can be accessed at https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016053494.

2.2.1 Inclusion Criteria

To be eligible for inclusion in the review, systematic reviews had to meet the criteria outlined in Table 3. The inclusion criteria are presented in the PICOS[39] form relating to specific participants, interventions, comparators, outcomes and study design. This gives a clear and unambiguous definition of the type of studies that were considered for inclusion.

Table 3 Eligibility criteria for included studies

	Inclusion
Population	Adults over 18 years of age who have sustained one or more rib fractures (including flail chest) following blunt chest wall trauma
Intervention	Any method of internally surgically fixing rib fractures, including a combination of therapies
Comparator	Non-surgical management (e.g. mechanical ventilation, epidural and regional anaesthesia); external fixation (e.g. traction, splints, Hoffman style pin and bar fixation)
Outcomes	Mortality, length of mechanical ventilation, Length of ICU stay, Length of hospital stay, Pneumonia
Study Design	Systematic Review Published and non-published works in English

2.2.2 Defining the population

Most patients' sustaining major trauma are adults, with very few paediatric cases in comparison.[40] Physiological differences in children result in paediatric cases of trauma being managed differently to adult cases. Bone healing in children is rapid and fracture stability is gained relatively quickly. Bone remodelling in children is

such that significant initial deformity is accepted as the bone will remodel back to its anatomical shape. For these reasons, only adults with rib fractures were considered eligible.

Both non flail unifocal rib fractures (NF) and bifocal flail chest (FC) injuries were included but these were considered as separate injuries and therefore analysed separately as a subgroup analysis. No penetrating injuries were considered as these are managed entirely differently. Studies that include both penetrating and non-penetrating injuries were eligible if data was presented independently. Only patients undergoing rib fracture fixation for acute injury were included, surgery for chronic non-union was excluded.

2.2.3 Defining the intervention

There are multiple types of internal fixation devices used for rib fracture fixation, all based on the principle that the fracture is reduced and held in place until healing occurs. As they all use the same principle of bridging the fractures to promote secondary bone healing, the devices are comparable in this way despite their design differences. No intervention has been proved superior and therefore all internal fixation devices were included. External fixation devices were only considered as a comparator.

2.2.4 Defining the comparator

Non-surgical management of rib fractures encompasses a multitude of different therapies and strategies. Which non-surgical therapies are employed in particular cases is dependent on symptoms and clinical signs. All non-operative treatments, such as supportive ventilation, epidural and local anaesthesia, traction and splinting were included, as well as external fixation.

2.2.5 Defining outcomes

There is no current core outcome set published for rib fracture fixation, therefore it was not possible to prioritise specific outcomes for inclusion in the review. In the absence of a core outcome set, outcomes were chosen from clinical experience and included measures of morbidity and mortality. Specifically, outcomes most often reported in primary studies include mortality, length of ventilation, ICU and hospital stay as well as rates of pneumonia. Studies had to include at least one of these outcomes to be eligible for inclusion. The primary outcome was length of

mechanical ventilation as this outcome is closely linked with two other outcomes, mortality and pneumonia.

2.2.6 Study design

Studies were included if they specified they were a systematic review, scoping review or meta-analysis. Systematic reviews were eligible for inclusion if they specified a search strategy in at least one literature database and included primary research. No restrictions were placed on the study design of the primary studies.

Mays et al.[41] define scoping reviews as aiming 'to map rapidly the key concepts underpinning a research area and the main sources and types of evidence available'. As described by Arksey and OMalley,[42] there are four different reasons why scoping reviews may be undertaken and all are relevant for the research objectives in this review;

- To examine the extent, range and nature of research activity
- To determine the value of undertaking a full systematic review
- To summarise and disseminate research findings
- To identify research gaps in the existing literature

Scoping reviews with a defined research question, literature search and systematic way of presenting the results were included despite the lack of quality assessment of the literature. Since one of the aims of this review was to find any gaps in the literature, it was felt scoping reviews would help refine the research questions and would increase the yield of known knowledge. It was recognised that not assessing the risk of bias within a scoping review could reduce the reliability; nonetheless it is recognised as a valid methodology of study synthesis.[42] The relevance of all the reviews would be assessed and reported in synthesis after considering the risk of bias assessment and quality appraisal.

2.2.7 Language

Only English language systematic reviews were included in the synthesis since there was no funding for translation services. It is acknowledged that this may introduce language bias, especially since the known published research in primary studies are from Japan and Egypt, although these are published in English language journals. A list of non-English language studies is reported for transparency.

2.2.8 Publication Type

All publication types, published and unpublished studies, conference abstracts and theses were included. Being inclusive rather than restrictive with the type of publication allowed a greater breadth of evidence to be gathered. It was useful to identify all available evidence even if not used in the synthesis.

2.2.9 Search Strategy

An electronic database search of published literature was undertaken on 14 December 2016 and these searches were updated on 2 March 2017. Searches included the following databases: MEDLINE including PreMEDLINE, EMBASE, Cochrane Database of Systematic Reviews (CDSR) and Science Citation Index. Clinical guidance and policy documents and relevant databases such as NICE Evidence were also searched. These included the Department of Health policy content, national clinical guidance centre, and Scottish Intercollegiate Guidelines Network (SIGN).

An additional search was undertaken for non-published literature within the Conference Proceedings Citation Index. The MEDLINE search was restricted to those published after 1976 because that was the year that Advance Trauma Life Support (ATLS) was introduced, incorporating new methods of resuscitation which have significantly improved outcomes. Comparing studies before 1976 to studies after the introduction of ATLS would be likely to confound outcome data as they are not comparable.

2.2.10 Search Terms and Selection

The search strategy developed for MEDLINE was adapted to run appropriately on other databases, and is provided in Appendix A.1. The searches were conducted with help from the Department of Health Sciences Librarian Adrian Clark, who helped define the search terms. Both keyword and Medical term to Subject headings (MeSH) searches were conducted (Table 4).

Table 4 Subject headings captured within the search terms

Search terms	Subject headings captured
rib (adj3) fracture*	Rib within three words of fracture, fractures, fractured, fracturing
(flail or stove? in) adj3 chest	Flail or stove(d) in within three words of chest
blunt chest adj3 trauma	**Blunt chest** within three words of t**rauma**
extra thoracic injur*	Extra thoracic injuries, Extra thoracic injury,
costal fracture*	Costal fracture(s)

Search terms	Subject headings captured
Flail Chest/	Flail chest
Rib Fracture/	Rib fracture
fracture* adj3 fixation	Fracture, Fractures, Fracturing within three words of Fixation
bone screw*	Bone screw(s)
Bone plate*	Bone plate(s)
Suture* adj3 fixation*	**Suture**(s) within three words of **fixation(s)**
judet strut*	Judet strut(s)
bioabsorbable plate*	Bioabsorbable plate(s)
heavy suture*	Heavy suture(s)
intramedullary splint*	Intramedullary splint(s)
metal adj2 fixation*	**Metal** within two words of **fixation(s)**
(plate* or strut*) adj3 fixation*	Plate(s) or Strut(s) with three words of fixation(s)
exp Internal Fixators/	Internal fixator(s)
fracture fixation/ or fracture fixation, internal/ or fracture fixation, intramedullary/	Internal fracture fixation, Intramedullary fracture fixation
fracture adj3 stabili?ation	fracture(s) within three words of stabilization or stabilisation

The search terms defining the injury were combined together with the Boolean logic function OR, similarly the search terms describing the intervention were also combined as OR. The resultant search terms were combined with the AND function (Figure 4).

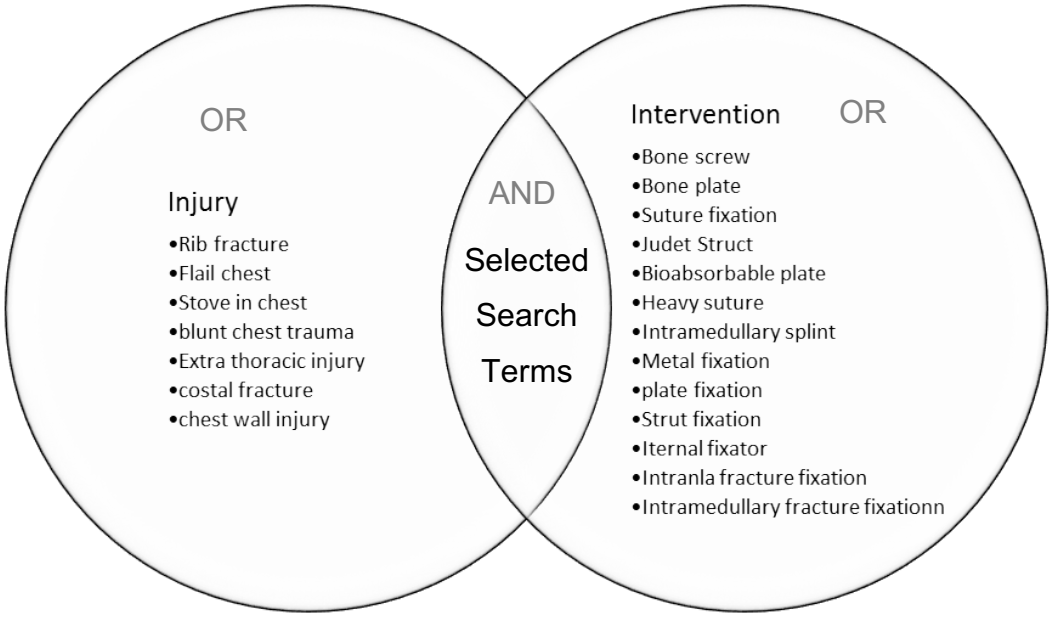


Figure 4 Search terms were selected using Boolean logic

2.2.11 Reference checking

To identify relevant further reviews, reference lists of included studies were assessed for eligibility.

2.2.12 Screening

A first screening reviewed titles and abstracts to identify potentially relevant studies and then a second screening reviewed the full texts of those records identified as potentially relevant by either researcher. Two researchers (HI and EC) completed both stages independently. A third researcher reviewed disagreements (CM) where a consensus could not be reached between the researchers. A log of all screening activity was kept within the software Endnote X7 (Clarivate Analytics, Version 7.1 release date 2/04/2014), which was used to organise all the gathered references. The responses of both researchers were kept partially blinded by hiding the response column of the other researcher. This was to ensure that independent decisions were made on each review. Reasons for exclusion were recorded on a hieratical scale.

2.2.13 Data extraction

Tables were used to present extracted data in a uniform and concise way so information could be assessed in a consistent manner. The table format was tested on a couple of reviews and adapted to the final format. Extracted data included patient characteristics, intervention and comparators, outcome measures as well as duration of follow up and effect estimates, standard deviations, standard errors and confidence intervals, as available. Statistical heterogeneity was extracted to assess the variability of the treatment effect between different studies. A description of the study methods and information about the study, including country and year, were also extracted.

One researcher completed data extraction (HI); a second researcher crosschecked 50% (EC). Both researchers crosschecked for discrepancies and a consensus was reached. No discrepancies required the intervention of a third researcher.

2.2.14 Review Validity, Quality Assessment and Risk of Bias

The methodological advantage of a systematic review over a scoping review is an assessment or appraisal of the synthesised evidence.[42] Although validity, risk of

bias and quality assessment are often used interchangeably they are considered different approaches to establish how reliable, generalisable and applicable the evidence is.[43]

Validity describes how well the review has answered its own research question. It is important to assess both external validity (describing the generalisability of the results) and internal validity (describing how well the research was conducted).[44]

Bias refers to the process by which errors can be made in reviews due to poor design or arising from how reviews are collected, selected and interpreted. Multiple agencies have made efforts to reduce the risk of bias in systematic reviews of primary studies, The PRISMA statement has been championed as the standard way to present systematic review findings to reduce bias.[45] The PRISMA checklist gives an easy format to follow so that all methodological aspects pertaining to the conduct of the study are transparently documented to reduce potential bias.

Uniquely, when synthesising reviews of reviews, one is assessing whether there is bias in the way the review was conducted and not necessarily the primary research. Multiple tools have been proposed to assess the risk of bias in a review of reviews. The first such tool developed was the AMSTAR tool,[46] but this is limited by a tendency to focus more on the quality assessment than the risk of bias. It is a quick and easy tool to use but lacks depth of questioning and only really scrapes the surface to identify true risk of bias. Two further problems include a lack of guidance on translating the score into the final rating (a problem also found in ROBIS) and lack of different weightings for different evaluated items. This process of evaluation makes it difficult to discriminate between those reviews with the same score without having a clarifying narrative.[47]

The ROBIS tool developed by researchers from the Universities of Bristol and York is a three-phase assessment of risk of bias (Table 5).

- Phase 1 Assessing relevance
- Phase 2 Identifying concerns with the review process
    - Study eligibility criteria
    - Identification and selection of studies
    - Data collection and study appraisal
    - Synthesis and findings

- Phase 3 Judging risk of bias

Phase 2 has four domains which are assessed independently with subdomain (“signalling”) questions. Each subdomain question is rated on a 5-item scale, “yes,’’ ‘‘probably yes,’’ ‘‘probably no,’’ ‘‘no,’’ and ‘‘no information,’’(Y, PY, PN, N, NI) with ‘‘yes’’ indicating low concerns [48]. An assessment of all the signalling questions will give an overall rating of high, low or unclear as a score for the whole domain. No exact criteria are given to assess high, low or unclear, with it being left up to the researcher after considering the answers from the signalling questions to assign a score, although some guidance is given within the handbook.

Table 5 Adapted* from the ROBIS tool showing three phases, four domains and signalling questions (*signalling questions presented without corresponding full explanation for each corresponding criteria)

Domains **Rated High/Low/Unclear**	**Signalling Questions** **Rated Y,PY,NI, PN, N**
Phase 1 Assessing relevance	
(Optional)	
Phase 2 Identifying concerns with the review process	
1. Study eligibility criteria	1.1 Did the review adhere to pre-defined objectives and eligibility criteria? 1.2 Were the eligibility criteria appropriate for the review question? 1.3 Were eligibility criteria unambiguous?1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? 1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)?
2. Identification and selection of studies	2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? 2.2 Were methods additional to database searching used to identify relevant reports? 2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? 2.4 Were restrictions based on date, publication format, or language appropriate? 2.5 Were efforts made to minimise error in selection of studies?
3. Data collection and study appraisal	3.1 Were efforts made to minimise error in data collection? 3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? 3.3 Were all relevant study results collected for use in the synthesis? 3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? 3.5 Were efforts made to minimise error in risk of bias assessment?
4. Synthesis and findings	4.1 Did the synthesis include all studies that it should? 4.2 Were all pre-defined analyses reported or departures explained? 4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? 4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? 4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? 4.6 Were biases in primary studies minimal or addressed in the synthesis?
Phase 3 Judging risk of bias	
	A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? B. Was the relevance of identified studies to the review's research question appropriately considered? C. Did the reviewers avoid emphasising results on the basis of their statistical significance?
Risk of bias in the review LOW/HIGH/UNCLEAR	

Quality assessment with the ROBIS Tool[48] was undertaken by one researcher and check by a second (CM). Risk of bias was completed by two researchers and did not require the intervention of a third as all disagreements were managed between the researchers. Although biases were identified within reviews, no review was excluded from the analysis based on the risk of bias assessment.

2.2.15 Data synthesis

The synthesis used several techniques described by the Centre for Reviews and Dissemination at the University of York. Firstly, tabulations of the review characteristics were constructed to give a concise summary of important facts about the reviews that could be compared easily. Summary tables were constructed to include titles, aims, country of publishing authors, information on search strategy as well as evidence of risk of bias assessment and study conclusions. The primary studies within each review were also displayed in this table with the known number of participants in each study. Each of the primary studies within the reviews was then highlighted within a second table; this allowed assessment of any overlap within the reporting of primary studies between the reviews. This format also served to highlight whether some reviews had missed important primary studies, possibly due to inadequate search techniques or error in identifying studies. A narrative synthesis then compared the review characteristics and highlighted important similarities and differences between the reviews.

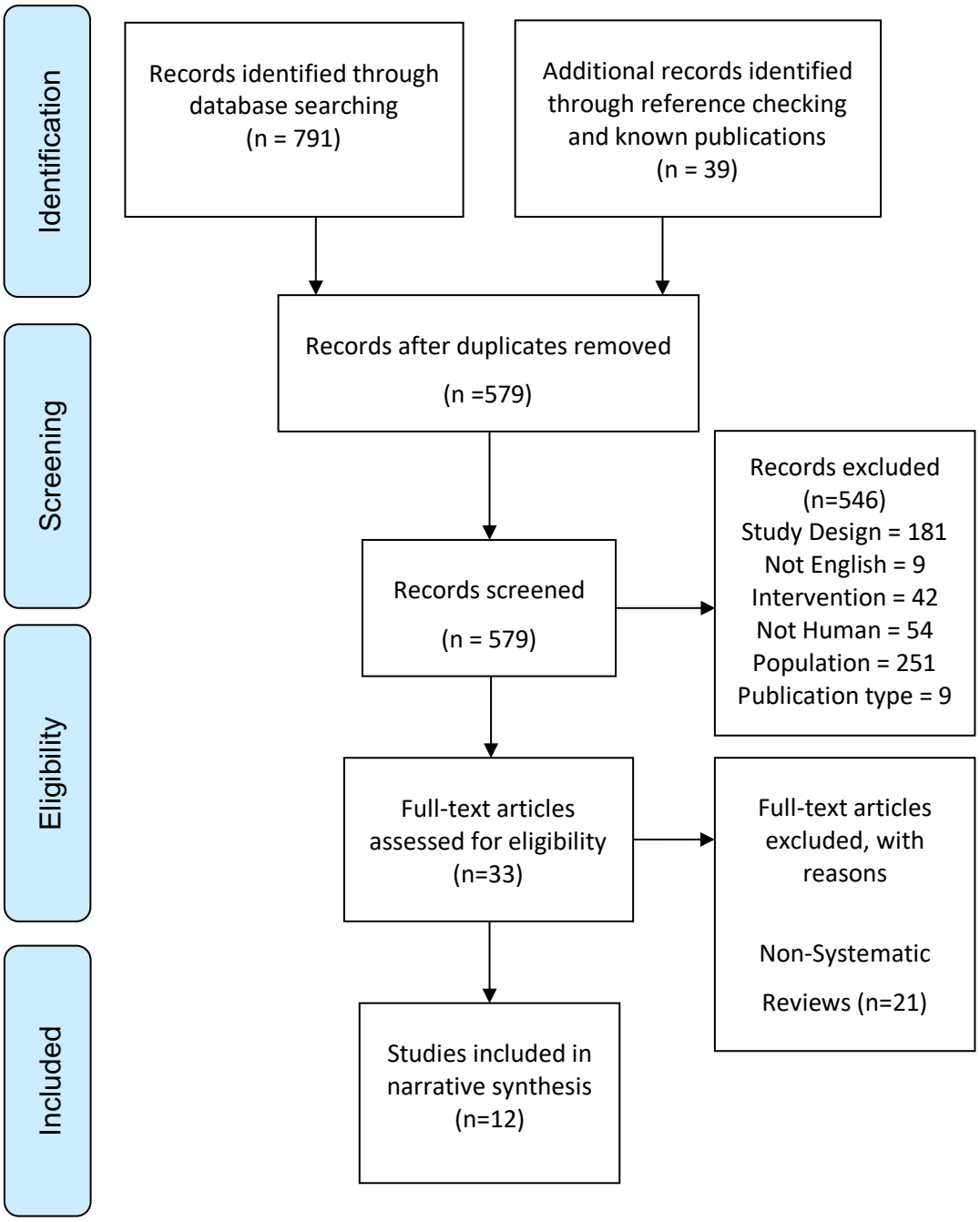
Flail chest and multiple unifocal rib fractures were considered as different injuries and were thus synthesised separately for each outcome extracted. Each outcome was narratively synthesised and included the number of reviews using this outcome as well as reporting effect estimates and confidence intervals as appropriate. Important numerical data was presented in tables when there was sufficient comparable data to allow such a comparison. All outcomes that were reported in the reviews were included in the synthesis ,even if only reported in one study, so as to avoid reporting bias.[49] A narrative synthesis was only undertaken if there were more than two reviews measuring the same outcome, otherwise the outcome was only reported within the study data tables.

The narrative synthesis discussed the aims, the heterogeneity of reviews and evidence relating to each outcome. It also describes the methodology and biases of each review process. Reporting guidance have not been developed for reviews of reviews and therefore reporting followed the guidance for the synthesis of primary studies. Although not fully applicable, reporting was as far as possible in accordance with the PRISMA statement.[45]

2.3 Results

Electronic searches undertaken on December 14, 2016 identified 791 records. An additional 39 records were identified following reference checking and a final search on March 13, 2017. Titles and abstracts revealed 33 potentially eligible records, and full text screening identified that 21 of these were descriptions of surgical techniques or types of literature reviews other than systematic reviews. The full text screening identified 12 systematic reviews eligible for inclusion. The PRISMA flow diagram in Figure 5 shows the screened records and reasons for exclusions. **Appendix A3** lists the excluded studies

Figure 5 PRISMA Flow Diagram



2.3.1 Review Characteristics

Eleven systematic reviews published between 2010 and June 2016, and one rapid evidence synthesis published by NICE as an overview for the Interventional Procedures Advisory Committee (IPAC),[25] met the inclusion criteria. Three of the reviews are presented as best evidence topics:[50] by Schulte et al.[51] Girsowicz et al.[52] and de Lesquen et al.[53] Several pieces of work included some form of systematic review but were not the focus of the research. A Delphi study[5] had included this work but had not published their synthesis and was therefore excluded.

Table 7 maps the aims of the included reviews, search strategy, included studies and the authors' conclusions. It is also describes whether quality appraisal of the primary studies was performed.

Nine reviews[2, 25, 36, 37, 51, 53-56] evaluated the effectiveness of internal surgical fixation in patients with flail chest, two included patients with multiple unifocal rib fractures[52, 57] and one review included all rib fractures but only reported outcomes for flail chest.[58] The inclusion criteria specified only adult patients in ten reviews, the review by Girsowicz et al.[52] specifically looked at patients over the age of 45 years old, and although the review by Cataneo et al.[2] included children, the primary research did not contain any participants less than 18 years of age. Studies specified all types of surgical fixation and did not specifically exclude external fixation, however no primary study had external fixation in their intervention or their comparator group. Table 8 summarises the primary studies that were included in each of the reviews.

Three reviews,[2, 37, 56] included only randomised evidence and eight included other study designs.[25, 36, 51-55, 57] As would be expected, there was overlap across the reviews in terms of the included studies. The number of unique primary studies was three randomised control trials (comparing internal fixation to usual care), 18 non-randomised studies (comparing internal fixation to usual care), 11 case series (evaluating internal fixation) and two case reports (evaluating internal fixation). The total number of patients who had internal fixation in primary studies (excluding duplicate studies) was 1036 and there were 1187 controls. Many reviews define the comparator as usual care but do not elaborate on what encompasses usual care. Non-standardised reporting within reviews of usual care protocols and nonsurgical treatments hindered a meaningful subgroup analysis of the

comparators against the intervention. For example, grouping reviews that used positive pressure ventilation or those that used external strapping.

The most commonly included primary study within the reviews (n= number of reviews the primary study was included in) was the RCT by Tanaka et al.[18] (n=9) published in 2001, followed by the RCT of Granetzny et al.[19] published in 2005 (n=8). The most recently published RCT, in 2013, was included in seven reviews. An early case series by Nirula et al.[59] was also commonly included (n=7). The review with the largest number of included studies was completed by Swart et al.,[54] which included three RCTs and 17 non-randomised studies. The reviews by Coughlin et al.,[37] Cataneo et al. [2] and Schuurmans et al.[56] included only the three RCTs [18-20].

The rapid evidence synthesis by NICE[25] was the first review included in this study, published in 2010. It included seven primary studies including an RCT published in 2001.[18] Another trial,[19] published in 2005, was not included in the NICE review, despite it appearing to meet the review's inclusion criteria. Search terms must have missed this study as it was not reported in the excluded studies list. A review in 2015 by Cataneo et al.[2] was the first meta-analysis published and included three RCTs.[18-20] Two further systematic reviews[37, 56] identified the same three RCTs[18-20] and repeated the same meta-analyses. The research question and eligibility criteria in both of the reviews are almost identical to the review by Cataneo et al.[2] and they were both published in 2016. Neither review was registered on the PROSPERO platform.[38] The review by Schulte et al.[51] only included the RCT by Marasco et al.[20] It is unclear why the earlier RCTs[18, 19] were not included as there were no study date restrictions or reasons why they should be excluded. The missed RCTs did satisfy the eligibility criteria, and it cannot be established whether the reported search terms identified these RCTs as a list of excluded studies was not published.

Girsowicz et al.[52] and de Jong et al.[57] did not include any RCTs since their research question was specifically designed to include only those with multiple unifocal rib fractures and not patients with flail chest.

2.3.2 Risk of Bias

Seven studies were rated as having low risk of bias,[2, 25, 36, 37, 53, 55, 56] three as unclear[52, 54, 57] and two as high[51, 58] (Table 6). The review by Schulte et al.[51] was

rated as having a high risk of bias due to the failure to report a clear search strategy, no attempt to minimise errors in data extraction by double checking with two researchers and no quality assessment of included studies. Schuurmans et al.[56] used the *'Cochrane Library Checklist for Randomized-Controlled Trials to assess quality'* quoting *'publications scoring 0–2, 3–4, or >5 were considered low, moderate, and high qualities, respectively.'* Despite following the citation, I could not locate the specific checklist referred to and the method did not follow the Cochrane risk of bias score, which is scored differently. Although this was highlighted as a discrepancy the authors were not contacted to explain this anomaly further. Although an overall scoring was given, how the author arrived at this conclusion was therefore not entirely clear. Similarly, in the review by Unsworth et al.[58] a level of quality was assigned to each study using a tool developed by the US Preventive Services Task Force. There was no breakdown of how the research team came to their conclusions about quality, however.

Table 6 Risk of bias using the ROBIS tool

Studies	Study eligibility criteria	Identification and selection of studies	Data collection and study appraisal	Synthesis and findings	Risk of bias in the review
Swart 2016 [54]	Low	Unclear	High	High	Unclear
Schuurmans 2016[56]	Low	Unclear	High	Low	Low
Schulte, 2016 [51]	High	High	High	High	High
Coughlin 2016 [37]	Low	Low	Low	Low	Low
Unsworth 2015 [58]	Low	Low	Unclear	Unclear	High
de Lesquen, 2015 [53]	Unclear	High	Unclear	Unclear	Low
Cataneo, 2015 [2]	Low	Low	Low	Low	Low
de Jong, 2014 [57]	High	Unclear	High	High	Unclear
Slobogean, 2013 [36]	Low	Low	High	Low	Low
Leinicke, 2013 [55]	Low	Low	Low	Low	Low
Girsowicz, 2012 [52]	High	High	High	High	Unclear
NICE Evidence, 2010 [25]	Low	Unclear	Unclear	Low	Low

Since this was the first time the researcher had used the ROBIS tool it was initially difficult to assign ratings for the signalling question as well as the overall score for each domain. Selecting PY or PN seemed easier than assigning a full No or Yes rating to the signalling questions due to lack of experience, whereas my more senior researcher found this easier to discriminate. This initial lack of confidence improved as more assessments were completed, however. Most of the ratings were middle of the road (PY, NI, PN) and the final rating of HIGH, LOW or

UNCLEAR rating was difficult to assign due to the lack of weight to the signalling questions. This was also confounded by a paucity of guidance in how the final score should be assigned from the ratings of the signalling questions.

A search of the PROSPERO database identified no registered protocols for any of the included reviews. Studies reporting meta-analysis all had some evidence to minimise data extraction errors. Appendix A2 contains the full assessment of risk of bias for each review.

.

Table 7 : Systematic review characteristics

Swart 2016 [54] **USA**	To perform a meta-analysis of high quality literature to evaluate both economic and medical benefits of early fixation of rib fractures in severe chest trauma	PubMed, Embase, Medline and Scopus, Search date June 2016 Search terms defined, No limitations described Evidence of hand searching Eligibility criteria - over 18 years of age and studies comparing operative vs non-operative treatment	3 RCT n =123 14 Case Control 3 Case Series	No evidence of quality assessment	Acute ORIF of Rib fractures in patients with flail chest injuries results in reduced mortality and medical complications in conjunction with being cost effective intervention. Limitations somewhat discussed.
Schuurman 2016 [56] **Netherlands**	Investigate how operative management improves patient care for adults with flail chest.	PubMed, Trip database, Google Scholar Search date November 2015 Search terms defined, No limitations described Evidence of reference checking Eligibility criteria - studies comparing operative vs non-operative treatment, RCT only and English	3 RCT n = 123	Quality assessment completed but criteria and explanation unclear	The operative management group showed a significant lower incidence of pneumonia, whereas mortality rate did not differ between treatment groups. Recognises some limitations in the evidence
Schulte 2016 [51] **UK**	In patients with acute flail chest does surgical rib fixation improve outcomes in terms of morbidity and mortality?	OVID MEDLINE® Search date January 2016 Search terms defined Search strategy description minimal, No limitations described No evidence of reference checking No specific inclusion or exclusion criteria defined.	1 Meta-analysis by separate author 1 RCT n=123 (2 further coded as RCT which are non-randomised studies) 3 Retrospective cohort studies	No evidence of quality assessment	Surgical stabilization of flail chest in thoracic trauma patients has beneficial effects with respect to reduced ventilatory support, shorter intensive care and hospital stay, reduced incidence of pneumonia and septicaemia, decreased risk of chest deformity and an overall reduced mortality when compared with patients who received non-operative management.
Coughlin 2016 [37] **UK**	Compare the efficacy or flail chest surgical stabilisation to non-	PubMed MEDLINE, Embase, Cochrane Library, clinical trials.gov. Search date February 2015 Search terms defined, No limitations	3 RCT n = 123	Clear quality appraisal of the studies	Surgical stabilisation for a traumatic flail chest is associated with significant clinical benefits including rate of pneumonia, length of hospital an ICU stay and duration of

	operative management	Evidence of reference checking Eligibility criteria - studies comparing operative vs non-operative treatment in flail chest and RCT only			mechanical ventilation in this meta-analysis of three relatively small RCTs
Unsworth 2015 [58] Australia	To review the treatments for blunt chest trauma and their impact on patient and hospital outcomes Specifically alludes to surgical stabilization of flail chest)	Cochrane, Medline, EMBASE and CINAHL databases Search date March 2014 Search terms defined. Limited to 1990 onwards, humans and adults Evidence of reference checking Eligibility criteria - original research, blunt chest trauma, intervention for blunt chest trauma including a comparator and contained measured outcomes	3 RCT n =123 5 Retrospective Case Controls n= 642 1 Retrospective cohort n = 21	Some quality assessment completed but criteria and explanation unclear	Across the literature there were consistent improvements in patients with flail chest and surgical fixation with fewer days of mechanical ventilation, ICU-LOS and cost savings compared to non-operative techniques. Three out of nine studies were randomized controlled trials, and the level of evidence in all studies was primarily fair or good.
De Lesquen 2015 [53] France	In flail chest is open reduction and internal fixation needed?	Medline and Science Direct Search dates January 2014 Search Terms defined limited to 1994 onwards No evidence of hand searching or reference checking Eligibility criteria - Exclusions of both child and vascular injuries	2 Meta-analysis 3 RCT n = 123 1 prospective cohort n = 60 5 Retrospective cohort n = 238	No evidence of quality assessment	For flail chest, early surgical stabilization can be considered in patients who would require mechanical ventilation for >48 h
Cataneo 2015 [2] Brazil	To evaluate the effectiveness and safety of surgical stabilization compared with clinical management for people with flail chest	Cochrane Injuries Group Specialised Register, CENTRAL, Medline, Embase, CINAHL, SCI, CPCI-S, Clinical trials.gov, ICTR Search Date 12th May 2014. Search terms defined, No limitations Evidence of reference checking Eligibility criteria - Limited to RCTs.	3 RCTs n = 123	Clear quality appraisal of the studies	There was no evidence that surgical intervention reduced mortality in people with FC compared with nonsurgical management. There was some evidence that surgical intervention could reduce the risk of developing pneumonia and thoracic deformity; need for tracheostomy; duration of mechanical ventilation, length of ICU stay, and hospital stay; and chronic pain, but the trials to date have been

					small. There is an urgent need for larger high-quality randomized con-trolled trials.
De Jong 2014 [57] Netherlands	To specify indications for rib fracture fixation of non-flail chests	Medline, Cochrane, Embase Search date December 2013 Search terms defined, limited to 2000 onwards. Evidence of reference checking . Eligibility criteria- Studies included at least 10 participants who were surgically treated for non-flail chest rib fractures. Reported in English, Dutch, or German. Excluded were case reports, biomechanical studies, animal studies, and expert opinions.	1 Case Control n = 60 2 Cohort studies n = 47	No evidence of quality assessment	The evidence for surgical treatment of non-flail chest rib fractures is limited
Slobogean 2013 [36] Canada	Compare the critical care outcomes of surgical fixation to non-operative management in patients with flail chest injuries	Medline, Embase, Cochrane Database of Systematic Reviews (CDSR), and the Cochrane Central, Register of Controlled Trials (CENTRAL) Search date May 2011, no limitations No evidence of reference checking or hand searching Eligibility criteria - Comparator studies with more than 10 cases.	2 RCT 1 case control n= 60 8 Cohort n = 676	No evidence of quality assessment	Improved outcomes of multiple critical care outcomes with narrow confidence intervals but based on small retrospective studies. Suggests prospective RCT to overcome potential biases
Leinicke 2013 [60] USA	Comparing operative to non-operative therapy in adult flail chest patients	MEDLINE (1966-2012), Embase (1947-2012), Scopus (all years), Cochrane Databases and ClinicalTrials.gov, Search date February 2012 Search terms defined, limited to English and human studies Evidence of reference checking	2 RCT 3 Case Control n=158 4 Cohort n = 303	Clear quality appraisal of the studies	As compared to non-operative therapy, operative fixation of FC is associated with reductions in DMV, LOS, mortality, and complications associated with prolonged MV. These findings support the need for an adequately powered clinical study to further define the role of this intervention

		Eligibility criteria - studies comparing operative vs non-operative treatment in patients with flail chest. Excluded case reports and case series			
Girsowicz 2012 [52] **France**	In patients over 45 years old with isolated, movable and painful rib fractures without true flail chest is surgical stabilization superior to non-operative management in improving outcomes?	OVID Medline, Search date June 2011 Search terms defined, limited to Human and English language, 1948 onwards Evidence of reference checking Eligibility criteria – excluded flail chest but inclusions not well described	4 Retrospective cohort n= 107 1 non-systematic Review 1 Case control = 30 2 Case report n= 2	Some comments on strengths and weaknesses but no quality or risk of bias assessment	Surgical stabilization in the management of isolated multiple non-flail and painful rib fractures improved outcomes (pain, respiratory function, quality of life and reduced socio-professional disability) Studies provided a low level of evidence (small studies with few numbers of patients and short-term follow-up or case reports). Large prospective controlled trials are thus necessary to confirm these encouraging results.
NICE Evidence 2010 [25] **UK**	To make recommendations about the safety and efficacy of surgical rib fracture fixation in flail chest	MEDLINE, PREMEDLINE, EMBASE, Cochrane Library. Search date May 2010 Search terms defined, no limitations No evidence of reference checking but other searches performed Eligibility criteria – clinical studies of patients with flail chest operated with metal rib reinforcements and published in English. Excluded conference abstracts and reviews	1 RCT 2 non randomized studies 4 case series Total 225 patients	No evidence of quality assessments	Surgical rib fracture fixation should be considered in patients with flail chest

Table 8 Primary studies included in each review and the number of included patients

Studies / Review	Leinicke et al. (2013)[60]	Slobogean et al. (2013)[36]	Tanaka (2001)[18]	Granetzny (2005)[19]	Marasco (2013)[20]	Paris (1975)[61]	Kim (1981)[62]	Karev (1997)[63]	Ahmed et al. (1995)[64]	Voggenreiter (1998)[65]	Balci et al. (2004)[66]	Teng (2009)[67]	Nirula et al (2006)[59]	Althausen et al. (2011)[68]	De Moya (2011)[69]	Granhed et al. (2014)[70]	Doben et al. (2014)[71]	Jayle et al. (2015)[72]	Pieracci et al. (2016)[73]	Zhang et al. (2015)[74]	Wada et al. (2015)[75]	Xu et al. (2015)[76]	Majercik (2015)[77]	Defreest (2016)[78]	Ohresser (1972)[79]	Hellberg (1981)[80]	Menard (1983)[81]	Moulton (1997)[82]	Cacchione et al., (2000)[83]	Lardinois (2001)[84]	Kerr -Valentic (2003)[85]	Gasparri et al., (2003)[86]	Borrelly (2005)[6]	Campbell (2009)[87]	Mayberry (2009)[88]	Richardson et al., (2007)[89]	Moreno De La (2010)[90]
Intervention patients			18	20	23	18	18	40	26	20	27	32	30	22	16	60	10	10	35	24	84	17	38	41	14	10	18	23	1	66	40	1	127	32	46	7	22
Control Patients			19	20	23	11	45	93	38	22	37	28	30	28	32	153	11	10	35	15	420	15	57	45	-	-	-	-	-	-	-	-	-	-	-	-	-
Swart [54]			●	●	●		●	●	●	●	●	●	●	●	●	●	●	●		●	●	●	●	●													
Schuurmans[56]			●	●	●																																
Schulte [51]		●												●	●	●	●	●	●	●	●	●															
Coughlin [37]			●	●	●																																
Unsworth [58]			●	●	●				●	●			●	●	●		●																				
de Lesquen [53]	●	●	●	●	●			●	●	●	●		●	●																							
Cataneo [2]																																					
de Jong [57]													●																					●	●		
Slobogean [36]			●	●			●	●	●	●	●	●	●												●								●				
Leinicke [55]			●	●				●		●	●		●	●	●																						
Girsowicz [52]													●																●		●	●		●	●	●	●
NICE [25]			●			●				●																●	●	●		●							
	SR		**RCT**			**Non Randomised Study**																			**Case Series or Report**													

2.3.3 Outcomes

All reviews undertook a narrative synthesis, six reviews included a meta-analysis.[2, 36, 37, 54-56] Table 9 summarises the results of the meta-analysis by outcome. Table 10 details the results from the systematic reviews for flail chest and Table 11for non-flail unifocal rib fractures.

Across all the reviews, twenty different outcomes were reported. Eleven outcomes were reported in more than one study, a narrative synthesis of the outcomes reported in this chapter is undertaken alongside the tabulated data. Ten studies reported the primary outcome of interest. Six further outcomes were identified which were reported by single reviews and their results are presented as tabulated data only (return to work, socio-professional disability, cost, pulmonary embolism, pneumo-and haemo-thorax).

Table 9 Outcome of reviews reporting meta-analysis in flail chest

Studies reporting outcome	N of studies (n of participants in analysis)	Study Types		Details of meta-analysis	Results	I^2
		RCT	NR			
Total length of invasive mechanical ventilation (Days)						
Cataneo[2]	3 (123)	3	0	MD [IV, Fixed, 95% CI]	Results not pooled	-
Coughlin [37]	3 (123)	3	0	MD [IV, Random, 95% CI]	-6.30 [-12.16, -0.43]	95
Leinicke [55]	8 (474)	2	6	MD [IV, Random 95% CI]	−4.52 [−5.54, −3.50]	48.6
Schuurmans [56]	3 (123)	3	0	MD [IV, Random, 95% CI]	−6.53 [−11.88, −1.18]	93
Slobogean [36]	8 Studies (563)	2	6	MD [IV, Fixed, 95% CI]	-7.5 [-9.9, -5.0]	48
Swart [54]	18 Studies (1150)	3	15	MD [IV, Random, SD]	-4.57 [0.59]	83
Mortality (frequency)						
Cataneo [2]	3 (123)	3	0	RR [M-H, Fixed, 95% CI]	0.56 [0.13, 2.42]	0
Coughlin [37]	2 (86)	2	0	RR [M-H Random 95% CI]	0.57 [0.13, 2.52]	0
Leinicke [91]	5 (343)	1	4	RR [95% CI]	0.43 [0.28, 0.69]	0
Schuurmans [56]	2 (86)	2	0	RR [M-H, Fixed, 95% CI]	0.56 [0.13, 2.42]	0
Slobogean [36]	7 (582)	2	5	OR [M-H, Fixed, 95% CI]	0.31 [0.20, 0.48]	-
Slobogean [36]	7 (582)	2	5	RR [M-H, Fixed, 95% CI]	0.19 [0.13, 0.26]	0
Swart [54]	13(1263)	3	10	RR [M-H, Random, SD]	0.44 [0.09]	0
Total length of stay in intensive care unit (Days)						
Cataneo [2]	2 (77)	2	0	MD [IV, Fixed, 95% CI]	Results not pooled	-
Coughlin [37]	3 (123)	3	0	MD [IV, Random, 95% CI]	-6.46 [-9.73, -3.19]	35
Leinicke [91]	5 (235)	2	3	MD [IV, Random, 95% CI]	−3.4 [−6.01, −0.80]	74.9
Schuurmans [56]	3 (123)	3	0	MD [IV, Fixed, 95% CI]	−5.18 [−6.17, −4.19]	40
Slobogean [36]	4 (261)	2	2	MD [IV, Fixed, 95% CI]	-4.8 [-7.9, -1.6]	0.1
Swart [54]	14 (840)	3	11	MD [IV, Random, SD]	-3.25 [1.29]	91
Total length of stay in hospital (Days)						
Coughlin [37]	2 (86)	2	0	MD [IV, Random, 95% CI]	-11.39 [-12.39, -10.38]	0
Leinicke [91]	5 (262)	1	4	MD [IV, Random 95% CI]	−3.83 [−7.12, −0.54]	68.9
Schuurmans [56]	2 (86)	2	0	MD [IV, Fixed, 95% CI]	−11.39 [-12.39,−10.38]	0
Slobogean [36]	4 (404)	1	3	MD [IV, Fixed, 95% CI]	-4.0 [-7.4, -0.7]	33
Swart [54]	11(438)	1	10	MD [IV, Random, SD]	-4.48 [1.98]	89

Studies reporting outcome	N of studies (n of participants in analysis)	Study Types		Details of meta-analysis	Results	I^2
		RCT	NR			
Pneumonia (frequency)						
Cataneo [2]	3 (123)	3	0	RR [M-H Random 95% CI]	0.36 [0.15, 0.85]	66
Coughlin [37]	3 (123)	3	0	RR [M-H Random 95% CI]	0.36 [0.15, 0.85]	66
Leinicke [91]	4 (260)	1	3	RR [95% CI]	0.43 [0.28, 0.69]	31
Schuurmans [56]	2 (83)	2	0	RR [M-H, Fixed, 95% CI]	0.45 [0.29, 0.7]	74
Slobogean [36]	8 (816)	2	6	OR [M-H, Fixed, 95% CI]	0.18 [0.11, 0.32]	4
Slobogean [36]	8 (816)	2	6	RR [M-H, Fixed, 95% CI]	0.31 [0.21, 0.41]	4
Swart [54]	15 (1005)	3	12	RR [M-H, Random, SD]	0.59 [0.10]	55
Tracheostomy (frequency)						
Cataneo [2]	2 (83)	2	0	RR [M-H Random 95% CI]	0.38 [0.14, 1.02]	64
Leinicke [91]	4 (215)	1	3	RR [95% CI]	0.25 [0.13, 0.47]	0
Schuurmans [56]	2 (83)	2	0	RR [M-H, Fixed, 95% CI]	0.4 [0.2, 0.7]	Not reported
Slobogean [36]	3 (165)	1	2	OR [M-H, Fixed, 95% CI]	0.12 [0.04, 0.32]	0
Slobogean [36]	3 (165)	1	2	RR [M-H, Fixed, 95% CI]	0.34 [0.10, 0.57]	0
Swart [54]	11 (975)	2	9	RR [M-H, Random, SD]	0.52 [0.07]	42
Sepsis (frequency)						
Slobogean [36]	4 (345)	0	4	OR [M-H, Fixed, 95% CI]	0.36 [0.19, 0.71]	0
Slobogean [36]	4 (345)	0	4	RR [M-H, Fixed, 95% CI]	0.14 [0.56, 0.23]	0
Spirometry (percentage of predicated)						
Coughlin [37]	-	-	-	-	-	-
FVC	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	1.53 [-13.49, 16.55] p = 0.84	Not reported
FEV1	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	-0.42 [-4.83, 3.98] p = 0.85	Not reported
TLC	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	3.69 [-3.08, 10.46] p = 0.29	Not reported
PEFR	2 (74)	2	0	MD [IV, Random, 95% CI] p-value	0.38 [-0.76, 1.53] p = 0.51	Not reported
Chest deformity (frequency)						
Cataneo [2]	2 (86)	2	0	RR [M-H, Fixed, 95% CI]	0.13 [0.03, 0.67]	0
Slobogean [36]	4 (228)	1	3	OR [M-H, Fixed, 95% CI]	0.11 [0.02, 0.60]	2.1
Slobogean [36]	4 (228)	1	3	RR [M-H, Fixed, 95% CI]	0.30 [0.00,0.60]	2.1

Studies reporting outcome	N of studies (n of participants in analysis)	Study Types		Details of meta-analysis	Results	I^2
		RCT	NR			
Dyspnoea (frequency)						
Slobogean [36]	3 (135)	1	2	OR [M-H, Fixed, 95% CI]	0.40 [0.16, 1.01]	0
Slobogean [36]	3 (135)	1	2	RR [M-H, Fixed, 95% CI]	0.15 [0.09, 0.39]	0
Chest pain (frequency)						
Slobogean [36]	2(71)	1	1	OR [M-H, Fixed, 95% CI]	0.40 [0.01, 12.60]	0
Slobogean [36]	2(71)	1	1	RR [M-H, Fixed, 95% CI]	0.18 [-0.46, 0.83]	0
RCT= Randomised controlled trial, NR = Non-randomised study, RR = Risk ratio, OR = Odds ratio, MD = Mean difference, SD = Standard deviation, CI = Confidence interval, IV - Inverse variance, M-H - Mantel-Haenszel, FVC = Force vital capacity, FEV1 = Forced expiratory volume, TLC = Total lung capacity, PEFR = Peak expiratory flow rate						

Table 10 Results of individual reviews that report a narrative synthesis for flail chest

Study details	Outcomes assessed	Included studies description	Narrative Synthesis)
Author Unsworth [58] **Year** 2015 **Country** Australia	RCT = 2 Granetzny(40) Tanaka (37) Marasco (46) Non-randomised= 6 Ahmed (64) Althausen (50) Doben (21) De Moya (48) Nirula(60) Voggenreiter (42) Total number of patients = 408	Mortality Pneumonia Pneumothorax and haemothorax LOS Hospital ICU stay Costings Treatment outcome	• significant decrease in mechanical ventilation requirements after surgical fixation. Decrease in ventilator-acquired pneumonia after surgical fixation • decrease in ICU-LOS, fewer days of mechanical ventilation and cost savings compared to non-operative management • decreased days of ventilator dependence, and shorter ICU-LOS • lower incidence of pneumonia, a higher return to full time work at six months • less persistent pain at six and 12 months in those receiving surgery • significantly fewer days of mechanical ventilation and a shorter hospital and ICU-LOS • The estimated cost savings was estimated at US dollars 10,000 and AU dollars 14,443 per patient with surgical rib fixation as a result of the decrease in ICU-LOS. • None of the studies were large enough to draw conclusions on the effect of this intervention on thromboembolism and death.
Author de Lesquen [53] **Year** 2015 **Country** France	Meta-analysis = 2 Leinicke 9 studies (538 patients) Slobogean 11 studies (732 patients) RCT = 3 Marasco (46) Granetzny(40) Tanaka (37) Non-randomised= 6 Ahmed (64) Karev (40) Voggenreiter (20) Balci (64) Nirula(60) Althausen(50) Total number of patients=421	Duration of IMV LOS ICU Pneumonia Mortality	For flail chest, early surgical stabilization can be considered in patients who would require mechanical ventilation for >48 h (Grade B, extrapolated recommendations from Level I evidences).

Study details	Outcomes assessed	Included studies description	Narrative Synthesis)
Author NICE [25] **Year** 2010 **Country** UK	RCT = 1 Tanaka (37) Non-randomised = 2 Voggenreiter (42) Paris (29) Case Series = 4 Lardinois (66) Mouton (23) Menard (18) Hellberg (10) Total number of patients=225 Intervention group = 173 Control group = 52	Duration of IMV Mortality LOS ICU Pneumonia Lung function Return to Employment Sepsis Pain or discomfort requiring removal of plates	Surgical stabilisation with metal rib reinforcements aims to allow earlier weaning from mechanical ventilation, reduce acute complications and avoid chronic pain sometimes associated with permanent malformation of the chest wall. Kirschner wire may be used on its own, but this method of rib stabilisation is not covered by this guidance.
Author Schulte [51] **Year** 2016 **Country** UK	Systematic Review = 1 Slobogean (753) RCT = 1 Marasco (23,23) Non-randomised studies = 9 Jayle (10,10) Pieracci (35,35) Zhang (24,15) Wada (84,336) Granhed (60,153) Doben (10,11) Xu (17,15) Althausen(22,28) De Moya (16,32) Total number of patients=1712 Intervention group = 301 Control group = 658	Duration of IMV Mortality LOS hospital LOS ICU Pneumonia Mortality	Surgical stabilization of flail chest in thoracic trauma patients has beneficial effects with respect to reduced ventilatory support, shorter intensive care and hospital stay, reduced incidence of pneumonia and septicaemia, decreased risk of chest deformity and an overall reduced mortality when compared with patients who received non-operative management.
ICU = Intensive care unit, IMV = invasive mechanical ventilation, LOS = Length of stay, RCT = Randomised control trial			

Table 11 Reviews reporting a narrative synthesis in multiple unifocal rib fractures

Study details	Outcomes assessed	Included studies description	
Author de Jong [57] **Year** 2014 **Country** Netherlands	RCT = 0 Non-randomised = 1 Nirula (60) Case Series = 2 Campbell (32) Mayberry (46, 15 non-flail) Total number of patients=138 Intervention group = 108 Control group = 30	Length of stay in hospital Duration of IMV Time of operation Chronic pain	Only Nirula et al. concluded that rib fracture fixation showed a trend toward fewer total ventilator days. Mayberry et al. investigated the quality of life after rib fixation, and concluded that there was low long-term morbidity and pain. Campbell et al. demonstrated low levels of pain and satisfactory rehabilitation.
Author **Girsowicz** [52] **Year** **2012** **Country** **France**	Non-systematic review =1 Nirula and Mayberry Non-randomised = 1 Nirula (30,30) Case Series = 4 Mayberry (46) Richardson (7) Moreno De La Santa Barajas (22) Campbell (32) Case report = 3 Gasparri (1) Cacchione (1) Kerr-Valentic (1) Total number of patients=169 Intervention group = 139 Control group = 30	Pain Disability Respiratory function Number of days lost from work	In general, of the nine studies presented, all indicated that surgical stabilisation in the management of isolated multiple non-flail and painful rib fractures improved outcomes. Indeed, the interest and benefit was shown not only in terms of pain and respiratory function but also in improved quality of life and reduced socio-professional disability. Hence, the current evidence shows surgical stabilisation to be safe and effective in alleviating post-operative pain and improving patient recovery, thus enhancing the outcome of the procedure. However, the retrieved studies provided a low level of evidence (small studies with few numbers of patients and short-term follow-up or case reports). Large prospective controlled trials are thus necessary to confirm these encouraging results.
IMV = invasive mechanical ventilation, RCT = Randomised control trial			

2.3.3.1 Primary Outcome - Length of mechanical ventilation (days)

2.3.3.1.1 Flail Chest

Ten systematic reviews reported length of mechanical ventilation; six of these reported a meta-analysis[2, 36, 37, 54-56] with four reviews[2, 37, 54, 56] reporting a meta-analysis of the same three RCTs.[18-20]

There was substantial variation in the pooled estimates for this outcome across the reviews, related to pooling different sets of studies. The largest reduction in mean difference (MD) in the duration of mechanical ventilation with surgical fixation compared to non-operative management was in the Slobogean et al.[36] review which pooled two RCTs[18, 19] and six non-randomised studies[59, 62, 63, 65-67] (MD (fixed) -7.5 days, 95% CI [-9.9,-5.5]). The mean difference was three days more than the pooled estimates offered by Leinicke et al.[55] and Swart et al.[54] Leinicke et al.[55] pooled six non-randomised studies[59, 63, 65, 66, 69, 92] and two RCTs,[18, 19] and reported a statistically significant reduction of -4.52 days, 95% CI [-5.54, -3.5]. Swart et al.[54] pooled three RCTs [18-20] and 15 non-randomised studies [59, 63-67, 69-72, 74, 76, 78, 92, 93] and reported a statistically significant reduction of -4.57 days, SD (0.59).

There were differences in the data reported for the four meta-analyses[2, 37, 54, 56] that included the same three RCTs.[18-20] Schuurmans et al.[56] extracted the median duration of mechanical ventilation post randomisation from the Marasco et al. RCT[20] (operative, median 9 days (SD 3.8) vs. non-operative, median 10.8 days (SD 5.9)) and pooled this in the meta-analysis along with studies that measured mean total time on ventilation. In contrast, Coughlin et al.,[37] Cataneo et al.[2] and Swart et al.[54] reported the total mean time on mechanical ventilation, which they state was obtained directly from the authors (operative, mean 6.32 (SD 3.46) vs. non-operative, mean 7.54 (SD 5.42)). The pooled estimates using the median and mean data from the Marasco RCT[20] are broadly similar, however. They show a reduction in mechanical ventilation of more than six days, although the difference is slightly larger in the Schuurman et al.[56] review (MD -6.53 days, 95% CI [-11.8,-1.18]. This is in contrast to the Cataneo et al.,[2] Coughlin et al.[37] and Swart et al.[54] reviews (MD -6.30 days, 95% CI [-12.16,-0.43]). Coughlin et al.[37] in their forest plot quoted the estimate by Marasco et al.[20] as an MD of -1.21 days, 95% CI [-3.84, -1.41] which would seem a significant result. The visual forest plot shows the

correct upper CI at 1.41 therefore this typographical error within the tables does not affect the overall pooled estimate.

Variations also arose in relation to the extraction of data from the RCT by Granetzny et al.,[19] who did not publish standard deviations for the outcome length of mechanical ventilation within their RCT report. Slightly different SD values were found in all six meta-analyses,[2, 36, 37, 54-56] which may have arisen from different methods of imputation

Cataneo et al.[2] report the SD for the non-operative group as 0.45 whereas Coughlin et al.[37] and Schuurmans et al.[56] report 1.45 (2 decimal places) and 1.5 (1 decimal place) for the RCT by Granetzny et al.[19]

The Swart et al.[54] review reported pooled estimated results only and did not report an individual study effect estimate for the Granetzny et al.[19] RCT, although it did report the SD for operative patients as 4.9 and non-operative patients as 8.8, which is substantially different to the other reviews. Using a random effects model as described in the review methods by Swart et al.,[54] a mean difference and confidence interval was calculated from these values as an MD of -10, 95% CI [-14.41,-5.59]. A random effects model should be used when studies of different methods or when clinical charateristics of the study patients vary. A further explanation of meta-analysis methods can be reviewed in section 3.2.14.1

Leinicke et al.[55] pooled the RCT by Granetzny et al.[19] with other studies but do not report the primary extracted data. The individual study effect estimate for the Granetzny et al.[19] RCT is MD -10, 95% CI [-15.41, -4.59], which is similar to the values imputed from the Swart review[54] (MD -14.41 Vs. -15.41 and SD -5.59 Vs -4.59 respectively). This variation could be due to imputational differences or the substitution of digits 4 and 5 could be a typographical error. Since primary data is not reported this cannot be confirmed.

Although the individual confidence intervals shown in Table 12 do not change substantially, the tabled results highlights the effect transcription errors and differences in imputation have on the individual study estimates..

Table 12 Reporting the differences between reviews of the Length of Mechanical Ventilation for the RCT by Granetzny et al.[19]

	Operative (Days)		Non –Operative (Days)		MD	CI 95%
	Mean	SD	Mean	SD		
Cataneo 2015	2	0.72	12	0.45	-10	-10.37, -9.63
Coughlin 2016	2	0.75	12	1.45	-10	-10.72, -9.28
Leinicke 2013	-	-	-	-	-10	-15.41, -4.59
Slobogean 2013	-	-	-	-	-10	-15.5, -4.5
Schuurmans 2016	2	0.7	12	1.5	-10	-10.73, -9.27
Swart 2016	2	4.9	12	8.8	-10*	-14.41, -5.59*
*imputed from reported data by methods reported in the review						

Substantial statistical heterogeneity was seen in all meta-analyses reporting mechanical ventilation[36, 37, 55, 56] (I^2=48-95%). Cataneo et al.[2] did not pool the data from the three RCTs they included for this outcome due to this heterogeneity, instead reporting the individual study effect estimates from all three RCTs.

The narrative synthesis from three reviews concluded that surgical fixation reduces the length of mechanical ventilation compared to non-operative management.[5, 53, 58]

2.3.3.1.2 Multiple unifocal rib fractures

Only one primary study, which was included in two systematic reviews,[52, 57] reported the length of mechanical ventilation for multiple unifocal fractures. A case series with matched controls[59] reported a statistically significant reduction in post-operative ventilator days (p =0.02) in the internal fixation group; however there was no statistical difference in total ventilator days (p = 0.12). This primary study compared internal surgical fixation with non-operative fixation but it was unclear what the non-operative fixation was.

2.3.3.2 Mortality

2.3.3.2.1 Flail Chest

Seven systematic reviews reported mortality; six of these pooled the data in a meta-analysis[2, 36, 37, 54-56] and one reported data without a narrative synthesis.[53] A single review explicitly defined mortality: Cataneo et al.[2] intended to report early (within 30 days) and late all-cause mortality rate, whereas in all other reviews it

was unclear what definition of mortality was used. Despite their intention, Cataneo et al. were unable to report mortality as planned due to the lack of a mortality definition in the primary studies. Three systematic reviews[2, 37, 56] pooled the same three RCTs[18-20] to show a non-statistically significant reduction in mortality with internal surgical fixation compared to non-operative management [RR (Fixed) 0.56, 95% CI [0.13, 2.42][2] and RR (Random) 0.57, 95% CI [0.13, 2.52][37, 56] Table 9].

Three systematic reviews pooled randomised and non-randomised studies.[36, 54, 55] Swart et al.,[54] the most recent review, pooled the three RCTs[18-20] and ten non-randomised studies.[59, 62-67, 69-72, 74-76, 78, 92, 93] This review demonstrated a statistically significant reduction in mortality with surgical fixation compared to non-operative treatment [RR (random) 0.44, SD [+/-0.09][54]]. The reviews by Leinicke et al.[55] and Slobogean et al.[36] were published before the RCT by Marasco et al. [20] and hence did not include this RCT in their meta-analyses. Leinicke et al.[55] pooled four non-randomised studies[63-66] and one RCT,[19] and showed a statistically significant reduction in mortality with internal fixation compared to non-operative management RR (fixed) of 0.43, 95% CI [0.28, 0.69]. Slobogean et al.[36] pooled five case control studies[6, 63-66] and one RCT,[19] showing a statistically significant reduction in mortality with surgical fixation RR (fixed) of 0.19, 95% CI [0.13, 0.26]. Overall, statistical heterogeneity for this outcome was low, I^2 = 0% in all reviews that presented this data.[2, 36, 37, 54-56]

One further review, de Lesquen et al.,[53] reported a narrative synthesis for mortality and includes nine primary studies, of which three are RCTs[20 18, 19] and six are non-randomised studies[59, 63, 64, 66, 92, 94]. de Lesquen et al.'s review also included two systematic reviews by Slobogean et al.[36] and Leinicke et al.[55] They provided study frequencies but did not perform a narrative synthesis of this outcome.

Unsworth et al.[58] did not report outcomes on mortality but concluded that the studies were not large enough to support surgical fixation compared to non-operative management for this outcome.

2.3.3.2.2 Multiple unifocal rib fractures

Mortality was not assessed in the reviews by de Jong et al.[57] or Girsowicz et al.[52]

2.3.3.3 Length of ICU Stay (days)

2.3.3.3.1 Flail Chest

Eight systematic reviews[2, 25, 36, 37, 53-56] assessed length of ICU stay; six of these performed a meta-analysis[2, 36, 37, 54-56]. Pooled estimates ranged from -3.25 days [SD 1.29] [54] to -6.46 days, CI 95% [-9.73, -3.19][37] and were all in favour of surgical fixation with a variety of comparators (Table 9). The range in pooled estimates may be partly explained by the pooling of different sets of studies.

Swart et al. pooled three RCTs[18-20] and 11 non-randomised studies[59, 64, 67, 69, 71, 72, 76, 78, 92, 93, 95] and had the lowest effect estimate with an MD (random) -3.25 days [SD 1.29].[54] This can be compared to the Schuurmans et al.'s[56] review, where the pooled estimate is significantly in favour of fixation MD (fixed) -5.18 days, 95% CI [-6.17, -4.19]. Leinicke et al.[55] pooled one RCT[19] and three non-randomised studies [59, 69, 92] with an overall significant effect in favour of fixation with an MD (random) -3.40 days, 95% CI [-6.01, -0.79]. Slobogean pooled two RCTs[18, 19] and two non-randomised studies,[59, 67] reporting a statistically significant mean difference in favour of fixation of -4.8 days, 95% CI [-7.9, -1.6].

Both Schuurmans et al.[56] and Coughlin et al.[37] pooled the same RCTs,[18-20] although a greater effect was cited by Coughlin et al.[37]: MD (random) -6.46 days, 95% CI [-9.73, 3.19]. This result looks to be non-significant since the confidence intervals cross zero, the line of no effect. This published data, however, includes a transcription error and the upper CI should in fact be -3.19, with the result therefore being significant, as depicted in the forest plot. Comparing this to the Schuurmans et al.,[56] review the pooled estimate was in significant favour of fixation with an MD (fixed) of -5.18 days, 95% CI [-6.17, -4.19]. Despite the estimation error by Coughlin et al., which underestimates the effect size, the overall pooled effect estimate is more than the pooled effect estimate in the Schuurmans et al.[56] review. This may be due to Coughlin et al.[37] using a random effects model and Schuurmans et al.[56] using a fixed effects model, which places different weights on the studies. For example, the Granetzny et al.[19] RCT is weighted at 96.3% in the paper by Schuurmans but only at 68.1% by Coughlin.

Three reviews included the same RCT[20] but the data extracted from primary studies for this outcome varied across reviews. Differences occurred since some pooled the median length of ICU stay while others pooled the mean. Furthermore, some used only the postoperative time in the ICU, while others used the total time

in the ICU[37, 54, 56] (Table 13). The Marasco et al.[20] RCT reported median time in the ICU post randomisation. The median time in the ICU post randomisation data extracted by Coughlin et al.[37] for this study is not comparable to data extracted as a mean total time in the ICU in the reviews by Schuurmans et al.[56] and Swart et al.[54]. The mean total time in the ICU was obtained from the authors, after a request by email communication. The individual study effect estimate for the Marasco et al.[20] RCT was higher in the Schuurmans et al.[56] review, with an MD of -9.50 days, CI 95% [-17.33, -1.67] than the review by Coughlin et al.,[37] where the MD was -8.73 days, CI 95% [-16.38, -1.08], but both are statistically significant.

Table 13 Length of ICU stay and individual study effect estimates for Marasco et al.[20] RCT reported by several systematic reviews

Marasco 2013	Operative (Days)		Non –Operative (Days)		MD	CI 95%
	Mean	SD	Mean	SD		
Coughlin 2016	11.2	3.87	19.94	18.32	-8.73	-16.38, -1.08
Schuurmans 2016	13.8	4.2	23.3	18.7	-9.50	-17.33, -1.67
Swart 2016	13.5	3	18.7	4.1	-	-
Obtained directly from Marasco et al.	13.96	4.63	23.5	18.8		

Variation also arose across reviews in respect to the data extracted from another trial due to standard deviations not being reported in the primary publication.[19] Imputed values were calculated or the raw data were obtained from the authors resulting in SD values ranging from 0.7 to 4.4 and 2.2 to 7.3 in the operative and non-operative groups respectively. Three reviews reported imputation methods, Cataneo et al. used methods by Higgins et al.,[96] while Leinicke et al.[55] used methods described by Deeks et al.,[97] and Swart et al.[54] used methods by Ma et al.[98] The mean difference and the inconsistencies in the standard deviation reported for the ICU stay outcome are shown in Table 14. Standard deviation values obtained from the authors were used by three studies;[2, 37, 56] Cataneo et al.[2] reported an SD of 2.7 (Cataneo et al.[2] obtained this from the author) instead of 2.18 that was reported by Coughlin et al.[37] in the non-operative group and may be either a transcription or rounding up error. I was unable to replicate the standard deviations supplied by Swart et al.,[54] using the methods by Ma et al.[98] in which sampling distributions were merged. The standard deviations reported by Swart et al.[54] were larger than those reported by the other reviews, and although the individual study effect estimate was not reported, this was calculated as -5 days,

95% CI [-8.74, -1.26] from the primary study data. The large confidence intervals could significantly affect the pooled effect despite its low weighting (13.83%). The overall pooled estimate by Swart et al.[54] had the lowest effect estimate with an MD (random) of -3.25 days [SD 1.29].

There was also variation across reviews in respect to the data extracted from the Granetzny et al.[19] RCT due to standard deviations not being reported in the primary publication. Imputed values were calculated, or the raw data were obtained from the authors, resulting in SD values ranging from 0.7 to 4.4 and 2.2 to 7.3 in the operative and non-operative groups respectively. There was also a substantial difference in the effect estimate in the Leinicke et al.[55] review (-10 days, 95% CI [-15.41, -4.59]), which was five days greater than the data from the same primary study included in other reviews. Ten days is the same as the length of the mechanical ventilation effect estimate used in the review, however, so it is possibly a transcription error.

Table 14 Reporting differences of Length of stay in ICU for the Study by Granetzny et al. [19]

	Operative (Days)		Non –Operative (Days)		MD	CI 95%
	Mean	SD	Mean	SD		
Cataneo 2015	9.6	0.72	14.6	2.7	-5	-6.22, -3.78
Coughlin 2016	9.6	0.72	14.6	2.18	-5	-6.01, -3.99
Leinicke 2013	-	-	-	-	-10*	-15.41, -4.59*
Slobogean 2013	-	-	-	-	-	-
Schuurmans 2016	9.6	0.7	14.6	2.2	-5	-6.01, -4.19
Swart 2016	9.6	4.4	14.6	7.3	-5.00**	-8.74, -1.26**

*Error showing results of length of mechanical ventilation instead of ICU length of stay
**Imputed using random effects model from data supplied by Swart et al. [54]

There was also a substantial difference in the data extracted from the Tanaka et al. RCT[18] in the Cataneo et al.[2] review compared to the other reviews: the mean length of intensive care stay was reported as 6.5 days compared to 16.5 days in other reviews. Although this data was not pooled, the individual estimate (MD -20.30, 95% CI [-24.01, -16.59]) was substantially different to Coughlin et al.[37] and Schuurmans et al.[56], with MD (random) of -10.30 days ,95% CI [-17.15, -3.45] and MD (fixed) of -10.2 days, 95% CI [-17.05,-3.35] respectively.

Moderate to substantial[32] heterogeneity was seen in this outcome across reviews: Leinicke et al.,[55] I^2 = 74.9%, Schuurmans et al.[56], I^2 = 40% and Coughlin et al.,[37] I^2= 35%. An I^2 value of 0.1% was reported by Slobogean et al., which is lower than

the other reports. Three out of the four studies within this pooled analysis were reported within the other three meta-analyses. A forest plot was not provided for this outcome so as to allow further exploration of the lower estimate of heterogeneity.

Narrative synthesis concluded that in patients with flail chest undergoing surgical fixation the length of ICU stay was reduced.[53, 58] Only de Lesquen et al.[53] reported numerical data showing a statistically significant reduction in total ICU length of stay in favour of surgical fixation, however. This was reported in three RCTs, showing a reduction of ICU days of 11.9 days vs. 15 days (p=0.03) by Marasco et al.,[20] 9.6 vs. 14.6 days in the RCT by Granetzny et al.,[19] and 10.8 days vs. 18.3 days reported by Tanaka et al. [18].

2.3.3.3.2 Multiple unifocal rib fractures

A single review reported length of ICU stay for patients with multiple unifocal rib fractures.[52] Within this review, one non-randomised study reported a reduction in ICU days but this was not statistically significant (p =0.51) and the mean difference and 95% CIs were not reported.[59]

2.3.3.4 Length of Hospital Stay (days)

2.3.3.4.1 Flail Chest

Nine studies[2, 25, 36, 37, 53-56, 58] assessed length of hospital stay, six of which undertook a meta-analysis[2, 36, 37, 54-56]. Both Coughlin et al.[37] and Schuurmans et al.[56] reported length of stay in hospital from the Marasco et al.[20] and Granetzny et al.[19] RCTs. The pooled effect estimate was the same in both studies and showed a statistically significant shorter hospital length of stay: MD -11.39 days 95% CI [-12.39, -10.38] in favour of the operative group compared to non-operative management. When combined with other case control studies the pooled effects were smaller, but still show a significant reduction in hospital stay in favour of fixation. Thus for Leinicke et al.[55] (RCT = 1,[19] non-randomised studies = 4[59, 66, 69, 92]) MD (random) was -3.83 days, 95% CI [-7.12,-0.54] and Slobogean et al.[36] (RCT = 1[19], non-randomised = 3[59, 66, 67]) MD (fixed) was -4 days, 95% CI [-7.4, -0.7]. Swart et al.,[54] included the largest number of pooled studies, one RCT[19] and eight non-randomised studies,[59, 66, 67, 69, 71, 72, 74, 75, 78, 92] and the effect estimate was significant and in favour of fixation: MD (Random) -4.48 days, SD (1.98).

Imputation differences for standard deviation are also present within the hospital length of stay outcome for the Granetzny et al.[19] RCT, outlined in Table 15.

Table 15 Reporting differences in respect to length of hospital stay for the RCT by Granetzny et al.

	Operative (Days)		Non-Operative (Days)		MD	CI 95%
	Mean	SD	Mean	SD		
Coughlin 2016	11.7	0.73	23.1	2.18	-11.40	-12.41,-10.39
Leinicke 2013					-11.40	-17.57, -5.23
Slobogean 2013						Not reported individually
Schuurmans 2016	11.7	0.7	23.1	2.2	-11.40	-12.41, -10.39
Swart 2016	11.7	6.8	23.1	10.4	-11.40*	-16.85, -5.95*
*Imputed using a random effects model from data supplied by Swart et al. [54]						

When pooling the two RCTs in the systematic reviews, heterogeneity was low I^2 = 0, [37, 56], however when pooling a greater number of studies, including non-randomised studies, the heterogeneity was moderate to substantial (I^2= 89%, I^2= 68.9% and I^2 = 33%, respectively.[37, 54, 56]

One review's[58] narrative synthesis concluded that, in patients with flail chest undergoing surgical fixation, the length of hospital stay was reduced in one non-randomised study[92] and in one RCT.[19] No data or significance values were reported in that review, however.

2.3.3.4.2 Multiple unifocal rib fractures

Two systematic reviews[52, 57] included a single non-randomised study that assessed length of hospital stay (days).[59] This study found a reduction in total hospital days from 21.1 [SD 3.9] to 18.8 [SD 1.8] in those with surgical fixation compared to non-operative treatment (p=0.59).

2.3.3.5 Pneumonia

2.3.3.5.1 Flail Chest

Ten systematic reviews[2, 25, 36, 37, 53-56, 99], assessed pneumonia and six of these reported a meta-analysis for this outcome.[2, 36, 37, 51, 54-56, 58] In all of the reviews, the risk of developing pneumonia was found to be lower in the surgical fixation group compared to the non-operative group. The pooled estimate of the three RCTs[18-20] reported by Coughlin et al.[37] and Cataneo et al.[2] showed a significant RR

(random) of 0.36, 95% CI [0.15, 0.85] in favour of surgical fixation. When non-randomised studies were combined, the reductions ranged from 0.31, [95% CI 0.21, 0.41] to 0.45, [95% CI 0.29, 0.70].

Schuurmans et al.[56] only reported two RCTs, despite including the third RCT by Granetzny et al.[19] in other analyses. No explanation was given for excluding this study from the analysis. The pooled estimate was reported as a significant RR (Fixed) of 0.45, 95% CI [0.29, 0.70].

Pooling with multiple case control studies reduced the effect estimate; the largest and most up to date review by Swart incorporated three RCTs[18-20] and 12 non-randomised studies [63-65, 67, 69, 70, 72, 74, 76, 78, 92, 93] and had a RR (random) of 0.59, SD (0.10). Leinicke et al.[55] included one RCT[18] and three non-randomised studies[63, 69, 92] the pooled estimate was reported as a significant RR (fixed) of 0.45, 95% CI [0.30,0.69] in favour of fixation. Slobogean et al. include two RCTs[18, 19] and six non-randomised studies[63-67] and gave a significant pooled estimate with an RR of 0.31, 95% CI [0.21, 0.41] in favour of fixation.

Substantial heterogeneity was seen in meta-analyses for this outcome[2, 37, 56] that included the three RCTs[18-20] (I^2=66 to 77%). In the reviews that pooled the RCTs alongside the non-randomised studies[36, 55] lower levels of heterogeneity were reported (I^2=4% and I^2=31%, respectively).

The narrative syntheses found that the risk of pneumonia was significantly reduced among patients with flail chest undergoing surgical fixation.[53, 58] One review,[53] included two non-randomised studies[64, 92] and two RCTs[18, 19] in the synthesis but the conclusions could not be verified as there were no effect estimates, confidence intervals or significance values reported. In the other review,[58] four non-randomised studies[63-65, 92] and three RCTs[18-20] were included. Four of the included studies report a significant reduction of $p<0.05$.[18, 63, 65, 92] They also report the meta-analysis results from the reviews by Leinicke et al.[55] and Slobogean et al.[36]

2.3.3.5.2 Non-flail unifocal rib fractures

No review reported the risk of pneumonia in patients with multiple unifocal rib fractures.

2.3.3.6 Tracheostomy

2.3.3.6.1 Flail Chest

Five systematic reviews included a meta-analysis of the outcome of tracheostomy. [2, 36, 54-56] Cataneo et al.[2] and Schuurmans et al. both report two RCTs[18, 20] in their pooled analysis. They were in favour of fixation but while the results were statistically significant for Schuurmans et al.,[56] with an RR (fixed) of 0.4 95% CI [0.2, 0.7], they were not significant for Cataneo et al.[2] with an RR (Random) of 0.38 95% CI [0.14, 1.02]. Slobogean et al.[20, 36] pooled one RCT[18] and two non-randomised studies[64, 66] using a fixed effects model to give an RR of 0.34 95% CI [0.1, 0.57] that was significantly in favour of surgical fixation. Leinicke et al.[55] pooled one RCT[18] and three non-randomised studies[64, 66, 92] to show the biggest significant effect size in favour of surgical fixation – an RR of 0.25 95% CI [0.13, 0.47]. The smallest effect size was produced by Swart et al.,[54] who included the largest number of studies (two RCTs [18, 20] and nine non-randomised studies[64, 66, 75, 76, 78, 92-95]); a random effect model showed a significant improvement with surgical fixation – and RR of 0.52, [p=0.07].

Moderate and substantial heterogeneity was seen in two reviews (I^2=42%[54], I^2=64% [2]) heterogeneity was not reported in one study[56] and had no heterogeneity in the two others (I^2=0% [36 55]).

2.3.3.6.2 Non-flail unifocal rib fractures

No review reported the risk of tracheostomy in patients with multiple unifocal rib fractures.

2.3.3.7 Sepsis

2.3.3.7.1 Flail Chest

In one review[36] the authors pooled four non-randomised studies[6, 62, 64, 65] and found an RR in respect to sepsis of 0.14, 95% CI (0.56, 0.23) with I^2=0%. This estimate reported is not possible, however, given that the confidence interval does not include the 0.14 value. The lower interval of 0.56 could possibly be -0.56 creating a wider CI. The odds ratio is also presented for the same pooled analysis and reported as 0.36, 95% CI [0.19, 0.71], I^2=0%.

2.3.3.7.2 Non-flail unifocal rib fractures

No review reported the risk of sepsis in patients with multiple unifocal rib fractures.

2.3.3.8 Spirometry

2.3.3.8.1 Flail Chest

One of the reviews[37] reported a meta-analysis of spirometry data which included two RCTs,[19, 20] with spirometry measured at two different time points (three and two months respectively). No statistically significant differences in any spirometry data were seen between surgical fixation and non-surgical approaches

2.3.3.8.2 Non-flail unifocal rib fractures

No review reported spirometry in patients with multiple unifocal rib fractures.

2.3.3.9 Chest Deformity

2.3.3.9.1 Flail Chest

Slobogean et al.[36] reported chest deformity as a pooled meta-analysis using one RCT and three non-randomised studies[19, 62, 64, 66] The effect estimate was significantly in favour of surgical fixation RR (fixed) 0.30, 95% CI [-0.00,0.60], I^2 = 2.1%. Cataneo et al.[2] report two RCTs[19, 20] that showed a significant reduction in chest deformity in favour of surgical fixation (RR 0.13, 95% CI [0.03, 0.67], I^2 = 0%). Granetzny et al.[19] reported chest deformity at two months but how this was measured was not reported. There were no reports on timing of outcome measurement or how outcomes were measured in the other studies.

2.3.3.9.2 Non-flail unifocal rib fractures

No review reported chest deformity in patients with multiple unifocal rib fractures.

2.3.3.10 Dyspnoea

2.3.3.10.1 Flail chest

One review pooled studies reporting dyspnoea in a meta-analysis[36] and included one RCT and two non-randomised studies.[18, 64 79] They reported a difference in favour of surgical fixation with a pooled risk ratio of 0.15, 95% CI 0.09 to 0.39; however, when these data were expressed as odds ratios the results were no longer statistically significant (OR 0.40, 95% CI 0.16 to1.01). Dyspnoea was reported at one year for two of the primary studies[79 18] but it was unclear in the other included primary study.[64] It was unclear how dyspnoea was measured or defined in the three primary studies included in the single systematic review assessing this outcome.

2.3.3.10.2 Non- flail unifocal rib fractures

No review reported dyspnoea in patients with multiple unifocal rib fractures.

2.3.3.11 Chest Pain

2.3.3.11.1 Flail chest

Chest pain was reported in one systematic review[36] which included two primary studies (one RCT [18]and one non-randomised study[79]) and data were pooled together in a meta-analysis (OR 0.40, 95% CI 0.01 to 12.60 and RR 0.18, CI 95% -0.46 to 0.83). Both studies had small sample sizes which may account for these differences.

2.3.3.12 Other reported outcomes

Several other outcomes were reported within the systematic reviews, but none of these were pooled in a meta-analysis. A narrative synthesis was not completed on the outcomes of wound infection, pain requiring removal of metalwork, return to work, socio-professional disability cost, pulmonary embolism, pneumothorax and haemothorax. In the reviews, data on these additional outcomes was minimal and presented as a narrative synthesis without numerical data (Table 10 and Table 11).

2.4 Discussion

Twelve separate reviews, published between 2010 and 2016, were identified as reporting on the effectiveness of the surgical fixation of flail chest and multiple unifocal rib fractures. This is the first systematic review of reviews on this subject and has highlighted that the included reviews have significant crossover, both in study aims and in the primary studies they included.

2.4.1 Flail chest

Six of the twelve systematic reviews presented meta-analyses for flail chest. These found reductions in the length of mechanical ventilation, length of stay, pneumonia and tracheostomy rates with surgical fixation, but inconsistent results for mortality. Across many of the meta-analyses there were moderate to high levels of heterogeneity and inconsistencies in effect estimates depending on the study design. Effect estimates were statistically significant when reviews synthesised mortality across multiple non-randomised studies but were not

significant when synthesising only RCT data. Heterogeneity is discussed further in 2.4.4. Length of hospital stay showed a statistically significant improvement when synthesising two small RCTs (n=86) and very low heterogeneity: −11.39 days 95 % CI [−12.39, −10.38] I^2= 0. When taking into account larger and multiple non-randomised studies, however, the heterogeneity increased and the strength of the effect decreased to an RR of -3.86 days, 95% CI [−7.12, −0.54], I^2=68%. Length of ICU stay (up to 6.3 days), however, showed a statistically significant improvement with fixation, although significant heterogeneity within all meta-analyses of these outcomes dilute the strength of the results, meaning that it is unclear who the findings might apply to and whether the pooled estimate is meaningful. Pneumonia and tracheostomy rates had substantial heterogeneity despite having statistically significant improvements following fixation when pooling RCT data. Pooling non-randomised studies for tracheostomy risk showed low heterogeneity and a RRs of 0.4, 95% CI [0.2, 0.7], 0.34, 95% CI [0.10, 0.57] and 0.25, 95% CI [0.13, 0.47] in three reviews.

A single systematic review found reductions in sepsis, dyspnoea chest deformity and chest pain. Since the definitions of these were not clearly set out, however, it is difficult to know whether these are clinically significant. Reporting of adverse outcomes was infrequent and may be subject to reporting bias, resulting in an overestimate of the benefits in light of the potential risks.[100] Underreporting of adverse events in clinical trials is endemic, even though guidance[101] and the CONSORT harms extension[102] do exist in an attempt to reduce reporting bias.

Since synthesising multiple meta-analysis data that use the same primary studies has the potential to overestimate the strength of the findings, the review conclusions reflect this. In addition, significant heterogeneity within all meta-analyses on these outcomes makes drawing firm conclusions difficult.

2.4.2 Multiple unifocal rib fractures

Evidence in support of multiple rib fracture fixation in the absence of flail chest was limited. Two systematic reviews[52, 57] reported overall one non-randomised study[59] that recruited four case series[87-90] and two case reports [83, 86] between 1996 and 2000. As a result of this lack of primary data no conclusive statements on effectiveness can be arrived at. Only one outcome showed a statistically significant improvement for multiple unifocal rib fractures after surgical fixation, namely a mean difference improvement of 4.7 post-operative ventilator days

p=0.02. This was derived from only one study, however.[59] The only other value reported overall compared the total ventilator days within this same study [59]and did not show a statistically significant improvement p=0.12.

2.4.3 Review quality

Data and synthesis of these twelve systematic reviews were closely examined and this highlighted significant research waste errors and high risk of bias. A significant amount effort and time is required to undertake a systematic review and thus should only be undertaken when there is sufficient cause[31, 103] (e.g. to incorporate the findings of a new RCT). None of the eight systematic reviews published within 18 months of each other were registered on the PROSPERO platform.[38] An unregistered review raises the question of the validity of the methods presented, due to the lack of transparency in the absence of a protocol. It also removes the opportunity for researchers to establish before commencing whether their research question is already being addressed by others. In the absence of this similar search strategies and search dates led to multiple duplications within the included studies.

Seven reviews do not report risk of bias or quality assessment, two studies appeared to undertake a systematic quality assessment with partially referenced methods but how they were undertaken was unclear. Conclusions drawn from studies with a narrative synthesis were treated with caution, as they were less likely to perform a risk of bias assessment. Despite the low risk of bias in some studies, errors were still evident.

The review by Schulte et al.[51] has several errors in assigning levels of evidence within their narrative synthesis, for example, quoting two studies[72, 73] as level 1b, Although they do not specify what scale they use to assign the levels of evidence, the methods in the two primary studies describe prospective recruitment with no evidence of randomisation. Even though the two studies were well designed they do not equate to level 1b evidence as assigned by the Oxford[29] or SIGN[28] levels of evidence.

Not all outcomes from primary studies were synthesised and only certain outcomes were selected introducing reporting bias.

2.4.4 Heterogeneity

The I^2 value describes the percentage of total variation across studies that is due to heterogeneity rather than chance.[104] Examining the RCT meta-analyses further shows that although the pooled estimates for length of mechanical ventilation were significant, the confidence intervals were often wide and I^2 values were considerable (93-95%). As heterogeneity increases the likelihood of correctly estimating and drawing true inferences decreases.[105] There are two types of heterogeneity. Statistical heterogeneity is formerly described and clinical heterogeneity arises due to clinical differences usually in the patient characteristics or methodological comparing different studies designs.[106] Surprisingly, when combining multiple study designs, the confidence interval of the pooled estimate narrowed and the I^2 value dropped (48 -83%). Usually, pooling different study designs leads to an increase in heterogeneity.[106] Slobogean et al.[36] completed a secondary analysis looking at two RCTs[18, 19] (the third RCT had not been published at the time of their analysis). Using only two RCTs showed the biggest pooled effect estimate, MD-8.8 days, 95% CI [5.2,11.4]. This pooled estimate had minimal heterogeneity and between study differences (I^2 = 0%) and confidence intervals was narrower. Both Slobogean et al.[36] and Leinicke et al.[55] do not include the Marasco et al. [20] This RCT specifically appears to generate substantial heterogeneity when pooled with other analyses. The only review that had low heterogeneity across most outcomes was by Slobogean et al. that used both small RCTs and large non-randomised studies for their synthesis. Since no original data was supplied with this review the heterogeneity could not be inspected for its accuracy.

Significant statistical heterogeneity was seen, specifically in the outcomes length of mechanical ventilation, ICU length of stay and pneumonia. Heterogeneity for mortality had an I^2 value for 0% for all meta-analyses. Using only RCT results (combined number of patients = 86), mortality did not show a statistically significant improvement with fixation, however pooling multiple other non-randomised studies did show a statistically significant improvement (combined number of patients = 582).

Outcomes, and how they were measured or quantified, were not clearly defined in the reviews and therefore whether the synthesised outcomes were equivalent was unknown. As an example, mortality was defined in only one study (as a 30-day mortality rate). Other mortality rates were measured but may not be equivalent

since no time points were defined. Differences in how outcomes were measured may have accounted for between study heterogeneity, but this could not be confirmed due to a failure to report whether the outcomes were equivalent in the pooled primary studies or overall between systematic reviews.

Conflicting results between small RCTs and multiple larger non-randomised studies makes developing an overall conclusion difficult due to methodological heterogeneity, despite several outcomes having low statistical heterogeneity.

The included primary studies lack uniformity in respect to indications and timing of surgery, and it is possible that these between study differences could be an important source of clinical heterogeneity. For example, in one RCT,[18] patients were randomised after five days of invasive ventilation, whereas another RCT[19] randomised and fixed within 24 to 72 hours, regardless of initial intubation state.

Outcomes related to long-term function and adverse events were reported infrequently, so, although short term outcomes appear promising, a full synthesis to include these other outcomes is lacking. Conclusions as to the efficacy of rib fracture fixation should be reported in the context of risks of adverse events. Reporting of adverse event outcomes was so infrequent that this may significantly increase reporting bias. This suggests that further high quality RCTs investigating the effectiveness (including adverse effects) of internal surgical fixation over non-operative management are warranted.

Although there was substantial statistical and clinical heterogeneity and lack of consideration of risk of bias in many of the reviews, conclusions tended to be similar and suggestive of benefit arising from fixation. Few studies appear to have considered the statistical, clinical or methodological heterogeneity when applying their conclusions, however.

2.4.5 Errors in meta-analysis

The methods sections of all the meta-analysis studies state the use of two researchers for data extraction so as to minimise errors.[2, 36, 37, 54, 55] Despite attempts to minimise errors and therefore an apparent low risk of bias, some significant errors (up to an MD of 10 days in the measurement of length of intensive care stay) have inadvertently over-estimated effects. There are no significant changes in the conclusions from these errors but, nonetheless, their presence highlights the necessity for care in preparing reviews of this nature.

2.4.6 Strengths and limitations

This is the first review of reviews to assess the effectiveness of rib fracture fixation. The protocol was published on PROSPERO allowing transparency in respect to the methods followed, which is in line with the guidance from Smith et al.[33] An extensive search was performed on multiple databases, grey literature and reference lists. Searches, study selection, data extraction and risk of bias was undertaken by two researchers to reduce the risk of error and bias. All outcomes were extracted to reduce reporting bias. Risk of bias within the reviews was assessed using the ROBIS tool. Although only English language studies were included, some sources of unpublished studies were searched. It was suspected from the publication of seven systematic reviews within two years that primary studies could have been synthesised in more than one review, therefore a mapping of the studies included in the reviews was undertaken to take into account individual studies being included in multiple reviews and hence double counting studies.

All systematic reviews were included irrespective of their risk of bias scoring. It could be argued that several reviews were stretching the traditional definition of a systematic review as they were either best evidence topics or rapid evidence syntheses, they did however hold the protocol definition that included an electronic database search strategy and included primary evidence. As best evidence topics and rapid evidence synthesis were included in this review alongside traditional systematic reviews it was then difficult to apply the ROBIS tool consistently. The ROBIS tool is not designed for rapid evidence synthesis and therefore this type of review showed high risk of bias as they were being assessed against a tool designed for full systematic reviews. Rapid evidence syntheses, by their nature, entail a trade-off between time, methodological rigour and comprehensiveness.[60]

2.5 Conclusion

The considerable duplication of work across reviews could be mitigated through protocol registration and greater attention to establishing whether a review is necessary by scoping the literature before commencing a new review. Despite this review identifying 12 systematic reviews, these only included 37 unique primary studies, only three of which were RCTs. Synthesis of the reviews showed some potential improvement in patient outcomes after surgical intervention for flail chest. There were differences in respect to indications for and timing of interventions in

the primary studies, however, and moderate to high levels of heterogeneity across reviews. For future review updates, meta-analysis for effectiveness may need to take into account indications for and timing of surgery as a subgroup analysis in order to address clinical heterogeneity between primary studies. Further robust evidence is required before conclusions can be drawn in respect to the effectiveness of surgical fixation for flail chest and in particular, multiple unifocal rib fracture.

Chapter 3 - A systematic review of the effectiveness, indications for and timing of internal surgical fixation of multiple unifocal rib fractures and flail chest

3.1 Introduction

As outlined in Chapter 2, several systematic reviews have assessed the effectiveness of internal fixation for patients who have sustained rib fracture injuries. Despite the existing reviews, a new review was considered of value for a number of reasons. The majority of systematic reviews were of poor quality and were assessed as being at high risk of bias in the review of systematic reviews. In addition, multiple errors were seen within meta-analyses. There was limited exploration of variation in treatment effects across different injury patterns in these reviews and the effect of timing of surgery on outcomes, and the effect of the heterogeneity of outcome measures used needs to be further explored. A new systematic review was therefore undertaken to address these deficiencies. A more detailed rationale for the new review is provided in sections 3.1.3.1 to 3.1.3.4 below.

3.1.1 Research Question

What is the current evidence base for the effectiveness, indications for and timing of rib fracture fixation?

3.1.2 Objectives

The aim of the synthesis was to identify and map the existing primary research evidence for internal rib fracture fixation in order to inform future research.

The specific objectives were:

- To identify and synthesise the evidence on the effectiveness of internal surgical rib fracture fixation
- To evaluate the effectiveness of surgical rib fracture fixation for different injury patterns
- To evaluate the effectiveness of surgical rib fracture fixation based on timing of fixation

- To identify the indications for surgical rib fixation, timing of interventions and outcome measures in studies evaluating surgical rib fracture fixation in order to inform a Delphi consensus questionnaire.

3.1.3 Overview

3.1.3.1 Effectiveness

The effectiveness of surgical rib fracture fixation has commonly been assessed by previous reviews based on the outcomes of mortality, length of stay in hospital, length of critical care stay and length of mechanical ventilation. This first objective is to incorporate all these common outcome measures so as to reduce reporting bias and incorporate subgroup analyses in respect to type of rib fractures and timing of fixation. Previous reviews have not taken into account the potential clinical heterogeneity arising from the differences in injury type and timing of fixation. This may be one reason why the statistical heterogeneity of the outcomes in previous reviews has been high. Previous reviews have also selected outcomes they wanted to report; a further review is required to address the reporting bias. A review of the PROSPERO register identified one systematic review that has been previously registered relating to rib fracture fixation, this review is ongoing and had been registered since 2014 without publication.[107] Since searches were likely to be almost two years out of date for this review it was felt that enough new material had been published to warrant a new review even if the previous were to be published.

3.1.3.2 The Indications

Selecting patients who are most likely to benefit from surgical rib fracture fixation is difficult in clinical practice. Surgeon preference, previous case experience, injury type and patient response to other treatments may affect selection.

An indication is defined as ‘a symptom or particular circumstance that indicates the advisability or necessity of a specific medical treatment or procedure’.[108] Indications for internal surgical fixation need to be clear and measurable if they are to inform the eligibility criteria for a prospective trial. Within this synthesis, an indication will be any factor indicating appropriateness for surgical fixation. Suggested indications include intractable pain, respiratory failure and chest wall deformity.[19] The defined eligibility criteria for entry into a surgical study are not synonymous with indications for fixation.

The second aim of the review is to understand further the reasons why the literature considers certain patient characteristics and types of chest injury are considered appropriate for rib fracture fixation. Identifying these indications for surgery will also feed into a second project in which indications for surgical fixation will inform a Delphi consensus panel.

3.1.3.3 Timing of Intervention

It is also important to identify the most appropriate time at which to undertake surgical fixation. Should surgeons wait until the failure of mechanical weaning, exposing the patient to the morbidity of mechanical ventilation? If fixed early would there be an excess of patients exposed to surgical risk who may have improved without surgical fixation? Looking into the effectiveness of early or late fixation is the third objective of this review. This is in order to support the rationale for the timing of randomisation within a randomised control trial. Previous reviews have not considered the timing of fixation as a possible source of clinical heterogeneity. The information gathered within this review in respect to the timing of fixation can also be used in further consensus work to establish when clinicians think they should operate.

3.1.3.4 The Outcomes

It is important to select the most appropriate outcomes and outcome measures when designing a clinical trial.[109] The Core Outcome Measures in Effectiveness Trials (COMET) group are an organisation that has helped develop a Core Outcome Set (COS) methodology. The COMET group defines a Core Outcome Set as; ‘an agreed minimum set of outcomes or outcome measures’. It is a recommendation of what should be measured and reported in all trials in a specific clinical area.[110]

The COMET group maintains an updated database of lists of COS and a register of those in development. The COMET website does not have a published protocol for an outcome set that is specific to rib fractures on their database and none are currently in development by researchers. The COMET Handbook, published in 2017 describes a methodology for identifying relevant outcomes and suggests a Delphi technique to develop a core outcome set.[110] Gathering outcomes by systematic review in advance of a Delphi exercise is advocated by the COMET group and methods on searching for these outcomes have been published by Brettle et al.[111] The fourth objective, therefore, is to record the currently measured

outcomes in studies of the effectiveness of treatments for rib fracture in order to inform the Delphi consensus process undertaken as part of this thesis.

3.2 Methods

A focused systematic review, meta-analysis and quality assessment of the literature was undertaken based on guidance in the Centre for Reviews and Dissemination handbook.[34] A protocol was developed in advance of undertaking the review and registered on the PROSPERO website (42016053494) and available online at: https://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016053494.

3.2.1 Inclusion criteria

To be eligible for inclusion in the review studies had to meet the criteria summarised below in Table 16.

Table 16 Inclusion criteria

Population	Participants with rib fractures (flail, non-flail and multiple unifocal rib fractures) following blunt chest trauma > 18 years old
Intervention	Internal surgical fixation (strut, plate, suture/wire, intramedullary splint)
Comparator	Any of the above, no treatment and non-surgical therapies (Ventilation, analgesic techniques and splints)
Outcome	Primary outcome is length of mechanical ventilation, All outcomes will be collected for synthesis
Study Design	RCTs, case control, cohort and case series with 10 participants or more. Ongoing clinical trials

3.2.2 Population

Studies of adults over 18 years of age who have sustained one or more rib fractures following blunt chest wall trauma were eligible for inclusion.

Blunt chest wall trauma was defined as a non-penetrating injury (i.e. the lung cavity or pleural space was not breached) following a blow to the chest. This could include a high energy injury but also a simple fall from standing height. Patients with additional injuries were also included within these criteria. All types of rib fractures were included: single rib fractures, multiple rib fracture as well as flail chest.

Patients with penetrating chest injuries were excluded. Studies with patients who had a mixed population of non-penetrating and penetrating trauma were included if results were presented as separate subgroups.

3.2.3 Interventions

Any method of internally surgically fixing rib fractures was eligible, including both plate and strut fixation; metal or synthetic material and internal suture fixation, as well as a combination of therapies.

External fixation methods were excluded as the primary intervention but could be used as a comparator to internal fixation. External fixation covers traction methods, splints and Hoffman style pin and bar fixation.

3.2.4 Comparators

Non-surgical management (e.g. mechanical ventilation, epidural and regional anaesthesia); external fixation (e.g. traction, splints, Hoffman style pin and bar fixation) and studies with no comparator were included. In studies comparing two types of internal surgical fixation (without a non-surgical comparator) the two types of fixation were assessed separately as case series. The purpose of the review was to evaluate the overall effectiveness of internal fixation, and not to assess the effectiveness of specific surgical devices used for internal fixation. Therefore, instead of excluding this type of study it was seen to add value as two separate series of internal fixation patients.

3.2.5 Outcomes

Given the exploratory nature of this review, all outcomes were considered relevant. The primary outcome chosen was length of mechanical ventilation. This was considered the most important outcome since the length of this ventilation is likely to affect ventilator complications and other outcomes such as mortality which are directly related to how long the patient is ventilated.[112] It is also often the most costly part of treatment in rib fracture care.

3.2.6 Study design

Randomised controlled trials, quasi-randomised, non-randomised comparison studies and case series that include ten or more patients were included. Following the review of reviews (chapter 2) only three small RCTs had previously been identified. In several of the previous reviews, non-randomised studies and case

series did yield useful information and highlighted adverse events and long-term outcomes which were not captured in RCTs. It was considered important to capture this evidence in the current review because not all outcomes were previously synthesised, leading to reporting bias. It was also considered necessary to go beyond randomised studies since, in addition to considering effectiveness, the review also aimed to capture evidence on indications, outcomes and timing of surgery for further consensus work. It is debatable whether using non-randomised evidence is appropriate when assessing the effectiveness of a healthcare intervention. Shier et al., however, argue that "excluding observational studies in systematic reviews a priori is inappropriate and internally inconsistent with an evidence-based approach".[113] That said, they recognise that there is a potential for bias which may be introduced by confounding factors in observational studies but also by the placebo effect.[113] Allocation and selection bias could account for some of the treatment effect seen in non-randomised studies, therefore the results of such studies would have to be carefully assessed and interpreted with this in mind. Accordingly, Valentine et al.'s recommendation to assess for potential confounders arising from selection bias in the original studies were followed.[114]

Only case series with more than ten participants were eligible for inclusion. Although no specific guidance is in place for this cut off it was thought that single case reports were not useful as rib fracture fixation is not a rare disease process or treatment and we wanted to assess standard techniques.[115] It is acknowledged that rare complications may be missed by excluding small case series and reports.[116] In a quantitative synthesis, small studies can also lead to a inappropriately large weighting in meta-analysis.[117] The definitions of types of non-randomised study design were taken from the Cochrane group of definitions.[118]

A case control trial

> *A study that compares people with a specific outcome of interest ('cases') with people from the same source population but without that outcome ('controls'), to examine the association between the outcome and prior exposure.[118]*

A historically controlled study

> *A study that compares a group of participants receiving an intervention with a similar group from the past who did not.[118]*

A cohort study

> *A study in which a defined group of people (the cohort) is followed over time, to examine associations between different interventions received and subsequent outcomes.*[118]

3.2.7 Publication type/status

Both published and unpublished works were included in this review, as well as conference proceedings where data could be extracted.[119] It is well known that unpublished studies tend to report negative results or results that are not statistically significant and therefore trying to include this grey literature important to reduce publication bias.[120] It is also known that very few (23.7%) conference presentations at orthopaedics conferences are in turn published as journal articles within five years.[121] Although one systematic review found that the inclusion of grey literature only affected very few pooled estimates in meta-analyses,[122] data can still be used for a narrative synthesis. Conference proceedings that were linked to included published papers were discounted.

3.2.8 Language

Only papers in English were included in the review. Nonetheless, no language restrictions were applied in the literature searches so non-English language papers were identified and recorded in an effort to identify the complete literature base.

3.2.9 Search Strategy

An electronic database search of published literature was undertaken on the 14th December 2016, with the last updated search on 2nd March 2017. Since Advance Trauma Life Support has been undertaken since 1976, this was used as the start date for the searches. The following databases were searched: MEDLINE, including PreMEDLINE, EMBASE, Cochrane database of systematic reviews (CDSR) and Central Register of Controlled Trials (CENTRAL) and the Science Citation Index. Additionally, the reference lists of included studies were scanned to identify relevant studies. Non-published work was searched for within the Conference Proceedings Citation Index, and ongoing trials within Clinicaltrials.gov and WHO clinical trials registry platform. It is important to include ongoing trial work for two reasons. Firstly, to allow greater characterisation of publication and outcome reporting bias by identifying unpublished studies of completed or

uncompleted trials.[123, 124] Secondly, it furthers knowledge of ongoing work relevant to the research question. Trial Registry Protocols were included for these reasons.

The searches were updated in March 2017 in MEDLINE and Science Citation Index as they yielded the most relevant studies, with relatively few being identified from other sources.

3.2.10 Search Terms

The search strategy developed for MEDLINE was adapted to run appropriately on other databases. The same search strategy was used as for the review of reviews in Chapter 2 and the MEDLINE search strategy is available in Appendix A1. An explanation of the search term selection and method is provided in Chapter 2.2.9

3.2.11 Study selection

Search results were downloaded into Endnote software X7 (Clarivate Analytics, Version 7.1 release date 2/04/2014). References were imported, de-duplicated and the software was used to aid screening and logging of decisions. Titles and abstracts from the search results were assessed by two researchers independently (HI and EC). A full text was requested if either researcher judged that a record met the criteria or if there was uncertainty. Each full text paper was assessed by the same two researchers against the eligibility criteria. The responses of the researchers were kept partially blinded by hiding the response column of the other researcher. Full text decisions were initially kept blinded, and then transposed onto the response column following the final decision. This was to ensure that independent decisions were made about each study. There were no disagreements that could not be solved between the two researchers and therefore a third researcher was not required.

3.2.12 Data extraction

Data extraction forms were developed and piloted on a few sample studies. Some adjustments were made through the extraction process as a pilot on five studies before a final form was agreed upon. The data was extracted by one researcher (HI) and 50% were cross checked by a second (EC). The data extracted for effectiveness are outlined below. A description of how data was extracted in preparation for the Delphi consensus work is provided in chapter 4.

3.2.12.1 Study characteristics

Study characteristics of interest included:

- A description of study methods and information about the study, including country and year
- Patient characteristics (age, gender, injury description, ISS Score, concomitant chest injuries)
- The study specific inclusion and exclusion criteria
- Intervention (type of surgical device, mean or median time of surgical intervention, number of ribs fixed as applicable)
- Comparator if applicable (description of comparator i.e. usual care/non-operative management or specific intervention)
- Outcomes measured as well as duration of follow up

Summary tables were constructed to differentiate between type of injury (injury description), type of fixation (plate, strut, intramedullary and combined) and type of study (RCT, case control, historically controlled, cohort and series). They included the country, sample size and maximum follow-up time.

3.2.12.2 Data extracted for effectiveness

Data extracted on outcome measures included, as appropriate:

- Means, median, quartiles and ranges
- Frequencies and percentages
- Effect estimates and standard deviation, standard errors and confidence intervals, as available

Outcome data was extracted so that confidence intervals and between group differences could be calculated as appropriate for the specific outcome measure (e.g. relative risk, hazard ratio, mean difference).

Imputation methods were used when the required data were not available after contacting the authors. This was done in accordance with guidance set out by the

Cochrane Handbook.[125] Standard errors were calculated from either P values by converting into a T value (equation 1) or from confidence intervals (equation 2).

Equation 1

$$Standard\ Error = \frac{Mean\ \ Difference}{T\ value}$$

Equation 2

$$Standard\ Error = \frac{(Upper\ 95\%\ confidence\ interval - Lower\ 95\%\ confidence\ interval)}{3.92}$$

Standard deviations were then calculated from standard error and sample sizes.

Equation 3

$$Standard\ Deviation = \frac{Standard\ Error}{\sqrt{\left(\frac{1}{sample\ size\ 1} + \frac{1}{sample\ size\ 2}\right)}}$$

3.2.12.3 Data extracted for indications

Indications for surgery were assessed separately to inclusion and exclusion criteria. Narrative accounts of the indications that were described in the methods section of papers were extracted into the study characteristics table.

3.2.12.4 Data extracted for timing of fixation

Timing of fixation was extracted as either a mean or a median time from the studies and converted into days.

3.2.12.5 Data extracted for outcome measures assessment

A list of all outcome measure were extracted from each study. Where studies specified a primary outcome this was identified as such. Both outcomes and outcome measurement instruments were extracted if reported. These were not extracted strictly as verbatim but were grouped under umbrella terms to be concise.

3.2.13 Quality Assessment

Quality assessment was undertaken for all included studies. The Cochrane Risk of Bias Tool was used for included RCTs;[32] the Newcastle-Ottawa tool[126] for non-randomised studies (case control and cohort); and the Joanna Briggs Institute Risk

of Bias tool for case series.[126] One researcher completed the quality assessment of all studies (HI). A second researcher checked (EC) 50% of the first researcher's assessment. Any discrepancies were discussed but none required the intervention of a third researcher.

3.2.14 Data Synthesis

The aim of the synthesis was to ascertain the gaps present in the evidence base and the implications for future research with specific regard to effectiveness, indication, timing and outcome measures. Both a narrative synthesis and meta-analysis of key outcomes were performed.

3.2.14.1 Synthesis for Effectiveness

Estimates of effect from individual trials are presented either as forest plots or tabulated where meta-analysis was not possible. Studies were pooled in a meta-analysis using a random-effects approach to incorporate between-study variation as well as in-study variance. A random effects model was used rather than a fixed effects model since it was believed although the studies were similar in method there could be significant population differences and the true effect size may not be the same in all studies. With the random effects model the true effect size can vary between studies[127] whereas in the fixed effect model it is assumed that the effect size is the same across studies.

RCTs, case-control and cohort studies were entered into meta-analysis for the following outcomes: length of mechanical ventilation, mortality, length of ICU stay, length of hospital stay, pneumonia and tracheostomy rates. These outcomes were chosen since they are the most commonly reported in controlled studies. Tables were constructed for the additional outcome measures grouped by the injury type and type of study and a narrative synthesis was undertaken.

Studies were not stratified by type of study but RCTs were highlighted within the extraction tables. Subgroup analyses were performed between early and late fixation (3.2.14.3) as well as flail chest (FC) only and flail chest plus multiple unifocal rib fractures (FC +MURF) (3.2.14.1). Tests of heterogeneity were performed (chi-squared test and I^2 statistic) and reported as per the Cochrane handbook as: might not be important, moderate, substantial and considerable.[128] All studies with the required data were included, no study was excluded from the meta-analysis due to quality assessment or risk of bias.

Case series were synthesised in a narrative review see 3.2.14.4.

3.2.14.2 Type of injury subgroup analysis

In order to identify and synthesise the evidence on the effectiveness of internal surgical rib fracture fixation, the studies were first grouped by injury type (i.e. those including only patients with flail chest and those studies including both flail chest and multiple rib fracture patients). Initially, it was planned to use the following definitions: flail chest, defined as rib fracture with bifocal rib fracture and paradoxical movement; and multiple unifocal rib fractures. This was not always possible, however, due to the variety of reporting and definitions of flail chest, segment and multiple unifocal rib fractures across the papers. A more pragmatic approach was therefore taken. A study was classified as having a flail chest injury population if it described the included population as having flail chest or flail segment and paradoxical movement. All other injuries were defined as having multiple unifocal rib fractures. Details of individual papers' inclusion criteria are provided in the data tables (Appendix B). For meta-analysis subgroups were split into flail chest only (FC) and flail chest and multiple unifocal rib fractures (FC+MURF) since no study looked at multiple rib fractures only.

3.2.14.3 Timing of fixation subgroup analysis

Recently published British Orthopaedic Association Standards for Trauma (BOAST) guidance states that patients should be operated on within two days of being identified as needing surgery, although the evidence behind this guidance is not published.[16] The timing of surgery has not been fully explored in a meta-analysis and the level of evidence for timing of surgery is described as an expert level of opinion (Level 5).[5] Pieracci et al. have completed some consensus work with fourteen surgeons, recommending fixation within 72 hours of the injury.[5] This consensus approach was chosen over the BOA standard to define early and late fixation because it was developed by a consensus method. Those with a mean or median time of surgery above or equal to 72 hours were classed as late fixation and those in which surgery occurred in less than 72 hours were classed as early fixation. Studies that reported a time to fixation with a comparator group were entered into meta-analysis comparing late and early fixation in a subgroup analysis

3.2.14.4 Narrative Synthesis

A narrative synthesis of outcomes and patient characteristics was completed on all included studies and reported by type of study (RCT, NRS and case series). Due to the complexities of the reporting, NRS were not reported by their subgroup of case-control (i.e. historically controlled study or cohort study).

A description of the types of injuries within each study was presented in the study characteristics tables. A narrative synthesis grouped studies by the type of injury (FC and FC+MURF) describing the mean, medians, SD, IQR and ranges as appropriate for each outcome. The timing of operative intervention was described in the narrative synthesis using the mean, median, SD, IQR and range as appropriate.

3.2.14.4.1 Outcome

Following data extraction, the measurement instruments were assembled into a relevant list of outcome measures in preparation for incorporation into a Delphi consensus.

The measurement instruments were arranged into six groups based on work by Williamson and Clarke:[110]

- Hospital resource use
- Adverse outcomes
- Lung function and arterial blood gas analysis (physiological)
- Chest deformity and range of movement (clinical)
- Pain and discomfort
- Quality of life

Similar instruments were amalgamated if appropriate. For example, metal work failure included the outcome broken metal work as well as migrated metal work. The number of studies using each measurement instrument was then presented in tables.

Although an attempt was made to distinguish time points in which the outcome measures were recorded this was difficult due to the lack of clear reporting,

especially for short term outcomes such as mortality, pneumonia and tracheostomy. See Chapter four for further explanation of how measurement instruments were used to form a list of overall outcome measures.

3.2.14.4.2 Indications

For analysis, the indications were simply counted as how many times an indication was advocated by each study. Indications with a similar theme were combined if feasible and rational, even if they did not have exactly the same wording.

The report was written in accordance with the PRISMA guidance.[129]

3.3 Results

The electronic searches identified 803 records and a further 38 were identified from hand searching and reference checking of included papers (Figure 6).

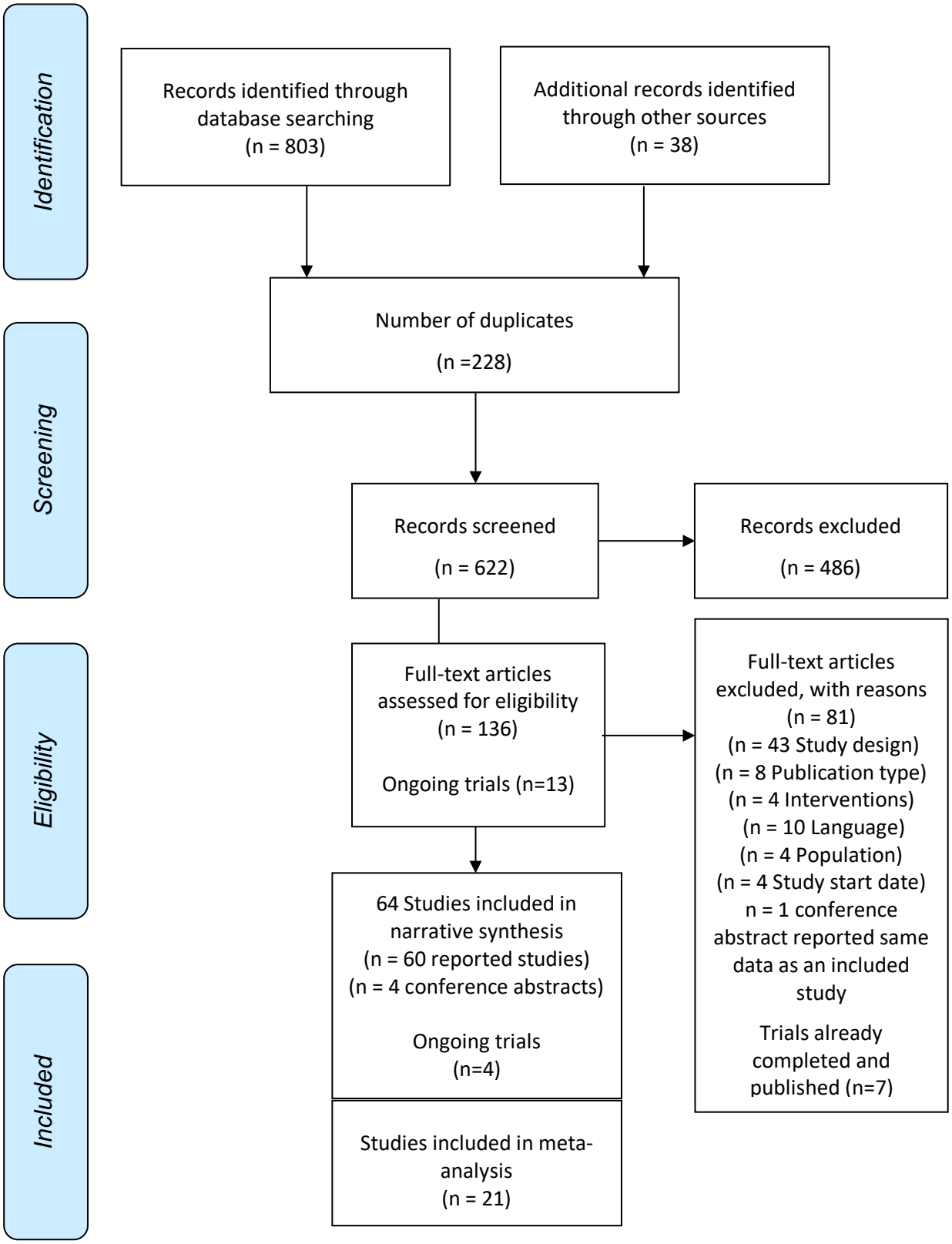


Figure 6 PRISMA Flow chart of study selection

Of the total of 841 papers, 228 duplicates were identified and removed, leaving 613 for screening of titles and abstracts. Full texts were ordered for 140 records that were identified as possible includes and assessed for eligibility. Sixty-four studies were included in the synthesis and four ongoing trials were identified. Only one full text was not retrievable and this was thought to be a non-English language text. Ten potentially eligible papers were identified as published in languages other than English: Czech (1 paper),[130] German (1 paper),[131] Italian (3 papers),[90, 132, 133] Japanese (1 paper),[134] Chinese (1 paper)[67] and Spanish (3 papers).[135-137] The most common reason for exclusion was an ineligible study design, and 87 case reports or series of less than ten patients were identified. The next most common reason was an ineligible publication type such as letters to the editor and commentaries. Five records were identified as conference abstracts,[138-142] but one abstract[142] was related to a journal article that had already been included, so was not reported twice.[143] Overall, therefore, 64 records were included rather than the 65 reported in the PRISMA diagram. The other conference abstracts were included in the synthesis since they reported data not included elsewhere in review.[138-141] There were three ongoing RCTs[144, 145,146] and one ongoing cohort study.[147] All are due to finish recruitment within 1 year (Table 17). Seven other studies that were identified through searches of trial registries have all been completed and published. These full papers were identified within the original searches [148-154]. A list of excluded studies is provided in Appendix A3 Excluded Studies

Table 17 Ongoing Trials

	Intervention	Inclusions	Outcomes
Treatment of Acute, Unstable Chest Wall Injuries RCT Canada Expected end of recruitment Dec 2017	Plate and screws Participants = 206 Timing Randomisation < 72 hours from injury ORIF < 96 hours from injury	Flail chest 3 unilateral segmental rib fractures; OR 3 bilateral rib fractures; OR 3 unilateral fractures combined with sternum fracture/dissociation Note: at least 3 of the rib fractures involved in the flail segment must demonstrate displacement. Severe deformity of the chest wall Severe (100%) displacement of 3 or more ribs OR marked loss of thoracic volume/caved in chest (>25% volume loss in involved lobe(s)); OR overriding of 3 or more rib fractures (by minimum 15 mm each); OR Two or more rib fractures associated with intra-parenchymal injury - i.e. ribs in the lung, in the parenchyma	Ventilator-free days Number of days in the Intensive Care Unit (ICU) Amount of pain medication administration, converted to oral morphine equivalence Rate of Pneumonia Pulmonary function assessment Rate of return to work Assessment of functional health and well-being SF-36
Medico-Economic Analysis of Management of Flail Chest Between Medical Treatment and Surgical Treatment With Stracos RCT France Expected end of recruitment Nov 2017	Plate and screws Participants = 310 Timing Within 48 hours	Patients with flail chest including bifocal fracture of three or more consecutive ribs in at least two places with or without paradoxical movement The surgical procedure was performed in the first 48 hours after admission pathology with prognosis for survival 6-month-old	Average cost hospitalisation length of hospital stays ICU, length of hospital stays Occurrence of pulmonary infection The vital capacity (VC), expiratory reserve volume (ERV), total lung capacity (TLC), residual volume (RV) 6 min walk test (6MWT) Visual analogue scorer for pain Patient Global Assessment date of return to work
A Multicentre Prospective Randomised Trial on the Intervention of Rib Fixation for Clinically Severe Rib Fractures From Trauma RCT USA	Plate and screws Participants = 300 Timing Not discussed	Flail chest, defined as 3 or more consecutive ribs fractured in more than one place Pain and disability of an FPS (Functional Pain Scale) rating of 3 or higher Deformity and Defect Non-Union Thoracotomy for other indications	ICU Length of Stay Quality of Life, as determined by SF-36 pneumonia Total cost of treatments Complication Rates including, but not limited to, pneumonia, urinary tract infection, arrhythmia, sepsis, reintubation, wound infection Pain Control documented by the Functional Pain Scale

	Intervention	Inclusions	Outcomes
Expected end of recruitment October 2018		3 or more rib fractures with rib displacement of more than 1 rib cortical diameter Failure to wean from ventilator	Ventilator/Ventilator Free Days Narcotic usage converted to units of morphine Hospital length of stay Pulmonary Function as measured by FVC, FEV1, and TLC Time to wean from ventilator Tracheostomy rates
Sheffield Multiple Rib Fractures Study: Evolution of Classification, Management and Outcomes Cohort Study UK Expected end of recruitment December 2017	Patients presenting from October 2015 to October 2017 with multiple rib fractures or flail chest, managed operatively or non-operatively Participants = 300 Timing Not discussed	Inclusion Criteria: Multiple simple rib fractures Flail chest	Acute Pain Visual Analogue Score Forced Expired Volume in 1 second (FEV1), Forced Vital Capacity (FVC) Length of critical care unit stay Complications during critical care unit stay adverse events as assessed by CTCAE v4.0 Length of hospital stay Complications during hospital stay adverse events as assessed by CTCAE v4.0 Quality of Life - SF36 (Short Form 36) SF-36, EQ5D, EORTC (European Organisation for the Research and Treatment of Cancer) QLQ-C30 (Quality of Life Questionnaire - Cancer-30), EORTC QLQ-LC13 (Lung Cancer13) Healthcare cost - procedural costs plus hospital cost plus community healthcare costs

3.3.1 Study Characteristics

Sixty four studies met the eligibility criteria: four RCTs, 28 NRS (four case controls, seven historically controlled studies and 17 cohort studies) and 32 case series. A summary of study characteristics is provided in Table 18 and Table 19, full details of study characteristics are available in Appendix B(Table 68 to Table 72) The RCTs were reported in 2002, 2005, 2013 and 2015 and since publication there has been a significant upsurge in the number of non-randomised study designs (Figure 7). Despite more publications, however, the grade or level of evidence has not increased.[29, 155]

Since 2009, there has been an upsurge in the amount of publications on surgical rib fracture fixation, with the most active country in terms of publishing results being the USA[59, 69, 71, 73, 78, 92, 93, 99, 156-164] (n=19), followed by China[74, 76, 165-169] (n=8). Only one case series has been published in the UK,[143], while China,[169] Australia,[20] Japan[18] and Egypt[19] have reported RCTs (Figure 8). The USA has published the most studies with ten NRS and ten case series but no RCT. Common centres that have produced rib fracture fixation research are the Alfred hospital (Australia), the Mayo and Portland Clinics (USA), Shanghai (China) and Gothenburg (Sweden).

Sample sizes of studies were typically small; the combined number of patient participants in all four RCTs was 287. The largest NRS with a control group was by Majercik et al.,[77, 93] and the same participant group was used in two published studies (counted separately) by the same author reporting different outcomes and containing 137 in the intervention group and 274 controls. The overall number of patients in control groups (discounting patients that were reported twice by authors) was 3879, while the number in intervention groups was 1044. There were an additional 1389 patients reported in case series. Most papers only reported ‘in-hospital’ outcomes such as length of stay; the maximum follow up was up to 96 months.

Table 18 Characteristics of studies reporting flail chest only

Randomised Control Trial	Country	Injury	Fixation	Sample I	Sample C	Follow up
Marasco 2013Ab [20]	Australia	Flail chest	Plate	23	23	6 months
Tanaka 2002 [18]	Japan	Flail chest	Strut	18	19	12 months
Historically controlled trial						
Buyukkarabaca 2015 [170]	Turkey	Flail chest	Plate	10	10	In hospital
Farquhar 2014 [171]	Canada	Flail chest	Plate	19	36	6 months
Doben 2014 [71]	USA	Flail chest	IM and Plate	10	11	6 months
Jayle 2014 [72]	France	Flail chest	Strut	10	10	3 month
Cohort						
Althausen 2011 [92]	USA	Flail chest	Plate	22	28	22 months
De Moya 2011[69]	USA	Flail chest	Plate	16	32	In hospital
Defeest 2016 [78]	USA	Flail chest	Plate	41	45	In hospital
Nirula 2006 [59]	USA	Flail chest	Strut	30	30	In hospital
Voggenreiter 1998 [65]	Germany	Flail chest	Strut	20	22	In hospital
Ahmed 1995 [64]	UAE	Flail chest	Intramedullary	28	38	9 months

Case Series	Country	Injury	Fixation	Sample	Follow up
Ivancic 2009 [172]	Croatia	Flail chest	Plate	15	In hospital
Lardoinois 2001 [84]	Switzerland	Flail chest	Plate	66	6 months
Majercik 2014 [159]	USA	Flail chest	Plate	101	16 months
Michelitsch 2016* [138]	Switzerland	Flail chest	Plate	23	68 months
Moslam 2015 [173]	Egypt	flail chest [A/L]	Plate	40	3 months
Mouton 1997 [82]	Switzerland	Flail chest	Plate	23	3 months
Olsen 2013 [174]	Sweden	Flail chest	Plate	24	6 months
Reber 1993[175]	Switzerland	Flail chest	Plate	11	26 months
Said 2014 [163]	USA	Flail chest	Plate	20	5 months

Case Series	Country	Injury	Fixation	Sample	Follow up
Taylor 2013 [164]	USA	Flail chest	Plate	21	5 months
Marasco 2009 Ab [176]	Australia	Flail chest	Plate	13	16 months
Marasco 2014 Ab [177]	Australia	Flail chest	Plate	60	3 months
Menard 1983 [81]	France	Flail chest	Strut	18	5 months
Wiese 2015 [178]	Switzerland	Flail chest	Strut	68	6 months
Schmitt 1982 [179]	Germany	Flail chest	Strut	20	In hospital
Tarng 2016 [166]	Taiwan	Flail chest	Intramedullary	12	12 months
Borerelly 2005 [6]	Iran	Flail chest	IM and Strut	127	In hospital
Bottlang 2013 [158]	USA	Flail chest	IM and Plate	20	6 months

AL – Anterolateral, Ab – Absorbable, I – Intervention, C- Control, *Conference abstract

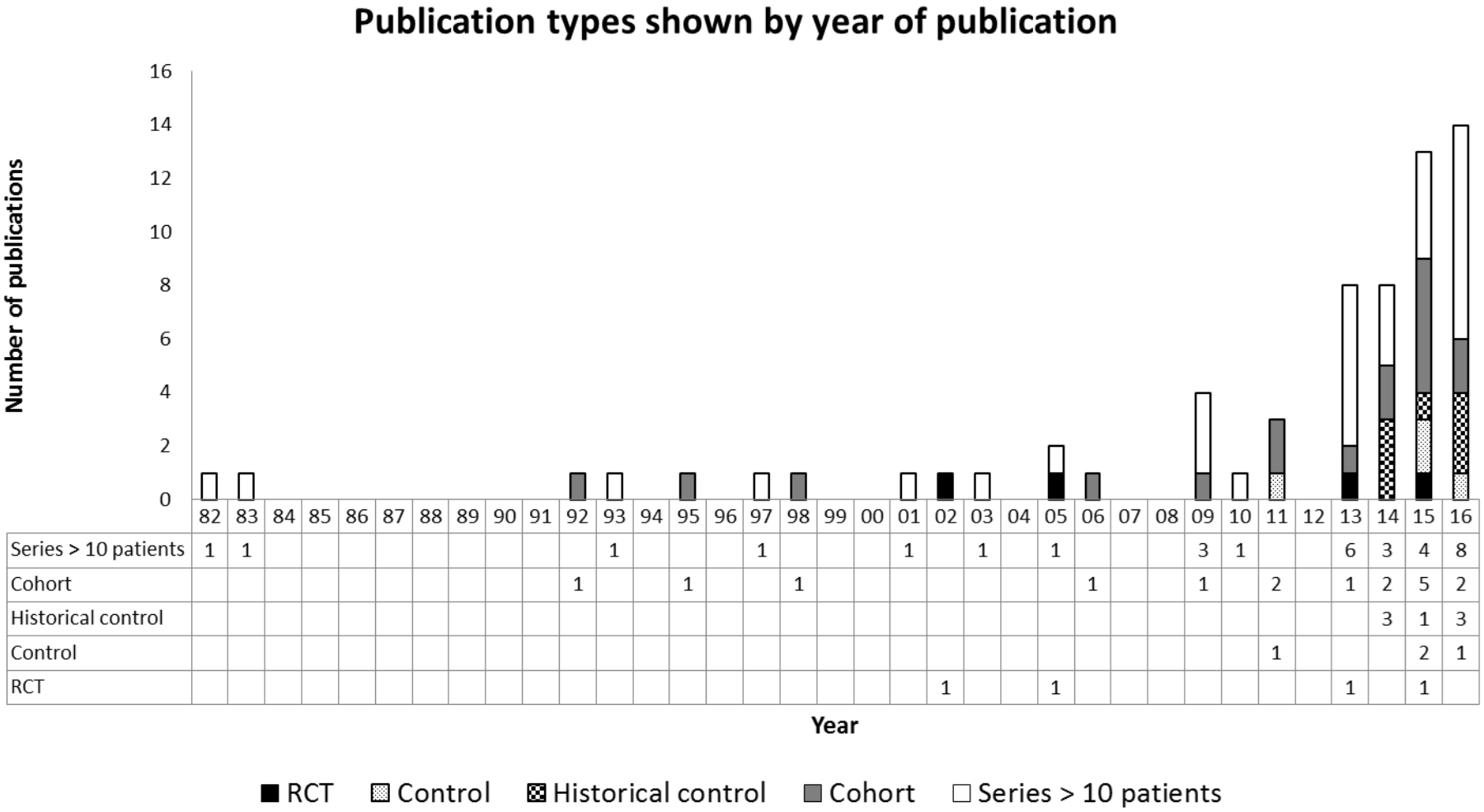
Table 19 Characteristics of studies reporting flail chest and multiple unifocal rib fractures

Study Type	Country	Injury	Fixation	Sample I	Sample C	Follow up
RCT						
Wu 2015 [169]	China	FC +MURF	Strut	75	89	2 months
Granetzny 2003 [19]	Germany	FC +MURF	Intramedullary	20	20	2 months
Case Control Study						
Khandelwal 2011 [180]	India	All rib fractures	Plate	32	29	30 days
Majercik 2015[a] [77]	USA	All rib fractures	Plate	137	274	In hospital
Majercik 2015[b] [93]	USA	All rib fractures	Plate	137	274	In hospital
Pieracci 2016 [73]	USA	FC and multiple >3 rib fractures	Plate	35	35	In hospital
Historical Control						
Olsen 2016 [181]	Sweden	FC and multiple >4 rib fractures	Plate	58	320	4.5 years
Qiu 2016 [168]	China	FC and multiple rib fractures	Plate	86	76	6 months
Velaquez 2016 [182]	Columbia	FC and multiple >3 rib fractures	Strut	20	20	In hospital
Cohort Study						
Galan 1992 [183]	Spain	Unclear	Strut	29	1667	In hospital
Granhed 2014 [70]	Sweden	FC +MURF	IM and Plate	60	762	In hospital
Muhm 2013 [184]	Germany	FC +MURF	Plate	21	23	In hospital
Pimakhov 2015* [139]	Ukraine	Unclear	Multiple methods	27	30	6 months
Pimakhov 2014* [140]	Ukraine	Unclear	Multiple methods	21	25	6 months
Solberg 2009 [156]	USA	Superolateral implosion deformity	Plate	9	7	16 months
Taylor 2016 [157]	USA	Flail chest and multiple >4 rib fractures	Plate	31	30	6 months
Wada 2015 [75]	Japan	FC +MURF	Multiple methods	84	336	28 days
Xu 2015 [76]	China	FC and multiple >4 rib fractures	Plate	17	15	14 days
Zhang 2015 a [95]	China	FC +MURF	Strut	23	29	In hospital
Zhang 2015 b [74]	China	FC +MURF	Strut	12	15	In hospital

Case Series	Country	Injury	Fixation	Sample	Follow up
Nickerson 2015 [99]	USA	FC +MURF	Plate	89	In hospital
Nickerson 2016 [162]	USA	FC +MURF	Plate	43	6 months

Caragounis 2016 [185]	Sweden	Flail chest and multiple >4 rib fractures	Plate	60	1 year
De Palma 2016 [186]	Italy	FC +MURF	Plate	10	1 year
Mayberry 2003 [ab 161]	USA	FC +MURF	Plate	10	19 months
Sellers 2013 [143]	UK	FC +MURF	Plate	10	18 months
Theils 2016 [187]	USA	FC +MURF	Plate	122	5 months
Metin 2016 [188]	Turkey	FC +MURF	Strut	44	36 months
Yang 2010 [165]	China	FC +MURF	Strut	17	10 months
Chai 2013 [167]	China	FC +MURF	Strut and IM	248	2 years
Marasco 2016 [189]	Australia	FC +MURF	IM and Plate	15	6 months
Campbell 2009 [ab 87]	Australia	FC +MURF	Multiple methods	10	34 months
Mayberry 2009 [88]	USA	FC +MURF	Multiple methods	46	96 months
Redwan 2015* [141]	Germany	Unstable rib fractures	Intramedullary	Unknown	Unknown

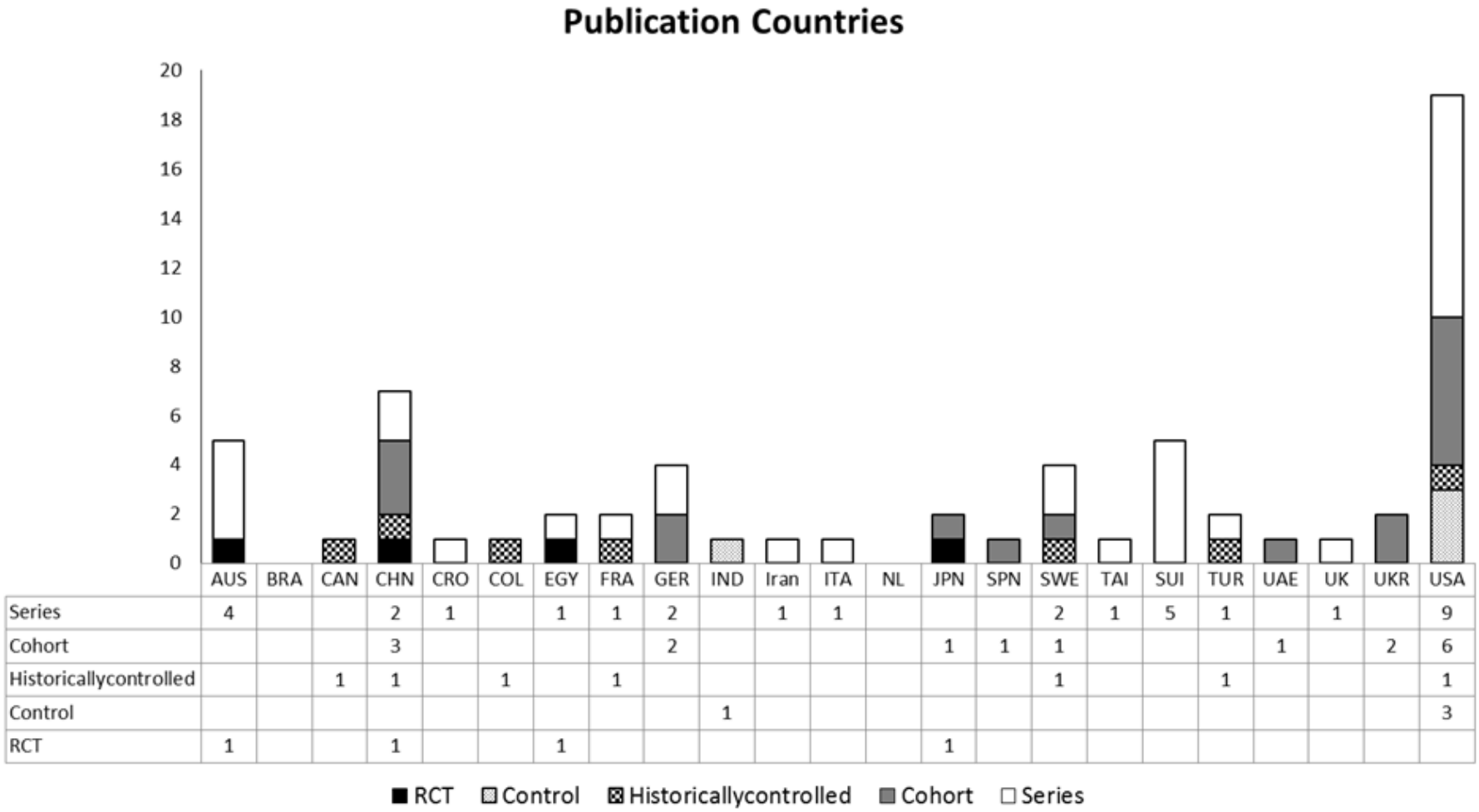
*Conference abstract, I = Intervention group , C = Control group, IMV Invasive mechanical ventilation, ICU Intensive Care Unit, Resp F Respiratory failure, ab= absorbable fixation



	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	00	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16
Series > 10 patients	1	1										1				1				1		1		1				3	1			6	3	4	8
Cohort											1			1			1								1			1		2		1	2	5	2
Historical control																																	3	1	3
Control																														1				2	1
RCT																					1			1								1		1	

Figure 7 Publication types shown by year of publication

Figure 8 Number of publication by country of origin



	AUS	BRA	CAN	CHN	CRO	COL	EGY	FRA	GER	IND	Iran	ITA	NL	JPN	SPN	SWE	TAI	SUI	TUR	UAE	UK	UKR	USA
Series	4			2	1		1	1	2		1	1				2	1	5	1		1		9
Cohort				3					2					1	1	1				1		2	6
Historicallycontrolled			1	1		1		1								1			1				1
Control										1													3
RCT	1			1			1							1									

3.3.2 Types of Fixation

Plate fixation was used in 35 studies and was reported in one RCT,[20] four case control studies,[73, 77, 93, 180] four historically controlled studies,[168, 170, 171, 181], seven cohort studies[69, 76, 78, 92, 156, 157, 184] and 19 case series.[82, 84, 99, 138, 143, 159, 161-164, 172-177, 185-187] Strut fixation was used in 14 studies, which included two RCTs[18, 169], two historically controlled studies,[72, 182] five cohort studies[59, 65, 74, 95, 183] and five case series.[81, 165, 178, 179, 188] Intramedullary fixation was used in four studies including one RCT,[19] one cohort study[64] and two case series.[141, 166] Intramedullary fixation was often used in combination with other fixations. Such combination fixation was used in 11 studies which included one historical case control,[71] four cohort studies[70, 75, 139, 140] and six case series.[6, 87, 88, 158, 167, 189]

While strut fixation was more common in the 1980s, metallic plate fixation is now the commonest fixation within the included literature (Figure 9). Studies have also used combinations of fixations; the most common being IM fixation supplemented with wires, wraps, plates or struts. IM fixations are useful to fix posterior rib fractures that are difficult to reach under the scapular. Absorbable plates, struts and wraps made of L-Lactide, D,L-Lactide, Polyglycolide and Trimethylene Carbonate are used infrequently (6 studies[20, 87, 161, 176, 177]) and have not been considered as a separate group within the synthesis but are highlighted within the tables with a superscript ab[(ab)].

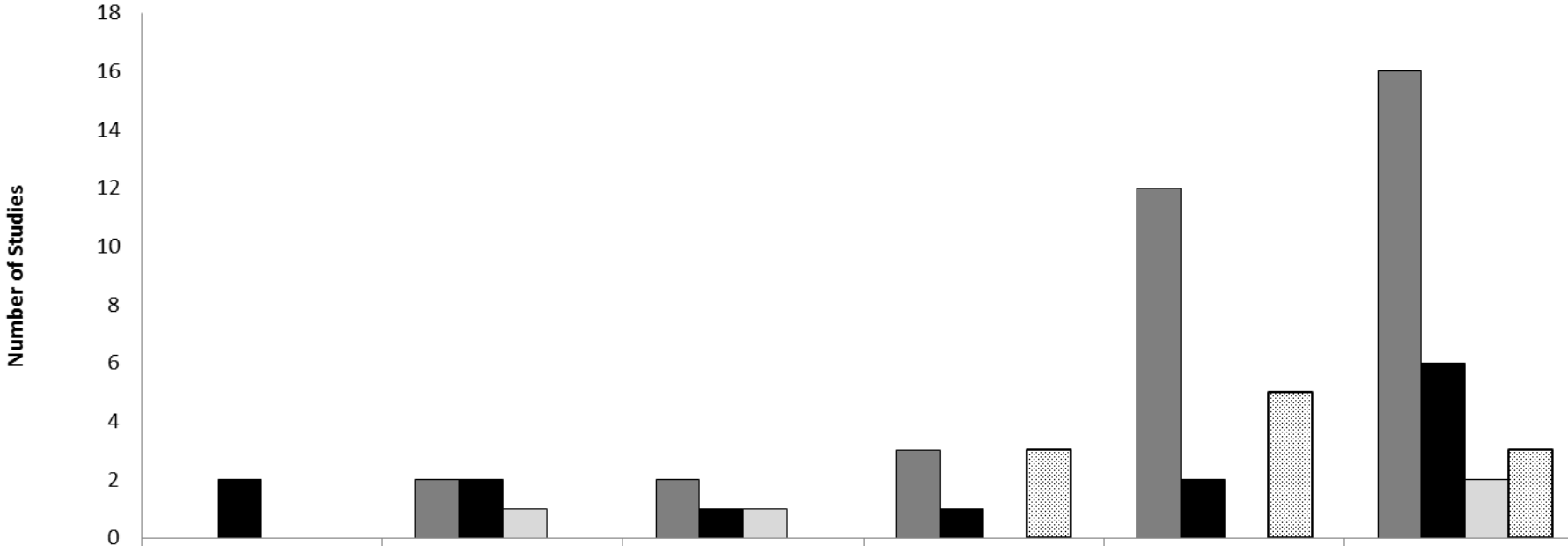
Two studies reported on different fixation techniques within the same study;[99, 162] each technique was reported separately so they were included but analysed as separate case series. Nickerson et al. in 2015 reported the use of a 90 degree screwdriver used for fixing plates to ribs compared to the standard screwdriver. [99] In 2016 ,Nickerson et al.[162] report a case series of 43 patients with flail chest who had two separate approaches to fixing flail segments. The first group of 23 patients had all fracture fragments stabilised whereas second group of 20 had a partial stabilisation where flail segments were converted into unifocal rib fractures. Anterior location of the fracture was the most common reason for PFS (45%).

3.3.3 Comparators

The comparator within the RCT studies included chest strapping with IMV, internal pneumatic stabilisation and usual care/non-operative management. Within the

NSR studies, comparators included usual care/non-operative management, which consisted of a range of regional and local anaesthetic techniques and, if necessary, mechanical ventilation. Comparators for each study are presented in the study characteristics tables in Appendix B1(Table 68 to Table 72).

Figure 9 Trends in methods of fixation of rib fractures reported in the literature



	1980's	1990's	2000-2004	2005-2009	2010-2014	2015-2017
Plate		2	2	3	12	16
Strut	2	2	1	1	2	6
IM		1	1		0	2
Combined				3	5	3

3.3.4 Patient characteristics

3.3.4.1 Age

Patients' ages were reported both in means and medians. In the studies with a control group, the mean age of the surgical fixation group ranged from 36.1 to 58.7 years and in the non-surgical arm it ranged from 35.5 to 59 years. In the case-series the mean age ranged from 42 to 59.5 years and the median from 57 to 63 years, the minimum age was 15 and the maximum age 90 years old across studies (Table 20). Five studies [19, 71, 74, 78, 184] reported mean ages that were clinically significantly different between control and intervention groups. The cohort studies by Doben et al.[71] and Defreest et al.[78] had control groups that were, on average, 9.2 and 5.5 years older than their intervention groups, which may bias results in favour of the intervention group as the ability to recover from trauma is proportional to age and comorbid status.[190] Zhang et al.[74] had a subgroup for early fixation which had a median age of 38 years compared to their late and non-fixation groups that had median ages of 45.5 and 47 years, respectively. The RCT by Granetzny et al.[19] and the cohort study by Muhm et al.[184] had control groups that were 4.5 and 4.7 years younger than the intervention group, which may lead to the effectiveness of rib fracture fixation being underestimated. Five studies did not report the ages of participants.[139, 140, 179, 183, 186]

Table 20 Study Participant Characteristics

		Randomised Control Trials				Non-Randomised Studies				Case series	
		Control		Surgery		Control		Surgery		Surgery	
Characteristic		Min	Max	Min	Max	Min	Max	Min	Max	Min	Max
Age	Mean	36	59.3	40.5	57.8	35.5	59	36.1	58.7	42	59.5
	Median	-	-	-	-	45.5	55	38	59	57	63
	Range	12	60	24	55	19	95	18	90	15	90
ISS	Mean	18	30	16.8	35	24.3	47.8	21.5	37	16	29.8
	Median	-	-	-	-	13	38	9	42		
	Range	-	-	-	-	9	75	9	75	4	66
Number of ribs	Mean	4.9	11.3	4.4	11	3.10	11	3.22	11.29	6	11.8
	Median	-	-	-	-	3	11	4	12	4	8
	Range	6	11	6	12	2	24	3	20	3	14
Gender	Percentage	89% ♂	21% ♀	81% ♂	29% ♀	75% ♂	24% ♀	76% ♂	24%♀	74% ♂	26% ♀

3.3.4.2 Gender

Within the RCTs, 81% of participants in the intervention group were male and 89% in the comparator group. However, the RCT by Wu et al.[169] is an exception and

only included male patients (Table 20). The NRS operated groups were 76% male, the controls 75% and the case series 74%.

3.3.4.3 Injury Severity

The injury severity score (ISS) has a range of 0, being no injury, to 75, severe. Of the studies that reported ISS the minimum and maximum means and medians, and the minimum and maximum range values are presented in Table 20. Three studies had ISS scores that were considerably different between intervention and control groups. One cohort study[71] had a control group with a mean ISS of 35.7 (SD 12.7) and an intervention group mean ISS of 26.3 (SD 9.5). It is possible that the intervention group may have overestimated the effectiveness of the intervention as the intervention groups were less severely injured. Similarly, another cohort study[70] had a control group mean ISS of 30.9 (SD 13.3) and an intervention mean ISS of 21.7 (SD 10.8). A further cohort study[170] reported an ISS of 75 in both intervention and control group, an explanation from the authors was not sought. These values represent extreme outliers compared to other values reported in other studies and whether this was a mean, median or a maximum value was not qualified. There were also significant differences in ISS in between studies, with means ranging from 16.8 to 47.8.

3.3.4.4 Number of ribs fractured

Mean, median and range values of the number of ribs fractured is presented in Table 20. Four studies [71, 77, 181, 184] had significant differences between control and intervention groups. Majercik et al.,[77] Muhm et al.[184] and Olsen et al.[181] had, on average, 1.9, 1.9 and 2 more ribs fractured in the intervention group than the control group, respectively. Doben et al.[71] had a median of 6.6 ribs fractured in the intervention group and 9 in the control group. More rib fractures in any one group may confer worse outcomes compared to a group with less ribs fractured due to increased instability of the chest wall and the potential for worse outcomes.

Characterisations of the injury by describing the number of fractured ribs, presence of flail or location of fractures was not reported in six non-randomised studies[65, 139, 140, 156, 171, 183] or nine case series.[82, 138, 141, 143, 161, 172, 176, 185, 186]

3.3.4.5 Flail chest and multiple unifocal rib fractures

The definition of a flail chest was inconsistent between studies, making the grouping into flail chest and multiple unifocal rib fractures difficult for this study.

The difference between the flail chest and flail segment may be central to the confusion. A flail segment is described as segmental fractures in adjacent ribs and is often diagnosed radiologically. The ability to diagnose paradoxical motion requires a clinical assessment and this definition is more common in prospective studies where this can be assessed. Retrospective studies were less likely to be able to distinguish a flail chest from a flail segment unless this had been carefully documented within clinical notes. Identification of most patients in retrospective reviews was via retrospective review of CT scans, which cannot distinguish between flail segments and flail chest.

None of the RCTs provided a definition of a flail chest injury within their selection criteria (Table 21). The most common definition used in other studies was three or more adjacent and segmental rib fractures. Paradoxical movement was only mentioned in half of the study definitions and was the sole definition in two studies. Respiratory compromise in combination with segmental adjacent rib fractures was the definition in three studies.

Two RCTs,[18, 20] ten non-randomised studies[59, 64, 65, 69, 71, 72, 78, 92, 170, 171] and 20 case series [6, 81, 82, 84, 138, 158, 159, 161, 163, 164, 166, 172-179, 183] included or described patients with flail chest (FC) injuries only (Table 18). Although 32 studies included multiple unifocal rib fractures within their inclusion criteria only one study[168] presented this data separately and therefore multiple unifocal rib fractures could not be investigated as a subgroup in the analysis. Two RCTs[19, 169], 18 non-randomised studies[70, 73-77, 93, 95, 139-141, 156, 157, 168, 180-182, 184] and 12 case series[87, 88, 99, 143, 162, 165, 167, 185-189] included both FC+MURF (Table 19). Two studies specifically looked at only one area of the chest: one case series looked at anterior-lateral flail[173] and one NRS looked at superior-lateral fractures.[156]

Table 21 Definition of flail chest within studies

Study	Number of adjacent ribs	Segmental	Paradoxical movement	Respiratory compromise
Althausen 2011	4 or more	Y	Not stated	Not stated
Borerelly 2005	Not stated	?Not stated	Y	Not stated
Bottlang 2013	3 or more	Y	Y	Not stated
Buyukkarabaca, 2015	2 or more	Y	Y	Not stated
Caragounis 2016	3 or more	Y	Not stated	Y
Defeest 2016	3 or more	Y	Y	Not stated
Doben 2014	3 or more	Y	Y	Not stated
Farquhar 2014	3 or more	Y	Not stated	Y
Jayle 2014	3 or more	Y	Not stated	Not stated
Majercik 2014	3 or more	Y	Y	Not stated
Marasco 2009	Multiple	Y	Y	Not stated
Marasco 2014	Not stated	Y	Not stated	Not stated
Mayberry 2009	Not stated	Not stated	Y	Not stated
Moslam 2015	3 or more	Y	Not stated	Not stated
Nirula 2006	3 or more	Y	Not stated	Not stated
Pieracci 2016	3 or more	Y	Not stated	Not stated
Qiu 2016	4 or more	Y	Not stated	Not stated
Said 2014	2 or more	Y	Not stated	Not stated
Sellers 2013	4 or more	Y	Not stated	Y
Taylor 2016	3 or more	Y	Y	Not stated
Voggenreiter 1998	4 or more	Not stated	Y	Not stated
Xu 2015	3 or more	Y	Y	Not stated
Zhang 2015 a	3 or more	Y	Y	Not stated
Zhang 2015 b	Multiple	Y	Y	Not stated

3.3.5 Risk of Bias

The risk of bias in RCTs, as assessed by the Cochrane risk of bias tool, is shown in Table 22, showing two studies[19, 20] with a low risk of bias, one unclear[18] and one high.[169] Three RCTs[18-20] showed a low risk of bias for the method of randomisation. Two RCTs had a high risk of allocation bias, one due to using a randomisation chart with no evidence of concealment,[18] and the other the randomisation method was not explained.[169] The RCT by Wu et al.[169] had significant risk of bias due to lack of blinding, randomisation protocol and poor reporting. Selection bias was especially high in this trial since after the patients were randomised they were then asked to decide whether they wished to continue with the allocated treatment. It was not reported how many patients crossed over and if any intention to treat model was employed. The trial identified 956 patients with chest trauma but was highly selective about the patients for inclusion, including only male patients with ‘pure chest trauma’, and thus only 164 were randomised. Groups were unequal, out of 164 randomised patients, 75 received surgery and 89 did not. Although this trial had a high risk of bias it was still included in pooled analysis as it still represented evidence that was comparable to NRS. With these significant potential biases, however, it cannot be classed as true randomised evidence.

Table 22 Quality appraisal of RCT using Cochrane Risk of Bias Tool

	Randomisation	Allocation	Performance Bias	Detection Bias	Attrition Bias	Reporting Bias	Other Bias
Tanaka 2002	Low	High	Unclear	Unclear	Low	Unclear	Unclear
Granetzny 2005	Low	Unclear	Unclear	Unclear	Low	Unclear	Low
Marasco 2013	Low	Low	Unclear	Unclear	Low	Low	Low
Wu 2015	Unclear	High	High	Unclear	Unclear	Unclear	High

All RCTs were unclear when reporting blinding of participants, personnel and outcome assessment. Blinding in surgical trials is often difficult, blinding of outcome assessment would reduce some detection bias but, despite this, there was no report of blinding of outcome assessments in any of the RCT reports.

Attrition bias was low within the studies that reported this information; in hospital outcomes were fully reported in all studies. Granetzny et al.[19] had full follow up at two months, Marasco et al.[20] lost 4 per group for three month's spirometry follow up, and Tanaka et al.[18] lost three from the surgical group and two from the pneumatic stabilisation group at 12 months. Wu et al.[169] did not specifically report attrition, therefore this was rated as unclear, but it was assumed to be low for the acute in hospital outcomes as they are extracted from medical notes. Assessment of the criterion of reporting bias requires checking the outcomes reported against the outcomes specified by the protocol in order to determine if there was selective under reporting of data.[49] Published protocols and trial registration could not be located for Tanaka et al.[18] and Granetzny et al.,[19] but they reported all the outcomes they list in their method. Marasco et al.[20] had a published protocol that was adhered to.

Table 23 and Table 24 provides the quality assessment for each of the NRS; four NRS achieved the full score.[59, 72, 77, 92] The case control studies consistently have a high risk of bias related to their selection of controls. The processes of control selection are often not stipulated and potentially could have been selected to enhance outcomes. The indication for surgery is a potential confounder that could account for differences between groups other than the intervention received. This confounding indication is common in non-randomised studies and can be accounted for if instrumental analysis techniques are undertaken when analysing the data.[114] Most cohort studies did not control for baseline characteristics such as injury severity, age or injury type, meaning that the groups were not directly comparable. Also, historical comparator groups are unlikely to have benefitted from significant advances in prehospital and intensive care and treatment outcomes and may have differed to the more recent intervention group.

Table 23 Quality Assessment of Case Control Trials Using Newcastle-Ottawa Tool

Case Control and Historically Controlled Trials	Newcastle-Ottawa Quality Assessment Tool		
	Selection	Comparability	Exposure
Flail chest only			
Buyukkarabaca, 2015	****		***
Farquhar, 2014	**	*	***
Doben 2014	**		**
Jayle 2014	****	**	***
Flail Chest and Multiple unifocal rib fractures			
Khandelwal, 2011	**		***
Pieracci, 2016	***	**	***
Velasquez 2016		**	
Majercik, 2015a	****	**	***
Majercik, 2015b	****		***
Olsen, 2016	*		*
Qiu 2016	****		**

cp = conference proceedings, Selection - maximum score ****, Comparability – maximum score **, Exposure – maximum score ***

Table 24 Quality Assessment of Cohort Studies Trials Using Newcastle-Ottawa Tool

Cohort Studies	Newcastle-Ottawa Quality Assessment Tool		
	Selection	**Comparability**	**Exposure**
Flail chest only			
Althausen, 2011	****	**	***
Defreest, 2016	**		***
De Moya, 2011	**	*	***
Nirula 2006	****	**	***
Voggenreiter 1998	****		***
Ahmed 1995	****		***
Flail Chest and Multiple unifocal rib fractures			
Granhed 2014	***		***
Galan 1992			
Muhm, 2013	****		***
Pimakhov 2015 cp	N/A	N/A	N/A
Pimakhov 2014 cp	N/A	N/A	N/A
Solberg, 2009	***		***
Taylor, 2016	***		***
Wada 2015	***	**	***
Xu, 2015	****		***
Zhang 2015 a	****	*	***
Zhang 2015 b	****		***

cp = conference proceedings, Selection - maximum score ****, Comparability – maximum score **, Exposure – maximum score ***

One factor that could account for lack of comparability between groups is the method of selection of patients. Examples are seen in two studies where patients who failed non-operative management were then selected into the fixation group.[78, 171] Allocating patients to the surgical group based on non-operative treatment being unsuccessful, rather than randomly allocating patients to non-operative or surgical treatment at the outset, means that the patients in the surgical group are likely to be *in extremis* and more likely to have a poorer outcome (Figure 10). The operated group in this situation is disadvantaged, even before surgical management has commenced, and thus the groups are not comparable even though comparisons of demographic and injury severity show no statistically significant differences.

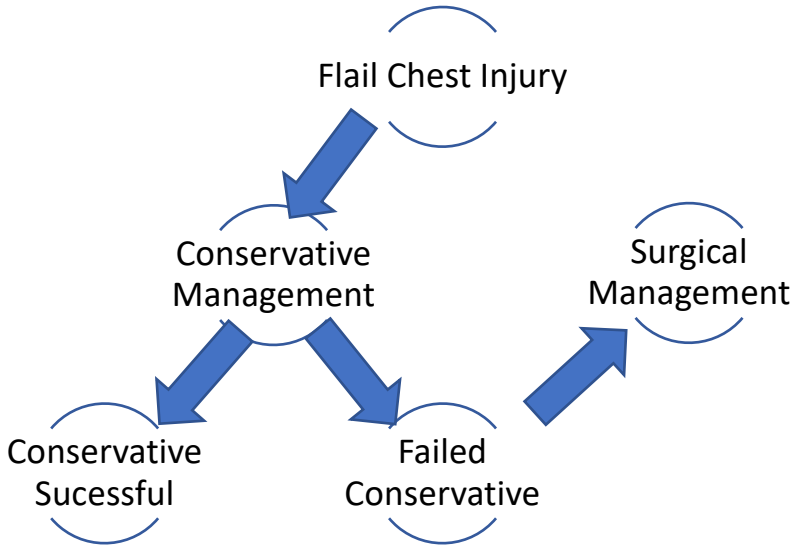


Figure 10 Patient selection in the studies by Defreest et al.[78] and Farqhuar et al.[171]

The method by which patients were selected to a non-randomised study was unclear, mostly due to lack of reporting and confusion between the reporting of an indication for surgery and the strict eligibility criteria for entry into a study. There was evidence of good comparability between groups using matched case controls in six studies, and these were generally of higher quality overall.[59, 72, 75, 92, 93, 182]

Thirty-one studies were assessed using the Joanna Briggs Institute Checklist for Case Series. Two case series were unable to be assessed as they were conference proceedings and did not give enough information to permit judgement (Table 25).[138, 141] Five studies were awarded the maximum score.[6, 162, 166, 172, 173] Several studies had low scores, indicating high risk of bias due to unclear reporting; specifically, whether the sample was consecutive and complete and whether the condition was measured in a standard way. Those case series scoring low were older studies which may have been written before current standards of reporting were widely used.[81, 175, 179] In almost all case series there was clear reporting of patient characteristics and outcomes.

Table 25 Quality assessment of Case Series using Joanna Briggs Institute Check list for Case Series Tool

Case Series	Joanna Briggs Institute Check List for Case Series									
Flail Chest	1	2	3	4	5	6	7	8	9	10
Borerelly 2005	+	+	+	+	+	+	+	+	+	+
Bottlang 2013	+	+	+	+	-	+	+	+	+	+
Ivancic 2009	+	+	+	+	+	+	+	+	+	NA
Lardoinois 2001	+	+	+	+	?	+	+	+	+	NA
Majercik 2014	+	+	+	+	-	+	+	+	+	+
Marasco Ab 2009	+	?	+	+	+	+	+	+	+	+
Marasco Ab 2014	+	+	+	+	-	+	+	+	+	?
MayberryAb 2003	+	?	+	+	+	+	+	?	+	NA
Menard 1983	?	?	?	+	?	+	+	+	+	NA
Michelitsch 2016 cp	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Moslam 2015	+	+	+	+	+	+	+	+	+	+
Mouton 1997	+	+	+	+	+	+	+	?	+	NA
Olsen 2013	+	?	?	+	-	+	+	+	+	+
Reber 1993	?	?	?	?	?	+	-	+	?	NA
Said 2014	+	+	+	?	?	+	+	-	+	?
Schmitt 1982	?	?	?	?	?	-	+	+	-	NA
Taylor 2013	-	?	?	?	?	+	+	+	?	NA
Tarng 2016	+	+	+	+	+	+	+	+	+	NA
Multiple unifocal rib fractures and flail chest										
Campbell 2009Ab	+	+	?	+	?	+	+	+	+	+
Caragounis 2016	+	+	+	+	-	+	+	+	+	+
Chai 2013	-	?	-	?	?	y	?	?	?	?
De Palma 2016	+	+	?	+	?	+	+	+	+	NA
Marasco 2016	+	+	+	+	?	+	?	+	+	NA
Mayberry 2009	+	+	+	?	?	+	+	+	+	+
Metin 2016	+	+	?	?	?	+	+	+	+	+
Nickerson 2015	+	+	+	?	?	+	+	+	+	+
Nickerson 2016	+	+	+	+	+	+	+	+	+	+
Redwan 2015 cp	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Sellers 2013	+	+	+	+	-	+	+	+	+	NA
Theils 2016	+	+	+	?	?	+	+	+	+	+
Wiese 2015	+	?	?	?	?	+	+	+	+	+
Yang 2010	-	?	?	?	-	+	+	+	+	+

cp = conference proceedings, ab = absorbable

+ yes - no ? unclear

1. Were there clear criteria for inclusion in the case series?
2. Was the condition measured in a standard, reliable way for all participants included in the case series?
3. Were valid methods used for identification of the condition for all participants included in the case series?
4. Did the case series have consecutive inclusion of participants?
5. Did the case series have complete inclusion of participants?
6. Was there clear reporting of the demographics of the participants in the study?
7. Was there clear reporting of clinical information of the participants?
8. Were the outcomes or follow up results of cases clearly reported?
9. Was there clear reporting of the presenting site(s)/clinic(s) demographic information?
10. Was statistical analysis appropriate?

3.3.6 Effectiveness

Meta-analysis was undertaken for six outcomes and these are reported individually in separate sections with a description of how they were measured. Four studies were not suitable for pooling in meta-analysis since they did not report sufficient information. These included two conference proceedings,[139, 140] one study that did not clearly distinguish outcomes between their fixation and non-fixation groups[183] and one that reported outcomes that were not reported by others.[181] All other studies were included in the meta-analysis; there was no quality threshold for studies to be excluded.

This synthesis included the overall pooling and two different subgroup analyses. The first section discusses overall effectiveness and the first subgroup by type of injury, FC only versus FC+MURF. The subsequent section 3.3.7 reports the second subgroup analysis investigating the timing of surgery, early versus late fixation. Summary tables of the meta-analysis are shown in the text (Table 26) with outcome tables presented in Appendix B2 and the forest plots reported in Appendix B3.

Summarising the results in Table 26 all outcomes favoured rib fracture fixation however, there was considerable heterogeneity within several outcomes including invasive mechanical ventilation, length of ICU stay and length of hospital stay. There was minimal overall heterogeneity in outcomes mortality and tracheostomy. There were statistically significant subgroup differences between the FC and FC+MURF for the outcome length of mechanical ventilation suggesting there is a difference in outcomes for the different injury types. There were no other statistically significant differences between the two injury types within the other outcomes.

Table 26 Meta-analysis results for overall effectiveness and subgroups FC and FC+MURF

Group	Mean difference	Lower CI	Upper CI	I^2	Favours	Subgroup differences	
						I^2	p value
Total length of mechanical ventilation (days)							
Overall (n=20)	-4.03	-5.48	-2.58	80%	Rib fixation		
FC (n=14)	-2.58	-4.39	-0.78	73%	Rib fixation	90.3%	0.001
FC+MURF(n=6)	-6.57	-8.21	-4.94	66%	Rib fixation		
Total length of stay in ICU (days)							
Overall (n=20)	-3.27	-4.78	-1.76	84%	Rib fixation		
FC (n=15)	-2.87	-4.88	-0.85	78%	Rib fixation	0%	0.41
FC+MURF(n=5)	-4.27	-6.94	-1.61	92%	Rib fixation		
Total hospital length of stay (days)							
Overall(n=15)	-2.53	-5.66	0.61	88%	Rib fixation		
FC (n=12)	-0.61	-3.71	2.50	66%	Rib fixation	59%	0.12
FC+MURF(n=3)	-7.62	-15.85	0.62	97%	Rib fixation		
Outcome	**Risk Ratio**	**Lower CI**	**Upper CI**	I^2	**Favours**	**Subgroup differences**	
						I^2	p value
Mortality							
Overall (n=17)	0.39	0.24	0.64	0%	Rib fixation		
FC (n=11)	0.26	0.13	0.51	0%	Rib fixation	64.1%	0.10
FC+MURF(n=6)	0.59	0.29	1.19	0%	Rib fixation		
Pneumonia							
Overall(n=14)	0.67	0.48	0.95	65%	Rib fixation		
FC (n=8)	0.74	0.40	1.39	74%	Rib fixation	0%	0.58
FC+MURF(n=6)	0.61	0.43	0.86	44%	Rib fixation		
Tracheostomy							
Overall(n=9)	0.50	0.38	0.65	0%	Rib fixation		
FC(n=6)	0.44	0.31	0.63	0%	Rib fixation	0%	0.46
FC+MURF(n=3)	0.57	0.32	0.98	29%	Rib fixation		

I^2 –the percentage variation across studies that is due to heterogeneity not due to chance.
I^2 subgroup differences the percentage variation between the subgroups that due to heterogeneity and not due to chance

3.3.6.1 Length of mechanical ventilation

How was the outcome measured?

Invasive Mechanical Ventilation (IMV) is used in patients with blunt chest trauma to support the mechanical work of breathing when the biomechanics of the chest are compromised or if the patient is in too much discomfort to perform sustainable ventilation. Mechanical ventilation should be used sparingly due to the complications of long-term use.[17] Length of mechanical ventilation is a good outcome measure to show improvement from rib fracture surgery since the reduction in this time reduces the complications of long-term use. Mechanical ventilation is also costly, requiring 24 hour one-to-one nursing care, as well as significant costs of drugs and equipment. Mechanical ventilation is often required for other injuries sustained within the presence of major trauma. For example, head injuries often require extended ventilator periods. Most papers excluded patients with significant head injuries, however, hence mechanical ventilation should only be required for the chest injury.

The threshold or indication for when patients require the support of IMV could affect the measurement of this outcome since certain clinicians may be liberal with the use of IMV while others may only use it in extremis. A clear indication or protocol for the instigation of IMV was documented in only one RCT[18] and 2 NRS.[65, 92] A clear protocol for mechanical weaning was reported in two RCTs[18, 20] and three NRS,[71, 92, 170] but, as with instigation of IMV, the discontinuation of IMV could vary widely between clinicians, hospitals and regions. It is assumed that the patients were not kept on mechanical ventilation for longer than needed but whether this was standardised is unknown.

Length of mechanical ventilation was measured from several different time points including as the time from when it was deemed needed and also as the time from surgery. All data reported was converted into time in days. The inclusion criteria in most studies required the need for IMV at the outset, however other studies had some patients who did not have any IMV pre-treatment. Between 55% and 76% of the intervention group required mechanical ventilation compared to the control groups, which required a higher percentage of ventilation, between 63% and 91%. The number of patients requiring mechanical ventilation was described in only two

studies.[157, 184] It was not clear whether the higher ventilation requirement was due to the control group initially being more severely injured or whether it was due to deterioration in condition due to treatment type, but the former could bias results in favour of the fixation group. One study changed their inclusion criteria halfway through their study due to seeing good results in patients who required IMV at the outset and started to include patients as soon as they required non-invasive mechanical ventilation.[71]

Since 1995 (the earliest study with a control group), patients receiving surgical fixation and non-operative care were spending less time on mechanical ventilation (Figure 39 in Appendix B2), most likely due to a change in evidenced-based practice. In the 1990s there was a trend to use mechanical ventilation for all flail chest injuries; the high risk of ventilator-associated complications, in particular pneumonia, is likely to have informed the reduction in the use of IMV since, however.[191, 192] Also local and regional anaesthetic interventions have been introduced since the 1990s and now appear to be part of many routine non-operative protocols.[73] Improvements in the techniques used in surgical intervention and in the timing of the intervention are also likely to have contributed to the reduction in mechanical ventilation time.

3.3.6.1.1 Randomised control trials and non-randomised studies

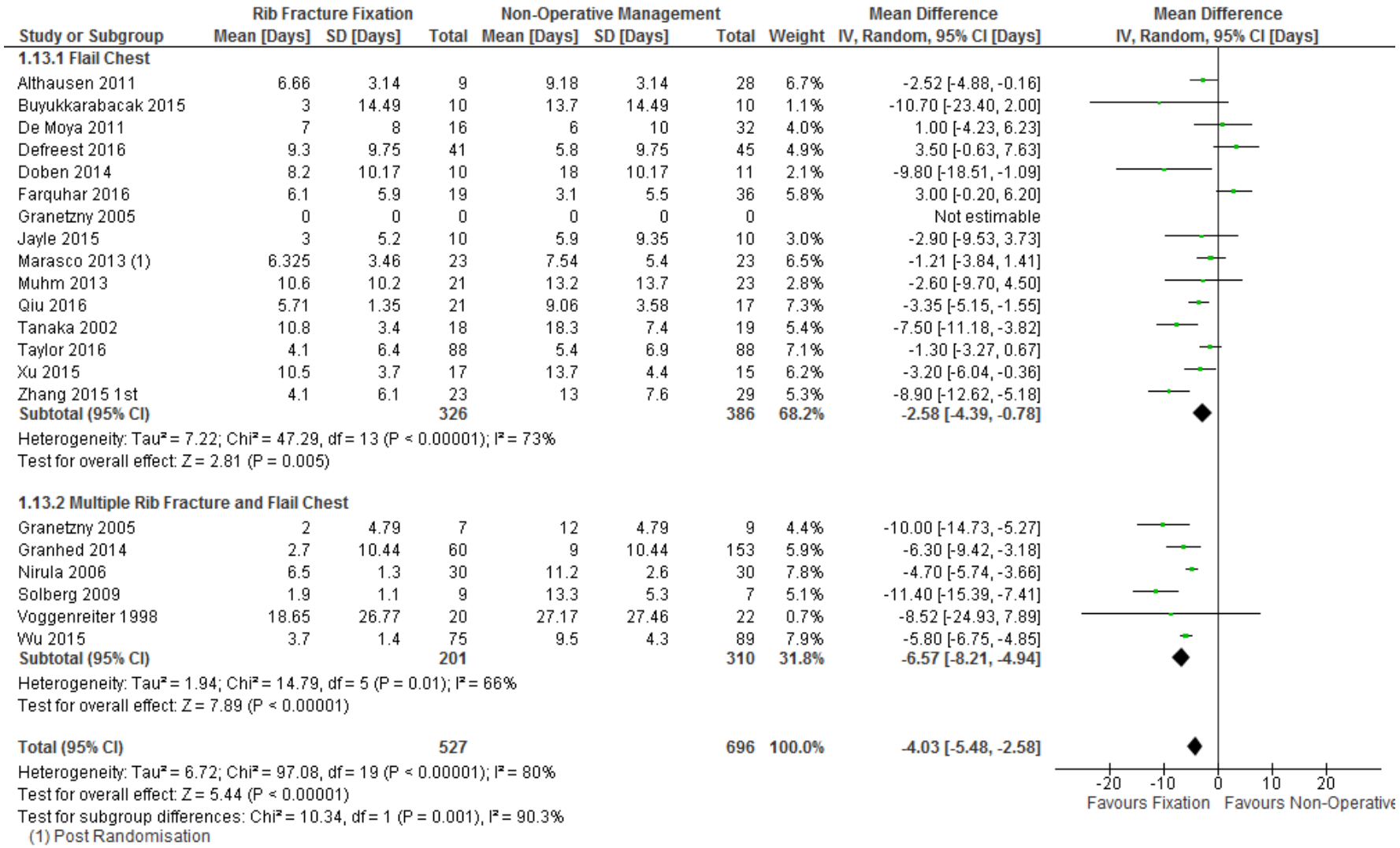
Overall, the surgical rib fixation group showed fewer days on mechanical ventilation in total than the non-operative group (Figure 11): mean difference -4.03 days, 95% CI [-5.48,-2.58], Heterogeneity was considerable, however, suggesting that the estimate is unlikely to be generalisable (I^2 = 80%).

Seventeen studies showed an improvement in total mechanical ventilation time with surgical intervention; three studies favoured non-operative management.[69, 78, 171]

Values were imputed in six studies, allowing their inclusion in the analysis (Appendix B3, Table 74).[19, 70, 71, 78, 92, 170] The paper by Voggenreiter et al.[65] separated their participants into those with pulmonary contusion and those without; the patients were pooled as these were not considered separately in other papers. When considered separately, the mean difference (MD) for the outcome in this study was +1.5 days in the contused group in favour of the control group and -20.2 days in the non-contused group in favour of surgical fixation.

Imputations were not possible in three studies. In the surgical versus the non-operative groups, respectively: Pieracci et al.[73] reported a median of 0 versus 5 days; Zhang et al.[74] 8 days versus 7 days; Ahmed et al.[64] 3.9 days versus 15 days.

Figure 11 Meta-analysis for outcome length of mechanical ventilation with subgroups FC and FC+MURF



3.3.6.1.2 Subgroup analysis FC versus FC+MURF

Subgroup analysis was undertaken to compare studies reporting flail chest only (FC) and those reporting both multiple unifocal rib fractures and flail chest (FC+MURF). There was a significant difference in length of IMV between the two groups (chi^2 = 10.34, df = 1, p = 0.001, I^2 = 90.3%).

Despite subgroup analysis of FC and FC+MURF substantial heterogeneity remained within subgroups (FC: chi^2 =47.29, df =13, p=0.00001, I^2 = 73% and FC+MURF: chi^2 =14.79, df = 5, p = 0.01, I^2 = 66%).

The subgroup FC+MURF had significantly fewer days on IMV in the rib fracture fixation compared to non-operative management with a MD -6.57, 95% CI [-8.21,-4.94]. The subgroup with FC had fewer days on IMV in the rib fracture fixation compared to non-operative management with a MD -2.58, 95% CI [-4.39, -0.78].

3.3.6.1.3 Case Series

Eleven case series reported the length of IMV post-surgery, eight included FC patients only with a mean length of IMV post-surgery ranging from 0.27 to 6.4 days.[81, 143, 158, 161, 163, 164, 172, 175] Three case series reported IMV post-surgery in patients with FC+MURF; recording a mean of 2.5 days, median 15 days and median 2.1 days, respectively(Table 73).[84, 166, 176]

Two case series reported total length of IMV in patients with FC+MURF; with means of 5.8 and 6.42 days respectively (Table 74).[6, 166] Papers reporting median and interquartile values most often showed a positive skew with most patients very quickly coming off mechanical ventilation and a minority requiring longer term ventilation.

3.3.6.2 Length of Stay in Intensive Care Unit

How was the outcome measured?

Length of Intensive Care Unit (ICU) stay is often related to IMV time since it is often the only setting in which IMV can take place. ICU stay may be extended longer than IMV time due to other factors such a concomitant injuries, sepsis and hemodynamic instability. It is an area where nursing to patient ratios are higher and invasive monitoring can occur. ICU care is expensive and reducing these costs would be beneficial as a societal cost as well as showing improved patient outcomes. Clear ICU discharge criteria were only documented in two NRS,[64, 156] but it is assumed that patients were not kept in ICU or discharged from ICU quicker or longer than what was required. Lack of reported concealment within RCTs and case control series were inevitable since ICU clinicians would know treatment allocation. There could be bias associated with this that could lead to disparities between groups if no clear prospective discharge policy was adhered to. Although other injuries could have prevented discharge from ICU this was mainly addressed by excluding patients with severe head spinal or pelvic injuries.

Length of ICU stay was measured as two separate time points; total time in ICU (Appendix B2 Table 75 and Table 76) and time in ICU post-surgery (Table 77). All data reported was converted into time in days. Time in ICU varied widely within studies, with patients either being discharged very early or requiring an extended period in ICU. Despite the likelihood of positively skewed data, very few studies with a control group reported medians and interquartile ranges. Case series reported statistical finding as medians and interquartile ranges and showed that the data was most often positively skewed. Unlike IMV, the ICU length of stay has not particularly altered over time (Appendix B2 Figure 40).

3.3.6.2.1 Randomised control trials and non-randomised studies

The overall effectiveness in the pooled meta-analysis was -3.27 days, 95% CI [-4.78, -1.76] in favour of surgical fixation compared to non-operative management (Figure 12). There was substantial heterogeneity overall, however, with I^2 = 84%. Sixteen studies showed a shorter ICU stay on average with surgical fixation. The same three studies that indicated that non-operative management resulted in shorter IMV duration were also in favour of the control group for length of ICU stay.[69, 78, 171] This corroborates the associations seen in relation to mechanical ventilation and ICU stay.

Four studies required standard deviations to be imputed as they were not reported.[71, 78, 92, 170] Three studies could not be imputed and pooled due to lack of data.[64, 73, 74] The study by Pieracci et al. showed a difference in median length of stay in ICU with values of six days in the plate fixation group and nine days in the control group.[73] Zhang et al.[74] was in favour of the control group with a length of stay of 21.5 days, whereas strut fixation had a longer median stay of 24.5 days. Ahmed et al. did not report any P values or confidence intervals to be able to impute standard deviations, but the mean days were significantly higher in the non-operative group than the fixation group, 21 days versus nine days respectively (Appendix B2 Table 75).[64]

One RCT[18] and one NSR[92] reported time in ICU post-surgery in patients with FC, reporting a mean time of 9.2 days and 2.68 days respectively. Only one study reported ICU time post-surgical fixation with FC+MURF the mean was 11.7 days and range 0 to 33 days.[184]

3.3.6.2.2 Subgroup analysis FC versus FC+MURF

Subgroup analysis was undertaken to compare studies reporting flail chest only[18, 20, 69, 71, 72, 76, 78, 92, 95, 164, 168, 170, 171, 184] and those reporting both multiple unifocal rib fractures and flail chest[19, 59, 77, 156, 169] (Figure 12) Despite the subgroup analysis of FC and FC+MURF in attempt to reduce clinical heterogeneity, substantial statistical heterogeneity remained within the subgroups. Comparing surgical fixation to non-operative management the FC group had an ICU stay of -2.87 days, 95% CI [-4.88, -0.85], I^2 = 78% and the FC+MURF group had an ICU stay of -4.27 days, 95% CI [-6.94, -1.61], I^2 = 92%. Both subgroups were independently in favour of surgical fixation compared to non-operative management and these values were statistically significant. There was no statistically significant difference in length of ICU stay between the subgroups (chi^2 =0.68, df=1, p=0.41), I^2= 0%

Although significant statistical heterogeneity was found between all the studies, the overall direction, apart from the three studies described [69, 78, 171], was in favour of surgical fixation. The severity of injuries vary between studies, creating clinical heterogeneity that may explain part of the overall statistical heterogeneity seen between the studies.

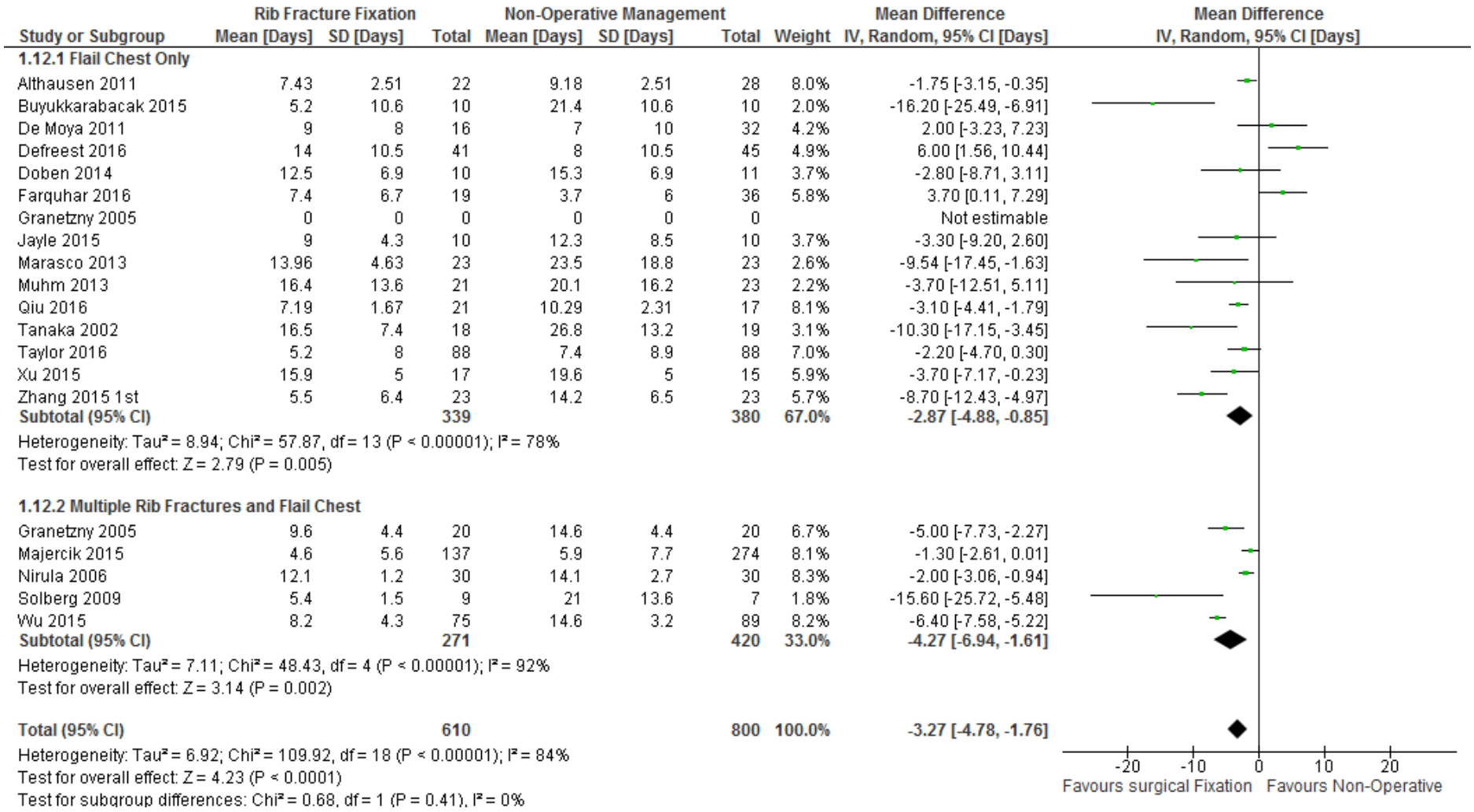
3.3.6.2.3 Case Series

Twelve studies[82, 84, 87, 99, 158, 162, 163, 166, 175, 176, 186, 187] measured total length of ICU stay (Appendix B2 Table 76); and seven studies[18, 92, 143, 159, 164, 172, 184] measured time after surgical fixation (Table 77).

Total time in ICU in FC patients was on average around 1 week (mean 6 to 8 days), minimum stay was 1 day[82, 84] and maximum stay was 48 days.[82] Median values were reported in the FC+MURF group and were lower (1 to 3 days, except one outlier of 16.9 days[176]) the minimum value was 0 and the maximum value was 29 days.

In the FC only group the mean time in ICU post-surgery ranged from 3.93 days[172] to 5.2 days,[164] median values were between 1 day[159] and 6 days[143] and the maximum time in one study was 111 days[143]. Several studies had patients that did not require an ICU admission post operatively.[164, 184, 186]. No case series reported time in ICU post-surgery with FC+MURF.

Figure 12 Meta-analysis for outcome total length of ICU stay with subgroups of flail chest only and FC+MURF



3.3.6.3 Length of hospital Stay

How was the outcome measured?

The length of hospital stay can be a marker of chest trauma severity, but factors such as rehabilitation facilities, step down to community hospitals and rehabilitation facilities and available social support may affect this outcome. In well-designed studies these factors should be balanced in both the intervention and non-operative management groups. As discussed with previous outcomes, those patients who had other severe brain, spinal and pelvic injuries were mostly excluded from studies so that the dominating injury was that to the chest. Length of hospital stay was measured in three RCTs[19, 20, 169], 14 NRS studies[59, 69, 71-75, 77, 78, 92, 157, 170, 171, 184] and 17 case series.[84, 87, 99, 158, 159, 162-166, 175, 176, 178, 186, 187] All data reported was converted into time in days.

3.3.6.3.1 Randomised control trials and non-randomised studies

The pooled analysis of all studies showed an overall improvement with surgical fixation (Figure 13) but this was not statistically significant and had substantial heterogeneity -2.53 days, 95% CI [-5.66, 0.61] I^2= 88%. Nine studies showed a reduction in the length of hospital stay with fixation compared to non-operative management.[19, 59, 71, 72, 92, 93, 157, 169, 170] Five studies were in favour of non-operative management, and three of these studies also did not show improvement of IMV and ICU length of stay with surgical fixation.[69, 78, 171] Only the study by Defreest et al.[78] was statistically significant and in favour of non-operative management. Two further studies by Muhm et al.[184] and Marasco et al.[20] were minimally in favour of non-operative management but had wide confidence intervals and were not statistically significant MD 1.8 days, 95% CI [-8.23, 11.83] and MD 1 day, 95% CI [-9.70, 11.70] respectively (Figure 13).

Five studies required imputation of standard deviations (Appendix B2, Table 78).[19, 71, 78, 92, 170] Three studies reported only median values, namely for fixation 38 days versus control of 60 days,[74] fixation, 33 days versus control, 42 days,[75] and fixation 13 days versus control 16 days.[73] These results could not be pooled. The RCT by Marasco et al.[20] reported both mean and median values. In this study, the mean difference was in favour of the control group, with those subject to fixation staying in hospital for 26 days versus 25 days for the control. The median values from the same data, however, indicated that the fixation group had a hospital

length of stay of 20 days and the control group 25 days. This highlights again the positive skew of the data and the potential limitation of using the mean difference. The median and interquartile ranges show a positive data skew in all studies who report them for this outcome and therefore the mean values reported may not be as representative.

3.3.6.3.2 Subgroup analysis FC versus FC+MURF

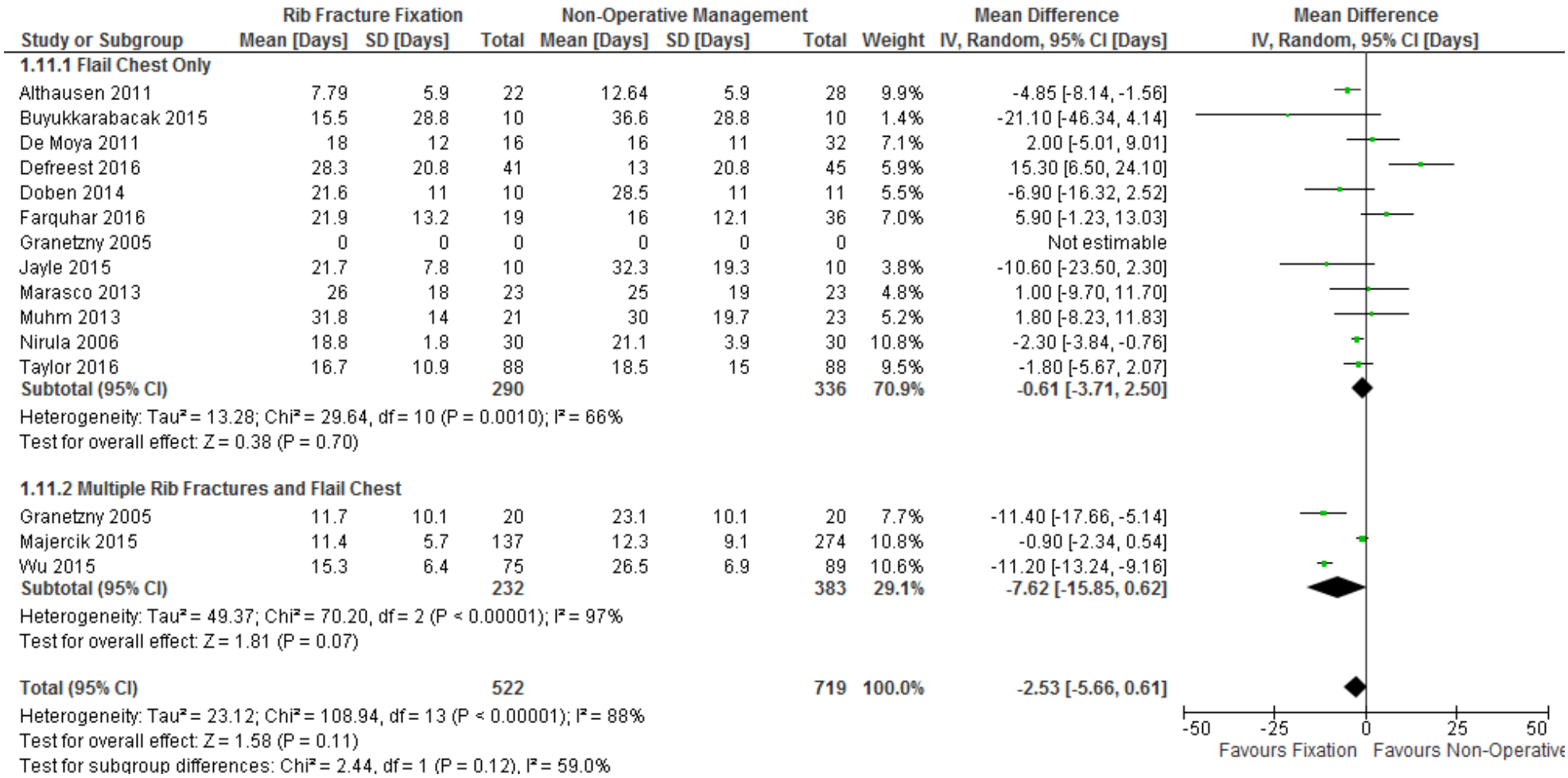
Subgroup analysis was undertaken to compare studies reporting flail chest only (FC) and those reporting both multiple unifocal rib fractures and flail chest (FC+MURF). Despite the subgroup analysis of FC and FC+MURF in attempt to reduce clinical heterogeneity, substantial statistical heterogeneity remained within the subgroups. The pooled subgroup analysis of those with FC+MURF was -7.62 days, 95% CI [-15.85, 0.62], I^2 = 97% and those with FC only was -0.61 days, 95% CI [-3.71, 2.50], I^2 = 66%. When the subgroups were compared there was no statistically significant difference in length of hospital stay between the two groups (chi^2 =2.44, df=1, p=0.12), I^2= 59%. The length of hospital stay was shorter in those in the FC+MURF subgroup compared to FC only, although confidence intervals overlapped and neither were statistically significant individually. Only three studies are pooled in the FC+MURF subgroup and substantial statistical heterogeneity was again evident, due to the narrow confidence intervals of these studies and relatively large sample sizes.[19, 77, 169]

3.3.6.3.3 Case Series

Nine studies[84, 158, 162-164, 166, 175, 176, 178] reported length of hospital stay in those with FC only and eight with FC+MURF[87, 99, 159, 165, 178, 186, 187] (Appendix B2 Table 79). Median values were most often reported within the case series, suggesting that the data is not normally distributed. In the FC only group length of hospital stay ranged from a lower quartile of two days[162] to a maximum length of stay for one patient of 80 days.[175] Mean time in hospital ranged from 9 days[163] to 18.4 days[158] and median values from 10 days[162] to 25.4 days.[176]

In the FC+MURF only group hospital length of stay ranged from a lower quartile of two days[99] to a maximum length of stay for one patient of 129 days.[186] Mean time in hospital was reported by one study at 6.47 days[188] and median values ranged from 8 days[159] to 13.5 days.[87] Interquartile ranges within the case series showed a positive skew suggesting that most patients were discharged early but a few patients required extended stays.

Figure 13 Meta-analysis for outcome length of hospital stay with subgroups of Flail chest only and FC+MURF



3.3.6.4 Mortality

How was the outcome measured?

Mortality was measured in three RCTs,[19, 20, 169] 13 control studies[64, 65, 73-76, 78, 95, 157, 168, 170, 171, 184] and 14 case series[6, 81, 82, 84, 142, 163, 166, 175, 176, 178, 179, 186, 187, 189] (Appendix B2 Table 80 and Table 81). Four studies gave a time frame of either 30 day[84, 178], 28 day[75] or 10 day[75] mortality rate. All other studies did not specify a time frame, however it was assumed to be an 'in hospital' mortality rate. Overall mortality has decreased since the 1980s due to a combination of factors including the introduction of ATLS, modern local anaesthetic block techniques, damage control orthopaedic surgery and modern rehabilitation techniques (Figure 42). Improvements have therefore been seen in both surgical fixation as well as non-operative patients.

3.3.6.4.1 Randomised control trials and non-randomised studies

The overall pooled analysis showed a statistically significant lower mortality rate in the surgical fixation group compared to the non-operative management risk ratio 0.39, 95% CI [0.24, 0.64] I^2 = 0%; (Figure 14). Overall heterogeneity was low with the studies having confidence intervals that all overlapped.

Twelve studies showed an improvement in mortality rate in the surgical fixation group compared to non-operative treatment (Appendix B2, Table 80).[19, 20, 64, 65, 74, 76, 78, 157, 168-170, 184] Two studies favoured non-operative management to surgical fixation.[75, 171]

In NRS it is important that the intervention and control groups are comparable, and one way of doing this is by using propensity score matching, which was completed by one study.[75]The study by Wada et al.[75] looked at multiple methods of fixation and did not show an improvement in mortality at 28 days in patients with multiple unifocal rib fractures and flail chest. This was a relatively large study with 84 surgical patients and 366 non-operative patients. The study used a 1:4 propensity matched case analysis and also excluded patients with other significant injuries. Since this was using 'real world' data from all types of hospitals, including those who potentially do not routinely undertake rib fracture fixation, it may not reflect the results achieved at specialist centres. Patients were excluded if the hospital they attended had less than one patient who had rib fracture fixation, if they died within ten days of admission and if surgical fixation occurred more than ten days after

admission. There may have been multiple other patients who may have been excluded who in fact died prior to day ten and therefore the mortality rate is lower than expected in both groups and not representative.

3.3.6.4.2 Subgroup analysis FC versus FC+MURF

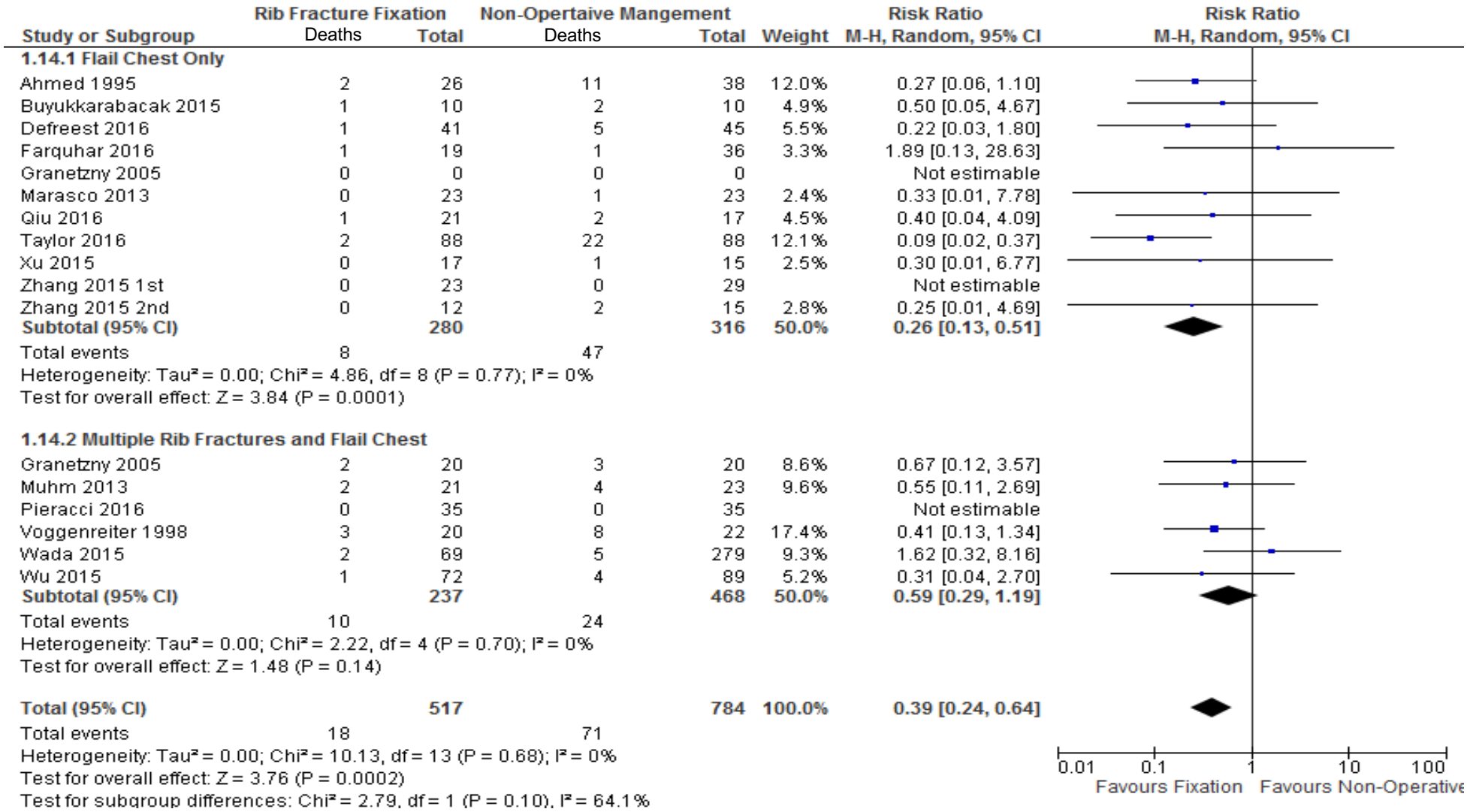
Risk ratios were calculated for NRS and are presented in a meta-analysis subgrouped by FC only and FC+MURF (Figure 14).

Subgroup analysis of FC and FC+MURF showed no heterogeneity within subgroups. The FC only group had a lower mortality rate in their fixation group compared to their non-operative group and was statistically significant with an RR of 0.26, 95% CI [0.13, 0.51] , I^2 = 0%.The FC+MURF also had a lower mortality rate in their fixation group compared to their non-operative group but this was not statistically significant with an RR of 0.59, 95% CI [0.29,1.19], I^2 = 0%) There was no significant difference between the two groups (chi^2 =2.79, df=1, p=0.10, I^2=64.1%).

3.3.6.4.3 Case Series

Ten case series[6, 81, 82, 84, 142, 163, 166, 175, 176, 178] looked at FC only and four[179, 186, 187, 189] looked at FC+MURF (Appendix B2, Table 81). In the FC only group, mortality rates ranged from 0- 28% and in the FC+MURF they ranged from 0-30%.

Figure 14 Meta-analysis for outcome mortality with subgroups of flail chest only and FC+MURF



3.3.6.5 Pneumonia

How was the outcome measured?

Three RCTs,[18-20] 11 NRS[69, 72, 73, 76, 78, 92, 95, 157, 170, 171, 184] and 14 case series studies[70, 81, 84, 158, 159, 162, 163, 175, 178, 187] report the incidence of pneumonia. Most reported the overall pneumonia rate for the hospital episode, although one study reported the rate at 7 and 21 days.[18] A lack of definition of pneumonia or respiratory infection reduces the reliability of this outcome measure in some studies. Three out of the four RCTs defined pneumonia, including: *' a new infiltrate on chest x-ray, with positive sputum culture'* was the definition by Marasco et al.[20], *'According to the patients' temperature, nature of sputum, lung examination combined with imaging examination results determine presence of lung infection, and deciding whether antibiotic treatment is needed'* was the definition used by Wu et al.[169] Tanaka et al.[18] used the definition *'the following criteria: purulent expectorate or end-tracheal aspirate from which known pathogens were grown (> 105/mL), continued high fever (38°C), leukocytosis (>10,000/μL), and recent infiltrate shadows on chest radiograph'*. Although similar, these definitions are not entirely comparable leading to potential differences between studies. Within the meta-analysis, six studies[20, 69, 73, 78, 92, 184] had a specified definition and five did not.[74, 76, 157, 170, 171]

3.3.6.5.1 Randomised control trials and non-randomised studies

The pooled meta-analysis showed a statistically significant lower rate of pneumonia in those with surgical fixation compared to non-operative management, with an RR of 0.67, 95% CI [0.48, 0.95] (Figure 15). The pooled analysis showed moderate to substantial heterogeneity I^2 = 65%.

The rate of pneumonia ranged from 0% to 63% in the fixation group. In the non-operative group the rate ranged from 22% to 93%. Nine studies showed an improvement in the pneumonia rate in the fixation group compared to the non-operative group.[18-20, 69, 73, 76, 92, 95, 157, 170] Three studies,[72, 78, 184] two[78, 184] of which had comprehensive definitions of pneumonia, were in favour of non-operative management compared to fixation.

3.3.6.5.2 Subgroup analysis FC versus FC+MURF

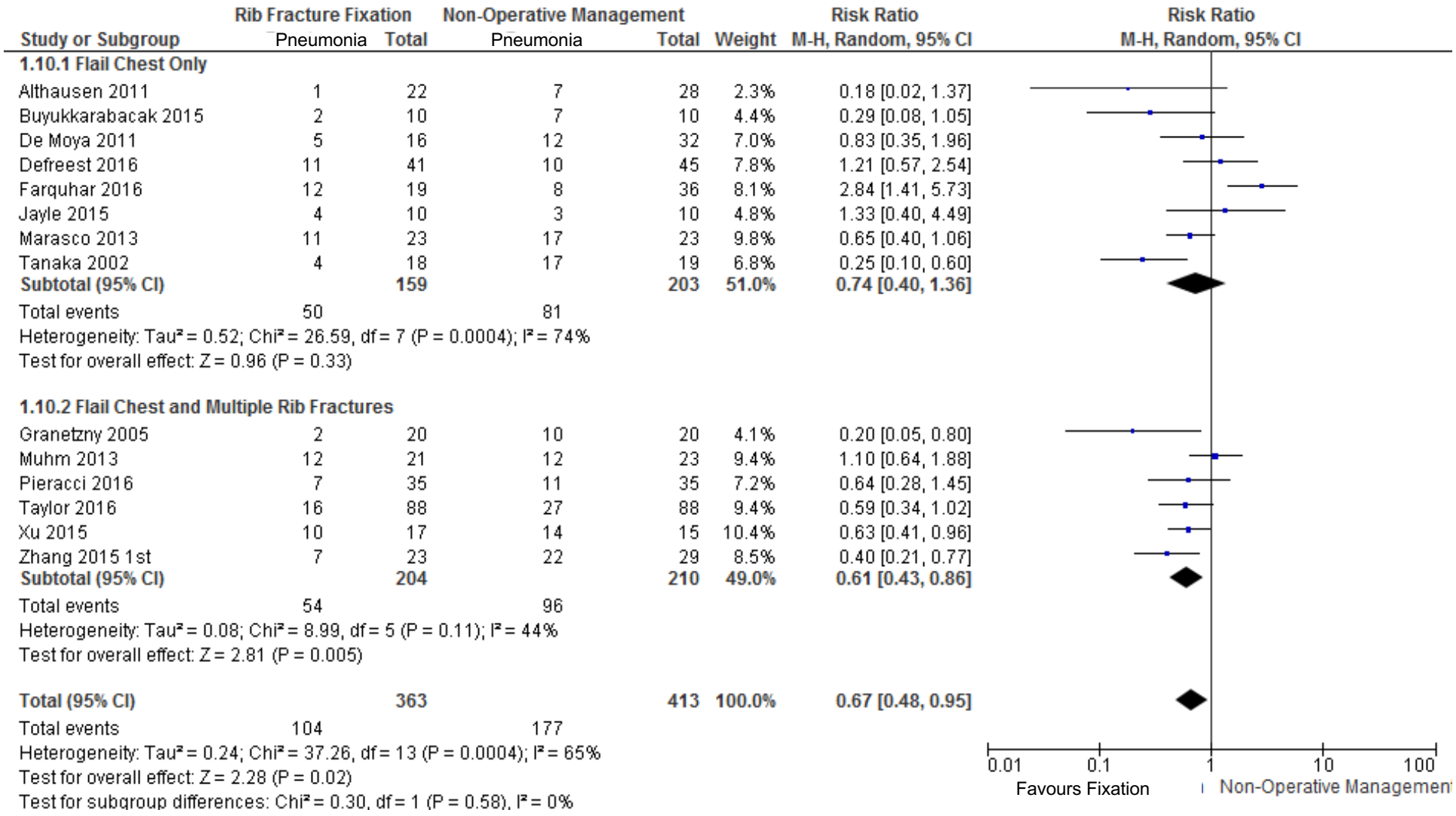
Subgroup analysis was undertaken to compare studies reporting flail chest only[18, 20, 69, 72, 78, 92, 170, 171] (FC) and those reporting both multiple unifocal rib fractures and flail chest[19, 73, 76, 95, 157, 184] (FC+MURF).

Despite subgroup analysis of FC and FC+MURF, substantial heterogeneity remained within subgroups. In the FC only subgroup the pneumonia rate was less in the fixation group than in the non-operative group, with an RR of 0.74, 95% CI [0.40, 1.36], I^2 = 74% (Figure 15). In FC+MURF there was a statistically significant reduction in the pneumonia rate in the fixation group compared to the non-operative group, with an RR of 0.61, 95% CI [0.43, 0.86] , I^2 = 44%. There were no statistically significant differences between the two groups (chi^2 =0.30, df=1, p=0.58), I^2= 0%.

3.3.6.5.3 Case Series

Seven case series[81, 84, 158, 162, 163, 175, 178] reported FC only and three case series[70, 159, 187] reported FC+MURF (Appendix B2, Table 83). In the FC only group pneumonia rates ranged from 6%[178] to 38%.[175] In the FC+MURF group pneumonia rates ranged from 0%[70] to 15.6%.[187]

Figure 15 Meta-analysis for outcome pneumonia with subgroups of flail chest only and FC+MURF



3.3.6.6 Tracheostomy

How was the outcome measured?

Three RCTs,[18, 20, 169] six NRS[73, 74, 76, 92, 157, 184] and four case series[161, 163, 164, 166] report the rate of tracheostomy placement. Tanaka et al.[18] reported the rate at 7 days and at 28 days, all other studies reported the overall rate. The presence of a tracheostomy is easy to record, the judgement of the need for the tracheostomy placement is more complex, however. The placement of tracheostomy was protocol driven in the study by Marasco et al.[20] and defined as:

> *An assessment by the treating physician after 7 days of mechanical ventilation that deemed the patient was unlikely to wean in 2-3 days prompted insertion of a tracheostomy.*

This may be quite an arbitrary protocol and it is unlikely that assessors could be reliably blinded. Pieracci et al.[73] left the decision up to the attending surgical intensivists. No other study defined their tracheostomy insertion protocol, making the measurement of this outcome unstandardised. Blinding of assessors would be desirable to reduce assessment otherwise known as detection bias however in real word practice this is not feasible as the treating team would know treatment allocation. To help negate assessment bias a protocol to initiate and cease tracheostomy treatment should be in place so there is transparency in measuring this outcome. It is normal practice to assess patients for tracheostomy insertion on a case-by-case basis, however, and so, pragmatically, this could reflect 'real world practice' rather than 'test conditions'. Despite the lack of standardised protocols, and lack of blinding, this is still an important outcome to measure since placement of a tracheostomy can cause significant long-term morbidity and has its own complications.

3.3.6.6.1 Randomised control trials and non-randomised studies

The overall pooled analysis risk ratio showed a statistically significant lower rate of tracheostomy in the surgical fixation group compared to the non-operative group, with an RR of 0.5, 95% CI [0.38, 0.65], The overall heterogeneity was low I^2= 0% (Figure 16). The rate of tracheostomy ranged from 0% to 39% in the intervention group and from 7.9% to 78.9% in the control group (Appendix B2, Table 84). All studies had a lower tracheostomy rate in their fixation group compared to their non-operative group. Nine studies[18, 20, 73, 74, 76, 92, 157, 169, 184] showed a lower

tracheostomy rate in favour of surgical fixation compared to non-operative management.

3.3.6.6.2 Subgroup analysis FC versus FC+MURF

Subgroup analysis was undertaken to compare studies reporting flail chest only[18, 20, 74, 76, 92, 157] and those reporting both multiple unifocal rib fractures and flail chest.[73, 169, 184]

Subgroup analysis of FC and FC+MURF showed minimal heterogeneity within subgroups (FC: chi^2 =3.30, df=5, p=0.65, I^2 = 29% versus FC+MURF:chi^2 =2.81, df=2, p=0.25, I^2 = 0%)

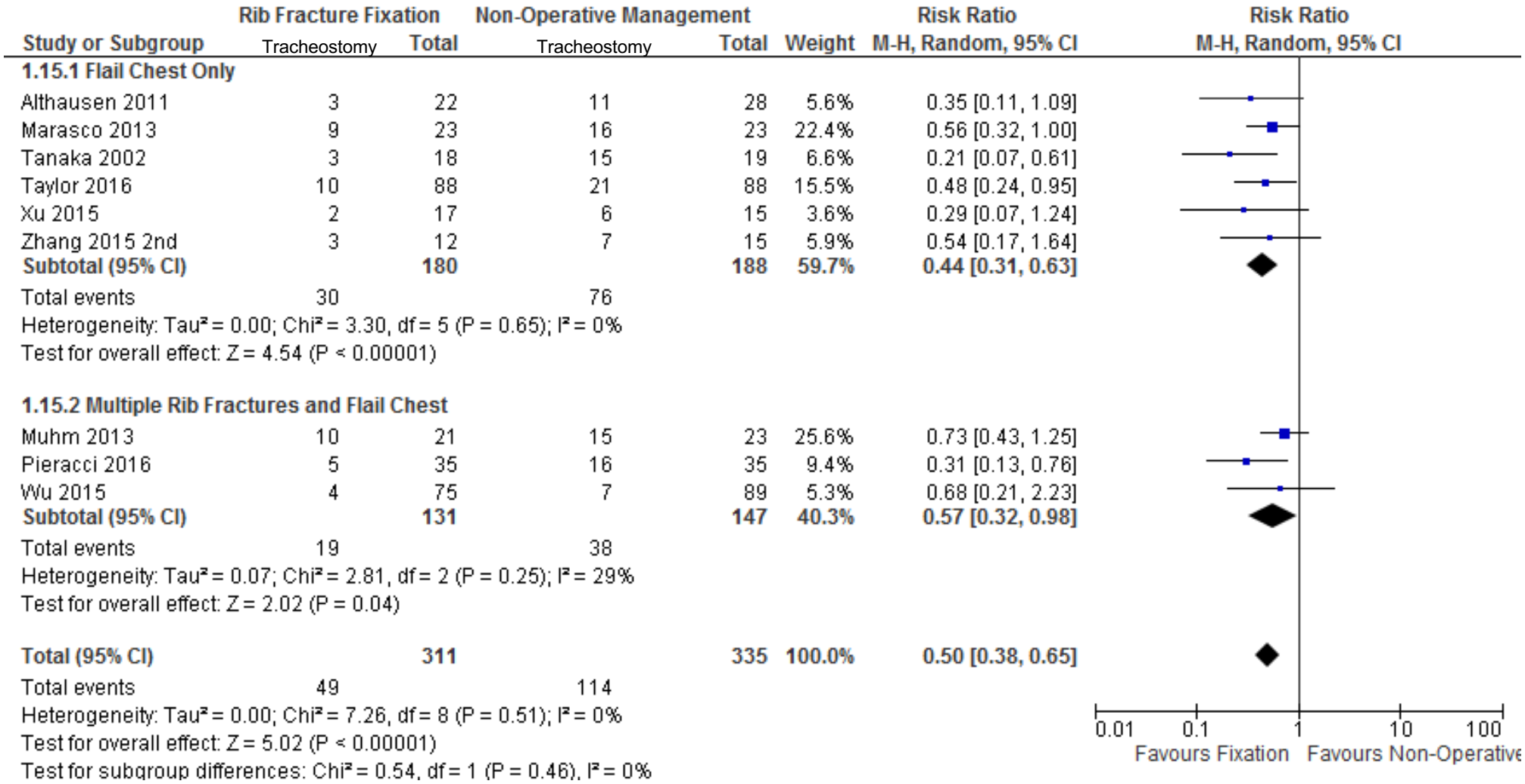
The subgroup analysis of FC only had a lower rate of tracheostomy in the fixation subgroup compared to the non-operative group RR 0.44, 95% CI [0.31, 0.63] (Figure 16). The FC+MURF subgroup was also in favour of fixation compared to non-operative treatment, RR 0.57, 95% CI [0.32, 0.98].

There was no statistically significant difference between the two groups (chi^2 =0.54, df=1, p=0.46), I^2= 0%.

3.3.6.6.3 Case Series

Four case series[161, 163, 164, 166] reported FC only and there were no case series that reported FC+MUR. Tracheostomy rates ranged from 0%[166] to 20%[161] (Appendix B2, Table 85)

Figure 16 Meta-analysis for outcome tracheostomy with subgroups of flail chest only and FC+MURF



3.3.6.7 Resource use

3.3.6.7.1 Cost

Cost analyses are undertaken in several studies, but these are measured in different years and in different currencies so are not comparable. The differences in cost between surgical and non-operative treatments were explored, however. Four studies calculated the hospital treatment costs of the surgical group to be cheaper than the non-operative group (Appendix B2, Table 86).[18, 20, 70, 170] This is due to a reduction in the highest levels of care including intensive care bed days, overall days in hospital and invasive mechanical ventilation days. A fifth study found that non-operative management was cheaper than rib fracture fixation in patients with flail chest and pulmonary contusion.[74] In the same study, late fixation was more expensive than early fixation (261236 Yuan Vs 207341 Yuan).

3.3.6.7.2 Chest Tube

Chest tube duration was measured in four studies as the time from insertion to removal; two of these studies were NRS[156, 157] and two were case series[164, 166] (Appendix B2, Table 87). In one study, chest tube duration was longer in the control group (16.8 days SD 5.1) compared to surgical fixation (5.6 days SD1.2) p= 0.001.[156] The study by Taylor et al. did not show a difference, however (p =0.95).[157] Taylor et al. also recorded that the number of patients requiring a tube thoracotomy was 23.9% in the non-operative group and 11.4% in the surgical group.

3.3.6.8 Adverse events

3.3.6.8.1 Wound Infection

Sixteen studies reported wound infection rates: one RCT,[19] three NRS[70, 74, 180] and 12 case series[81, 82, 84, 87, 158, 159, 161, 163, 176, 178, 179, 187] (Appendix B2, Table 88). Wound infection rates ranged between 0% to a maximum of 25%. The percentages were pooled from all studies and the average rate of wound infection of all the reported studies was 9.9%, SD 7.7. Most infections were reported as mild and resolved with antibiotic treatment. Significant infections occurred in the paper by Mayberry et al. in which one patient required an incision and drainage for exposed metal work at ten weeks.[161] The wound infection settled after five months of serial packing and seven months of antibiotic treatment. Secondary operations occurred in the studies by Lardinois et al.[84] (n=1 out of 66 patients) and Thiels et

al.[187] (n=5 out of 122 patients). Implant removal was required in one patient in each study by Bottlang et al. (20 patients),[158] Campbell et al. (32 patients)[87] and Granhed et al. (60 patients),[70] for two patients in the study by Wiese et al.(94 patients)[178] and four in that by Schmitt-Neuerberg (15 patients)[179]. All were as a result of serious infections causing significant and lengthy morbidity.

3.3.6.8.2 Metal work failure

Metal work failure was reported in six studies; one NRS[180] and 5 case series[81, 163, 177, 179, 189] (Appendix B2, Table 89) Up to 12% of patients had failure of metalwork requiring removal. Three intramedullary splints migrated and 'cut out' superiorly requiring removal in the study by Marasco et al.[193]. One other k wire migrated in the study by Menard et al.[81] Two plates loosened and required re-operation in the paper by Schmitt-Neuerberg et al.[179] and is in addition to the operations performed for wound infection.

3.3.6.8.3 Respiratory failure

Four non-randomised studies [65, 73, 78, 140] and one case series[81] reported respiratory failure (Appendix B2, Table 90). The definition of respiratory failure varied between studies and is discussed further in 3.3.9.3. The non-operative group had a higher rate of respiratory failure compared to the fixation group in all studies and this was statistically significant in two studies.[73, 140]

3.3.6.8.4 Overall complication rate

Overall complication rate, measured as a frequency of all complication combined together, was reported in one RCT[19] and one case series[178] (Appendix B2, Table 91). The complication rate was higher in the fixation group compared to the non-operative group but this was not significant (65% vs 40%).[19]

3.3.6.8.5 Reintubation

One RCT [20] and three NRS [76, 92, 170] reported the reintubation rate (Appendix B2, Table 92). The reintubation rate was higher in the non-operative group compared to the fixation group in two NRS[76] but this was only statistically significant in one (17.9% vs 4.55%, p = 0.34).[92] The reintubation rate was higher in the rib fracture fixation group compared to the non-operative group in the RCT,[20] but this was not significant (13% vs 4%, p = 0.61), and the remaining NRS (10% vs 0%).[170]

3.3.6.8.6 Sepsis

Three non-randomised studies reported sepsis.[64, 65, 81] The rate of sepsis was higher in the non-operative group compared to the fixation group in one study[64] and one study subgroup of non-pulmonary contusion.[65] The subgroup with pulmonary contusion had a higher rate of sepsis in the fixation group compared to the non-operative group.[65] No significance values were reported.

3.3.6.8.7 Retained haemothorax

Retained haemothorax was measured in one NRS[77] and two case series[159, 163] (Appendix B2, Table 94). Retained pneumothorax was higher in the non-operative group compared to the fixation group and was statistically significant (16 % vs. 5.1%, p = 0.001).[77] One case series had a 1% retained haemothorax complication rate[159] and another reported no cases of retained haemothorax.[163]

3.3.6.9 Lung Function and Arterial blood gas analysis

3.3.6.9.1 Forced Expiratory Volume 1 second (FEV1)

Two RCTs[19, 20], two NRS[72, 95] and five case series[158, 173, 174, 185 162] reported FEV1 (Appendix B2, Table 95). The intervention group had a statistically significant improvement in FEV1 in the fixation group compared to the non-operative group (1.8 L Vs 1.43 L P<0.001).[95] The two RCTs showed no significant difference between the fixation and the non–operative groups measured at two months (p = n.s.)[19] and three months (p= 0.31)[20]. The case series predicted values ranging from 64% at one month and 82% at six months. In the Nickerson et al. case series study, complete flail chest stabilisation had a greater predictor percentage compared to partial flail chest stabilisation at all-time points, but this was not significant.[162]

3.3.6.9.2 Forced Vital Capacity (FVC)

Two RCTs[19, 20], two non-randomised studies[72, 181] and six case series[158, 173, 185 162, 163, 178] reported forced vital capacity (FVC) (Appendix B2, Table 96). Forced vital capacity is measured as a volume and as a predicted percentage of a matched patient on age, height and gender. Granetzny et al.[19] was the only study that showed an improvement with surgical fixation compared to non-operative management measured at two months (75% predicted Vs 66.5 % predicted p <0.001). Marasco et al.[20] showed a larger predicted FVC at three months in the non-operative group compared to the fixation group but this was not statistically

significant (85% predicted Vs 78 % predicted p =0.198). Serial evaluations of FVC within case series showed a steady improvement over time, continuing up to 12 months.[158, 173, 185 162, 163, 178] In Nickerson et al.'s case series study the complete flail chest stabilisation had a greater predictor percentage compared to the partial flail chest stabilisation at all-time points, but this was not significant.[162]

3.3.6.9.3 Total Lung Capacity (TLC)

Two RCTs[19, 20], one NRS[72] and one case series[162] reported TLC (Appendix B2, Table 97).The Marasco et al.[20] RCT was in favour of the non-operative group compared to fixation but this was not significant (88% Vs 84% p= 0.61). The Granetzny et al.[19] RCT was in favour of operative fixation compared to non-operative management and this was statistically significant (91% vs 86% P= 0.01). Nickerson et al.[162] compared complete flail chest stabilisation to partial flail chest stabilisation, finding that the former had higher TLC at all time points (1, 3 and 6 months) and was statistically significant at 3 and 6 months.

3.3.6.9.4 FEV1/FVC

One RCT[20] and two case series[162, 173] report FEV1/FVC (Appendix B2, Table 98). Measured at two months, there was a slightly higher percentage FEV1/FVC ratio in the fixation group compared to the non-operative group but this was not significant (96% vs 95% P = 0.92). In Nickerson et al.'s case series study the complete flail chest stabilisation had a greater predictor percentage compared to the partial flail chest stabilisation at all time points but this was not significant.[162]

3.3.6.9.5 Peak expiratory flow rate (PEFR) and Maximal mid expiratory flow (MMEF)

PEF was reported by two RCTs,[19, 20] one NRS[72] and three case series[173, 174, 185] (Appendix B2, Table 99). In one RCT the fixation group had a greater PEFR than the non-operative group at two months (92.2% vs 91.8%).[19] In the other RCT, the non-operative group had the larger PEFR at three months but this was not statistically significant (62.8% vs 68.1%, p= 0.63).[20] The case series PEFR ranged from 79% to 81.4% at three months, 77.3% to 83.7% at six months and 109.0% at 12 months. Only one study reported MMEF, indicating that the percentage predicted was higher in the non-operative group compared to the fixation group, but this was not significant (82.1% vs 76.2%, p = 0.64).

3.3.6.9.6 Partial pressure of oxygen (PaO_2)

PO_2 is measured on arterial blood gas analysis with the unit's mmHg (millimetres of mercury). One RCT[19] reported PO_2 pre operation and 7-10 days post intervention; one case series [173] reported post-stabilisation PO_2. (Table 100). Comparisons were made between the pre-operative and post-operative measurements showing statistically significant improvement in both the fixation and non-operative groups. No comparisons were made between the fixation and non-operative groups, although the pre-op surgical fixation group had a worse PO_2 value compared to the non-operative group (56 mmHg vs 64 mmHg), while at 7-10 days the rib fracture fixation group had a better PO_2 value than the non-operative group (99 mmHg vs 90 mmHg). Post intervention, the fixation group had a mean (SD) PO_2 of 98.7(21) and the non-operative group was 89.3(8). The mean (SD) PO_2 in the case series study was 97.6 (6.4).[173]

3.3.6.9.7 Partial pressure of carbon dioxide ($PaCO_2$)

PCO_2 is measured on arterial blood gas analysis with the unit's mmHg (millimetres of mercury). One RCT[19] reported PCO_2 pre-operation and 7-10 days post intervention and one case series study[173] reported post-stabilisation PCO_2. (Appendix B2, Table 100). Comparisons were made between the pre-operative and post-operative measurements, showing improvement in both the fixation and non-operative groups. While this was not statistically significant in the fixation group it was in the non-operative group. No comparisons were made between the fixation and non-operative groups. The non-operative group had a worse PCO_2 level, at 39.7 mmHg pre-op compared to the fixation group value of 34.2 mmHg. At 7-10 days post intervention the fixation group had a mean (SD) PCO_2 of 31.2 mmHg (5.9) while that of the non-operative group was 30.9 mmHg (3). The mean (SD) PCO_2 in the case series study was 32.4 mmHg (8.4).[173]

3.3.6.9.8 O_2 Saturation

O_2 saturation is measured on arterial blood gas analysis as a percentage. One RCT[19] reported O_2 saturation pre-operation and 7-10 days post intervention, and one case series study[173] reported post-stabilisation O_2 saturation. (Appendix B2, Table 100). Comparisons were made between the pre-op and post-operative measurements, showing statistically significant improvement in both the fixation and non-operative groups. No comparisons were made between the fixation and non-operative groups. Post-fixation, the fixation group had a mean (SD) O_2

saturation of 96.8% (3) and the non-operative group was 96.2 %(2). The mean (SD) PO_2 in the case series[173] was 98.4% (1.5).

3.3.6.10 Chest deformity and range of movement

3.3.6.10.1 Breathing movements

Breathing range of movement was reported in two NRS[181, 185] and one case series study[174] (Appendix B2, Table 101). Breathing movements were measured in all three studies by *'using a Respiratory Movement Measuring Instrument, RMMI® (ReMo Inc. Keldnaholt, Reykjavik, Iceland). The range of motion in the thorax was assessed by measuring thoracic excursion (at the level of the 4th costae and the xiphoid process), flexion and lateral flexion in a standardized manner* '[185]

There was crossover between all three studies as they had similar authors and it is not clear how many patients could have been reported twice. Olsen et al. reported the difference between the breathing movements on the injured side to the normal side.[181] The fixation group had statistically significantly more movement in the lower thorax during breathing than the non-operative group (p=0.002), but the timing of this measurement was not reported. The upper thoracic breathing movements also had more movement in the fixation group, but this was not significant (P = 0.606).

No statistically significant difference was found in the study by Caragounis et al.[185] comparing the fixation groups to the non-operative group at three months, six months or 1 year.

The second study by Olsen et al., in 2013, was a case series and only compared the difference between the non-injured and injured sides.[174] The upper thoracic breathing movements was significantly reduced on the injured side compared to the uninjured at three months (0.005) and six months (0.009) after fixation. The lower thoracic breathing movement on the injured side was not significantly different compared to the uninjured side at three months (0.948) and at six months (0.131).

3.3.6.10.2 Flexion extension of the thorax

Thoracic range of movement was reported in two NRS[181, 185] and one case series study[174] (Appendix B2, Table 101). Again, however, there was crossover of the authors. Olsen et al. 2013[174] and 2016[181] measured the range of thoracic flexion and extension in cm. In the NRS, the fixation group had a statistically significantly increased range of flexion ($p<0.001$) and extension ($p<0.001$) than the non-operative group. In the study by Caragounis et al.[185] the fixation group had statistically significant increased range of flexion ($P<0.05$) and extension ($p<0.01$) at one year compared to the non-operative group. In the case series, the measured values were compared against known reference values to show a statistically significantly reduced range of motion in the injured patient compared to the reference values in thoracic extension ($p<0.001$) and flexion ($p = 0.054$) at three months.

3.3.6.10.3 Range of movement of shoulder

Shoulder movements were reported in two studies (Appendix B2, Table 101). Shoulder movements were reduced on the injured side compared to the uninjured side in the fixation group ($p= 0.171$) and in the non-operative group ($p=0.062$)[181] but this was not statistically significant. It is possible that there was no difference between the injured and non-injured sides in both treatment groups, as shoulder movements as an outcome may not being relevant to the injury.

3.3.6.10.4 Chest wall deformity

Chest wall deformity was reported in three RCTs,[19, 20, 169] three NRS[64, 95, 168] and three case series[177, 178, 189] (Appendix B2, Table 102). There is no uniform reporting of chest deformity and definitions are rarely used. Un-blinded assessments could be open to significant bias. Overall chest deformity was consistently found to have improved after surgical fixation compared to the non-operative group Granetnzy et al. ($p=0.008$), Zhang et al. ($p<0.005$), Wu et al. ($p=0.017$) and Qiu et al. ($p=0.002$). Internal fixation reduced rib angulation ($p =0.01$) but did not significantly improve overlapping ($p =0.35$) or displacement ($p=0.16$) compared to non-operative management.

3.3.6.11 Pain and discomfort

3.3.6.11.1 Visual Analogue Scale (VAS) pain scale

One RCT,[169] four NRS[168, 171, 180, 188] and five case series studies[87, 141, 165, 173, 181] measured pain using VAS in millimetres (Appendix B2, Table 103). Both the RCT and NRS had lower VAS pain scores in the fixation group compared to the non-operative group at all time points (15 days, 30 days, two months and six months) except five days post-surgery, and where reported were statistically significant.[168, 171, 180, 188] The case series measured pain directly post operatively (mean range 20 mm to 74 mm) and up to 6 months (mean 50 mm).

3.3.6.11.2 Chronic pain

One RCT,[18] one NRS[181] and four case series[82, 84, 159, 185] reported the incidence of chronic pain (Appendix B2, Table 104). The percentage of chronic thoracic pain was reduced in the fixation group compared to the non-operative group at 12 months and was statistically significant (32% Vs 50% P<0.05).[18] Olsen et al. recorded patients who did not report any pain, hence the inverse of this result was calculated to allow a comparison with other studies (patients experiencing pain).[181] Chronic pain was experienced more in the non-operative group compared to the fixation group but this was not statistically significant (50% vs 32% p = 0.253). They also measured pain disturbing sleep (p=0.944) and pain during breathing (p=0.389) which was reported to be lower in the fixation group compared to the non-operative group but not statistically significantly so. The timing of these outcome measures was not reported.

Within the case series, chronic pain did reduce with time. At three months, 52% of patients reported chronic pain, reducing to 35% at six months and 13% at 12 months.[185] Another series reported that 16% reported chronic pain at 16 months.[159]

3.3.6.11.3 Narcotic Use

Narcotics use was measured by the mean amount of morphine equivalents in milligrams and the days spent on IV morphine in one NRS.[69] It was also reported as a frequency of patients requiring morphine regularly at different time points in two case series [159, 185] (Appendix B2, Table 105). There was slightly higher daily morphine use in the fixation group compared to the non-operative group but this was not statistically significant (79 mg vs 7 mg, p = 0.65).[69] The fixation group also

spent more days using IV morphine than the non-operative group and this was statistically significant (p =0.04).[69] In one case series, the percentage of patients requiring analgesia was 53% at six weeks, 38% at three months, 14% at six months and 8.9% at 12 months.[185] Another case series reported analgesia use by 4% of patients at 16 months.[159]

3.3.6.11.4 Chest discomfort and tightness

Two RCTs[18, 169] and three case series [87, 165, 178] reported chest discomfort and tightness measured by self-reported questionnaire (Appendix B2, Table 106). Both RCTs indicate a lower rate of chest tightness in the fixation group compared to the non-operative group (33% vs 84%, p<0.05 [18] and 13.3 Vs 51% p= 0.014[169]). The case series, meanwhile, show a rate of chest discomfort of 19% at 6 months.[178]

3.3.6.11.5 Dyspnoea

Dyspnoea was reported in two RCTs[18, 169] and two case series[87, 185] and measured by self-reported questionnaires (Appendix B2, Table 107). At 12 months, the non-operative group had a statistically higher percentage of patients reporting dyspnoea compared to the fixation group in one RCT (63% vs 28%, p<0.05).[18] The other RCT had similar results, however the timing of this outcome was not reported (22.4% vs 5.3%, p = 0.029).[167] In one case series, the percentage of patients requiring analgesia was 42.1% at six weeks, 35.3% at three months, 27% at six months and 15.6% at 12 months.[185] The study by Farquhar et al. measured dyspnoea but did not report how this was measured.[171]

3.3.6.12 Quality of life and function

3.3.6.12.1 Return to work

Return to work was measured in two ways; as a measure in days by three case series [84, 87, 159] (Appendix B2, Table 108) and by reporting frequency at different time points (3, 6, 12 and 16 months) by one RCT[18] two NRS[168, 171] and five case series[82, 87, 158, 159, 165] (Appendix B2, Table 109).

Patients had returned back to work on average 7.9 weeks,[159] 8 weeks[84] and 3.9 months[87] after surgery. In the three controlled studies there were, on average, more patients back at work in the fixation group compared to the non-operative group, and this was statistically significant in two studies at six months (p= 0.014)[168] and 12 months (<0.05).[18] Within the case series, the percentage of

patients back at work was between 0% to 31% at three months, 33% to 95% at six months and 96% at 16 months.

3.3.6.12.2 Quality of life scores

Multiple quality of life scores are reported at multiple time points, however none were measured consistently so they cannot be compared. There was no significant difference in either the mental (p =0.65) or physical component (p=0.98) of the SF-36 score in the only controlled study reporting a quality of life score.[20]

3.3.6.12.3 Return to activities

Two NRS[168, 180] measured return to normal activities in time from injury (Appendix B2, Table 108). Patients in these studies were back to normal activities in fewer days, on average, in the fixation group compared to the non-operative group (28.2 days vs 42.4 days, P= 0.028[168] and 26.6 days vs 54.2 days, p<0.0001).[180]

3.3.6.12.4 Satisfaction

One case series reported through a questionnaire, delivered on average 16 months after surgery, that 82% of patients felt they were ‘somewhat better’ immediately following surgery.[159] In the same survey, satisfaction with their overall experience and with the results of the procedure scored 9.2 (SD 0.2) out of 10. The authors explain a polarised view of scores with all patients (except two) giving a rating of 8, 9 or 10. The other two patients gave a rating of 2 out of 10, both of whom were suffering from chronic pain. Ninety-four percent of the patients reported they would recommend the procedure to a friend if they had the same injury. This particular case series had no significant adverse events. If satisfaction scores had included patients with ongoing deep infection and chronic pain then the satisfaction would be likely to be less favourable.

3.3.7 Timing of Surgery

Introduction

Studies were separated into those whose mean or median timing of surgery was less than or equal to 72 hours and those more than 72 hours (three days). Three days (72 hours) was chosen since this had an evidence base.[5] In hospital outcomes were analysed in a meta-analysis to explore any differences in effectiveness between early and late fixation and whether this would explain the substantial heterogeneity seen in the meta-analysis for effectiveness.

How was timing measured?

In the 34 studies that reported timing, time to surgery varied from the same day of injury to a maximum of 59 days after injury. The mean length of time from admission to receiving surgery varied between 0.75 days and 12 days. Twelve studies[19, 59, 64, 65, 73, 77, 81, 84, 92, 156, 161, 165] were considered to have implemented early fixation (Table 27 and Appendix B3, Figure 43) and 22 [18, 20, 69, 70, 87, 88, 143, 157-159, 161, 163, 164, 166, 171, 172, 177, 178, 180, 184, 187] implemented fixation after more than 72 hours (three days) (Table 28 and Figure 43). Five studies[72, 75, 95, 170, 179] gave maximum values but not mean or median values so could not be classed into early or late fixation. Twenty five studies did not report the timing of surgery (Appendix B3, Table 110).

Most non-randomised studies had a possible positive skew in respect to their surgical timing data since their means or medians were significantly closer to the minimum value than the maximum value. Most patients, therefore, received relatively early fixation and the mean values may be higher than expected due to a few patients having significantly late fixation. For example, in Granhed et al. the median was four days, but the range was 1-59 days.[70] With evidenced-based consensus being to undertake early fixation,[5] it would be expected that recent studies would be more likely to follow this model. When comparing either median or mean time by the year of publication, however, there does not seem to be a trend towards earlier surgical fixation over the time period 1983 to 2016. The country in which the study took place or the type of chest injury also did not seem to influence whether there is early or late fixation (Table 27 and Table 28).

Table 27 Early Fixation (before three days)

				Days							
Author/Year	**Country**	**Type of study**	**Type of rib fractures**	**Mean**	**SD**	**Median**	**Min**	**Max**	**Q1**	**Q3**	**IQR**
Solberg 2009	USA	NRS	FC + MURF	0.75			0.25	1.75			
Majercik 2015	USA	NRS	FC + MURF			2	0	22	2	4	2
Voggenreiter 1998	Germany	NRS	Flail Only			2		7			
Mayberry 2003	USA	Series	FC + MURF	2							
Althausen 2011	USA	NRS	Flail Only	2.3			1	5			
Pieracci 2016	USA	NRS	FC + MURF	2.4	0.78						
Menard 1983	France	Series	Flail Only	2.6			0	13			
Nirula 2006	USA	NRS	FC + MURF	2.7			0	20			
Lardoinois 2001	Switzerland	Series	Flail Only			2.8	0	21			
Yang 2010	China	Series	FC + MURF					1			
Granetzny 2003	Germany	RCT	Flail Only				1	1.5			
Ahmed 1995	UAE	NRS	Flail Only				0.5	2			

Table 28 Late Fixation (over three days)

				Days							
Author/Year	**Country**	**Type of study**	**Type of rib fractures**	**Mean**	**SD**	**Median**	**Min**	**Max**	**Q1**	**Q3**	**IQR**
Majercik 2014	USA	Series	FC + MURF	3.4	0.5						
Wiese 2015	Switzerland	Series	Flail Only			3.4	0	17			
Tarng 2016	Taiwan	Series	Flail Only	3.83	0.83						
Granhed 2014	Sweden	NRS	FC + MURF			4	1	59			
Said 2014	USA	Series	Flail Only			4	1	33			
Marasco 2013	Australia	RCT	Flail Only	4	1.5						
Taylor 2016	USA	NRS	Flail Only	4.6			1	13			
Taylor 2013	USA	Series	Flail Only	4.6			2	11			
Marasco 2014	Australia	Series	Flail Only			5	0	21			
Campbell 2009	Australia	Series	FC + MURF			5			3	7	4
Seller 2013	UK	Series	Flail Only			5	2	12			
De Moya 2011	USA	NRS	FC + MURF	5			1	10			
Bottlang 2013	USA	Series	Flail Only	5.3			1	17			
Mayberry 2003	USA	Series	Flail Only	6			5	10			
Farquhar 2014	Canada	NRS	Flail Only	6.3	3.6						
Theils 2016	USA	Series	FC + MURF	6.92	2.67						
Mayberry 2009	USA	Series	FC + MURF	7	5		0	33			
Mayberry 2003	USA	Series	FC + MURF [P]	7			3	30			
Muhm 2013	Germany	NRS	FC + MURF	7.1	4.4	6	1	15			
Ivancic 2009	Croatia	Series	Flail Only	7.73	3.57		3	13			
Tanaka 2001	Japan	RCT	Flail Only	8.2	4.1						
Khandelwal 2011	India	NRS	FC + MURF	12		12	12	12			

P = Pain and Instability

3.3.7.1 Randomised and non-randomised studies

The eligibility for inclusion for surgery and randomisation protocols differed between the RCTs. Tanaka et al. randomised on day 5 after admission and were operated on a mean of 8.2 days,[18] but required patients to be on mechanical ventilation prior to randomisation. Marasco et al.'s randomisation protocol did not specify a time at which patients should be randomised or enrolled but, on average, they were randomised at 61.6 hours after admission to ICU and operated on 49.4 hours after randomisation (mean five days post admission).[20] Eligibility criteria for inclusion in the study by Marasco et al. were that patients had already been ventilated and had no prospect of weaning, and therefore were deemed to have failed medical management.[20] Both these studies were classified as late fixation.

Patients in the RCT by Granetzny et al. were all randomised and fixed between 24-36 hours of being admitted to ICU, which was classed as early fixation.[19] The RCT by Wu et al. did not specify at what time their surgical group were randomised or when they were surgically fixed.[169]

One NRS grouped their patients into non-operative, early and late fixation, defined as within seven days (n=12) and after seven days (n=12).[74] This retrospective study of patients did not elaborate on the reasons why certain patients were fixed earlier than others but those with early (within seven days) fixation had a reduced length of mechanical ventilation and rate of tracheostomy compared to the non-operative group. Mortality, length of ICU stay or total length of stay did not significantly change between the fixation and non-operative groups in this study.

One NRS used regression analysis to show that the time to operation was strongly associated to in hospital outcomes.[92] There was a statistically significant association between time to fixation with ICU length of stay, with a Pearson's correlation coefficient of 0.0487 (p= 0.029), time on IMV 0.477 (p=0.033) and hospital length of stay 0.483 (p=0.031).

3.3.7.2 Subgroup meta-analysis of early and late fixation

A summary of the meta-analysis of early and late fixation is presented in Table 29 and the forest plots are presented in Appendix B3, Figure 44 to Figure 48.

3.3.7.2.1 Length of mechanical ventilation

Five studies[19, 59, 65, 92, 156] that reported length of mechanical ventilation were classed as early fixation, and five studies[20, 69, 70, 157, 171] were classed as late fixation. All studies in the late fixation group had all their patients mechanically ventilated (except for Taylor et al.[157] in which 54% were initially ventilated). Within the early fixation group no paper had a prerequisite that included patients should be on mechanical ventilation, and most papers only a third were mechanically ventilated prior to surgery.

Overall effectiveness using these ten studies was in favour of fixation compared to non-operative management -3.66 days 95% CI [-5.92, -1.39] (Appendix B3, Figure 44).

Table 29 Results of subgroup meta-analysis for early and late fixation

Outcome	Mean difference	Lower CI	Upper CI	I^2	Favours	Subgroup differences	
						I^2	P value
Total length of mechanical ventilation (days)							
Overall n=10	-3.66	-5.92	-1.39	84%	Rib fixation		
Early Fixation n=5	-6.61	-9.75	-3.48	79%	Rib fixation	84.8 %	0.01
Late Fixation n=5	-1.12	-3.91	1.68	77%	Rib fixation		
Total length of stay in ICU (days)							
Overall n=11	-2.35	-3.89	-0.81	71%	Rib fixation		
Early Fixation n=5	-2.47	-3.92	-1.03	69%	Rib fixation	0%	0.97
Late Fixation n=6	-2.56	-6.71	1.60	71%	Rib Fixation		
Total hospital length of stay (days)							
Overall n=9	-2.12	-4.09	-0.15	58%	Rib fixation		
Early Fixation n=4	-3.47	-6.03	-0.91	78%	Rib fixation	70.4 %	0.07
Late Fixation n=5	0.17	-2.75	3.08	0%	Non-Operative		
Outcome	**Risk Ratio**	**Lower CI**	**Upper CI**	**I2**	**Favours**	**Subgroup differences**	
						I^2	P value
Mortality							
Overall n=5	0.54	0.25	1.17	0%	Rib fixation		
Early Fixation n=2	0.48	0.18	1.27	0%	Rib fixation	0%	0.70
Late Fixation n=3	0.66	0.19	2.32	0%	Rib fixation		
Pneumonia							
Overall n=7	0.86	0.54	1.36	67%	Rib fixation		
Early Fixation n=2	0.47	0.16	1.39	26%	Rib fixation	28.3 %	0.24
Late Fixation n=3	0.98	0.58	1.64	73%	Rib fixation		

I^2 –the percentage variation across studies that is due to heterogeneity not due to chance.
I^2 subgroup differences the percentage variation between the subgroups that due to heterogeneity and not due to chance

Despite subgroup analysis of early and late fixation substantial heterogeneity remained within subgroups. In the early fixation group, the duration of mechanical ventilation was shorter in the fixation group compared to the non-operative group -6.61 days, 95% CI [-9.75, -3.48] , I^2 = 79%. In the late fixation subgroup, the length of mechanical ventilation was shorter in the surgical fixation group than in the non-operative -1.12 days, 95% CI [-3.91, 1.68] , I^2 = 84%. Confidence intervals did not overlap, therefore there was a significant difference between early and late fixation for this outcome.

There was also a statistically significant difference between the early and late groups (chi^2 =6.59, df=1, p=0.001), I^2= 84.8%.

3.3.7.2.2 Length of stay in intensive care unit

Five studies[19, 59, 77, 92, 156] that reported length of mechanical ventilation were classed as early fixation and five studies[18, 20, 69, 171, 184] were classed as late fixation. Overall effectiveness using these ten studies was in favour of fixation compared to non-operative management -2.35 days 95% CI [-3.89, -0.81] (Appendix B3, Figure 45).

Despite subgroup analysis of early and late fixation, substantial heterogeneity remained within subgroups. In the early fixation subgroup, the length of ICU stay was shorter in the fixation group compared to the non-operative group -2.47 days, 95% CI [-3.92, -1.03] , I^2 = 69%. In the late fixation subgroup the length of ICU stay was shorter in the surgical fixation group compared to the non-operative group -2.56 days, 95% CI [-6.71, 1.60] , I^2 = 76%. There was no statistically significant difference between the early and late groups (chi^2 =0.00, df=1, p=0.097), I^2= 0%.

3.3.7.2.3 Length of hospital stay

Four studies[19, 59, 77, 92] that reported length of mechanical ventilation were classed as early fixation, and five studies[20, 69, 157, 171, 184] were classed as late fixation. Overall effectiveness using these nine studies was statistically significantly in favour of fixation compared to non-operative management -2.12 days 95% CI [-4.09, -0.15] (Appendix B3, Figure 46) .

Subgroup analysis showed substantial heterogeneity in the early fixation group and none in the late fixation group. In the early fixation subgroup the length of hospital stay was shorter in the fixation group compared to the non-operative

group -3.47 days, CI 95% [-6.03, -0.91], I^2 = 78%. In the late fixation subgroup, the length of hospital stay was longer in the surgical fixation group compared to the non-operative group, 0.17 days, 95% CI [-2.75, 3.08], I^2 = 0%.There was no statistically significant difference between the early and late groups (chi^2 =3.38, df=1, p=0.07), I^2= 70.4%.

3.3.7.2.4 Mortality

Two studies[19, 65] were classed as early fixation and three studies[20, 171, 184] were classed as late fixation. Overall effectiveness using these five studies showed that the rate of mortality rate was less in the surgical fixation group compared to the non-operative group RR 0.54, 95% CI [0.25, 1.17] (Appendix B3, Figure 47).

The subgroup analysis of early and late fixation showed no heterogeneity within subgroups. In the early fixation group, the mortality rate was lower in the fixation group compared to the non-operative group, with an RR 0.48, 95% CI [0.18, 1.27], I^2 = 0%. In the late fixation group, the mortality rate was lower in the fixation group compared to the non-operative group RR 0.66, 95% CI [0.19, 2.32], I^2 = 0%.

There was no statistically significant difference between the early and late groups (chi^2 =0.15, df=1, p=0.70), I^2= 0%.

3.3.7.2.5 Pneumonia

Two studies[73, 92] were classed as early fixation and five studies[20, 69, 157, 171, 184] were classed as late fixation. Overall effectiveness using the seven studies showed that the rate of pneumonia was less in the surgical fixation group compared to the non-operative group, with an RR of 0.86, 95% CI [0.54, 1.36],(Appendix B3, Figure 48).

Subgroup analysis showed minimal heterogeneity in the early group and substantial heterogeneity in the late group. In the early fixation group, the rate of pneumonia was less in the fixation group compared to the non-operative group, with an RR of 0.47, 95% CI [0.016, 1.39], I^2 = 26%. In the late fixation group, the rate of pneumonia was less in the fixation group compared to the non-operative group RR 0.9, 95% CI [0.58, 1.64], I^2 = 73%.

There was no statistically significant difference between the early and late groups (chi^2 =1.40, df=1, p=0.24), I^2= 28.3%.

3.3.7.3 Case Series

Seventeen case series[81, 84, 87, 88, 143, 158, 159, 161, 163-166, 172, 176-178, 187] measured time to fixation from admission. Means ranged from 2 to 7.73 days and minimum and maximum values ranged between 0 to 33 days (Table 27 and Table 28)

3.3.8 Outcome Measurements

The aim of this part of the synthesis was to describe what outcomes were being measured and how they were being measured within studies, which can then be fed into a Delphi consensus. This is a separate from the preceding section 3.3.6 that presented the evidence for effectiveness using these outcomes. The measured outcomes were classified into six categories, of which in hospital outcomes in the acute phase of treatment were measured most consistently.

- In-hospital resource use outcomes
- Adverse outcomes
- Physiological - Lung function and arterial blood gas analysis
- Clinical - Chest deformity and range of movement
- Pain and discomfort
- Quality of life and function

All outcomes were presented in tables for each outcome category, describing how the outcome was measured, at what time points and in how many studies it was measured. Outcomes that are reported as a unit of time were described as being measured within the duration of the study. Separately, outcome data was extracted and presented in data tables in Appendix B2 as described in 3.3.6 and 3.3.7

The reviewed literature had 64 separate outcome measures, of which over half were measured at several different time points.

3.3.8.1 In-hospital resource use outcomes

In hospital outcomes describes the outcomes that are a consequence of the early hospital treatment measured within the hospital admission. Twelve in hospital outcomes are reported (Table 30).

Table 30 In-hospital resource use outcome measures

Outcome	How it was measured	Time points	Studies
Length of hospital stay	Time since admission to hospital discharge Time since injury to hospital discharge	Duration of study	36
Length of ICU Stay	Time since admission to ICU to discharge Time from surgery to discharge from ICU	Duration of study	35
Total duration of IMV	Time from intubation to extubation Time from surgery to extubation	Duration of study	26
Tracheostomy	Number of patients	7 days and 21 days	18
Chest Drain	Number of patients Time from insertion to removal	Duration of study Duration of study	4
Cost	Overall estimated cost of treatment, US dollar, Turkish Lira, Yuan	Duration of the study	5
NIV	Number of patients	Duration of study	1
ICU Readmission	Number of patients	Duration of study	1
Epidural Use	Number of patients, days	Duration of study	1
Timing of Surgery	Days	Duration of study	34
Antibiotics timing	Hours	Duration of study	1
Hospital readmission	Days	Duration of study	1
Requirement of antibiotics	Number of patients	Duration of study	1
Blood Product Transfusion	Number of units, number of patients	Duration of study	1
Plasma Transfusion	Number of units, number of patients	Duration of study	1

3.3.8.2 Adverse Outcomes

Adverse outcomes occur as a consequence of treatment or as a worsening of the patient condition which has not been prevented by treatment. Outcomes measuring surgical effectiveness are contrasted by the adverse outcomes and complications that can occur during treatment and should be reported together. Twenty-one adverse outcomes were measured within the included studies, but most are only reported once (Table 31).

Table 31 Adverse outcomes

Outcome	How it was measured	Time points	Studies
Mortality	Number of patients	7 days,10 days, 21 days, 28 days, 30 days, duration of study	33
Pneumonia	Number of patients	All time points, 7 days and 21 days	30
Wound Infection	Number of patients	Duration of study	16
Metal work failure	Number of patients	Duration of study	6
Respiratory failure/ARDS	Number of patients	Duration of study	5
Overall complication rate	Number of patients	Duration of study	2
Perioperative complications	Number of patients	Duration of study	1
Reintubation/Failed extubation	Number of patients	Duration of study	4
Sepsis	Number of patients	Duration of study	3
Retained Haemothorax	Number of patients	Duration of study	3
Barotrauma	Number of patients	Duration of study	1
Pleural Effusion	Number of patients	Duration of study	1
Multi Organ Failure	Number of patients	Duration of study	1
Pulmonary Embolism	Number of patients	Duration of study	1
Mediastinitis	Number of patients	Duration of study	1
APACHE II	Score		1
Reoperation	Number of patients	Duration of study	1
Empyema	Number of patients	Duration of study	1

3.3.8.3 Lung Function and Arterial blood gas analysis

Measurement of lung function and gas exchange by arterial blood gas are an objective measure of overall ventilation. The pulmonary function test assesses the chest biomechanics whereas the arterial blood gas assesses gas exchange. Both are important in ventilation.

Table 32 Studies reporting lung function and arterial blood gas analysis

Outcome	How it was measured	Time points	Studies
Forced Vital Capacity	Percentage of normal values and Litres	1 month, 2 months, 3 months, 6 months, 12 months	10
Forced Expiratory Volume 1 second	Percentage of normal values and in Litres	1 month, 2 months, 3 months, 6 months, 12 months	9
FEV1/FVC	Percentage of normal values	1 month, 3 months, 6 month	3
Total Lung Capacity	Percentage of normal values, number of patients less than 85% predicted	1 month, 2 months, 3 months, 6 months	4
Residual Volume	Percentage of normal values	6 months	1
FEV 75%	Percentage of normal values	2 months	1
PO2	ABG	Pre intervention, 7-10 days, post-operative day 1	2

Outcome	How it was measured	Time points	Studies
PCO2	ABG	Pre intervention, 7-10 days, post-operative day 1	2
O2 Sats	ABG	Pre intervention, 7-10 days, post-operative day 1	2
MMEF	Percentage of normal values		1
PEF	Percentage of normal values		6

3.3.8.4 Chest deformity and range of movement

Nine different outcomes relating to chest deformity and range of movement were reported in the studies (Table 33)

Table 33 Chest deformity and range of movement

Outcome	How it was measured	Time points	Studies
Chest Wall Deformity	Number of patients with overlapping/displacement/angulation or mild, moderate or severe deformity	3 months, 4 months, 5 months, 9 months	9
Breathing Movements	Respiratory Movement Measuring Instrument	3 months, 6 months, 1 year	3
Range of movement of thorax	Circumference at 4th costae and xiphoid process Thoracic flexion in mm between 7th cervical vertebra and a skin mark 30cm below Lateral flexion in mm distance moved of index finger on thigh on lateral flexion	3 months, 6 months, 1 year	3
Range of movement of shoulder	Active flexion and abduction with goniometer	3 months, 6 months	2
Brostrom Score	Points system based on functional movements maximum bilateral score 60	3 months, 6 months	1
Kinesiophobia Tampa Score	Fear of movement >37 defined as having kinesiophobia	3 months, 6 months	1
Constant Score	Measure of range of shoulder movements, pain and sleep disturbance	6 weeks, 3 months	1
Scoliosis	Clinical judgement, number of patients	Duration of Study	1
CT assessment of healing	Clinical judgement	3 months	1

3.3.8.5 Pain and discomfort

Six outcomes relating to pain and discomfort were measured by 30 studies (Table 34). Outcomes related to chronic pain and discomfort are difficult to measure and are subjective. Chronic pain encases multiple terms such as pain syndrome and can be qualified into pain during activities such as at rest or taking a deep breath. Acute pain measured on visual analogue attempts to reduce this bias and is measured serially to assess change in pain. Measurements were taken during treatment at six weeks and measured up to one year.

Table 34 Studies reporting pain and discomfort

Outcome	How it was measured	Time points	Studies
Pain VAS	100mm	15 days, 30 days, 3 months, 6 months, 12 months	10
Chronic Pain	Number of patients experiencing pain at rest and during breathing	6 weeks, 3 months, 6 months, 1 year	6
McGill Pain Index		Unknown	1
Narcotics Use	Morphine equivalents, days of IV morphine use	6 weeks, 3 months, 6 months, 12 months, 16 months	3
Chest discomfort/ tightness	Number of patients	3 months, 6 months	5
Dyspnoea	Number patients experiencing dyspnoea	6 weeks, 3 months, 6 months, 12 months	5

3.3.8.6 Quality of life and function

Twelve outcomes were measured by studies reporting quality of life and function (Table 35).

Table 35 Studies reporting quality of life and function

Outcome	How it was measured	Time points	Studies
SF 36	Questionnaire	6 months	1
HRQOL	Questionnaire	Unknown	1
RAND-36	Questionnaire	3 months, 6 months	2
AQOL	Questionnaire	Unknown	1
EQ5D 5L	Questionnaire	6 weeks, 3 months, 6 months, 1 year	1
EQ 5D 3L	Questionnaire		1
Physical function and Level Disability Rating Scale	Questionnaire 0-100mm	Unknown	1
Return to Work	Number of patients – self reporting	3 months, 6 months, 12 months	8
Return to Activities	Self-reporting number of days		2
Discharge Destination	Number of patients discharged to home, rehab or skilled nursing facility	Upon discharge	1
Home Oxygen Therapy	Number of patients	Duration of study	1
Satisfaction	0-10 rating on questionnaire	16 months	1

3.3.9 Indications for surgical fixation of rib fractures

The criteria for which patients are prospectively selected for surgery by surgeons on the basis that they believe they would benefit from surgery are known as the surgical indications. Indications for surgery were collected from studies and recorded verbatim into the data extraction tables. Indications were then grouped into similar themes and a narrative synthesis was undertaken. The most common way to describe an indication was to describe a type of chest injury (FC or MURF) and qualify this with a condition such as respiratory compromise or failure to wean

from mechanical ventilation. Some other studies had indications that were independent of type of injury. For this reason, a table was constructed that differentiated between FC, MURF and those indications independent of injury type.

Within the reviewed literature it was difficult to identify what authors believed their indications for surgery were. There was often confusion with the inclusion and exclusion criteria of the study which may have been different from the indications for surgery. An indication for surgery was only taken as such if this was specifically described in these terms and described separately to the inclusion criteria for the study. Within the data extraction tables the inclusion and exclusion criteria are reported separately from the indications for surgery (Appendix B1, Table 68 to Table 72).

Indications for surgery were not often reported in the retrospective studies. Most often, they compared patients undergoing fixation of rib fractures and a historical cohort of non-operative patients. These studies often had a specific inclusion and exclusion criteria which fitted with their research question but did not discuss the original prospective surgical indication. In an RCT or NRS, where surgical intervention was prospectively allocated, the inclusion criteria and indications for surgery were usually clearly described. This is down to the fact that if the patient did not fit the surgical indications then they would not have been prospectively entered into the trial in the first place. Most studies had several indications for surgery.

3.3.9.1 Flail chest injury

The most common indication for surgery was flail chest (Table 36). Between studies, however, this indication varied due to the definition of a flail chest described in 3.3.4.5. Surgical fixation was indicated based solely on the flail chest injury in 16 studies.[6, 59, 65, 70, 73, 75, 77, 99, 158, 159, 162, 170, 173, 178, 186, 189]

Table 36 Indications for surgical fixation

Flail Chest	Indication	Number of Studies
	Injury only	16
	Respiratory Compromise	16
	IMV	15
	Pain	10
	Paradoxical Movement	10
	Failure to Wean	7
	Deformity	7
	Tracheostomy	2
	Displacement	2
	Hemodynamic Instability	1
	Anterolateral flail only	2
Multiple unifocal rib fractures		
	Injury only	4
	Respiratory Compromise	11
	IMV	4
	Pain	9
	Paradoxical Movement	5
	Failure to Wean	2
	Chest Deformity	5
	Tracheostomy	0
	Displacement	5
	Haemodynamic Instability	2
Independent of injury		
	Other thoracic operation	16
	Irritation of underlying organs	5
	Severe displacement/dislocation	2
	Failure of medical management	1
	30% volume loss of hemithorax	1
	Anticipated non-union	3
	Underlying chronic lung disease	1
	Pulmonary Contusion	0

3.3.9.2 Multiple unifocal rib fractures

Multiple unifocal rib fractures were described as an indication in only four studies based on the injury type alone (Table 36).[75, 77, 186, 189]

3.3.9.3 Respiratory failure

Respiratory failure combined with flail chest was a common indication, being described in 16 studies[19, 59, 65, 71, 81, 82, 84, 87, 92, 142, 157, 163, 171, 172, 181, 186] and with multiple unifocal rib fractures in 11 studies.[69, 70, 87, 99, 143, 157, 162, 181, 184, 185, 187] Respiratory failure was not clearly defined, but studies often used arterial blood gas measurements showing hypoxia, or hypercarbia of similar values to PaO2<60 mmHg, PaCO2 > 50 mm Hg, or required a high respiratory rate >35 breaths per minute.[65, 92, 172, 185] Spirometry measures of a FVC of less than 50% predicted[71] or less than 20mL/Kg,[171] or progression to invasive or non-invasive ventilation also constituted respiratory failure.[71]

3.3.9.4 Mechanical ventilation

Mechanical ventilation in combination with flail chest was reported in 15 studies[18, 20, 59, 64, 69, 71, 74, 78, 92, 156, 171, 172, 176, 177, 188] and with multiple unifocal rib fractures in four studies.[76, 156, 175, 187] A defined protocol of instigation of mechanical ventilation was only rarely described (see section 3.3.6.1). Development of respiratory failure coincided with the instigation of mechanical ventilation since this is the emergency treatment for respiratory failure and so the indications are closely linked.

3.3.9.5 Failure to wean

Failure to wean from mechanical ventilation with a flail chest was reported in seven studies[84, 88, 143, 159, 161, 172, 176] and in two studies[143, 159] for multiple unifocal rib fractures. Post-operative weaning protocols are described much more clearly than the initial instigation of IMV. The time in which the patient failed to wean was only specified as an indication by Marasco et al.[20] Doben et al.[71] and Mayberry et al.[161] Marasco et al. defined not likely to wean within 48 hours as an indication within their study protocol.[20] Mayberry et al. commented that they believed that the ideal candidate was a patient who failed to wean by 5-7 days and had limited extra thoracic injuries but it was unclear if this was followed in their study protocol.[161] Doben et al., meanwhile, describe a prospective weaning regime that was specific and measurable and included a spontaneous breathing trial which was attempted every 12 hours after commencement of mechanical ventilation.[71] Three

consecutive failures of the spontaneous breathing trial amounting to 36 hours was considered an indication for surgical fixation.

'A failure of the spontaneous breathing trial was defined as any of the following: respiratory rate greater than 35 sustained for more than 5 minutes, tachycardia increase of greater than 30% from baseline, hypertension increase greater than 30% from baseline, hypotension requiring intervention, cardiac arrhythmia, or desaturation 88% or less sustained for more than 3 minutes'[71].

3.3.9.6 Paradoxical movement

Confusingly flail chest with paradoxical movement was reported in ten studies as an indication.[70, 72, 74, 81, 87, 95, 163, 170, 173, 176] This represents the difference in definitions of flail chest and flail segment. Paradoxical movement with multiple unifocal rib fractures was reported in five studies.[70, 76, 87, 159, 173]

3.3.9.7 Chest wall deformity and displacement

Chest wall deformity combined with flail chest was reported in seven studies[64, 65, 69, 84, 143, 156, 163] and multiple unifocal rib fractures in five studies,[88, 99, 143, 156, 166] but the definition of deformity was only provided in two papers. Voggenreiter et al. described deformity as *'stove in chest'* or *'> 5cm impression of chest wall'*.[65] Solberg et al. describe a superior-lateral implosion injury but their description is not clear about the expected degree of severity of this injury.[156]

Displacement of flail segments was reported in two studies,[92, 159] but the displacement was not quantified within the study methods. Displacement in multiple unifocal rib fractures was described by Thiels et al.[187] and Nickerson et a l.[162] as more than 1 rib width but was not quantified in a further three studies[88, 99, 159]. No study tested the degree of deformity or displacement as a dependent factor on surgical outcomes.

3.3.9.8 Pulmonary contusion

Pulmonary contusion (PC) was not described as an indication in any study. Many studies did, however, include patients with pulmonary contusion although other studies have described that pulmonary contusion is a contraindication.

Zhang et al. did not describe pulmonary contusion as a specific indication for surgery but nonetheless only included patients with pulmonary contusion in their

study.[74] In their retrospective cohort study of 39 patients with flail chest and pulmonary contusion (FC-PC) they saw an improvement in hospital length of stay in those who had fixation to 38 days Vs 60 Days p=0.049 for those who were managed non-operatively. There was a reduction in the length of mechanical ventilation (MV) 8 Vs 15.5 days (p = 0.19) and tracheostomy (OR 0.0111, p = 0.039) when they analysed those patients who had early fixation (within seven days) compared to late fixation (after seven days).[74] So although pulmonary contusion is not described as a specific indication there is some evidence to show hospital length of stay can improve with surgical fixation compared to non-operative management in the presence of pulmonary contusion.

A retrospective cohort [157] of patients were subgrouped into those with a chest wall lung injury score of 2 or less compared to greater than 2. Surgical fixation was favoured across all outcomes, and the strength of this association did not change when severe pulmonary injury was compared to minor pulmonary injury. A retrospective study by Voggenreiter et al.[65] divided their cohort into four groups; Group 1 FC and surgery, Group 2 FC-PC and surgery, Group 3 FC and MV and Group 4 FC-PC and MV. The study concluded that surgical fixation in patients with pulmonary contusions is not beneficial over mechanical ventilation and thus they regard pulmonary contusion as a contraindication. Their indications described by their clinical protocol are as follows:

1. *Flail chest with indication for thoracotomy from intrathoracic injury ("stabilisation on retreat")*
    - *Initial haemothorax of > 1.5L or*
    - *Haemodynamic instability due to continuous blood loss via chest tube > 200 mL/h*
    - *Pulmopleural air leak with loss of > 40% of minute ventilation*

2. Flail chest ***without pulmonary contusion*** *but respiratory insufficiency and without severe head injury (AIS-head□4)*

- *Respiratory rate > 35 breaths/min*
- *Hypoxemia with PO2 < 60 mmHg*
- *Hypercapnia with PCO2 > 55 mmHg*
- *Oxygen saturation under supplementive oxygen < 90%*

3. Paradoxical movement of a chest wall segment in the weaning period from the ventilator

4. Severe deformity of the chest wall ("stove-in chest")

Impression of the chest wall > 5cm

All the patients in group 1 were operated on for respiratory insufficiency secondary to chest wall instability, with no patient having an intrathoracic injury. Patients in group 2 who had pulmonary contusion were not operated on due to their contusion injury but were instead as a '*retreat indication'* after emergency surgery following intrathoracic injury, severe blood loss or haemodynamic instability (n=8), or for chest wall instability after an attempt of weaning (n=2). The injuries sustained, and subsequent treatment, between groups 1 and 2 were significantly different and should not be compared. A more sensible conclusion would state that patients who have surgical fixation on retreat spend longer on mechanical ventilation than patients who have surgery for chest wall instability only.

Again, no comparison can be made between groups 2 and 4 due to the small sample size of group 4 (n=4), but also due to the differences in injury severity and type. Although all patients in groups 2 and 4 had pulmonary contusions (severity not classified), if intrathoracic injuries had been comparable between groups then they would all have required surgery. No patient in group 4 had a serious thoracic injury that required emergency surgery, and therefore this group is not comparable to group 2.

3.3.9.9 Haemodynamic instability

Haemodynamic instability and flail chest was reported in one study[173] and with multiple unifocal rib fractures in two studies.[166, 173] Haemodynamic instability was qualified in only one study, described in 3.3.9.8.[65]

3.3.9.10 Independent of injury type

The following indications are described as an independent indication not relating to either FC or MURF. Sixteen studies [6, 59, 64, 65, 69, 70, 87, 88, 92, 157, 163, 170, 179, 181, 184, 185] report that having another thoracic operation for a different indication is an opportunity to fix the rib fractures as a *'retreat indication'.*

Five studies [162, 163, 179, 184, 188] report that surgery is indicated if rib fractures irritate underlying organs and one[73] further describes a 30% loss of volume of the hemi thorax. Only one study reported that an indication would be based on a patient's pre-morbid state and stipulated that those with underlying chronic lung disease should be considered for surgery.[143] Three studies described that anticipated non-

union was an indication for surgery but the conditions that constituted anticipated non-union were not defined.[162, 163, 187]

3.4 Discussion

The systematic review included 64 studies of which only four were described as RCTs and only two had low risk of bias. The meta-analysis is the largest pooled analysis conducted within the published literature and is the only review to encompass a fourth randomised control trial, albeit a trial at risk of bias.

3.4.1 Principal Findings

In this section the principal findings are discussed.

3.4.1.1 Effectiveness

The meta-analysis found that patients who have rib fracture fixation within the included studies exhibit, on average, an improvement in length of mechanical ventilation -4.03 days, 95% CI [-5.48,-2.58] compared to the non-operative group. There was considerable heterogeneity in the included studies, however, reducing the strength of this evidence and the conclusions that can be drawn from it.

There was a statistically significant improvement in length of ICU stay (-3.27 days, 95% CI [-4.78, -1.76],) mortality (RR 0.39, 95% CI [0.24, 0.64]), pneumonia (RR 0.67, 95% CI [0.48, 0.95]) and tracheostomy (RR 0.5, 95% CI [0.38, 0.65]) with rib fracture fixation compared to non-operative management. There was no statistically significant improvement in length of hospital stay (-2.53 days, 95% CI [-5.66, 0.61]) in patients who had fixation compared to non-operative management. Substantial heterogeneity was seen in all outcomes except mortality and tracheostomy which are outcomes that are factual and less likely to be open to interpretation. It may be that the heterogeneity for some outcomes is due to differences in discharge criteria of hospitals and intensive care units, as well as the definition of the outcome, for example pneumonia. Several studies reported on groups that were historical controls or non-comparable control groups, increasing within study variation. Due to considerable heterogeneity across all other outcomes, subgroup analyses were performed to explore the injury type and the timing of fixation.

Other secondary outcomes that showed statistically significant improvement following surgery included the cost of treatment, lung function tests, PaO_2, chest deformity, thoracic movements, acute and chronic pain.

Outcomes that did not show improvement include $PaCO_2$, shoulder movements, overlapping or displacement of ribs and chest tube duration.

3.4.1.2 Study risk of bias

Studies on the whole were of poor quality; three RCTs specifically had an unclear or high risk of allocation and reporting bias. It was possible to locate a pre-specified protocol for only one RCT, which overall scored a low risk of bias. Non-randomised studies were also of poor quality, with only four achieving the full score. The risk of bias was higher in those using a historical cohort, which may not have had similar levels of initial advanced trauma life support or the most modern ventilation and regional anaesthetic regimes. A few studies reduced this bias by using matched case analysis and prospective collection of data. Blinding of assessors and clinicians who were both treating and conducting the trial was questionable. Studies were included regardless of risk of bias, limiting the meta-analysis conclusions since treatment effects are often over-estimated in high risk of bias studies.[194]

3.4.1.3 Injury type

Although it was initially planned that a subgroup analysis would explore FC versus MURF since included studies were inconsistent in their definitions of flail chest and did not report these injuries separately this turned out not to be feasible. A compromise to differentiate between injury types was to include those studies that fixed only flail chest and those that also included multiple unifocal rib fractures, comparing these against non-operative management. There were statistically significant differences between the two subgroups for the outcome total length of mechanical ventilation. The length of mechanical ventilation was shorter in the FC+MURF group than the FC only group compared to non-operative management since confidence intervals did not overlap. The subgroup analysis did not meaningfully change the levels of heterogeneity found within studies in respect to any other outcome.

Patients with rib fractures and pulmonary contusion exhibited improvement with surgical fixation compared to non-operative management in one study,[74] but

fixation did not confer significant benefit in another study where pulmonary contusion was described as a contraindication.[65] Due to substantial bias allocating patients to these groups retrospectively in this study these conclusions were not valid, however.

3.4.1.4 Timing of surgery

Published consensus, based on Level 5 evidence, advises fixation within 72 hours.[5] Studies that reported on the timing of surgery were entered into a subgroup analysis of those that on average operated before 72 hours and those that operated after 72 hours. Since not all studies reported timings there were fewer studies for a pooled analysis but a similar effectiveness estimate was seen as the original overall effectiveness analysis. This held true for all outcomes except for mortality in which the direction was in favour of rib fixation compared to non-operative management but was not statistically significant. In so reducing the number of studies has not substantially affected the overall pooled effectiveness. The subgroup analysis shows that early fixation results in a shorter length of mechanical ventilation compared to late fixation. Across all outcomes, late fixation was still in favour of operative fixation compared to non-operative but the only statistically significant subgroup difference is seen in respect to length of mechanical ventilation.

3.4.1.5 Outcome measurements

Sixty-five different outcome measures were reported and each of those were measured at different time points. There was difficulty in comparing outcomes for their effectiveness in the meta-analysis due to the variety in reporting of outcome measures as well as the timing of the measurement.

Multiple studies have concluded that rib fracture fixation improves short term in-hospital outcomes, suggesting that this surgery is safe and effective. Long-term morbidity and adverse events were reported less frequently in the studies, however. When they were, adverse outcomes were relatively high. Thus, wound infections were around 10% and up to 12% of patients required metalwork removal following migration of intramedullary k wires. Although these adverse events seem high and would not be tolerated in elective practice, the potential for gains in early mortality and morbidity could outweigh the risk of adverse events.

Patient-reported outcomes (PROMs) are reported infrequently and therefore there is limited evidence of patient experience. Patient satisfaction and assessment of whether patients would recommend this procedure to a family member or friend provided mostly positive results, but was polarised with several patients having poor satisfaction due to complications. Patient satisfaction was assessed in one case series but has not been undertaken in a controlled study. This would be an asset for future studies into effectiveness. A patient perspective on outcome measures, as well as the experience of treatment and recovery would be essential in the preparation of a trial. Qualitative research, which could include in-depth interviews or focus groups[195] with patients who have undergone either surgical or non-operative treatment for rib fracture fixation may yield important insights into their experiences and preferences, and identify further outcomes that are important to them. Qualitative research could also explore the willingness to be randomised in a trial setting in respect to a potential surgical fixation.

3.4.1.6 Indications for surgery

Evidence for indications for surgery was difficult to extract and synthesise since the definitions of injuries, measurements and diagnosis of respiratory failure, failure to wean and need for tracheostomy were poorly defined or inconsistent. Time and again authors describe flail chest injury specifically as an indication for surgical intervention and in combination with respiratory failure, failure to wean, and paradoxical movement. Multiple unifocal rib fractures as a sole indication was only advocated in four studies but was consistently advocated by authors in combination with other factors, such as paradoxical movement, failure to wean, respiratory failure, chest deformity and rib fracture displacement.

3.4.2 Strengths, limitations and protocol deviations

This review has followed strict protocols with an a priori method and has included the checking of at least 50% of the data by a second researcher. An assessment of risk of bias has been undertaken for all studies and the findings for this have been taken into consideration in the conclusions made based on the evidence. One further RCT has been added to the evidence synthesis. This may have been missed by some other recent systematic reviews as it has only recently been indexed, although published in 2015. Extra data was requested from primary study authors so competed data was available to meta-analyse all the RCTs for the planned outcomes. Data was shared by Marasco et al.[20] so that meta-analysis of

mean difference could be undertaken for all outcomes. Grey literature was searched and synthesised, however it did not yield any additional studies that could be used in meta-analysis. Several conference abstracts were identified but were not followed up with published articles. This may have been because they were from non-English speaking countries and may have been published elsewhere. Since only English-language papers were synthesised important data may have been missed

Classifying studies into FC and FC+MURF was a deviation from the protocol. Since there was a lack of studies reporting multiple unifocal rib fractures separately they were grouped as FC+MURF and this reduced the applicability of the evidence generated on multiple unifocal rib fractures. Other limitations to this meta-analysis include the pooling of both RCT and NRS which may be problematic because non-randomised studies are subject to selection bias which in turn could affect study results.[196] NRS were less likely to have standardised treatment protocols, consistently apply indications for surgery, and comparable treatment groups, all of which could bias results. No sensitivity analyses were completed but subgroup analyses tried to tackle some between study differences. Using aggregated patient data has its limitations but individual participant data is labour intensive and often gives similar results as aggregated data.[197] Subgroup analyses only partly addressed these between study differences. Future studies should look to power their study to complete subgroup analyses on early and late fixation and differences of injury patterns as these differences have affected outcomes. This may require a sample size that is not feasible to recruit to. A more practical solution to address heterogeneity may therefore be to require that fixation is at least within 72 hours. Given that the evidence, albeit with limitations, suggests that outcomes may be better within this timeframe.

It is hypothesised that length of mechanical ventilation, length of ICU stay and length of hospital stay is potentially skewed data and therefore using the mean difference would not be appropriate within a meta-analysis. Although very few studies with a control group reported medians, the data from case series studies did show some skewing of this data. To investigate this further the procedures set out by Altman et al.[198] could be used to assess whether skewness could be found from the presented summary statistics. If found to be skewed this could then be transformed using formulas derived by Higgins et al.[199] This has not been undertaken and potentially is a significant limitation of the meta-analysis.

The ideal solution would be to use individual patient data that could be transformed into normalised data prior to analysis, but this was not feasible with the resources available. The mean difference has been used in a similar way by the six previous meta-analyses described in chapter two without consideration of accounting for skewed data.

As with any trauma research there is always difficulty in assessing the patient characteristics, as well as documenting and comparing other injuries. No two patients are the same and therefore the intervention and control groups are not always comparable. The lack of transparent weaning and tracheostomy protocols, and of agreed definitions of respiratory failure and pneumonia could allow significant bias within studies. UK patients were only included in one case series of twelve patients, however, significant difference in management is not expected compared to other countries.

Since studies often failed to report their definition of flail chest, it was difficult to say whether the same injuries were being compared equally. Not one of the RCTs defined flail chest injury within their selection criteria. Failure to report multiple unifocal rib fractures separately meant that it was not possible to compare directly between flail chests only and multiple unifocal rib fractures only.

There was also a lack of descriptions of the indications for surgery in the retrospective studies. Most often, they compared patients undergoing fixation of rib fractures and a historical cohort of non-operative patients. These papers often had a specific inclusion and exclusion criteria that fitted with their research question but did not discuss the original surgical indications. Not knowing the specific indications has a potential to bias results since the indication for surgery is a possible confounding variable. An example for this could be of two separate patients included in a retrospective cohort with the inclusion criteria of flail chest. In one patient, the indication for surgery is massive haemorrhage, requiring an emergency thoracotomy with the patients flail ribs fixed as a ‘retreat’ indication. Within the same series, a patient with flail chest who had been on an invasive ventilation for five days and was unable to wean from the ventilator was included. These very different injuries would fit the same inclusion criteria even though it is clear that there are significant differences within these cases that could affect overall outcomes. It may be, in fact, that the indication for surgery is more important than the differentiation between the injury types. In future, it may be

more meaningful for trials to stratify for indication for surgery at randomisation rather than injury type. Even though the subgroup analysis of flail chest only and FC+MURF describes the included injuries and not specifically the indication, effectiveness can be shown between these two groups notwithstanding that the indications were unknown in most studies.

3.4.3 Improving the evidence

'The IDEAL framework describes the stages through which interventional therapy innovation normally passes'.[24] Within the IDEAL Framework,[200] it is expected when researching a new surgical procedure or device that the idea will be developed, explored and assessed before beginning a long-term study. It is expected that the level of evidence will increase with time, progressing from structured case reports to routine registry data for surveillance as evidence is gathered. This is to ensure, first, that the intervention is safe before progressing to show that it is effective in patients with a specific indication. Ideally, evidence would then seek to find validation for a broader spectrum of indications before defining the specific indications and following patients in a long-term study. There appears to be no such stepwise approach found in the development of rib fixation evidence, however. Following the publication of an RCT by Marasco et al.[20] in 2013 there has been a surge in the publication of case reports, series and some NRS. This is probably due to the fact that this study showed that rib fracture fixation could be successful in a specific patient group and new studies are expanding indications for the population receiving surgical fixation and reporting their experience in case series and non-randomised controlled studies, but not committing this yet to randomised evidence. As the indications for fixation of surgery are broadening it is essential that new randomised evidence should be sought so as to assess rigorously whether the intervention is effective in a broader population. It is clear that any new planned research should take into account the importance of defining the injury, the indications for surgery and should aim to tackle the issue of the timing of surgical fixation more fully. Further consensus work following this review aims to tackle these issues further in preparation for future trial work.

3.4.4 Conclusions

Meta-analysis has shown some improvement arising from the internal surgical fixation of flail chest and multiple unifocal rib fractures on outcomes of length of

mechanical ventilation, length of stay in ICU, risk of mortality, pneumonia and tracheostomy placement. As indications for such treatment are not well defined, however, current large randomised control trials were deficient and NRS were lacking comparable groups. Accordingly, further evidence is required before concluding that internal fixation is effective. Further study is needed to identify the specific indications and timing for surgery as these are still ill defined and the variability within and between studies makes it difficult to interpret who the evidence might be generalisable to. Long-term outcome measures and adverse events need to be captured and reported consistently in future studies. There is a need for a minimum outcome dataset so future studies can be compared in evidence syntheses and also to ensure that the outcomes assessed are relevant for patients.

Chapter 4 - Developing a Consensus on Indications, Timing and Core Outcomes for Surgical Fixation of Rib Fractures

4.1 Introduction

A consensus on outcome measures appears to be the biggest gap within the available knowledge base. The lack of such a consensus means that meta-analysis of previous studies was difficult since multiple studies had presented a multitude of outcomes that were not comparable. This increases research waste since standalone studies may not have the statistical power that comes when comparable studies are entered into meta-analysis. The effect of fewer studies being entered into meta-analysis reduces the strength of the evidence that recommendations can be based on. The number outcomes measured by studies that could not be compared makes developing a core outcome set a specific priority in rib fracture research, especially since there is currently no evidence to suggest that the most appropriate outcomes are being assessed.

In addition, the synthesised evidence has revealed that rib fractures are fixed for a variety of indications.

4.1.1 Research Questions

What are the indications for rib fracture fixation in an effectiveness trial, what time frame should surgical fixation be undertaken and what outcomes should be measured?

4.1.2 Objectives

To develop a consensus on:

- a Core Outcome Set (COS) for patients undergoing rib fracture fixation following blunt chest trauma to be used in clinical trials to assess the effectiveness of rib fracture fixation
- indications for surgical rib fracture fixation and timing of interventions in a clinical trial following blunt chest trauma

4.1.3 Overview

4.1.3.1 Outcomes

It is important to select the most appropriate outcome measures when designing a clinical trial in order to maximise the quality of evidence and the generalisability of research findings.[201] The benefits of COS include the ability to make comparisons and meta-analyse multiple studies but also the opportunity to engage with multiple stakeholder groups so as to make sure research is relevant to a wider audience. Interventions should be appropriately assessed for efficacy and efficiency. Arguably, more importantly, we should assess whether treatment benefits patients, since this is the primary reason for undertaking research. Well designed and rigorous studies can be flawed by the choice of a poor outcome measure if they do not capture the impact of the intervention. The measure needs to be sensitive to the change expected from the intervention. The researcher's ability to measure the outcome, and whether this is acceptable to patients, also needs to be addressed. In summary, a measure needs to be truthful (measures what it intends to), discriminative (sensitive to change) and feasible (easily and acceptably measured).[202]

The Core Outcome Measures in Effectiveness Trials (COMET) group is an organisation that has developed a methodology for developing a Core Outcome Set (COS). The COMET group defines a Core Outcome Set as:

*'an agreed minimum set of outcomes or outcome measures. It is a recommendation of **'what'** should be measured and reported in all trials in a specific area' [110]*

In addition to developing methods for establishing a COS the COMET group describe methodologies for the development of Core Outcome Measurement Instruments. A Core Outcome Measurement Instrument is how we measure a quality or quantity of an outcome variable, specifically:

'An outcome measurement instrument refers to how the outcome is being measured. It is a tool to measure a quality or quantity of the outcome. The tool can be a single question, a questionnaire, a score obtained through physical examination, a laboratory measurement, a score obtained through observation of an image, etcetera.'[203]

In the context of rib fracture fixation, therefore, this could be the forced vital capacity (instrument) measuring within the outcome domain of physiological or clinical lung function.

There are other groups who are championing outcome sets, the OMERACT group specifically support outcome development in rheumatology and have produced their own handbook, published in March 2017,[202] built on a previous publication, the OMERACT filter 2.0.[204] Although the aims of OMERACT are similar to COMET the methodology of developing what they term a Core Domain Set differs slightly. OMERACT have a hierarchy of Concepts, Core areas and Domains, which should be developed first before completing a consensus on a Core Domain Set.[202] The OMERACT group describes domains as a *'component or core area: concept to be measured, as further specification of an aspect of health, categorized within a core area.'*

The Core Domain Set is developed for studies of health interventions, being *'the minimum set of Domains to fully measure all relevant concepts of a specific health condition within a specified setting'.*[202] Although a CORE domain set is developed, other domains may still be important depending on the study question or a particular research domain of interest. This is visualised in a diagram within the OMERACT handbook, which describes domains placed in concentric spheres by decreasing importance. [202]

The COMET group, meanwhile, brings together clinicians, researchers and patient representatives who are interested in the development of COS to advise methodological frameworks. The COMET group published a handbook in 2017 describing the methodological processes that need to be followed in order to develop a COS, as shown in Figure 17.[110] The protocol developed for this project predated the publication of the handbook, however its design was heavily based on the same methodological papers that have since fed in to the handbook.

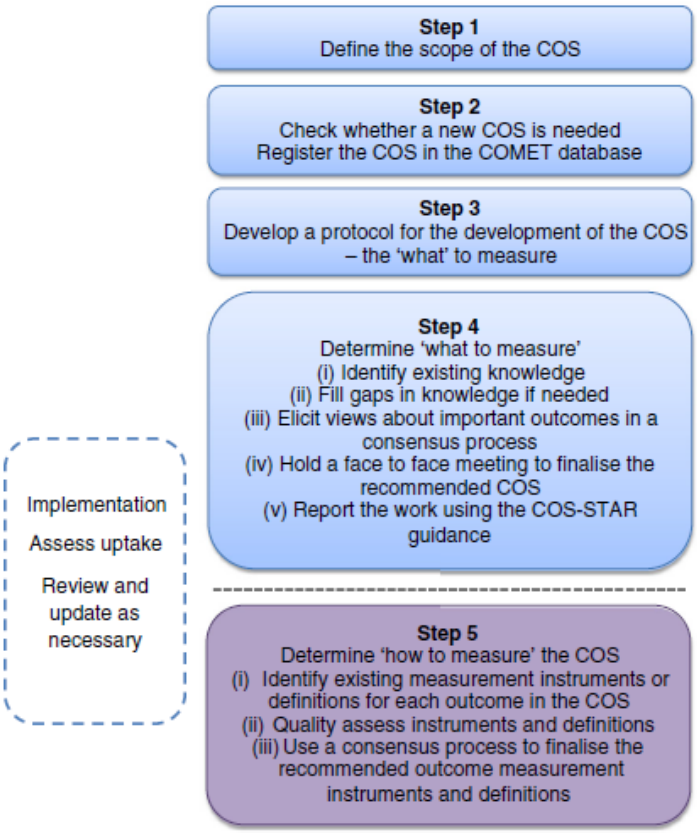


Figure 17 The core outcome set (COS) development process – taken from COMET Handbook[110]

4.1.4 Indications and timing

Published trials on rib fixation have lacked consistency in respect to the situations in which surgery is offered and also in the timing of when surgical fixation is performed. Synthesising this evidence has proved difficult within a systematic review due to lack of clarity about specific indications and timings. A consensus on the indications and timing of surgical fixation within a trial is therefore imperative since it allows future studies to give a clear statement within their protocol that their indications and timing of fixation is based on a methodically sound consensus of experts.

Several methods have been described to develop a consensus on clinical evidence. Consensus statements can be constructed from a review of the literature and can be assigned a GRADE level of evidence. A consensus conference or Delphi technique can also be used. A consensus conference has been used in a previous consensus on indications for rib fracture fixation, but only included a small number of cardiothoracic and general surgeons.[5] The decision was made to use the Delphi method to develop the consensus on the indications

and timing of surgical fixation since a captive audience would have already been gathered for the outcome consensus.

4.2 Method

A Delphi consensus was undertaken to achieve consensus on outcomes, indications and timing of surgical rib fixation in a clinical trial. The COMET approach was used not on the basis that it had demonstrable superiority over other potential approaches but because I had attended the COMET annual conference and therefore had more experience of these methods. The overall method of consensus is described in Figure 18.

The Delphi consensus on indications and timing of fixation, including the core outcome set, was based on the PICOS (Population, Intervention, Comparator, Outcomes and Study design) structure described in Chapter 2. The PICO is specifically for those patients who have either multiple rib fractures or flail chest that would be considered for surgical intervention.

The reporting of this chapter is structured as recommended by the guidance in the COMET Handbook[110] and subsequently published COS-STAR checklist.[205]

Figure 18 Outline of consensus study

4.2.1 Is a Core Outcome Set needed?

The first steps were to identify and fill in the gaps in the existing knowledge prior to beginning consensus work so as to determine whether a Core Outcome Set is needed. COMET has a platform on which to register completed and ongoing work on developing core outcome sets. A search of the COMET group database revealed there was no published protocol for an outcome set specific to rib fractures and none were in development by researchers (search date 14th September 2017).

A protocol was then developed and published.[206] The COS protocol was also registered on the COMET database of developing outcomes to avoid other researchers duplicating this work and to give them the opportunity to collaborate with the project. This can be accessed at http://www.comet-initiative.org/studies/details/1104.

4.2.2 Search strategy

The COMET group advocates gathering outcomes from existing work.[110] They recommend that this achieved by way of a systematic review as such reviews are an effective and unbiased method of collecting a comprehensive list. This systematic review method of gathering outcomes has been used successfully in other studies, and was also applied here.[109, 207]

The purpose of this search was to identify studies that have used outcomes and outcome measurement instruments to assess the effectiveness of rib fracture fixation and to identify what were the indications used to identify patients as well as the timing of fixation to treat them.

Brettle et al.[111] suggest that it is usually sufficient to complete a basic search to identify sufficient detail on outcomes. Increasing the search terms in a stepwise manner to an intermediate or comprehensive strategy is an option if the question is not answered by the basic search. Since a comprehensive search had already been completed for the systematic review in chapters two and three this was used so work was not duplicated. The comprehensive searches, and how the studies were selected, are reported in Chapter two, three and in Appendix A. The last search date was in March 2017.

Additionally, there are two guidance documents that are not available in electronic databases as they are not primary research but were also included since they describe recommendations for the timing of surgical interventions.

4.2.3 Data extraction, determining inclusions and wording of items to be considered for the consensus exercise on outcomes

Data extraction consisted of study characteristics as well as all the outcomes and outcome measurement instruments reported in each study. Following the selection of the relevant studies, the outcomes were extracted into a list and then grouped into similar categories so that they could be transformed into a subsequent Delphi questionnaire.

These categories are called outcome domains, which are described as 'constructs which can be used to classify broad aspects of the effects of interventions'.[110] There are multiple ontologies for grouping individual outcomes into outcome domains, however there is no such guidance for indications and timing. Grouping outcomes into domain is helpful to disentangle how outcomes either measure or classify disease over time, or whether they measure change as a consequence of an intervention. Five conceptual frameworks for COS selection have been described in a scoping review by Idzerda et al.[208] These include the WHO tripartite definition of health;[209] the 5 Ds (discomfort, disability, drug toxicity, dollar cost and death);[210] the International Classification of Functioning (ICF);[211] PROMIS (Patient-Reported Outcomes Measurement System);[212] and the Outcomes Hierarchy. Other conceptualized models include the Wilson and Cleary[213] model, from 1995, showing the relationship between patient outcomes and health-related quality of life, and updated models by Ferrans et al.,[214] Smith et al,.[28] Gliklich et al. and OMERACT.[204] COMET, however, have adopted the Williamson and Clarke model, as described below.

A new conceptualised framework has been developed by the COMET group and was presented at the 6th COMET conference, held in 2016,[215, 216], although at the time of undertaking this thesis this had not yet been published. The prologue to the new framework, described by Williamson and Clarke, refers to five Core domains, shown in Table 37. These include adverse events, death, physiological or clinical life impact and resource use, with 36 subdomains as detailed in Table 37 and Table 38. The Williamson and Clarke five core domains framework was chosen as

it fits with the methodology of the COMET group; however, there is no evidence to suggest this is better than any other model.

Table 37 Conceptualised framework of outcomes from presentation by Susanna Dodd at COMET VI conference in Amsterdam 2016 [216]

Core domain	Smith	Williamson/Clarke (original)	Williamson/Clarke (revised)
Adverse events	1: AEs	1: AEs	1: AEs
Death	2: Mortality/survival	2: Mortality/survival	2: Mortality/survival
Physiological or clinical	3: Physiological/ clinical	3: Physiological/ clinical	3-24: **Physiological/clinical**
	4: Infection	4: Infection	
	5: Pain	5: Pain	
Life impact	6: ADLs	6: ADLs	**Functioning** 25: Physical 26: Social 27: Role 28: Psychological/wellbeing 29: Cognitive
	7: Psychosocial	7: Psychosocial	
		8: Mental Health	
	8: QoL	9: HRQL	30: HRQL
	9: Compliance	10: Compliance	31: Delivery of care (includes satisfaction, patient preference, adherence, withdrawal, tolerability, etc.)
	10: Withdrawal		
	11: Satisfaction	11: Satisfaction	
Resource Use	12: Medication	12: Resource Use	**Resource Use** 32: Economic 33: Medication 34: Hospital 35: Operative 36: Societal/carer burden
	13: Economic		
	14: Hospital		
	15: Operative		

Table 38 Physiological and clinical domains in the revised Williamson and Clarke outcome domains framework, presented by Susanna Dodd at the COMET VI Conference Amsterdam 2016 [216]

- Blood and immune system conditions
- Cancer
- Cardiovascular conditions
- Diabetes and other endocrinal, nutritional and metabolic conditions
- Digestive tract conditions
- Ear, nose and throat conditions
- Eye conditions
- Fertility, pregnancy and childbirth
- Genetic conditions
- Gynaecological conditions
- Infections
- Injuries, accidents and wounds
- Kidney conditions
- Liver conditions
- Mental health and behavioural conditions
- Musculoskeletal conditions
- Neurological conditions
- Oral and dental health
- Respiratory conditions
- Skin conditions
- Urological conditions
- **General symptoms**

In the context of this study, extraction of outcomes was complex due to multiple similar definitions or descriptions were used between studies, for example chest

pain and chest discomfort. To be transparent, the COMET handbook recommends that outcomes and their measurement instruments should be extracted verbatim under an outcome heading, with grouping occurring at a later stage if they are similar. Unfortunately, data extraction was completed before the final COMET Handbook was published and therefore this was not undertaken as described in the handbook. In practice, therefore, outcomes were extracted from each study and were placed into a table of the relevant domains. Verbatim outcomes were not collected for each study, instead outcomes with similar definition were combined together. For example, under the domain ‘adverse events’, the outcomes of pneumonia, chest infection and lower respiratory tract infection were collectively extracted as pneumonia. A single researcher completed extraction of outcomes and categorisation into domains and sub-domains.

The list of outcomes derived from the systematic review was used to construct the Delphi questionnaires. The structure of the questionnaire in the outcome consensus exercise was ordered as per the framework by Williamson and Clarke.[110, 216] It has been shown in social science research that ordering of questions could affect responses,[217] since it is likely that later responses will be based on or related to earlier responses.[218] The outcomes listed under each domain heading were listed in alphabetical order to prevent imbalance of questions or bias in outcome list order. It was hoped this would encourage participants to rate each outcome individually on its own merit and not in comparison to the previously rated outcome.

All outcomes extracted from the review were retained in a full list to ensure that all outcomes were considered. If the list was restricted this could have led to outcomes important to participants being missed. An explanation was developed for each question and written in lay terms at a reading age of 8 years old. These ensured that each outcome was understandable with a consistent definition and that participants were able to make informed decisions in respect to each outcome.

4.2.4 Data extraction and grouping of indications for surgical fixation and timing of interventions

4.2.4.1 Indications

Indications for surgical fixation were extracted from primary studies and taken directly from the systematic review. An explanation of how these indications were extracted into the study characteristic tables is reported in chapter three sections 3.2.12.3. A distinct separation had to be made between indications for surgery and inclusion criteria for the study as these are two separate entities. For example, authors may advocate fixation in all patients who have flail chest. The same study, however, may only include those who were over 45 years old. Although this is the inclusion criteria, being over 45 years old is not explicitly an indication for surgery. The same reasoning was applied to timing of surgery.

The list of indications was initially trialled by taking verbatim quotes from the manuscripts; this became very complex and difficult to manage in tabular form, however. To simplify the extraction, similar indications were grouped upon extraction to make a simplified concise list. The simplified list distinguishes primarily by the definition of the rib fracture injury (flail chest and non-flail chest) and secondarily by additional conditions, such as chest deformity, intubation need, or failure to wean from ventilation. (Figure 19).

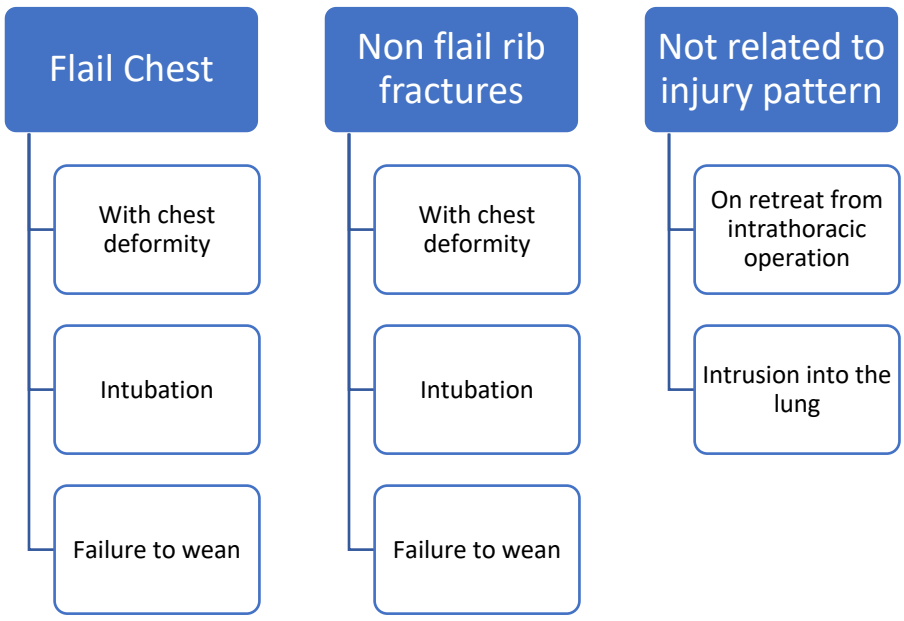


Figure 19 Data extracted into three groups of different indications, showing Injury by anatomical distinction and sub-grouped by other clinical conditions, as an example

4.2.4.2 Timing of interventions

The timing of surgery was extracted from trials or studies that outlined their rationale for timing of surgery. These were taken verbatim and then transformed into useable statements for the Delphi questionnaire. Timings of interventions were also presented as means, medians and ranges in the study characteristics tables, as stated in chapter three section 3.2.12.4. Using these timings, statements were constructed to encompass the range of timings of fixations. The primary studies based their timing of fixation on several different caveats. As an example, one study would randomise at the earliest at five days, while another study would require a period of trial of weaning and other studies suggested that they would not perform surgery after a given period of time as the window of opportunity had passed. This gave rise to three types of timing of fixation. The first group of statements relates to the earliest time a clinician would advocate conducting surgical fixation on any patient in a clinical trial, regardless of ventilation status or injury morphology. The second group of statements relates to the latest time a clinical would advocate and the third group how long a ventilated patient should have a trial of weaning from a ventilator before proceeding with fixation. Each statement on timing describes a range in hours or days, this was to try to make clinicians commit to a specific timing range during the rating stage. Timings were presented as several scenarios based on several caveats on timing that were presented in primary studies, where timing options ranged from 0 days, most operating in the first three days and very few operating after 14 days had passed. A scale of before 24 hours, 24 to 48 hours, 48 to 72 hours, 3 to 5 days, 5 to 7 days, 7 to 14 days and over 14 days reflected the most common timings, therefore.

Recommendations were extracted verbatim from the two additional guidance documents identified on the clinical management of chest trauma and then transformed into statements that could be used in a Delphi questionnaire. These related to the timing of referral for consideration of rib fracture fixation, the timing of transfer and how soon following the decision to operate surgery had to take place. Since these quotes were taken verbatim from guidance the timing of these statements was left unchanged from the original documents, but the presentation of the questions was adjusted to fit within a questionnaire format for clinical trial.

Delphi consensus for clinical practice guidelines often assign GRADE levels of evidence[155] so clinicians can use this knowledge to inform their choice in the rating stage. Since the purpose of this consensus was for clinical trial and not clinical practice, however, these GRADE levels were not assigned.

4.2.4.3 Participant Information and recruitment

Three stakeholder groups were involved in the Delphi consensus process (Figure 20)

- Medical panel
- Allied health care panel
- Patient and public panel

A multi-stakeholder panel is accepted as a gold standard approach to developing a COS.[110] The benefits of involving patients and the public include the potential to identify outcomes that have previously not been identified as important by clinicians or researchers.[219-221] Separate to the COS consensus, but delivered concurrently, a further consensus was sought from the medical panel to encompass indications for and timing of surgery. Each participant within each panel was considered an expert.

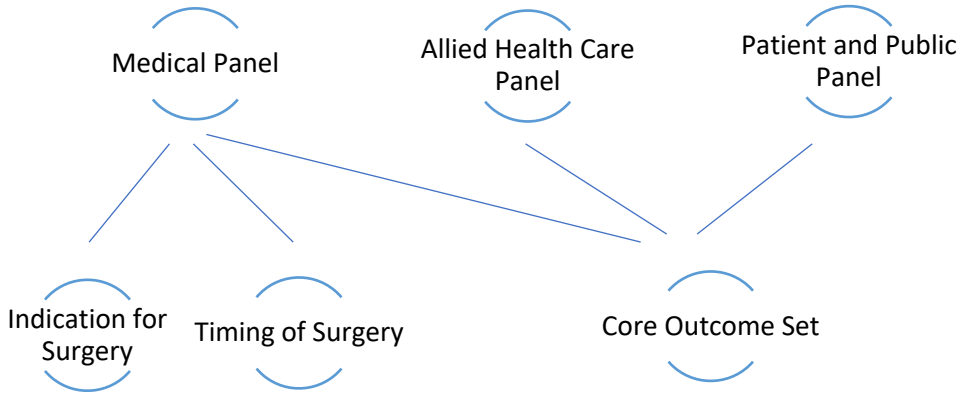


Figure 20 Composition of Delphi consensus panels

4.2.4.4 Medical panel

Clinicians who undertake the care of patients with rib fractures and who are part of the multidisciplinary team who decide on rib fracture fixation formed the clinical expert panel. This included surgeons who perform rib fracture surgery, general

surgeons who often undertake day-to-day care of rib fracture patients in district general hospitals, and intensive care physicians who provide ventilator support and acute pain management. Rehabilitation specialists were also eligible for inclusion in the panel.

Societies and associations were asked if they had relevant clinicians in their societies who undertake the care of rib fracture patients and who may be interested in taking part. Major Trauma Centres in the UK were contacted to identify those who are undertaking rib fracture care. Authors' contact details were collected from all studies included within the review as possible candidates for an expert panel. To increase participation, and to keep the sample representative, those who decline to take part in the medical panel were asked to suggest a person with similar knowledge or expertise who may take part in their place as well as a relevant allied health professional.

This panel formed the consensus on indications for surgery, timing of surgery and a core outcome set and was drawn from the international community.

4.2.4.5 Allied healthcare panel

This panel included allied health professionals who specialised in trauma rehabilitation or chest physiotherapy, such as physiotherapists, occupational therapists or specialist trauma or intensive care nurses. This panel participated in the consensus on core outcomes and was recruited internationally.

The Chartered Society for Physiotherapy published a recruitment call in their monthly newsletter and Major Trauma Centres were contacted via email to identify physiotherapists, specialist trauma and intensive care nurses and occupational therapists.

4.2.4.6 Patient and public panel

Patients and carers of patients who had knowledge of the condition were invited to take part. Patients as experts is believed to be important within the Delphi methodological process as it allows each participant to have an equal opinion whether medically trained or not. Patients were considered experts if they had suffered flail chest or multiple rib fractures or had received rib fracture fixation. Carers and family members were also be eligible to participate if they had cared for or supported a person with multiple rib fractures, flail chest or had rib fracture

fixation. This panel participated in the consensus on core outcomes and was recruited from the UK only.

Patients from relevant public and patient involvement groups and patients identified by clinicians were invited to take part. To prevent selection bias of participants, and to make the group representative, a one year sample of all admitted chest injuries from James Cook University Hospital were identified. Patient leaflets (Appendix C1) were delivered to patients at James Cook University Hospital. The onus was on the participant to contact the research team if they wished to take part. Recruitment also involved posts on trauma support website 'After Trauma' and was publicised with Twitter. The charity ICU Steps also sent out emails to their members in the form of their newsletter. Details of the research contact were provided and potentially interested individuals were required to get in touch with the research team if they wished to participate.

To take part the individual needed access to the Internet and an email address.

4.2.4.7 Group size

The COMET handbook has no advice on the size of each panel[110] and the consensus is not bounded by statistical power.[110] Attrition was anticipated to be considerable through the subsequent rounds. Patients and allied health professionals views on outcomes are particularly important to the consensus process to insure outcomes that are relevant to patients and carers therefore, as many as possible were invited.

4.2.5 Attrition

Attrition of participants after the first round was a concern. As an incentive to participate in the Delphi consensus, medical and allied health professional participants were offered a certificate of participation when they completed all three rounds. Although monetary incentives have been shown to improve response rate in some circumstances[222] they were not possible within the scope and budget of this project.

Even if a participant's opinions were in the minority they were encouraged to continue to take part as the consensus could be overestimated if they dropped out.[223]

4.2.6 Consensus Process

A maximum three round Delphi consensus was undertaken, as shown in Figure 241.

If consensus was not agreed after the third questionnaire round no further feedback was given and the consensus process was ended. Outcomes and statements without a consensus were then eliminated.

4.2.6.1 Round One

Invitations describing the study were sent via email and included a link to the first Delphi consensus questionnaire (Appendix C1). A participant information sheet was attached to the invitation (Appendix C1).

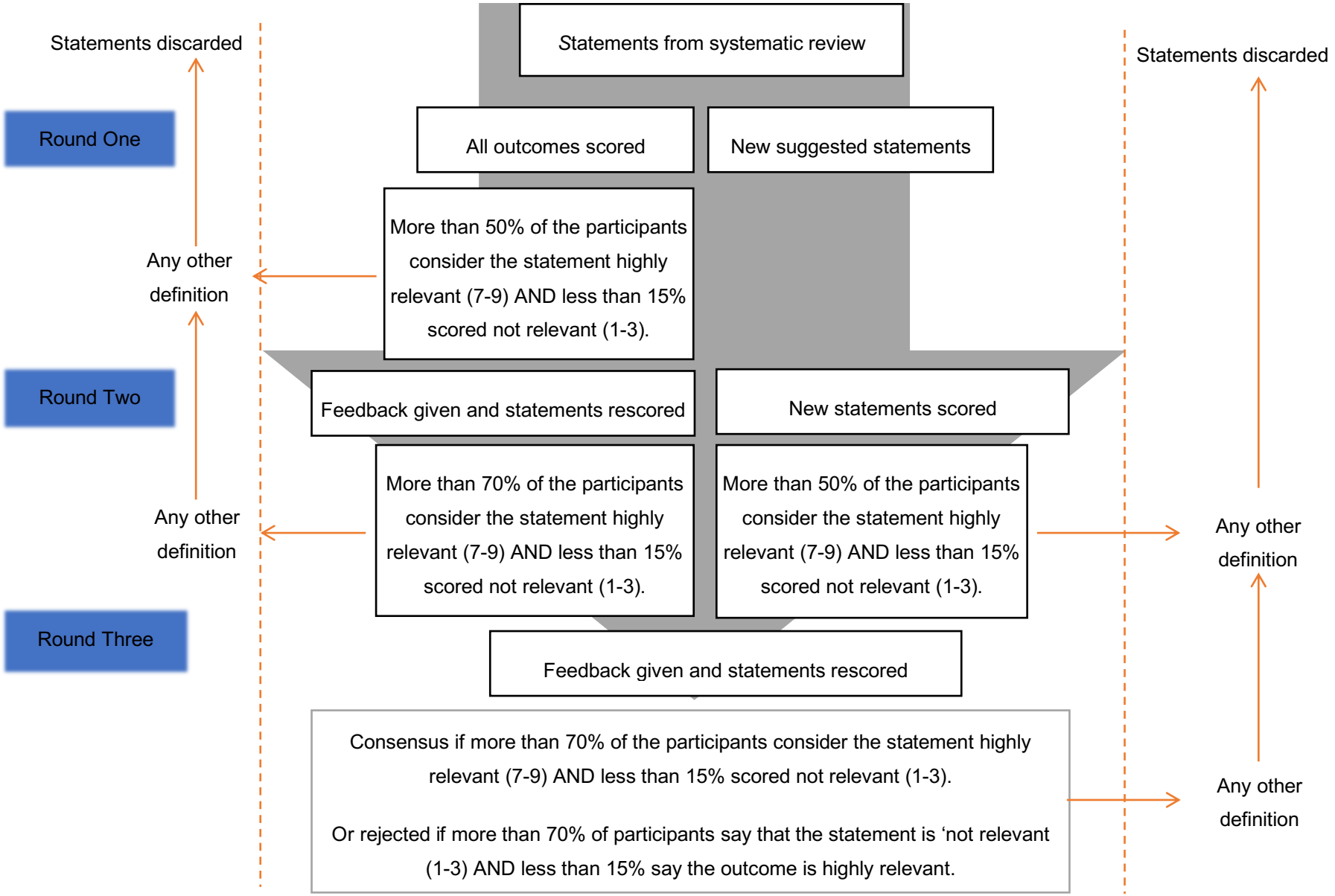
Qualtrics software (Qualtrics, Provo, UT) licensed by the University of York was used to administer all rounds of the Delphi questionnaire via email link (Appendix C2)

Consent was obtained through Qualtrics software since a written consenting process was likely to burden with wet ink signatures and face-to-face meetings were likely also to represent a burden and reduce response rate. Consent was taken within the questionnaire with participants needing to tick a box to acknowledge the conditions of undertaking the study. The survey was piloted and the COS element took no more than 15 minutes to fill out. The indications and timing element took an additional 10 minutes for the medical panel.

The Delphi questionnaire was open for four weeks to maximise the intake of participants. Three reminder emails were sent at weekly intervals. An unsubscribe box was available within the email if people did not wish to receive any further communication.

The consensus method for outcomes, indications and timing of surgery by the medical panel was completed concurrently with the outcomes consensus delivered to all respective panels.

Figure 21 The Delphi consensus rounds, scoring and feedback



4.2.6.2 Additional open questions

As recommended by COMET,[110] the first round of the Delphi asked participants an open question. This allowed participants to list what indications, timing of fixation and outcomes they feel should be included. If identified without prompting, these are likely to be important to that individual and prevent researcher bias in the study. Getting participants to identify their own outcomes may prevent overstatement of the researcher's favoured statements and would expand the list of outcomes that may not have previously been considered. Additional outcomes were hoped to be identified in the patient panel, since their views had not been explored prior to this point.

A further free comment box was added at the end of the Delphi questionnaire to allow participants to recommend further additional outcomes/indications that were not included within the initial list. Completing the Delphi questionnaire was expected to stimulate further items after considering those already listed. As recommended by the COMET Hanbook,[110] an open question at the end of the Delphi questionnaire gave a final chance for participants to identify outcomes that had been omitted.

Additional items suggested by participants were accepted into the next round if they were not included within the initial list. No item was excluded.

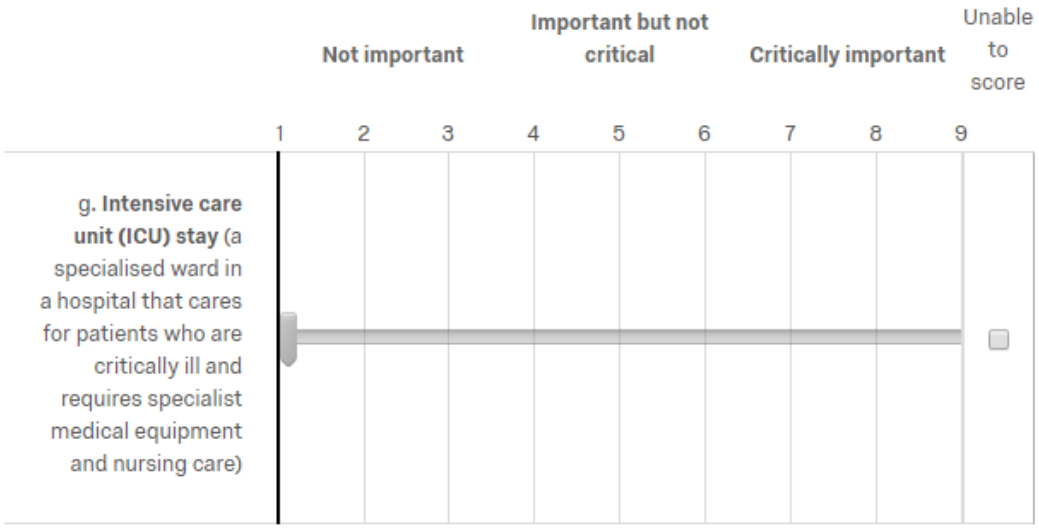
4.2.6.3 Survey questions

The second part of the Delphi, for the medical panel only, comprised of a list of statements on indications and timing of surgery. These were extracted from primary studies in a systematic review and presented as previously described.

4.2.7 Scoring

Participants were asked to rate the relevance of each item to be included within the minimum dataset or final consensus statement. The ratings used was a Likert scale from one to nine, one being not important and nine being critically important, Figure 22.

Figure 22 Example of scoring the outcome Intensive care unit stay



4.2.8 Retaining or dropping items between rounds

Items were retained and entered into the next round if 50% or more of participants in all three panels scored an item between seven and nine (highly relevant or important) and less than 15% scored the item one to three (not relevant or important). Items not meeting these criteria were dropped from the consensus process. Keeping the level at which items were retained low at 50% in this first round allows feedback to be given on a greater number of outcomes but excludes quickly those that are unlikely to achieve consensus.

Although having a stricter criterion in the first round could have achieved a consensus sooner it would not allow feedback on those outcomes or statements not achieving consensus straight away. Since it was necessary to rate large numbers of outcomes, however, this had to be balanced against the rate of attrition among participants if all outcomes were to be rated for a second time after feedback.

Using the 50%/15% rating in the first round and increasing this to 70%/15% for the second and third rounds provided enough outcomes for sufficient feedback without overwhelming the participants and without being too restrictive or over accommodating. This has been previously used in in a core outcome study for oesophageal cancer,[224] however there is no evidence to suggest what the best way to retain or drop items is.[110] The scores from the three panels were grouped together for ease of analysis, although it is recognised that this has some drawbacks. There is a risk that the patient group, being the smallest panel is likely

to be dominated by the medical and allied healthcare panel. In addition, if there are too few members within a single panel when the definitions were applied then consensus may not be achievable. On the other hand, studies have shown that patient panels are likely to be more polarised in their scoring compared to medical professionals and therefore their strong opinions could dominate medical opinions.[225] Neither method (combining panel results or requiring consensus within each panel) has been proved superior so, for balance and convenience, they were combined.

4.2.8.1 Feedback

Although retention or removal of items was based on the scoring of all three panels combined, feedback was delivered for each stakeholder panel. Ratings 1 to 3, 4 to 6 and 7 to 9 were presented for each item with the percentage score from each of the stakeholder panels. All stakeholder panels were shown the percentage rating for all other panels (Figure 23). This approach was used since being able to reflect on what other stakeholder groups feel was important and likely to lead to a stronger agreement.[225] If feedback was only presented from the participant's own stakeholder group agreement across the panels would be less likely.[225] On the other hand, if all participants received overall feedback without distinction between stakeholder groups then participants would be unable to reflect on the views of other stakeholder groups. A reminder of a participant's previous ratings were not provided. This was due to the complexities of maintaining anonymity during rounds, although it is acknowledged that a reminder of a participant's previous ratings would have enhanced the reflective process.

Intensive care stay	Not Important	Important but not critical	Critically Important
Doctors	0%	25.8%	74.2%
AHP	12.5%	12.5%	75%
Patients/Carers	0%	80%	20%
Overall	**2.3%**	**29.5%**	**68.2%**

Figure 23 Example of feedback between rounds from each stakeholder group

4.2.8.2 Round Two

A second round was undertaken with only the respondents who completed the first round or had completed more than 50% of the questionnaire. Suggestions from the first round of additional items were included within this second Delphi questionnaire but not duplicated if the item had been covered in the first round. If items were able to be combined due to similarity this was also considered if there were comments to support this.

4.2.8.3 New statement scoring

The new statements identified from the first round were submitted into the second round for rating between one to nine. Retaining and dropping of outcomes was reached according to the same criteria as in round one with any new outcomes first being scored at 50%/15% in the second round and then 70%/15% in the third round.

4.2.8.4 Consensus definition

- A consensus was reached if more than 70% of the whole participant group considered an item highly relevant (seven to nine) AND less than 15% scored an item not relevant (one to three).
- A consensus was also reached if more than 70% of the whole participant group said that the statement was ‘not relevant (one to three) AND less than 15% said the statement is highly relevant.

All items that did not satisfy these criteria were considered not to have consensus and were therefore dropped. Similar types of criteria have been used in several Delphi studies.[35, 226-228] The 70/15 consensus definition was anticipated as being likely to result in sufficient outcomes being included within the COS without being too restrictive or over accommodating.[110]

The consensus process ceased at this point. Although face-to-face meetings are described in the OMERACT and COMET handbooks as a good way to confirm and agree to the final outcome set this was beyond the scope of the work of this MD. The full process of feedback and scoring within rounds is shown in Figure 21.

4.2.9 The level of consensus

A brief assessment was made on the degree of consensus in each round by looking at the spread of group scoring and the change in group scoring between

rounds. It is important to assess the degree of consensus to ensure that the survey is working towards consensus. This can be done by assessing the change in scores of individuals. The best way to do this has not yet been described, although both standard deviations and interquartile ranges have been used previously.[110] The difference between the scoring in the first and second rounds was analysed using a paired student T test to show an overall trend compared to the individual scores and thereby to assess the direction of consensus.

4.2.10 Ethics

Ethical approval was obtained from the University of York Health Science Research Governance Committee. HRA (235596) and North West Research Ethics Committee (18/WM/0018) granted approvals on 11 January 2018. Further R&D approvals were granted by James Cook University Hospitals on the 26th January 2018 for access to patient addresses.

All data was anonymised and stored in accordance with the guidelines of the York Trials Unit. A full explanation of the procedures followed is available in the published protocol.[206]

4.3 Results

4.3.1 Recruitment

Two hundred and twenty-two clinicians were identified and invited directly via email to take part. Sixty-six patients were sent invitation leaflets by post and advertisements were posted online and by email. Ten patients' and fourteen allied health professionals replied through the various recruitment methods inviting participants.

Sixty-five individuals started the Delphi process: 52 clinicians, seven patients and six allied health professionals. The characteristics of the participants included in each panel are displayed for each survey round in Table 39. The medical panel was international and consisted of clinicians practicing in multiple countries and from multiple specialties.

Table 39 Panel characteristics for each round

	Round 1	Round 2	Round 3
Patients	7	4	2
Allied health Professional	6	6	5
Medical	52	19	16
Specialty			
Accident and Emergency	3	2	1
Anaesthetics	2	1	1
Intensive Care	2	1	1
Cardiothoracic Surgery	10	9	7
Thoracic surgery	2	0	0
General Surgery	4	1	1
Trauma and Orthopaedic Surgery	16	5	5
Trauma and Emergency Surgery	1	0	0
Resident in Training	1	0	0
Other (not specified)	11	0	0
Country (all panels)			
Columbia		1	1
Germany		2	1
Italy		1	1
South Korea		1	0
Spain		2	2
Sweden		1	1
UK		13	11
USA		7	6
Unknown	65*	1	0
*Country data was not collected in round one			

4.3.2 Gathering of items

From the systematic review, 30 items on indications, 28 on timing and 60 on outcomes were entered into the round 1, as in Figure 24.

4.3.3 First round

Fifty-two clinicians, seven patients and six allied health professionals took part in the first round. Although they completed the survey some participants answered ‘unable to comment’ for multiple questions, reducing the number of participants assigning a score to each statement; Appendix C3, Table 112 to Table 114 shows the scoring for each item in each round.

Using the 50%/15% threshold 15 indications, 7 items on timing and 46 outcomes were retained and entered into round 2, Figure 24. There were eight new indications and three new outcomes identified that were also entered into the second round (Table 40), no statements were amalgamated.

Figure 24 Flow diagram showing the dropping and retaining of statements and outcomes in the consensus rounds

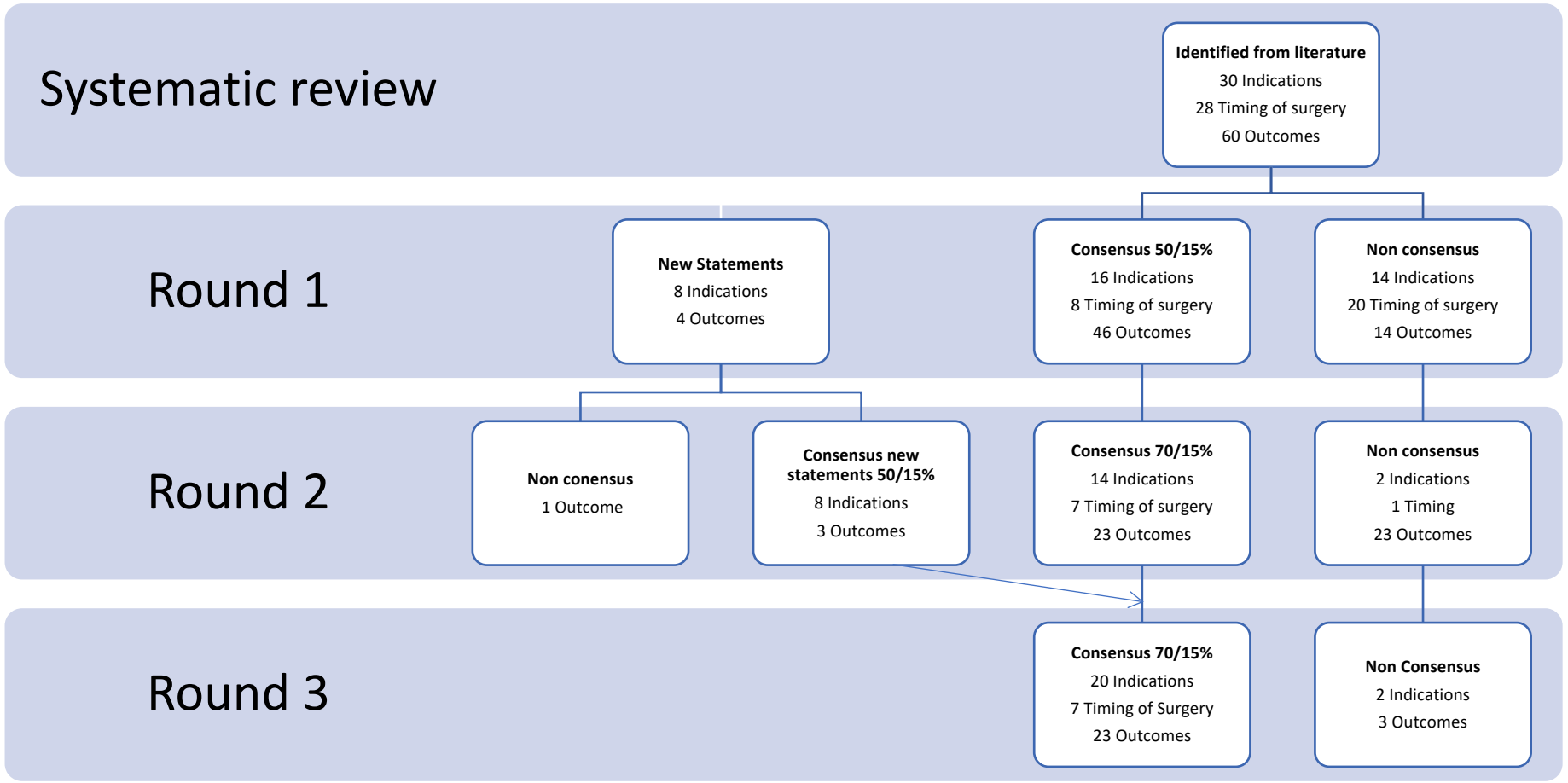


Table 40 New suggested indications and outcomes

New Indications
FLAIL Chest with concomitant sternal fracture
MULTIPLE rib fractures with concomitant sternal fracture
Bilateral FLAIL Chest
Bilateral MULTIPLE rib fractures
Any rib fracture with intrusion into underlying lung
Any rib fracture with concern for diaphragm laceration
MULTIPLE rib fractures with haemothorax
FLAIL Chest With Haemothorax
New Outcomes
Health related quality of life (the standard of health, comfort, and happiness experienced by an individual related specifically to their health
Pulmonary toilet (the ability to clear lung secretions)
Narcotic addiction (whether someone is dependent on using pain medication such as morphine)
Cosmetic look of the chest (the shape of the chest)

4.3.4 Second round

Nineteen clinicians, six allied health professionals and four patients completed the second round. The new statements were scored using the 50/15% threshold: all eight new indications were retained, as well as three out of four new outcomes. Using the higher 70/15% threshold for items presented at round one, 23 outcomes and 14 indications were retained, seven related to timing of surgery (Figure 24 and Appendix C3, Table 113). No new statements or outcomes were suggested in this round.

4.3.5 Third round

The final consensus panel consisted of five allied health professionals, two patients and 16 clinicians. All statements were re-rated using the threshold 70/15% and consensus was gained on 20 indications (Table 41) seven timings of interventions (Table 42) and 23 outcomes (Table 43). Appendix C3, Table 114 contains the results for each of the three panels. Flail chest gained a higher percentage of consensus compared to multiple rib fractures or sternal fractures. The earliest a person should be fixed gained consensus at between 24 and 48 hours. Eight adverse events outcomes, three mortality, five physiological or clinical, six life impact and one resource use, gained consensus.

Table 41 Final scoring of indications for rib fracture fixation after three rounds

Percentage for each score category in Round 3			
Indications for surgery	**1-3**	**4-6**	**7-9**
Any Flail SEGMENT with paradoxical movement (flail chest)	0	6.3	93.8
Flail CHEST with respiratory compromise	0	0	100
Flail CHEST and patient requiring invasive ventilation	0	012.5	100
Flail CHEST and intractable pain despite regional and epidural anaesthesia	0	0	100
Flail CHEST and failure to wean from ventilation within 48 hours	0	0	100
Flail CHEST requiring tracheostomy placement	0	25	75
Flail CHEST and underlying chronic lung disease	0	12.5	87.5
MULTIPLE adjacent rib fractures with paradoxical movement	0	6.3	93.8
MULTIPLE adjacent rib fractures with respiratory compromise	0	6.3	93.8
MULTIPLE adjacent rib fractures and patient requiring invasive ventilation	0	6.3	93.8
MULTIPLE adjacent rib fractures and intractable pain despite regional and epidural anaesthesia	0	0	100
MULTIPLE adjacent rib fractures and failure to wean from ventilation within 48 hours	0	6.3	93.8
MULTIPLE adjacent rib fractures with deformity	0	25	75
MULTIPLE adjacent rib fractures requiring tracheostomy placement	0	18.8	81.3
FLAIL Chest with concomitant sternal fracture	0	12.5	87.5
MULTIPLE rib fractures with concomitant sternal fracture	0	25	75
Bilateral FLAIL Chest	0	0	100
Bilateral MULTIPLE rib fractures	0	18.8	81.3
Any rib fracture with intrusion into underlying lung	0	25	75
FLAIL Chest With haemothorax	0	6.3	93.8

Table 42 Final scoring for timing of interventions after three rounds

Percentage for each score category in the final consensus round			
Timing of interventions	**1-3**	**4-6**	**7-9**
The EARLIEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 24 and 48 hours after injury	0	12.5	87.5
Patients should be REFERRED to a multidisciplinary trauma unit within 24 hours for consideration of surgical rib fracture fixation	0	18.8	75
Patients should be REFERRED to a multidisciplinary trauma unit within 48 hours for consideration of surgical rib fracture fixation	0	12.5	87.5
Patients should be TRANSFERRED to a multidisciplinary trauma unit for rib fracture fixation within 24 hours of the decision to transfer or the patient becoming fit for transfer.	0	18.8	81.3
Patients should be TRANSFERRED to a multidisciplinary trauma unit for rib fracture fixation within 48 hours of the decision to transfer or the patient becoming fit for transfer.	0	81.3	87.5
Patients with rib fractures (independent of ventilation status or type of injury) should have surgical fixation within 24 hours of the DECISION to operate unless patient becomes unwell or there are complications	0	18.8	81.3
Patients with rib fractures (independent of ventilation status or type of injury) should have surgical fixation within 48 hours of the DECISION to operate unless patient becomes unwell or there are complications	0	6.3	93.8

Table 43 Final Core Outcome Set after three rounds

Percentage for each score category in the final consensus round			
Outcome Measure	**1-3**	**4-6**	**7-9**
Adverse Event			
Acute Respiratory Distress Syndrome	0	13.6	86.4
Empyema	0	18.2	81.8
Pneumonia	0	27.3	72.7
Reintubation or Failed extubation	0	23.8	76.2
Respiratory failure	0	27.3	72.7
Iatrogenic mediastinal injury	0	27.3	72.7
Iatrogenic thoracic injury	0	22.7	77.3
Iatrogenic vascular injury	0	27.3	72.7
Mortality			
Mortality	0	9.1	90.9
7 Day Mortality	4.5	13.6	86.4
30 Day Mortality	4.3	8.7	87
Physiological or clinical			
Chronic Pain	4.3	21.7	73.9
Dyspnoea	4.5	22.7	77.3
Lung Function	4.5	13.6	81.8
Ventilation	0	13.6	86.4
Pulmonary toilet	0	13.6	86.4
Life Impact			
Disability	4.3	8.7	87
Physical function	0	13	87
Quality of life	0	8.7	91.3
Health related quality of life	0	4.3	95.7
Return to Activities	0	17.4	82.6
Return to Work	0	21.7	78.3
Resource Use			
Invasive mechanical ventilation	0	13.6	86.4

For all 20 indications for surgery and seven timings of interventions the level of consensus increased through the rounds. The level of consensus agreement decreased through the rounds for two of the final outcomes, however: ‘respiratory failure’ as an adverse event and ‘return to work’ as a life impact outcome. For all other outcomes, the level of consensus increased. Within the different panels there was some disagreement between ratings on outcomes, however, since the AHP and patient panels were small and thus the final level of consensus was most influenced by the clinician panel. Sepsis was rated highly by the patient and AHP panels but less so by the clinician group (percentage scoring 7 to 9 critically important: AHP = 88.9%, patients = 100% and clinicians = 62.1%) Appendix C3, Table 114, leading to this item not meeting the consensus definition for round 3 and being rejected from the final outcome set. Similarly, the outcome of chronic pain seemed much more important to patients and AHPs than clinicians who rated

this as a less important outcome, however this was still adopted in the outcome set.

A t test explored the differences in scoring between participants who completed all three rounds and those that only completed round one. Several statements on indications and one outcome scored differently between these two groups, highlighting potential biases. Four or more unilateral rib fracture (-1.38, p=0.043), MRF with paradoxical motion (-2.11, p=0.05), MRF with respiratory failure (-1.15, p=0.02) and MRF with invasive mechanical ventilation (-1.10, p=0.04) were scored on average less by the group who discontinued, but pulmonary embolism (1.16, p= 0.044) was scored on average higher.

4.4 Discussion

This is the first Delphi consensus to deliver a core outcome set for rib fracture surgery involving multiple stakeholders. Twenty-three outcomes, twenty indications and seven timing of interventions gained consensus.

The indications for surgery gained consensus easily, with those indications scoring highly in round one continuing to score even higher in subsequent rounds (Table 41). The specific injury of flail chest, described as bi cortical fractures in more than three consecutive ribs and paradoxical movement, demonstrated strong consensus as an indication for rib fracture fixation. Combining this with respiratory compromise, invasive ventilation, intractable pain or failure to wean from ventilation further increased this consensus to 100%. Less favourable, although still gaining consensus, was flail chest injury with tracheostomy, underlying chronic lung disease, haemothorax and concomitant sternal fracture. Similarly, for multiple rib fractures, this injury plus paradoxical movement, respiratory compromise, invasive ventilation, tracheotomy, sternal fracture and intractable pain gained consensus. Consensus ratings on multiple rib fractures increased with each round, however it is not possible to say conclusively that this was due to an increase in consensus or due to drop out of panel members whose opinions were not in line with the consensus.

Seven of the timing of surgery statements gained consensus (Table 42). Statements that lacked consensus may have been too generalisable for clinicians to commit to a specific time due to other factors that would influence this decision

making it difficult to interpret the scoring and feedback received. It could be that there was such a range of timings at which a surgeon could consider fixation that it was difficult to rate one timing statement over another. Our statements specified that the timing should be for a patient who needs surgery irrespective of the indication. This was a potential sticking point as multiple other factors could be required to make this decision, such as different injuries or indications. Certain injuries could be perceived to be more urgent and thus require operating on earlier, making it difficult to assign a score irrespective of injury or indication. Since many clinicians did assign scores, however, and only a few selected 'unable to score' this is less likely to be the case.

The statement that patients should be operated on, transferred or referred within 24 hours gained good consensus (75%, 81.3% and 81.3% respectively) but this consensus strengthened in all three of the clinical scenarios presented if this was extended to 48 hours (87.5%, 87.5% and 93.8% respectively) (Table 42). This suggests that there was greater affinity for these tasks being undertaken within 48 hours rather than 24 hours, which is in line with the BOAST guidance.[16]

The final core outcome set has 23 outcomes, of which eight are adverse events. It is important to distinguish an adverse event, which is an injury caused by medical treatment instead of the underlying disease, from a complication; which refers to a treatment with an adverse effect that produces a new health problem.[229] It should be noted that an adverse event does not necessarily have a causal relationship with the treatment and that sequalae are the residual effects after an acute injury and are not related the treatment. The adverse events that gained consensus were more serious in nature than those that did not gain consensus (Table 43). It is possible that the perceived seriousness of the adverse event, rather than the importance or frequency, dominated the scoring of these items. Adverse events are important to collect when using medical devices that do not have an extensive proven safety profile.

The patient panel assigned high scores to these outcomes, since serious adverse events, although usually rare, are likely to affect the patient panel more than any other group and would make these outcomes feel more important. This has also been noted in a Delphi exercise in respect to polypharmacy in older adults, in which the seven top items that gained consensus were adverse outcomes.[230]

Overall, 7 day and 30 day mortality gained consensus but 90 day mortality did not, suggesting that the early mortality best assesses the effectiveness of rib fracture fixation (Table 43).

Only four clinical or physiological outcomes gained consensus. These related to a person's feeling of breathlessness or ability to clear secretions, which are both subjective, as well as ventilation and lung function which can be specifically measured. Although the measurement instruments are yet to be derived by COSMIN methodology it is likely lung function will be measured by spirometry at baseline and as medium to long term follow up(Table 43).

Six outcomes under the life impact domain gained consensus (Table 43). Health-related quality of life was rated highest of these outcomes and relates closely with others such as physical function and disability. Despite the similar themes of these outcomes they were all felt necessary to be assessed separately. Surprisingly, return to work seemed more important to the clinicians and AHP compared to patients, although returning to activities rated higher with patients. The age of patients was not asked for so this may reflect the retired population who would rate return to activities above return to work.

The only resource use outcome gaining consensus was invasive mechanical ventilation, which is already measured in several systematic reviews. It is of note that the other resource use outcomes were not thought to be useful in measuring effectiveness in rib fracture fixation trials even though these have been the mainstay of measuring effectiveness in most primary studies and systematic reviews. Length of stay and length of ICU stay are the primary outcomes of most primary studies but were rejected in the early rounds of the consensus process. This suggests a gap between what is regarded as important by participants in the panel and what is being measured in trials.

The focus of research of rib fracture fixation is swayed by the United States being the biggest research publisher on this procedure (Chapter 3 section 3.3.1). Research into new procedures and devices in the United States is heavily biased by resource use outcomes that measure efficiency. Spiralling health costs in the United States make it difficult for clinicians to justify delivering research solely for patient benefit and their research therefore mainly focusses on whether a patient is discharged earlier or requires less ICU time, which has an associated cost.[231]

This has also been seen in the roll out of robotic surgery where evidence has focused primarily on the cost of procedures rather than patient outcomes.[232] Anecdotally, while discussing these issues at the chest wall injury summit 2018, US surgeons did not feel resource use outcomes assessed the effectiveness of the surgery but were specifically measured to gain approval from their hospital boards to continue their use of this procedure.

The patient panel scored the resource use outcomes low, with their most important outcomes being identifying serious adverse events and life impact.

One of the factors that needs to be considered when developing a core outcome set is the burden of using the outcomes in research for patients, clinicians and others involved in gathering data. Although the outcome set developed is extensive, generally, the burden of these potential measurement instruments is low. Collecting eight separate adverse events and two separate mortality rates and length of mechanical ventilation is unlikely to be unduly difficult for a trial team to collect without patient burden. Ventilation and lung function are easily measured using bedside tests, an example would be spirometry. Outcomes of dyspnoea, pulmonary toilet, return to work, activities and health-related quality of life can be successfully measured as patient-reported outcomes. Further work is required to assess which instruments should be used to measure these outcomes, however, and whether these are burdensome for patients.

4.4.1 Strengths and limitations

The Delphi panel consisted of three different sets of expert stakeholders, encompassing an international clinician panel that were recruited using a range of methods to create a diverse sample. The Delphi process was completed within the guidance of the COMET handbook and the identification of outcomes and indications was completed through systematic searches. Participants were given the opportunity to suggest their own items before the items gathered from the systematic review were presented to them. More statements were retained initially and could be re-rated using the initial lower threshold of 50%. Having multiple opportunities to rate following feedback gave maximum exposure to statements and therefore the final retained statement consistently gained consensus in each round

The main limitations of this study are the relatively small overall panel size. Although there is no guidance on panel size or ratio of group sizes, it is recognised that results could be sensitive to small groups if the consensus is defined by those groups. COMET advice in this situation is to pool the stakeholder results to ensure items are not penalised by small panels if the large groups did gain consensus. In this study, the patient and AHP groups were much smaller than the clinician group, unbalancing the consensus in favour of the clinician group; however this approach is still preferable to underrepresentation in a clinician-only consensus.

Attrition was high between rounds and although this was predicted, especially in the clinician group, the patient and AHP panels also suffered high attrition. Since these individuals had self-selected by contacting the research team to take part, it was thought that the retention between rounds would have been higher in these groups. Excluding those that did not fully complete the rounds also significantly decreased the group sizes. Within the participant information it explicitly stated that even if participants felt their opinions were out of line with the groups they should nonetheless continue as their withdrawal may bias the results. Despite this, statistical analysis showed that in respect to several statements, specifically those relating to multiple rib fractures, those participants that did not continue through all of the rounds, scored differently to those who did continue. Considering multiple rib fractures as an indication for surgical fixation is controversial within the clinical literature and could have deterred participants from continuing to the next round, creating selection bias.

In several studies have used consensus conferences to condense large outcome sets resulting from the formal survey rounds.[233] The COMET Handbook[110] also recommends that a face-to-face meeting of stakeholders is undertaken and additional voting is undertaken before a COS is agreed. This is not essential, however, and is not performed in several Delphi studies.[234, 235] A consensus conference was not held following the survey rounds as it was beyond the scope of the MD funding. The potential downside of this is that there was a large number of statements and outcomes retained that perhaps could have been focused down further.

4.4.2 Conclusions

There was consensus amongst clinicians that both flail chest and multiple rib fractures are indications for multiple rib fracture fixation, especially if the patient

has respiratory compromise, invasive ventilation or has intractable pain. The earliest fixation should occur is between 24 and 48 hours, however the lack of consensus on other statements means that the latest timing of fixation and whether patients should have a trial of weaning still appears controversial. Patients should generally be referred, transferred and operated on within 48 hours, with a smaller proportion of clinician agreeing this should be within 24 hours. Consensus was achieved on 23 outcomes across five domains. Collecting serious adverse outcomes was important to all stakeholders, life impact outcomes such as quality of life, physical function and return to activities was also important. Less important were resource use outcomes. This new set of 23 outcomes has been developed robustly with multiple stakeholders and are feasible to embed in future trials.

Chapter 5 - An analysis of the Trauma Audit Research Network Chest Wall Injury Dataset -The relationship of patient factors, injury type, treatment decisions and outcome

5.1 Introduction

Although rib fractures are a common injury following trauma, there is currently no clear description of the rib fracture population in the UK and the outcomes following treatment are also unknown. A better understanding of these facts may influence the decisions related to how to fix rib fractures and thus needs further exploration.

5.1.1 Research Questions

The research questions for this Chapter are:

What is the relationships between patient factors, injury type, treatment decisions and outcomes in rib fracture patients? In England and Wales, what patient and injury factors influence the decision to undergo rib fracture fixation?

5.1.2 Objectives

- To answer the research questions, the following statements outline the objectives presented within this Chapter:
- To describe the chest wall trauma population, the treatment they receive and to map the patient journey from ambulance to discharge (Figure 25).
- To determine what factors influence the decision to undergo rib fracture fixation.
- To assess the effectiveness of rib fracture fixation compared to non-operative management in terms of length of ventilation, length of ICU stay, length of hospital stay, adverse events and mortality.
- To identify potential confounding factors and further develop evidenced-based treatment pathways.

To help direct future areas of research.

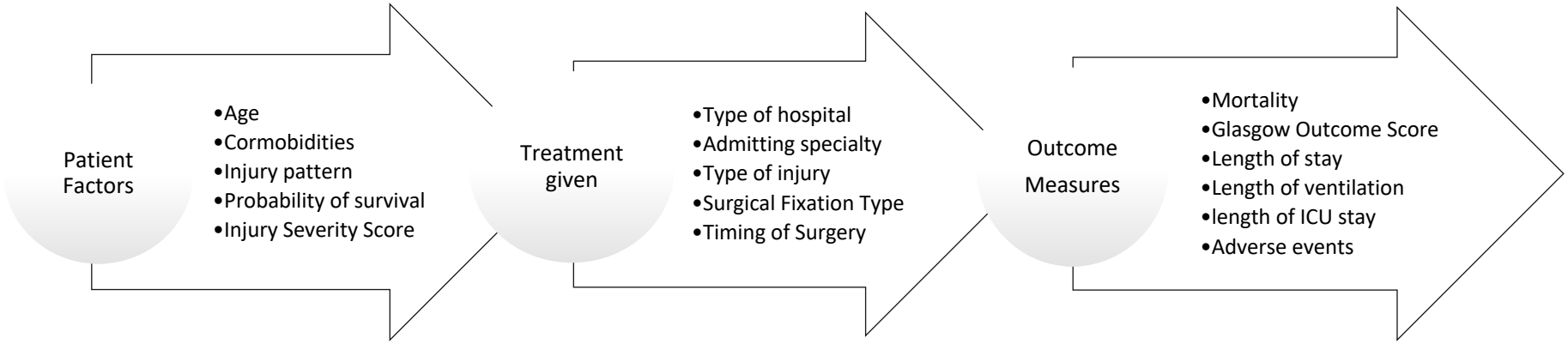


Figure 25 The Patient Journey - Understanding the relationship between patient factors, treatment given and outcomes

5.1.3 Overview

Despite some promising evidence from trials of surgical rib fixation the uptake of this treatment is neither standardised nor consistent across the United Kingdom.[18-20] Patients undergoing operative fixation are only one element of this patient group, however. Whilst it is evident that the appropriate management of those deemed suitable for fixation remains unclear, the optimum management of patients with rib fractures managed non-operatively is equally unclear. In addition, there are multiple factors to consider, including injury mechanism, age, co-morbidity and frailty.

5.1.3.1 Trauma Audit and Research Network

The Trauma Audit and Research Network (TARN) is a non-profit organisation based at the University of Manchester that collaborates with hospitals in England, Wales, Ireland and other European countries. Their aim is to improve trauma care through the collection of audit data to provide a population-based epidemiology of trauma and identify potential areas of research. It is hoped that this information may influence health policy and help local and national commissioners to develop trauma services.

5.1.3.2 Data collection

Twenty trauma networks from England and Wales (encompassing 27 major trauma centres and 170 trauma units) submit their data on major trauma to TARN. To be included in the TARN database several criteria must be satisfied. Length of stay is based on a stay of more than three days (combined if transferred to another hospital for treatment) or admission to a higher level of care such as ICU or HDU irrespective of length of stay. All patients who have died from trauma are also entered irrespective of cause of death. Injury types include: all head or brain injuries, internal injures of the thorax and abdomen, asphyxia, drownings, explosions and electrical injuries. Certain fractures, including pelvis, femur, open fractures and multiple limb fractures, are included, as well as nerve, vessel and de-gloving injuries. All patients are included irrespective of age.

The Chest Wall Trauma screen was introduced in April 2016 as an extended dataset to TARN. This element of trauma data collection was introduced to address an evidence void in the management of this type of injury. To be eligible for inclusion to the chest wall dataset the patient must have had a fracture to the

rib(s) and/or sternum. All cases with this injury have an extended set of questions related to the management of the chest injury that are completed.[14]

Data submitted to TARN is at the level of the hospital and data completeness varies between hospitals. Most hospitals identify their patient population from the ICD 10 codes that are given to each patient in hospital. The S or T codes that identify potential cases can then be used to inspect case notes for inclusion. Injury details are recorded from medical notes and radiology reports. Often, a copy of the radiology or post mortem report is attached to the submitted case, hence TARN coders are able to verify any injuries. Only confirmed injuries are recorded.

5.1.3.3 Data set

The TARN Core dataset is mandatory and consists of demographics, a description of the incident and the injuries, observations, operations and outcomes at discharge. Multiple other data fields are mandatory and include: date of injury, date of birth (or age), gender, mechanism of injury and injury severity score. The chest wall dataset introduced in April 2016 explores cases with rib(s) and/ or sternal fracture and those that have had thoracic and rib fracture operations. Specifically, the type of rib fixation, the number of ribs fractured and the inspection of intrathoracic viscera are recorded. Outcome measures such as tracheostomy, use of non-invasive ventilation, reintubation and complications are also collected. Pre-specified responses are used for categorical data and an option is available for ‘not recorded’ however these data points are not mandatory and may not be complete.

5.1.3.4 Data completeness

TARN regularly monitors its own data collection for completeness and validity. Only valid entries are able to be uploaded to the TARN database, and this is electronically verified to make sure all mandatory fields are completed. Coders at TARN receive the electronically validated data and screen for completeness and validity. Any cases not meeting the TARN inclusion criteria or requiring further information are returned for review at the hospital site. Only records approved by this process are uploaded into the database.

5.2 Methodology

The intention of the research presented in this Chapter is to explore factors that could be targeted for further research. Consequently, the statistical methods used will initially be descriptive. Further analyses will look at what factors predict a patient receiving rib fracture fixation and then what factors affect outcomes.

5.2.1 Overview

The methods include the process of acquiring, storing and handling data, and the methods for cleaning and dealing with missing values. Following data cleaning and preparation, the first output consists of describing the patient population in terms of demographics and injury type. The second output builds upon the basic demographics and looks at what patient, injury and hospital factors predict whether a person receives rib fracture fixation or has an adverse event. Thirdly, rib fracture fixation is compared to non-operative treatment to see if this affects outcomes (e.g. length of ventilation, length of tracheostomy, Glasgow outcome score and complication rates).

5.2.2 Data

5.2.2.1 Access and data security

Acquisition of the TARN data followed an application to the TARN executive board. A data transfer agreement was set up between the University of Manchester, which holds the TARN data, and the University of York. This data transfer agreement stipulated that data could be used for the purpose of the analysis for one year unless extensions were applied for and granted. A further extension was applied for and accepted at the end of year one. Data was stored securely on a networked computer at the University of York, with password protection and encryption. The data was never stored on any temporary media. On receiving the data this was password protected at the University of York. No personal identifiable information was sent or used as part of this study. On receipt of the data, it was processed in accordance with the Data Protection Act 1998 (as described in the agreement and under Standard Operating Procedures) within the York Trials Unit. The study author completed the data analyses and access was granted to academic supervisors to provide statistical advice, guidance and support.

5.2.2.2 Data Availability

The TARN database collects data on all patients presenting to English and Welsh major trauma centres and trauma units who satisfy the inclusion criteria. Before delivering the data to the University of York, the University of Manchester selected the chest wall screen data with elements from the core dataset. The last date for data entry was the 30th May 2017.

5.2.2.3 Data Handling

17,793 records were transferred in Microsoft Excel worksheet extension files. This was imported into IBM Corp Released 2016. IBM SPSS Statistics for Windows, Version 24.0. (Armonk, NY: IBM Corp). Data was cleaned and prepared for analyses within the statistical software. Since the chest wall dataset was delivered separately to the core dataset they were merged using the merge function within SPSS, matched on study ID. Only 13,376 cases had data available on complications so analyses using these variables were limited to this complete case set. All transformations, recoding and analyses undertaken in SPSS were written in syntax files to ensure an audit trail.

Several functions within SPSS were used to prepare the variables for analysis, including:

- Explore – used to inspect the spread of the data
- Binning - used to change continuous data into categorical data where required
- Recode – used to create new variables from old variables
- Compute – used to calculate total length of stay variables from different length of stay variables

Further transformation of data and statistical analyses were completed in Stata (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC) as required, using similar transformation procedures.

5.2.2.4 Data Cleaning

Data cleaning involved the inspection of variables for accuracy and validity. Cases were removed from the analysis if they were not adults and/or did not have a rib fracture or sternal injury (Table 44). Although penetrating injury was not the focus

of this thesis it was thought important to describing the rib fracture population and so were included as a population descriptor.

Table 44 Cases excluded from analysis

	Included	Excluded
Age	16 - 112 years	Data for those aged less than 16 was removed from the analysis the oldest known resident in the UK is 112 so figure outside this were excluded
Injury type	Fracture one rib, Fracture two ribs, Fracture greater than 3 ribs, Multiple rib fractures NFS, Fracture greater than 3 ribs on each side, Fracture ribs with flail NFS, Fracture ribs with unilateral flail, Fracture ribs with 3-5 ribs, fracture more than 5 ribs with unilateral flail, Fracture ribs with bilateral flail, Fracture ribs: complex, Sternum fracture	Injury codes that did not contain a rib or sternal fracture were removed from the analysis

Both continuous and categorical data were included in the core and chest wall datasets. A visual inspection of data using summary statistics, histograms, box and whisker plots looked for outliers, errors and missing data. Erroneous data was removed from the analysis and recorded as missing data unless a valid explanation could account for and correct the anomaly (Table 45).

Table 45 Variables recoded to missing if erroneous

	Erroneous variables recoded to missing	Included
Charlson Index	Out with range 0-29	0-29
PS14	Out with range 1-100	1-100
Injury Severity Score	Out with range 0-75	0-75
Transfer time	Transfer time longer than total length of stay	All other values
Pre-op ventilation time	Pre-op or ventilation time longer than length of stay	All other values
Post op intubation time	Post op Intubation time longer than 1) length of stay or 2) length of critical care stay	All other values
Length of stay	Implausible results that were longer than total time of TARN data collection	All other values
Critical Care stay	Critical care longer than length of stay	All other values
Transfer Type	Must have occurred if a second length of stay is entered	All other values
Lead Specialty	Paediatric specialties (recoded to respective adult specialty)	All other values
Time to rib operation	0 to Longer than total length of stay	All other values

During data cleaning several errors were noted in the coding of the injury variables. Seventy-one cases had rib fracture fixation without a corresponding rib fracture or sternal fracture injury. This issue was raised with the TARN data

collection team and it was noticed that there had been a problem with coding several variables together. A further update of the 71 patient injury codes was subsequently received and incorporated into the original dataset.

5.2.2.5 Missing data

Bennett [236] states that significant bias could occur if more than 10% of a variables data is missing meanwhile Schaffer et al.[237] believe that if less than 5% of variables data is missing then cases could be discounted without causing any statistical bias. To be cautious, imputation was undertaken to prevent bias by missing data. Missing data was imputed using multiple imputation if less than 25% of a variables data was missing. Five iterations of imputation were undertaken using all other variables as predictors. If more than 25% of a variables data was missing then the variable was excluded from any statistical analysis. Guidance on the handling of missing data was followed.[238].

5.2.2.6 Preparation of variables for modelling

Histograms were used to explore the distributions of continuous data; transformations were considered for any substantial skew. Transformations included log10, natural log,x^2,x^3, $\sqrt[2]{x}$ and $\frac{1}{x}$. Q-Q plots and the Kolmogorov–Smirnov test for normality were used. If transformations were not successful then continuous data were transformed into categories that were common to other major trauma outcome reporting or to groups that were balanced by similar frequencies per category or dichotomised at their median value.

Some variables were recorded at several time points and were combined together using the compute function in SPSS (Appendix D1,Table 115Table 116Table 117Table 118). This includes length of stay outcomes, which were reported at multiple time points.

Continuous variables that were planned for inclusion in the model were explored in a scatterplot matrix to show any relationship between variables. This gave an overall impression of which variables had a relationship and whether they should be included in the model to avoid multicollinearity.

Categorical data included, among others, mechanism of injury, admitting service, gender, transfer type, chest injury type and Glasgow Outcome Score. Some categorical variables had large numbers of categories with small frequencies and

these categories were therefore combined where meaningful (Appendix D1, Table 105-108). In general, TARN publications quantify those patients that have an ISS score as either (i) 15 or more, or (ii) less than 15 as this is often used as the general cut off for admission to an MTC. It should be noted that in this analysis the dichotomy is different, and the ISS is either (i) less than 15 or, (ii) 15 or more.

5.2.3 Statistical Analysis

5.2.3.1 Univariate analysis

The first objective was to describe the chest wall injury population using summary statistics. This was performed as a whole population but also as subgroups in order to be able to compare differences narratively between those who had a rib operation and those who did not. Continuous variables were summarised as means, standard deviations, medians and ranges. Categorical data was presented as frequencies and percentages.

Continuous data was compared using independent samples t-tests between those that had a rib operation and those that did not. Categorical data was presented as cross tabulations and analysed using Chi-squared tests or Fisher's exact test as appropriate. If transformation did not normalise the data then non-parametric (Mann-Whitney U) tests were used.

5.2.3.2 Predicting which patients are receiving rib fracture fixation - binary logistic regression

Since multiple factors are likely to influence whether a person is selected for rib fracture fixation, binary logistic regression models were constructed to explore the influence of several explanatory variables on whether rib fracture fixation was performed or not. In these models, cases were removed if patients died within 24 hours of admission, regardless of treatment. This is on the basis that cause of death in such circumstances is unlikely to have been reversible with rib fracture fixation. In addition, within 24 hours of admission, chest trauma patients are in any case unlikely to have had the opportunity to be offered surgical fixation. This is in line with other literature in assessing the factors that contribute to prolonged use of ventilation in rib fracture patients.[239]

Since the purpose of the models was to explore factors that influence the decision for rib fracture fixation, those covariates that were thought to be clinically important

and had sufficient complete data were entered into the model. It was hypothesised that certain surgeons or hospitals may have a preference for undertaking a rib operation compared to other surgeons or hospitals hence the logistic regression models incorporated potential clustering by hospital admission site.

The categorical variable of pre-operative ventilation, indicating that the patient had ventilation prior to having an operation was excluded from the model. This variable was not specific to a rib fracture operation and could indicate ventilation prior to any other type of operation, hence it was excluded from the model.

Missing data was imputed using multiple imputation (MI) and combined using Rubin's rules.[240] The precision of the MI estimate was assessed by inspecting the variability within imputations based on the number of imputations and observations. Two measures were assessed; the Fraction of Missing information (FMI) and the relative increase in variance due to nonresponse (RIV). These measures are derived from values of the between, and within imputation variance and the total variance. The average RIV was satisfactory if it was less than 0.1. The largest FMI was multiplied by 100 and if the resulting number was less than the number of imputations (5) then the specified number of imputations was considered sufficient.

To assess the level of simulation error within the MI results, Monte Carlo error (MCE) estimates were calculated. MCE estimates are 'the standard deviation of the results across repeated runs of the same imputation procedure using the same data'.[241] The statistical reproducibility of the results were satisfied if:

- MCE coefficients were less than 10% of the standard errors of the coefficients
- MCE estimates of test statistics were approximately 0.1
- MCE estimates of p-values were approximately 0.01 when the true p-value is 0.05 and 0.02 when the true p-value is 0.1.

To test the hypothesis that all the coefficients were equal to zero, and thus rule out a constant only model, the model's F-test were calculated. The hypothesis is rejected if $P \leq 0.05$.

Results are presented as Odd Ratios (OR) with associated 95% Confidence intervals (CI) and p-values.

5.2.3.3 Does rib fracture fixation affect outcomes? (Glasgow outcome score, length of stay, length of intubation, length of critical care stay, number of adverse events)

The second aim was to explore whether rib fracture fixation affects outcomes compared to non-operative management. Comparing rib operation patients directly to non-operative patients to explain outcomes is inappropriate as there are several confounding factors; therefore adjusted statistical models were constructed.

Binary logistic regression models were developed to predict mortality, ICU admission and presence of intubation, controlling for a range of confounding factors and adjusting for potential clustering by admission site.

The length of ICU admission, length of intubation and total hospital stay were other outcomes that were of interest. Overall hospital length of stay was measured in all comers and was not sub-grouped into those that had an ICU stay or not. This distinction was not made as the surgical intervention was being tested rather than the ICU treatment. It was originally intended that linear regression models would be developed, but the data was highly skewed and did not satisfy the assumption that the residuals are normal. The outcomes were dichotomised at their median value and remodelled using binary logistic regression using similar models to those described above. The final outcomes assessed were as follows in Table 46.

Table 46 Dichotomised outcomes at the median value in preparation for modelling

Outcome	Indicator		Model
Length of hospital stay	< 9 days	9 days ≤	Binary Logistic Regression
Length of ICU stay	< 4 days	4 days ≤	Binary Logistic Regression
Length of intubation	< 4 days	4 days ≤	Binary Logistic Regression
Mortality	Alive	Dead	Binary Logistic Regression
Glasgow Outcome Score	1 = Dead	2 =Prolonged Disorder of Consciousness 3 =Severe Disability 4 =Moderate Disability 5 =Good Recovery	Ordinal Logistic Regression
Number of adverse events	None	1 or 2 adverse events 3 or more adverse events	Ordinal Logistic Regression

The three following approaches to the analyses were undertaken and results compared:

1. Binary logistic regression and ordinal regression, controlling for multiple covariates identified in 5.2.3.2
2. A propensity matched score analysis that matched with a 4:1 ratio
3. Binary logistic regression and ordinal regression controlling for multiple covariates identified and the effect of early versus late fixation in the operative population
4. A competing risks regression model was developed since death is a competing risk for time to discharge.

The above models were implemented in Stata (StataCorp. 2017. *Stata Statistical Software: Release 15*. College Station, TX: StataCorp LLC) and adjusted for the potential clustering by admission site. Multiple imputation was used to account for missing data (except propensity score matching) for both outcomes and covariates, using the processes described in section 5.2.3.2.

5.2.3.3.1 Using binary logistic regression to predict mortality

A binary logistic regression model was constructed to predict mortality, controlling for all identified covariates (including whether a rib operation was performed or not) and were adjusted for the potential clustering by admission site.

5.2.3.3.2 Binary logistic regression and ordinal regression to predict outcomes

Binary logistic regression was used to predict length of stay, length of intubation and length of ICU stay. Ordinal regression was used to predict Glasgow Outcome score. Models were constructed using covariates that were suggested to be predictive in 5.2.3.2 and adjusted for potential clustering by admission site.

5.2.3.3.3 Propensity matched score analysis that matched with a 4:1 ratio to predict treatment effect

The second analysis explored differences in outcomes between rib fracture fixation patients and non-operative patients using matched cohorts. In non-randomised studies, or studies of prospectively collected cohorts, treatment groups are likely to differ systematically from one another.[13] To overcome the

problem of multiple confounders, some scholars have suggested using matched cohorts.[242-244]

Propensity scores are created to measure the probability of an assigned treatment given observed covariates. Scores given to each case can then be matched in either a one-to-one or one-to-many ratio by treatment type. This propensity score matching technique is used to adjust for treatment effects in studies that have measured confounders.[242, 245] Propensity scores were calculated and matched on a 1 to 4 ratio (rib operation to non-operative management, respectively) using the 'treatment effects' function in Stata. The matched cohorts were entered into binary logistic regression models to explain the effect of rib fracture fixation on the four outcomes. The treatment effects function does not allow the use of multiple imputed data and therefore imputed data was not used for this model.

5.2.3.3.4 Does the timing of fixation affect outcomes?

The impact of timing of fixation on outcomes was also explored.

A distinction made by the British Orthopaedic Association Standards for Trauma[16] (BOAST 15) guidance suggests that patients should be operated on within 72 hours. This was further explored in Chapter 3 as part of the meta-analysis of primary evidence. To follow on from this work, patients who were operated on were separated into those operated before and after 72 hours.

These two groups were entered into the binary logistics models described in 5.2.3.3.2 plus a further covariate representing whether the patient was ventilated preoperatively and was adjusted for potential clustering by admission site. The ventilated preoperatively covariate could not be used in the previous models as it compared patients who had an operation with those that who did not, but here all cases had a rib operation. Estimates were reported along with associated 95% CI and p-values from each model.

5.2.3.3.5 Competing risks regression analysis accounting for death in hospital

Length of stay, length of ICU stay and length of intubation can be graphically represented as a function of survival using a univariate Kaplan-Meier curve but this accounts only for one binary factor. Cox proportional hazards models, meanwhile, allow the assessment of multiple continuous or categorical covariates

using regression techniques. In normal time to event analysis, when an individual dies in hospital they would be censored (as the event occurred). This is not appropriate in this analysis, however, since a person who dies in hospital could not also be discharged from hospital and therefore length of stay could be affected.[246] Kaplan Meier and Cox Proportional hazards do not take into account these factors and would therefore not model this scenario adequately.

In contrast, a competing risks analysis[247] allows for multiple causes of 'failure' to be accounted for, including death to hospital/ICU discharge or extubation. The competing risks regression has been shown to be superior to other methods such as restricting the analysis to those who lived, right censoring patients at the time they died or a worse outcome analysis, where those who die are right censored at the longest possible length of stay.[248]

A competing risk regression analysis was therefore used to model three time-dependent outcomes with one competing risk and were adjusted for potential clustering by admission site (Table 47). Results were presented as sub-hazard ratios with associated 95% CI and p-values.

5.2.3.3.6 A competing risks regression analysis accounting for death in hospital and time to rib operation as a time varying covariate

As discussed in previous chapters, rib fracture fixation surgery is performed at varying times between cases for a multitude of reasons. The timing of fixation could affect outcomes such as mortality and pneumonia, which are binary endpoints. The outcomes such as length of stay, ICU stay and length of intubation could therefore be dramatically altered if the timing of treatment is taken into account. An example case would be a patient who begins to deteriorate at day five and who thus may only receive the benefit of rib fixation at this point and will need time to recover post-surgery (~four days) creating a length of stay of nine days. Comparing this to a patient who was severe enough on day one to have surgery and accounting for the same recovery period (four days) will take their length of stay to only 6 days. The time to event analysis in this case is confounded by the timing of rib fixation. Several examples have shown that using time varying covariates affects the conclusions of competing risks analyses.[249, 250]

A competing risks model was therefore constructed where the timing of fixation was controlled when a case entered the model. For example, if a patient had an

operation on day four they were not considered at risk for the purposes of the model until they had this treatment. If no operation was performed then the case entered the model at T_0 (Table 47). Results were presented as sub-hazard ratios, with associated 95% CI and P values. In this model the timings were modelled as continuous variables.

Table 47 Competing risks model set up showing standard first model and a second model that incorporates the timing of treatment as the time of entry to the model.

First model			**Second model**
Failure	**Time to failure**	**Competing risk**	**Entering into model at time (n)**
Alive	Hospital length of stay (days)	Death	n = Time to rib operation T_0 if no operation
Alive	ICU length of stay (days)	Death	n = Time to rib operation T_0 if no operation
Alive	Intubation length (days)	Death	n = Time to rib operation T_0 if no operation

5.3 Results

5.3.1 Overview and data handling

1. Of 17,793 records 181 paediatric patients and 974 patients without rib fractures were excluded from the analyses (Figure 26).

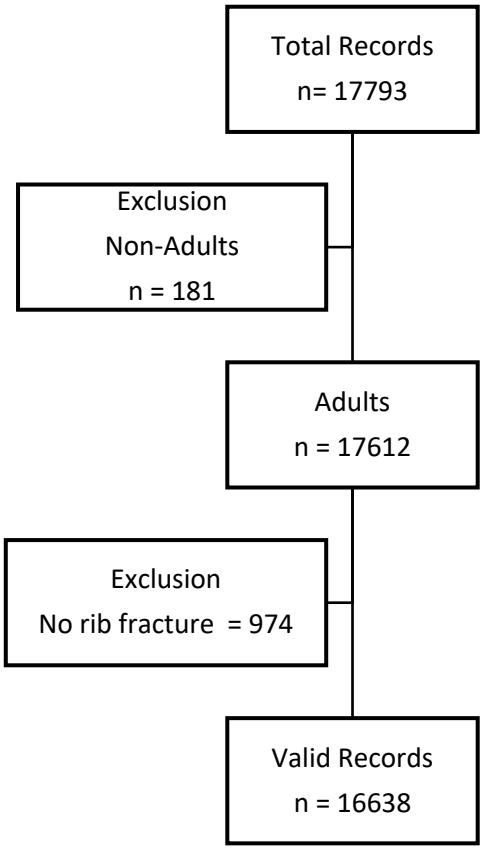


Figure 26 Flow chart describing inclusion criteria

5.3.1.1 Erroneous data

Age, Charlson index, PS14 and injury severity score had no erroneous outliers. Sixteen cases had a transfer time longer than the total length of stay. One case had a pre-operative ventilation time longer than their length of stay. Eighteen cases had a hospital length of stay, and 287 cases had a critical care length of stay longer than their post-operative intubation time. One case had a length of stay that was 771 days, that would be longer than the time that data had been collected for and without any other factors to support this length of stay. There were no cases where length of critical care stay was more than the length of stay. One case was recorded as having no transfers but had a second length of stay. All

erroneous data was recoded to missing. Three adult patients (more than 16 years old) were admitted under paediatric specialties for and therefore were recoded to the respective adult specialties.

5.3.1.2 Missing data

The dataset was inspected for missing data. Data was recorded as a valid response, recorded as 'not recorded' from the dataset or recoded as missing as a blank response. Certain variables are mandatory within the TARN dataset and therefore were fully complete. Charlson index (4.5% missing), and PS14 (3.4% missing) variables had a high response rate despite not being mandatory; the Glasgow outcome score, meanwhile, had 20.9% of data missing. As eight cases had a length of hospital stay recoded to missing after they were found to be erroneous, these cases were also entered into the multiple imputation analyses.

5.3.2 Patient and admission factor variables

The patient and admission factor results are tabulated in Table 48. The differences between the groups are presented as p-values.

5.3.2.1 Age

Reflecting the growth in the elderly population in the United Kingdom, the age distribution of patients presenting with chest wall trauma is skewed towards the older population.[251] The cohort's average age was 63.45 years (95% CI 63.14, 63.76) the maximum recorded age was 106 years old (Table 48). The mean age of those undergoing rib fracture fixation was significantly younger than those not undergoing rib fracture fixation -3.1(95% CI -4.70 to -1.50) years, independent t-test ($p<0.0001$).

Table 48 Patient and admission factor demographics

		Treatment		Differences between groups	
Variable	**All Patients**	**Rib fixation patients**	**No rib fixation**	**Original**	**Imputed**
Total patients n (%)	**16638 (100)**	**402 (2.4)**	**16236 (97.6)**	**P-value**	**P-value**
Age, mean (sd)	63.45 (20.30)	60.42 (16.03)	63.52 (20.39)	<0.0001†	-
Median (range)	66.20(16.00-106.01)	61.20(19.20-93.70)	66.4(16.00-106.10)		
16-24.9	744 (4.5)	5 (1.2)	739 (4.6)		
25-49.9	3642 (21.9)	94 (23.4)	3548 (21.9)	0.03≠	
50-74.9	6397 (38.4)	218 (54.4)	6179 (38.1)		
75+	5855 (35.2)	84 (20.9)	5771 (35.5)		
Charlson index, mean (sd)	2.45(3.24)	2.00 (2.87)	2.41 (3.24	<0.065†	<0.065
Median (range)	1.00(0.00-25.00)	0.00(0.00-18.00)	1.00(0.00-25.00)		
None – 0, n (%)	7478 (44.9)	196 (48.8)	7283 (44.9)		
Mild 1-2, n (%)	3089 (18.6)	82 (20.4)	3007 (18.5)		
Moderate 3-4, n (%)	2744 (16.5)	63 (15.7)	2681(16.5)	0.054	
High more than 5, n (%)	3327 (20.0)	61 (15.1)	3266 (20.1)		
Mechanism of injury, n (%)				<0.0001	-
Fall less than 2m – Low energy	6908 (41.5)	88 (21.9)	6820 (42)		
Vehicle incident	5621 (33.8)	199 (49.6)	5422 (33.4)		
Fall more than 2m High energy	3104 (18.7)	94 (23.4)	3010 (18.5)		
Penetrating injury	161 (1.0)	0 (0.0)	161 (1.0)		
Non-Penetrating Injury	844(5.1)	20 (5.0)	824 (5.1)		
PS-14, mean (sd)	91.25 (15.3)	88.4 (18.24)	91.32 (15.22)	<0.0001†	<0.0001†
Median (range)	96.71(0.96-99.85) 9797	95.96(5.04-99.85) 219	96.71(0.96-99.85) 9578		
95% and above n (%)	(58.9)	(54.7)	(59.0)	0.068	
Below 95% n(%)	6841 (41.1)	182 (45.3)	6659 (41.0)		
Transfer Time mean (sd)	1.30 (3.72)	0.93 (1.87)	1.33 (3.83)	0.255	-
Median (range)	0.14(0.00-72.40)	0.20(0.00-13.12)	0.13(0.00-72.40)		
Gender, n (%)				<0.0001	-
Male	10518 (63.2)	297(74.1)	10221(62.9)		
Female	6120 (36.8)	104 (25.9)	6016 (37.1)		

		Treatment		Differences between groups	
Variable	**All Patients**	**Rib fixation patients**	**No rib fixation**	**Original**	**Imputed**
Total patients n (%)	**16638 (100)**	**402 (2.4)**	**16236 (97.6)**	**P-value**	**P-value**
Admitting specialty, n (%)				<0.0001	-
Orthopaedics	1207(19.1)	38 (26.0)	1169 (18.9)		
Emergency Medicine	1046 (16.6)	8 (5.5)	1038 (16.8)		
General Surgery	1121(17.7)	12 (8.2)	1109 (18.0)		
General Medicine	692 (10.9)	2 (0.3)	690 (11.2)		
Major Trauma Service	707(11.2)	21 (14.4)	686 (11.1)		
'Cardiothoracic Surgery'	552 (8.7)	42 (28.8)	510 (8.3)		
'Neurosurgery and Spinal'	299 (4.7)	6 (2)	293 (4.7)		
Geriatric Medicine	255 (1.5)	0 (0.0)	255 (4.1)		
ITU	160 (2.5)	5 (3.4)	155 (2.5)		
'Other Medicine'	136 (2.2)	10 (6.8)	126 (2.0)		
'Other Surgery'	145 (2.3)	2 (1.4)	143 (2.3)		
ISS, mean (sd)	16.90(11.47)	26.34 (13.23)	16.65 (11.32)	<0.0001†	-
Median (range)	13.00 (1.00-75.00)	21.00 (4.00-75.00)	13.00(1.00-75.00)		
Less than 15	8820 (53.0)	47 (11.7)	8773 (54.0)	<0.0001	-
15 or more	7818 (47.0)	354 (88.3)	7464 (46.0)		
Type of hospital, n (%)				<0.0001	-
Major Trauma Centre	8243 (49.5)	364(90.8)	8358 (51.5)		
Non-MTC	8395 (50.5)	37 (9.2)	7879 (48.5)		
Transfer Type, n (%)				<0.0001	-
No Transfer	13631 (81.9)	239 (59.6)	13392 (82.5)		
Transfer In	793 (4.8)	37 (9.2)	756 (4.7)		
Transfer Out	2024 (12.2)	116 (28.9)	1908 (11.8)		
Transfer In & Out	190 (1.1)	9 (2.2)	181 (1.1)		
Injury description, n (%)				<0.0001	-
Less than three rib fractures (non-flail)	4299 (25.8)	2 (0.5)	4297 (26.5)		
3 or more rib fractures (non-flail)	6854 (41.2)	62 (15.5)	6792 (41.8)		
Unilateral flail chest	2809 (16.9)	246 (61.3)	2563 (15.8)		
Bilateral flail chest or complex rib fracture pattern	2676 (16.1)	91 (22.7)	2585 (15.9)		

		Treatment		Differences between groups	
Variable	**All Patients**	**Rib fixation patients**	**No rib fixation**	**Original**	**Imputed**
Total patients n (%)	**16638 (100)**	**402 (2.4)**	**16236 (97.6)**	**P-value**	**P-value**
Pulmonary contusion				<0.0001	
No lung contusion	13378 (80.4)	204 (50.9)	13174 (81.1)		
Lung contusion unilateral	2307 (13.9)	140(34.9)	2167 (13.3)		
Lung contusion bilateral	953 (5.7)	57 (14.2)	89 (5.5)		
Analgesia overall usage					
Entonox	966 (5.8)	19 (4.7)	947 (5.8)	0.389	
Intravenous paracetamol	5433 (32.7)	149 (37.1)	5284 (32.5)	0.052	
Intravenous opioid	7948 (47.8)	252 (62.8)	7696 (47.4)	<0.0001	
PCA	870 (5.2)	62 (15.4)	808 (5.0)	<0.0001	
Ketamine	475 (2.9)	35 (8.7)	440 (2.7)	<0.0001	
LA patches	141 (0.8)	2 (0.5)	139 (0.9)	0.778	
LA blockade	260 (1.6)	19 (4.0)	241 (1.5)	<0.0001	
Paravertebral block	178 (0.1)	19 (5.0)	159 (0.1)	<0.0001	
Epidural block	289 (2.0)	35 (8.7)	254 (1.6)	<0.0001	
Highest level of analgesia usage					
Entonox	217 (0.0)	2 (0.5)	215 (1.3)		
Intravenous paracetamol	2147 (12.9)	32 (8.0)	2115 (13.0)		
Intravenous opioid	6581 (39.6)	148 (36.8)	6433 (8.8)		
PCA	652 (3.8)	40 (10.0)	612 (3.8)		
Ketamine	127 (0.8)	1 (0.3)	126 (0.8)	<0.0001≠	
LA patches	435 (2.6)	27 (6.7)	408 (2.5)		
LA blockade	251 (1.5)	17 (4.2)	234 (1.4)		
Paravertebral block	172 (1.0)	18 (4.5)	154 (0.9)		
Epidural block	289 (2.0)	35 (8.7)	254 (1.6)		

sd – standard deviation, n = frequency, MTC = Major trauma centre, ISS = Injury severity score, PS14 = Probability of survival, Independent T test (continuous data variables), Chi squared/Fishers Exact test (categorical data variables), †Non-parametric Mann Whitney-U, ≠Linear by linear association

Table 49 Outcomes

		Treatment		Differences between groups	
Variable	**All Patients**	**Rib fixation**	**No rib fixation**	**Original**	**Imputed**
Total patients n (%)	**16638 (100)**	**402 (2.4)**	**16236 (97.6)**	**P-value**	**P-value**
Any rib operation, n (%)			-	-	-
Yes in first procedure	315(1.9)	-			
Yes in second procedure	87 (0.5)				
Two rib operations	2 (0.0)				
No rib fracture operation	16234 (97.6)				
Thoracic operation, n (%)				<0.0001	
Yes in first procedure	139 (0.8)	83 (20.7)	56 (0.3)		
Yes in second procedure	899 (5.4)	312 (77.8)	587 (3.6)		
Two thoracic operations	7 (0.0)	3 (0.7)	4 (0.0)		
No thoracic operation	15593 (93.7)	3 (0.7)	15590 (96)		
Any thoracic operation, n (%)				<0.0001	-
Yes	1452 (8.7)	400 (99.8)	1052 (6.5)		
No	15186 (91.3)	1 (0.2)	15185 (93.5)		
Tracheostomy, n (%)				<0.0001	-
Yes (once)	365 (2.2)	52 (13)	313 (1.9)		
Yes (twice)	70 (0.4)	7 (1.7)	63 (0.4)		
No	16203 (97.4)	342 (85.3)	15861(97.7)		
Glasgow Outcome Score, n (%)				<0.0001	-
Death	1558 (9.2)	20 (5.0)	1538 (9.5)		
Prolonged Disorder of Consciousness	16 (0.1)	0 (0.0)	16 (0.1)		
Severe Disability	780 (4.7)	27 (6.7)	754 (4.6)		
Moderate Disability	3059 (18.4)	87 (21.7)	2972 (18.3)		
Good Recovery	11225 (67.5)	267 (66.6)	10958 (67.5)		
Total length of stay, mean (sd)	15.75 (22.27)	24.69 (25.85)	15.53, (22.13)	<0.0001†	-
Median (range)	9.00 (1.00-402.00)	16.00 (2.00-284.00)	9.00 (1.00-402.00)		
<7 days	5959 (35.8)	43 (10.7)	5916 (36.4)	<0.0001	-

		Treatment		Differences between groups	
Variable	**All Patients**	**Rib fixation**	**No rib fixation**	**Original**	**Imputed**
Total patients n (%)	**16638 (100)**	**402 (2.4)**	**16236 (97.6)**	**P-value**	**P-value**
7-13.99 days >14 days	4907 (29.5) 5772 (34.7)	133 (33.2) 225 (56.1)	4774 (29.4) 5546 (34.2)		
At least one admission to critical care n (%)	4701 (28.2)	285 (71.1)	4416 (27.0)		
Total length of critical care stay, mean (sd) Median (range) No CCU stay 0-2.99 days 3-6.99 days 7+ days	8.02 (11.92) 4.00 (1.00-230.00) 11937 (71.7) 1715 (10.3) 1334 (8.0) 1652 (9.9)	11.86 (10.79) 8.00 (1.00-49.00) 116 (28.9) 62 (15.5) 63 (15.7) 160 (39.9)	7.77 (11.95) 4.00 (1.00-230.00) 11821 (72.8) 1653 (10.2) 1271 (7.8) 1492 (9.2)	<0.0001† <0.0001	-
Intubated prior to operation n (%)	930 (5.6)	106 (26.4)	824 (5.1)	<0.0001	-
Length of pre-op ventilation, mean (sd) Median (range)	3.08 (13.38) 0.66(0.00-366.02)	2.53(3.33) 1.24(0.01 -18.28)	3.16 (14.20) 0.60(0.00-366.02)	0.001†	-
Intubated at any time n (%)	1372 (8.0)	105 (26.2)	1267 (7.8)	<0.0001	-
Total length of intubation, mean (sd) Median (range)	7.09 (8.94) 4.00(1.00-155.00)	8.10 (6.93) 7.00(1.00-42.00)	7.00 (9.08) 4.00(1.00-155.00)	0.02†	-
Tracheostomy Yes (once) Yes (twice) No	 365 (2.2) 70 (0.4) 16203 (97.4)	 52 (13.0) 7 (1.7) 342 (85.3)	 313 (1.9) 63 (0.4) 15861 (97.7)	<0.0001	-
Total length of tracheostomy, mean (sd) Median (range)	20.89 (26.04) 14.5 (1.00-234.00)	15.07 (6.76) 15.00(3.00-35.00)	21.94 (28.06) 14.00(0.00-235.00)	0.879†	-
NIV at any time n (%)	157 (0.9)	32 (8.0)	125 (0.8)	<0.0001	-

		Treatment		Differences between groups	
Variable	**All Patients**	**Rib fixation**	**No rib fixation**	**Original**	**Imputed**
Total patients n (%)	**16638 (100)**	**402 (2.4)**	**16236 (97.6)**	**P-value**	**P-value**
Total length of NIV, mean (sd) Median (range)	12.00 (55.51) 3.00 (0.00-646.00)	4.41 (5.58) 2.00 (1.00-21.00)	13.92 (62.04) 3.00 (1.00-646.00)	0.097†	-
Re-intubation, n (%) Yes (once) Yes (twice) No	 124 (0.7) 14 (0.1) 16500 (99.2)	 16 (4) 2 (0.5) 383 (95.5)	 108 (0.7) 12 (0.1) 16117 (99.3)	 0.574	 -
sd – standard deviation, n = frequency, MTC = Major trauma centre, ISS = Injury severity score, PS14 = Probability of survival Independent T test (continuous data variables) or Chi squared/Fishers Exact test (categorical data variables), †Non-parametric Mann Whitney-U					

5.3.2.2 Gender

Data on gender was complete with 10,518 (63.2%) males and 6,120 (36.8%) females recorded (Table 48). When age and gender are considered together a greater spread is seen within the male distribution showing a small peak in younger males which is not present in younger females. Age is positively skewed in females towards older age (Figure 27), but overall male patients have rib fracture operations more frequently than female patients (Males rib operation 74.1% vs. Males No rib operation 62.9% Fishers Exact (p<0.0001)).

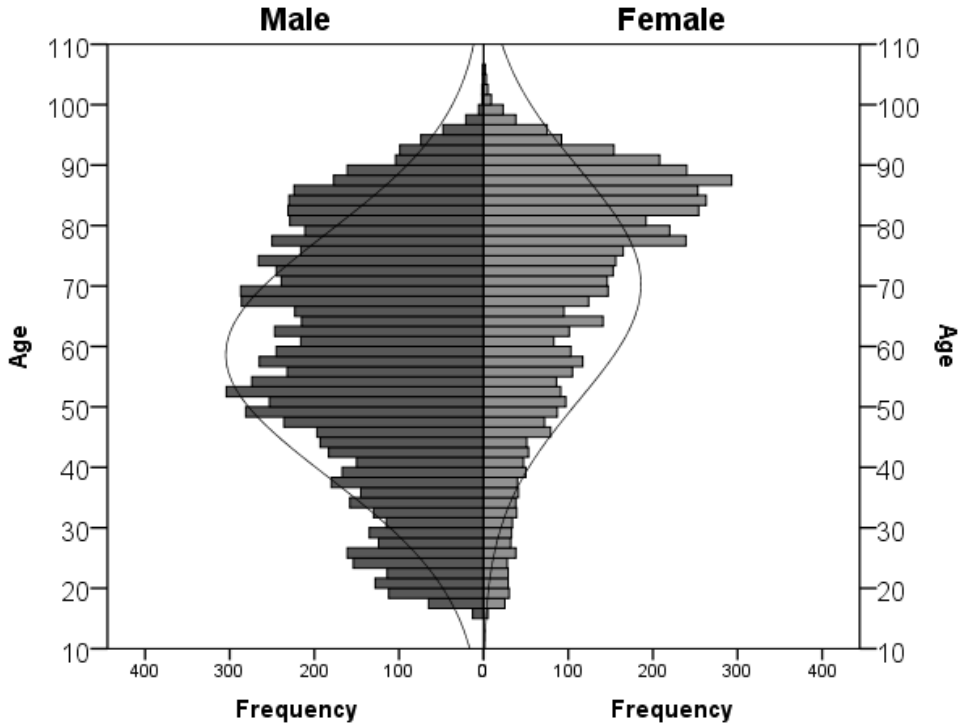


Figure 27 Age distribution by gender

5.3.2.3 Charlson Index

The Charlson comorbidity index is used in many epidemiological studies to control for potential confounders.[252] The Charlson index was complete and was right skewed with 7,478 cases (44.9%) scoring zero. This right skew is normal within the standard population and it is common when analysing this score to convert it into a categorical variable and distribute the data evenly between the four categories of none, mild, moderate and severe. Using the Chi squared test, there was no significant association between the fixation and no fixation groups and the Charlson comorbidity index (p= 0.062; Table 48).

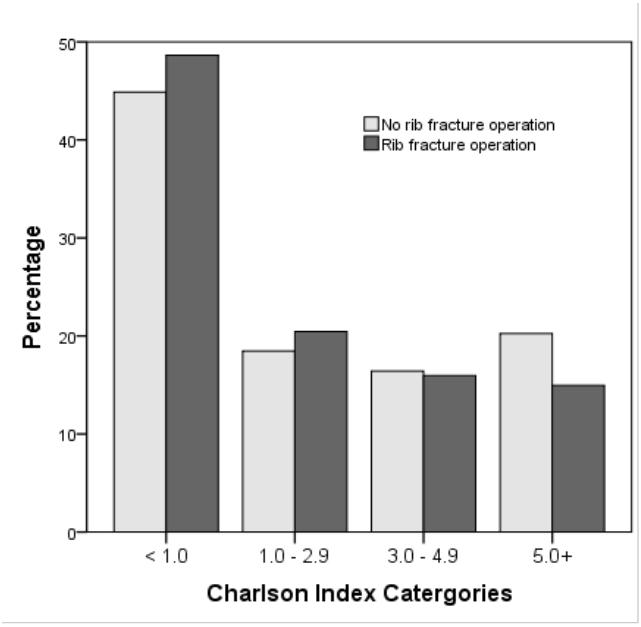


Figure 28 Percentage within each rib fracture operation group for the Charlson Index

5.3.2.4 Injury Severity Score

Injury severity score (ISS) was fully complete and was right skewed. Graphically, log transformed data appeared more normally distributed, however tests of normality rejected this as normalised data. Those with rib fixation had a significantly higher ISS (median 21.00, IQR 16.00 to 34.00) than those that did not have an operation (median 13.00, IQR 9.00 to 21.00) Mann-Whitney U Test (p <0.0001)) (Table 48). ISS was further grouped into ISS<15 (n= 8,820) and ISS>15 (n=7,818). Rib fracture fixation occurred more often in the ISS group 15 or more (i.e. those who were more severely injured and often presented to a Major Trauma Centre), Fishers exact test (p<0.0001).

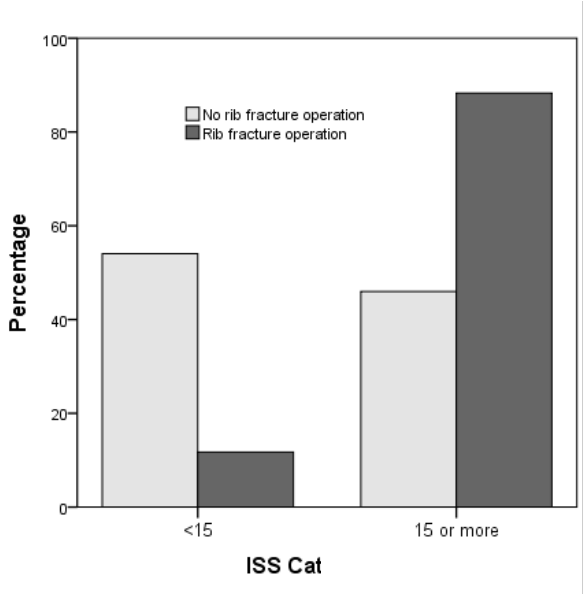


Figure 29 Percentage within each rib fracture operation group for ISS categories

5.3.2.5 Probability of survival

There were 563 values missing for the probability of survival (PS14) score (Table 119) and these were imputed (Table 121). Initial inspection of the histograms revealed a severely right skewed distribution. Multiple transformations were applied but none resulted in sufficient correction, hence a non-parametric test was used (Figure 30). Using non-parametric tests, the rib fixation group (median 95.96%, IQR 87.87 to 98.17%) on average had a lower probability of survival than the non-operative group (median 96.71%, IQR 91.44 to 98.91%) Mann-Whitney U Test ($p < 0.0001$; Table 48). PS 14 was transformed into categories above and below 95% (Figure 30). A greater percentage of patients whose probability of survival was less than 95% had rib fracture fixation (n=182, 45.3%) compared to non-operative management (n=6659, 41.0%) however this difference was not significant, Fishers exact test (p=0.068)

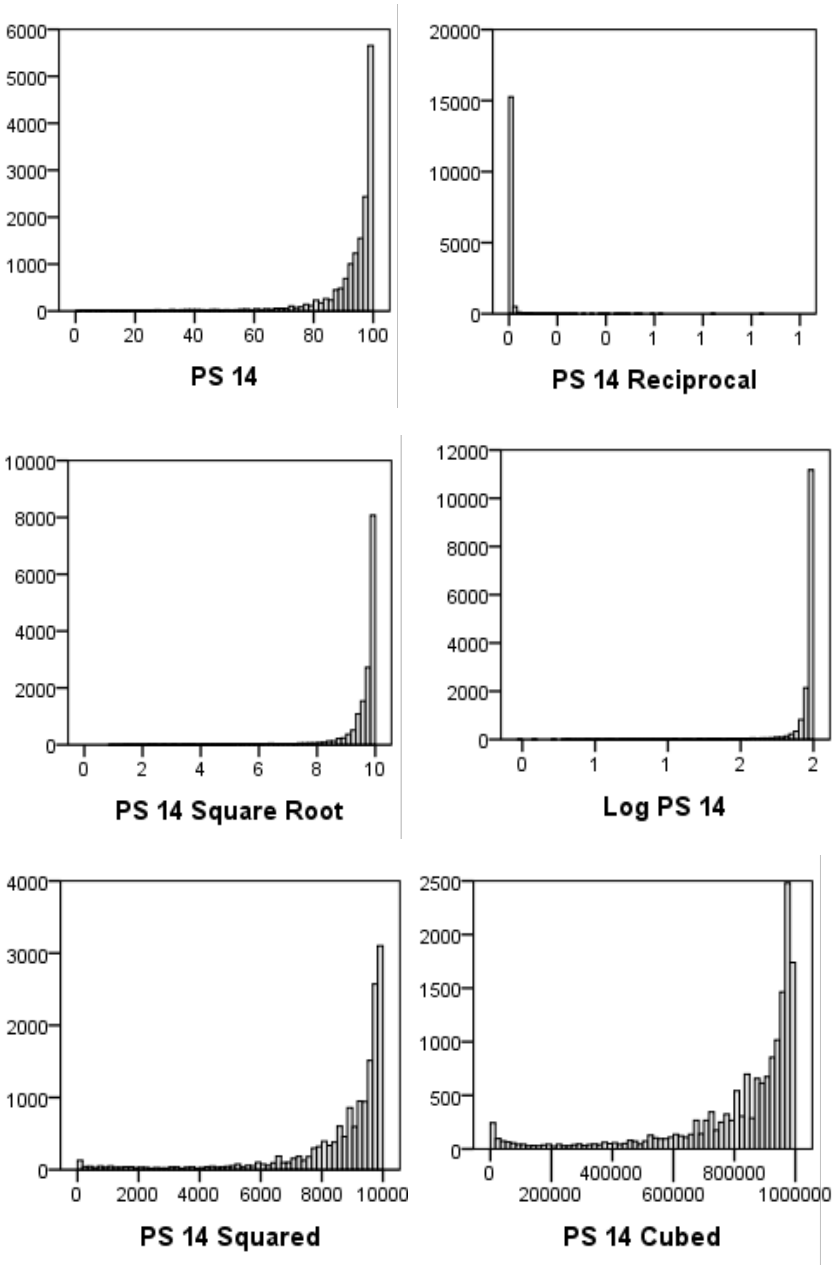


Figure 30 Histograms showing transformations of variable PS 14 of right skewed data

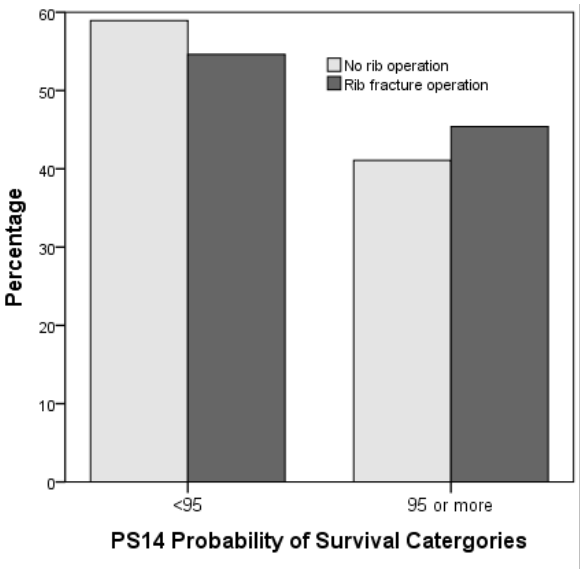


Figure 31 Percentage within each rib fracture operation group for PS14 categories

5.3.2.6 Mechanism of Injury

Complete records were available for the mechanism of injury variable, which was grouped into five categories: 41.5% (n=6,908) of patients had low energy injuries (fall from less than two metres). A vehicle incident was the next most common mechanism of injury at 33.8% (n=5,621) followed by a fall from more than two metres at 18.7% (n=3,104; Table 48). There were substantial differences between the operative and the non-operative groups in terms of the number of high energy injuries (vehicle incidents, fall from more than two metres, (Figure 32) with more individuals with high energy injuries going on to have rib fracture fixation (Fisher's Exact, $p<0.0001$). Within the penetrating injury group there were no patients who received rib fracture fixation.

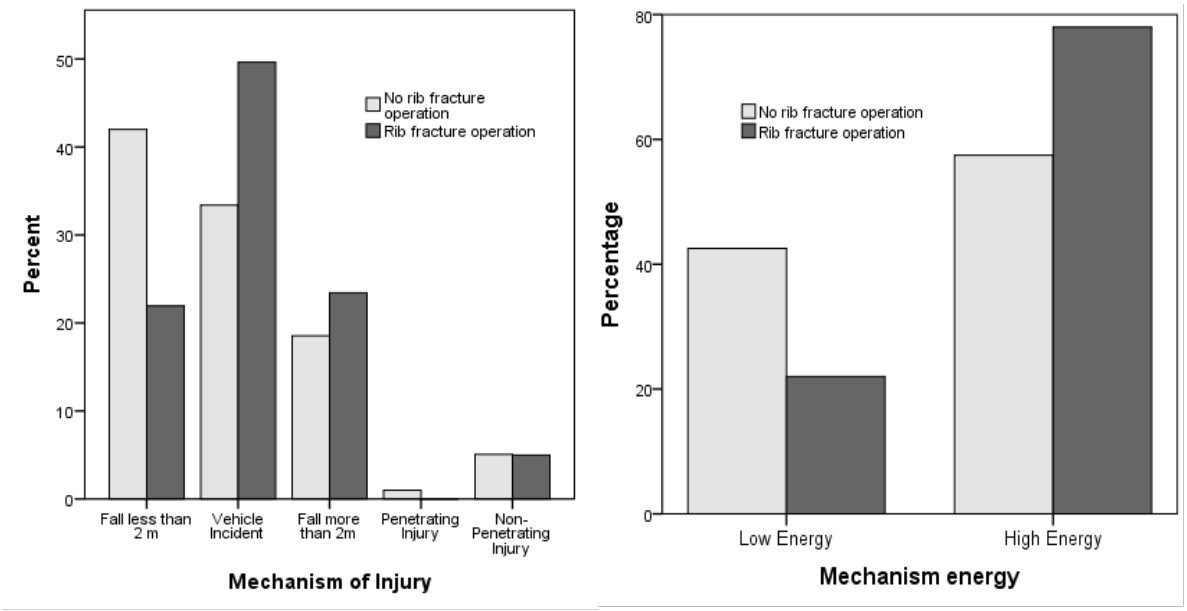


Figure 32 Percentage within each rib fracture operation group for mechanism of injury

5.3.2.7 Hospital Type

Care of chest trauma was split equally between Major Trauma Centres (MTC) and Trauma Units (TU) (MTC:TU; 49.5%, n=8,243:50.5%, n=8,395; Table 48). In the rib fracture operation group, however, 90.8% (n=364) were treated in an MTC compared to 51.5% (n=8,358) in the non-rib fracture operation population (Fisher Exact Test, p<0.0001). There were 201 admission sites that treated rib fracture patients, 37 sites were identified as undertaking rib fracture fixation and 17 sites performed more than ten procedures in a 14 month period.

5.3.2.8 Transfer Type

Transfer type was almost fully complete within the dataset (Table 48). Most patients were not transferred (81.9%, n=13,631), but a higher percentage of patients were transferred in the rib fracture fixation population (Fisher's Exact Test= P<0.0001;Figure 33). Of those that had a rib operation, 28.9% (n=116) were transferred out of their admitting hospital compared to 11.8% (n=1908) of those who did not have a rib fracture operation (Table 48).

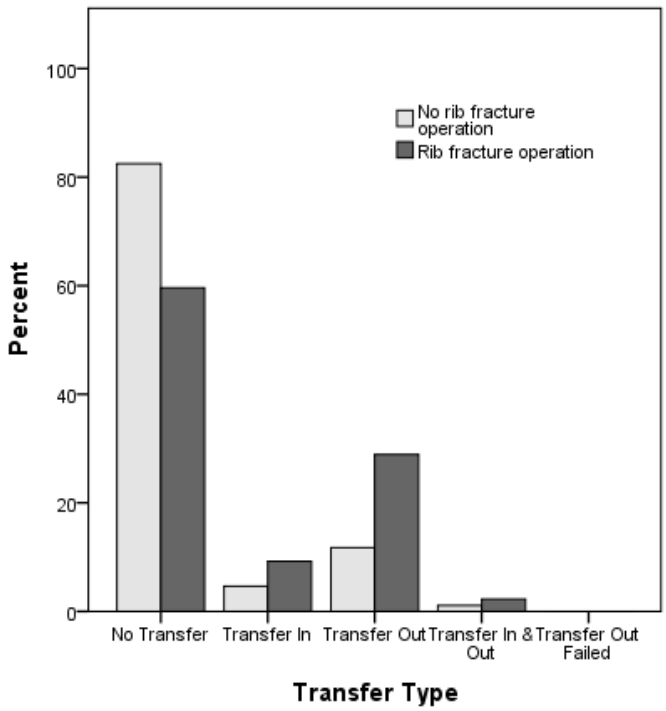


Figure 33 Percentage within each rib fracture operation group of transfer type

5.3.2.9 Admitting Speciality

Admission specialty was poorly recorded, with 62.2% of cases missing (Table 48). Due to large amounts of missing data this variable was not imputed. Overall, the top three specialties that patients were admitted under were orthopaedics (19.1%, n=1,207), general surgery (17.7%, n=1,121), and emergency medicine (16.6%, n=1,046) (Table 48). A greater proportion of patients who underwent rib fracture fixation were under the care of orthopaedics (26.0%, n=38), cardiothoracic surgery (28.8%, n=42) and the major trauma service (14.4%, n=21; Figure 34). Overall, there was a significant difference between the rib fracture operation and non-operative groups by admitting specialty (Fishers Exact Test p <0.0001). Since a significant proportion of the data was missing this variable was not used in any further statistical analyses.

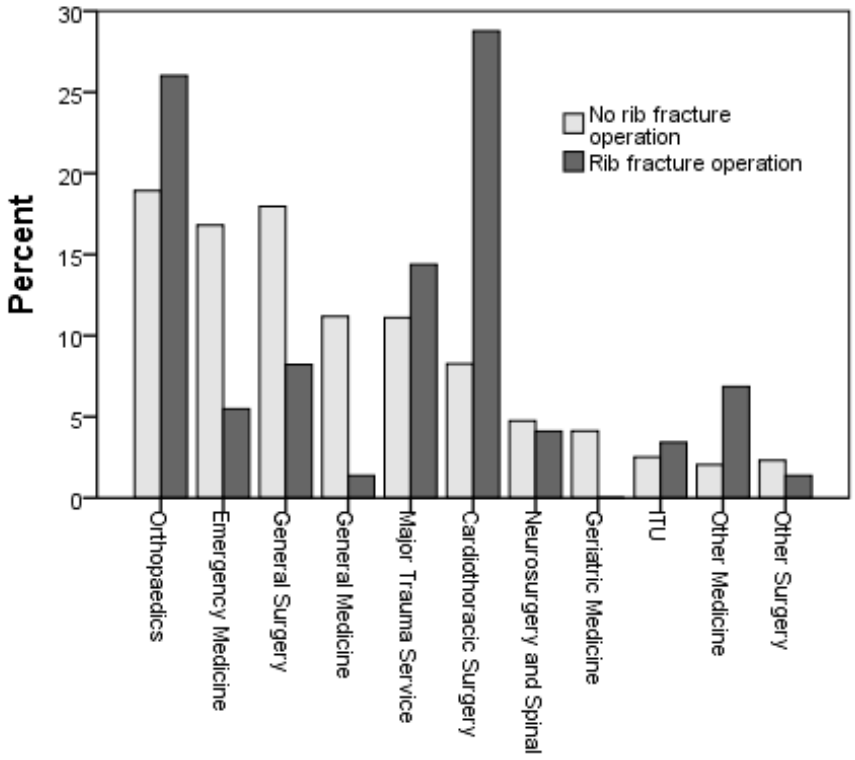


Figure 34 Percentage within each rib fracture operation group of admitting speciality

5.3.2.10 Analgesia

In terms of analgesia use, just under half of the sample had intravenous opioid (47.8%) and just under a third had intravenous paracetamol (32.7%). A small percentage had entonox (5.8%), PCA (5.2%), Ketamine (2.9%), Epidural block (2%) or LA blockade (1.6%). The other analgesia was used in under 1% of the sample. There was significantly higher use of a number of the analgesics (intravenous opioid, PCA, Ketamine, LA blockade, paravertebral block and epidural block) in the rib fixation group compared to the non-operative group. There was no evidence of a difference in the use of intravenous paracetamol, Entonox and LA patches between the two groups (Table 48).

5.3.2.11 Chest Injury Type

Rib fracture injury descriptions were grouped into four categories to represent the most common type of injuries. Most patients presented with three or more non-flail rib fractures 41.2% (n=6,854) followed by less than three non-flail rib fractures 25.8% (n=4,299). One third of patients had a flail injury (Table 48). Those who were operated on had a higher proportion of unilateral flail injuries (61.3%, n=246)

and bilateral flail injuries (22.7%, n= 91) compared to those not being operated on (Fishers exact test p<0.0001;Figure 35).

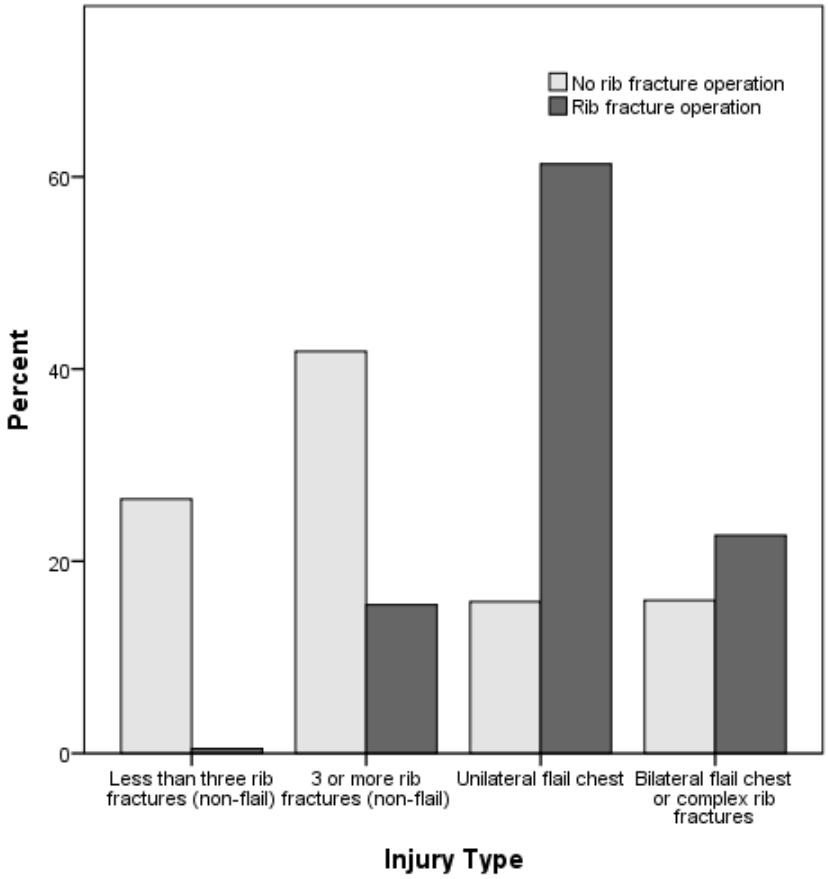


Figure 35 Percentage within each rib fracture operation group for injury type

5.3.2.12 Rib fracture and thoracic operations

The vast majority of patients with a rib fracture did not have an operation, however 315 patients had a rib operation as their first procedure, 87 had a rib operation as their second procedure and two patients had two rib operations (Table 49). A thoracic operation was defined as a procedure that was undertaken within the theatre setting on thoracic cavity, this could include; Video assisted thoracoscopy (VAT), open surgery or the drainage of haemothrorax. Slightly more patients had thoracic operations, with 139 having a thoracic operation in their first procedure, 899 having a thoracic operation in a second procedure and seven patients having two thoracic operations. Patients who had rib fracture surgery also had a greater percentage of thoracic operations (99.8%, n=400) than those who did not have rib fracture surgery (6.5%, n=1052; Fishers exact test p<0.0001). In subsequent

analyses, patients who had more than one procedure were counted singly and analyses were based on the first procedure.

5.3.2.13 Glasgow Outcome Score

The Glasgow Outcome Score (GOS) was not complete and 3,483 values needed to be imputed. Most patients (n =11,223, 67%) had a good recovery with very few patients with a severe disability (n=780, 4.7%) or a prolonged disorder of consciousness (n= 16, 0.1%). A substantial proportion of patients died, which may represent a confounder within any further analyses as there will be a proportion of this group who would have been dead on arrival or within 24 hours. These patients would not have had any rib fracture treatment to influence their outcome; a higher proportion of patients who did not have a rib operation therefore died in comparison to those who had a rib operation (n=1,538, 9.5% vs. n=20, 5.0%, Fishers Exact Test $p<0.0001$).

5.3.2.14 Total length of stay and critical care length of stay

Total length of stay of all comers and critical care length of stay were severely skewed and none of the transformations corrected this sufficiently. Length of hospital stay (LOS) was grouped into categories <7 days; 7≤ LOS<14 days and more than 14 days (Figure 36). Patients stayed a median time of 9 (IQR 5 to 18) days (Table 49). Patients who had a rib operation (median 16, IQR 9 to 30 days) stayed on average longer in hospital than those that did not have a rib operation (median 9, IQR 5 to 18 days; Mann-Whitney U Test, $p<0.0001$).

A higher percentage of patients who had a rib fracture operation were in critical care compared to those who did not have rib fracture operations (n=285, 71.1% vs. n=4,416, 27.2%). Patients stayed a median of 4 days (IQR 2 -10 days); those patients who had a rib operation stayed longer in critical care on average (median 8.5, IQR 3 to 18 days) than those who did not have an operation (median 4, IQR 2 to 9 days; Mann-Whitney U Test $p<0.0001$). Critical care length of stay (CCLOS) was also grouped into categories due to its severe skew. The four groups included: no CCU stay, 0<CCLOS<3, 3≤CCLOS<7 and more than 7 days. A greater number of operative patients had a longer CCLOS in these groups than non-operative patients (Fishers Exact, $p<0.0001$; Figure 36)

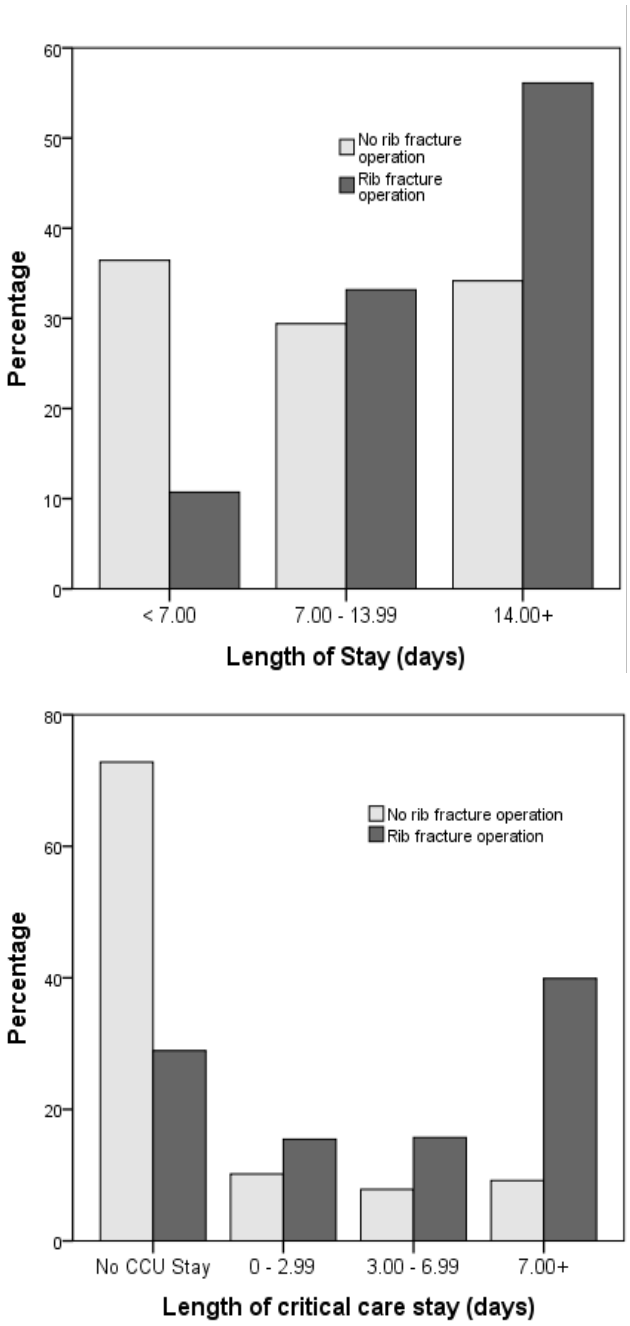


Figure 36 Percentage within each rib fracture operation group for length of stay and critical care length of stay (days)

5.3.2.15 Ventilator support

Patients who were intubated prior to having any operation had a longer median intubation time preoperatively (1.24, IQR 0.14 to 2.31 days) if having a rib fracture operation compared to other operations (0.60, IQR 0.14 to 2.31 days; Mann-Whitney U, p=0.001; Table 49).

The overall intubation time was longer in the rib fracture operative patients, however (median 7, IQR 2 to 12 days) compared to those that did not have a rib fracture operation (median 5, IQR 2 to 10 days; Mann-Whitney U Test p=0.02). Numbers of patients re-intubated were small and there was no evidence of an association between those who had a rib fracture operation (4.5%, n=18) and those that did not (0.8%, n=120; Fisher exact test, p= 0.574).

Rib fracture operation patients had a higher rate of tracheostomy (26%, n=105) compared to those patients that did not receive an operation (7.8%, n=1267). The tracheostomy time in the rib fracture operation patients (median 15, IQR 10.5 to 20 days) was longer than those who did not have operative management (median 14, IQR 8 to 25), but this was not statistically significant (Mann-Whitney U, p=0.879).

A higher proportion of patients who had a rib fracture operation had non-invasive ventilation (8.0%, n=32) compared to those who did not have a rib fracture operation (0.8%, n=125). Those who had a rib operation spent less time on NIV (median 2, IQR 1 to 6 days) than those that did not have a rib fracture operation (median 3, IQR 1 to 6.5 days), but this was again not statistically significant (Mann-Whitney U Test, p =0.097).

Intubation time, tracheostomy time and NIV time were severely skewed and none of the transformations corrected this sufficiently; therefore they were not used as a continuous variable and were dichotomised for further analyses.

5.3.3 Rib Fracture Operation Factors

There were 404 rib fracture operations performed on 402 patients (two patients had a second rib operation). Of the 402 patients who had a rib operation the median time to their first rib fracture operation was 2.70 (IQR 1.42 to 5.19) days in the 377 patients who had recorded data (Table 50). In those cases where data was recorded (combining both the first and second rib fracture operations) the most common type of endotracheal tube used in theatre was the single lumen tube (n=109, 27.0%) and the most common position was lateral (n=225, 55.7%). The most common method of intrathoracic inspection was by Video Assisted Thoracoscopic Surgery (VATS) (n=238, 58.9%), and a thoracotomy was performed 54 times. An air leak was found in 23 patients and was repaired in seven of these. A pleural lavage was performed in 38 patients and a pleural tear

was found in ten patients. The method of repair was reported in six cases (glue n=2, suture n=3 and staples n=1)

Table 50 Operative factors

Variable	All Rib fixation patients n (%)
Time to rib operation (days) (n = 375) mean (sd)	4.00 (4.19)
Median (range)	2.70 (0.04-35.06)
Early fixation less than 72 hours	208 (51.9)
Late fixation more than 72 hours	169 (42.1)
Tube Type 1 (n = 317)	
Single lumen	76 (24.0)
Double lumen	52 (16)
Tube Type 2 (n=89)	
Single lumen	33 (37.1)
Double lumen	9 (10.1)
Position for surgery 1 (n = 317)	
Prone	9 (2.8)
Lateral	166 (52.4)
Supine	34 (10.7)
Position for surgery 2 (n=87)	
Prone	0 (0)
Lateral	59 (66.3)
Supine	10 (11.2)
Rib plating(n=402)	
Yes in first procedure (n =315)	250 (61.9)
Yes in second procedure (n= 87)	79 (19.6)
Two plating procedures (n=2)	1 (0.2)
Unknown	74 (18.3)
Type of plating 1 (n = 317)	
Specific	141 (44.8)
Generic	56 (17.8)
Combination	19 (6.0)
Type of plating 2 (n=87)	
Specific	50 (56.1)
Generic	16 (18.0)
Combination	4 (5.5)
Any Intramedullary splint (n=402)	
Yes in first procedure	38 (9.4)
Yes in second procedure	3(0.7)
Two Intramedullary procedures	0 (0.0)
Unknown	(89.9)
Total number of ribs fixed 1(n = 273) mean (sd)	4.31 (2.23)
(range)	(1-18)
Total number of ribs fixed 2 (n=82) mean (sd)	4.21 (1.78)
(range)	(1-10)
Intrathoracic viscera inspected (n=402)	
First Intrathoracic viscera inspected	109(27.2)
Second Intrathoracic viscera inspected	45(11.2)
Intrathoracic viscera inspected on both procedures	1(0.2)
Unknown	246 (61.3)
Method of inspection of viscera 1 (n = 317)	
VATS	208 (65.6)
Thoracotomy	38 (12.0)
Unknown	71(22.4)

Variable	All Rib fixation patients n (%)
Method of inspection of viscera 2 (n=87) VATS Thoracotomy Unknown	 30 (33.7) 16 (18.0) 41 (47.1)
Air leak found (n=402) First procedure air leak Second procedure air leak Air leaks in both procedures Unknown	 16 (3.9) 7 (1.7) 0 (0) 378 (94.3)
Air leak repaired (n=402) First procedure air leak repaired Second procedure air leak repaired Two air leaks repaired Unknown	 6 (1.5) 1 (0.2) 0 (0) 394 (98.2)
Pleural lavage (n=402) First procedure pleural lavage Second procedure pleural lavage Pleural lavages in both procedures Unknown	 30 (8.0) 8 (2.0) 0 (0) 363 (90.5)
Pleural Tear (n=402) First procedure pleural tear Second procedure pleural tear Pleural tears in both procedures Unknown	 9 (2.2) 1(0.2) 0 (0) 391 (97.5)
Method of repair (n=402) Glue Sutures Staples Unknown	 2(0.5) 3 (0.7) 1(0.2) 395(98.5)
The first procedure is the operation of any type the patient had on their first time to theatre. The second procedure refers to the operation performed on the patients second time in theatre.	

5.3.3.1 Types of fixation

Plate fixation (n=330) was the most common type of fixation overall in comparison to intramedullary fixation, which was performed in 41 patients. The mean total number of ribs fixed in a single procedure ranged from 4.31 (SD 2.23) in a first operation to 4.21 (SD 1.78) in a second operation. The most common type of plate used was a specific rib plate fixation (n=191, 47.2%) followed by a generic plate (n=72, 17.8%). A combination of the two was used less frequently (n=23, 5.7%).

5.3.4 Adverse events

In general, complications or adverse events were low in rib fracture patients, with the incidence of most complications being less than 1% (Table 51). Certain complications have a high incidence in rib fracture patients, however. Specifically,

atelectasis (n=395, 2.95%), bronchopneumonia (n=686, 5.13%), pleural effusion (n=556, 4.16%), respiratory failure (n=325, 2.43%), pulmonary embolism (n=146, 1.96%) and sepsis (n=227, 1.7%) have higher complication rates in these patients. When comparing complications using a Fishers Exact test, complications of atelectasis (p= 0.003), bronchopneumonia (p=0.005), respiratory failure (p<0.0001), sepsis (p=0.015), pleural effusion (p<0.0001), aspiration (p=0.001) and empyema (p=0.03) appear statistically higher for operative patients than for non-operative patients. This is thought to be due to rib fracture operations being reserved for the sickest patients who are therefore more exposed to the risks of complications.

Table 51 Complications reported in all patients and by sub-group of rib operation and no rib operation

		Treatment		Differences between groups
Variable	**All Patients**	**Rib fixation patients**	**No rib fixation**	**Fishers Exact test**
Total patients n (%)	**13376 (100)**	**335 (2.50%)**	**13041 (97.50%)**	**P-value**
Fat Embolism	4 (0.03%)	0 (0%)	4 (0.03%)	0.904
Pulmonary Embolism	146 (1.96%)	4 (1.19%)	142 (1.09%)	0.787
Metabolic	39 (0.29%)	0 (0%)	39 (0.30%)	0.627
Atelectasis	395 (2.95%)	20 (5.97%)	375 (2.88%)	0.003
Pneumothorax (iatrogenic)	25 (0.19%)	2 (0.60%)	23 (0.18%)	0.129
Thrombosis	9 (0.07%)	0 (0%)	9 (0.07%)	0.796
DVT	59 (0.44%)	2 (0.6%)	57 (0.44%)	0.660
Bronchopneumonia	686 (5.13)	29 (8.66%)	657 (5.04%)	0.005
Shock	15 (0.11%)	1 (0.30%)	14 (0.11%)	0.334
Pleural Effusion	556 (4.16%)	38 (11.34%)	518 (3.97%)	<0.0001
Pulmonary- Other	144 (1.08%)	4 (1.19%)	140 (1.07%)	0.785
Sepsis	227 (1.70%)	12 (3.38%)	215 (1.65%)	0.015
ARDS	12 (0.09%)	0 (0%)	12 (0.09%)	0.737
Respiratory Failure/Arrest	325 (2.43%)	25 (7.46%)	300 (2.30%)	<0.0001
Aspiration	41 (0.31%)	6 (1.79%)	35 (0.27%)	0.001
Pulmonary Oedema	39 (0.29%)	2 (0.60%)	37 (0.28%)	0.256
Empyema	11 (0.08%)	2 (0.60%)	9 (0.07%)	0.030
Multi organ failure	98 (0.73)	2 (0.60%)	96 (0.74%)	0.554
ARDS = Acute Respiratory Distress Syndrome, DVT = Deep Vein Thrombosis				

5.3.5 Predictors for rib fracture operations

There were 434 patients who died within one day of admission and who were therefore removed prior to analyses; only one of these patients had rib fracture fixation. This patient had a high ISS of 66 and was taken to theatre within 71

minutes of arrival into hospital with a major thoracic arterial bleed. The patient also sustained bilateral and sternal fractures and bilateral contusions. No data was recorded for this patient as to the number of ribs fixed or what was used for the fixation.

Scatter plots of the continuous variables were plotted (Figure 37). There was some correlation between outcome variables but no convincing collinearity in the explanatory variables. All explanatory variable were retained for inclusion in the model.

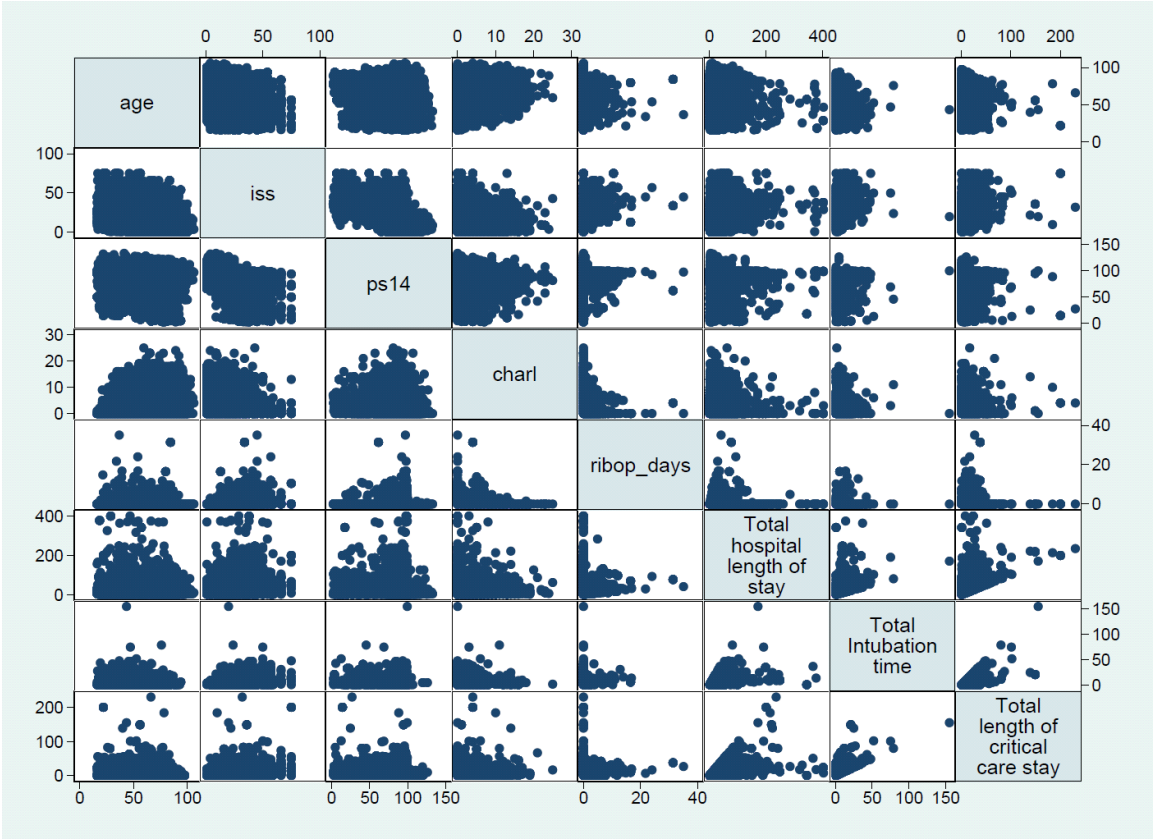


Figure 37 Scatterplot matrix of continuous explanatory variables

The first analysis looked at what factors predict which cases that receive a rib fracture operation by including all predictor groups. In this analysis, the mechanism of injury sub-group of 'penetrating injury' was a perfect predictor since no case had rib fracture fixation. The mechanism of injury subgroups were combined to make a new variable; high-energy injury (fall greater than 2 metres, vehicle incident, penetrating injury and non-penetrating injury) and low energy injury (fall of less than two metres) and re-entered into the model.

The biggest predictors of rib fracture fixation were the type of injury and the admission to an MTC when controlling for age, ISS, Charlson index, Contusion and type of injury energy. The odds of rib fracture fixation in unilateral flail chest was 107.51 (95% CI 28.61 to 404.05, p <0.0001), in bilateral flail or combined complex sternal fracture 47.63 (95% CI 13.35 to 169.92, p=0.007) and in three or more non-flail ribs 15.62 (95% CI 4.84 to 50.41, p<0.0001) compared to less than three non-flail rib fractures (Table 52).

Table 52 Independent predictors of rib fracture fixation: binary logistic regression analysis with MI data

Covariate	OR	95% C.I.		P-value
TU				
MTC	6.00	2.90	12.41	0.000
Low Energy				
High Energy	1.43	1.03	1.98	0.033
< 3 rib fractures NF				
≥3 rib fractures NF	15.62	4.84	50.41	0.000
Unilateral FC	107.51	28.61	404.05	0.000
Bilateral FC	47.63	13.35	169.92	0.000
No Contusion				
Unilateral contusion	2.16	1.69	2.77	0.000
Bilateral contusion	1.87	1.18	2.96	0.007
Age	1.01	1.01	1.02	0.000
ISS	1.02	1.01	1.03	0.000
Charlson Index	1.01	0.97	1.05	0.655
Constant	0.00	0.00	0.00	0.000

The odds of rib fracture fixation were higher in an MTC (OR 6.00, 95% CI 2.98 to 12.41, P<0.0001) compared to the odds of being in a trauma unit.

The odds of rib fracture fixation were higher the older the patient (OR 1.02, 95% CI 1.01 to 1.02, p<0.0001) and the higher the ISS (OR 1.02, 95% CI 1.01 to 1.03, p<0.0001). The odds of rib fracture fixation were also higher with an increase in the Charlson index, but this was not statistically significant (OR 1.01, 95% CI 0.97 to 1.03, p=0.655). The odds of rib fracture fixation in those with high-energy injuries were 1.43 times (95% CI 1.03 to 1.98, p<0.033) the odds of those with a low energy injury. The odds of rib fracture fixation in patients were higher with

unilateral pulmonary contusion (OR 2.16, 95% CI 1.69 to 2.77, p<0.0001) and bilateral contusion (OR 1.87, 95% CI 1.18 to 2.96, p=0.007) compared to the odds of no contusion. Although there was a significant difference in odds in these two variables (contusion and energy mechanism), and the odds ratios were low compared to MTC and injury type.

5.3.6 Does rib fracture fixation affect outcomes?

5.3.6.1 Mortality

The odds of patient mortality were less in patients who had rib fracture fixation compared to non-operative management (OR 0.14, 95% CI 0.06 to 0.31, p<0.0001), and in those who had high energy injuries compared to low energy injuries (OR 0.77, 95% CI 0.64 to 0.93, p= 0.006). The odds of mortality were higher with increasing age (OR 1.06, 95% CI 1.06 to 1.07, p<0.0001), increasing ISS (OR 1.06, 95% CI 1.06 to 1.07, p<0.0001) and increasing Charlson index (OR 1.11, 95% CI 1.08 to 1.13, p<0.0001). The odds of mortality were higher amongst those with one or two adverse events (OR 3.17, 95% CI 2.39 to 4.20, p<0.0001) and three or more adverse events (OR 8.12, 95% CI 5.14 to 12.82, p<0.0001) compared to those having no adverse events, and were the highest predictors of mortality.

Table 53 A binary logistic regression model predicting mortality following rib fracture surgery

Covariate	OR	95% C.I.		P-value
No Rib Op				
Rip Op	0.14	0.06	0.31	0.000
TU				
MTC	0.94	0.72	1.21	0.616
Low Energy				
High Energy	0.77	0.64	0.93	0.006
< 3 rib fractures NF				
≥3 rib fractures NF	1.09	0.88	1.35	0.435
Unilateral FC	0.87	0.65	1.17	0.362
Bilateral FC	1.18	0.88	1.58	0.269
No Contusion				
Unilateral contusion	1.02	0.76	1.35	0.913
Bilateral contusion	1.42	0.92	2.19	0.110
Age	1.06	1.06	1.07	0.000
ISS	1.06	1.06	1.07	0.000
Charlson Index	1.11	1.08	1.13	0.000
No adverse events				
1 or 2 adverse events	3.17	2.39	4.20	0.000
3 or more adverse events	8.12	5.14	12.82	0.000
Constant	0.00	0.00	0.00	0.000

5.3.6.2 Adverse events

Despite controlling for multiple factors, the odds of developing an adverse event were higher in the rib operation group compared to the non-operative group (OR 1.89, 95% CI 1.28 to 2.80, p=0.001). Increasing age, ISS, Charlson index and bilateral contusions (compared to no contusion) also increased the odds of developing an adverse event (Table 54). High energy injury decreased the odds of developing an adverse event compared to having a low energy injury (OR 0.84, 95% CI 0.74 to 0.95 p=0.005).

Table 54 Ordinal logistic regression using MI data to predict the odds of adverse events

Covariate	OR	95% C.I.		P-value
No rib op				
Rib op	1.89	1.28	2.80	0.001
TU				
MTC	1.04	0.62	1.75	0.884
Low Energy				
High Energy	0.84	0.74	0.95	0.005
< 3 rib fractures NF				
≥3 rib fractures NF	1.19	1.01	1.39	0.032
Unilateral FC	1.10	0.92	1.31	0.304
Bilateral FC	1.30	1.10	1.53	0.002
No Contusion				
Unilateral contusion	0.99	0.86	1.14	0.869
Bilateral contusion	1.32	1.09	1.60	0.004
Age	1.01	1.00	1.01	0.000
ISS	1.03	1.02	1.04	0.000
Charlson	1.09	1.07	1.12	0.000
/cut1	3.01	2.62	3.40	
/cut2	5.71	5.24	6.18	
MTC = Major Trauma Centre, TU = Trauma Unit, OR = Odds Ratio, CI = Confidence Interval, ISS = Injury Severity Score, NF = Non Flail, FC = Flail Chest				

5.3.6.3 Length of hospital stay (days)

Length of hospital stay was dichotomised at nine days since the outcome data was skewed. A binary logistic model describing the odds of staying in hospital for nine days or more revealed higher odds in the rib operation group compared to the non-operative group (OR 2.52, 95% CI 1.90 to 3.35, p<0.0001). Other factors that increased the odds of staying in hospital for nine days or longer were MTC compared to TU, increasing age, increasing ISS, increasing Charlson index score and one or two adverse events and three or more adverse events compared to no adverse events (Table 56).

Propensity score matching was not possible for imputed data and therefore the original data was used. Using the matching technique, the odds of staying in hospital for more than nine days were higher in the rib operation group compared to the non-operative group (OR 1.33, 95% CI 1.28 to 1.40, p<0.0001) (Table 56).

When categorising this into early (less than 72 hours) versus late fixation (more than 72 hours) the odds of being in hospital for longer than nine days were lower with early rib fixation compared to late rib fixation (0.14, 95% CI 0.05 to 0.34, p<0.0001).

A competing risks regression analysis showed that rib fracture fixation was associated with a higher incidence of being discharged from hospital, accounting for the competing risk of death (SHR 1.04, 95% CI 0.94 to 1.15, p = 0.478, Table 57), but this was not statistically significant. In the competing risks regression model incorporating the timing of rib fracture, fixation was associated with a higher incidence of being discharged from hospital, also accounting for the competing risk of death (SHR 1.16, 95% CI 1.05 to 1.29, p=0.005), but this time the result was statistically significant. Other covariates in the competing risks models did not change when adding the additional caveat of timing of fixation. In both models, being admitted to an MTC rather than a TU, increasing age, increasing ISS and increasing Charlson score, as well as having an adverse event, decreased the incidence of being discharged (Table 57). High energy injury compared to a low energy injury, and having three or more non-flail rib fractures or a unilateral flail chest compared to less than three non-flail rib fractures, all increased the incidence of being discharged from hospital (Table 57).

In summary, the effect of rib fracture fixation on length of stay (or time to discharge) varies between the models (Table 55). Conclusions as to the length of stay (time to discharge) change when taking into account the competing risk of death for rib fracture fixation, conferring an advantage to rib fracture fixation.

Table 55 The effect of rib fracture fixation on the length of hospital stay

		95% C.I.		P-value	Interpretation
Binary logistic regression (OR)	2.52	1.90	3.35	<0.0001	Odds of being in hospital longer than nine days are higher with rib fracture fixation.
Propensity score matching (OR)	1.33	1.28	1.40	<0.0001	Odds of staying nine days or longer are higher in the rib operation group.
Early Vs Late fixation (OR)	0.14	0.05	0.34	<0.0001	Odds of being in hospital longer than nine days are lower with early rib fixation.
Competing risks regression (SHR)	1.04	0.94	1.15	0.478	Incidence of discharge from hospital is higher with a rib operation when there is a competing risk of death (not significant).
Competing risks with time to rib op (SHR)	1.16	1.05	1.29	0.005	Incidence of discharge from hospital is higher with a rib operation when there is a competing risk of death and taking into account the timing of surgery.
OR = Odds Ratio, SHR = Sub-Hazard Ratio, CI =Confidence Interval					

Table 56 Prediction of length of hospital stay of more than nine days. Binary logistic regression and MI data in all cases and the effect on early or late fixation in operated cases.

Rib op vs non-operative (all cases)					Early Vs Late fixation (in operated cases)				
Covariate	**OR**	**95% CI**		**P value**		**OR**	**95% CI**		**P value**
No Rib Op					Late Fixation				
Rip Op	2.52	1.90	3.35	0.000	Early Fixation	0.14	0.05	0.34	0.000
TU					TU				
MTC	1.25	1.09	1.44	0.002	MTC	0.13	0.01	2.05	0.146
Low Energy					Low Energy				
High Energy	0.88	0.80	0.97	0.010	High Energy	0.61	0.22	1.68	0.336
< 3 rib fractures NF					< 3 rib fractures NF				
≥3 rib fractures NF	0.90	0.81	0.99	0.033	≥3 rib fractures NF	0.92	0.06	15.32	0.954
Unilateral FC	0.64	0.56	0.73	0.000	Unilateral FC	0.65	0.03	12.96	0.780
Bilateral FC	1.06	0.92	1.22	0.426	Bilateral FC	0.66	0.03	17.06	0.803
No Contusion					No Contusion				
Unilateral contusion	0.91	0.81	1.02	0.107	Unilateral contusion	1.15	0.61	2.17	0.673
Bilateral contusion	1.04	0.84	1.30	0.700	Bilateral contusion	1.09	0.26	4.55	0.908
Age	1.02	1.02	1.03	0.000	Age	1.04	1.01	1.07	0.020
ISS	1.07	1.06	1.08	0.000	ISS	1.10	1.04	1.17	0.001
Charlson Index	1.07	1.05	1.08	0.000	Charlson Index	0.97	0.88	1.08	0.635
					No pre-op ventilation				
					Pre-op ventilation	4.24	1.16	15.41	0.028
No AE					No AE				
1 or 2 AE	2.14	1.86	2.46	0.000	1 or 2 AE	4.90	2.11	11.36	0.000
3 or more AE	3.66	2.19	6.13	0.000	3 or more AE	1.00			
Constant	0.07	0.06	0.09	0.000	Constant	1.93	0.05	81.16	0.731

OR = Odds Ratio, CI =Confidence Interval, AE = Adverse Events, FC = Flail Chest, NF = Non Flail MTC= Major Trauma Centre, TU = Trauma Unit

Table 57 Outcome of length of stay model using a competing risk regression analysis and a second analysis incorporating the time to rib operation.

Covariate	Length of hospital stay (days) Competing Risk in hospital death							
	All entering at T_0				Operated patients entering at T_n (time to rib op)			
	SHR	95% C.I.		P-value	SHR	95% C.I.		P-value
No Rib Op								
Rip Op	1.04	0.94	1.15	0.478	1.16	1.05	1.29	0.005
TU								
MTC	0.89	0.82	0.96	0.005	0.89	0.82	0.96	0.004
Low Energy								
High Energy	1.14	1.08	1.20	0.000	1.14	1.08	1.20	0.000
< 3 rib fractures NF								
≥3 rib fractures NF	1.11	1.05	1.18	0.000	1.11	1.05	1.17	0.000
Unilateral FC	1.34	1.25	1.44	0.000	1.34	1.25	1.44	0.000
Bilateral FC	1.01	0.96	1.08	0.619	1.01	0.96	1.07	0.647
No Contusion								
Unilateral contusion	1.05	0.99	1.12	0.087	1.05	0.99	1.12	0.098
Bilateral contusion	0.97	0.90	1.04	0.347	0.96	0.90	1.03	0.303
Age	0.98	0.98	0.98	0.000	0.98	0.98	0.98	0.000
ISS	0.96	0.96	0.96	0.000	0.96	0.96	0.96	0.000
Charlson Index	0.95	0.94	0.96	0.000	0.95	0.94	0.96	0.000
No adverse events								
1 or 2 adverse events	0.58	0.53	0.64	0.000	0.58	0.53	0.64	0.000
3 or more adverse events	0.36	0.31	0.43	0.000	0.37	0.31	0.44	0.000

SHR = Sub Hazard Ratio, CI =Confidence Interval, AE = Adverse Events, FC = Flail Chest, NF = Non Flail, MTC = Major Trauma Centre, TU = Trauma Unit

5.3.6.4 Length of intensive care stay (days)

Length of intensive care stay was dichotomised at four days since the outcome data was skewed. A binary logistic model describing the odds of staying in an ICU for four days or more is higher in the rib operation group compared to the non-operative group (OR 3.07, 95% CI 2.08 to 4.52, p<0.0001). Other factors that increased the odds of staying in ICU 4 days or longer are being admitted to an MTC compared to TU, high energy injury compared to low energy injury, increasing ISS and Charlson index score. One or two adverse events and three or more adverse events, compared to no adverse events, and three or more ribs fractured and bilateral flail chest compared to less than three non-flail rib fractures, and unilateral contusion compared to no contusion all also increased the odds (Table 59).

Propensity score matching was not possible for imputed data and therefore original data was used. Using this matching technique, the odds of staying in an ICU for more than four days were higher in the rib operation group compared to the non-operative group (OR 1.28, 95% CI 1.17 to 1.30, p<0.0001) (Table 58).

When categorising this into early (less than 72 hours) versus late fixation (more than 72 hours) the odds of being in ICU longer than four days were lower with early rib fixation compared to late fixation (OR 0.38, 95% CI 1.19 to 1.60, p<0.0001).

A competing risks regression analysis showed that rib fracture fixation was associated with a higher incidence of being discharged from ICU accounting for the competing risk of death. (SHR 1.06, 95% CI 0.91 to 1.22, p=0.4651, Table 60) but this result was not statistically significant. The competing risks regression model incorporating the timing of treatment, showed that rib fracture fixation was associated with a higher incidence of being discharged from ICU; a result which was statistically significant (SHR 1.38, 95% CI 1.19 to 1.60, p<0.0001). Other covariates in the competing risks models did not change when adding the additional caveat of timing of fixation. In both models, increasing age, increasing ISS, increasing Charlson score, and having an adverse event all decreased the incidence of being discharged from ICU with a competing risk of death (Table 60). A unilateral flail chest compared to less than three non-flail rib fractures increased the incidence of discharge from ICU with a competing risk of death (Table 57).

In summary, the effect of rib fracture fixation on length of stay (time to discharge) varied between the models (Table 58). Conclusions on the length of stay (time to discharge) change when taking into account the competing risk of death for rib fracture fixation, especially when performed earlier than 72 hours from admission.

Table 58 The effect of rib fracture fixation on the length of ICU stay

		95% C.I.		P-value	Interpretation
Binary logistic regression (OR)	3.07	2.08	4.52	0.000	Odds of being in the ICU longer than four days are higher with rib fracture fixation.
Propensity score matching (OR)	1.28	1.07	1.30	0.000	Odds of staying in the ICU longer than four days are higher in the rib operation group.
Early Vs Late fixation (OR)	0.40	0.25	0.62	0.000	Odds of being in ICU longer than four days are lower with early rib fixation.
Competing risks regression (SHR)	1.06	0.91	1.22	0.465	Incidence of discharge from the ICU is higher with a rib operation when there is a competing risk of death (not significant).
Competing risks with time to rib op (SHR)	1.38	1.19	1.60	0.000	Incidence of discharge from the ICU is higher with a rib operation when there is a competing risk of death and taking into account the timing of surgery.
OR = Odds Ratio, SHR = Sub-Hazard Ratio, CI =Confidence Interval					

Table 59 Prediction of length of ICU stay of more than four days modelled using binary logistic regression and MI data in all cases, and the effect on early or late fixation in operated cases.

Length of ICU stay more than four days									
Rib op vs non-operative (all cases)					**Early Vs Late fixation (in operated cases)**				
Covariate	**OR**	**95% CI**		**P**	**Covariate**	**OR**	**95% CI**		**P**
No Rib Op					Late Fixation				
Rip Op	3.07	2.08	4.52	0.000	Early Fixation	0.40	0.25	0.62	0.000
TU					TU				
MTC	1.45	1.09	1.93	0.011	MTC	0.42	0.15	1.18	0.098
Low Energy					Low Energy				
High Energy	1.59	1.36	1.86	0.000	High Energy	2.27	1.23	4.20	0.009
< 3 rib fractures NF					< 3 rib fractures NF				
≥3 rib fractures NF	1.28	1.06	1.55	0.009	≥3 rib fractures NF	0.83	0.25	2.75	0.754
Unilateral FC	1.16	0.97	1.38	0.100	Unilateral FC	0.77	0.37	1.59	0.479
Bilateral FC	1.40	1.16	1.69	0.000	Bilateral FC	1.00			
No Contusion					No Contusion				
Unilateral contusion	1.22	1.01	1.46	0.036	Unilateral contusion	0.72	0.32	1.61	0.424
Bilateral contusion	1.20	0.97	1.48	0.087	Bilateral contusion	1.47	0.53	4.09	0.461
Age	0.99	0.99	1.00	0.000	Age	1.02	1.00	1.04	0.058
ISS	1.09	1.08	1.10	0.000	ISS	1.04	1.00	1.09	0.057
Charlson Index	1.04	1.02	1.06	0.000	Charlson Index	1.03	0.93	1.14	0.581
					No pre-op ventilation				
					Pre-op ventilation	12.44	5.18	29.89	0.000
No AE					No AE				
1 or 2 AE	3.66	2.99	4.49	0.000	1 or 2 AE	2.80	1.31	6.00	0.008
3 or more AE	12.85	8.18	20.20	0.000	3 or more AE	1.00			
Constant	0.01	0.01	0.02	0.000	Constant	0.11	0.01	1.39	0.089
OR = Odds Ratio, CI =Confidence Interval, AE = Adverse Events, FC = Flail Chest, NF = Non Flail, MTC = Major Trauma Centre, TU = Trauma Unit									

Table 60 Outcome length of ICU stay model using a competing risk regression analysis and a second analysis incorporating the time to rib operation.

Covariate	Length of ICU stay (days) Competing Risk in hospital death							
	All entering at T_0				Operated patients entering at T_n (time to rib op)			
	SHR	95% C.I.		P-value	SHR	95% C.I.		P-value
No Rib Op								
Rip Op	1.06	0.91	1.22	0.465	1.38	1.19	1.60	0.000
TU								
MTC	1.02	0.87	1.21	0.797	1.02	0.87	1.20	0.790
Low Energy								
High Energy	1.07	0.96	1.21	0.225	1.08	0.97	1.22	0.172
< 3 rib fractures NF								
≥3 rib fractures NF	1.11	1.00	1.23	0.059	1.10	1.00	1.22	0.056
Unilateral FC	1.21	1.07	1.38	0.002	1.21	1.07	1.37	0.002
Bilateral FC	1.05	0.92	1.19	0.480	1.05	0.93	1.19	0.446
No Contusion								
Unilateral contusion	1.04	0.95	1.13	0.420	1.04	0.95	1.13	0.4250
Bilateral contusion	0.94	0.86	1.04	0.242	0.94	0.86	1.03	0.177
Age	0.99	0.98	0.99	0.000	0.99	0.98	0.99	0.000
ISS	0.97	0.97	0.97	0.000	0.97	0.97	0.97	0.000
Charlson Index	0.96	0.95	0.98	0.000	0.96	0.95	0.98	0.000
No AE								
1 or 2 AE	0.66	0.59	0.74	0.000	0.67	0.60	0.75	0.000
3 or more AE	0.41	0.34	0.50	0.000	0.41	0.34	0.50	0.000
SHR = Sub Hazard Ratio, CI =Confidence Interval, AE = Adverse Events, FC = Flail Chest, NF = Non Flail, MTC = Major Trauma Centre, TU = Trauma Unit								

5.3.6.5 Length of intubation (days)

Length of intubation was dichotomised at four days since the outcome data was skewed. A binary logistic model described the odds of being intubated for four days or more as higher in the rib operation group compared to the non-operative group (OR 2.13, 95% CI 1.10 to 4.11, p=0.024, Table 61). Other factors that increased the odds of being intubated in an ICU for four days or longer were high energy injury compared to low energy injury, increasing ISS and Charlson index score. One or two adverse events and three or more adverse events compared to no adverse events also increased the odds of being intubated for four days or more (Table 62). Increasing age decreased the odds of spending more than four days intubated.

Propensity score matching was not possible for imputed data and therefore original data was used. Using this matching technique, the odds of being intubated for longer than four days were higher in the rib operation group compared to the non-operative group (OR 1.03, 95% CI 1.00 to 1.06, p=0.021) (Table 61).

When categorising this into early (less than 72 hours) versus late fixation (more than 72 hours) the odds of being intubated longer than four days were lower with early rib fixation compared to late fixation (OR 0.28, 95% CI 0.13 to 0.60, p=0.001).

A competing risks regression analysis was performed to include the outcome of being extubated in the presence of the risk of death. The incidence of being extubated was higher with a rib operation when there is a competing risk of death (SHR 1.28, 95% CI 1.01 to 1.64, p=0.044,Table 63); a result that was statistically significant. In the competing risks regression model incorporating the timing of treatment, the incidence of being extubated was higher with a rib operation (SHR 2.01, 95% CI 1.58 to 2.54, p<0.0001). No other covariate statistically improved this incidence. Other covariates in the competing risks models did not change when adding the additional caveat of timing of fixation. In both models, increasing age, increasing ISS and increasing Charlson score, and having an adverse event, were associated with a decreased incidence of being extubated, with a competing risk of death (Table 62).

In summary, the effect of rib fracture fixation on length of intubation varied between the models (Table 61). Conclusions on the intubation length change when taking into account the competing risk of death for rib fracture fixation, conferring an advantage of rib fracture fixation, especially when fixation is performed less than 72 hours from admission.

Table 61 The effect of rib fracture fixation on the length of Intubation stay

		95% C.I.		P-value	Interpretation
Binary logistic regression (OR)	2.13	1.10	4.11	0.024	Odds of being intubated for four days or longer are higher with rib fracture fixation.
Propensity score matching (OR	1.03	1.00	1.06	0.021	Odds of being intubated for four days or longer are higher with rib fracture fixation.
Early Vs Late fixation (OR)	0.28	0.13	0.60	0.001	Odds of being intubated for four days or longer are lower with early rib fixation.
Competing risks regression (SHR)	1.28	1.01	1.64	0.044	Incidence of being discharged from intubation is higher with a rib operation when there is a competing risk of death.
Competing risks with time to rib op (SHR)	2.01	1.58	2.54	0.000	Incidence of being discharged from intubation is higher with a rib operation when there is a competing risk of death and taking into account the timing of surgery.
OR = Odds Ratio, SHR = Sub-Hazard Ratio, CI =Confidence Interval					

Table 62 Prediction of length of intubation of four days or longer modelled using binary logistic regression and MI data in all cases and the effect on early or late fixation in operated cases

Rib op vs non-operative (all cases)					**Early Vs Late fixation (in operated cases)**				
Covariate	OR	95% CI		P		OR		95% CI	P
No Rib Op					Late Fixation				
Rip Op	2.13	1.10	4.11	0.024	Early Fixation	0.28	0.13	0.60	0.001
TU					TU				
MTC	1.16	0.83	1.64	0.379	MTC	0.26	0.06	1.17	0.079
Low Energy					Low Energy				
High Energy	1.99	1.41	2.81	0.000	High Energy	4.61	0.92	23.09	0.063
< 3 rib fractures NF					< 3 rib fractures NF				
≥3 rib fractures NF	1.10	0.82	1.47	0.523	≥3 rib fractures NF	0.30	0.09	0.98	0.046
Unilateral FC	0.77	0.58	1.02	0.070	Unilateral FC	0.74	0.31	1.75	0.491
Bilateral FC	1.10	0.83	1.47	0.509	Bilateral FC	1.00			
No Contusion					No Contusion				
Uni contusion	1.10	0.86	1.43	0.446	Uni contusion	0.77	0.22	2.74	0.690
Bi contusion	1.38	0.98	1.93	0.066	Bi contusion	0.25	0.08	0.79	0.018
Age	0.99	0.99	1.00	0.001	Age	1.03	0.99	1.06	0.105
ISS	1.09	1.08	1.10	0.000	ISS	0.99	0.96	1.02	0.406
Charl Index	1.05	1.01	1.08	0.015	Charl Index	1.18	1.07	1.30	0.001
					No pre-op ventilation				
					Pre-op ventilation	46.31	16.31	131.44	0.000
No AE					No AE				
1 or 2 AE	4.45	3.28	6.03	0.000	1 or 2 AE	5.95	1.65	21.42	0.006
3 or more AE	20.69	12.19	35.14	0.000	3 or more AE	23.54	3.92	141.26	0.001
Constant	0.00	0.00	0.01	0.000	Constant	0.02	0.00	0.44	0.015

OR = Odds Ratio, CI =Confidence Interval, AE = Adverse Events, FC = Flail Chest, NF = Non Flail, MTC = Major Trauma Centre, TU = Trauma Unit

Table 63 Outcome length of intubation model using a competing risk regression analysis and a second analysis incorporating the time to rib operation

Covariate	Length of intubation (days) Competing Risk in hospital death							
	All entering at T_0				Operated patients entering at T_n (time to rib op)			
	SHR	95% C.I.		P-value	SHR	95% C.I.		P-value
No Rib Op								
Rip Op	1.28	1.01	1.64	0.044	2.01	1.58	2.54	0.000
TU								
MTC	1.16	0.94	1.44	0.154	1.17	0.96	1.42	0.119
Low Energy								
High Energy	1.10	0.86	1.42	0.434	1.12	0.87	1.44	0.389
< 3 rib fractures NF								
≥3 rib fractures NF	0.87	0.72	1.05	0.147	0.87	0.72	1.06	0.165
Unilateral FC	0.99	0.75	1.31	0.952	1.00	0.76	1.32	0.984
Bilateral FC	0.88	0.68	1.13	0.319	0.89	0.70	1.14	0.346
No Contusion								
Unilateral contusion	1.10	0.95	1.27	0.208	1.10	0.95	1.26	0.212
Bilateral contusion	0.94	0.79	1.12	0.499	0.94	0.79	1.12	0.490
Age	0.99	0.98	0.99	0.000	0.99	0.98	0.99	0.000
ISS	0.98	0.97	0.99	0.000	0.98	0.97	0.99	0.000
Charlson Index	0.97	0.95	0.99	0.009	0.97	0.95	1.00	0.020
No adverse events								
1 or 2 adverse events	0.74	0.64	0.86	0.000	0.73	0.62	0.84	0.000
3 or more adverse events	0.52	0.41	0.65	0.000	0.52	0.42	0.66	0.000

SHR = Sub Hazard Ratio, CI =Confidence Interval, AE = Adverse Events, FC = Flail Chest, NF = Non Flail, MTC= Major Trauma Centre, TU Trauma Unit

5.3.6.6 Glasgow Outcome Score (GOS)

An ordinal logistic regression model was constructed to describe the effect of rib fracture fixation on the Glasgow outcome score. For rib fracture fixation, the proportional odds of a Glasgow outcome score of 5 (good recovery) compared to a combined score (1 to 4) was 1.61 times higher compared to the non-operative management, when all other variables are held constant (OR 1.61, 95% CI 1.06 to 2.46, p= 0.025, Table 64)

Table 64 Prediction of Glasgow Outcome Score modelled using ordinal logistic regression and MI data in all cases and the effect on early or late fixation in operated cases

Glasgow outcome Score									
Rib op vs non-operative (all cases)					**Early Vs Late fixation (in operated cases)**				
Covariate	**OR**	**95% CI**		**P**		**OR**	**95% CI**		**P**
No Rib Op					Late Fixation				
Rip Op	1.61	1.06	2.46	0.025	Early Fixation	1.00	0.62	1.63	0.994
TU					TU				
MTC	1.00	0.68	1.48	0.985	MTC	3.38	0.51	22.37	0.207
Low Energy					Low Energy				
High Energy	1.15	1.02	1.30	0.025	High Energy	0.63	0.20	1.95	0.427
< 3 rib NF					< 3 rib NF				
≥3 rib NF	1.14	1.01	1.29	0.038	≥3 rib NF	0.00	0.00	0.00	0.000
Unilateral FC	1.74	1.45	2.09	0.000	Unilateral FC	0.00	0.00	0.00	0.000
Bilateral FC	1.01	0.85	1.20	0.888	Bilateral FC	0.00	0.00	0.00	0.000
No Contusion					No Contusion				
Unilateral contusion	1.13	0.98	1.30	0.084	Unilateral contusion	1.07	0.51	2.25	0.848
Bilateral contusion	1.02	0.83	1.24	0.864	Bilateral contusion	1.38	0.45	4.20	0.574
Age	0.97	0.96	0.97	0.000	Age	0.95	0.93	0.97	0.000
ISS	0.93	0.93	0.94	0.000	ISS	0.95	0.91	0.98	0.005
CI	0.93	0.92	0.95	0.000	CI	0.88	0.75	1.04	0.141
					No pre-op ventilation				
					Pre-op ventilation	0.40	0.17	0.96	0.040
No AE					No AE				
1 or 2 AE	0.46	0.35	0.60	0.000	1 or 2 AE	0.99	0.49	2.03	0.989
3 or more AE	0.21	0.13	0.33	0.000	3 or more AE	0.16	0.03	0.95	0.043
OR = Odds Ratio, CI =Confidence Interval, AE = Adverse Events, FC = Flail Chest, NF = Non Flail, MTC = Major Trauma Centre, TU = Trauma Unit									

For unilateral flail chest and three or more non-flail rib fractures, the proportional odds of a high GOS versus the combined lower scores are 1.74 and 1.14 higher compared to less than three non flail rib fractures, given that the other variables remain constant (Table 64). For high energy injuries, the proportional odds of a high GOS (good recovery) versus the combined lower scores are 1.15 times higher compared to lower energy injuries. For one or two adverse events and three or more adverse events the proportional odds of a high GOS versus the combined lower scores are 0.46 and 0.21 times lower compared to no adverse events. For one unit of increasing age, ISS and Charlson index the proportional

odds of GOS versus the combined lower scores is 0.97, 0.93 and 0.93 times lower.

In operated patients, there was no evidence of a difference in GOS between early rib fracture fixation versus late rib fracture fixation (OR 1.00, 0.62 to 1.63, p=0.994).

For preoperative ventilation the proportional odds of a high GOS (good recovery) versus the combined lower scores was 0.40 times lower compared to no preoperative ventilation. For three or more adverse events, the proportional odds of a high GOS (good recovery) versus the combined lower scores were 0.16 times lower compared to no adverse events. Injury types was a perfect predictor of GOS in this model.

5.4 Discussion

The TARN database is the largest dataset of rib fracture patients in the UK to date. The database allows the current population demographics of rib fracture patients to be summarised overall as well as by whether someone had rib fracture fixation or non-operative management. The analysis conducted in this chapter has identified what factors predict surgical rib fracture fixation and has used several statistical models to explore the effect of rib fracture fixation on outcomes, and similarly the impact of the timing of this fixation on outcomes.

5.4.1 Patient demographics

The rib fracture population within the UK is diverse with no typical rib fracture patient defined. In general terms, however, some factors appear to be more common. For example, rib fracture patients tended to be male, over 50 years old and with fractures that were non-flail in nature. Rib fracture fixation patients, meanwhile, tended to be younger, less comorbid (Charlson less than 1), have a lower probability of survival and a higher injury severity score. The most common injury operated on was the unilateral flail chest, followed by bilateral flail chest. Higher levels of analgesia were used in rib fracture patients suggesting that patients who have significant pain are receiving rib fracture fixation; an indication that gained consensus in the Delphi survey. A variety of pain interventions were recorded as being used.

The mechanism of injury most commonly reported in all rib fracture patients was a fall from standing height followed by a vehicle accident. In the rib fixation group, high energy injuries were more likely to be fixed. In future work it may be useful to distinguish between these two groups of very different injuries as it seems that the mechanism of injury affects the type of injury sustained and subsequent surgical decision, making either directly or indirectly. In some of the regression models it was seen that a high energy injury was advantageous (reduced odds of an adverse event and reduced odds of mortality).

5.4.2 Predictors of rib fracture surgery

The biggest predictor of rib fracture fixation was the type of rib fracture injury. Patients with unilateral flail chest (OR 107.51), bilateral flail chest (OR 47.63) and more than three non-flail ribs (OR 15.62) had greater odds of receiving rib fracture fixation. This supports the conclusions of the Delphi consensus that both flail and non-flail segments of more than three adjacent ribs are selected for rib fracture fixation. If admitted to an MTC, patients had greater odds of receiving rib fracture fixation (OR 6.00).

5.4.3 Does rib fracture fixation affect outcomes?

The odds of mortality were less in rib fracture fixation patients (OR 0.14); high energy injury was also a protective factor. Contusion and type of rib fracture injury did not affect mortality, however increasing age, increasing ISS, increasing Charlson index score and increasing the number of adverse events did increase the odds of mortality. Adverse events were higher in the rib fracture population, despite controlling for multiple confounders.

It was found that length of stay was more likely to be greater than nine days in those that had rib fracture fixation when controlling for multiple factors. An increased length of stay was also seen in a recently published paper conducted in the USA from a single centre using the national trauma database.[253] This published study did not account for death as a competing risk, however. Analysis of the TARN dataset when accounting for death as a competing factor it was found that rib fracture fixation increases the incidence of being discharged from hospital when taking into account the timing of fixation. In operated patients the odds of staying in hospital longer than nine days were lower in the early fixation group

compared to those fixed after 72 hours (late fixation) conferring an advantage to early fixation in respect to this outcome.

Patients who had a rib operation had a higher odds of spending more than four days in ICU and four days intubated but had greater odds of a higher Glasgow outcome score (good recovery) than those that were not operated on. When considering the competing risk of in-hospital death, the incidence of discharge from ICU stay and from intubation was higher with a rib fracture operation compared not non-operative treatment.

In operated patients, early fixation decreased the odds of being in an ITU or of being intubated for four or more days compared to no fixation but this did not seem to alter the overall Glasgow Outcome Score.Simple univariate and binary logistic regression models that did not account for hospital death appear to be insufficient to model this complex intervention. By taking into account the risk of hospital death and the timing of fixation, outcomes that are measured as a unit of time are more appropriately modelled.

5.4.4 Strengths and Limitations

The database used for this analysis was prospectively collected and comprised multiple checks and validations before data was uploaded to the system in order to improve its accuracy. For core demographic data it was complete, however the data supplied within the chest wall data set was less complete, with multiple data fields missing for the descriptions of surgical technique. Multiple imputation (MI) addressed some issues with missing data, however large amounts of potentially useful information was unable to be used for modelling due to incompleteness. Multiple imputed data reduces bias (assuming the correct mechanism for the missing data is modelled), preserves sample size and statistical power; these advantages were lost with the propensity score analyses since MI could not be used within the analyses. Continuous outcomes were skewed and transformations were insufficient. Using categorical data was more appropriate in this scenario but it was at the expense of losing some detailed information. An alternative would have been to use non-parametric approaches.

Models included multiple covariates to reduce confounding. Data was collated from 201 hospitals within England and Wales, with 37 sites performing rib fracture fixation, thus giving a population-based general overview of rib fracture care which

has not been demonstrated before. Other studies have reported single centre data in which surgeon preference could be a significant confounder.[93, 253] Clustering for admission site is intended to account for this potential bias although this did not significantly affect the models here.

5.4.5 Work emerging

Including in-hospital death as a competing risk substantially altered the results of the analysis and, going forward, this should be included in analyses looking at length of stay. Other studies have accounted for in-hospital mortality by excluding those patients, but this may introduce bias.[253] Further research should define the intubation state and admission to ICU pre- and post-operatively, and not just the total time.

Although data was prospectively collected, the decision to undertake rib fixation was not known in each case. It is hypothesised that different indications could influence outcomes, which is not accounted for in this analysis. The difference of outcomes in respect to a patient intubated at the outset and fixed early compared to a patient experiencing intractable pain but otherwise maintaining ventilation and potentially fixed later, if they deteriorate, are anecdotally very different, but these differences have yet to be demonstrated in a big data set or as a subgroup in a trial. Early and late fixation may be a surrogate marker for indication type in this circumstance as they are almost inextricably linked. Future studies should seek to determine the indication for surgery so comparisons can be made in these sub-populations.

5.4.6 Conclusions

Rib fracture has demonstrated an improvement in mortality and has shown clinically important improvements in the incidence of being discharged from hospital, ICU stay and length of intubation, when taking into account timing of fixation and in-hospital death. The odds of a good recovery were higher in the rib fracture fixation group compared to the non-operative group when controlling for multiple other factors. Early fixation conferred an advantage compared to late fixation for these outcomes, but did not improve Glasgow Outcome Scores. Indications for surgery need to be defined in future data collection in order to be able to investigate whether outcomes are affected by indication.

Chapter 6 – A Nationwide Survey of Practice on Available Services and Current Clinical Input to the Care of Patients with Rib Fractures

6.1 - Introduction

To develop a randomised control trial that is adequately powered and relevant to current clinical practice, certain aspects need clarification. Undertaking a large clinical trial involving multiple sites and specialties in the trauma setting poses challenges on how to standardise the identification, recruitment and delivery of interventions to patients.

Current management of blunt chest trauma is based on the British Orthopaedic Standard for Trauma (BOAST) guidance, which has been developed so that all patients, no matter where they present, have access to high quality care.[16] The guidelines stipulate that chest wall injury patients should be managed within a Major Trauma Network and that there should be resuscitation protocols, agreed guidance for the management of severe chest trauma and clearly defined pathways for identification of patients who may benefit from surgical fixation. Decisions on rib fracture fixation should be multidisciplinary between specialties and the surgical team undergoing rib fracture fixation should have experience in the management of all intrathoracic trauma. Ongoing care should be facilitated by specialist physiotherapists and consultants in rehabilitation medicine. This guidance was devised by a multidisciplinary consensus meeting and published in April 2016, and is fully auditable.

It is important to understand the current provision of care to see if trial delivery is feasible within these current care models. Although standards are set we have no evidence to suggest they are being adhered to, or if services are working well. To identify those who are likely to participate in a trial it is important to understand which specialties are undertaking care as this is an injury that is often managed by different specialties dependent on service provision and expertise. It is necessary to understand the provision of specialist physiotherapy, occupational therapy and rehabilitation consultants to know whether the UK has the infrastructure to deliver comparable care in multiple potential recruitment sites.

6.1.1 Research question

Is a randomised controlled trial feasible with the current provision of rib fracture care in the UK?

6.1.2 Objectives

To describe hospital demographics, existing pathways and current clinical care of patients with rib fractures, and to establish whether clinicians would be willing to randomise patients into a surgical trial of rib fracture fixation in the future.

6.2 Method

Since the aim was to gather information about hospital protocols and management of blunt chest trauma patients, the trauma leads at each trust were considered to be the most likely individuals to have overall knowledge of hospital protocols and service management. An anonymous electronic survey was considered the most appropriate method for this type of information gathering since this approach is able to reach many participants in a short time at low cost.[254] A disadvantage of this approach, however, was the risk that, although I was attempting to gather data on their unit and protocols, there was the potential for participants to discuss their own opinions rather than stick strictly to factual data. An attempt was made to mitigate this by reiterating the need to stick to factual data in the documentation accompanying the survey. Ethical approval for the survey was granted by the Research Governance Committee of the Department of Health Sciences at the University of York.

6.2.1 Sampling frame and recruitment

The Trauma Network is a collaboration between hospitals and services that provide trauma care. Networks are often area based and are headed by a trauma network lead.[21] Trauma network services include Major Trauma Centres (MTC), Trauma Units (TU) as well as prehospital care and rehab services. Twenty-seven hospitals are dedicated MTCs, providing specialist care for multiply-injured patients, as well as quality improvement programmes for other hospitals within their network.[255] Trauma Units provide care for most other trauma patients and have systems in place should patients need to be transferred for specialist treatment at other hospitals.[21]

The sampling frame comprised the trauma leads from each trust on the basis that they would have overall knowledge of hospital protocols and service management. Identification of the trauma leads of all MTC and TUs was difficult, however, since no generic email list was available. National guidance and updates are distributed through the trauma network managers to the respective trauma leads, however, so this method of distribution was followed. The trauma network manager for Northern England was asked to forward onto the national trauma network managers a request for the email contact details of their respective local trauma leads. Emails were sent to all trauma network managers who were asked to identify their respective MTC and TU leads, or any other person they thought would be the most appropriate to complete the survey, e.g. another clinician or an operating service manager.

6.2.2 Survey content

An invitation email was sent to those identified by trauma network managers. This included an information sheet (Appendix E1) as an attachment, with the contact number and email address of the chief investigator (CI). The information sheet detailed how the data would be used and distributed and stated that individual sites and personal anonymity were protected.

6.2.2.1 Consent

The first page of the survey included a summary information sheet with a box that needed to be ticked to confirm consent. Before the respondent could start the survey questions. Consent was obtained through the survey software, since a full consenting process requiring wet ink signatures was likely to burden participants and reduce the response rate.[256]

6.2.2.2 Survey questions

The full questionnaire is available in appendix E2. The first part of the survey gathered hospital demographic data and the services available within that hospital. This information is valuable in assessing whether a trial can be delivered in certain settings. It is important to know how many sites have surgeons who undertake rib fracture fixation, and whether they have thoracic surgery services available, since this will determine how many potential sites could recruit to a trial. Questions related to whether hospitals have already undertaken steps to create their own treatment protocols and dedicated referral pathways, so as to gain insight into

whether these would need to be set up prior to undertaking an RCT comparing surgical rib fixation to non-operative management. A description of the hospital setting and distances from regional major trauma centres since if patients need to be transferred to other hospitals for the research purposes this may affect their willingness to be randomised into a trial. Only general information was sought on the location of the trust (rural or city based) and the population size in order to ensure that Trusts and responding individuals were not identifiable. These questions could be opted out of if participants wished.

The second part of the survey looked at current clinical care of patients with rib fractures, including the setting and the specialty that assumed care in different scenarios. Anecdotally, it is known that multiple specialties are involved in the delivery of rib fracture patients and this is thought to be different by region, type of hospital and local expertise and service provision. This part of the survey wanted to determine what specialties were undertaking this care in several scenarios, including those with chest drains, ventilation requirements, and whether the patients was elderly or comorbid. This would identify which specialties would need to be approached if undertaking a trial.

The third part of the questionnaire related to the willingness to take part in further research including randomising patients with rib fractures in a clinical trial assessing the effectiveness of rib fixation. Knowing whether a surgeon has equipoise and would be willing to recruit to trial is critical as this underpins any trial recruitment process.[257]

6.2.3 Survey delivery

The survey was designed in Qualtrics (Qualtrics, Provo, UT). The email addresses of the identified MTC and TU leads were entered into the survey software as well as a link to the survey sent to trauma network managers at the opening of the survey. The survey link was also made available if network managers were unwilling to share email addresses of trauma leads but were willing to deliver the survey through their internal email systems to TU and MTC leads to maximise reach and response rates. This also allowed those who felt unable to complete the questionnaire to share it with an appropriate colleague.

Prior to fielding the questionnaire, the functionality of the electronic survey and appropriateness of survey questions were tested by several clinicians. Questions

were designed to reduce burden in order to increase the response rate. There were six pages, with a maximum of five questions per page. All questions required an answer to proceed to the next screen. A ‘don’t know’ option or a free text box were available for certain questions where it was felt that they may have been difficult to answer, thus ensuring that participants could proceed through the questions. This option was only available on a few questions, however; participants were required to choose an answer to most questions. Participants were allowed to scroll back and forth through the question pages to amend any errors.

Since response rate is an important issue, a certificate to show participation in research was offered as a small non-monetary incentive. It is understood that survey burden and lack of time are the commonest reason for poor response rate to surveys in medical professionals.[258, 259] To increase response rate in this specific cohort it has been shown that surveys delivered by direct email with a reminder email increases response rate compared to a survey posted online. One or two follow ups has been shown to increase response rate however, a third does not significantly improve rate of response.[260] Although non-monetary incentives have not been shown statistically to improve response rate, it was thought that in this instance such an incentive may encourage some further responses. Participation in research is an important part of continuing professional development in medical specialties and often hard to evidence. An offer of a certificate of participation within the invitation email to enhance participants research portfolio was hoped to be an incentive to complete this survey. Monetary incentives, although shown to improve response rate are unable to be provided within the scope and budget of this project.[222] A certificate of participation was emailed on completion, as well as a copy of the report if requested.

6.2.4 Analysis

Responses analysed using SPSS (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp). Data was described descriptively using counts and percentages. Hospital demographics and specialties undertaking rib fracture care in several scenarios were compared statistically between MTCs and TUs using chi-squared tests or Fishers exact tests, as appropriate.

6.3 Results

6.3.1 Responses

The survey was open from 26th May 2017 until 19th July 2017. Reminders were sent at two and four weeks after the survey opening, generating a greater yield of participants after each reminder. Of 62 email invites a complete set of data was available for 39 responders; three were partially complete. All entries were completed by unique individuals at unique IP addresses and the respondents represented at least 32 unique trusts.

All but four of the 20 trauma networks were represented by the survey.

6.3.2 Major Trauma Centre and Trauma Unit demographics

There were eight responses from MTCs and 34 from TUs. All surveyed TUs were part of a trauma network. Seven (21%) TUs were less than 10 miles from the nearest MTC,13 (38%) were between 10 and 29 miles, nine (27%) were between 30-49 miles, three (9%) were between 49-74 miles and two (6%) were more than 75 miles. MTCs are mostly serving a population of over 750,000 (n=5, 62%) and are based in cities (n=5, 62%). Five (15%) TUs were also serving a population of over 750,000 but were mostly town (n=16, 47%) or rural (n=11, 32%) (Table 65). All nine trusts providing rib fracture surgery also had thoracic surgery provision within the same hospital. As would be expected, compared to TUs, MTCs had a significantly higher proportion of thoracic surgery services within their hospitals (five, 63% versus four, 12%, $p = 0.006$) and surgeons undertaking rib fracture surgery (seven, 88% versus two, 6%, $p < 0.0001$).

There were no significant differences between MTCs and TUs in having an emergency department protocol (seven, 88% versus 27, 79%, p=1), guidance identifying possible surgical candidates (five, 63% versus 16, 66%, p=1) or having a dedicated referral pathway (five, 63% versus 14, 41%, p=0.544). There was poor provision of specialist physiotherapy and rehabilitation medicine in both MTCs and TUs. There were no significant differences between MTC and TU in physiotherapy provision (three, 38% versus 14, 41%, p=1) however, rehabilitation medicine was provided in significantly more MTCs than TUs (five, 63% versus two, 6%, p=0.001).

Table 65 Trauma unit demographics and available services, N = frequency of responses (percentage per type of trauma unit (MTC/TU))

		Trauma Unit Type frequency (%)			
Question	**Answer**	**MTC**	**TU**	**Total (%)**	**P Value**
Does your hospital service incorporate mostly city, town or rural communities?	City	5 (62.2%)	7 (20.6%)	12 (28.5%)	P=0.058
	Town	1 (12.5%)	16 (47.1%)	17 (40.4%)	
	Rural	2 (25%)	11 (32.4%)	13 (30.9%)	
How many Trauma and Orthopaedic Surgeons do you have delivering trauma care in your hospital?	5 or less	0 (0%)	2 (5.9%)	2 (4.7%)	P<0.0001
	6-10	0 (0%)	14 (41.2%)	14 (33.3%)	
	11-15	0 (0%)	12 (35.5%)	12 (28.5%)	
	16-20	7 (87.5%)	1 (2.9%)	8 (19%)	
	More than 20	1 (12.5%)	5 (14.7%)	6 (14.2%)	
Do you have a thoracic surgery service in your hospital?	Yes	5 (62.5%)	4 (11.8%)	9 (21.4%)	P=0.006
	No	3 (37.5%)	30 (88.2%)	33 (78.6%)	
Do you have a pathway or protocol for patients presenting to your emergency department with rib fractures?	Yes	7 (87.5%)	27 (79.4%)	34 (80.9%)	P=1
	No	1 (12.5%)	6 (17.6%)	7 (16.7%)	
	Don't know	0 (0%)	1 (2.9%)	1 (2.4%)	
Has this been developed by the Trust/Hospital or disseminated from a regional trauma network?	Trust level	3 (37.5%)	18 (52.9%)	21 (61.8%)	P=0.575
	Regional level	4 (50%)	9 (26.5%)	13 (38.2%)	
	Don't know	0 (0%)	0 (0%)	0 (0%)	
Does anyone in your hospital undertake rib fracture fixation?	Yes	7 (87.5%)	2 (5.9%)	9 (21.4%)	P<0.0001
	No	1 (12.5%)	32 (94.1%)	33 (78.6%)	
	Don't know	0 (0%)	0 (0%)	0 (0%)	
Do you have a guideline or pathway for identifying which patients are suitable for rib fracture fixation?	Yes	5 (62.5%)	19 (55.9%)	24 (57.1%)	P=1
	No	3 (37.5%)	13 (38.2%)	16 (38.1%)	
	Don't know	0 (0%)	2 (5.9%)	2 (4.8%)	
Do you have a dedicated referral pathway for rib fracture fixation (either within hospital or between hospitals)?	Yes	5 (62.5%)	14 (41.2%)	19 (45.2%)	P=0.544
	No	3 (37.5%)	19 (55.9%)	22 (52.4%)	
	Don't know	0 (0%)	1 (2.9%)	1 (2.4%)	
Do you have a rehabilitation service led by a rehabilitation consultant to undertake care of patients with rib fractures?	Yes	5 (62.5%)	2 (5.9%)	7 (16.7%)	P=0.001
	No	3 (37.5%)	31 (91.2%)	34 (80.9%)	
	Don't know	0 (0%)	1 (2.9%)	1 (2.4%)	
Do you have a specialised respiratory physiotherapy service to undertake care of patients with rib fractures?	Yes	3 (37.5%)	14 (41.2%)	17 (40.4%)	P=1
	No	5 (62.5%)	17 (50%)	22 (52.4%)	
	Don't know	0 (0%)	3 (8.8%)	3 (7.1%)	

Would your centre be willing to take part or identify patients suitable for a randomised controlled trial of rib fracture fixation for FLAIL Chest?	Yes	5 (62.5%)	8 (23.5%)	13 (31%)	P=0.001
	Maybe	0 (0%)	21 (61.8%)	21 (63.6%)	
	No	1 (12.5%)	4 (11.8%)	5 (11.9%)	
	Abstained	2 (25%)	1 (2.9%)	3 (7.1%)	
Would your centre be willing to take part or identify patients suitable for a randomised controlled trial of rib fracture fixation for simple rib fractures (non-flail)?	Yes	5 (62.5%)	9 (26.5%)	14 (33.3%)	P=0.003
	Maybe	0 (0%)	21 (61.8%)	21 (50%)	
	No	1 (12.5%)	3 (8.8%)	4 (9.5%)	
	Abstained	2 (25%)	1 (2.9%)	3 (7.1%)	
MTC = Major trauma centre, TU = Trauma unit					

6.3.3 Specialties undertaking inpatient care

Multiple specialties undertake the care of rib fracture patients but differ between trusts and the levels of support required by patients (Table 66). General surgery is more likely to undertake rib fracture care when patients require no extra respiratory support in a TU (n=26, 77%) compared to an MTC (n=2, 77%); however, thoracic surgeons are most commonly reported to undertake this type of care in MTCs (n=3, 38%) compared to a TU (n=1, 3%).

In TUs, patients with chest drains are managed by general surgery (n=28, 82%) with only three respondents confirming emergency medicine, intensive care or thoracic surgery would undertake this care routinely. This differed in MTCs where thoracic surgery (n=3, 38%) shared the care more often with general surgery (n=4, 50%).

When non-invasive ventilator (NIV) support is required, the care continues predominantly under general surgery in a TU (MTC: n=3, 38% versus TC: n=14, 41%), with intensive care assuming the next biggest proportion of care (MTC: n=2, 25% versus TC: n=11, 32%). Respiratory medicine undertook the care of those with NIV in some TUs (n=4, 12%) but none in MTCs.

Table 66 Specialty who would undertake the in-patient care in the following scenarios stratified for MTC and TU. N = frequency of responses (percentage within the unit type)

	Emergency Medicine	General Surgery	Anaesthetics Intensive Care	Thoracic Surgery	Respiratory Medicine	Trauma and Orthopaedic Surgery	Elderly Medicine	Other	Total	P value
Rib fractures or flail chest requiring no support										
MTC	0 (0%)	2 (25%)	0 (0%)	3(37.5%)	1 (12.5%)	0 (0%)	0 (0%)	2 (25%)	8 (100%)	0.004
TU	2 (5.9%)	26(76.5%)	0 (0%)	1 (2.9%)	1 (2.9%)	3 (8.8%)	0 (0%)	1 (2.9%)	34 (100%)	
Rib fractures or flail chest requiring chest drain										
MTC	0 (0%)	4(50%)	0 (0%)	3 (37.5%)	0 (0%)	0 (0%)	0 (0%)	1 (12.5%)	8 (100%)	0.022
TU	1 (2.9%)	28 (82.4%)	1 (2.9%)	1(2.9%)	0 (0%)	3 (8.8%)	0 (0%)	0 (0%)	34 (100%)	
Rib fractures or flail chest requiring non-invasive ventilation										
MTC	0 (0%)	3 (37.5%)	2 (25%)	2 (25%)	0 (0%)	0 (0%)	0 (0%)	1(12.5%)	8 (100%)	0.164
TU	1 (2.9%)	14 (41.2%)	11 (32.4%)	0 (0%)	4 (11.8%)	0 (0%)	0 (0%)	4 (11.8%)	34 (100%)	
Rib fractures or flail chest requiring intubation										
MTC	0 (0%)	3 (37.5%)	3 (37.5%)	2 (25%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	8 (100%)	0.072
TU	0 (0%)	12 (35.3%)	19 (55.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	3 (8.8%)	34 (100%)	
Rib fractures or flail chest requiring no support and over 75 years old										
MTC	0 (0%)	3 (37.5%)	0 (0%)	1 (12.5%)	0 (0%)	0 (0%)	2 (25%)	2 (25%)	8 (100%)	0.416
TU	2 (5.9%)	18 (52.9%)	0 (0%)	0 (0%)	1 (2.9%)	3 (8.8%)	6 (17.9%)	4 (11.8%)	34 (100%)	

MTC = Major trauma centre, TU = Trauma unit

Intubated patients are looked after by general surgery (n=12, 35%) and intensive care (n=19, 56%) in a TU, and 9% (n=3) would transfer care to thoracic surgery at an MTC. In MTCs, meanwhile, intubated patients are cared for by general surgery (n=3, 38%), intensive care (n=3, 38%) and thoracic surgery (n=2, 25%)

In the case of patients who are over 75 years of age, generally, care would not change from those less than 75 years of age. Some respondents declared that most cases are dealt with on a case-by-case basis, with consultant discussion between teams depending of patients' frailty and clinical needs. Elderly care specialists would manage their care in an MTC (n=2, 25%) and a TU (n=6, 18%) based on their age if they required no other respiratory support.

6.3.4 Trial Participation

Overall, a reasonable proportion of centres reported that they would be willing (n=13, 31%) or potentially be willing (n=21, 50%) to take part or identify patients for an RCT of rib fracture fixation for flail chest and non-flail chest (n=14, 33% and n=21, 50 %), respectively.

6.4 Discussion

6.4.1 Hospital demographics

This survey represented responses from 16 (80%) trauma networks, the sample ratios, MTC to TU (8:34) responses are representative of the population of MTCs and TUs (27:170) in England and Wales. More than half of the TUs were within 30 miles of an MTC (n=20, 59%). If undertaking a study which required transfer of patients this is achievable in most centres based on an acceptable distance to transfer trauma patients due to safety. Patient transfers may be challenging, however, since TUs serve mostly rural areas and transfers may take longer n=11 (32%). In a UK study patients were found to be willing and found it acceptable to travel up to 1 hour and 45 minutes for better outcomes in routine secondary care.[261] Further patient and public participation work is required to establish whether patients would be willing to travel for emergency surgical intervention for rib fracture fixation in a trial setting.

6.4.2 Available services

The British Orthopaedic Association has prepared an audit standard for trauma in conjunction with the Cardiothoracic Surgery Society of Great Britain and Ireland for the management of blunt chest wall trauma, published in April 2016.[16] Specifically, the audit standard details that protocols should be in place for the resuscitation of patients with severe chest wall trauma and ongoing multidisciplinary management to include consultant led surgical, anaesthetic, pain management, physiotherapy and rehabilitation teams. The recent introduction of the audit standards may have increased the number of hospitals with dedicated rehabilitation services and relevant treatment and referral protocols; however these numbers are still low and protocols are mostly developed locally (n=21, 62%) and not as a trauma network (n=13, 38%). As part of a trial, there may be a need to develop protocols that address variations in local care pathways across trial sites, and to explore ways of ensuring comparable care across UK centres in terms of specialist physiotherapy and rehabilitation services. A consensus trial physiotherapy regime could address some variation in practice but if specialist physiotherapists are not available to deliver this care in a trial setting, transfer of all trial participants to the MTCs providing rib fracture fixation may be required. This could create a significant burden on the MTC service and may be a barrier to site set up and patient recruitment.

6.4.3 Current clinical input

This survey has highlighted the wide variety of specialities undertaking the care of patients with rib fractures. It is clear that, in TUs, general surgery is the most common specialty managing this population, even when patients require ventilator support. Rib fracture care is multidisciplinary and lead speciality clinicians are key to instigating overall management, referring for higher levels of care and seeking opinions for surgical fixation. In this survey, trauma and orthopaedics (T&O) did not lead the care of a patient with isolated chest trauma in an MTC. In general, the decision to fix rib fractures is multidisciplinary at a MTC between T&O surgery, thoracic surgery and intensive care and surgery undertaken jointly between T&O and thoracic surgery.[16] It seems counterintuitive that general surgery is the specialty that leads the majority of rib fracture patient care when they are unlikely to take part in the decision for rib fracture fixation or undertake the surgery. Nonetheless, since general surgery and intensive care specialities lead most of

the rib fracture care in trauma units any trial or national guidance should seek to engage with general surgical and intensive care societies at the outset.

6.4.4 Willingness to engage in future research

It is encouraging that some UK centres are willing to recruit to a clinical trial on rib fracture fixation. Further research in the form of a feasibility study is required to understand why the majority of clinicians were only potentially willing to participate in a trial and to understand more fully how any barriers to patient recruitment due to variation in patient pathways could be overcome. These points will be more thoroughly discussed in Chapter 7.

6.4.5 Strengths and Limitations

Although there was an adequate response from invited participants and multiple methods of circulation were used, the original sampling frame could have identified further participants. An exact number of persons that the survey reached was unknown so a response rate cannot be calculated. Thirty percent (n=8) of major trauma centres and 19% (n=32) trauma units were represented in the study, however. Identifying participants was difficult and relied on trauma network managers sharing the email addresses of their MTC and TU leads. Where this was not the case, we were then reliant on network managers being willing to send an email to their MTC and TU leads with an anonymous link. Since sample sizes were unequal, caution must also be taken in the interpretation of the Fisher exact test of association.

The survey was designed and delivered with the Checklist for Reporting Results of Internet E-Surveys (CheRRIES) in mind to provide a robust a clear report of the survey results.[262]

6.5 Conclusion

Care of rib fracture patients in England and Wales is delivered in a variety of MTCs and TUs with different care protocols, referral pathways, lead specialties and rehabilitation services. Several challenges have been highlighted in the context of preparing for a clinical trial in a rib fracture population and a feasibility trial based in the UK should be the next step to establish whether a full scale trial addressing the question of the effectiveness of rib fracture fixation is feasible.

Chapter 7 - Discussion

7.1 Overview of chapter

In this chapter, the results of the thesis are summarised and presented showing the evidence gathered for each research objective. The overall thesis aims were to inform the design and delivery of a future randomised control trial to assess the effectiveness of internal rib fracture fixation. The specific research questions were: (i) What is the current evidence for the effectiveness of rib fracture fixation? (ii) What is the current evidence for the indications and timing of rib fracture fixation? (iii) In England and Wales, what patient and injury factors predict rib fracture fixation? (iv) What are the relationships between patient factors, injury type, treatment decisions and outcome in rib fracture patients? (v) What are the indications for rib fracture fixation and at what time following injury should surgery be undertaken in an effectiveness trial? (vi) What outcomes should be measured in a rib fracture fixation effectiveness trial? (vii) Is a randomised controlled trial feasible with the current provision of rib fracture care in the UK? The strengths and limitations of the methods and the results gathered in the thesis are discussed. They frame how this thesis contributes to the literature and what impact it has on future study. Finally, the recommendation for future trial work is set out in the PICOS style.

7.2 Summary of main findings

The main findings are discussed in sections 7.2.1 to 7.2.7 and are based on the initial research questions asked as part of the study aim.

7.2.1 What is the current evidence base for the effectiveness of rib fracture fixation?

The current evidence base for effectiveness was assessed by way of a systematic review. It became apparent from the initial searches that there had been several systematic reviews published and that a synthesis of the systematic evidence was required.

Twelve systematic reviews of which six included meta-analysis concluded that rib fracture fixation in the presence of flail chest significantly improved resource use outcomes, i.e. days on invasive ventilation, total length of ICU stay and hospital

stay, despite significant statistical and clinical heterogeneity. Mortality was statistically reduced in half of the meta-analyses but this reduction was not statistically significant if RCT evidence was incorporated. Adverse events (sepsis and pneumonia), and physiological and clinical measures (chest deformity, dyspnoea and chest pain) showed some improvements in the surgical group, but there was substantial statistical heterogeneity in most of these outcomes. Spirometry showed no difference between surgically managed and non-surgically managed patients. The heterogeneity of these outcomes, as well as the error inherent in the meta-analyses reduced the overall strength of the conclusions that could be drawn from these reviews, however.

There were several issues with the conduct of some reviews, bring into question the validity of their results and conclusions. Overall, seven reviews were considered to have a low risk of bias. Of these seven reviews, three were considered low risk for data collection and study appraisal, and six for synthesis. High risk of bias in the other reviews was due to the lack of risk of bias assessment of the primary papers but also interpreting results with a high degree of confidence despite significant statistical heterogeneity. Errors were found in data extraction and meta-analysis in several reviews despite low risk of bias scores. Although there was substantial statistical and clinical heterogeneity and lack of consideration of risk of bias in many of the reviews, conclusions tended to be similar and in the direction of benefit with fixation. Few studies appear to have considered the statistical, clinical or methodological heterogeneity when applying their conclusions, however. There were also several differences noted in the included studies, with a number of studies being missed or excluded without evidence or explanation.

Due to the different injury types and timing of interventions in the primary studies, and the multiple errors and invalid conclusions within the systematic reviews a further review of primary studies was completed. This sought to provide the methodological rigour that was lacking in previous reviews but also to explore clinical and statistical heterogeneity.

Sixty-four studies were included in the review of primary studies making this the largest review to date. A further RCT was identified that had not been included in previous reviews, as well as 28 non-randomised studies and 32 case series.

Common types of surgical fixation included combined plate or strut fixation with intramedullary fixation; absorbable plates, struts and wraps were used infrequently compared to metallic fixations. In recent publications, plate fixations were more commonly used than the more historical strut style fixations. Authors who commented on their decision to fix rib fractures stated that they did not fix every rib fracture but turned flail segments into non-segmental rib fractures.[162] Several comparator interventions including packing, strapping and internal pneumatic stabilisation were described as therapies. Usual care was infrequently described but was the commonest comparator. Where described, usual care often comprised multimodal analgesics and respiratory support, including non-invasive and invasive ventilation. In general, the non-operative and surgical fixation groups were closely matched on patient factors however there were some exceptions where surgical groups had more favourable characteristics which potentially introduced selection bias.

For the primary outcome of mechanical ventilation, surgical fixation led to fewer days of mechanical ventilation than with non-operative patients, -4.03 days, 95% CI [-5.48, -2.58] (19 NRS and 3 RCT). Secondary outcomes also showed a statistically significant reduction in length of intensive care stay (-3.27 days, 95% CI [-4.78, -1.76], 17 NRS and 4 RCTs), mortality (RR 0.39, 95% CI [0.24, 0.64], 13 NRS and 4 RCTs), pneumonia (RR 0.67, 95% CI [0.48, 0.95], 11 NRS and 3 RCT) and tracheostomy (RR 0.5, 95% CI [0.38, 0.65], 6NRS and 3 RCTs) in the fixation group. Hospital length of stay was unaffected by surgical fixation. Substantial heterogeneity was seen for all outcomes except mortality and tracheostomy. The results mirror the results seen in the previous reviews however the heterogeneity quandary still needed to be addressed.

Several clinical differences where noted within the primary literature that could account for the statistical heterogeneity, including the clinical characteristics that determine need for surgery and the timing of interventions; this was further explored with a new subgroup analysis of injury type and timing of fixation discussed in section 7.2.2. Early death in hospital is, obviously, a poor outcome but since it can be measured as a short length of hospital stay it can, perversely, appear as a good outcome. Overall, how mortality was accounted for in primary studies was poorly documented and is a possible confounder.

To date, the body of evidence for surgical rib fixation is based on a mix of prospective and retrospective non-randomised studies and case series. The four published RCTs[18-20, 169] have small numbers of patients, survey surgical techniques that are used infrequently in current practice in the UK, and report outcomes that are not aligned with the newly developed COS. The stepwise IDEAL framework for development of evidence in surgery has been followed up until the publications of the RCTs. Published studies have established that rib fracture fixation is safe and the indications for surgery have expanded to now include non-segmental rib fractures. Following the initial small RCTs within the IDEAL framework[200] larger scale RCT evidence should have evolved, potentially followed by registry studies for surveillance and to assess regional variation. It is proposed that the RCT evidence was enough to convince multiple surgeons of the procedure's merits, and that surgeons have therefore gone on to produce their own evidence in case series to show the performance of their units. The quantity of evidence since Marasco et al.[20] published their RCT in 2013 goes beyond what is required to establish safety, which had been demonstrated by the NICE evidence synthesis in 2010[25] and has not advanced the effectiveness evidence base. TARN data collection has a role in monitoring surgical fixation of rib fracture but lacks the strength of randomised evidence, despite the large numbers of patients it collects data on. Following the IDEAL Framework,[200] future research should focus on assessment of the intervention via a large scale randomised control trial focussing on medium to long term patient centred outcomes.

7.2.2 What is the current evidence for the indications and timing of rib fracture fixation?

The current evidence for the indications and timing of surgical fixation were assessed by way of systematic review. A meta-analysis of several outcomes was completed, with subgroup analysis of injury type as well as timing of fixation, followed by a narrative synthesis. In general, indications for surgery and the timing of fixation are linked, since some indications are time dependent. For example 'flail chest and fails to wean from ventilation within 48 hours' implies that a delay embarking on fixation is planned and not deleterious to the outcome.

7.2.2.1 Indications and injury type

The systematic review identified a paucity of evidence for multiple non-segmental rib fractures presented independently of flail chest. Originally it was planned that a subgroup analysis could be completed for studies of flail chest compared to multiple unifocal rib fractures (MURF), however the existing studies did not have sufficient distinction between the two groups to make this possible. The second-best option was to subgroup those studies that looked at flail chest only (FC) and studies that also included patients who had unifocal rib fractures (FC+MURF).

The meta-analysis suggests there was a significant difference in length of IMV between the two subgroups ($chi^2 = 10.34$, df = 1, p = 0.001), $I^2 = 90.3\%$. The subgroup analysis did not meaningfully alter within subgroup heterogeneity, which persisted in all outcomes. The results suggest that injury type subgrouping influences outcomes and should be considered for stratified randomisation. This conclusion is based on studies that are not randomised, however, and there could be other study characteristics that introduce confounding factors.

Definitive indications for rib fracture fixation were difficult to extract and synthesise from the published literature. The most common indication was a flail chest only but often an injury description was also qualified by clinical parameter. For example, flail chest with respiratory failure or multiple non-segmental rib fractures with chest deformity. Multiple non-segmental rib fractures were only advocated as an indication without an additional clinical parameter in four studies, suggesting that this injury alone is not usually enough to justify rib fixation and must be qualified by another clinical parameter such as intractable pain. Several indications were described independent of an injury type, these included operation for another thoracic operation (retreat indication) or irritation/intrusion of underlying organs.

Definitions of injury type, respiratory compromise, failure to wean and chest deformity were poorly described and not consistent between studies. The distinction between flail chest (segmental fractures with paradoxical motion) and flail segment (a segmental fracture without paradoxical motion) was inconsistently applied due to the lack of description of the injuries by the studies. Since most of the evidence within the synthesis was gathered from retrospective studies, the determination of what factors originally prompted the decision to operate was rarely reported. The injuries were often described as a radiological diagnosis which did not take into account the clinical examination aspect of determining

paradoxical movement which is thought to be crucial in the decision to operate. This created difficulty in determining whether the intervention was effective since the indications for surgery may not have been comparable between studies. In a future controlled study, indications should be clarified with a specific and reproducible eligibility criterion that can be consistently applied with little ambiguity. The narrative synthesis was further used to formulate a Delphi questionnaire section 7.2.3.

7.2.2.2 Timing of fixation

Timing of fixation varied considerably in the systematic review of primary studies, hence it was difficult to compare studies through meta-analysis and a subgroup analysis needed to be employed.

Studies were sub-grouped into those that operated before and after 72 hours; this standard was set by a consensus panel in 2016.[5] Studies that on average operated earlier (before 72 hours) had a reduced total length of mechanical ventilation (subgroup difference = 84.8%, p =0.01), although risk of mortality and pneumonia, as well as length of ICU stay, did not have significant subgroup differences in this analysis. Substantial or considerable heterogeneity was seen in all outcomes except mortality and, for most outcomes, there was still heterogeneity in the individual subgroups.

Overall, timing of fixation should be considered as part of a subgroup analysis or as part of pre-randomisation stratification since the subgroups for the primary outcome had statistically significant differences. The narrative results from the consideration of timing of fixation were used as the basis of a Delphi consensus questionnaire in section 7.2.3.

7.2.3 What are the timing and indications for rib fracture fixation in an effectiveness trial?

The timing and indications for a rib fracture fixation trial for effectiveness were determined by an international Delphi consensus exercise. A three round Delphi consensus was completed anonymously online by a final group of 16 clinicians from a variety of specialties.

7.2.3.1 Indications

Thirty indication items from the systematic review and eight newly suggested indication items were rated in a minimum of two rounds. Twenty indications gained consensus. Flail chest (flail segment with paradoxical movement) was a favoured indication. Flail chest injury with the additional caveat of respiratory compromise or intubation, failing to wean from a ventilator or experiencing intractable pain all strengthened the consensus. Flail segments (no paradoxical movement), concomitant pulmonary contusions and traumatic brain injury did not gain consensus. Multiple non-segmental rib fractures did not gain consensus when categorised by injury alone, but did in combination with intractable pain, respiratory compromise and failure to wean.

It appears the presence of paradoxical motion or an element of respiratory compromise or intractable pain appears to be the driver of surgical rib fracture fixation rather than the radiological type of rib fracture. This suggests that the qualification of these secondary parameters should be specified in the eligibility criteria of future trials as they are directly derived from consensus-based work

7.2.3.2 Timing

Twenty-eight items related to timing of rib fracture fixation were whittled down to seven items that gained consensus after three rounds. The Delphi exercise highlighted that there is a lack of consensus amongst clinicians on the timing of surgical fixation. Consensus was achieved on only one statement ‘the earliest a patient should be considered for fixation should be between 24 and 48 hours’. How late patients should have fixation, or whether patients should have a period weaning from ventilation prior to fixation, gained no consensus at any point. This suggests that deciding when a patient should be offered surgery is based on multiple factors such as different injuries or indications. Certain injuries could be perceived to be more urgent and thus needing surgical fixation earlier, making it difficult to reach agreements on particular statements irrespective of injury or indication. This suggests that strict trial protocols adhering to specific timings for surgery are unlikely to gain favour with surgeons since there is such a wide variation in practice or other determining factors and that a more pragmatic approach may need to be taken.

It was generally accepted by consensus that patients should be referred, transferred and operated on within 48 hours of a decision to treat surgically and therefore this should be the benchmark for time to operating in a trial scenario.

7.2.4 What outcomes should be measured in a rib fracture fixation effectiveness trial?

A core outcome set was derived by way of a Delphi consensus developed following the methods described by the COMET Group. Outcomes were identified by systematic review and entered into an anonymous questionnaire. The systematic review of reviews identified six meta-analyses looking at 11 separate outcomes (one mortality outcome, four resource use, three adverse events, and three clinical or physiological outcomes). The primary evidence synthesis identified 65 different outcomes that were measured in 64 studies. The array of outcomes reported at multiple time periods that are unable to be synthesised in meta-analysis highlighted the need for a core outcome set.

A three round Delphi consensus exercise was undertaken by a multi-stakeholder panel including patients, clinicians and allied health professionals, selecting 23 outcomes that are now incorporated into a core outcome set. Recent outcome sets have ranged from 13 outcomes[235] in prostate cancer to 29 outcomes in childhood asthma.[109] This core outcome set differed from the most common measured outcomes in previous evidence syntheses. The most common outcome domains accepted in the core outcome set were adverse events (eight outcomes), physiological or clinical (five outcomes), mortality (three outcomes) and life impact (six outcomes). Only one resource use outcome gained consensus despite a multitude of resource use outcomes being reported in more than 30 of the primary studies and in all systematic reviews. Resource use outcomes were rated poorly across all stakeholder panels. Consensus was achieved with little disparity between clinicians, AHPs and patients. Adverse outcomes were rated more highly by patients than clinicians and return to work was rated more highly to clinicians than patients but consensus was nonetheless achieved on these outcomes.

Only four clinical or physiological outcomes gained consensus, relating to a person’s feeling of breathlessness or ability to clear secretions, both of which are subjective, as well as ventilation and lung function, which can be specifically measured. Measurement of all 23 outcomes is achievable in future studies since only four outcomes are potentially patient reported or clinically measured and

generally the burden of these measures is likely to be low. Future studies should adopt the core outcome set although further work is required to identify specific outcome measurement instruments.

7.2.5 What is the relationship between patient factors, injury type, treatment decisions and outcomes in rib fracture patients?

The Trauma Audit Research Network chest wall injury dataset was explored to describe the patient factors, injury factors and treatment decisions that affect outcomes of rib fracture patients. These are described in the following sections 7.2.5.1 to 7.2.5.4.

7.2.5.1 Patient factors

The TARN chest wall dataset of 17793 patients between April 2016 and May 2017 presents a broad demographic of patients who have sustained rib fractures. Although there was no one archetypal rib fracture patient, there does appear to be some trends in the characteristics of patients. Female patients were characteristically over 75 years of age; in contrast, their male counterparts had multi-modal peaks not present in the female population. A peak in the younger working age male and middle age was likely to be due to higher risk-taking behaviours. This is a concern as this group are generally the economically productive population and reducing morbidity in this age group could be of socioeconomic importance. In the same vein, it may also be of socioeconomic importance to maintain the independence of elderly population since social care is increasingly expensive and difficult to deliver.[263]

Those that go on to rib fracture fixation were generally male, had higher injury severity scores and were less comorbid, compared to their non-operative cohort. The most commonly-operated age group was those between 50 and 75 years old. This particular age group is likely to have some physiological decompensation and, in terms of mortality, potentially has the most to gain from restoring chest wall biomechanics. It is hypothesised that those under 50 years old have a greater physiological reserve to overcome the injury and therefore the potential gains by operating are reduced. In the over-75 age category other factors may influence the decision to operate including; medical comorbidities that would preclude an operation being in the best interest of the patient and the notion of being ‘too sick’ to operate on the basis that the surgery would be unlikely to change outcomes.

7.2.5.2 Injury type

The most common overall mechanism of injury was a low energy fall from standing height (two metres). Despite this being the most common cause of injury, these fractures were fixed less often than those resulting from higher energy injuries such vehicle incidents (including pedestrians and road traffic collisions) and falls from over two metres. No patients with fractures resulting from penetrating injuries (e.g. stabbings or gunshot wounds) had a rib fracture fixation operation.

Injury severity scores were significantly higher in the rib fixation group (median 21, IQR 16 to 34) compared to the non-operative group (median 13, IQR 9 to 21), suggesting that the severely injured, who were normally admitted to MTCs, were more likely to receive fixation.

The median predicted probability of survival, measured as the PS14 score, was 96.7% across all patients, however the data was skewed, with a tendency for most patients to have a high probability of survival. Surgical rib fracture fixation patients, on average, had a lower predicted probability of survival score then their non-surgical counterparts.

Most patients presented with three or more non-flail rib fractures 41.2% (n=6854), followed by less than three non-flail rib fractures 25.8% (n=4299). One third of patients had a flail injury; unilateral flail chest 16.9% (n= 2809) and bilateral flail chest, or complex rib fracture pattern 16.1% (n= 2676).

Overall, the most common rib fracture injury was the non-flail fractures that were rarely operated on in this dataset, the most commonly-operated patients had either a unilateral flail chest (61.3%) or a bilateral flail chest (22.7%).

7.2.5.3 Surgical management

Since 2016, the most common rib fracture operation in England and Wales was plate fixation using specifically designed plates; intramedullary fixation was used infrequently. Systematic review evidence corroborates these findings, citing that the most common type of fixation was plate fixation, followed by strut fixation and intramedullary fixation. Almost all patients who had a rib operation also had a thoracic operation, with most being conducted via the video assisted thoroscopic approach. The average number of ribs fixed was 4.31 per operation. On average, the TARN data indicates that ribs were surgically fixed at a median of 2.70 days

(65 hours, IQR 1.42 to 5.19 days), and that there was a tendency to operate early on patients.

TARN data also shows that rib fracture fixation patients were receiving higher levels of analgesics than their non-operative counterparts, including ketamine (8.7%), local anaesthetic blockade (4%) paravertebral blocks (5.0%) and epidural blocks (8.7%) see 7.2.5.4. This suggests that either high analgesic requirements correspond with an indication to fix rib fractures surgically or that rib fracture fixation was more painful. From the dataset it is unknown whether the higher levels of analgesia were given pre or post op.

Multiple specialties undertook the inpatient care of rib fracture patients: trauma and orthopaedic surgery (26%), cardiothoracic surgery (28.8%) and the major trauma service (14.4%) were the admitting specialty of the majority of the rib fracture fixation patients. It is unclear from this data whether the patients who were likely to need fixation were referred initially to the correct surgical specialty, or whether those admitted to specialist surgeons were more likely to get an operation than those admitted under non-surgical specialties. Only 9.2% of patients who had rib fracture fixation were initially admitted to TUs, suggesting that patients who required fixation were generally presenting first to MTCs. Conversely, it may be that only those patients attending MTC were offered surgery and those presenting to TUs were disadvantaged.

TARN also shows us that while MTCs and TUs shared the burden of care of rib fracture patients equally, rib fracture fixation patients were generally admitted or transferred to MTCs. Transfers between hospitals was common for rib fracture patients with 40% having a transfer in or out of an MTC.

7.2.5.4 Non-operative management

The majority of the patients within the TARN database were managed non-operatively (97.6%); the most common injuries were uni-focal fractures (68.3%) and 81.1% did not have any pulmonary contusion. A greater proportion of non-operative patients were older than rib fracture fixation patients and their mechanism of injury tended to be a low energy fall. This was a feature in several retrospective studies in the systematic review, making the comparison of operative and non-operative groups potentially biased towards the operative groups.[19, 71, 74, 78, 184] Orthopaedic surgery (18.9%), general surgery (18.0%) and emergency

medicine (16.8%) were the most common admitting specialties for non-operative patients.

A range of treatments were available to non-operative patients, including multimodal analgesia and supportive ventilation. In general, non-operative patients received simpler analgesic methods such as Entonox, intravenous paracetamol and opioids and patient controlled analgesia (PCA). A smaller proportion of patients received ketamine (2.7%), local anaesthetic blockade (1.5%), paravertebral blocks (0.1%) and epidural blocks (1.6%). A greater proportion of non-operative patients received local anaesthetic patches compared to operative patients. Anecdotally, this may be due to reluctance to apply these patches near an operative site.

7.2.5.5 Outcomes

A binary logistic model was used to predict mortality in hospital following a rib fracture, accounting for multiple identified confounders such as patient age and comorbidity, type of rib fracture, injury severity and adverse events. While the odds of mortality were lower in patients who had rib fracture fixation (OR 0.14, 95% CI 0.06 to 0.31, $p<0.0001$), the odds of developing an adverse event were higher in this group (OR 1.89, 95% CI 1.28 to 2.80, $p=0.001$).

Outcomes describing length of stay have multiple confounding factors. These outcomes were compared between the rib fracture fixation population and the non-operative population using sophisticated statistical modelling that was able to account for death in hospital and timing of intervention. Accounting for death as a competing factor to hospital discharge, rib fracture fixation was found to increase the incidence of being discharged from hospital when taking into account the timing of intervention (SHR 1.16, 95% CI 1.05 to 1.29, $p=0.005$). When considering the competing risk of in-hospital death, both the incidence of discharge from ICU stay (SHR 1.38, 95% CI 1.19 to 1.60, $p<0.000$) and from intubation (SHR 2.01, 95% CI 1.58 to 2.54, $p<0.0001$) was higher with a rib fracture operation compared to non-operative treatment.

In operated patients, the odds of staying in hospital longer than nine days was lower in the early fixation group compared to those fixed after 72 hours (late fixation), conferring a potential advantage of early fixation in respect to this outcome (0.14, 95%CI 0.05 to 0.34, $p<0.0001$). Early fixation also decreased the

odds of being in an ITU (OR 0.38, 95%CI 1.19 to 1.60, p<0.0001) or intubated (OR 0.28, 95%CI 0.13 to 0.60, p=0.001), for more than four days, compared to no fixation, although it did not seem to alter the overall Glasgow Outcome Score (OR 1.00, 0.62 to 1.63, p=0.994).

7.2.6 In England and Wales, what patient and injury factors predict rib fracture fixation?

Independent factors that predicted rib fracture fixation were the type of injury, being admitted to an MTC (OR 6.00), high energy injuries (OR 1.45), increasing ISS (OR 1.02), increasing age (OR 1.02) and degree of contusion (unilateral OR 2.16, bilateral contusion OR 1.87). The strongest predictor was a unilateral flail chest (OR 107), followed by bilateral flail or concomitant complex or sternal fractures (OR 47) suggesting that, in the England and Wales, injury type heavily influences the decision to fix fractures surgically. The comorbidity score was a poor predictor of rib fracture fixation (OR 1.01, 95% CI 0.97 to 1.03, p=0.655).

Injury description is something to focus on in a future trial since this appears to be the biggest predictor of rib fracture fixation, and statistically contributes to the length of hospital stay, ICU stay and intubation length outcomes in regression analysis.

7.2.7 Is a randomised controlled trial feasible with the current provision of rib fracture care in the UK?

To assess whether a randomised control trial was feasible in the UK, a survey was undertaken to assess current provision and equipoise for a trial. There were 39 participants from 32 unique hospital trusts.

The survey of major trauma centres and trauma units in England and Wales revealed that 21.4% of centres offer rib fracture fixation (MTC 87.5% versus TU 5.8%). Most had an A+E protocol for patients with rib fractures that was generally developed at trust level. Just over half of hospitals had a guideline for identifying which patients were suitable for rib fracture fixation. Only 45.2% of hospitals were aware of dedicated referral pathways for rib fracture fixation in their hospital. Even though BOAST[16] recommends that those undertaking rib fracture fixation surgery should be able to undertake intrathoracic procedures, only 62.5% of the surveyed MTCs had a thoracic surgery service, despite the high percentage of MTCs providing rib fracture fixation surgery.

A variety of scenarios were presented and personnel were asked to indicate which specialties would normally be the admitting specialty. The greatest proportion of patients were said to be admitted under general surgery, intensive care, thoracic surgery and respiratory medicine. Trauma and orthopaedic surgery were the admitting specialty in two situations: those requiring no support (8.8%) or requiring no support and over 75 years old (8.8%).

While BOAST[16] recommends that chest wall injury services should provide specialist chest physiotherapy and rehabilitation services, services were still falling short of this ideal, with just 16.7% of hospitals having access to specialist rehabilitation and 40.4% having access to specialist physiotherapy. This has the potential to affect the delivery of future trials; especially if intervention and comparators are unable to receive equal rehabilitative care. Confounding factors may be introduced if randomised patients are transferred to an MTC for surgery, where physiotherapy is more readily available, whereas patients randomised to non-surgical management and remaining in a TU may not receive specialist physiotherapy. Potential trial sites would need to standardise care of patients and this may require training and the development of rehabilitative services. A consensus trial physiotherapy regime could address some variation in practice, and indeed this has previously been done in other orthopaedic surgery trials, such as the UKFROST, which is a three-arm trial, with one being structured physiotherapy.[264] If specialist physiotherapists are not available to deliver this care in a trial setting, it may be necessary to transfer all trial participants to the MTCs, but this could create significant burdens on the MTC service and may be a barrier to site set up and patient recruitment. Alternatively, a more pragmatic approach may be adopted to conservative management in which non-specialist physiotherapists deliver this care, on the basis that this is pragmatically closer to current provision.

Thirteen centres in the UK are enthusiastic about recruiting to a surgical fixation trial but a large proportion of centres remain tentative about participation in such a trial. This may be due to a lack of detail about the proposed trial design with clinicians being unwilling to commit without prospective information. Further research in the form of a feasibility study is required to understand why the majority of clinicians were only potentially willing to participate in a trial and to understand more fully how any barriers to patient recruitment due to variation in patient pathways could be overcome.

Respondents from only nine centres undertaking rib fracture fixation participated in the survey. The TARN database identified 37 separate sites, but only 17 sites performed more than ten procedures within a 14-month period. Multiple centres are now offering rib fracture fixation showing that there is the potential to recruit from a range of sites within England and Wales that will make the results of a trial generalisable.

7.3 Strengths and Limitations

This section presents the strengths and weaknesses of the thesis overall so that its results can be interpreted in context; a more detailed critique of the methods is presented within the relevant chapters.

The strength of this thesis lies in its methodological rigour since it follows strict formalised guidance on the conduct of systematic reviews. The systematic review was published on PROSPERO and protocol deviations were clearly reported for transparency.[38] The PRISMA reporting guidelines were followed.[45]

Moderate to substantial clinical and statistical heterogeneity was found within the systematic review of reviews (chapter 2). This was not appropriately picked up in the individual reviews, highlighting the weaknesses of the original reviews. The synthesis of primary evidence was improved and extended by having a prior registered protocol and updated searches of multiple databases for published and unpublished data. In an attempt to limit clinical heterogeneity in the review of primary studies (chapter 3), a subgroup analysis stratifying for injury type and timing of surgery was applied. This review synthesised 64 studies, including one newly identified RCT. This is the largest synthesis on this topic and was based on robust searches, unbiased selection methods and quality assessment of studies.

A potential weakness of the systematic research evidence is the difficulty of separating multiple unifocal rib fractures and flail chest patients as the injury patterns were not described in the primary evidence. Meta-analysis of the length of stay outcomes using mean difference was undertaken in six previous systematic reviews and this was also the metric used in this meta-analysis. The analysis of the TARN data highlighted that these outcomes were heavily skewed, which was not apparent from published primary research, which commonly presented the results as a mean. Following the TARN analysis, further careful inspection of the

case series data showed that those studies that presented medians and quartile ranges also had negatively skewed data. While it is possible that the means in the RCT and non-randomised studies were not skewed, and that their data was appropriately presented as means but, in light of the TARN data, this does bring into question the method of using mean difference in the meta-analysis. No sensitivity analyses were completed but subgroup analyses tried to tackle some between study differences. Although it is recognised that subgroup analyses do have limitations, these were pre-specified and the analyses did show a clinically plausible direction of results. Future work should look to power their studies to complete subgroup analyses on early and late fixation and differences in injury patterns, since these factors have been shown to affect outcomes.

An international multi-stakeholder Delphi exercise developed a core outcome set by consensus. Strict formalised guidance on the process of developing core outcome sets was followed,[265] and both the COMET databases and the Delphi consensus protocol were formally published.[206] Great care was taken in the recruitment of multiple expert stakeholder groups from multiple clinical specialties, the international community and patient groups. This diverse group of participants enriched the already well-developed list of items systematically gathered from the published literature; and adding these un-primed responses prior to scoring the Delphi survey reduced researcher bias. From a relatively small community of eligible participants, 65 participants started and a respectable 23 participants completed all three rounds of the Delphi survey. Small Delphi consensus panels are commonplace, especially in areas in which treatment experience and clinical expertise is rare. It is recognised, however, that a greater number of participants from all stakeholder groups would increase confidence in the findings.

The ‘in-hospital’ outcomes such as length of stay, length of mechanical ventilation and ICU stay were thought to be of importance as they had been measured in multiple studies. These in-hospital outcomes did not make it through to the final core outcome set, however, calling into question the relevance to the actual priorities of patients, AHPs and clinicians of the outcomes being measured in current case series, RCTs and by TARN.

The Delphi survey suffered high attrition of all stakeholder groups, meaning that by the last round the patient panel had shrunk to just two participants. Although this meant that the consensus was eventually unbalanced in favour of the relatively

larger clinician group, this approach is still preferable to a biased clinician-only consensus. Due to the small numbers in the stakeholder panels, the overall scores were pooled so that items were not penalised by small panels. This meant that the autotomy of the stakeholder groups was lost for the eventual consensus definition but feedback from each panel was still able to be independently deliberated.

Analysis of the TARN data followed a pre-specified analysis plan and the RECORD reporting guidelines[266]. The Trauma Audit and Research Network is a non-profit organisation based at the University of Manchester and is directed by a collection of researchers, data handlers and clinicians. Each hospital is responsible for submission of its own patient data, which then undergoes strict validation before submission to the database. Research derived from this database benefits from large case numbers with accurate and complete data on important variables. In predicting what factors influence rib fracture fixation, multiple factors were entered into this analysis based on clinical judgement. Completeness of data was important, therefore multiple imputation plugged the relatively small amounts of incomplete data. A complex competing risk model, combined with time varying covariate treatment analysis, ensured that length of stay outcomes were not influenced by the death of a patient in hospital or by the timing of the treatment. Overall, this analysis improves upon other similar research,[75] both in the number of cases but also in the complexity of the modelling to reduce confounders.

While, in general, data completeness of the important variables in the TARN data is a strength of this research, admitting specialty, types of analgesia used and the specifics of each rib operation were not able to be used in the analysis due to incompleteness. Care was taken to identify and address confounders within the TARN data. Other injuries were accounted for by the injury severity score, however further derivation by either abbreviated injury score (based on anatomical region) or by presence of head injury or pelvic injury may have given greater insight as to the outcomes with these additional injury types.

Intubation and intensive care time prior to a rib operation were not distinguishable from the total time of intubation and intensive care. It was therefore difficult to distinguish whether the outcomes of intubation time or ICU stay were directly due to rib fixation or whether they were part of the general clinical course. As with all retrospective studies, it is difficult to disentangle what specific clinical vignette led

to the decision to offer surgery. With no insight as to the particulars of the decision to operate, conclusions can only be interpreted in a general sense and not tied to a specific indication. This highlights the importance of predetermined indications informing an eligibility criteria for controlled trials, and such indications may need to be stratified in prospective cohort studies so outcomes can be monitored for different indications.

Although the small sample size in the survey limits the conclusions that can be drawn from it, 16 out of the 20 trauma networks were represented, and thus the survey can be said to give a good general feeling of the current UK practice and available services if a trial is to be undertaken.

7.4 Contribution to the literature

Owing to the differing methods used in the approach to the thesis, its contribution to the literature is considerable. Future trial work should consider the recommendations from this thesis in line with other ongoing projects.

Prognostic models have been developed and are helping to identify patients who are likely to develop complications as a result of their injuries. [267] The assessment of the effectiveness of these prognostic models, which are based on age, number of rib fractures, oxygen saturations, chronic lung disease and pre-injury anticoagulants is currently ongoing.[268] Analysis of the TARN data suggests that admission to an MTC, the presence of adverse events, ISS and Charlson Index also increases the risk of prolonged hospital stay and should also be considered in addition to the already identified parameters for future prognostic modelling.

Clinical practice guidelines have been developed by consensus in the USA and included 14 surgeons.[5] This work was very detailed in respect to the specifics of the operative technique but did not go into the nuances of specific indications or the timing of fixation specifically for research purposes. Building on the three broad indications that gained consensus in the US study,[5] this thesis describes a consensus of 20 specific indications for rib fracture fixation derived from 16 international participants from a range of specialties. A search of the literature did not identify a consensus on timing of fixation and this is clearly needed for the future development of trials. Another consensus survey, published in February 2018 (during round two of the Delphi consensus for this thesis),[269] looked

specifically at indications for surgical fixation in the non-flail chest, however. The authors of that study presented complex scenarios to determine surgeon equipoise in certain clinical situations. Their conclusions state that the cut-off for equipoise appeared to be 'a patient 21-79 years old with no or mild traumatic brain injury, two abnormal pulmonary parameters regardless of fracture location'. This concurs with the findings from the Delphi exercise conducted here, since this also identified that injury pattern was less important than the disruption of the clinical parameters associated with the injury.

Research into the impact of surgical rib fracture fixation from the patient perspective is uncomfortably rare. Qualitative interviews have identified that feelings of breathlessness, being unable to cough, the chronicity of pain and functional limitations affected patients' quality of life.[270] This very much echoes the outcomes that were accepted into the core outcome set, and validates that the outcomes suggested are in line with the patient perspective, even though few patients completed the Delphi rounds. Adoption of a core outcome set in future trials could reduce research waste since studies could be compared, contrasted and ultimately synthesised in meta-analysis.

7.5 Work emerging and recommendations for trial

This section will outline recommendations for future trials arising as a direct result of the thesis findings. These will be presented in the PICOS format.

7.5.1 Patient

Specific patient characteristics were identified from the TARN data and systematic review evidence and were further defined by Delphi consensus.

7.5.1.1 Eligibility

The effectiveness of rib fracture fixation compared to non-operative management needs to be established in the adult population before extending the indications into the relatively small paediatric population. A future trial should focus on the adult population and specifically look to include the elderly. Rib fractures are prevalent in the elderly, who commonly undergo fixation since they potentially have the most to gain. Chronic lung disease was considered to be an indication for rib fracture fixation in flail chest patients and should not preclude entry into a trial. Similarly, pulmonary contusion should not be considered a contraindication to

surgical rib fixation and therefore entry into a trial.[5] Treatment, which could include invasive ventilation, surgical fixation and invasive anaesthetic techniques, must be in the best interest of the patient. Instances where treatment may be inappropriate could include the multi-comorbid patient with little quality of life or severe traumatic brain injury. This has been qualified by a survey of the chest wall injury society members as moderate to severe brain injury.[269]

Inclusion criteria

- Adult patients, 16 years or older
- Injury type

1. Any flail chest (described as paradoxical movement in more than two adjacent bifocal rib fractures)

or

2. Multiple rib fractures (more than two adjacent unifocal rib fractures) or flail segment (more than two segmental rib fractures no paradoxical movement) with one of the following:
   - Paradoxical movement
   - Respiratory compromise (to be defined)
   - Invasive ventilation
   - Intractable pain despite regional and epidural anaesthesia (to be defined)
   - Failure to wean from ventilation within 48 hours (to be defined)
   - Chest deformity (to be defined)
   - Requiring tracheostomy (to be defined)
   - Bilateral multiple rib fractures
   - Concomitant sternal fracture

or

3. Any rib fracture with intrusion into the underlying lung

Exclusion criteria

1. Not expected to survive 24 hours
2. Moderate or severe brain injury (to be defined)

7.5.1.2 Stratification

If multiple indications for surgery are to be included, then it may be important to stratify patients by their indication for surgery as well as injury type. This is to account for two differing scenarios:

1. the patient who is already in respiratory extremis and already subject to increased risks of associated with invasive ventilation
2. the patient not in respiratory extremis but experiencing pain and deformity and for whom surgery is used to prevent deterioration

It is important to recognise the subgroup differences between allocated groups since if subgroups are unbalanced this could lead to differences in outcome for specific prognostic factors. Completing a subgroup analysis of these indications post random allocation is less favourable as this may lack power due to small sample sizes or interactions. Stratifying for these indications prior to randomisation reduces the confounders at baseline compared to by chance in simple randomisation.[271] This means that outcome differences are more likely to be due to differences in treatment rather than baseline characteristics, which is important in small samples.[272] Stratifying for critical features that are potentially prognostic reduces the type I errors, especially in small trials <400 patients.[273] Stratification increases the efficiency of trials since it is not necessary to detect differences between groups with such high power, therefore reducing the sample sizes needed to detect differences between treatments.[274]

It is important to choose strata carefully, however, since a greater number of strata increases the likelihood of unbalancing the block sizes, which defeats the purpose of stratification. Although there is no guidance as to how many strata should be used, in general more than three or four strata makes it difficult to fill allocation groups, potentially making the groups unbalanced, especially in smaller trials.[274] The balancing of strata could be explored within a feasibility study and would give some idea of the balance likely to be achieved within the blocks.

Other important stratifications derived from the TARN data include the difference between non-segmental rib fractures, flail segment and flail chest, injury severity score and age.

There needs to be a stratification strategy for chest injury type as this subgroup was found to affect outcomes; also, chest injury type was the strongest predictor

within the regression modelling of rib fracture fixation and could be a confounding factor. Paradoxical movement is a key factor in the decision to operate and therefore this distinction should be made in the stratification strategy. The distinction should be between non-segmental rib fractures, flail segment with no paradoxical movement and flail chest with paradoxical movement.

In other publications derived from TARN results are dichotomised according to an injury severity score above or below 15. This almost dichotomises the TARN population equally with 53% being below ISS15 and 47% being above ISS15, meaning that allocation is likely to be equal between groups. ISS was a significant predictor of mortality, adverse events, length of stay, length of ICU stay, length of intubation as well as Glasgow outcome score so would be an ideal stratum.

Age was a strong predictor of outcomes and should be used to stratify patients' pre-randomisation. Age groups should reflect the current rib fracture population and to reduce the number of strata it would be sensible to allocate age groups for 16 to 49 years, 50 to 74 years and 75 years and older. This covers the physiologically young, the physiologically old as well as the age group in between.

Accounting for treatment site as a potential confounder, the TARN data did not identify differences in outcomes. Clustering on individual treatment sites is therefore not a priority for pre-randomisation stratification.

Table 67 presents the stratification in a hierarchical order with 48 separate stratification groupings. This would need to be tested in feasibility studies to see if there would be enough patients to balance the groupings.

An equally valid alternative would be the use of minimisation, which ensures that groups are allocated equally by pre-specified factors [275]. Allocation is made to the group in which the patient would minimise any differences in these factors.

Table 67 Stratification - Treatment assignment will be stratified on the basis of the following criteria

Independent of injury type all other patients that include those with intractable pain, deformity, intrusion into underlying organs and for whom surgery is used to prevent deterioration	Flail chest	16 to 49 years	ISS>15
			ISS<15
		50 to 74 years	ISS>15
			ISS<15
		75 years +	ISS>15
			ISS<15
	Flail segment	16 to 49 years	ISS>15
			ISS<15
		50 to 74 years	ISS>15
			ISS<15
		75 years +	ISS>15
			ISS<15
	Unifocal rib fractures	16 to 49 years	ISS>15
			ISS<15
		50 to 74 years	ISS>15
			ISS<15
		75 years +	ISS>15
			ISS<15
Independent of injury type a patient with invasive ventilation, respiratory failure, failure to wean or tracheostomy.	Flail chest	16 to 49 years	ISS>15
			ISS<15
		50 to 74 years	ISS>15
			ISS<15
		75 years +	ISS>15
			ISS<15
	Flail segment	16 to 49 years	ISS>15
			ISS<15
		50 to 74 years	ISS>15
			ISS<15
		75 years +	ISS>15
			ISS<15
	Unifocal rib fractures	16 to 49 years	ISS>15
			ISS<15
		50 to 74 years	ISS>15
			ISS<15
		75 years +	ISS>15
			ISS<15

7.5.2 Intervention

The surgical fixation should be undertaken in a hospital that performs the procedure routinely, has a thoracic surgery service and intensive care facilities. TARN identified 201 sites undertaking the care of rib fracture patients, with 37 site undertaking rib fracture fixations and 17 performing more than 10 rib fixations in a 14-month period (91% were MTCs).

7.5.2.1 Fixation type

The commonest fixation in the UK is plate fixation, which is often supplemented with intramedullary fixation. Ideally, an efficacy trial would have exactly the same intervention and surgical fixations would be limited to the same type of plate or intramedullary fixation for the whole study population. In the real-world, however, retraining surgeons to use a specific device is likely to deter surgeons from taking part, especially with the learning curve required to master a new technique. In this sense, since the trial is aiming to provide generalisable results from multiple centres, a more pragmatic approach should be adopted. This has been successful in other surgical trials such as PROPHER, in which the type of surgical intervention was not specified.[276] The number of ribs to be fixed and whether segmental fractures should be converted into non-segmental rib fracture by only fixing one of the fractures should also be left to the surgeon's discretion. This information will still be gathered as an exploratory outcome, however, as it may be useful in defining future research. A standardised and reproducible classification tool to help describe the location and severity of rib fractures has been developed and is being used in the SMuRFS trial.[147] No publications of this tool are currently available and its validity and applicability to the targeted outcome measures is unclear; nonetheless, it gives a standardised way to describe injuries, which is invaluable.

7.5.2.2 Timing of intervention

The Delphi consensus concurred that the earliest that surgical fixation should take place in a trial is between 24 to 48 hours. Randomisation of patients should therefore only be taken after 24 hours. This is likely to exclude patients who potentially would not survive within 24 hours and for whom rib fracture fixation would potentially not have changed outcomes (i.e. the notion of being too sick for surgery). Potential participants should be assessed at 24 hours for eligibility. Those eligible should be approached for entry into the study and randomised at

this point. Patients should then be operated on within 48 hours of the randomisation, if entered into this arm. As evidenced by the Delphi consensus, referral and transfer of patients to a site that performs rib fracture surgery needs to be within 48 hours of decision to treat. The delivery of this will be further discussed in 7.5.5.3

7.5.3 Comparators

Comparative care needs to include all the modalities of treatment, rehabilitation and support that is available to the intervention group. This is to ensure that change in outcomes can be attributed solely to the intervention. Surveying the current provision in England and Wales showed that some hospitals are not meeting the current audit standard set by BOAST[16] and are lacking the recommended specialist physiotherapy and rehabilitation provision. Recruited patients would need to be treated as an active control in a hospital able to provide specialist anaesthetic blocks and supportive therapies, and should have protocols in place to transfer to a hospital that provides surgical fixation if randomised to this arm. Although specific comparator treatments were not the subject of this thesis, protocols for comparator treatments should include a standard regimen for analgesia, which should include in the armamentarium, paracetamol, non-steroidal anti-inflammatories, oral opioids, intravenous opioids as standard, as well as being able to offer at least one of epidural catheter or regional block. The TARN data shows these are most commonly used analgesia regimens in UK practice. A comparator consensus treatment protocol should also be available, entailing a stepwise approach to analgesia and specific physiotherapy interventions such as incentive spirometry. To be included, recruiting sites should be able to deliver these interventions as a minimum. This is further explored in 7.5.5.3.

7.5.4 Outcome

Outcomes should be based on the core outcome set developed by consensus in chapter 4. A paucity of long-term life impact outcomes and adverse events in previous studies makes these a priority in future trials. As to which outcome should be a primary outcome, this is yet to be specifically evidenced. There is a difference between (i) a patient who is in respiratory extremis for whom surgical intervention is potentially life saving and (ii) a patient for whom surgery is performed to prevent respiratory deterioration or to improve long term sequelae of chronic pain and deformity. These two very different patient scenarios present the dilemma of

choosing a primary outcome that is able to encompass the effectiveness of the same treatment when used for different gains. There is a potential to use two primary outcomes that could be combined as a composite outcome, and this would have the advantage of potentially reducing the sample size and improving the statistical efficacy.[277] It is recognised that the interpretation of composite outcomes is often complex and misunderstood, however. [278] Outcomes that gained the most consensus between all stakeholders were mortality and health-related quality of life (HRQOL). It is suggested that these two outcomes encompass the two patient scenarios above and would be covered by using the EQ-5D[279].

Measurement instruments and recommendations on the timing of outcome measurement are still to be defined. Further work in line with the COMET methodology[203] needs to be completed in respect to defining what the HRQOL instrument should be. An ongoing study is assessing the patient-reported outcome measures as an impact on the radiological diagnosis of rib fractures.[147] This study is assessing the Quality of Life - SF36 (Short Form 36); up to two years; Quality of Life - EQ5D[279]; up to two years; Quality of Life - EORTC (European Organisation for the Research and Treatment of Cancer) QLQ-C30 (Quality of Life Questionnaire - Cancer-30); up to two years; Quality of Life - EORTC QLQ-LC13 (Lung Cancer13); up to two years. Results of this study may help focus which HRQOL scores relate specifically to rib fracture injuries.

7.5.5 Study design and trial delivery

A randomised control trial for effectiveness of surgical rib fracture fixation has yet to be undertaken in the UK. The trial design needs to balance pragmatism and efficacy (section 7.5.5.1) as well as an element of feasibility work (Section 7.5.5.2) before a full trial is undertaken. Collaborative working between sites is crucial since a single centre study is unlikely to be able to recruit enough patients to power a study adequately. A single site would also be inherently biased and outcomes would be unlikely to be reproducible or generalisable. One RCT that aimed to recruit 100 patients was terminated as a result of recruiting less than 25% of their target.[280] Another ongoing RCT aims to recruit 206[146] patients. A Cochrane review[2] states that even if these two studies recruit to target they would be unlikely to answer the research question of effectiveness definitively due to

their small sample sizes. Updates of the ongoing trial appear to suggest that recruitment is incomplete.

7.5.5.1 Efficacy versus Pragmatism

The distinction between efficacy and pragmatism is made by Schwartz and Lellouch [281]. Explanatory trials confirm a physiological or clinical hypothesis, whereas pragmatic trials inform a clinical or policy decision by providing evidence for the adoption of the intervention into real-world clinical practice.

The efficacy of an intervention should ideally be shown to be superior under ideal conditions before expanding this to a real world pragmatic trial of effectiveness. An explanatory randomised trial with tight inclusion and exclusion criteria, experienced surgeons and strictly adhered protocol would be the gold standard. While it is possible to achieve this, the time taken to recruit this highly selected population would be impractical, costly and lengthy. On the other hand, a fully pragmatic trial may be unable to disentangle the nuances of whether the intervention is ineffective or whether the delivery of the intervention and the organisational factors that surround the intervention is influencing the outcome instead. In such circumstances, the impact of intervention remains unknown.[282] In an intervention that has already been proven efficacious, however, a pragmatic trial is useful to see if the results are reproducible in the real world against standard current practice.

For this intervention, a combination of the two approaches is thought to be best, in order both to establish efficacy and whether the intervention is able to deliver these outcomes in the real world. The PRECIS 2 tool[283] is used to assess how pragmatic or explanatory a trial is. In applying the current proposed trial design to the PRECIS 2 tool there is a balanced mix between pragmatism (score 5) and explanatory styles (Score 1). Domains in which explanatory themes predominated were eligibility, recruitment, organisation, flexibility: adherence and follow up. Pragmatism dominated in the primary analysis and neither dominated in flexibility: delivery, primary outcome and setting (Figure 38).

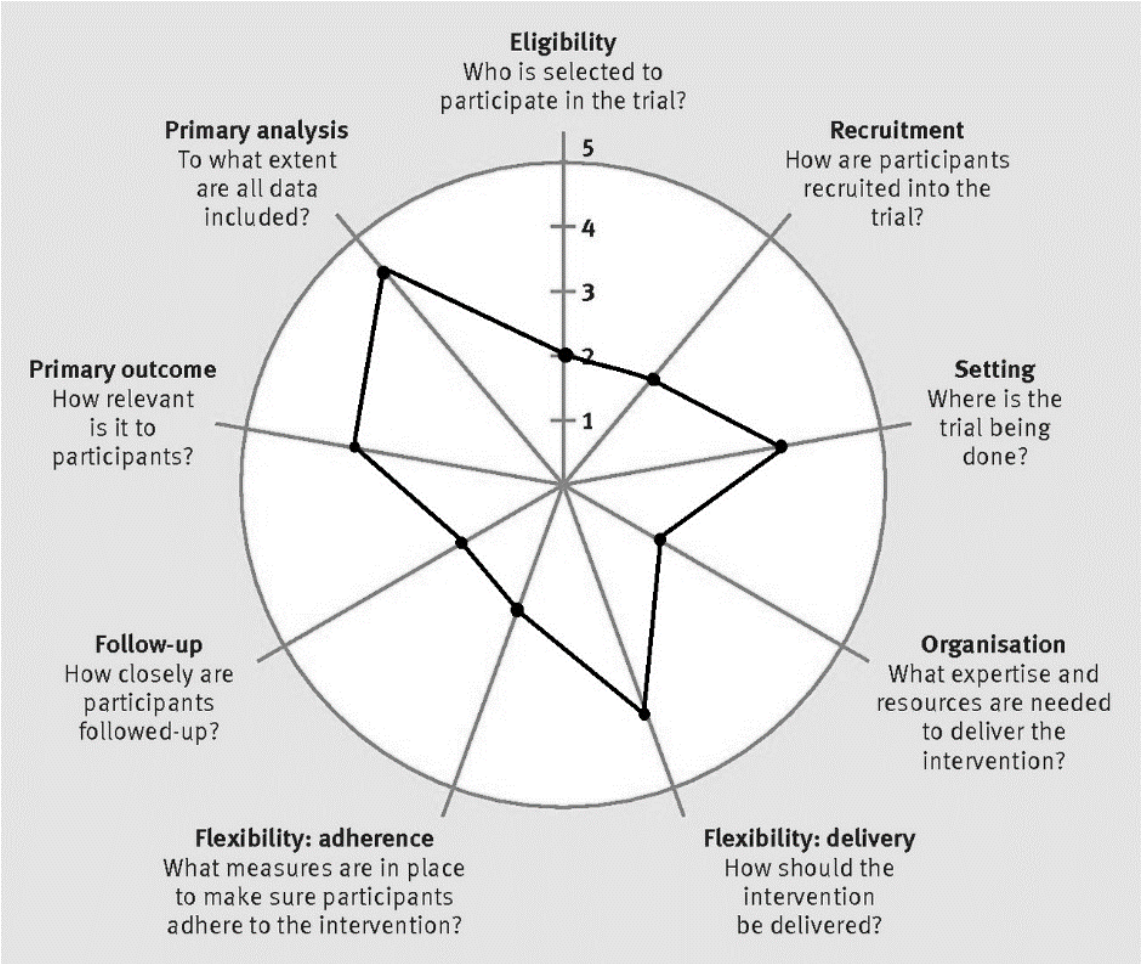


Figure 38 PRECIS- 2[283] wheel diagram describing the design of the current proposed trial

7.5.5.2 Feasibility versus pilot study

Survey evidence suggests that there is some appetite from surgeons to undertake a randomised trial. There are still several areas of ambiguity in respect to how a final trial should be conducted, however, and it is recommended to undertake feasibility work to understand these further before undertaking a full trial. There are varying definitions of feasibility and pilot studies. A pilot study is a version of the main study to assess whether the study can be done.[284] Afeasibility study , meanwhile, looks at whether the components of the main study can work together and includes optimisation of the study design, assessing issues with recruitment, adherence to protocols and allocated treatments.[285]

In the first instance, a feasibility study would test whether patients would be willing to be randomised. One method of doing this is by a prospective preference assessment,[286] in which potential participants would be assessed prior to recruitment in order to evaluate their motivations for taking part in an RCT, as well

as any hesitations, and thus providing information to make enrolment more attractive to a wider range of participants and thereby to improve the generalisability of the results. The survey data highlighted that a substantial number (42%) of district general hospitals who undertake rib fracture care are more than 30 miles from their nearest MTC. Whether patients would accept such a transfer to an MTC a greater distance from their local hospital for trial purposes is unknown and could be explored as part of feasibility work or as a pilot study. Further patient and public participation work is required to establish whether patients would be willing to travel for emergency surgical intervention for rib fracture fixation in a trial setting. Patient and public involvement (PPI) is an important part of feasibility work since it helps to ensure that the proposed methods are acceptable to patients, that the information provided is appropriate so participants can make informed choices, and that the process of recruitment is practical and feasible. The National Institute Health Research (NIHR) INVOLVE guidance recommends the use of PPI at an early stage in designing research so as to 'build and strengthen the relevance, quality and the ethics of the research'.[287]

A randomised pilot study would test whether identifying, randomising, transferring and operating within 48 hours is practicable within the NHS. It would also test the ability to apply an active control group and whether there is true clinician equipoise. Adherence to protocol and the number of crossovers of allocated treatments is also unknown and a randomised pilot study would give an indication of this.

Progression to a full trial would be dependent on progression criteria,[285] whether this can proceed to main trial or whether modifications are required. This has been explored by Avery and colleagues, who have devised a traffic light system that is pre-specified but also flexible so early problems can be rectified.[285]

7.5.5.3 Trial delivery

Developing an efficacy trial protocol which would need to be strictly adhered to from a national multi-centre trial perspective would be the ideal solution for a complex interventional trial on rib fracture fixation. It would be naïve to suggest that this could be rolled out universally throughout the trauma services, however, since such a protocol does not take into account the nuances that encompass each rib fracture service. One solution to the complex area of recruitment to trial from multiple specialties in the emergency setting could be the use of the national

trainee research collaborative. National trainee research collaboratives bring together speciality trainee doctors and medical students throughout the UK and the world with the aim of undertaking collaborative multicentre research projects.[288]

Advantages would include the ability to identify potential trial participants in the out of hours setting, as well as engaging with multiple specialities that form part of the trainee research collaboratives, such as anaesthetics, general surgery and trauma and orthopaedics. One RCT in emergency orthopaedics has recruited to trial eight months before the target time when involving trainee research collaboratives, showing that trainees are effective at identifying and recruiting patients in the emergency setting.[289]

7.6 The Operative RIb Fixation (ORIF) Trial

Since the completion of this MD thesis a Health Technology Assessment (HTA) grant was awarded to undertake a randomised control trial of surgical rib fracture fixation versus non-operative management. The Operative RIb Fixation (ORIF) Trial (ISRCTN10777575, https://doi.org/10.1186/ISRCTN10777575) is a pragmatic interventional multi-centre two-arm parallel group randomised controlled trial nested within a population registry. The inclusion criteria of patients who present with multiple (three or more) rib fractures suitable for surgical repair and one or more of the following:

- Clinical flail chest
- Respiratory difficulty requiring respiratory support
- Uncontrollable pain using standard modalities

The exclusion criteria include the following:

- Aged under 16 years
- Thoracic injury requiring emergent operative or interventional radiology
- Cannot be operated on within 72 hours as deemed unfit for surgery

The inclusion and exclusion criteria are very similar to the study recommendations set out in 7.5.1.1 and supports the consensus defined timings adding strength to these conclusions. Furthermore, the stratification protocol includes age; polytrauma; mechanical ventilation and study site which are equally similar to the

recommendation for trial in 7.5.1.2. What is not clear is the definition of flail chest and respiratory difficulty requiring support and could be open to interpretation or bias however this may be more qualified in the trial documentation. The primary outcomes are (i) all-cause mortality at 12 months and (ii) quality of life measured using the EQ-5D-5L questionnaire at baseline, 30 days, 3 months, 6 months and 12 months. These are directly related to the core outcome set developed in Chapter 4 and the conclusions derived in section 7.5.4. Secondary outcomes include pain, length of stay and cost effectiveness but not the full core outcome set. Not measuring the full core outcome set leaves newer studies not being able to pool outcomes and thus reducing the strength of future systematic review evidence due to lack of comparability.

7.7 Conclusion

The findings from this thesis contribute to the ongoing investigation of the effectiveness of surgical rib fracture fixation. Synthesis of the literature has identified a need for further randomised evidence since no clear benefit is attributable to rib fracture fixation over non-surgical management for the consensus-defined outcomes. Evidence synthesis has shown that the procedure is safe and has the potential to be effective. Meta-analysis has shown some improvement using internal surgical fixation of flail chest and multiple rib fractures on outcomes of length of mechanical ventilation, length of stay in ICU, risk of mortality, pneumonia and tracheostomy placement. A plethora of heterogeneous studies (in which indications are ill defined and many outcomes are of potentially low relevance to stakeholders) has reduced the strength of the systematic review conclusions.

This research adds valuable insights into clinical decision making for rib fracture patients by clinicians and identifies indications for surgical rib fracture fixation that are consensus defined. Flail chest and non-segmental rib fractures are indications for surgical intervention, by consensus. The decision to fix surgically, and the timing of the intervention, are often based on other factors, including prevention of respiratory function deterioration, as well as to assist liberation from invasive ventilation. Future trials will need to make the distinction between these two scenarios at randomisation, since they will invariably deliver different outcome results.

The rib fracture population is diverse and important factors associated with outcomes include; injury severity score, age, the presence of pre-operative ventilation, the presence of a flail chest. Future trials should look to include these factors to either stratify prior to randomisation or as a priori subgroup analyses.

In conclusion, this thesis supports the need for a feasibility trial that will randomise adult patients with an eligibility criterion based on clinical consensus for rib fracture fixation in contrast to non-operative treatment. Further work is required to identify and develop measurement instruments to be used in the trial setting from the consensus-defined core outcome set.

Publications List

The following publications are derived directly from work completed as part of the MD thesis

Ingoe HM, Coleman E, Eardley W, Rangan A, McDaid C, Hewitt C Systematic review of systematic reviews for effectiveness of internal fixation for flail chest and rib fractures in adults. BMJ Open 2019;9:e023444. doi: 10.1136/bmjopen-2018-023444

Ingoe H, McDaid C, Eardley W, Hewitt C. Developing a consensus on indications, timing and core outcomes for surgical fixation of rib fracture: a Delphi technique protocol. Clinical Trials in Orthopedic Disorders 2018; 3: 1-6. Research Article. DOI: 10.4103/2542-4157.233622

Ingoe H, McDaid C, Eardley W, Rangan A, Hewitt C A nationwide survey of practice on available services and current clinical input to the care of patients with rib fractures. The Journal of Cardiothoracic Trauma 2018; 3: 5-10. Original Article. DOI: 10.4103/jctt.jctt_1_18.

Ingoe H, Eardley W, Rangan A, McDaid C, Hewitt C, An international multi-stakeholder delphi consensus exercise to develop a core outcomes set (COS) for surgical fixation of rib fractures. Injury, Published online: October 31, 2019. doi.org/10.1016/j.injury.2019.10.031

Ingoe H, Eardley W, McDaid C, Rangan A, Lawrence T, Hewitt C, Epidemiology of adult rib fracture and factors associated with surgical fixation: Analysis of a chest wall injury dataset from England and Wales. Injury, Published online: October 15, 2019. doi.org/10.1016/j.injury.2019.10.030

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Appendices

Appendix A1 MEDLINE search strategy (OVID interface)

1. (rib adj3 fracture*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

2. ((flail chest or stove? in) adj3 chest).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

3. (blunt chest adj3 trauma).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

4. extra thoracic injur*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

5. costal fracture*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

6. Flail Chest/

7. Rib Fractures/

8. 1 or 2 or 3 or 4 or 5 or 6 or 7

9. (fracture* adj3 fixation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

10. bone screw*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

11. Bone plate*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

12. (suture adj3 fixation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

13. judet strut.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

14. bioabsorbable plate*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

15. heavy suture*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

16. intramedullary splint*.mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

17. (metal adj2 fixation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

18. ((plate* or strut) adj3 fixation*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier]

19. exp Internal Fixators/

20. fracture fixation/ or fracture fixation, internal/ or fracture fixation, intramedullary/

21. (fracture adj3 stabili?ation).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol

supplementary concept word, rare disease supplementary concept word, unique identifier]

22. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21

23. 8 and 22

24. limit 23 to (humans and yr="1976 -Current")

Appendix A2 Risk of Bias Assessment using ROBIS

Coughlin, T.A., et al., *Management of rib fractures in traumatic flail chest A META-ANALYSIS OF RANDOMISED CONTROLLED TRIALS.* Bone & Joint Journal, 2016. **98B**(8): p. 1119-1125.

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Flail Chest
Intervention(s): Surgical fixation
Comparator(s): Normal care
Outcome(s): Pneumonia rate, Length of mechanical ventilation, ICU stay , hospital stay and Mortality

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PY
1.2 Were the eligibility criteria appropriate for the review question? Y
1.3 Were eligibility criteria unambiguous? Y
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? Y
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? Y
Concerns regarding specification of study eligibility criteria LOW
Rationale for concern: No important causes for concern except for no publicly available prtotocol

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic
sources for published and unpublished reports? PY
2.2 Were methods additional to database searching used to identify relevant reports? Y
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? PY
2.4 Were restrictions based on date, publication format, or language appropriate? Y
2.5 Were efforts made to minimise error in selection of studies? Y
Concerns regarding methods used to identify and/or select studies LOW
Rationale for concern: All clearly presented and appropriate

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? Y
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? PY

3.3 Were all relevant study results collected for use in the synthesis? Y
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? Y
3.5 Were efforts made to minimise error in risk of bias assessment? NI
Concerns regarding methods used to collect data and appraise studies LOW
Rationale for concern: No evidence that efforts were made to reduce error in quality assessment. Risk of bias tool was used and clearly reported. Despite efforts to reduce error, errors were found

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? Y
4.2 Were all pre-defined analyses reported or departures explained? Y
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? PY
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? PY
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? PY
4.6 Were biases in primary studies minimal or addressed in the synthesis? PY
Concerns regarding the synthesis and findings LOW
Rationale for concern: Significant heterogeneity was found in several outcomes

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria LOW
2. Concerns regarding methods used to identify and/or select studies LOW
3. Concerns regarding methods used to collect data and appraise studies LOW
4. Concerns regarding the synthesis and findings LOW

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? PY
B. Was the relevance of identified studies to the review's research question appropriately considered? Y
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? PY
Risk of bias in the review RISK: LOW
Rationale for risk: All conclusions were valid and high level of heterogeneity could have been discussed further. Take home message seems a bit optimistic given the limitations in the evidence. Also, conclusion broad in that it does not identify which outcomes.

de Jong, M.B., et al., *SURGICAL MANAGEMENT OF RIB FRACTURES: STRATEGIES AND LITERATURE REVIEW.* Scandinavian Journal of Surgery, 2014. **103**(2): p. 120-125.

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Non-flail Rib fractures
Intervention(s): Surgical management
Comparator(s): Non-Surgical management
Outcome(s): Timing of operative management, duration of hospital stay and duration of ventilation

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PN
1.2 Were the eligibility criteria appropriate for the review question? N
1.3 Were eligibility criteria unambiguous? PN
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? PN
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? PY
Concerns regarding specification of study eligibility criteria HIGH
Rationale for concern: Dates limited to 2000 to 2013 due to surgical techniques changing dramatically. 3 different techniques are then described within the included papers which are techniques used prior to 2000.

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic
sources for published and unpublished reports? PN
2.2 Were methods additional to database searching used to identify relevant reports? Y
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? NI
2.4 Were restrictions based on date, publication format, or language appropriate? PY
2.5 Were efforts made to minimise error in selection of studies? PY
Concerns regarding methods used to identify and/or select studies UNCLEAR
Rationale for concern: Search terms could have been more inclusive using more terms for fixation other than ‘plate’ Search strategy was not published in full. Dates made the identification of studies restrictive.

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? Y

3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Y
3.3 Were all relevant study results collected for use in the synthesis? N
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? N
3.5 Were efforts made to minimise error in risk of bias assessment? N
Concerns regarding methods used to collect data and appraise studies HIGH
Rationale for concern: No evidence of quality assessment in any form

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? Y
4.2 Were all pre-defined analyses reported or departures explained? NI
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? N
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? N
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? NI
4.6 Were biases in primary studies minimal or addressed in the synthesis? N
Concerns regarding the synthesis and findings HIGH
Rationale for concern: No meta-analysis to comment on. Data was presented in tables but descriptive statistics were not clearly identified. A full synthesis of the literature was not undertaken.

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria HIGH
2. Concerns regarding methods used to identify and/or select studies UNCLEAR
3. Concerns regarding methods used to collect data and appraise studies HIGH
4. Concerns regarding the synthesis and findings HIGH

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? N
B. Was the relevance of identified studies to the review's research question appropriately considered? PY
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? NI
Risk of bias in the review RISK: UNCLEAR
Rationale for risk: Identified the lack of heterogeneity and low level of evidence. Did not address limitations. Lacks clarity in clinical and statistical significance.

de Lesquen, H., et al., *Surgical management for the first 48 h following blunt chest trauma: state of the art (excluding vascular injuries).* Interactive Cardiovascular and Thoracic Surgery, 2015. **20**(3): p. 399-408.

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Flail Chest (excluding vascular injuries and children)
Intervention(s): Internal fixation
Comparator(s): No operative treatment
Outcome(s); Duration of ICU stay, pneumonia, duration of mechanical ventilation

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PN
1.2 Were the eligibility criteria appropriate for the review question? NI
1.3 Were eligibility criteria unambiguous? PN
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? NI
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? NI
Concerns regarding specification of study eligibility criteria UNCLEAR
Rationale for concern: Eligibility criteria was not defined

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? PN
2.2 Were methods additional to database searching used to identify relevant reports? N
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? PN
2.4 Were restrictions based on date, publication format, or language appropriate? NI
2.5 Were efforts made to minimise error in selection of studies? NI
Concerns regarding methods used to identify and/or select studies HIGH
Rationale for concern: Search term not inclusive enough to identify rib fracture fixation surgery. No search term for 'rib fracture'. No evidence of hand searching. Two searchers but no plan on how to minimise error selection discussed. Search strategy should have produced more hits as more studies are known.

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? N
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? PN

3.3 Were all relevant study results collected for use in the synthesis? PY
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? PN
3.5 Were efforts made to minimise error in risk of bias assessment? NI
Concerns regarding methods used to collect data and appraise studies UNCLEAR
Rationale for concern: No evidence of efforts to reduce data collection errors, Levels of evidence were quoted but not assessment of quality was made.

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? PY
4.2 Were all pre-defined analyses reported or departures explained? PN
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? NI
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? PY
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? NI
4.6 Were biases in primary studies minimal or addressed in the synthesis? NI
Concerns regarding the synthesis and findings UNCLEAR
Rationale for concern: No meta-analysis completed despite some homogeneous studies.

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria UNCLEAR
2. Concerns regarding methods used to identify and/or select studies HIGH
3. Concerns regarding methods used to collect data and appraise studies UNCLEAR
4. Concerns regarding the synthesis and findings UNCLEAR

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? PY
B. Was the relevance of identified studies to the review's research question appropriately considered? Y
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? Y
Risk of bias in the review RISK: LOW
Rationale for risk: Did not over emphasize results and recognised difficulty in assimilating evidence in different studies which recommended surgery on different indications

Girsowicz, E., et al., *Does surgical stabilization improve outcomes in patients with isolated multiple distracted and painful non-flail rib fractures?* Interactive Cardiovascular and Thoracic Surgery, 2012. **14**(3): p. 312-315.

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Over 45 with isolated rib fractures without true flail chest
Intervention(s): Surgical stabilisation
Comparator(s): Non operative management
Outcome(s): Pain, disability, respiratory function, number of days lost from work

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PN
1.2 Were the eligibility criteria appropriate for the review question? NI
1.3 Were eligibility criteria unambiguous? PN
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? PN
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? PY
Concerns regarding specification of study eligibility criteria HIGH
Rationale for concern: A clear three part question is discussed how ever study characteristics are not discussed and therefore ambiguous.

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? PN
2.2 Were methods additional to database searching used to identify relevant reports? Y
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? PY
2.4 Were restrictions based on date, publication format, or language appropriate? PN
2.5 Were efforts made to minimise error in selection of studies? NI
Concerns regarding methods used to identify and/or select studies HIGH
Rationale for concern: Only one database searched. No evidence that efforts were made to minimise error

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? NI
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? PY

3.3 Were all relevant study results collected for use in the synthesis? NI
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? N
3.5 Were efforts made to minimise error in risk of bias assessment? N
Concerns regarding methods used to collect data and appraise studies HIGH
Rationale for concern: No risk of bias assessment was made and not clarified in the methods described in the reference. Some comments on weakness were made but not in a validated way. No systematic assessment of ROB.

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? PY
4.2 Were all pre-defined analyses reported or departures explained? NI
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? PN
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? PY
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? NI
4.6 Were biases in primary studies minimal or addressed in the synthesis? No
Concerns regarding the synthesis and findings HIGH
Rationale for concern: No meta-analysis completed due to significant heterogeneity Synthesis clear in tables

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria HIGH
2. Concerns regarding methods used to identify and/or select studies? HIGH
3. Concerns regarding methods used to collect data and appraise studies HIGH
4. Concerns regarding the synthesis and findings HIGH

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? PN
B. Was the relevance of identified studies to the review's research question appropriately considered? PY
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? PN
Risk of bias in the review RISK: UNCLEAR
Rationale for risk: Has slightly overemphasized the findings but has recognised that the evidence base is low level

Leinicke, J.A., et al., *Operative management of Rib fractures in the setting of flail chest: A systematic review and meta-analysis.* Annals of Surgery, 2013. **258**(6): p. 914-921.

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Flail Chest
Intervention(s): Operative fixation
Comparator(s): Non operative management
Outcome(s): Outcomes were duration of mechanical ventilation, (DMV), intensive care unit length of stay (ICULOS), hospital length of stay (HLOS), mortality, incidence of pneumonia, and tracheostomy

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PY
1.2 Were the eligibility criteria appropriate for the review question? Y
1.3 Were eligibility criteria unambiguous? Y
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? Y
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? Y
Concerns regarding specification of study eligibility criteria LOW
Rationale for concern: All clearly stated

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic
sources for published and unpublished reports? Y
2.2 Were methods additional to database searching used to identify relevant reports? Y
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? Y
2.4 Were restrictions based on date, publication format, or language appropriate? PN
2.5 Were efforts made to minimise error in selection of studies? Y
Concerns regarding methods used to identify and/or select studies LOW
Rationale for concern: All clearly stated

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? Y
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? PY
3.3 Were all relevant study results collected for use in the synthesis? Y

3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? Y
3.5 Were efforts made to minimise error in risk of bias assessment? Y
Concerns regarding methods used to collect data and appraise studies LOW
Rationale for concern: All clearly stated

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? Y
4.2 Were all pre-defined analyses reported or departures explained? Y
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? Y
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? Y
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? Y
4.6 Were biases in primary studies minimal or addressed in the synthesis? Y
Concerns regarding the synthesis and findings LOW
Rationale for concern: All clearly stated

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria LOW
2. Concerns regarding methods used to identify and/or select studies LOW
3. Concerns regarding methods used to collect data and appraise studies LOW
4. Concerns regarding the synthesis and findings LOW

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? Y
B. Was the relevance of identified studies to the review's research question appropriately considered? Y
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? Y
Risk of bias in the review RISK: LOW
Rationale for risk: Conclusions were valid

NICE., *Insertion of metal rib reinforcements to stabilise a flail chest wall.* Interventional procedures guidance 2010. **[IPG361]**

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Flail Chest
Intervention(s): Insertion of metal rib reinforcements.
Comparator(s): Normal care
Outcome(s): Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? Y
1.2 Were the eligibility criteria appropriate for the review question? Y
1.3 Were eligibility criteria unambiguous? Y
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? Y
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? Y
Concerns regarding specification of study eligibility criteria LOW
Rationale for concern: All clearly presented and appropriate

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic
sources for published and unpublished reports? Y
2.2 Were methods additional to database searching used to identify relevant reports? N
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? PY
2.4 Were restrictions based on date, publication format, or language appropriate? Y
2.5 Were efforts made to minimise error in selection of studies? NI
Concerns regarding methods used to identify and/or select studies Unclear
Rationale for concern: No evidence of additional hand searching or reference checking. No evidence of efforts made to reduce selection error

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? NI
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Y
3.3 Were all relevant study results collected for use in the synthesis? Y

3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? N
3.5 Were efforts made to minimise error in risk of bias assessment? NI
Concerns regarding methods used to collect data and appraise studies Unclear
Rationale for concern: No evidence that efforts were made of formal quality assessment.

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? Y
4.2 Were all pre-defined analyses reported or departures explained? Y
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? PY
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? PY
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? PN
4.6 Were biases in primary studies minimal or addressed in the synthesis? PY
Concerns regarding the synthesis and findings LOW
Rationale for concern: Significant heterogeneity was found in several outcomes

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria LOW
2. Concerns regarding methods used to identify and/or select studies Unclear
3. Concerns regarding methods used to collect data and appraise studies Unclear
4. Concerns regarding the synthesis and findings LOW

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? PY
B. Was the relevance of identified studies to the review's research question appropriately considered?PY
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? PY
Risk of bias in the review RISK: LOW
Rationale for risk: Minimal conclusions higlighted but validity and generalisability discussed

Schulte, K., D. Whitaker, and R. Attia, *In patients with acute flail chest does surgical rib fixation improve outcomes in terms of morbidity and mortality?* Interactive Cardiovascular and Thoracic Surgery, 2016. **23**(2): p. 314-319.

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Flail Chest
Intervention(s): Surgical rib fixation
Comparator(s): Non-surgical management
Outcome(s): Morbidity and Mortality

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PN
1.2 Were the eligibility criteria appropriate for the review question? PY
1.3 Were eligibility criteria unambiguous? PN
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? NI
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? NI
Concerns regarding specification of study eligibility criteria HIGH
Rationale for concern: Little information on study eligibility

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? PN
2.2 Were methods additional to database searching used to identify relevant reports? NI
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? PN
2.4 Were restrictions based on date, publication format, or language appropriate? NI
2.5 Were efforts made to minimise error in selection of studies? NI
Concerns regarding methods used to identify and/or select studies HIGH
Rationale for concern: although a structure protocol is given in the introduction as a reference it is unclear what was followed. Only one search database was used and search terms were limited.

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? NI
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? Y
3.3 Were all relevant study results collected for use in the synthesis? NI
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? N
3.5 Were efforts made to minimise error in risk of bias assessment? N
Concerns regarding methods used to collect data and appraise studies HIGH
Rationale for concern: No evidence to suggest risk of bias was assessed. At least two levels of evidence were assigned wrongly and therefore significant errors were made

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? N
4.2 Were all pre-defined analyses reported or departures explained? NI

4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? PY
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? PN
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? PN
4.6 Were biases in primary studies minimal or addressed in the synthesis? PN
Concerns regarding the synthesis and findings HIGH
Rationale for concern: Several RCT's and systematic reviews were not included that should have been picked up within this review. Suggestion of Level 1 evidence for two studies which innappropriate as there was no randomisation.

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria HIGH
2. Concerns regarding methods used to identify and/or select studies UNCLEAR
3. Concerns regarding methods used to collect data and appraise studies HIGH
4. Concerns regarding the synthesis and findings HIGH

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? PN
B. Was the relevance of identified studies to the review's research question appropriately considered? PY
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? PN
Risk of bias in the review RISK: HIGH
Rationale for risk: Conclusions were overemphasised for the level of evidence and bias in the primary studies. No attempt was made to discuss level of evidence in the conclusions or results.

Schuurmans, J., J.C. Goslings, and T. Schepers, *Operative management versus non-operative management of rib fractures in flail chest injuries: a systematic review.* European Journal of Trauma and Emergency Surgery, 2016: p. 1-6.

ROBIS: Tool to assess risk of bias in systematic reviews

Phase 1: Assessing relevance (Optional)

ROBIS is designed to assess the risk of bias in reviews with questions relating to interventions, aetiology, diagnosis and prognosis. State your overview/guideline question (target question) and the question being addressed in the review being assessed:

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Flail Chest (Flail chest occurs when three or more adjacent ribs are fractured in at least two places, creating a chest wall segment that moves paradoxically from the chest wall)
Intervention(s): Operative
Comparator(s): Non-Operative
Outcome(s): mechanical ventilation, duration of ICU stay, pulmonary infection rate, days in hospital, incidence of lung contusion, rate of tracheostomy, and management costs

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PY
1.2 Were the eligibility criteria appropriate for the review question? Y
1.3 Were eligibility criteria unambiguous? PY
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? PY
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? PN
Concerns regarding specification of study eligibility criteria LOW
Rationale for concern:

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic
sources for published and unpublished reports? PN
2.2 Were methods additional to database searching used to identify relevant reports? Y
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? PY
2.4 Were restrictions based on date, publication format, or language appropriate? PY
2.5 Were efforts made to minimise error in selection of studies? N
Concerns regarding methods used to identify and/or select studies UNCLEAR
Rationale for concern: No evidence to minimise error in selection of studies however they have selected the relevant studies. Limited search with no quality assurance processess

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? N
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? PN
3.3 Were all relevant study results collected for use in the synthesis? Y
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? NI
3.5 Were efforts made to minimise error in risk of bias assessment? N
Concerns regarding methods used to collect data and appraise studies HIGH
Rationale for concern: No evidence that authors have minimised risk of error in data extraction or risk of bias. Risk of bias tool Is not applied properly

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? Y
4.2 Were all pre-defined analyses reported or departures explained? PY
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? PN
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? PN
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? PN
4.6 Were biases in primary studies minimal or addressed in the synthesis? PY
Concerns regarding the synthesis and findings LOW
Rationale for concern: Heterogeneity varied between outcomes, no sensitivity analysis was performed

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria Low
2. Concerns regarding methods used to identify and/or select studies Unclear
3. Concerns regarding methods used to collect data and appraise studies High
4. Concerns regarding the synthesis and findings Low

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? PY
B. Was the relevance of identified studies to the review's research question appropriately considered? Y
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? Y
Risk of bias in the review RISK: LOW
Rationale for risk: Collection of data bias was not addressed but all other were. Conclusions were valid for the limited strengths of the studies.

Slobogean, G.P., et al., *Surgical fixation vs nonoperative management of flail chest: A meta-analysis.* Journal of the American College of Surgeons, 2013. **216**(2): p. 302-311.e1.

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Flail Chest
Intervention(s): Operative management
Comparator(s): Non-Operative Management
Outcome(s): Relevant critical care outcomes

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PY
1.2 Were the eligibility criteria appropriate for the review question? PY
1.3 Were eligibility criteria unambiguous? PY
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? Y
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? Y
Concerns regarding specification of study eligibility criteria LOW
Rationale for concern: Most of the eligibility criteria were specified but not all.

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? PN
2.2 Were methods additional to database searching used to identify relevant reports? N
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? Y
2.4 Were restrictions based on date, publication format, or language appropriate? Y
2.5 Were efforts made to minimise error in selection of studies? Y
Concerns regarding methods used to identify and/or select studies LOW
Rationale for concern: Clear selection method was described and was robust.

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? Y
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? PY
3.3 Were all relevant study results collected for use in the synthesis? NI
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? N

3.5 Were efforts made to minimise error in risk of bias assessment? PN
Concerns regarding methods used to collect data and appraise studies HIGH
Rationale for concern: Efforts were made to reduce error in data collection however there was no clear assessment of risk of bias

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? Y
4.2 Were all pre-defined analyses reported or departures explained? Y
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? Y
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? PY
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? PY
4.6 Were biases in primary studies minimal or addressed in the synthesis? PY
Concerns regarding the synthesis and findings LOW
Rationale for concern: A robust analysis of the findings

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria LOW
2. Concerns regarding methods used to identify and/or select studies LOW
3. Concerns regarding methods used to collect data and appraise studies HIGH
4. Concerns regarding the synthesis and findings LOW

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? PY
B. Was the relevance of identified studies to the review's research question appropriately considered? Y
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? PY
Risk of bias in the review RISK: LOW
Rationale for risk: Level of evidence bias was attributed to the results but not all bias were discussed

Swart, E., et al., *Operative Treatment of Rib Fractures in Flail Chest Injuries: A Meta-Analysis and Cost Effectiveness Analysis.* Journal of Orthopaedic Trauma, 2016. **Publish Ahead of Print**.

ROBIS: Tool to assess risk of bias in systematic reviews

Phase 1: Assessing relevance (Optional)

ROBIS is designed to assess the risk of bias in reviews with questions relating to interventions, aetiology, diagnosis and prognosis. State your overview/guideline question (target question) and the question being addressed in the review being assessed:

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Adult Acute Flail Chest
Intervention(s): Operative
Comparator(s): Non Operative
Outcome(s):Ventilator days, ICU stay, hospital LOS Mortality, Pneumonia rate, tracheostomy rate

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PY
1.2 Were the eligibility criteria appropriate for the review question? Y
1.3 Were eligibility criteria unambiguous? PY
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? PY
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? Y
Concerns regarding specification of study eligibility criteria LOW
Rationale for concern:

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic
sources for published and unpublished reports? PN
2.2 Were methods additional to database searching used to identify relevant reports? Y
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? PY
2.4 Were restrictions based on date, publication format, or language appropriate? PN
2.5 Were efforts made to minimise error in selection of studies? Y
Concerns regarding methods used to identify and/or select studies UNCLEAR
Rationale for concern: Two researchers performed and checked identification of studies

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:

3.1 Were efforts made to minimise error in data collection? Y
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? N
3.3 Were all relevant study results collected for use in the synthesis? PY
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? N
3.5 Were efforts made to minimise error in risk of bias assessment? N
Concerns regarding methods used to collect data and appraise studies HIGH
Rationale for concern: No risk of bias was performed

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? Y
4.2 Were all pre-defined analyses reported or departures explained? Y
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? Y
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? PY
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? Y
4.6 Were biases in primary studies minimal or addressed in the synthesis? NO
Concerns regarding the synthesis and findings HIGH
Rationale for concern: Significant heterogeneity reported but not addressed

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria Low
2. Concerns regarding methods used to identify and/or select studies Unclear
3. Concerns regarding methods used to collect data and appraise studies Low
4. Concerns regarding the synthesis and findings High

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? PN
B. Was the relevance of identified studies to the review's research question appropriately considered? PY
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? PN
Risk of bias in the review RISK: UNCLEAR
Rationale for risk: Don’t take into account risk of bias or heterogeneity

Unsworth, A., K. Curtis, and S.E. Asha, *Treatments for blunt chest trauma and their impact on patient outcomes and health service delivery.* Scandinavian Journal of Trauma Resuscitation & Emergency Medicine, 2015. **23**.

Intervention reviews:
Category Target question (e.g. overview or guideline) Review being assessed
Patients/Population(s): Adult blunt chest trauma (specifically flail)
Intervention(s): Multidisciplinary intervention
Comparator(s): Other intervention
Outcome(s): Patient and health care outcomes

Phase 2: Identifying concerns with the review process

DOMAIN 1: STUDY ELIGIBILITY CRITERIA
Describe the study eligibility criteria, any restrictions on eligibility and whether there was evidence that objectives and eligibility criteria were pre-specified:
1.1 Did the review adhere to pre-defined objectives and eligibility criteria? PY
1.2 Were the eligibility criteria appropriate for the review question? PY
1.3 Were eligibility criteria unambiguous? PY
1.4 Were all restrictions in eligibility criteria based on study characteristics appropriate (e.g. date, sample size, study quality, outcomes measured)? PY
1.5 Were any restrictions in eligibility criteria based on sources of information appropriate (e.g. publication status or format, language, availability of data)? PY
Concerns regarding specification of study eligibility criteria LOW
Rationale for concern:

DOMAIN 2: IDENTIFICATION AND SELECTION OF STUDIES
Describe methods of study identification and selection (e.g. number of reviewers involved):
2.1 Did the search include an appropriate range of databases/electronic sources for published and unpublished reports? PN
2.2 Were methods additional to database searching used to identify relevant reports? Y
2.3 Were the terms and structure of the search strategy likely to retrieve as many eligible studies as possible? PY
2.4 Were restrictions based on date, publication format, or language appropriate? Y
2.5 Were efforts made to minimise error in selection of studies? PY
Concerns regarding methods used to identify and/or select studies LOW
Rationale for concern: eoor slection was not discussed however all other modality were clear

DOMAIN 3: DATA COLLECTION AND STUDY APPRAISAL
Describe methods of data collection, what data were extracted from studies or collected through other means, how risk of bias was assessed (e.g. number of reviewers involved) and the tool used to assess risk of bias:
3.1 Were efforts made to minimise error in data collection? NI
3.2 Were sufficient study characteristics available for both review authors and readers to be able to interpret the results? PN
3.3 Were all relevant study results collected for use in the synthesis? PY
3.4 Was risk of bias (or methodological quality) formally assessed using appropriate criteria? Y

3.5 Were efforts made to minimise error in risk of bias assessment? NI
Concerns regarding methods used to collect data and appraise studies UNCLEAR
Rationale for concern: Data collection and risk of bias errors were not minimised. Not all data that was relevant was presented.

DOMAIN 4: SYNTHESIS AND FINDINGS
Describe synthesis methods:
4.1 Did the synthesis include all studies that it should? PY
4.2 Were all pre-defined analyses reported or departures explained? NI
4.3 Was the synthesis appropriate given the nature and similarity in the research questions, study designs and outcomes across included studies? PN
4.4 Was between-study variation (heterogeneity) minimal or addressed in the synthesis? N
4.5 Were the findings robust, e.g. as demonstrated through funnel plot or sensitivity analyses? N
4.6 Were biases in primary studies minimal or addressed in the synthesis? N
Concerns regarding the synthesis and findings UNCLEAR
Rationale for concern: Biases were not adequately addressed within the synthesis with minimal recognistion of the between study variation

Phase 3: Judging risk of bias

Summarize the concerns identified during the Phase 2 assessment:

Domain Concern Rationale for concern
1. Concerns regarding specification of study eligibility criteria LOW
2. Concerns regarding methods used to identify and/or select studies LOW
3. Concerns regarding methods used to collect data and appraise studies Unclear
4. Concerns regarding the synthesis and findings Unclear

RISK OF BIAS IN THE REVIEW

Describe whether conclusions were supported by the evidence:
A. Did the interpretation of findings address all of the concerns identified in Domains 1 to 4? PN
B. Was the relevance of identified studies to the review's research question appropriately considered? PY
C. Did the reviewers avoid emphasizing results on the basis of their statistical significance? PN
Risk of bias in the review RISK: HIGH
Rationale for risk: although level of literature was high the in study bias were in fact high and these were not picked up on

Appendix A3 Excluded Studies

1	Galan G, Penalver JC, Paris F, et al. BLUNT CHEST INJURIES IN 1696 PATIENTS. Eur J Cardiothorac Surg. 1992; 6: 284-7.	Study Design
2	Actis Dato GM, Aidala E and Ruffini E. Surgical management of flail chest. Ann Thorac Surg. 1999; 67: 1826-7.	Study Design
3	Ahmed Z and Mohyuddin Z. Management of flail chest injury: Internal fixation versus endotracheal intubation and ventilation. Journal of Thoracic and Cardiovascular Surgery. 1995; 110: 1676-80.	Study Design
4	Akkus M, Utkusavas A, Hanozu M, Kaya M and Bakir I. Stabilization of Flail Chest and Fractured Sternum by Minimally Invasive Repair of Pectus Excavatum. Thoracic and Cardiovascular Surgeon Reports. 2015; 4: 11-3.	Study Design
5	Althausen PL, Shannon S, Watts C, et al. Early surgical stabilization of flail chest with locked plate fixation. J Orthop Trauma. 2011; 25: 641-7.	Study Design
6	Ananiadou O, Karaiskos T, Givissis P and Drossos G. Operative stabilization of skeletal chest injuries secondary to cardiopulmonary resuscitation in a cardiac surgical patient. Interact Cardiovasc Thorac Surg. 2010; 10: 478-80.	Study Design
7	Attia RQ, Schulte KL and Whitaker DC. eReply: In patients with acute flail chest does surgical rib fixation improve outcomes in terms of morbidity and mortality? Interactive Cardiovascular and Thoracic Surgery. 2016; 23: 319-20.	Study Design
8	Bailey J, VanderHeiden T, Burlew CC, et al. Thoracic hyperextension injury with complete "bony disruption" of the thoracic cage: Case report of a potentially life-threatening injury. World Journal of Emergency Surgery. 2012; 7.	Study Design
9	Beelen R, Rumbaut J and De Geest R. Surgical stabilization of a rib fracture using an angle stable plate. Journal of Trauma - Injury, Infection and Critical Care. 2007; 63: 1159-60.	Study Design
10	Beltrami V, Martinelli G, Giansante P and Gentile K. An original technique for surgical stabilisation of traumatic flail chest. Thorax. 1978; 33: 528-9.	Study Design
11	Berthet JP, Solovei L, Tiffet O, et al. Chest-wall reconstruction in case of infection of the operative site: Is there any interest in titanium rib osteosynthesis. Eur J Cardiothorac Surg. 2013; 44: 866-74.	Study Design
12	Bibas BJ and Bibas RA. Operative stabilization of flail chest using a prosthetic mesh and methylmethacrylate. Eur J Cardiothorac Surg. 2006; 29: 1064-6.	Study Design
13	Bille A, Okiror L, Campbell A, Simons J and Routledge T. Evaluation of long-term results and quality of life in patients who underwent rib fixation with titanium devices after trauma. General Thoracic and Cardiovascular Surgery. 2013; 61: 345-9.	Study Design
14	Bille A, Okiror L, Karenovics W and Routledge T. Experience with titanium devices for rib fixation and coverage of chest wall defects. Interactive Cardiovascular and Thoracic Surgery. 2012; 15: 588-95.	Study Design

15	Bonne SL, Turnbull IR and Southard RE. Technique for repair of fractures and separations involving the cartilaginous portions of the anterior chest wall. Chest. 2015; 147: e199-e204.	Study Design
16	Borrelly J and Aazami MH. New insights into the pathophysiology of flail segment: The implications of anterior serratus muscle in parietal failure. Eur J Cardiothorac Surg. 2005; 28: 742-9.	Study Design
17	Bottlang M, Long WB, Phelan D, Fielder D and Madey SM. Surgical stabilization of flail chest injuries with MatrixRIB implants: A prospective observational study. Injury. 2013; 44: 232-8.	Study Design
18	Brotzu G, Montisci R, Pillai W and Sanna S. Chest injuries. A review of 195 patients. Ann Chir Gynaecol. 1988; 77: 155-9.	Study Design
19	Buyukkarabacak YB, Sengul AT, Celik B, et al. The Usefulness of Early Surgical Rib Stabilization in Flail Chest. Acta Chir Belg. 2015; 115: 408-13.	Study Design
20	Cacchione RN, Richardson JD and Seligson D. Painful nonunion of multiple rib fractures managed by operative stabilization. Journal of Trauma - Injury, Infection and Critical Care. 2000; 48: 319-21.	Study Design
21	Campbell N, Conaglen P, Martin K and Antippa P. Surgical stabilization of rib fractures using inion OTPS wraps-techniques and quality of life follow-up. Journal of Trauma - Injury, Infection and Critical Care. 2009; 67: 596-601.	Study Design
22	Caragounis EC, Olsen MF, Pazooki D and Granhed H. Surgical treatment of multiple rib fractures and flail chest in trauma: a one-year follow-up study. World Journal of Emergency Surgery. 2016; 11.	Study Design
23	Chapman BC, Herbert B, Rodil M, et al. RibScore: A novel radiographic score based on fracture pattern that predicts pneumonia, respiratory failure, and tracheostomy. J Trauma Acute Care Surg. 2016; 80: 95-101.	Study Design
24	Charafeddine AH, Stone ME, Reddy SH, Teperman SH, Kaban JM and Cohen-Levy WB. Anterior chest wall disassociation: A pattern associated with serious underlying injury. Am Surg. 2015; 81: E244-E5.	Study Design
25	Cho YH, Kim HK, Kang DY and Choi YH. Reoperative surgical stabilization of a painful nonunited rib fracture using bone grafting and a metal plate. J Orthop Trauma. 2009; 23: 605-6.	Study Design
26	De La Santa Barajas PM, Polo Otero MD, Delgado Sanchez- Gracian C, Leal Ruiloba S, Trinidad C and Choren Duran M. Surgical treatment for flail chest. Interactive Cardiovascular and Thoracic Surgery. 2012; 15: S5.	Study Design
27	De Moya M, Bramos T, Agarwal S, et al. Pain as an indication for rib fixation: A bi-institutional pilot study. Journal of Trauma - Injury, Infection and Critical Care. 2011; 71: 1750-4.	Study Design
28	de Palma A, Sollitto F, Loizzi D, et al. Chest wall stabilization and reconstruction: Short and long-term results 5 years after the introduction of a new titanium plates system. Journal of Thoracic Disease. 2016; 8: 490-8.	Study Design
29	Dean NC, Van Boerum DH and Liou TG. Rib plating of acute and sub-acute non-union rib fractures in an adult with cystic fibrosis: a case report. BMC Res Notes. 2014; 7: 681.	Study Design
30	Defreest L, Tafen M, Bhakta A, et al. Open reduction and internal fixation of rib fractures in polytrauma patients with flail chest. Am J Surg. 2016; 211: 761-7.	Study Design
31	Dehghan N, de Mestral C, McKee MD, Schemitsch EH and Nathens A. Flail chest injuries: A review of outcomes and treatment practices from the National Trauma Data Bank. Journal of Trauma and Acute Care Surgery. 2014; 76: 462-8.	Study Design

32	Doben AR, Eriksson EA, Denlinger CE, et al. Surgical rib fixation for flail chest deformity improves liberation from mechanical ventilation. J Crit Care. 2014; 29: 139-43.	Study Design
33	Dunlop RLE, Tiong W, Veerasingam D and 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-e3.	Study Design
34	Engel C, Krieg JC, Madey SM, Long WB and Bottlang M. Operative chest wall fixation with osteosynthesis plates. Journal of Trauma - Injury, Infection and Critical Care. 2005; 58: 181-6.	Study Design
35	Evman S, Kolbas I, Dogruyol T and Tezel C. A Case of Traumatic Flail Chest Requiring Stabilization with Surgical Reconstruction. Thoracic and Cardiovascular Surgeon Reports. 2015; 4: 8-10.	Study Design
36	Fagevik Olsén M, Pazooki D and Granhed H. Recovery after stabilising surgery for 'flail chest'. Unfallchirurgie. 2013; 39: 501-6.	Study Design
37	Farquhar J, Almahrabi Y, Slobogean G, et al. No benefit to surgical fixation of flail chest injuries compared with modern comprehensive management: results of a retrospective cohort study. Canadian Journal of Surgery. 2016; 59: 299-303.	Study Design
38	Flagel BT, Luchette FA, Reed RL, et al. Half-a-dozen ribs: the breakpoint for mortality. Surgery. 2005; 138: 717-23; discussion 23-5.	Study Design
39	Gabram SGA, Devanney J, Jones D and Jacobs LM. Delayed hemorrhagic pericardial effusion: Case reports of a complication from severe blunt chest trauma. Journal of Trauma. 1992; 32: 794-800.	Study Design
40	Galvin IF, Costa R and Murton M. FRACTURED RIB WITH PENETRATING CARDIOPULMONARY INJURY. Ann Thorac Surg. 1993; 56: 558-9.	Study Design
41	Gardenbroek TJ, Bemelman M and Leenen LPH. Pseudarthrosis of the ribs treated with a locking compression plate: A report of three cases. Journal of Bone and Joint Surgery - Series A. 2009; 91: 1477-9.	Study Design
42	Gasparri MG, Almassi GH and Haasler GB. Surgical management of multiple rib fractures. Chest. 2003; 124: 295S-6S.	Study Design
43	George RJ and Stern HS. An approach to surgical fixation of traumatic costosternal diastasis. ANZ J Surg. 2014; 84: 594-5.	Study Design
44	Gerov I and Yablanski V. Damage control - Increasing the survival rates through emergency bone stabilization in a polytraumatized young patient. Injury. 2011; 42: S29.	Study Design
45	Ginsberg RJ and Kostin RF. 5. New approaches to the management of flail chest. Can Med Assoc J. 1977; 116: 613-5.	Study Design
46	Govaert G, Schuetz M and Peters P. Rib fixation for a traumatic 'stove-in chest': An option to consider. ANZ J Surg. 2012; 82: 276-7.	Study Design
47	Granetzny A, Abd El-Aal M, Emam E, Shalaby A and Boseila A. Surgical versus conservative treatment of flail chest. Evaluation of the pulmonary status. Interact Cardiovasc Thorac Surg. 2005; 4: 583-7.	Study Design
48	Granhed HP and Pazooki D. A feasibility study of 60 consecutive patients operated for unstable thoracic cage. J Trauma Manag Outcomes. 2014; 8: 20.	Study Design
49	Guernelli N, Bragaglia RB, Briccoli A, Mastrorilli M and Vecchi R. Technique for the management of anterior flail chest. Thorax. 1979; 34: 247-8.	Study Design
50	Gunn JM, Savola J and Isotalo K. Left-sided diaphragmatic and pericardial ruptures with subluxation of the heart after blunt trauma. Ann Thorac Surg. 2012; 93: 317-9.	Study Design

51	Haasler GB. Open fixation of flail chest after blunt trauma. Ann Thorac Surg. 1990; 49: 993-5.	Study Design
52	Hasenboehler EA, Bernard AC, Bottiggi AJ, et al. Treatment of traumatic flail chest with muscular sparing open reduction and internal fixation: Description of a surgical technique. Journal of Trauma - Injury, Infection and Critical Care. 2011; 71: 494-501.	Study Design
53	Hellberg K, de Vivie ER, Fuchs K, et al. Stabilization of flail chest by compression osteosynthesis--experimental and clinical results. Thorac Cardiovasc Surg. 1981; 29: 275-81.	Study Design
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521	Wright DEP and Johnstone AJ. The floating shoulder redefined. Journal of Trauma - Injury, Infection and Critical Care. 2010; 68: E26-E9.	Population
522	Wu YS, Lin Y, Zhang XL, et al. Management of hangman's fracture with percutaneous transpedicular screw fixation. Eur Spine J. 2013; 22: 79-86.	Population
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529	Zong ZW, Bao QW, Liu HY, et al. Diagnosis and treatment of rare complications of pelvic fractures. Chinese Journal of Traumatology - English Edition. 2016; 19: 199-205.	Population
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533	Sartorelli KH and Vane DW. The Diagnosis and Management of Children with Blunt Injury of the Chest. Seminars in Pediatric Surgery. 2004; 13: 98-105.	Population
534	Yasuda R, Okada H, Shirai K, et al. Comparison of two pediatric flail chest cases. Scandinavian Journal of Trauma Resuscitation & Emergency Medicine. 2015; 23.	Population

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537	Fabricant L, Ham B, Mullins R and Mayberry J. Prospective clinical trial of surgical intervention for painful rib fracture nonunion. Am Surg. 2014; 80: 580-6.	Population
538	Ahmed Z. On internal fixation for flail chest - Reply. Journal of Thoracic and Cardiovascular Surgery. 1996; 112: 850-.	Publication Type
539	Doben AR and Pieracci FM. Reply to "open reduction and internal fixation of rib fractures in polytrauma patients with flail chest" by DeFreest et al. American Journal of Surgery. 2016.	Publication Type
540	Fabian TC, Hawkins M, Bland K, et al. Discussion. Am Surg. 2007; 73: 596-7.	Publication Type
541	Haasler GB. Use of 3.5-mm acetabular reconstruction plates for internal fixation of flail chest injuries - Invited commentary. Ann Thorac Surg. 1998; 65: 1474-.	Publication Type
542	Hajj-Chahine J, Jayle C, Houmaida H and Corbi P. eComment. Titanium devices in children. Interact Cardiovasc Thorac Surg. 2012; 15: 595.	Publication Type
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546	Oyarzun JR, Bush AP, McCormick JR and Bolanowski PJP. Reconstruction plates for internal fixation of flail chest - Reply. Ann Thorac Surg. 1998; 66: 2158-.	Publication Type
547	Bastos R, Calhoon JH and Baisden CE. Flail Chest and Pulmonary Contusion. Seminars in Thoracic and Cardiovascular Surgery. 2008; 20: 39-45.	Literature Review
548	Bemelman M, Poeze M, Blokhuis TJ and Leenen LPH. Historic overview of treatment techniques for rib fractures and flail chest. European Journal of Trauma and Emergency Surgery. 2010; 36: 407-15.	Literature Review
549	Fitzpatrick DC, Denard PJ, Phelan D, Long WB, Madey SM and Bottlang M. Operative stabilization of flail chest injuries: review of literature and fixation options. European Journal of Trauma and Emergency Surgery. 2010; 36: 427-33.	Literature Review
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551	Fowler TT, Taylor BC, Bellino MJ and Althausen PL. Surgical Treatment of Flail Chest and Rib Fractures. Journal of the American Academy of Orthopaedic Surgeons. 2014; 22: 751-60.	Literature Review
552	Gasparri MG, Tisol WB and Haasler GB. Rib stabilization: lessons learned. European Journal of Trauma and Emergency Surgery. 2010; 36: 435-40.	Literature Review
553	Kiraly L and Schreiber M. Management of the crushed chest. Crit Care Med. 2010; 38: S469-S77.	Literature Review
554	Lafferty PM, Anavian J, Will RE and Cole PA. Operative treatment of chest wall injuries: indications, technique, and outcomes. J Bone Joint Surg Am. 2011; 93: 97-110.	Literature Review
555	Marasco S and Saxena P. Surgical rib fixation - Technical aspects. Injury. 2015; 46: 929-32.	Literature Review
556	Mayberry JC and Trunkey DD. The fractured rib in chest wall trauma. Chest Surgery Clinics of North America. 1997; 7: 239-61.	Literature Review
557	Nirula R, Diaz Jr JJ, Trunkey DD and Mayberry JC. Rib fracture repair: Indications, technical issues, and future directions. World J Surg. 2009; 33: 14-22.	Literature Review
558	Nirula R and Mayberry JC. Rib fracture fixation: Controversies and technical challenges. Am Surg. 2010; 76: 793-802.	Literature Review
559	Parry NG, Moffat B and Vogt K. Blunt thoracic trauma: recent advances and outstanding questions. Current Opinion in Critical Care. 2015; 21: 544-8.	Literature Review
560	Pettiford BL, Luketich JD and Landreneau RJ. The Management of Flail Chest. Thorac Surg Clin. 2007; 17: 25-33.	Literature Review
561	Pharaon KS, Marasco S and Mayberry J. Rib Fractures, Flail Chest, and Pulmonary Contusion. Current Trauma Reports. 2015; 1: 237-42.	Literature Review
562	Qasim Z and Gwinnutt C. Flail chest: Pathophysiology and management. Trauma. 2009; 11: 63-70.	Literature Review
563	Ranasinghe AM, Hyde JAJ and Graham TR. Management of flail chest. Trauma. 2001; 3: 235-47.	Literature Review
564	Senekjian L and Nirula R. Rib Fracture Fixation: Indications and Outcomes. Critical Care Clinics. 2017; 33: 153-65.	Literature Review
565	Simon B, Ebert J, Bokhari F, et al. Management of pulmonary contusion and flail chest: An Eastern Association for the Surgery of Trauma practice management guideline. Journal of Trauma and Acute Care Surgery. 2012; 73: S351-S61.	Literature Review
566	Sirmali M, Turut H, Topcu S, et al. A comprehensive analysis of traumatic rib fractures: morbidity, mortality and management. Eur J Cardiothorac Surg. 2003; 24: 133-8.	Literature Review

567	Zreik NH, Francis MI, Ray A, Rogers BA and Ricketts DM. Blunt chest trauma: bony injury in the thorax. British Journal of Hospital Medicine. 2016; 77: 72-7.	Literature Review

Appendix B1 Study Characteristics

Randomised Controlled Trials

Table 68 Study caracteristics - Randomised Controlled Trials

Granetzny A, El-Aal MA, Emam E, Shalaby A, Boseila A. Surgical versus conservative treatment of flail chest. Evaluation of the pulmonary status. Interactive Cardiovascular and Thoracic surgery 2005;4:583–7. [PUBMED: 17670487]							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Granetzny, Year 2005 Study Type RCT Setting Egypt- Single centre Intervention Internal fixation Comparator Packing strapping and IMV	Flail chest including fracture of three ribs or more with paradoxical movement	Inclusion Flail chest including fracture of three ribs or more with paradoxical movement Exclusion 1. Head trauma with disturbed conscious level. 2. Associated injuries as myocardial contusion that might be adversely affected by general anesthesia. 3. Severe associated trauma to other systems. 4. Fractures of the upper three ribs only, as immobilizing bandages are inefficient in fractures of the upper ribs for anatomic reasons.	Intervention: N=20 Age Mean age (SD) 40.5 (8.2) Range 24–55 Gender Male:17 Female:3 Diag/location Flail ribs N = 4.4 Anterolateral 8 (40%) Posteriolateral 6 (30%) Costochondral junction 5 (25%) Sternum 1 (5%) ISS = 16.8 (43.5) Pneumothorax 2 (10%)	Control: N= 20 Age Mean age (SD) 36 (14.9) Range 12–60 Gender Male:14 Female:6 Diag/location Flail ribs N= 4.9 Anterolateral 5 (25%) Posteriolateral 15 (75%) Costochondral junction 0 (0%) Sternum 0 (0%) ISS = 18 (5.1) Pneumothorax 1 (5%)	Type K wires and stainless steel wire 14 Stainless steel wire 6 Time Fixed within 24 to 36 h after admission to the ICU	PRIMARY OUTCOMES Duration of mechanical ventilation ICU stay SECONDARY OUTCOMES No complications Chest infection Empyema Pulmonary embolism Mediastinitis Wound infection Chest wall deformity Scoliosis Mortality Duration of hospital stay ABG analysis before and after intervention 2 months spirometry	2 months

Marasco SF, Davies AR, Cooper J, Varma D, Bennett V, Nevill R, et al. Prospective randomized controlled trial of operative rib fixation in traumatic flail chest. Journal of American College of Surgeons 2013;on line:1–9. [PUBMED:23415550]							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Marasco Year 2013 Study Type RCT Setting Single centre Australia Intervention Fixation Comparator Usual Care (nonoperative management)	Not discussed	Inclusion Presence of a flail segment defined as 3 or more consecutive ribs fractured in more than 1 place, producing a free floating segment of chest wall Patients were enrolled only if they were ventilator dependent with no prospect of successful weaning within the next 48 hours. Exclusion age greater than 80 years spinal injuries open rib fractures with soiling or infection, sepsis severe traumatic brain injury (GCS <10)at the scene of accident or at presentation to the hospital uncorrected coagulopathy.	Intervention: N= 23 (22 received intervention) Age Mean age (SD) 57.8 (17.1) Gender Male:20 Female: 3 Diag/location Flail ribs N = 5.1 (1.7) Multiple ribs N = 11 (3.1) Bil :unilateral 12:11 ISS = 35 (11.4) Lung contusion None 3 Mild 16 Mod 4 Severe 0 Pneumothorax 20 (90%)	Control: N= 23 Age Mean age (SD): 59.3(10.4) Gender Male:20 Female: 3 Diag/location Flail ribs N=5.5 (2) Multiple ribs N=11.3 (4.7) Bil :unilateral 13:10 ISS = 30 (6.3) Lung contusion None 2 Mild 16 Mod 4 Severe 1 Pneumothorax 21 (91%)	Type Inion resorbable (Inion OTPS) 6- or 8-hole plates and bicortical screws were used for every rib fixation. These plates and screws are made of a polylactide copolymer that resorbs over 18 to 24 months. Time Randomised at 48 hours Hours + 49.4 (35.9) mean (SD)	PRIMARY OUTCOMES Duration of mechanical ventilation ICU stay SECONDARY OUTCOMES N of respiratory complications (pneumonia, pneumothorax, intercostal catheter usage) Rate of failed extubation Rate of tracheostomy Blood products Readmission to ICU Duration of hospital stay Cost of the operation Patients were reviewed at 3 months postoperatively for clinical assessment, spirometry, and CT scan. All patients were sent a (SF-36) at 6 months	3 months CT Operative group (n=21) Non-operative (n =17) Spirometry (n= 17 each group) 6 months SF36 Operative group (n=19) Non-operative group (n =18)

Tanaka H, Yukioka T, Yamaguti Y, Shimizu S, Goto H, Matsuda H, et al. Surgical stabilization of internal pneumatic stabilization? A prospective randomized study of management of severe flail chest patients. Journal of Trauma Injury, Infection, and Critical Care 2002;52:727–32. [PUBMED: 11956391]							
Study details	Indications	Inclusion/Exclusion Criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author: Tanaka et al Year: 2002 Study Type :RCT Setting Single centre, Japan Intervention Fixation Comparator Internal pneumatic stabilization .	Not discussed	Inclusion Flail chest requiring mechanical ventilation more than six rib fractures Exclusion did not require mechanical ventilation; had fractures of fewer than six ribs did not develop acute respiratory failure severe closed head injury (head Abbreviated Injury Scale score 3 with unconsciousness) spinal injury age 14 years consent not given chronic preexisting heart pulmonary, hepatic or renal disease; questionnaire not completed	Intervention: N= 18 Age Mean age (SD) 43 (12) Gender Male:12 Female:6 Diag/location Flail ribs N = 8.2 (3.3) Ant/Lat 11 Post/Lat 4 ISS = 33 (11) Tube thorcotoamy 18/18 Lung contusion None Mild 36 % Mod 27 % Severe 36 % Pneumothorax 18 (100%)	Control: N= 19 Age Mean age (SD): 46 (9) Gender Male:14 Female:5 Diag/location Flail ribs N= 8.2 (2.6) Ant/Lat 14 Post/Lat 3 ISS = 30 (8) Tube thorcotoamy 19/19 Lung contusion None Mild 31 % Mod 38 % Severe 31 % Pneumothorax 19 (100%)	Type Judet Struts Time Randomised at 5 days hours Fixed at 8.2 days (4.1)	PRIMARY OUTCOMES Severity of lung contusion Rate of pneumonia at 7 and 21 days Rate of tracheotomy at 7 and 21 days Length of mechanical ventilation Length of ICU stay total medical expense Tube thoracotomy SECONDARY OUTCOMES Long term respiratory function by spirometry Chest Tightness Thoracic cage pain Dyspnea on effort Subjective dyspnea Return to work 6m Return to work 12m	Spirometry at 1, 2, 3, and 4 weeks; and at 2, 3, 6, and 12 months after injury. Questionnaire at 6 and 12 months After discharge from the hospital, patients' respiratory function and subjective complaints were followed in the outpatient clinic until 12 months after injury

Wu, W.-M., et al., Which is better to multiple rib fractures, surgical treatment or conservative treatment? International Journal of Clinical and Experimental Medicine, 2015. 8(5): p. 7930-7936.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Wu Year 2015 Study Type Randomized control trial Setting Single Centre, China Intervention: Nickel-titanium alloy device Comparator Not described	3 or more rib fractures frame fracture dislocation 50% or higher Serious chest wall deformity or chest cavity active bleeding Flail chest.	Inclusion Male patients Exclusion Other traumatic injuries	Fixation n= 75 Age Mean 52 ± 4.5(SD) Gender 100% male Diag/location Fractues Mean = 8.1 (6-12) Flail chest n = 31 (41.3%) Contusion n = 71 (94.5%) Pneumothorax n= 23 (30.7%) AIS = 4.5 ± 1.7	Control n=89 Age Mean 51 ± 3.1(SD) Gender 100% male Diag/location Fractues Mean = 7.9 (6-11) Flail chest n = 35 (39.3%) Contusion n = 82 (92.1%) Pneumothorax n=28 (31.4%) AIS = 4.3 ± 1.3	Type Nickel-titanium alloy device Timing Not discussed	PRIMARY OUTCOMES Mortality Mechanical ventilation time ICU LOS Hospital LOS Incidence of pneumonia Rate of Tracheotomy SECONDARY OUTCOMES Chest pain condition Difficulty in breathing The chest wall tension Chest wall deformity	2 months

Case Control Studies

Table 69 Study characteristics - Case Control Studies

Khandelwal, G., et al., A prospective single center study to assess the impact of surgical stabilization in patients with rib fracture. International Journal of Surgery, 2011. 9(6): p. 478-481.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Khandelwal Year 2011 Study Type Prospective Case Control Setting Single Centre, India Intervention: Titanium Plates Comparator Usual Care	Intractable pain at day 11 patients having pain scale of 8, 9, and 10 were selected for operative management	Inclusion Age above 18 year All rib fractures Controls = Pain scale 5-7 at day 10 Exclusion Patients having pain scale less than 5 Glasgow Coma Scale of less than seven at presentation	Intervention: N= 32 Age Mean 47.38 20-30 = 3 31-40 = 7 41-50 = 8 >51 = 14 Gender –total group Male: 40 (65.57%) Female: 21 (34.42%) Diag/location Rib fractures mean = 3.34	Control: N= 29 Age Mean 45.30 20-30 = 3 31-40 = 6 41-50 = 11 >51 = 9 Gender Male: 40 (65.57%) Female: 21 (34.42%) Diag/location Rib fractures mean = 3.10	Type Titanium Plate Fixed Day 12	PRIMARY OUTCOMES Pain Return to normal activity SECONDARY OUTCOMES Complication	30 Days
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Majercik, S., et al., Surgical stabilization of severe rib fractures decreases incidence of retained hemothorax and empyema. American Journal of Surgery, 2015. 210(6): p. 1112-1117.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Majercik Year 2015 Study Type Retrospective Case control Setting Single Centre, USA Intervention: Fixation Comparator Usual Care	Not discussed	Inclusion Patients with both rib fractures and flail who had surgical fixation Control group no fixation Exclusion Not discussed	Intervention: N= 137 Age Mean age (SD) 55.9 (16) Gender Male: 110 (80%) Female: 27 (20%) Diag/location Rib fractures mean (SD) = 6.5 (2) ISS = mean (SD) 21 (10.7)	Control: N= 274 Age Mean age (SD) 54.6 (19.5) Gender Male: 218 (80%) Female: 56 (20%) Diag/location Rib fractures mean (SD) = 4.6 (2.3) ISS = mean (SD) 22 (11.8)	Type Matrix Rib Fixed Median 2 day IQR 2-4 Range 0-22	PRIMARY OUTCOMES Retained Haemothorax SECONDARY OUTCOMES Duration ICU stay Duration of hospital stay Complications (Empyema, Readmission)	In hospital
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Majercik, S., et al., In-hospital outcomes and costs of surgical stabilization versus nonoperative management of severe rib fractures. Journal of Trauma and Acute Care Surgery, 2015. 79(4): p. 533-539.							
Study details	Indications	Inclusion/Exclusion	Participant characteristics		Fixation and Timing	Outcomes assessed	Follow up
Author Majercik Year 2015 Study Type Retrospective Case Control Setting Single Centre, USA Intervention: Fixation Comparator Usual Care	Flail chest Severely displace rib fractures without flail Intractable pain In ability to wean from ventilation as defined by failed extubation	Inclusion Patients with both rib fractures and flail who had surgical fixation Control group no fixation Exclusion Not discussed	Intervention: N= 137 Age Median age (IQR) 55 (49-65) Gender Male: 110 (80%) Female: 27 (20%) Diag/location Flail 101(74%) ISS Median (IQR)= 17 (13-29) Lung contusion 72 (53%)	Control: N= 274 Age Median age (IQR) 56 (40-68) Gender Male: 218 (80%) Female: 56 (20%) Diag/location Flail 87 (32%) ISS Median (IQR)= 20 (14-17) Lung contusion 153 (56%)	Type Matrix Rib Fixed Median 2 day IQR 2-4 Range 0-22	PRIMARY OUTCOMES ICU stay Ventilator days SECONDARY OUTCOMES Duration of hospital stay Cost	In hospital
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Pieracci, F.M., et al., A prospective, controlled clinical evaluation of surgical stabilization of severe rib fractures. Journal of Trauma and Acute Care Surgery, 2016. 80(2): p. 187-194.							
Study details	Indications	Inclusion/Exclusion	Participant characteristics		Fixation and Timing	Outcomes assessed	Follow up
Author Pieracci Year 2016 Study Type Prospective Case Control Setting Single Centre, USA Intervention: Plate fixation Comparator Usual Care	Not discussed	Inclusion Age over 18 Flail Chest 3 or more severely displaced ribs 30% volume loss of the hemi thorax Any fracture pattern with failure of medical management Exclusion Identified after 72 hours of injury	Intervention: N = 35 Age Mean age 51 (15.3) Gender Male 30 (85.7%) Female 5 (14.5%) Diagnosis/location Number of ribs Median 9 IQRange (7-11) Flail n = 28 (80%) Bilateral: Unilateral 13:22 ISS = Median 21.5 IQR (17-26) Rib Fracture Score Median 10 IQR (8-22)	Control: N = 35 Age Mean age 50.3 (15.1) Gender Male 24 (68.6%) Female 11 (31.4%) Diagnosis/location Number of ribs Median 8 IQRange (6-11) Flail n = 11 (31.4%) Bilateral: Unilateral 13:22 ISS = Median 22 IQR (17-38) Rib Fracture Score Median 10 IQR (7-24)	Type Titanium plate (Matrix Rib) Timing Mean 2.4 SD (0.78)	PRIMARY OUTCOMES Respiratory Failure Tracheostomy Pneumonia Duration of Mechanical Ventilation Duration of hospital Stay Duration of ICU Stay Mortality SECONDARY OUTCOMES Perioperative complications	In hospital
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Historically controlled studies

Table 70 Study characteristics - Historically controlled studies

Jayle, C.P., et al., Flail chest in polytraumatized patients: surgical fixation using Stracos reduces ventilator time and hospital stay. BioMed Research International, 2015. 2015: p. 624723.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Jayle Year 2014 Study Type Prospective Case Control Setting Single Centre, France Intervention: Titanium Clips (Stracos) Comparator Usual Care	Not discussed	Inclusion Flail chest including bifocal fracture of three or more consecutive ribs in at least two places with or without paradoxical movement Exclusion Aorta hematoma or rupture and patients with tetraplegia or paraplegia and patients having the necessity of neurosurgical treatment.	Intervention: N= 10 Age Mean age (SD) 47.9 (10.6) Gender Male: 8 (80%) Female:2 (20%) Diag/location Rib fractures mean (SD) = 7 (2.4) ISS = 28.6 (8.7) Lung contusion 8 (80%) Pneumothorax 8 (80%)	Control: N= 10 Age Mean age (SD) 50.5 (12.5) Gender Male: 8 (80%) Female: 2 (20%) Diag/location Rib fractures mean (SD) = 6.6 (2.9) ISS = 26.1 (6.2) Lung contusion 8 (80%) Pneumothorax 8 (80%)	Type Titanium Clips (Stracos) Fixed within 48 hours of admission	PRIMARY OUTCOMES Duration of mechanical ventilation Duration ICU stay Duration of hospital stay SECONDARY OUTCOMES FVC FEV1 TLC PEFR Pneumonia	3 months
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Velasquez, M., et al., Operative versus Nonoperative Management of Multiple Rib Fractures. American Surgeon, 2016. 82(5): p. E103-E105.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Velasquez Year 2016 Study Type Case control Setting Single Centre, Columbia Intervention: Strut fixation Comparator Usual Care	Three or more consecutive ribs fractured with respiratory failure Pain control failure deformity of the thoracic wall Flail chest (three or more consecutive ribs fractured in two different segments) Severe rib displacement	Inclusion Adults over 16 with multiple rib fractures and flail chest Exclusion severe closed head injuries (Glasgow Coma Scale < 8) severe cervical spinal cord injury pregnancy open contaminated rib fractures chronic pre-existing cardiopulmonary disease	Intervention: N = 20 Age Median 51.1 IQR 41-63 Diagnosis/location Number of ribs Median 5 IQR 4-8 ISS = Median 9 IQR 9-16 Chest AIS Median 3	Control: N = 20 Age Median 44.5 IQR 36-54.5 Diagnosis/location Number of ribs Median 5 IQR 4-6.5 ISS = Median 13 IQR 9-17 Chest AIS Median 3	Type Metallic Struts Stratos Timing Not discussed	PRIMARY OUTCOMES Duration of Hospital stay Duration of ICU stay Tube duration Mortality Pneumonia Duration of ventilation	In hospital
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Olsen, M.F., et al., Physical function and pain after surgical or conservative management of multiple rib fractures - a follow-up study. Scandinavian Journal of Trauma Resuscitation & Emergency Medicine, 2016. 24.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Olsen Year 2016 Study Type Retrospective Case Control Setting Single Centre, Sweden Intervention: Plate fixation Comparator Usual Care	Flail chest defined as three or more adjacent ribs each fractured in more than one location, with respiratory insufficiency Multiple rib fractures (>4) with respiratory insufficiency and also in need of a thoracotomy due to bleeding or air leakage	Inclusion Not discussed Exclusion In surgical group Deceased n = 4 Comorbidity n = 10 Living too far away n = 6 Not Swedish speaking n = 1 <18 years n = 0 Non-Surgical Group Deceased n = 65 ≤4 or an unspecified rib fractures n= 56 Comorbidity n = 26 Living too far away n = 73 <18 years n = 1 Comorbidity = previous disease or trauma affecting lung function or range of motion in the rib cage (as COPD, rheumatoid arthritis, stroke and major scoliosis)	Intervention: Total= 58 Excluded = 21 Declined = 6 Included n = 31 Age Mean age 58.3 (14.6) range 23–88 Gender Male 22 (71%) Female 9 (29%) Diagnosis/location Number of ribs Median 9 Range (4-20) ISS = Median 22 Range 9-48	Control: Total = 320 Excluded 221 Declined = 69 Included n = 30 Age Mean age 58.4 (16.1) Range 23–87 years Gender Male 25 (83%) Female 5 (17%) Diagnosis/location Number of ribs Median 7 Range (5-13) ISS = Median 18.5 Range 9-45	Type Titanium plate (Matrix Rib) Timing Mean 2.7 Range 0-20 days	PRIMARY OUTCOMES Pain SECONDARY OUTCOMES Spirometry (FEV, PEF) Breathing Movements Range of motion of the thorax Range of movement of the shoulder Physical Function and level of physical activity Kinesiophobia	Surgical Group 1.8 (0.5)Years Non-surgical Group 4.5 (1.2) Years
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Farquhar, J., et al., No benefit to surgical fixation of flail chest injuries compared with modern comprehensive management: results of a retrospective cohort study. Canadian Journal of Surgery, 2016. 59(5): p. 299-303.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Farqhuar Year 2016 Study Type Retrospective Case Control Setting 2 centres, Canada Intervention: Plate and screw fixation Comparator Usual Care	Criteria for flail chest fixation required that the patient have 3 or more adjacent, displaced, segmental rib fractures with evidence of respiratory compromise (functional vital capacity < 20 mL/kg or need for noninvasive or invasive mechanical ventilation), despite adequate analgesia	Inclusion Aged 19 years or older who underwent operative repair of their flail chest and in whom 3 or more fractured ribs were repaired with the MatrixRIB system Exclusion Not discussed	Intervention: N= 19 Age Mean age (SD) 53.1 (14.3) Gender Male:11 (79%) Female: 4 (21%) ISS = 31.4 (9.6) Lung contusion Present 19 (100%) Absent 0 (%)	Control: N= 36 Age Mean age (SD) 56.5 (15.9) Gender Male: 25 (69%) Female: 11 (31) ISS = 29.3 (8.1) Lung contusion Present 21 (58%) Absent 15 (42%)	Type Matrix Rib Plate and screw fixation Fixed 6.3 ± 3.6 days	PRIMARY OUTCOME Duration of mechanical ventilation SECONDARY OUTCOMES VAS Pain VAS Chest Pain Dysopnea Return to employment EQ-5D-5L Length of stay (LOS) in the intensive care unit (ICU), total hospital LOS Rate of pneumonia Mortality Long-term quality of life measures	6 months
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Buyukkarabacak, Y.B., et al., The Usefulness of Early Surgical Rib Stabilization in Flail Chest. Acta chirurgica Belgica, 2015. 115(6): p. 408-413.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Buyukkarabacak Year 2015 Study Type Retrospective Case Control Setting Single Centre Turkey Intervention: Plate fixation Comparator IMV	Large anterolateral flail chest Flail chest area causing paradoxical respiration Flail chest requiring MV Pain and nonunion rib fractures Thoracotomy due to intrathoracic hematoma drainage and decortication	Inclusion Two or more unilateral or bilateral adjacent ribs broken in two or more places and/or Full thickness sternum fractures accompanied by costochondral separation in two or more joints and/or Paradoxical motion caused by flail chest visible to the naked eye Exclusion Not discussed	Intervention: N=10 Age Mean age 58.1(SD) (4.07) Gender Male:10 (100%) Female:0 (0%) Diag/location Flail ribs N = 7.4 median 7 range (5-11) ISS = 75 Lung contusion Mean 3.7 median 3 Range (1-6)	Control: N= 10 Age Mean age 55.2 (SD): (6.07) Gender Male:10 (100%) Female:0 (0%) Diag/location Flail ribs N= 6.7 median 6.5 Range (5-8) ISS = 75 Lung contusion Mean 4 median 5 Range (1-6)	Type Locking plate fixation Time Fixed within 5 days	PRIMARY OUTCOMES Duration of mechanical ventilation Duration ICU stay SECONDARY OUTCOMES Pneumonia Rate of tracheostomy Duration of hospital stay Hospital cost Mortality Complications	In hospital only
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Qiu, M., et al., Potential Benefits of Rib Fracture Fixation in Patients with Flail Chest and Multiple Non-flail Rib Fractures. Indian Journal of Surgery, 2016. 78(6): p. 458-463.									
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics				Type of Fixation and Timing	Outcomes assessed	Follow up
			Flail Chest n = 38		Non flail multiple rib fractures n =124				
Author Qiu Year 2016 Study Type Retrospective control study Setting Single Centre, China Intervention: Plate fixation Comparator Usual Care	Not discussed	Inclusion Flail Chest, fractures of four or more ribs fractured at more than two sites Multiple non-flail rib fracture (number≥2) that are broken in one point but along a straight line, causing the patient to have chronic pain and pulmonary complications Exclusion head trauma Myocardial contusion history of serious cardiac or respiratory disease, thoracic deformity,hepatic dysfunction, chronic renal failure on hemodialysis, cerebral infarction, pregnancy and bleeding diathesis	Intervention: N = 21 Age Mean age 34.7 (12.92) Gender Male 15 (71%) Female 6 (29%) Diagnosis Number of ribs Mean 6.02 (1.25)	Control: N = 17 Age Mean age 35.53 (14.32) Gender Male 12 (71%) Female 5 (29%) Diagnosis Number of ribs Mean 5.88 (1.34)	Intervention: N = 65 Age Mean age 37.62 (11.97) Gender Male 46 (71%) Female 19 (29%) Diagnosis Number of ribs Mean 3.22 (1.15)	Control: N = 59 Age Mean age 36.39 (11.74) Gender Male 42 (71%) Female 17 (29%) Diagnosis Number of ribs Mean 3.84 (1.24)	Type AO steel plates with cancellous screws Timing Not discussed	PRIMARY OUTCOMES Duration of ICU stay Tracheostomy Deformity Mortality Duration of ventilation SECONDARY OUTCOMES Pain VAS Fracture healing Pneumonia Duration of Hospital stay Return to normal activity	6 months
Newcastle Ottawa Assessment		Selection		Comparability				Exposure	
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Doben, A.R., et al., Surgical rib fixation for flail chest deformity improves liberation from mechanical ventilation. Journal of Critical Care, 2014. 29(1): p. 139-143.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Doben Year 2014 Study Type: Retrospective Case Control Setting Single centre, USA Intervention: Plate and screw fixation or intramedullary rods Comparator Usual Care	Failure of standard therapy for spontaneously breathing patients was defined by either progression to invasive mechanical ventilation or the need for supportive noninvasive ventilation. Bedside PF tests were obtained during optimal pain control. Clinical deterioration FEV less than 50% of predicted was assessed for NIV. Patients who progressed to NIV were considered failure of standard therapy. Failure of standard therapy for patients who were MV from admission was defined as an inability to wean from MV.	Inclusion All patients admitted with a diagnosis of flail chest (ICD, Ninth Revision, code 807.4, 3 ribs fractured in ≥2 places) who survived to hospital discharge and with a hospital length of stay (LOS) of 5 days or more between September 2008 and June 2010 were included. Exclusion GCS less than 8. Two octogenarians were excluded as they had do-not-resuscitate and do not-intubate orders and declined surgery	Intervention: N= 10 Age Mean age (SD) 47.4 (14.7) Gender Male: 9 (90%) Female: 1 (10%) Diag/location Mean 8.3 Median 6.5 Range 4-20 Flail ribs = Mean 3.7 Median 4 Range0-10 ISS = 26.3 (9.5)	Control: N= 11 Age Mean age (SD):) 56.6 (16.9) Gender Male: 7 (64%) Female: 4 (46%) Diag/location Mean 9.4 Median 9 Range 6-16 Flail ribs = Mean 4.2 Median 4 Range 0-8 ISS = 35.7 (12.7)	Type Osteosyntheses plates and intramedullary nails. Fixed 2-25 days Median 3	PRIMARY OUTCOMES Duration of mechanical ventilation ICU stay Duration of hospital stay SECONDARY OUTCOMES	6 months
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Cohort Studies

Table 71 Study characteristics - Cohort studies

Ahmed and Mohyuddin 1995 Management of flail chest injury: internal fixation versus endotracheal intubation and ventilation. J THORAC CARDIOVASC SURG 1995;110:1676-80							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author: Ahmed and Mohyuddin Year: 1995 Study Type Retrospective Case Control Setting 2 centres UAE Intervention Surgical fixation Comparator IMV	Not discussed	Inclusion Flail chest Requiring intubation Haemothorax (10) Major air leak (6) Gross chest wall deformity (6) Operated on for associated orthopedic or abdominal injuries the opportunity was availed to stabilize the chest wall (4) Exclusion Other injury affected outcome	Intervention: N=26 Age Decade n 2 0 3 10 4 8 5 5 6 6 Gender Male:23 (88%) Female:3 (12%) Diag/location Flail ribs N= 5-8 AntLat 4 (15%) PosLat 22 (85%)	Control: N= 38 Age Decade n 2 8 3 12 4 8 5 7 6 3 Gender Male:36 (95%) Female:2 (5%) Diag/location Flail ribs N= 5-8 AntLat 9 (24%) PosLat 29 (76%)	Type Kirshner Wires – fixing only one of the ribs in the flail Time Internal fixation of ribs was done within 12 to 48 hours after admission to the ICU	PRIMARY OUTCOMES Duration of mechanical ventilation Duration of ICU stay SECONDARY OUTCOMES Chest infection Rate of tracheostomy Mortality Barotrauma Septicemia Chest deformity (Mild moderate severe) Peri-operative Complications	3-9 Months
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Althausen, P. L. Shannon, S. Watts, C. Thomas, K. Bain, M. A. Coll, D. O'Mara, T. J. Bray, T. J. Early surgical stabilization of flail chest with locked plate fixation Journal of Orthopaedic Trauma 2011							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Althausen, Year : 2011 Study Type Retrospective Case-Control Setting Single centre, USA Intervention: Plate fixation Comparator Usual Care	Non-intubated patients with respiratory failure despite continuous epidural anaesthesia and pulmonary secretion clearance Extensive anterolateral flail chest and progressive displacement of fractured ribs, intubated Flail chest who failed to wean from the ventilator Flail chest who required a thoracotomy due to associated intrathoracic injury	Inclusion Patients aged 19–65 years who presented with the diagnosis of flail chest Patients with a visible flail segment or lung herniation. Only patients with a supplemental O2 requirement were considered for surgical intervention. Exclusion Severe spinal cord injury (loss of diaphragm control), GCS ,8, ICP monitoring, ARDS, active preexisting infection, preexisting cardiac or pulmonary conditions, and pregnant women.	Intervention: N= 22 Age Mean age 47.7 Gender Male:17 (77%) Female:5 (23%) Diag/location Flail ribs mean = 5.9 ISS = 25.1 Lung Contusion Grade 1.72	Control: N= 28 Age Mean age 50.8 Gender Male:23 (79%) Female:6 (21%) Diag/location Flail ribs mean= 7.3 ISS = 24.3 Lung Contusion Grade 1.65	Type Locked plate fixation Time days Fixed at mean 2.3 days Range 1-5	PRIMARY OUTCOMES Duration of mechanical ventilation Duration of ICU stay Duration of hospital stay SECONDARY OUTCOMES Pneumonia Rate of failed extubation Rate of tracheostomy Home O2 Hardware complications Wound infection Non union	17.84 (4.51) months Range 13-22 months
Newcastle Ottawa Quality Assessment							
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Defreest L, Tafen M, Bhakta A, et al. Open reduction and internal fixation of rib fractures in polytrauma patients with flail chest. American Journal of Surgery. 2016; 211: 761-7.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author DeFreest Year 2016 Study Type Retrospective Case Control Setting Single centre[78], USA Intervention: Plate and screw fixation Comparator Usual Care	There was no formal protocol for surgical management of flail chest. In general, all patients chosen for fixation had failure to wean from the ventilator, intractable pain after optimal medical therapy, or failure of conservative management requiring intubation or noninvasive positive pressure ventilation. Fractures occurring in the 1st, 2nd, 11th, and 12th ribs or paravertebral were not plated.	Inclusion Age >=17 January 1, 2008-October 2014 ISS >=16 “Flail Chest” Exclusion Not discussed	Intervention: N= 41 Age Mean age (Range) 50.8 (19-80) Gender Male: 36 (88%) Female: 5 (22%) Diag/location 11.2 (6-19) ISS = 27.5 (16-48) Lung contusion 73% Pneumothorax 85%	Control: N= 45 Age Mean age (Range):56.3 (2-89) Gender Male: 39 (87%) Female: 6 (13%) Diag/location 10.6 (6-23) ISS = 29.3 (16-66) Lung contusion 71% Pneumothorax 87%	Type Plate fixation Fixed at No timings given	PRIMARY OUTCOMES Duration of hospital stay Duration of mechanical ventilation ICU stay SECONDARY OUTCOMES Mortality Rate of Tracheostomy Pneumonia ARDS	In hospital only
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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De Moya, M., et al., Pain as an indication for rib fixation: A bi-institutional pilot study. Journal of Trauma - Injury, Infection and Critical Care, 2011. 71(6): p. 1750-1754.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristic		Type of Fixation and Timing	Outcomes assessed	Follow up
Author De Moya Year 2011 Study Type Retrospective Case Control Setting Two centres, USA Intervention: Plate and screw fixation Comparator Usual Care	Painful rib fractures, and in addition to pain the indications for rib fixation were if a patient had more than two severely displaced rib fractures with unrelenting pain and worsening respiratory function, the option of rib fixation was offered Flail chest with ongoing respiratory compromise (in 10 patients, 62.5%) Major chest wall deformity (in 2 patients,12.5%) Pain and respiratory compromise with worsening oxygenation requiring intubation (in 1 patient, 6.3%) Thoracotomy for another reason (in 3 patients, 18.7%).	Inclusion Not discussed Exclusion Not discussed	Intervention: N= 16 Age Mean age (SD) 45 (16) Gender Male:14 (88%) Female: 2 (12%) Diag/location Number of fractured ribs: 8 (4) Flail ribs N = 9 (56%) Bilateral : Unilateral 5:11 ISS = 24 (7) Lung contusion 2.5 (1.4) Pneumothorax 12 (75%)	Control: N= 32 Age Mean age (SD):47 (14) Gender Male: 26 (81%) Female:6 (19%) Diag/location Number of fractured ribs: 8 (3) Flail ribs N= 11(36%) Bilateral : Unilateral 12:20 ISS = 25 (9) Lung contusion 2.1 (1.4) Pneumothorax 22 (69%)	Type Plate fixation Fixed Mean 5 days Range 1-10 days	PRIMARY OUTCOMES Narcotics Use SECONDARY OUTCOMES Duration of mechanical ventilation Duration ICU stay Pneumonia Respiratory complications (empyema, lobar collapse/atelectasis, persistent pulmonary effusion, pulmonary embolism, and retained hemothorax) Duration of hospital stay	In hospital only
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Galan, G., et al., BLUNT CHEST INJURIES IN 1696 PATIENTS. European Journal of Cardio-Thoracic Surgery, 1992. 6(6): p. 284-287.						
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes assessed	Follow up
Author Galan Year 1992 Study Type Retrospective Cohort Setting Single Centre, Spain Intervention: Steel struts	Not discussed	Inclusion Not discussed Exclusion Not discussed	Fixation N = 29	Type Strut fixation Timing Not discussed	PRIMARY OUTCOMES Mortality	

Granhed, H.P. and D. Pazooki, A feasibility study of 60 consecutive patients operated for unstable thoracic cage. J Trauma Manag Outcomes, 2014. 8(1): p. 20							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Granhed Year 2014 Study Type Prospective Case Control Setting Single Centre, Sweden Intervention: Locking plates and intramedullary splints Comparator Usual Care	Flail segment Respiratory insufficiency and pain with multiple rib fractures (n= 6) Thoracotomy for another reason (n=22) Unstable thoracic cage with flail or multiple rib fractures (n=60)	Inclusion Blunt chest trauma with rib fractures impaired saturation in spite of oxygen administration and suffering from severe pain Exclusion Not discussed	Fixation N = 60 Age Mean age 57 (range 19-86) Gender Male:44 (73%) Female:16 (27%) Diag/location Rib fractures mean = 6.3 Flail = 56 Rib fractures = 4 Bilateral :unilateral 1:59 ISS = 21.7 (10.8)	Control N = 762 ISS = 30.9 (13.3)	Type Matrix rib fixation titanium plates, cerclage wires, IM fixation Timing Median 4 days Range 1-59	PRIMARY OUTCOMES Duration of mechanical ventilation Respiratory Infection Re-operation rate Mortality SECONDARY OUTCOMES Hospital costs Complications	In hospital
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Nirula, R., et al., Rib fracture stabilization in patients sustaining blunt chest injury. American Surgeon, 2006. 72(4): p. 307-309.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Nirula Year 2006 Study Type Retrospective Case Control Setting Single Centre, USA Intervention: Struts plus wire or suture Comparator Usual Care	Severe flail chest Pain (16.7%). Bleeding (6.7%), Inability to wean from the ventilator (6.7%).	Inclusion Not discussed Exclusion Not discussed	Intervention: N= 30 Age Mean age 51.8 Diag/location Flail = 15 (50%) ISS = 25.7	Control: N= 30 Age Mean age 50.4 Diag/location Flail 9(30%) ISS = 27.5	Type Struts plus wire or suture Timing Mean 2.7 Range 0-20 days	PRIMARY OUTCOMES Duration of mechanical ventilation ICU stay Duration of hospital stay SECONDARY OUTCOMES	In hospital
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Muhm, M., et al., Severe trauma of the chest wall: surgical rib stabilisation versus non-operative treatment. European Journal of Trauma and Emergency Surgery, 2013. 39(3): p. 257-265.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Fixation and Timing	Outcomes assessed	Follow up
Author Muhm Year 2013 Study Type Retrospective Case Control Setting Single Centre, Germany Intervention: Plate fixation Comparator Usual Care	Thoracotomy because of associated thoracic injuries Flail chest and uni- or bilateral serial rib fractures with respiratory failure and deteriorating pulmonary function (with or without pulmonary contusion) Massive dislocations of fractured ribs and irritation of underlying organs, e.g. lung, liver or spleen, and consecutive pulmonary affection, e.g. pneumo-, haemo- or serothorax	Inclusion Not discussed Exclusion Not discussed	Intervention: N= 21 Age Mean age 58.7 Median 10.6 Range 36-78 Gender Male: 15 (71%) Female: 6 (29%) Diag/location Flail = 15 (71%) Ribs N = Mean 9.2 SD(3.8) Median 8 Range 3-18 Bilateral : Unilateral 6:15 (29%:71%) ISS = Mean 36.1 SD(8.7) Median 29 Range 10-66 Lung contusion Mild 3 (14%) Moderate 10 (48%) Severe 8 (38%) Pneumothorax 16 (76%)	Control: N= 23 Age Mean age 54 Median 55 Range 22-80 Gender Male: 18 (78%) Female: 5 (22%) Diag/location Flail 11(48%) Ribs N = Mean 7.3 SD(3.2) Median 7 Range 3-18 Bilateral : Unilateral 6:17 (26%:74%) ISS = Mean 36 SD(10.5) Median 34 Range 17-59 Lung contusion Mild 2 (9%) Moderate 15 (52%) Severe 8 (35%) Pneumothorax 21 (91%)	Type Synthes plates Timing Mean 7.1 SD(4.4) Median 6 Range 1-15	PRIMARY OUTCOMES Duration of mechanical ventilation Duration ICU stay Duration of hospital stay SECONDARY OUTCOMES Mortality Pneumonia Tracheostomy	In hospital
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Pimakhov, V. and O. Belov, Optimization of chest stabilization methods for acute respiratory distress-syndrome prophylaxy and treatment in patients with craniothoracic trauma. Interactive Cardiovascular and Thoracic Surgery, 2014. 18: p. S60.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Pimakhov Year 2014 Study Type Retrospective Control Study (Conference Abstract) Setting Single Centre, Ukraine Intervention: Intramedualllry osteosynthesis and Extra pleural technique Comparator Internal pneumatic stabilization	Not discussed	Inclusion Craniothoracic trauma rib fracture of 3 and 4 degree according to the Oxford classification Exclusion Not discussed	Intervention: Intramedullary fixation n = 6 Extra-pleural fixation n =15 Total Group ISS Median 20.2 SD(2.82) (10 to 34)	Control: N = 25	Type Intramedullary fixation Or Extra pleural fixation Timing Not discussed	PRIMARY OUTCOMES Mortality SECONDARY OUTCOMES ARDS	3 months 6 months

Pimakhov, V., Assessmentof long-term outcome of different rib fracture stabilization methods for patients with craniothoracic trauma. Interactive Cardiovascular and Thoracic Surgery. Conference: 23rd European Conference on General Thoracic Surgery. Lisbon Portugal. Conference Start, 2015. 21(no pagination).							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Pimakhov Year 2015 Study Type Retrospective Control Study (Conference Abstract Only) Setting Single Centre, Ukraine Intervention: Intramedualllry osteosynthesis and Extra pleural technique Comparator Internal pneumatic stabilization	Not discussed	Inclusion Craniothoracic trauma Exclusion Not discussed	Intervention: Intramedullary fixation n =11 Extrapleural fixation n =16 Total Group ISS Median 19.1 SD(6.2)	Control: N = 30	Type Intramedullary fixation Or Extra pleural fixation Timing Not discussed	PRIMARY OUTCOMES HRQOL SECONDARY OUTCOMES Callous formation Tiffino Index	1 month 3 months 6 months

Solberg, B.D., et al., Treatment of chest wall implosion injuries without thoracotomy: Technique and clinical outcomes. Journal of Trauma - Injury, Infection and Critical Care, 2009. 67(1): p. 8-13.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Solberg Year 2009 Study Type Retrospective Case Control Setting Single Centre, USA Intervention: Plate fixation Comparator Usual Care	Not discussed	Inclusion high-energy blunt chest wall trauma with side impact mechanism and radiographically documented supero-lateral implosion deformity of the thoracic cage Exclusion displaced anterior flail chest injuries less than 12 months clinical follow-up severe closed head injury with initial presenting Glasgow Coma Scale score of 10 or less severe head injury requiring prolonged mechanical ventilation and tracheostomy	Intervention: N= 9 Age Mean age 38.8 (16.7) Gender Male 6 female 3 ISS = Mean 24.9 SD (6.5)	Control: N = 7 Age Mean age 41.1 (13) Gender Male 5 Female 2 ISS = Mean 24.8 SD (6.2) Range 9-45	Type Titanium plate (Matrix Rib) Timing Mean 0.75 days Range 0.25- 1.75 days	PRIMARY OUTCOMES Duration of mechanical ventilation Duration of ICU Stay SECONDARY OUTCOMES Constant Score Chest Tube Duration	Operative 16 months (6.7) Non-operative 12 months (2.3) 3 and 6 weeks and every 3 months thereafter.
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Taylor, B.C., et al., Clinical Outcomes of Surgical Stabilization of Flail Chest Injury. Journal of the American Academy of Orthopaedic Surgeons, 2016. 24(8): p. 575-580.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Taylor Year 2016 Study Type Retrospective Case Control Setting Single Centre, USA Intervention: Plate fixation Comparator Usual Care	Not discussed	Inclusion Flail chest Exclusion Not discussed	Intervention: N = 88 Age Mean age 54.2 (16.8) Range 18-90 Gender Male 59 (67%) Female 29 (43%) Diagnosis/location Number of ribs Mean 9 (3.8) Range (3-19) ISS Mean = 24.16 (11.3) (Range 9-51)	Control: N = 88 Age Mean age 53.8 (18.3)Range 19-95 Gender Male 69 (78.4%) Female 19 (21.6%) Diagnosis/location Number of ribs Mean 8.4 (4.3) Range (3-24) ISS Mean = 29.46 (12.7) (Range 10-75)	Type Titanium plate (Matrix Rib) or Zimmer Biomet Sternalok Blu Timing Mean 4.6 Range 1-13 days	PRIMARY OUTCOMES Hospital length of stay SECONDARY OUTCOMES Intensive care length of stay Ventilator status Ventilator requirement Thoracostomy tube Pneumonia Tracheostomy Mortality Comparisons between those with pulmonary contusion and those without	3 months 6 months
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Voggenreiter, G., et al., Operative chest wall stabilization in flail chest--outcomes of patients with or without pulmonary contusion. J Am Coll Surg, 1998. 187(2): p. 130-8.									
Study details	Indications	Inclusion/Exclusion	Participant characteristics				Fixation and Timing	Outcomes assessed	Follow up
Author Voggenreiter Year 1998 Study Type Retrospective Case-Control Setting Single Centre, Germany Intervention: Strut fixation	Flail chest with indication for thoracotomy from intrathoracic injury ("stabilization on retreat") (n6). Flail chest without pulmonary contusion but with respiratory insufficiency (n9). Paradoxical movement of a chest wall segment in the weaning period from the respirator (n3). Severe deformity of the chest wall (stove-in chest) (n2).	Inclusion Not discussed Exclusion Not discussed	Group 1: flail chest without pulmonary contusion (n =10) Age Mean (SD) age 55.2 (8.4) ISS = 31 (7)	Group 2: flail chest with pulmonary contusion (n=10) Age Mean (SD) age 50.4 (15.5) ISS = 37 (7.9)	Group 3: flail chest without pulmonary contusion and without operative chest wall stabilization (n=8) Age Mean (SD) age 44.2 (19.1) ISS = 36.3(12.3)	Group 4: flail chest with pulmonary contusion and without operative chest wall stabilization (n=4) Age Mean (SD) age 47.8 (26.5) ISS = 47.8 (26.5)	Type Strut fixation Timing Usually within 48 hours Max 7 days	PRIMARY OUTCOMES Duration of mechanical ventilation SECONDARY OUTCOMES Pneumonia Sepsis ARDS Mortality	In hospital
Newcastle Ottawa Quality Assessment		Selection	Comparability				Exposure		
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Wada, T., et al., Effectiveness of surgical rib fixation on prolonged mechanical ventilation in patients with traumatic rib fractures: A propensity score-matched analysis. Journal of Critical Care, 2015. 30(6): p. 1227-1231.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Fixation and Timing	Outcomes assessed	Follow up
Author Wada Year 2015 Study Type Retrospective Case Control Propensity score matched Setting Multicentre, Japan Intervention: Any surgical fixation Comparator Usual Care	Not discussed	Inclusion injuries including rib fractures (S223, S224, or S225) and admission to hospitals where surgical fixation for rib fractures was performed The surgical group contained patients who received surgical rib fixation within 10 days of hospital admission Exclusion Patients who died within 10 days of hospital admission Patients younger than 20 years	Intervention: N = 84 Age <60 = 36 (42.9%) 60-74 = 27 (32.1) >75 = 21 (25%) Gender Male 39 (70.2%) Female 25 (29.8%) Diagnosis/location Flail = 10 (11.9%)	Control: N = 336 Age <60 = 126 (37.5%) 60-74 = 121 (36%) >75 = 89 (26.5%) Gender Male 225 (67%) Female 111 (33%) Diagnosis/location Flail = 48 (14.3)	Type Any surgical fixation Timing Within 10 days	PRIMARY OUTCOMES Prolonged mechanical ventilation for 5 or more days or death within 28 days death within 28 days tracheotomy or death within 28 days length of hospital stay SECONDARY OUTCOMES	28 days
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Xu, J.Q., et al., Better short-term efficacy of treating severe flail chest with internal fixation surgery compared with conservative treatments. European Journal of Medical Research, 2015. 24.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Xu Year 2015 Study Type Retrospective case control Setting Single Centre, China Intervention: Plate fixation Comparator Usual Care	Not discussed	Inclusion Four or more rib fractures; Abnormalities of the thoracic cage and paradoxical breathing Requirement for mechanical ventilation during treatment Exclusion Age <14 or >75 years Severe cranio-cerebral trauma [GCS] score <8 No spontaneous breath after high-level spinal cord injury History of chronic cardiopulmonary disease.	Intervention: N = 17 Age Mean age 36.4(13.5) Gender Male 12 (70.5%) Female 5 (29.5%) Diagnosis/location Number of ribs Mean 6.8 (2.1) ISS=Mean 21.8 (7.8) APACHE II admission Mean = 13.7 (5.5)	Control: N = 15 Age Mean age 39 (11.6) Gender Male 12 (80%) Female 3 (20%) Diagnosis/location Number of ribs Mean 7.4 (1.6) ISS = Mean 24 (8) APACHE II admission Mean = 15.3 (7.2)	Type Titanium plate Timing Not discussed	PRIMARY OUTCOMES Mechanical ventilation time intensive care unit (ICU) stay time pulmonary infection therapeutic time of anti-biotics acute physiology and chronic health evaluation II (APACHE II) score 7 and 14 days after trauma rate of tracheostomy rate of endotracheal re-intubation SECONDARY OUTCOMES	14 days
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Zhang, X.F., et al., Management of patients with flail chest by surgical fixation using claw-type titanium plate. Journal of Cardiothoracic Surgery, 2015. 10.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes assessed	Follow up
Author Zhang Year 2015 Study Type Retrospective case control Setting Single Centre, China Intervention: Plate fixation Comparator Usual Care	Flail chest with ≥ 3 consecutive rib fractures in ≥ 2 locations Severe paradoxical breathing	Inclusion Not discussed Exclusion age <20 years or > 80 years; severe associated trauma to head or spinal cord; severe extra-thoracic injuries that was like to cause death during the follow-up pregnancy	Intervention: N = 23 Age Mean age 57.8 (12) Gender Male 16 (69.5%) Female 7 (30.4%) Diagnosis/location Number of ribs Mean 7.8 (1.5) Anterolateral flail 7(30.4%) Posterolateral flail 16 (69.6%) Bilateral: Unilateral 2:21 (87%:13%) Contusion Score1.24	Control: N = 29 Age Mean age 59.5 (9.9) Gender Male 21 (72%) Female 8 (18%) Diagnosis/location Number of ribs Mean 7.4 (1.7) Anterolateral flail 10 (34.5%) Posterolateral flail 19 (65.5%) Bilateral: Unilateral 3:26 (10.3%:89.7%) Contusion Score1.21	Type Steel claw plate Timing Within 10 days	PRIMARY OUTCOMES Mechanical ventilation time Mechanical ventilation Intensive care unit (ICU) stay time pulmonary infection Mortality Chest deformity SECONDARY OUTCOMES	14 days
Newcastle Ottawa Quality Assessment		Selection		Comparability		Exposure	
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Zhang, Y. et al., Comparison of surgical fixation and nonsurgical management of flail chest and pulmonary contusion. American Journal of Emergency Medicine, 2015. 33(7): p. 937-40.								
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics			Type of Fixation and Timing	Outcomes assessed	Follow up
Author Zhang Year 2015 Study Type Retrospective Case control Setting Single Centre, China Intervention: Plate fixation Early fixation ≤7days Late fixation >7days Comparator Usual Care	Not discussed	Inclusion Flail Chest and pulmonary contusion age older than 16 multiple rib fractures and pulmonary contusion confirmed by CT paradoxical movement in the physical exam requirement for mechanical ventilation Exclusion age older than 80 or younger than 16 combined spine injury or other fracture that precluded a proper surgical position combined severe brain injury that caused prolonged DMV because of central nerve system damage other conditions that exclude the use of general anaesthesia uncorrected coagulopathy disorder that would exclude the patient from surgery.	Early Fixation N = 12 Age Median (IQR) 38 (31.25-47) Gender Male 9 (75%) Female 3 (25%) Diagnosis/location Number of ribs Median 11 IQR (7.75-16.25) ISS Median (IQR) 38 (34-38) Pneumothorax (total fixation) = 75% APACHE II Median (IQR) 7 (5-14)	Late fixation N = 12 Age Median (IQR) 45.5 (41-61.5) Gender Male 10 (83.3%) Female 2 (16.7%) Diagnosis/location Number of ribs Median 12 IQR (8.25-15) ISS Median (IQR) 42 (35-43) Pneumothorax (total fixation) =75% APACHE II Median (IQR) 7 (4.25-15.5)	Control: N = 15 Age Median (IQR) 47 (35-55) Gender Male 14 (93.3%) Female 1 (6.7%) Diagnosis/location Number of ribs Median 11 IQR (7-16) ISS Median (IQR) 38 (35-43) Pneumothorax = 9 (60%) APACHE II Median (IQR) 9 (6-19)	Type Steel claw plate Timing Within 10 days	PRIMARY OUTCOMES Mechanical ventilation time Mechanical ventilation Duration ICU stay Mortality SECONDARY OUTCOMES Antibiotic use RBC trans Plasma trans Expense Tracheotomy Pleural effusion Pain Visual Analogue DMV, ICULOS, HLOS incision infection incidence of ventilator associated pneu-monia (VAP)	In hospital
Newcastle Ottawa Quality Assessment		Selection		Comparability			Exposure	
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Case Series

Table 72 Study Characteristics - Case Series

Borrelly, J. and M.H. Aazami, New insights into the pathophysiology of flail segment: The implications of anterior serratus muscle in parietal failure. European Journal of Cardio-thoracic Surgery, 2005. 28(5): p. 742-749.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Borrelly Year 2005 Study Type Retrospective Case Series Setting Single Centre, Iran Intervention: Kirschner wires and Judet staples sliding-staples-struts	Retreat indication (RIn) was defined if threatened visceral lesions were associated, where surgical fixation was carried out at the end of the operation Primary parietal indication (PPIn) was considered if surgical fixation was attempted to restore parietal mechanical integrity within the first 2 days after initial trauma; Secondary parietal indication (SPIn) was considered if surgical fixation was attempted to offer a better respiratory or functional outcome in view of parenchymal lesions, impossibility of pursuing conservative therapy, shrinkage of chest wall, secondary respiratory deterioration or to shorten the time on the ventilator after the first 3 days following initial trauma.	Inclusion Surgical reduction/fixation of a flail segment (multi-focal fractures of at least three consecutive ribs regardless of clinical evidence for paradoxical motion or initial degree of deformation) Exclusion Not discussed	Early Fixation N = 127 Age Mean (SD) 56 (14.4) Range (20-84) Gender Male 108 (85%) Female 19 (15%) Diagnosis/location Mean number of ribs 6 (0.35) Anterolateral 38 (30%) Posterolateral 89 (70%) Pneumothorax = 60% Haemothorax 93%	Type Kirschner wires and Judet staples n = 36 (30%) Sliding-staples-struts 91 (70%) Timing Within 10 days	PRIMARY OUTCOMES Mechanical ventilation time Mechanical ventilation Mortality SECONDARY OUTCOMES Tracheotomy Wound infection Return to work	In hospital	1 Yes 2 Yes 3 Yes 4 Yes 5 Yes 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Bottlang, M., et al., Surgical stabilization of flail chest injuries with MatrixRIB implants: A prospective observational study. Injury, 2013. 44(2): p. 232-238.							
Study details	Indications	Inclusion/Exclusion Criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Bottlang Year 2012 Study Type Prospective Case Series Setting Single Centre, USA Intervention: Intramedullary Splint Plate fixation	Flail chest injury with three or more consecutive ribs fractures in at least two locations	Inclusion Flail Chest Exclusion age <21 years or >80 years, pregnancy severe closed head injury severe spinal cord injury associated extra-thoracic injuries that made survival during the follow-up period unlikely	Fixation N = 20 Age Mean (SD) 50.7 Range (29-70) Diagnosis/location Mean 11.8 (Range 5-21) Anterolateral 6 (32%) Posterolateral 9 (47%) Lateral 4 (21%) ISS Mean 28 Range (16-66) Contusion Mean 17% Range (0-56%) Pneumothorax = 14 (74%)	Type Intramedullary Splint Plate fixation Timing 5.3 days (range 1–17 days) from admission	PRIMARY OUTCOMES Mechanical ventilation time Mechanical ventilation Mortality RAND-36 SECONDARY OUTCOMES Tracheotomy Wound infection Return to work Epidural use Spirometry	6 months	1 Yes 2 Yes 3 Yes 4 Yes 5 No 6 Yes 7 Yes 8 Yes 9 Yes 10 NA Overall appraisal: Include

Campbell N, Conaglen P, Martin K and Antippa P. Surgical stabilization of rib fractures using inion OTPS wraps-techniques and quality of life follow-up. Journal of Trauma - Injury, Infection and Critical Care. 2009; 67: 596-601.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Campbell Year 2009 Study Type Retrospective Case Series Setting Single Centre, Australia Intervention: Inion OTPS Wraps	level of pain degree of chest wall instability respiratory distress thoracotomy for other reasons (whereby fractures may be stabilized on retreat)	Inclusion Not discussed Exclusion irreversible severe head injury active local or systemic sepsis hemodynamic instability	Fixation N = 32 Age Median 53 years IQR (40-64) Gender Male = 23 (72%) Female = 9 (28%) Diagnosis/location Median number of ribs 3 (IQR 2-4) ISS Mean(SD) 26 (9.5) Contusion Mean 14 Range (47%) Pneumothorax = 32 (100%)	Type Inion OTPS Wraps Timing Median 5 days (IQR 3-7 days)	PRIMARY OUTCOMES Mechanical ventilation time Mechanical ventilation Duration in ICU Duration of hospital stay Mortality SECONDARY OUTCOMES Wound infection Return to work Pain Chest Tightness Subjective Dysopnea Return to Work Return to Activities AQOL	1039 Day (480)	1 Yes 2 Yes 3 Unclear 4 Yes 5 Unclear 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Caragounis, E.C., et al., Surgical treatment of multiple rib fractures and flail chest in trauma: a one-year follow-up study. World Journal of Emergency Surgery, 2016. 11.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Caragounis Year 2016 Study Type Prospective Case Series Setting Single Centre, Sweden Intervention: Plate fixation	Blunt trauma Flail chest defined as three or more adjacent ribs each fractured in more than one location with respiratory insufficiency Multiple rib fractures (>4) with respiratory insufficiency in need of a thoracotomy due to bleeding or air leakage. Respiratory insufficiency was defined as failing arterial oxygenation despite oxygen administration	Inclusion Blunt trauma Exclusion severe head injury and spinal cord injury	Fixation N = 60 54 followed up Age Median 57 (IQR) (20-86) Gender Male 40 (74%) Female 14 (26%) ISS Median 20 (IQR) (9-66)	Type Titanium plate Matrix Rib Timing Within 10 days	PRIMARY OUTCOMES Pain Local discomfort Breathlessness Analgesics EQ-5D-3 L SECONDARY OUTCOMES Spirometry	6 Weeks 3 Months 6 Months 1 Year	1 Yes 2 Yes 3 Yes 4 Yes 5 No 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Chai, X., et al., The clinical application of absorbable intramedullary nail and claw plate on treating multiple rib fractures. Minerva Chirurgica, 2013. 68(4): p. 415-420.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Chai Year 2013 Study Type Retrospective case series Setting Single Centre, China Intervention: Intramedullary fixation	Flail chest defined as multi rib and multiple fractures	Inclusion Not discussed Exclusion Not discussed	Intervention: N = 248 Age Mean age 45.17 Range 19-76 Gender Male 169 (68%) Female 79 (32%) Diagnosis/location Bilateral :Unilateral 185:63 (75%:25%)	Type Absorbable Intramedullary nailing 28 Claw plates 141 Combined 79 Timing Not discussed	PRIMARY OUTCOMES Mortality Pneumonia Metal work removal	6 months – 2 years	1 No 2 Unclear 3 No 4 Unclear 5 Unclear 6 Yes 7 Unclear 8 Unclear 9 Unclear 10 Unclear Overall appraisal: Include

de Palma, A., et al., Chest wall stabilization and reconstruction: Short and long-term results 5 years after the introduction of a new titanium plates system. Journal of Thoracic Disease, 2016. 8(3): p. 490-498. de Palma, A., et al., Chest wall stabilization and reconstruction: Short and long-term results 5 years after the introduction of a new titanium plates system. Journal of Thoracic Disease, 2016. 8(3): p. 490-498.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author De Palma Year 2016 Study Type Retrospective Case Series Including neoplastic cases as well as traumatic Setting Single Centre, Italy Intervention: Plate fixation	Not discussed	Inclusion Patients with flail chest Multiple rib fracture Exclusion Not discussed	Fixation N = 10 5 flail 5 multiple rib fractures Demographics unable to distinguish from neoplastic cases	Type Titanium plate Synthes Matrix Rib Timing Not discussed	PRIMARY OUTCOMES Duration ICU stay Duration hospital stay 30 day mortality SECONDARY OUTCOMES Spirometry – unable to distinguish form neoplastic cases SF 12 – unable to distinguish form neoplastic cases Pain VAS – unable to distinguish form neoplastic cases	6 Weeks 3 Months 6 Months 1 Year	1 Yes 2 Yes 3 Unclear 4 Yes 5 Unclear 6 Yes 7 Yes 8 Yes 9 Yes 10 NA Overall appraisal: Include

Ivancic, A., et al., Initial experience with external thoracic stabilization by the "figure of eight" osteosynthesis in polytraumatized patients with flail chest injury. Collegium antropologicum, 2009. 33(1): p. 51-56.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Ivancic Year 2009 Study Type Prospective Case Series Setting Single Centre, Croatia Intervention: Figure of 8 Osteosynthesis	Flail chest with deteriorating pulmonary function despite aggressive clearance of bronchial secretions and adequate analgesia, requiring IMV and without pulmonary contusion (candidates for early surgical stabilization) intubated patients with previous severe pulmonary contusion and cerebral injuries, in order to reduce the duration of internal pneumatic stabilization when the patient fails to wean from the mechanical ventilation low PaO2/FiO2 quotient which demand internal pneumatic stabilization; oxygen blood saturation drop (SO2%), during the attempt of weaning from IMV	Inclusion Flail Chest Exclusion severe head injury and spinal cord injury	Fixation N = 15 54 followed up Age Mean 52 (SD) (13.69) Range 18-65 Gender Male 11 (73%) Female 4 (27%) Bilateral : Unilateral 5:10 ISS Mean 29.8 Range 20-41	Type Titanium plate Matrix Rib Timing Mean 7.73 days (3.57) Range 3-13	PRIMARY OUTCOMES Duration ICU stay Duration of mechanical ventilation SECONDARY OUTCOMES	In hospital	1 Yes 2 Yes 3 Yes 4 Yes 5 Yes 6 Yes 7 Yes 8 Yes 9 Yes 10 NA Overall appraisal: Include

Lardinois, D., et al., Pulmonary function testing after operative stabilisation of the chest wall for flail chest. European Journal of Cardio-thoracic Surgery, 2001. 20(3): p. 496-501.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Lardinois Year 2001 Study Type Prospective Case Series Setting Single Centre, Switzerland Intervention: Plate fixation	Non-intubated patients with respiratory failure despite continuous peridural analgesia and aggressive clearing of bronchial secretions (n=28) Extended anterolateral flail chest and progressive dislocation of the fractured ribs (n=15) Intubated patients who did not require prolonged intubation in the absence of severe pulmonary contusion or cerebral injuries in order to reduce the use of mechanical ventilation when the patient failed to wean (n=21) Patients who required tracheostomy due to associated intrathoracic injury (n=2)	Inclusion Internal fixation of flail chest Exclusion Not discussed	Fixation N = 66 Age Mean 52.6 (Range 21-82 years) Gender Male 56 (85%) Female 10 (15%) Diagnosis/location Mean number of ribs 6 (Range 4-11) Bilateral:Unilateral 6:60 Pneumothorax = 57 (86%) Haemothorax = 62 (94%) Lung contusion = 53 (80%)	Type Synthes standard 3.5mm plates Timing Median 2.8 days Range (0-21)	PRIMARY OUTCOMES Spirometry ABG SECONDARY OUTCOMES Mechanical ventilation time Mechanical ventilation Duration in ICU Duration of hospital stay 30 day Mortality Post-operative Complications	6 Months	1 Yes 2 Yes 3 Yes 4 Yes 5 Unclear 6 Yes 7 Yes 8 Yes 9 Yes 10 NA Overall appraisal: Include

Majercik, S., et al., Long-term patient outcomes after surgical stabilization of rib fractures. American Journal of Surgery, 2014. 208(1): p. 88-92.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Majercik Year 2014 Study Type Retrospective Case Series Setting Single Centre, USA Intervention: Plate fixation	radiographic or clinical flail chest fracture displacement chest wall deformity pain inability to wean from mechanical ventilation	Inclusion Internal fixation of flail chest Exclusion Not discussed	Fixation N = 101 only 50 available for follow up Age Mean (SD) 57 (2 years) Gender Male 37 (74%) Female 13 (16%) Diagnosis/location Mean number of ribs 6.3 (0.3) ISS Mean 22 (1.7)	Type Matrix rib Titanium plates Timing Mean 3.4 (0.5)	PRIMARY OUTCOMES incidence of chronic pain chest wall deformity, Satisfaction Return to work SECONDARY OUTCOMES Mechanical ventilation time Mechanical ventilation Duration in ICU Duration of hospital stay Post-operative Complications Pneumonia Wound infection Pulmonary Embolism Discharge destination	Mean 16 (1) Months	1 Yes 2 Yes 3 Yes 4 Yes 5 No 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Marasco, S., et al., Pilot study of operative fixation of fractured ribs in patients with flail chest. ANZ Journal of Surgery, 2009. 79(11): p. 804-808.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Marasco Year 2009 Study Type Prospective Case Series Setting Single Centre, Austrailia Intervention: Plate fixation	multiple segmentally fractured ribs, leading to paradoxical chest wall motion extubated but requiring increasing non-invasive ventilatory support (three patients) requiring invasive mechanical ventilation without any improvement in ventilatory parameters over a number of days and/or failed attempt to wean invasive mechanical ventilation (10 patients)	Inclusion multiple segmentally fractured ribs, leading to paradoxical chest wall motion Exclusion Not discussed	Fixation N = 13 Age Mean (SD) 59.3 (13.4 years) Gender Male 6 (60%) Female 4 (40%) ISS Mean 33.1 (8) APACHE II 13.15 (7.06) predicted risk of death = 10.24% APACHE III 43.54 (19.8) predicted risk of death = 6.9%	Type absorbable polylactide plate and screw system (Inion OTPS) Timing Not discussed	PRIMARY OUTCOMES Mechanical ventilation time Mechanical ventilation Duration in ICU Duration of hospital stay Mortality SECONDARY OUTCOMES	Mean 16.1 Months	1 Yes 2 Unclear 3 Yes 4 Yes 5 Yes 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Marasco, S., et al., Analysis of bone healing in flail chest injury: Do we need to fix both fractures per rib? Journal of Trauma and Acute Care Surgery, 2014. 77(3): p. 452-458.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Marasco Year 2014 Study Type Case SeriesRetropective Setting Single Centre, Australia Intervention: Plate fixation	Flail chest	Inclusion invasive and non invasive ventilator-dependent patients with a flail segment Exclusion significant head injury (which would dictate their extubation time), sepsis,or spinal injury precluding lateral positioning on the operating table	Fixation N = 60 52 followed up Age Mean (SD) 55 (18 years) Gender Male 46 (77%) Female 14 (23%) Diagnosis/location Mean number of ribs 10 (4.3) Bilateral:Unilateral 22:38 Posterior n=22 Lateral n=43 Anterior n=46 ISS Mean 32 (7.2)	Type absorbable polylactide plate and screw system (Inion OTPS) Timing Median 5 days (range 2-21)	PRIMARY OUTCOMES CT assessment of healing at 3 months Hard ware failure Deformity SECONDARY OUTCOMES	3 Months	1 Yes 2 Yes 3 Yes 4 Yes 5 No 6 Yes 7 Yes 8 Yes 9 Yes 10 Unclear Overall appraisal: Include

Marasco, S., et al., An assessment of outcomes with intramedullary fixation of fractured ribs. Journal of Cardiothoracic Surgery, 2016. 11.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Marasco Year 2016 Study Type Case Series Retropective Setting Single Centre, Australia Intervention: Plate fixation and intramedullary k wire fixation	Fractures under the scapular is a indication to use Intramedullary fixation	Inclusion Not discussed Exclusion Not discussed	Fixation N = 15 6 = k wire exclusively 9 = combination of both techniques Age Mean (SD) 52 (32-77 years) [After removing patient aged77 who died] Gender Male 14 (93%) Female 1 (7%) Diagnosis/location Median number of ribs 7 (range 4-14)	Type Synthes Titantium Plates and k-wires used singly and in combination Timing Median 5 days (range 2-21)	PRIMARY OUTCOMES CT assessment of healing at 3 months Hard ware failure Deformity SECONDARY OUTCOMES	3 & 6 Months	1 Yes 2 Yes 3 Yes 4 Yes 5 Unclear 6 Yes 7 Unclear 8 Yes 9 Yes 10 NA Overall appraisal: Include

Mayberry, J.C., et al., Absorbable Plates for Rib Fracture Repair: Preliminary Experience. Journal of Trauma - Injury, Infection and Critical Care, 2003. 55(5): p. 835-839.								
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics			Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Mayberry Year 2003 Study Type Retrospective Case Series Setting Single Centre, USA Intervention: Absorbable plates with absorbable suture	Flail chest who are not weaning from mechanical ventilation and who in the opinion of the attending surgeon would benefit from flail chest stabilization Flail = 5	Inclusion Fixation of rib fractures Exclusion Not discussed	N = 10 Age Mean (SD) 44 (15-86 years)			Type Absorbable plates with absorbable suture Timing Flail Median 6 days (range 5-10) Pain and instability Median 7 days (range 3-30)	PRIMARY OUTCOMES Wound infection Mechanical ventilation Return to work SECONDARY OUTCOMES	Mean (SD) 26.3 (27.6) (median 18, range 0-96 months)	1 Yes 2 Unclear 3 Yes 4 Yes 5 Yes 6 Yes 7 Yes 8 Unclear 9 Yes 10 NA Overall appraisal: Include
			Flail n=5 Age Mean 50 (range 44-86) ISS Mean = 24 (range 9-38)	Rib fracture pain instability = 4 Age Mean 44 (range 31-59) ISS Mean = 19 (range 9-32)	Chest wall defect = 1 Age 15 years				

Mayberry, J.C., et al., Long-Term Morbidity, Pain, and Disability after Repair of Severe Chest Wall Injuries. American Surgeon, 2009. 75(5): p. 389-394.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Mayberry Year 2009 Study Type Retrospective Case Series Setting Single Centre, USA Intervention: Plate fixation, cerclage wire and absorbable plates	Flail and Failure to wean from ventilator =18 Intractable pain with displaced rib fractures =15 Chest deformity =5 Lung herniation =3 Thoracotomy for other indications = 5	Inclusion Fixation of rib fractures Exclusion Not discussed	Fixation N = 46 Age Mean (SD) 50 (15-85 years) Gender Male 36 (93%) Female 10 (7%) Diagnosis/location Mean number of ribs (SD) = 7.6 (3.1) (range 3-18) ISS Mean (SD) = 30 (12)	Type Plate fixation, cerclage wire and absorbable plates Timing Mean 7 days (5) (range 0-33)	PRIMARY OUTCOMES McGill Pain questionnaire Rand- 36 SECONDARY OUTCOMES Level daily activity	Mean (SD) 26.3 (27.6) (median 18, range 0-96 months)	1 Yes 2 Yes 3 Yes 4 Unclear 5 Unclear 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Menard, A., et al., Treatment of flail chest with judet struts. Journal of Thoracic and Cardiovascular Surgery, 1983. 86(2): p. 300-305.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Menard Year 1983 Study Type Retrospective Case Series Setting Single Centre, France Intervention: Judet Struts	Flail chest with Paradoxical movement Displacement Tracheostomy Pain Respiratory failure	Inclusion Adult patients with flail chest Exclusion Not discussed	Fixation N = 18 Age Mean 48 (Range 21-72) Gender Male 15 (83%) Female 3 (17%) Location of rib fractures Anterior = 3 Anterolateral = 7 Posterolateral = 7 Not determined = 1	Type Judet struts Timing Within 1 week except 1 which was day 13	PRIMARY OUTCOMES Mortality Duration of mechanical ventilation Intubation time SECONDARY OUTCOMES pneumonia	Maximum 5 months	1 Unclear 2 Unclear 3 Unclear 4 Yes 5 Unclear 6 Yes 7 Yes 8 Yes 9 Yes 10 NA Overall appraisal: Include

Metin, B. and Y.S. Intepe, Operative ease and efficiency of nitinol memory rib plaque on the multiple costa and sternum fractures: Three-year clinical experience. International Journal of Clinical and Experimental Medicine, 2016. 9(6): p. 11510-11517.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Metin Year 2016 Study Type Retrospective Case Series Setting Single Centre, Turkey Intervention: Plate fixation	displaced rib fractures and whose displaced costa ends harmed the pulmonary parenchyma and caused deformity on the thoracic wall underwent the fixation flail chest leading to hemodynamic instability, and on those with hypoxemia finding as the result of their pulse oximetric examinations and ABG (pO2< 90) as well as those likely to be in need of IMV	Inclusion Flail chest, costal or sternal fractures Exclusion Not discussed	Fixation N = 44 Age Mean 57.38 (Range 18-79) Gender Male 38 (86%) Female 6 (14%) Location of rib fracture Flail = 14 (31.81%) Bilateral :unilateral: sternal 9:33:2 (20:75:5)	Type Nitinol memory rib plaque Timing Not discussed	PRIMARY OUTCOMES Pain Duration of hospital stay SECONDARY OUTCOMES mechanical ventilation	Mean 13.2 Months Range 3-36	1 Yes 2 Yes 3 Unclear 4 Unclear 5 Unclear 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Michelitsch, C., et al., Operative stabilisation of chest wall trauma: Single center report of initial management and longterm outcome. Respiration, 2016. 91 (5): p. 456.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Mitchelitsch Year 2016 Study Type Prospective Case Series Conference Abstract Setting Single Centre, Switzerland Intervention: Plate fixation	Not discussed	Inclusion Not discussed Exclusion Not discussed	Fixation N = 23 Age Mean 49.3 (Range 18-79) ISS Mean = 22.9	Type Titanium Plate Matrix Rib Timing Not discussed	PRIMARY OUTCOMES Metal work failure Pain SECONDARY OUTCOMES	27.6 (12–68) months	1 Unclear 2 Unclear 3 Unclear 4 Yes 5 Yes 6 Yes 7 Unclear 8 Unclear 9 Unclear 10 Unclear Overall appraisal: Seek further info

Moslam, K.E., M.S. Badawy, and S.M. Asida, Evaluation of respiratory functions in chest trauma patients treated with thoracic wall stabilization. Egyptian Journal of Chest Diseases and Tuberculosis, 2015. 64(1): p. 213-217.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Moslam Year 2015 Study Type Prospective Case Series Setting Single Centre, Egypt Intervention: Plate fixation	Not discussed	Inclusion Anterolateral only five or more rib fractures in a row, or three or more segmental) rib fractures and confirmed by the presence of a flail segment dyspnea with respiratory rate (RR)>25 cycles/min oxygen saturation (SpO2) 90% or more while breathing 6 L oxygen/min ratio of the partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO2/FiO2) 300 while receiving FiO2 >0.5 in the ICU. Exclusion requiring endotracheal intubation immediately on admission due to severe respiratory distress, hemodynamic instability, encephalopathy, and emergency surgery following admission; non-cooperative patients unable to use face mask; severe acidosis; patients who could not perform pulmonary function test	Fixation N = 40 Age (years) Mean 42.6 SD (9.68) Gender Male, 30 (75%) Female, 10 (25%) Location of fractures Lateral 28 (70%) Anterolateral 12 (30%)	Type Titanium Plate Matrix Rib Timing Not discussed	PRIMARY OUTCOMES Spirometry ABG SECONDARY OUTCOMES Analgesia requirement	3 months	1 Yes 2 Yes 3 Yes 4 Yes 5 Yes 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Mouton, W., et al., Long-term follow-up of patients with operative stabilisation of a flail chest. Thoracic & Cardiovascular Surgeon, 1997. 45(5): p. 242-4.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Mouton Year 1997 Study Type Prospective Case Series Setting Single Centre, Switzerland Intervention: Plate fixation	Flail chest with respiratory insufficiency not responding to epidural anaesthesia	Inclusion patients who did not need prolonged intubation or mechanical ventilation for other reasons Exclusion Not discussed	Fixation N =23 Age mean (years) 52.2 (Range 22-81) Gender Male, 21 (91%) Female, 2 (9%)	Type 3.5mm thick steel plates Timing Not discussed	PRIMARY OUTCOMES 30 day Mortality SECONDARY OUTCOMES Wound infection Pain Return to work Deformity	3 months	1 Yes 2 Yes 3 Yes 4 Yes 5 Yes 6 Yes 7 Yes 8 Unclear 9 Yes 10 NA Overall appraisal: Include

Nickerson, T.P., et al., Use of a 90degree drill and screwdriver for rib fracture stabilization. World journal of surgery, 2015. 39(3): p. 789-793.								
Study details	Indications	Inclusion/Exclusion	Participant characteristics		Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Nickerson Year 2015 Study Type Prospective Case Series Setting Single Centre, USA Intervention: Plate fixation fixation with straight drill and 90 degree drill	chest wall implosion flail chest severely displaced rib fractures early intractable pain	Inclusion Not discussed Exclusion Not discussed	90 degree drill N= 29 Age (years) Median = 61 Range (55-67) Gender Male 20 (69%) Female 9 (31%) Flail 14 48% ISS Median 22 (range 9-41)	Straight drill N = 60 Age (years) Median = 60 Range (55-64) Gender Male 46 (77%) Female 16 (23%) Flail 24 40% ISS Median 16 (range 4-29)	Type Synthes Matrix rib titanium plates Timing Not discussed	PRIMARY OUTCOMES Duration of ICU stay Duration of hospital stay Highest rib stabilised SECONDARY OUTCOMES	In hospital only	1 Yes 2 Yes 3 Yes 4 Unclear 5 Unclear 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Nickerson, T.P., et al., Outcomes of Complete Versus Partial Surgical Stabilization of Flail Chest. World journal of surgery, 2016. 40(1): p. 236-241.								
Study details	Indications	Inclusion/Exclusion	Participant characteristics		Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Nickerson Year 2016 Study Type Prospective Case Series Setting Single Centre, USA Intervention: Synthes Matrix rib titanium plates	Rib fractures with respiratory failure requiring mechanical ventilation Nonintubated patient with deteriorating pulmonary function (with or without pulmonary contusion in association with rib fractures) Non-flail rib fracture(s) with or without significant (C1 rib width) displacement Impalement of ribs into pulmonary parenchyma, other solid organs (e.g.hepatic or splenic parenchyma), or diaphragm Significant and refractory patient pain in association with rib fractures Anticipated nonunion or malunion of rib fracture(s) or flail segment	Inclusion Not discussed Exclusion Not discussed	Complete flail chest N= 23 Age (years) Median = 63 Range (30-85) Gender Male 12 (52%) Female 11 (48%) Flail median number of ribs=3 (range 1-4) ISS Median 20 (range 5-34)	Partial flail chest N = 20 Age (years) Median = 58 Range (34-83) Gender Male 13 (65%) Female 7 (35%) Flail median number of ribs= 4 (range 3-6) ISS Median 17 (range 9-27)	Type Synthes Matrix rib titanium plates Timing Not discussed	PRIMARY OUTCOMES Duration of ICU stay Duration of hospital stay Narcotics use Spirometry SECONDARY OUTCOMES	1 month 3 months 6 months	1 Yes 2 Yes 3 Yes 4 Yes 5 Yes 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Reber, P., et al., Osteosynthesis of the injured chest wall: Use of the AO (Arbeitsgemeinschaft fur Osteosynthese) technique. Scandinavian Journal of Thoracic and Cardiovascular Surgery, 1993. 27(3-4): p. 137-142.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Reber Year 1993 Study Type Retrospective Case Series Setting Single Centre, Switzerland Intervention: Thick 3.5mm steel plates	Not discussed	Inclusion Flail Chest Exclusion Not discussed	N= 11 Age (years) Range 32-67 Gender Male : 10 Female : 1 Lateral = 7 Anterolateral = 4 Bi:Unilateral 2:9	Type Synthes Matrix rib titanium plates Timing Not discussed	PRIMARY OUTCOMES Duration of ICU stay Duration of hospital stay Duration of post-operative ventilation SECONDARY OUTCOMES Pneunomia	Mean 11 months Range 2-26	1 Unclear 2 Unclear 3 Unclear 4 Unclear 5 Unclear 6 Yes 7 Unclear 8 Yes 9 nclear 10 NA Overall appraisal: Seek further info

Redwan, B., et al., Video-assisted minimally invasive rib osteosynthesis using intramedullary titanium splints in patients with unstable rib fractures: Treatment algorithm and first clinical results. Interactive Cardiovascular and Thoracic Surgery. Conference: 23rd European Conference on General Thoracic Surgery. Lisbon Portugal. Conference Start, 2015. 21							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Redwan Year 2015 Study Type Prospective Case Series Conference proceedings Setting Single Centre, Germany Intervention: IM fixation	Not discussed	Inclusion Not discussed Exclusion Not discussed	Fixation N = 21 Age Mean 56 Gender Male 18 (86%) Female 3 (14%)	Type Titanaium intramedullary splints Timing Not discussed	PRIMARY OUTCOMES Pain SECONDARY OUTCOMES	Not discussed	1 Unclear 2 Unclear 3 Unclear 4 Unclear 5 Unclear 6 Unclear 7 Unclear 8 Unclear 9 Unclear 10 Unclear Overall appraisal: Seek further info

Said, S.M., et al., Surgical stabilization of flail chest: the impact on postoperative pulmonary function. European Journal of Trauma and Emergency Surgery, 2014. 40(4): p. 501-505.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Said Year 2014 Study Type Retrospective Case Series Setting Single Centre, USA Intervention: Plate fixation	Significant chest wall collapse or deformation with paradoxical respiratory dysfunction and with or without pulmonary contusions Impalement of ribs into pulmonary parenchyma and or other solid organs or diaphragm necessitating concomitant repair Significant and refractory pain Anticipated non-union or malunion.	Inclusion Flail chest with surgical stabilisation Exclusion non-flail rib fractures who underwent surgical fixation	N= 20 Age (years) Median 60 Range 30-83 Gender Male 13 (65%) Female 7 (35%) Number of rib fractures Median 4 Range 2-9 ISS Median 17 Range 9-41	Type Synthes Matrix rib titanium plates and Acute innovations RibLoc Timing Median 4 days Range 1-33 days	PRIMARY OUTCOMES Wound infection Tracheostomy Mortality Duration of ICU stay Duration of hospital stay Duration of post-operative ventilation SECONDARY OUTCOMES Spirometry	Mean 5.6 (SD) months	1 Yes 2 Yes 3 Yes 4 Unclear 5 Unclear 6 Yes 7 Yes 8 No 9 Yes 10 Unclear Overall appraisal: Seek further info

Schmit-Neuerburg KP, Weiss H and Labitzke R. Indication for thoracotomy and chest wall stabilization. Injury. 1982; 14: 26-34.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Schmit-Neuerberg Year 1982 Study Type Retrospective Case Series Setting Single Centre, West Germany Intervention: Plate fixation	Stablisation on retreat n= 5 Instability with pleural and lung injuries n=8 Flail chest with severe respiratory insufficiency n=7	Inclusion Not discussed Exclusion Not discussed	Fixation N = 20 Location Flail n = 7 Lateral n=16 Anterior n=14	Type Synthes plate fixation Timing 11 same day surgery 6 were operated 2-4 days and 3 at 6-10 days	PRIMARY OUTCOMES Mortality Complications	In hospital	1 Unclear 2 Unclear 3 Unclear 4 Unclear 5 Unclear 6 No 7 Yes 8 Yes 9 No 10 NA Overall appraisal: Seek further info

Sellers, E.L., et al., The introduction of rib fracture fixation for traumatic flail chest injury: A single centre experience. Trauma (United Kingdom), 2013. 15(3): p. 245-251.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Sellers Year 2013 Study Type Retrospective Case Series Setting Single Centre, UK Intervention: Plate fixation	Flail segment (of usually>4 ribs in more than one place) associated with respiratory failure and failure to wean from mechanical ventilation. Significant chest deformity as a result of multiple rib fractures. Multiple rib fractures causing pain and failure to wean in patients with underlying chronic lung disease. Impending requirement for mechanical ventilation due to pain and/or failure of chest wall mechanics.	Inclusion Flail chest with surgical stabilisation Exclusion non-flail rib fractures who underwent surgical fixation	N= 10 Age (years) Mean 52.1 Range 28-83 Gender Male 7 (70%) Female 3 (30%) ISS Mean 26.5 Range 16-41	Type Synthes Matrix rib titanium plates Timing Median 5 days Range 2-12 days	PRIMARY OUTCOMES Tracheostomy Mortality Duration of ICU stay Duration of post-operative ventilation SECONDARY OUTCOMES	6-18 months	1 Yes 2 Yes 3 Yes 4 Yes 5 No 6 Yes 7 Yes 8 Yes 9 Yes 10 NA Overall appraisal: Include

Tarng, Y.W., et al., The surgical stabilization of multiple rib fractures using titanium elastic nail in blunt chest trauma with acute respiratory failure. Surgical Endoscopy and Other Interventional Techniques, 2016. 30(1): p. 388-395.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Tarng Year 2016 Study Type Retrospective Case Series Setting Single Centre, Taiwan Intervention: Intramedullary fixation	Not discussed	Inclusion blunt thoracic injuries were included in this study. multiple rib fractures (more than 4 ribs) accompanied by acute respiratory failure Hemodynamically stable, with no hypovolemic shock Between 18 and 75 years old Exclusion non-flail rib fractures who underwent surgical fixation associated injuries that were too severe AIS 3	N= 12 Age (years) Mean 47.25 (14.37) Gender Male 11 (91.6%) Female 1 (8.4%) Numbers of ribs (mean, SD) 7.33 (1.15) Contusion score (mean, SD) 6.25 (1.05) ISS Mean (SD) 21.17 (4.13)	Type 2.0- or 2.5-mm intramedullary TENS Nails Timing Mean 3.83 days (0.83)	PRIMARY OUTCOMES Time from trauma to perform VATS Numbers of ribs fixed by TENs Time of ventilator use Time of ventilator use after rib fixations Time of chest tube use ICU length of stay In-hospital length of stay SECONDARY OUTCOMES	mean follow-up period was 21 months (range 18–24 months)	1 Yes 2 Yes 3 Yes 4 Yes 5 Yes 6 Yes 7 Yes 8 Yes 9 Yes 10 NA Overall appraisal: Include

Taylor, B.C., B.G. French, and T.T. Fowler, Surgical approaches for rib fracture fixation. Journal of Orthopaedic Trauma, 2013. 27(7): p. e168-e173.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Taylor Year 2013 Study Type Retrospective Case Series Setting Single Centre, USA Intervention: Plate fixation	Not discussed	Inclusion Flail Chest Exclusion Not discussed	N= 21 Age (years) Mean 51.5 (range 18-90) Gender Male = 14 (66.7%) Female = 7 (43.3%) Numbers of fractured ribs mean 6 (range 3-10)	Type Matrix rib titanium plates Timing Mean 4.6 days (range 2-11)	PRIMARY OUTCOMES Time of ventilator use Time of ventilator use after rib fixations Time of chest tube use ICU length of stay In-hospital length of stay Tracheostomy SECONDARY OUTCOMES Radiographic union	Maximum 5 months	1 No 2 Unclear 3 Unclear 4 Unclear 5 Unclear 6 Yes 7 Yes 8 Yes 9 Unclear 10 NA Overall appraisal: Seek further info

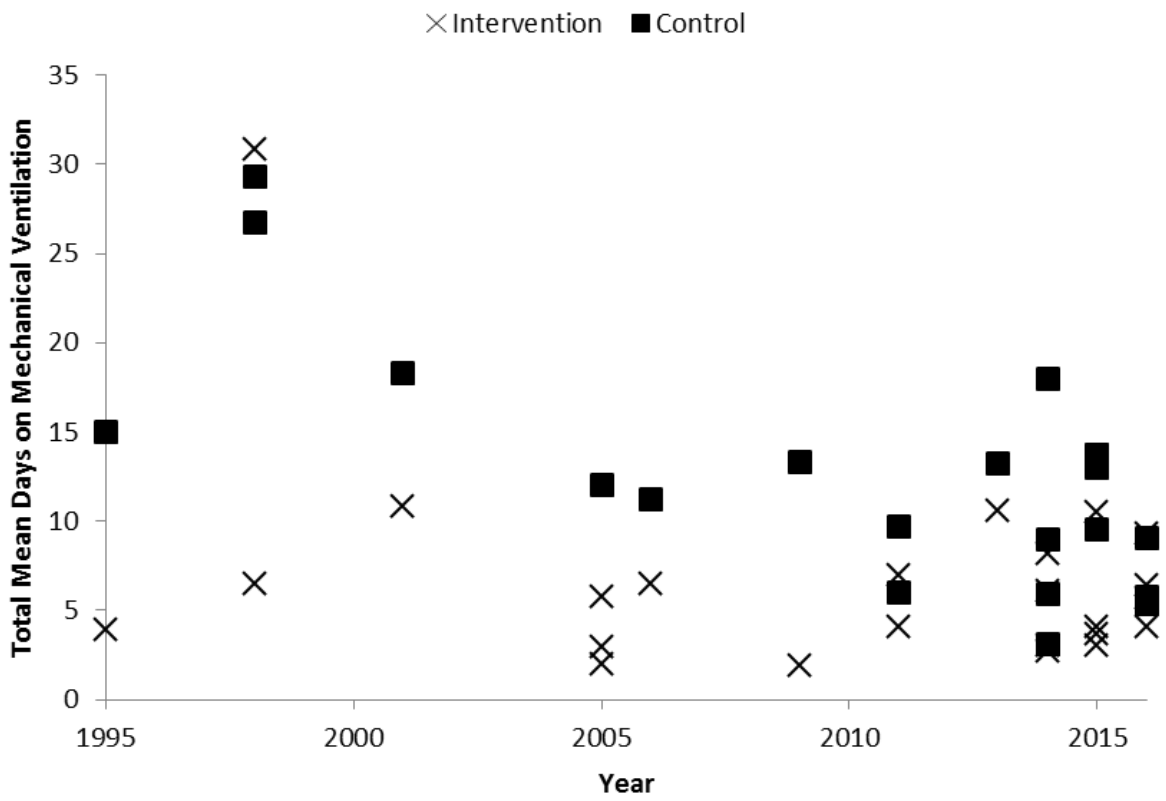
Thiels, C.A., et al., Infected hardware after surgical stabilization of rib fractures: Outcomes and management experience. Journal of Trauma and Acute Care Surgery., 2016. 17.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Theils Year 2016 Study Type Prospective Case Series Setting Single Centre, USA Intervention: Plate fixation	Rib fractures associated with respiratory failure requiring mechanical ventilation Nonintubated patient with deteriorating pulmonary function in association with rib fractures Nonflail rib fracture(s) with or without at least 1 rib width) displacement Impalement of ribs into pulmonary paracheyma or other solid organs or diaphragm Substantial and refractory pain associated with rib fractures Anticipated non-union or malunion of rib fractures	Inclusion 18 years or older with surgically fixed rib fractures Exclusion Not discussed	N= 122 Age (years) Mean 59.5 (SD 16.4) Gender Male 89 (72.9%) Female 33 (17.1%) Numbers of fractured ribs Median 7 (IQR 5-9) ISS Median 17 (IQR 13-22) Flail :58 (48%)	Type Matrix rib titanium plates Timing Mean 6.92 days (SD 2.67)	PRIMARY OUTCOMES ICU length of stay In-hospital length of stay SECONDARY OUTCOMES Pneumonia Wound infection sub group analysis	Maximum 5 months	1 Yes 2 Yes 3 Yes 4 Unclear 5 Unclear 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Wiese, M.N., et al., Functional results after chest wall stabilization with a new screwless fixation device. European Journal of Cardio-Thoracic Surgery, 2015. 47(5): p. 868-875.								
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics		Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Wiese Year 2014 Study Type Retrospective Case series Setting Two centres – Switzerland and Spain Intervention: Strut fixation	Flail chest in non-intubated patients with respiratory failure despite continuous epidural analgesia and aggressive clearance of bronchial secretions extended antero-lateral flail chest and progressive dislocation of the fractured ribs intubated patients who did not require prolonged in-tubation in the absence of severe pulmonary contusion or cerebralinjuries, in order to reduce the use of mechanical ventilation when the patient failed to wean thoracotomy or thoracoscopy due to associated extended haemothorax	Inclusion Not discussed Exclusion Not discussed	Flail N =68 Age Median age 57 (IRQ 45-68) Gender Male 28 (85%) Female 5 (15%) Diagnosis/location Number of ribs Median 8 (IQR 6-10) Bilateral : Unilateral 3:65	Dislocated painful ribs fractures N = 26 Age Median age 52 (IRQ 47-68) Gender Male 19 (73%) Female 7 (27%) Diagnosis/location Number of ribs Median 6 (IQR 5-10) Bilateral : Unilateral 3:65	Type Stratos Struts Timing Flail Median 3.4 Range 0-17 days	PRIMARY OUTCOMES Duration of Hospital stay 30 day mortality SECONDARY OUTCOMES Pneumonia Post-operative complications Functional lung capacity and mobility of the chest wall after ORIF in the subgroup of patients with a flail chest	6 months	1 Yes 2 Unclear 3 Unclear 4 Unclear 5 Unclear 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Yang, Y., L.-w. Dong, and J. Wang, Memory alloy embracing fixator in treatment of multiple fractured ribs and flail chest. World Journal of Emergency Medicine, 2010. 1(3): p. 212-215.							
Study details	Indications	Inclusion/Exclusion criteria	Participant characteristics	Type of Fixation and Timing	Outcomes	Follow up	Risk of Bias
Author Yang Year 2010 Study Type Prospective Case Series Setting Single Centre, China Intervention: Ni-Ti shape memory alloy embracing fixator	Not discussed	Inclusion Not discussed Exclusion Not discussed	Fixation N = 17 Age Mean (SD) 42 (15.4) Range 21-65 Gender Male n=12 Female n=5 Flail n = 6 Multiple ribs n = 5 Other reasons for thoracotomy n = 5	Type Ni-Ti shape memory alloy embracing fixator Timing Within 24 hours	PRIMARY OUTCOMES Chest tube duration Hospital length of stay Pneumonia Pain VAS Return to work	10 months	1 No 2 Unclear 3 Unclear 4 Unclear 5 No 6 Yes 7 Yes 8 Yes 9 Yes 10 Yes Overall appraisal: Include

Appendix B2 Outcome Tables

Figure 39 Time on mechanical ventilation between 1995 and 2016



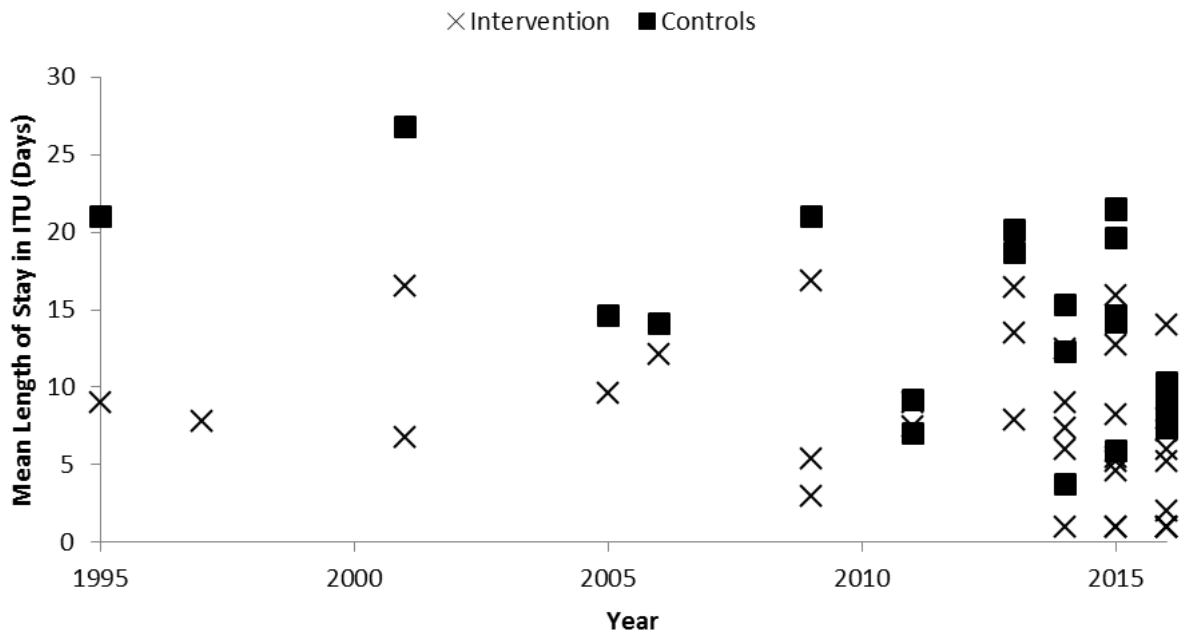


Figure 40 Total length of ICU length of stay between 1995 and 2016

Figure 41 Difference in length of hospital stay from 1993 to 2016

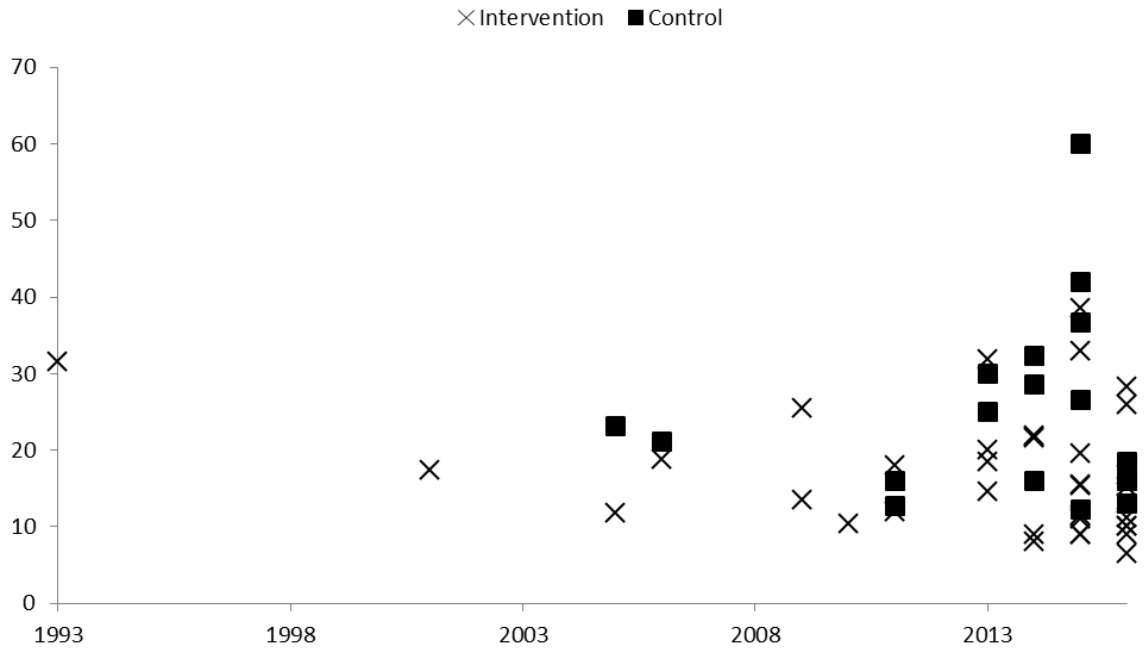
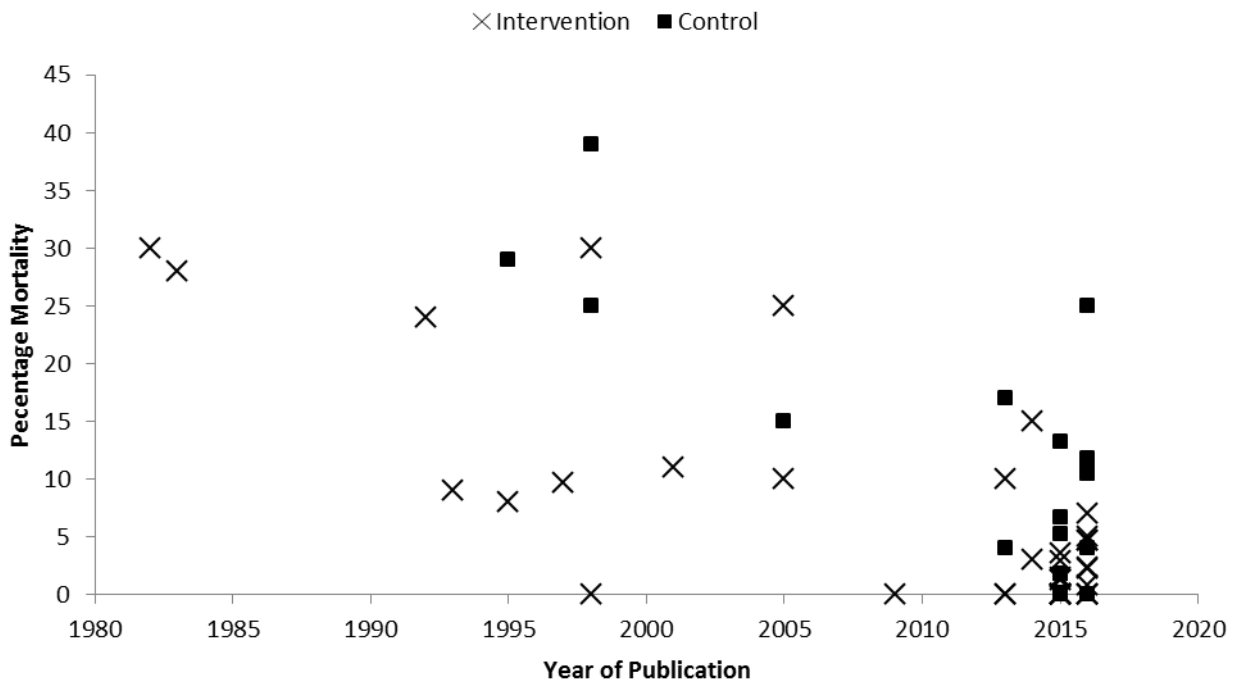


Figure 42 Difference in mortality rates between 1983 and 2016


Intervention
Control
Pecentage Mortality
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1980
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2020
Year of Publication

Figure 43 Timing of Surgical Fixation from 1983 to 2016

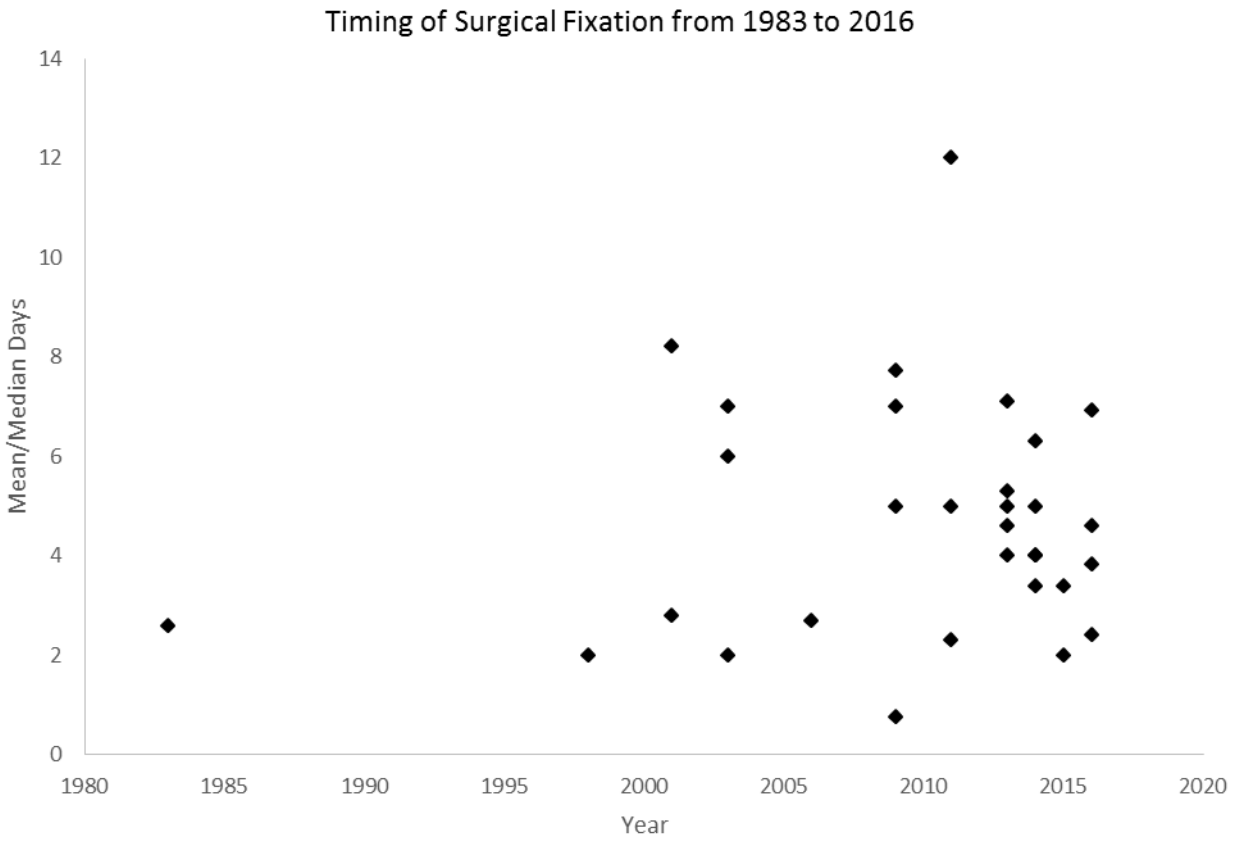


Table 73 Time on mechanical ventilation after surgical fixation (days)

Flail Only	Study Type	Type of Fixation	Mean	SD	Median	Min	Max
Tanaka 2001	RCT	Strut	2.5	3.2			
Althausen 2011	NRS	Plate	1.81				
Doben 2014	NRS	IM and Plate	3		1.5	0	8
Bottlang 2013	Case Series	IM and Plate	6.4			0	37
Ivancic 2009	Case Series	Plate	0.27	0.59	0	0	2
Marasco 2013	RCT	Absorbable Plate	6.25	4.93	4.15	1	15.9
Mayberry 2003	Case Series	Absorbable Plate			9	1	20
Menard 1983	Case Series	Strut	13	12		0	28
Reber 1993	Case Series	Plate	3.7			1	12
Said 2014	Case Series	Plate	3				
Seller 2013	Case Series	Plate	2.5	1.04	2	1	4
Taylor 2013	Case Series	Plate	4.8			0	26
Flail and Multiple Rib Fractures							
Muhm 2013	NRS	Plate	6.9	6.5	5	0	19
Nirula 2006	NRS	Strut	2.9	0.6			
Lardoinois 2001	Case Series	Plate			2.1	0.5	26
Marasco 2009	Case Series	Absorbable Plate			15	5.3	26
Tarng 2016	Case Series	IM	2.5	0.67			3

Table 74 Total length of mechanical ventilation in all studies (days)

Total length of mechanical ventilation			Rib fracture fixation							Non-operative							
	Study Type	Fixation Type	Mean	SD	Med	Min	Max	Q1	Q3	Mean	SD	Med	Min	Max	Q1	Q3	P Value
Flail Only																	
Althausen 2011	NRS	Plate	6.66	3.14*	4.14					9.18	3.14*	9.68					0.007
Buyukkarabaca 2015	NRS	Plate	3	14.49*	0	0	20			13.7	14.49*	7	0	74			0.116
De Moya 2011	NRS	Plate	7	8						6	10						0.44
Defreest 2016	NRS	Plate	9.3	9.75*	6	0	39			5.8	9.75*	1.8	0	39			0.1
Farquhar 2016	NRS	Plate	6.1	5.9						3.1	5.5						0.012
Taylor 2016	NRS	Plate	4.1	6.4		0	30			5.4	6.9		0	30			0.02
Xu 2015	NRS	Plate	10.5	3.7						13.7	4.4						0.033
Qiu 2016	NRS	Plate	5.71	1.35						9.06	3.58						0.005
Muhm 2013	NRS	Plate	10.6	10.2	11	0	26			13.2	13.7	10	0	57			ns
Marasco 2013 PR,R	RCT	Plate	6.325	3.46						7.54	5.4						
Tanaka 2001R	RCT	Strut	10.8	3.4						18.3	7.4						<0.05
Jayle 2014	NRS	Strut	3	5.2						5.9	9.35						0.026 multivariate
Zhang 2015a	NRS	Strut	4.1	6.1		11	48			13	7.6		24	82.2			<0.01
Doben 2014	NRS	Combined	8.2	10.17*	4.5	0	30	18	10.17*	16	4	40	0.04				
Ahmed 1995	NRS	Combined	3.9							15							
Flail and Multiple Unifocal Rib Fractures																	
Pieracci 2016	NRS	Plate			0			0	8			5			0	18	<0.01
Solberg 2009	NRS	Plate	1.9	1.1						13.3	5.3						<0.01
Wu 2015R	RCT	Strut	3.7	1.4						9.5	4.3						0.037

Total length of mechanical ventilation			Rib fracture fixation							Non-operative							
	Study Type	Fixation Type	Mean	SD	Med	Min	Max	Q1	Q3	Mean	SD	Med	Min	Max	Q1	Q3	P Value
Voggenreiter 1998	NRS	Strut	6.5	7						26.7	29						
Voggenreiter1998 PC	NRS	Strut	30.8	33.7						29.3	22.5						
Nirula 2006	NRS	Strut	6.5	1.3						11.2	2.6						0.12
Zhang 2015 2	NRS	Strut			12			7.5	17.8			7			4	14	0.233
Granhed 2014	NRS	Combined	2.7	10.44*	0.5	0	21	9.0	10.44*	5	1	176	0.0001				
Granetzny 2005 R	RCT	Combined	2	4.79*		9	45	12	4.79*		7	35	<0.001				
Tarng 2016	Series	IM	6.42	0.79						N/A							
Borrelly 2005	Series	Combined	5.8	0.76						N/A							
*Standard deviations (SD) that are imputed. ns = Not significant, ,PR = Post-randomisation time, PC= Pulmonary Contusion																	

Table 75 Total length of ICU Stay in Controlled Studies (days)

Total length of ICU stay			Rib fracture fixation							Non-operative							
Flail Only	**Study**	**Fixation**	**Mean**	**SD**	**Med**	**Min**	**Max**	**Q1**	**Q3**	**Mean**	**SD**	**Med**	**Min**	**Max**	**Q1**	**Q3**	**P Value**
Althausen 2011	NRS	Plate	7.43	2.51*	7.59					9.18	2.51*	9.68					0.018
Buyukkarabaca 2015	NRS	Plate	5.2	10.6*	3.5	2	20			21.4	10.6*	10.5	4	95			0.003
De Moya 2011	NRS	Plate	9	8						7	10						0.75
Defreest 2016	NRS	Plate	14	10.5*	12.4	0	43			8	10.5*	4.6	0	43			0.01
Farquhar 2016	NRS	Plate	7.4	6.7						3.7	6						0.009
Taylor 2016	NRS	Plate	5.2	8		0	43			7.4	8.9		0	38			0.09
Xu 2015	NRS	Plate	15.9	5						19.6	5						0.05
Qiu 2016	NRS	Plate	7.19	1.67						10.3	2.3						0.016
Muhm 2013	NRS	Plate	16.4	13.6	17	1	46			20.1	16.2	16	3	60			ns
Marasco 2013[PR]	RCT	Plate	13.96	4.63				9.9	15.8	23.5	18.8						0.03
Tanaka 2001	RCT	Strut	16.5	7.4						26.8	13.2						<0.05
Jayle 2014	NRS	Strut	9	4.3						12.3	8.5						0.076 multivariate
Zhang 2015 a	NRS	Strut	5.5	6.4						14.2	6.5						<0.05
Doben 2014	NRS	Combined	12.5	6.9*	9	5	31			15.3	6.9*	18	5	32			0.37
Ahmed 1995	NRS	Combined	9							21							
Flail and Multiple Rib Fractures																	
Pieracci 2016	NRS	Plate			6			3	10			9			4	15	0.15
Solberg 2009	NRS	Plate	5.4	1.5						21	13.6						0.01
Majercik 2015	NRS	Plate	4.6	5.6						5.9	7.7						0.5
Wu 2015	RCT	Strut	8.2	4.3						14.6	3.2						0.041
Nirula 2006	NRS	Strut	12.1	1.2						14.1	2.7						0.51
Zhang 2015 b	NRS	Strut			24.5			21.3	30.8			21.5			18	33.5	0.719
Granetzny 2005	RCT	Combined	9.6	4.4						14.6	4.4						<0.001

*Standard deviations (SD) that are imputed. ns = Not significant, PR = Post randomisation time

Table 76 Case Series total length of ICU Stay

Flail Only	Study Type	Fixation Type	Mean	SD	Median	Min	Max	Q1	Q3
Marasco 2009	Case Series	Absorbable Plate			16.9	8.1	33.3		
Tarng 2016	Case Series	IM	8	0.95					
Bottlang 2013	Case Series	IM and Plate	7.9			1	34		
Lardoinois 2001	Case Series	Plate	6.8			1	48		
Reber 1993	Case Series	Plate	7.3			2	14		
Said 2014	Case Series	Plate	6						
Mouton 1997	Case Series	Plate	7.8			1	48		
Flail and Multiple Rib Fractures									
Nickerson 2015	Case Series	Plate			1			0	39
Nickerson 201590	Case Series	Plate			1			0	17
Nickerson 2016 C	Case Series	Plate			1			0	39
Nickerson 2016 P	Case Series	Plate			2			0	26
Campbell 2009	Case Series	Absorbable Strut/Wrap			3			0.8	6.3
De Palma 2016	Case Series	Plate			1	0	29		
Theils 2016	Case Series	Plate			1			0	4
90 = using 90 degree screw driver, P = Partial stabilisation, C=Complete stabilisation									

Table 77 Time in ICU after surgical fixation

Flail Only	Study Type	Fixation Type	Mean	SD	Median	Min	Max	Q1	Q3
Tanaka 2001R	RCT	Strut	9.2	5.2					
Althausen 2011	NRS	Plate	2.68						
Ivancic 2009	Case Series	Plate	3.93	2.99	3	1	12		
Majercik 2014	Case Series	Plate			1			0	3
Seller 2013	Case Series	Plate			6	2	111		
Taylor 2013	Case Series	Plate	5.2			0	13		
Flail and Multiple Rib Fractures									
Muhm 2013	NRS	Plate	11.7	10.3	8	0	33		

Table 78 Total length of hospital stay in non-randomised studies and randomised control trial

Length of hospital stay			Rib fracture fixation							Non-operative							
Flail Only	**Study Type**	**Fixation Type**	**Mean**	**SD**	**Med**	**Min**	**Max**	**Q1**	**Q3**	**Mean**	**SD**	**Med**	**Min**	**Max**	**Q1**	**Q3**	**P Value**
Althausen 2011	NSR	Plate	7.79	5.9*	11.9					12.64	5.9*	19					0.006
Buyukkarabaca 2015	NSR	Plate	15.5	28.8*	13.5	5	30			36.6	28.8*	22	10	180			0.119
De Moya 2011	NSR	Plate	18	12						16	11						0.67
Defreest 2016a	NSR	Plate	28.3	20.8*	22	9	69			13	20.8*	10.1	3	43			<0.001
Farquhar 2016 a	NSR	Plate	21.9	13.2						16	12.1						0.044
Muhm 2013	NSR	Plate	31.8	14	33	9	56			30	19.7	25	5	77			ns
Marasco 2013	RCT	Plate	26	18	20			18	28	25	19	25			18	38	0.24
Taylor 2016 a	NSR	Plate	16.7	10.9		3	62			18.5	15		1	73			<0.01
Jayle 2014	NSR	Strut	21.7	7.8						32.3	19.3						0.024 multivariate
Nirula 2006	NSR	Strut	18.8	1.8						21.1	3.9						0.59
Doben 2014	NSR	Combined	21.6	11.0*	13	8	59			28.5	11.0*	22	6	50			0.169
Pieracci 2016	NSR	Plate			13			9	21			16			10	23	0.11
Majercik 2015	NSR	Plate	5.7							12.3	9.1						0.52
Wu 2015	RCT	Strut	6.4							26.5	6.9						0.036
Zhang 2015 b	NSR	Strut		38		33	54					60			38	99	0.049
Wada 2015	NSR	Combined		33		24	45					42			23	58	0.427
Granetzny 2005	RCT	Combined	10.1*							23.1	10.1*						<0.001

Table 79 Total Time of hospital stay in case series

Flail Only	Study Type	Type of Fixation	Mean	SD	Median	Min	Max	Q1	Q3
Bottlang 2013	Case Series	IM and Plate	18.4			4	68		
Lardoinois 2001	Case Series	Plate			17.4	8	60		
Marasco 2009	Case Series	Absorbable Plate			25.4	12.8	52		
Reber 1993	Case Series	Plate		31.5		12	80		
Said 2014	Case Series	Plate	9						
Tarng 2016	Case Series	IM	15.17	2.69					
Taylor 2013	Case Series	Plate	14.6			4	47		
Wiese 2015	Case Series	Strut			19.5	13	31		
Nickerson 2016 CS	Case Series	Plate			10			2	39
Nickerson 2016 PS	Case Series	Plate			10			4	36
Flail and Multiple Rib Fractures									
Campbell 2009	Case Series	Absorbable Wrap			13.5			8.8	22
De Palma	Case Series	Plate			13	5	129		
Majercik 2014	Case Series	Plate			8			6	11
Metin 2016	Case Series	Strut	6.47	2.98					
Nickerson 2015[90]	Case Series	Plate			9			6	21
Nickerson 2015	Case Series	Plate			9			2	39
Theils 2016	Case Series	Plate			9			6	12
Wiese 2015	Case Series	Strut			11	7	20		
Yang 2010	Case Series	Strut		3.14	10.3				
R = RCT, CS = complete stabilisation, PS = Partial stabilisation 90 = 90 degree screwdriver									

Table 80 Mortality rate in randomised and non-randomised studies

Mortality			Fixation		Non-operative		
Flail Only	**Study Type**	**Type of Fixation**	**n**	**%**	**n**	**%**	**RR**
Marasco 2013	RCT	Absorbable Plate	0	0	1	4	0.00
Zhang 2015[1]	NRS	Strut	0	0	0	0	0.00
Xu 2015	NRS	Plate	0	0	1	6.7	0.00
Taylor 2016	NRS	Plate	2	2.3	22	25	0.09
Qiu 2016	NRS	Plate	1	4.76	2	11.76	0.40
Zhang 2015 [2]	NRS	Strut	0	0	2	13.3	0.00
Farquhar 2014	NRS	Plate	1	5	1	4	1.89
Defreest 2016	NRS	Plate	1	2.4	5.00	11.1	0.22
Buyukkarabaca 2015	NRS	Plate	1	0.1	2	0.2	0.50
Ahmed 1995	NRS	IM	2	8	11	29	0.27
Flail and multiple rib fractures							
Wu 2015R	RCT	Strut	1	1.3	4	5.3	0.30
Wada 2015[28,a]	NRS	All fixations	2	2.9	5	1.8	1.64
Wada 2015 [28]	NRS	All fixations	3	3.6	6	1.8	2.00
Wada 2015 [10]	NRS	All fixations	0	0	0	0	0.00
Voggenreiter 1999 [PC]	NRS	Strut	3	30	1	25	1.20
Voggenreiter 1998	NRS	Strut	0	0	7	39	0.00
Pieracci 2016	NRS	Plate	0	0	0	0	0.00
Muhm 2013	NRS	Plate	2	10	4	17	0.55
Granetzny 2005	RCT	IM and Wire	2	10	3	15	0.67

PC = Pulmonary Contusion
10 = measured at 10 days
28 = measured at 28 days,
a = excluding patients with craniotomy spinal fusion, laparotomy, Pelvic ORIF and embolization

Table 81 Mortality rate in case series

Flail Only	Study Type	Type of fixation	n	%
Tarng 2016	Case Series	IM	0	0
Seller 2013	Case Series	Plate	0	0
Said 2014	Case Series	Plate	3	15
Reber 1993	Case Series	Plate	1	9
Mouton 1997	Case Series	Plate	2	8.7
Menard 1983 [e]	Case Series	Strut	5	28
Marasco 2009	Case Series	Absorbable Plate	0	0
Lardoinois 2001[30]	Case Series	Plate	7	11
Borerelly 2005	Case Series	IM and Strut	16	13.3
Wiese 2015[30]	Case Series	Strut	1	1.5
Flail and multiple rib fractures				
Theils 2016	Case Series	Plate	1	0.8
Schmitt 1982	Case Series	Strut	6	30
Marasco 2016	Case Series	Absorbable Plate	1	7
De Palma[30]	Case Series	Plate	0	0
30 = 30 day mortality rate, e = early treatment mortality				

Table 82 Randomised and Non-Randomised Studies Reporting Pneumonia

Pneumonia			**Fixation**		**Non-operative**		
Flail Only	**Study Type**	**Type of Fixation**	n	%	n	%	RR
Tanaka 2001, [7]	RCT	Strut	1	5.6	3	15.7	0.35
Tanaka 2001, [21]	RCT	Strut	4	22.2	17	89.5	0.25
Marasco 2013	RCT	Absorbable Plate	11	48	17	74	0.65
Althausen 2011	NRS	Plate	1	4.55	7	25	0.18
Buyukkarabaca 2015	NRS	Plate	2	20	7	70	0.29
De Moya	NRS	Plate	5	31	12	38	0.83
Defreest	NRS	Plate	11	26.8	10	22.2	1.21
Farquhar 2016	NRS	Plate	12	63	8	22	2.84
Jayle 2014	NRS	Strut	4	40	3	30	1.33
Flail and multiple rib fractures							
Muhm 2013	NRS	Plate	12	57	12	52	1.10
Granetzny 2005	RCT	IM and Wire	2	10	10	50	0.20
Pieracci 2016	NRS	Plate	7	20	11	31.4	0.64
Taylor 2016	NRS	Plate	16	18.2	27	30.7	0.59
Xu 2015	NRS	Plate	10	58.8	14	93	0.63
Zhang 2015	NRS	Strut	7	30.43	22	75.86	0.40
7 = measured at 7 days, 21= measured at 21 days							

Table 83 Case Series Reporting Pneumonia

Flail Only	Study Type	Type of fixation	n	%
Bottlang 2013	Case series	IM and Plate	6	30
Lardoinois 2001	Case series	Plate	5	7.6
Menard 1983	Case series	Strut	3	16.7
Nickerson 2016CS	Case series	Plate	5	22
Nickerson 2016PS	Case series	Plate	4	20
Reber 1993	Case series	Plate	4	38
Said 2014	Case series	Plate	2	10
Wiese 2015	Case series	Strut	4	6
Flail and multiple rib fractures				
Majercik 2014	Case series	Plate	5	10
Theils 2016	Case series	Plate	19	15.6
Granhed 2014	Case series	IM and Plate	0	0
CS =Complete Stabilisation, PS = Partial Stabilisation				

Table 84 Randomised and Non Randomised Studies reporting Tracheostomy

Tracheostomy			Fixation		Non-operative		
Flail Only	**Study Type**	**Type of Fixation**	**n**	**%**	**n**	**%**	**RR**
Marasco 2013	RCT	Absorbable Plate	9	39	16	70	0.056
Althausen 2011	NRS	Plate	3	13.6	11	39.3	0.35
Xu 2015	NRS	Plate	2	11.8	6	40	0.29
Taylor 2016	NRS	Plate	10	11.4	21	23.9	0.48
Zhang 2015b	NRS	Strut	12	25	7	46.7	0.54
Tanaka 2001[7]	RCT	Strut	0	0	5	26.3	
Tanaka 2001[28]	RCT	Strut	3	16.7	15	78.9	0.21
Flail and multiple rib fractures							
Wu 2015	RCT	Strut	4	5.3	7	7.9	0.68
Pieracci 2016	NRS	Plate	5	14.3	16	45.7	0.31
Muhm 2013	NRS	Plate	10	48	15	65	0.67
7 = rate at 7 days, 28 = Rate at 28 days							

Table 85 Case Series Tracheostomy

Flail Only	Study Type	Type of fixation	n	%
Mayberry 2003	Case Series	Absorbable Plate	2	20
Tarng 2016	Case Series	IM	0	0
Taylor 2013	Case Series	Plate	2	9.5
Said 2014	Case Series	Plate	2	10

Table 86 Cost of overall treatment

		Rib fracture fixation		Non-operative		
	Currency	Mean	Median	Mean	Median	Difference
Tanaka 2001	US Dollar	13445		23423		-9978
Marasco 2013	US Dollar					-14443
Buyukkarabaca 2015	Turkish Lira	13600		15257		-1657
Zhang 2015 (2)	Yuan		207341		182632	24706
Granhed 2014	US dollar	32300		37100		-4800

Table 87 Length of chest tube duration (days)

	Rib fracture fixation		Non-operative	
Author/Year	Mean	SD	Mean	SD
Solberg 2009	5.6	1.2	16.8	5.1
Taylor 2016	6.3	4.7	6.2	6.8
Tarng 2016	10.5	1.17		
Taylor 2013	7.4			

Table 88 Frequency of wound infection

Wound infection	Internal fixation	
Author/Year	**Frequency**	**Percent**
Granetzny 2005	2	10
Khandelwal 2011	3	8
Zhang 2015 No 2	3	25
Bottlang 2013	1	
Campbell 2009		19
Majercik 2014	2	2
Marasco 2009	1	8
Mayberry 2003	1	10
Menard 1983	2	22
Said 2014	2	10
Theils 2016	5	4
Wiese 2015	2	3
Granhed 2014	1	2
Schmitt-Neuerberg 1982	4	20
Mouton	1	5
Lardinois 2001	1	

Table 89 Frequency of metal work failure

Author/Year	Sample size	Frequency	Percentage
Khandelwal 2011	38	0	0
Marasco 2014	52	5	9.6
Marasco 2016	15	2	12
Menard 1983	18	1	11
Said 2014	20	0	0
Schmitt-Neuerberg 1982	20	2	10

Table 90 Studies reporting respiratory failure

Respiratory failure	Internal fixation		Non-Operative		
Author/Year	**Frequency**	**Percent**	**Frequency**	**Percent**	**P value**
Defeest		4.9		8.9	0.47
Pieracci 2016	17	48.6	25	71.4	0.05
Pimakhov 2014 [CP]		9.5		36	<0.05
Menard 1983	1	11			
Voggenreiter 1998	0	0	3	17	
Voggenreiter 1998 [PC]	0	0	0	0	
CP – Conference proceedings, PC = Pulmonary contusion					

Table 91 Studies reporting overall complication rate

Complications	Internal fixation		Non-operative management		
Author/Year	**Freq**	**Percent**	**Freq**	**Percent**	**P value**
Granetzny 2005	13	65	8	40	n.s
Wiese 2015	6	8.8			

Table 92 Studies reporting re-intubation rate

Re intubation	Rib fracture fixation		Non-operative management		
Author/Year	**Frequency**	**Percentage**	**Frequency**	**Percentage**	**P value**
Althausen 2011	1	4.55	5	17.9	0.034
Marasco 2013	3	13	1	4	0.61
Buyukkarabaca 2015	1	10	0	0	
Xu 2015	1	5.8	3	20	0.228

Table 93 Studies reporting rate of sepsis

Sepsis	Rib fracture fixation		Non-operative management	
Author/Year	**Frequency**	**Percent**	**Frequency**	**Percent**
Ahmed 1995	1	4	9	24
Menard 1983	1	11		
Voggenreiter 1998	0	0	10	39
Voggenreiter 1998 PC	3	30	1	25
PC = Pulmonary contusion				

Table 94 Studies reporting retained haemothorax

Retained Haemothorax	Internal fixation		Control		
Author/Year	**Frequency**	**Percent**	**Frequency**	**Percent**	**P Value**
Majercik 2015	7	5.1	44	16	P = 0.001
Majercik 2014	1	1			
Said 2014	0	0			

Table 95 Results of studies performing lung function tests Forced Expiratory Volume (FEV1)

FEV1 Percentage predicted		Rib fracture fixation					Non-operative		
Author/Year	**Follow Up**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**P value**
Marasco 2013	3months	74	15				80	18	0.31
Granetzny 2005	2 months	76	9				75	0	n.s.
Jayle 2014	3 months	78	12						
Zhang 2015[a L]	? months	1.58	0.08				1.43	0.06	<0.001
Bottlang 2013	3 months	77							
Bottlang 2013	6 months	79							
Caragounis 2016	3 months	79	23						
Caragounis 2016	6 months	82	25						
Caragounis 2016	12 months	80	30						
Moslam 2015	3 months	79	4						
Nickerson 2016 CS	1 months			64	39	90			0.88
Nickerson 2016 PS	1 months			65	33	105			
Nickerson 2016 CS	3 months			75	43	97			0.92
Nickerson 2016 PS	3 months			81	39	98			
Nickerson 2016 CS	6 months			71	53	99			0.87
Nickerson 2016 PS	6 months			77	44	107			
Olsen 2013	3 months	76	21						
Olsen 2013	6 months	77	26						
L = Litres PS = Partial flail chest stabilistation CS = Complete flail chest stabilistation									

Table 96 Results of studies performing lung function tests Forced Vital Capcity (FVC)

FVC Percentage predicted		Rib fracture fixation					Non-operative		
Author/Year	**Follow Up**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**P value**
Marasco 2013	3 months	78	16				85	14	
Granetzny 2005	2 months	75	5				67	7	
Jayle 2014	3 months	90	13						
Bottlang 2013	3 months	84							
Bottlang 2013	6 months	85							
Caragounis 2016	3 months	86	19						
Caragounis 2016	6 months	93	21						
Caragounis 2016	12 months	106	18						
Moslam 2015	3 months	79	6						
Nickerson 2016 CS	1 months			72	51	91			0.68
Nickerson 2016 PS	1 months			69	45	103			
Nickerson 2016 CS	3 months			83	52	99			0.61
Nickerson 2016 PS	3 months			81	39	98			
Nickerson 2016 CS	6 months			85	65	105			0.40
Nickerson 2016 PS	6 months			77	44	107			
Olsen 2013	3 months		21						
Olsen 2013	6 months		28						
Said 2014 [L]	?	1.86	1.43	4					
Wiese 2015	?	88	61	124	79	95			
L = Litres PS = Partial flail chest stabilistation CS = Complete flail chest stabilistation									

Table 97 Results of studies performing lung function tests Total Lung Capacity (TLC)

TLC Percentage predicted		Rib fracture fixation					Non-operative		
Author/Year		**Mean**	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**P value**
Marasco 2013	3 months	84	24				88	23	0.61
Granetzny 2005	2 months	91	4				86	11	0.01
Jayle 2014	3 months	93	2						
Nickerson 2016 CS	1 months			86	50	99			0.63
Nickerson 2016 PS	1 months			82	68	111			
Nickerson 2016 CS	3 months			90	83	108			0.02
Nickerson 2016 PS	3 months			72	68	92			
Nickerson 2016 CS	6 months			94	79	101			0.04
Nickerson 2016 PS	6 months			75	67	89			
PS = Partial flail chest stabilistation CS = Complete flail chest stabilistation									

Table 98 Results of studies performing lung function tests FEV1/FVC ratio

FEV1/FVC Percentage predicted		Rib fracture fixation					Non-operative		
Author/Year	**Follow Up**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**P value**
Marasco 2013	3 months	96	10				95	17	0.92
Moslam 2015	3 months	101	7						
Nickerson 2016 CS	1 months			72	60	90			0.76
Nickerson 2016 PS	1 months			75	57	85			
Nickerson 2016 CS	3 months			73	57	82			0.35
Nickerson 2016 PS	3 months			75	67	81			
Nickerson 2016 CS	6 months			68	56	82			0.06
Nickerson 2016 PS	6 months			74	71	81			
PS = Partial flail chest stabilistation CS = Complete flail chest stabilistation									

Table 99 Results of studies performing lung function tests (PEFR and MMEF)

	PEFR						MEFR				
	Rib fracture fixation			Non-operative			Rib fracture fixation		Non-operative		
Author/Year	Follow Up	Mean	SD	Mean	SD	P Value	Mean	SD	Mean	SD	P Value
Marasco 2013	3 months	62.8	28.5	68.1	36.5	0.63	76.2	36.9	82.1	35	0.64
Granetzny 2005	2 months	92.2	2	91.8	1.7						
Jayle 2014	3 months	92.2	2.2								
Moslam 2015	Post stabilisation	80.23	4.1								
Olsen 2013	3 months	79	18.6	Predicted value		<0.001					
Olsen 2013	6 months	77.3	27	Predicted value		<0.001					
Caragounis 2016	3 months	81.4	19.5								
Caragounis 2016	6 months	83.7	24.3								
Caragounis 2016	12months	109.9	24.8								

Table 100 Results of studies reporting arterial blood gas

		PO_2				**PCO_2**				**Saturation**			
		Rib fracture fixation		**Non-operative**		**Rib fracture fixation**		**Non-operative**		**Rib fracture fixation**		**Non-operative**	
Author/Year	Follow Up	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Granetzny 2005	Pre-Op	56.2	9.2	63.6	9	34.2	6.3	39.7	4	88.1	3.4	90.7	2
Granetzny 2005	7-10 days	98.7	21	89.3	8	31.2	5.9	30.9	3	96.8	3	96.2	2
	P value	<0.001		<0.001		n.s		<0.001		<0.001		<0.001	
Moslam 2015	Post stabilization	97.6	6.4			32.4	8.4			98.4	1.5		

Table 101 Range of movement

	Olsen 2015			Caragounis 2015			Olsen 2013		
	Mean (SD) Internal fixation Vs Control			Mean Δ Operated vs Non-Operated side			Mean Δ Operated vs Non-Operated side		
Range of movement	**Fixation**	**Control**	**P**	**3 month**	**6 month**	**1 year**	**3 month**	**6 month**	**1 year**
Δ Upper thorax during rest, mm	0.15 (1.27)	0.10 (0.42)	0.856	-0.76 ± 1.12	0.40 ± 0.68	0.49 ± 1.32b**	-0.76 ± 1.12	-0.40 ± 0.68	0.49 ± 1.32b**
Δ Lower thorax during rest, mm	0.13 (1.02)	−0.02 (0.36)	0.451	-0.22 ± 0.88	0.10 ± 0.56	0.27 ± 0.82	-0.22 ± 0.88	0.10 ± 0.56	0.27 ± 0.82
Δ Abdominally during rest, mm	-0.61 (1.90)	−0.01 (0.77)	0.136	-0.20 ± 1.67	0.43 ± 1.63	0.14 ± 1.40	-0.20 ± 1.67	0.43 ± 1.63	0.14 ± 1.40
Δ Upper thorax during maximal breathing movements, mm	−0.39 (4.69)	−0.11 (1.91)	0.606	-3.04 ± 5.24	-1.24 ± 1.77	0.10 ± 4.88	-3.04 ± 5.24	-1.24 ± 1.77	0.10 ± 4.88
Δ Lower thorax during maximal breathing movements, mm	4.98 (4.67)	−1.19 (2.04)	0.002	-0.05 ± 4.57	1.48 ± 3.62	1.05 ± 4.46	-0.05 ± 4.57	1.48 ± 3.62	1.05 ± 4.46
Δ Abdominally during maximal breathing movements, mm	-0.41 (4.67)	−0.46 (2.58)	0.398	-0.91 ± 4.92	-0.58 ± 2.64	0.65 ± 5.09	-0.91 ± 4.92	-0.58 ± 2.64	0.65 ± 5.09
Upper level, cm	5.2 (2.1)	3.7 (1.8)	0.005	3.84 ± 1.71	4.09 ± 1.53	3.98 ± 1.58	3.84 ± 1.71	4.09 ± 1.53	3.98 ± 1.58
Lower level, cm	4.3 (1.92)	4.3 (2.3)	0.944	3.41 ± 1.29	4.38 ± 1.70a*	3.82 ± 1.61	3.41 ± 1.29	4.38 ± 1.70a*	3.82 ± 1.61
Range of motion in the thorax Thoracic flexion, cm	4.0 (1.8)	2.4 (0.8)	<0.001	1.75 ± 0.88	2.06 ± 1.03	2.25 ± 0.75b*	1.75 ± 0.88	2.06 ± 1.03	2.25 ± 0.75b*
Thoracic extension, cm	2.5 (1.1)	1.3 (0.5)	<0.001	0.66 ± 0.47	0.88 ± 0.43	1.17 ± 0.45b**	0.66 ± 0.47	0.88 ± 0.43	1.17 ± 0.45b**
Lateral flexion towards the injured side, cm	15.9 (5.0)	14.8 (5.6)	0.494	14.50 ± 3.80	15.50 ± 5.30	14.10 ± 6.20	14.50 ± 3.80	15.50 ± 5.30	14.10 ± 6.20
Lateral flexion away from the injured side, cm	15.4 (5.1)	14.8 (5.8)	0.743	14.80 ± 5.40	15.90 ± 4.20	14.40 ± 6.40	14.80 ± 5.40	15.90 ± 4.20	14.40 ± 6.40
Flexion injured side, °	154 (31)	158 (37)	0.747						
Flexion non-injured side, °	154 (38)	163 (27)	0.341						
Abduction, injured side, °	159 (27)	161 (34)	0.846						
Abduction, non-injured side, °	156 (37)	165 (30)	0.373						

	Olsen 2015			Caragounis 2015			Olsen 2013		
	Mean (SD) Internal fixation Vs Control			Mean ∆ Operated vs Non-Operated side			Mean ∆ Operated vs Non-Operated side		
Range of movement	**Fixation**	**Control**	**P**	**3 month**	**6 month**	**1 year**	**3 month**	**6 month**	**1 year**
* p-value <0.05 **, p-value <0.01, a Difference from 3 months to 6 months, b Difference from 3 months to 1 year									

Table 102 results of studies reporting chest wall deformity

Chest wall deformity			Rib fracture fixation		Non-operative		
Author/Year	**Follow Up**		**Frequency**	**Percentage**	**Frequency**	**Percentage**	**P Value**
Marasco 2013	3 months	Overlapping	8	38	10	59	0.35
	3 months	Displacement	4	18	7	0.41	0.16
	3 months	Angulation	3	14	9	0.53	0.01
Granetzny 2005			1	5	9	45	0.008
Ahmed 1995	3-9 months	Mild	3		0		
	3-9 months	Moderate	0		4		
	3-9 months	Severe	0		6		
Zhang[a] 2015	Unknown		0	0	12	41.38	<0.005
Marasco 2014	3 months		7	13.5			
Marasco 2016	3 months		0	0			
Weise 2016	6 months		0	0			
Wu 2015	2 months		3	4	72	93.5	0.017
Qiu 2016	2 months		3	14.29	11	64.71	0.002

Table 103 VAS pain scale 0-100mm.

Visual analogue pain		Rib fracture fixation					Non-operative		
Author/Year	**Follow Up**	**Mean**	**SD**	**Median**	**Q1**	**Q3**	**Mean**	**SD**	**P Value**
Farquhar 2016	6 months	65					67.2		
Khandelwal 2011	5 Days	91.5					62.5		<0.0001
Khandelwal 2011	15 Days	23.1					59.6		<0.0001
Khandelwal 2011	30 Days	11.2					45		<0.0001
Wu 2015	2 months	29	10				56	17	0.043
Qiu 2016	2 months	14.5	10				45	10.5	0.003
Metin 2016*	Post-Operative	31.6					63.6		
Moslam 2015	Post-Operative	63							
Redwan 2015	Post-Operative	20							
Yang 2010*	Day 1 post op	74	20						
	1 week post op	56	20						
	1 month	51	10						
Campbell 2009	Rest			10	0	23			
	Coughing			13	0	37.5			
	Deep breathing			10	0	24			
Olsen 2016	3 months	30							
Olsen 2016	6 Months	50							
(*Converted into 0-100 scale)									

Table 104 Studies reporting frequency of chronic pain

Chronic Pain		Rib fracture fixation		Non-operative		
Author/Year	**Follow Up**	**Frequency**	**%**	**Frequency**	**%**	**P Value**
Tanaka 2001	12 months	7	39	17	90	<0.05
Olsen 2016	Unknown	10	32	15	50	
Zhang 2015 No 2	Unknown	7	58	16	66.7	
Qiu 2016	2 months	1.45	0.7	4.5	1.05	
Caragounis 2016	6 weeks	12	35			
Caragounis 2016	3 months	4	12			
Caragounis 2016	6 months	6	16			
Caragounis 2016	12 months	6	13			
Lardoinois 2001	6 months	6	11			
Majercik 2014	16 months	8	16			
Mouton 1997	More than 3 months	5	24			

Table 105 Studies reporting analgesia use

Narcotic mg equivalents		Rib fracture fixation				Non-operative		
Author/Year	**Follow up**	**Mean**	**SD**	**Frequency**	**Percentage**	**Mean**	**SD**	**P value**
De Moya	Mean daily dose	79	63			76	55	0.65
De Moya	Mean days on IV morphine	10	5			7	5	0.04
Frequency of patients using opiates								
Caragounis 2016	6 weeks			18	53			
Caragounis 2016	3 months			13	38			
Caragounis 2016	6 Months			5	14			
Caragounis 2016	12 months			4	8.9			
Majercik 2014	16.1 months			2	4			

Table 106 Studies reporting chest discomfort

Chest Tightness/Discomfort		Rib fracture fixation		Non-operative		
Author/Year	**Follow up**	**Frequency**	**Percentage**	**Frequency**	**Percentage**	**P value**
Tanaka 2002	12 months	6	33	16	84	<0.05
Wu 2015	?	10	13.3	51	57.3	0.014
Campbell 2009	?	12	60			
Wiese 2015	6 months	13	19			
Yang 2010	3 months	7				
Yang 2010	6 months	7				

Chest discomfort VAS

Author/Year	Follow up	Mean	Lower CI	Upper CI	Mean	Lower CI	Upper CI	P value
Farquhar 2014	?	1.9	0.6	3.3	0.8	0.1	1.5	

Table 107 Studies reporting dyspnoea

Dyspnoea		Internal fixation		Non-operative		
Author/Year	**Follow Up**	**Frequency**	**Percentage**	**Frequency**	**Percentage**	**P Value**
Tanaka 2001	12 months	5	28	12	63	<0.05
Wu 2015	?	4	5.3	20	22.4	0.029
Campbell 2009	?	4	20			
Caragounis 2016	6 weeks	14	42.1			
Caragounis 2016	3 months	12	35.3			
Caragounis 2016	6 Months	10	27			
Caragounis 2016	12 months	7	15.6			
Dyspnoea Class		**Mean**		**Mean**		
Farquhar 2014	6 months	1		0.6		

Table 108 Studies reporting return to work in weeks and return to normal activities in days

Return to work		Rib fracture fixation		Non-operative		
Author/Year	**Type**	**Mean**	**SD**	**Mean**	**SD**	**P Value**
Qiu 2016	Normal activities	28.2 days	9.21	42.4 days	10.1	0.028
Khandelwal 2011	Normal activities	26.6 days		54.2 days		<0.0001
Lardoinois 2001	Return to Work	8 weeks				
Campbell 2009	Return to Work	3.9 weeks	3.3			
Majercik 2014	Return to Work	7.9 weeks	1			

Table 109 Studies reporting frequency of patients returning to employment

Returning to work		Rib fracture fixation		Non-operative		
Author/Year	**Follow Up**	**Frequency**	**Percentage**	**Frequency**	**Percentage**	**P Value**
Tanaka 2001	12 months	16	89	12	63	<0.05
Farquhar 2014	Unknown		36		23	
Qiu 2016	6 months	18	86	8	47.1	0.014
Bottlang 2013	3 months	5	31			
Bottlang 2014	6 months	7	47			
Majercik 2014	16 months	33	96			
Campbell 2009	Unknown		55			
Yang 2010	3 months	0	0			
Yang 2010	6 months	5	33			
Mouton	6 months		95			

Appendix B3 Meta-analysis result with subgroups of early and late fixation

Table 110 Studies that could not be classified into early or late fixation

Author/Date	Country	Type of Study	Injury	Maximum time in days
Wada 2015	Japan	NRS	FC + MRF	10
Buyukkarabaca 2015	Turkey	NRS	Flail Only	5
Schmitt-Neuerberg 1982	Germany	Series	FC + MRF	10
Jayle 2014	France	NRS	Flail Only	48
Zhang 2015	China	NRS	Flail Only	10
Marasco 2016	Australia	Series	FC + MRF	No timings given
Borerelly 2005	Iran	Series	Flail only	No timings given
Xu 2015	China	NRS	FC + MRF	No timings given
Olsen 2016	Sweden	NRS	FC + MRF	No timings given
Defreest 2016	USA	NRS	Flail Only	No timings given
Caragounis 2016	Sweden	Series	FC + MRF	No timings given
De Palma 2016	Italy	Series	FC + MRF	No timings given
Michelitsch 2016	Switzerland	Series	FC + MRF	No timings given
Moslam 2015	Egypt	Series	FC + MRF	No timings given
Nickerson 2015	USA	Series	FC + MRF	No timings given
Nickerson 2016	USA	Series	Flail Only	No timings given
Reber 1993	Switzerland	Series	Flail only	No timings given
Olsen 2013	Sweden	Series	Flail Only	No timings given
Mouton 1997	Switzerland	Series	Flail Only	No timings given
Qiu 2016	China	NRS	FC+ MRF	No timings given
Zhang 2015 b	China	NRS	Flail Only	No timings given
Galan 1992	Spain	NRS	Flail Only	No timings given
Metin 2016	Turkey	Series	FC + MRF	No timings given
Wu 2015	China	RCT	FC + MRF	No timings given
Velaquez 2016	Columbia	NRS	FC + MRF	No timings given
Chai 2013	China	Series	FC + MRF	No timings given
Pimakov 2014	Ukraine	Series	Unclear	No timings given
Pimakov 2015	Ukraine	Series	Unclear	No timings given
Redwan 2016	Germany	Series	FC + MRF	No timings given

Figure 44 Mechanical ventilation (subgroup early and late fixation

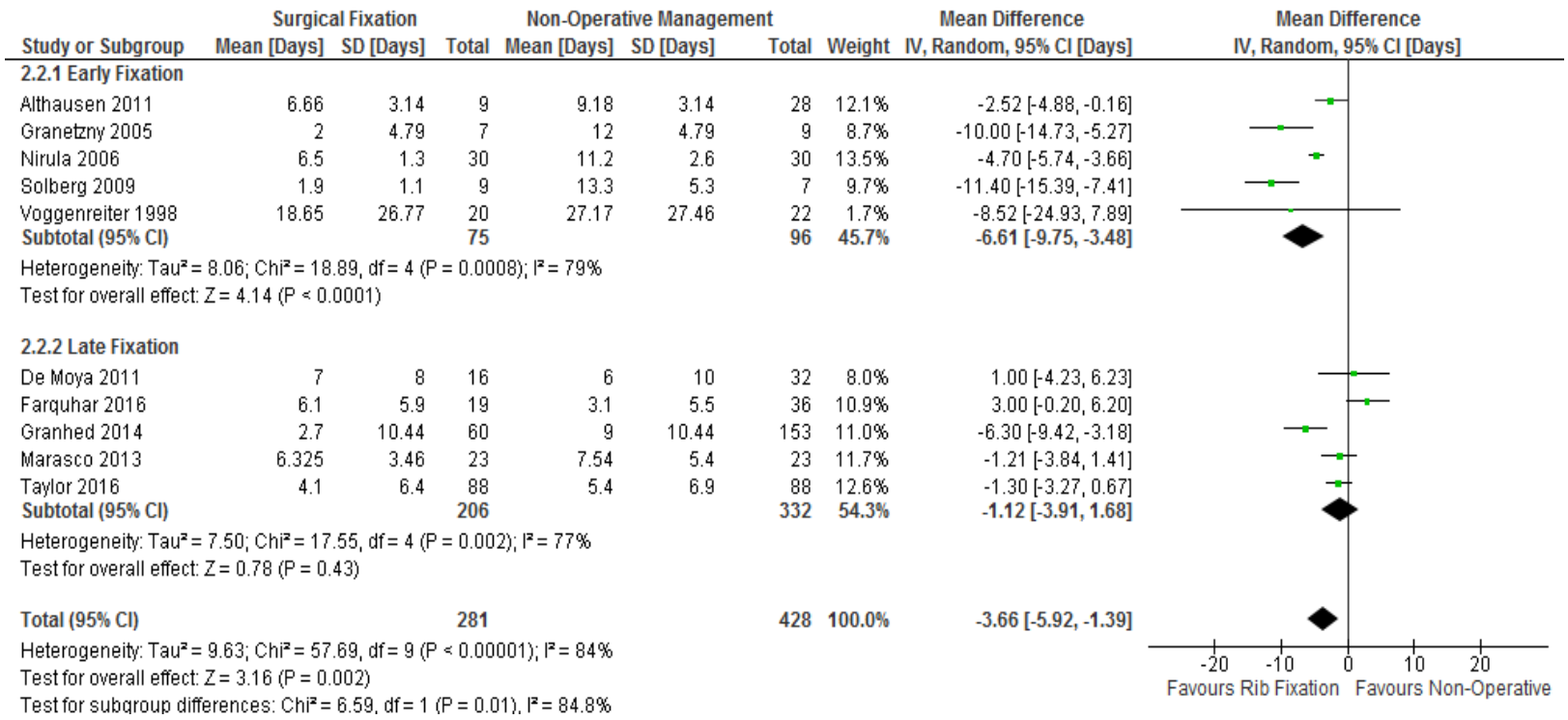


Figure 45 ICU Length of Stay (subgroup early and late fixation

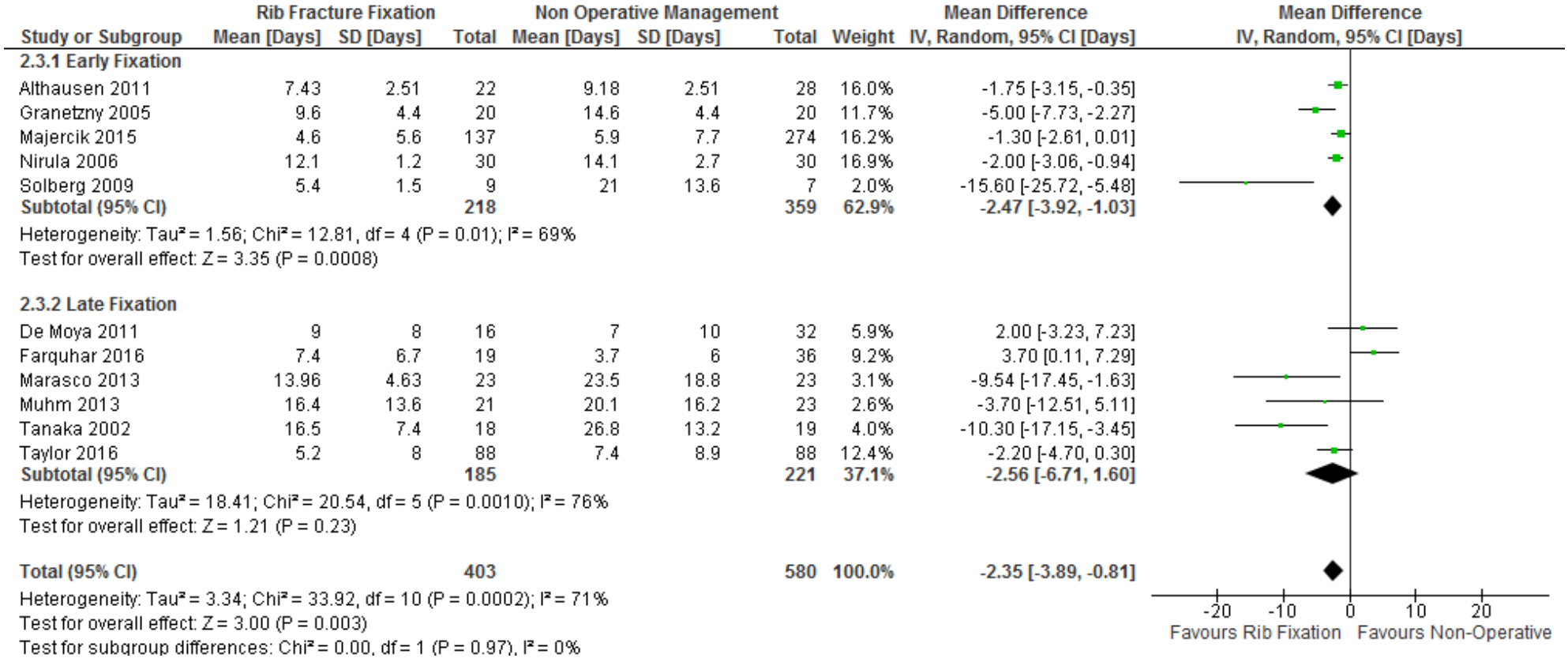


Figure 46 Length of hospital stay (subgroup early and late fixation)

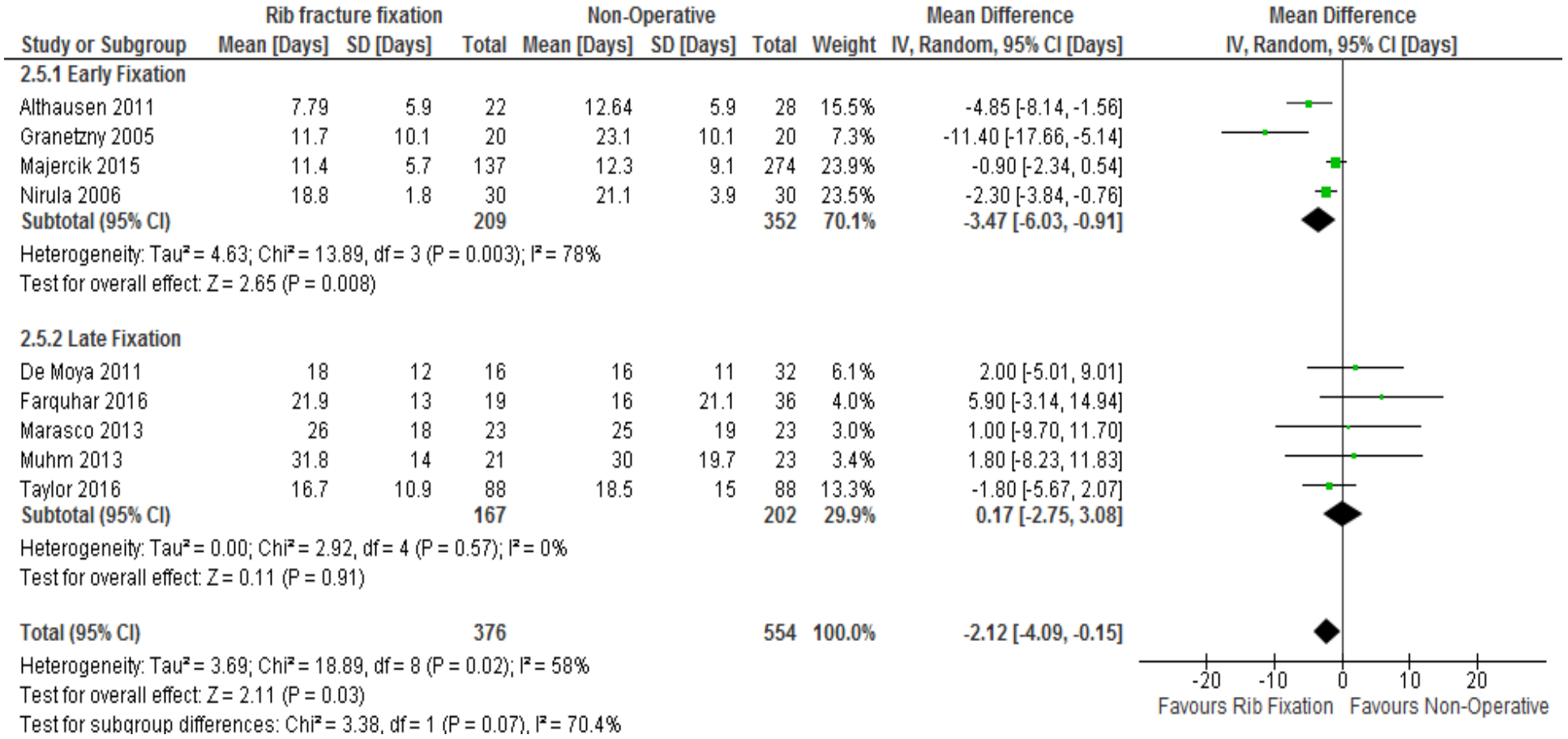


Figure 47 Mortality (subgroup early and late fixation)

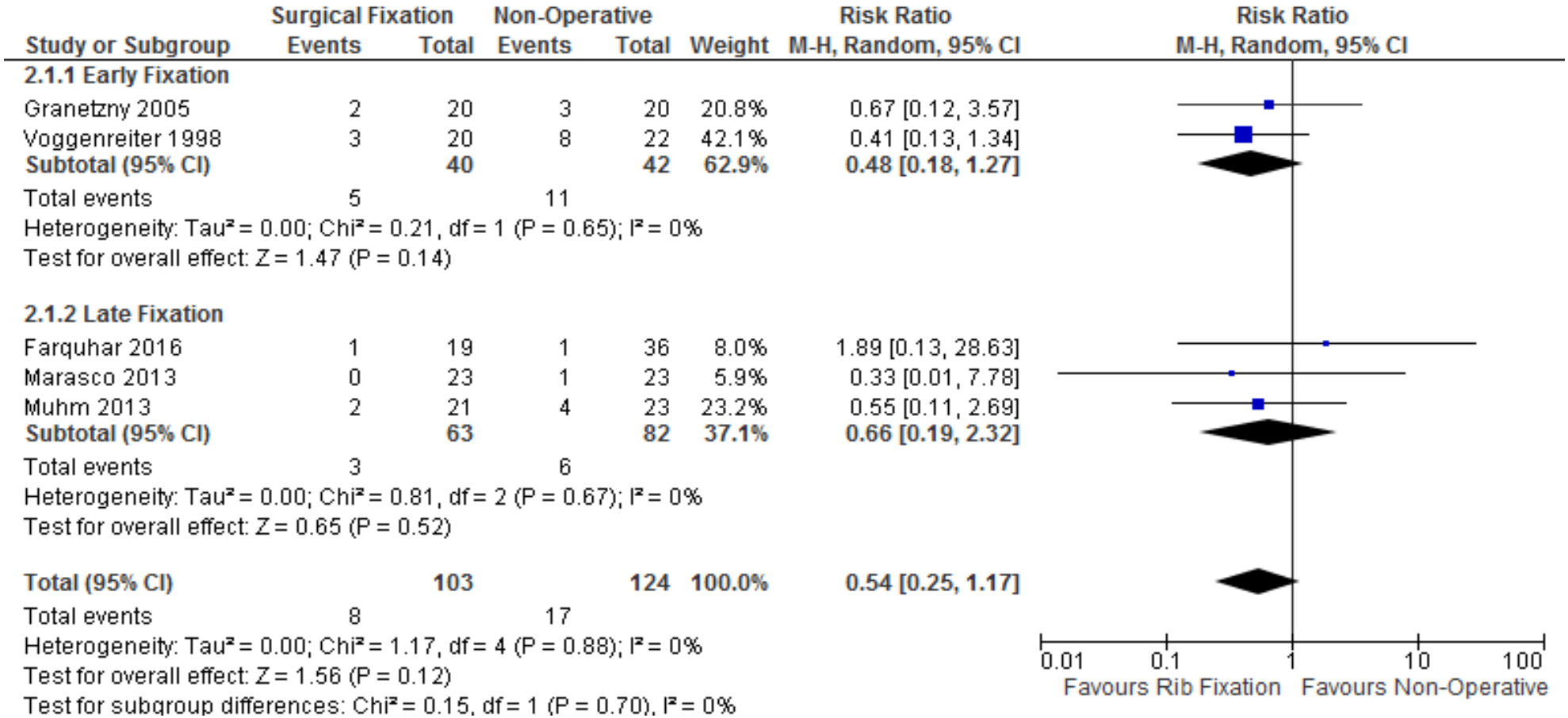
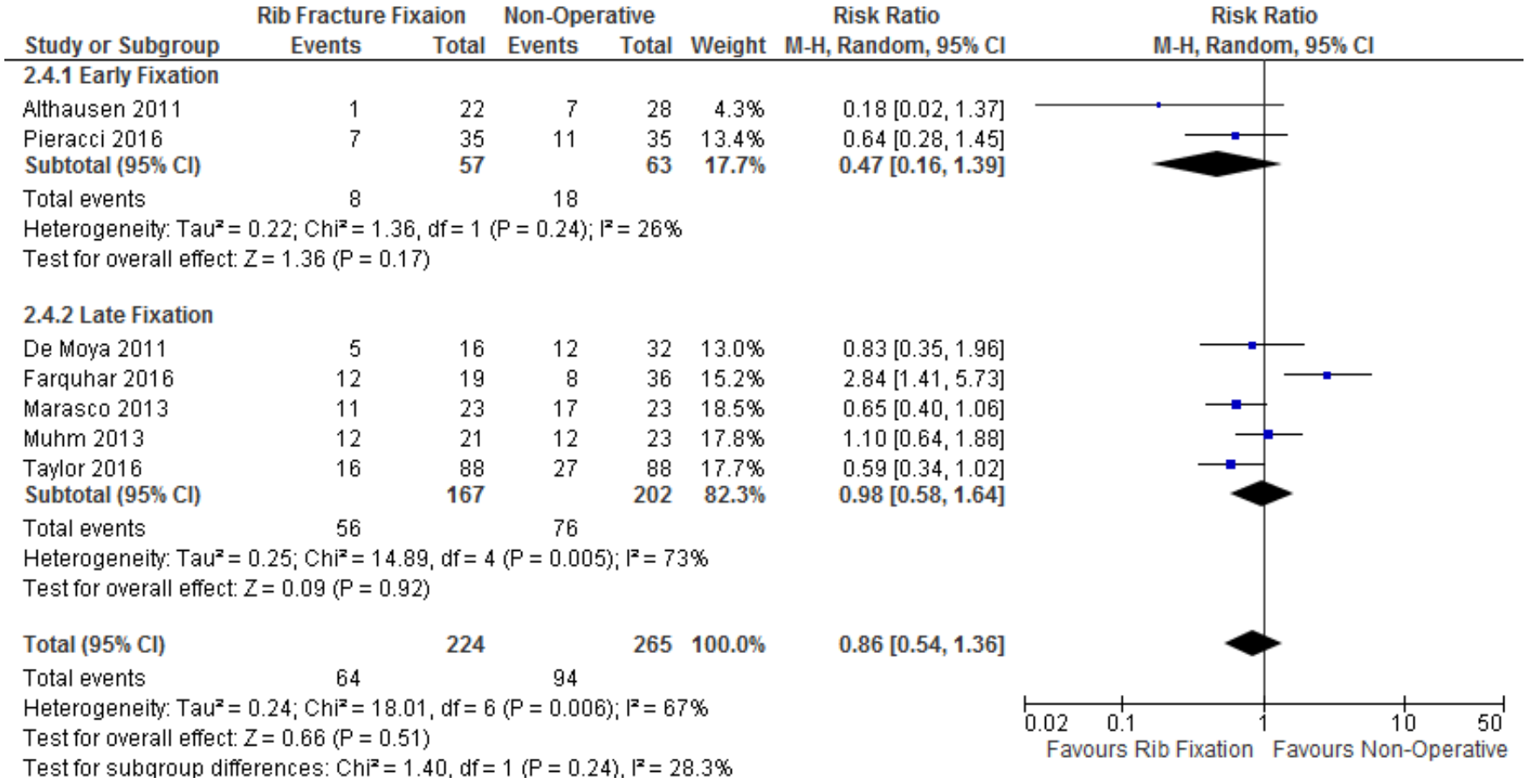


Figure 48 Pneumonia (subgroup early and late fixation)



Appendix C1 Recruitment leaflets and emails

Who is being asked to participate? *or* Why have I been asked to participate?

You are being asked to participate, as you have experienced a blunt chest trauma injury with rib fractures or you care for someone who has had this injury.

Do I have to take part?

The questionnaires are voluntary, you will be asked to consent to take part by accepting the terms at the beginning of the questionnaire.

Can I withdraw from the study at any time?

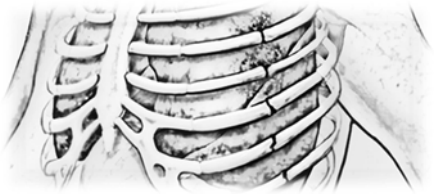
You can withdraw at any point up until the questionnaire is submitted. It is regrettable but data can't be withdrawn following questionnaire completion as all the data is anonymised and we will not be able to identify the data to withdraw.

A Core Outcome Set for Surgical Rib Fracture Fixation Trials – A Delphi Study

Have you experienced rib fractures as a patient or carer?

Have you had surgery for fractured ribs?

Do you want to influence research that could improve care of chest trauma in the future?



Who is doing the study?

The Chief Investigator is Dr Helen Ingoe who is an Orthopaedic Surgeon in Training based at the University of York Trials Unit. The York Trials Unit is sponsored by the British Orthopaedic Association to develop and expand the portfolio of trials in the UK related to trauma and orthopaedics. This work is being completed as part of an MD project.

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Y T U

Join Our Delphi Study Today

Please contact us if you would like further information or would like to take part in the study
The questionnaires will be open until xxx date xx
helen.ingoe@york.ac.uk

Appendix A 15/09/2017 Version 1.0

What is the purpose of this study?

To help patients, doctors and other health professionals make decisions about treatments, we need evidence about what works best. To do this researchers need to look at the effects those treatments have on patients. Researchers do this by measuring an 'outcome'.

When researchers design research studies to investigate treatments for health conditions they need to measure outcomes that are important and relevant to those people affected by the condition. To decide which outcomes are important researchers need to get everyone's opinion and try to reach agreement, or "**consensus**", on the most important outcomes.

What will I need to do?

If you decide to take part, you will be asked to give an opinion on what outcomes are most important to you. The study will include doctors and other health professionals but is anonymous to make sure everyone has an equal say. The aim of the study is to develop a consensus statement on the minimum recommended outcomes we should measure if undertaking a clinical study on surgical rib fracture fixation. Examples of outcome measures would include complications such as wound infections, clinical measures such as how well your lungs are working, life impact and use of services such length of stay in hospital or time to get back to work.

How do you choose core outcomes?

The research team has developed a long list of possible outcomes. You will be sent the list in an online questionnaire through an email link and asked to score the importance of each outcome. If, in your opinion, there are key outcomes missing from the list, you are encouraged to add these to the list. We refer to this as "**Round 1**" The ratings are sent back to the research team, who then summarise the responses from the group as a whole.

We will send a summary back to you in what we refer to as **Round 2**. You will be given a reminder of how the rest of the group scored. Using this information you will be asked to reflect on your own view and on the view of the group and to decide whether to stick with your original rating or change it. Through the whole process, you are not under any pressure to change your rating if you do not want to.

The responses are then sent back again to the research team who again collate the information. Every time we ask you for your opinion we call this a 'round'. There will be a maximum of three rounds lasting a **maximum of 15 minutes each**.

At the end of this process the research team produces a report on what the group has agreed as the most important outcomes. **These are called the 'core outcomes'**

Medical Panel Invitation email

Dear Participant,

Developing a Consensus on Indications, Timing and Core Outcomes for Rib Fracture Surgical Fixation

I am a Trauma and Orthopaedic Trainee surgeon undertaking a MD project at the University of York with funding from Orthopaedic Research UK.

I am inviting you to take part in a study in which we are bringing together clinicians who undertake rib fracture surgery and blunt chest trauma care, allied health professionals, rib fracture patients and carers. The aim of the study is to develop a consensus statement on the minimum recommended outcomes we should measure if undertaking a clinical study and the indications and timing of surgery. Clear outcomes and indications are key to developing robust research methods and increase the efficiency and value of research.

The consensus process will follow the Delphi method and completed as an anonymous online questionnaire. You will be asked to rate on a scale of 1 to 9 how much you agree with the outcomes and statements on timing and indications for surgery proposed in a list. Those outcomes that have a low relevance score will be discarded but all others will be scored again in a second round. A maximum of three rounds will take place.

All results will be anonymised using a study ID embedded within the questionnaire software. It is important that you complete all rounds as the reliability of the results could be compromised if you drop out. Even if you feel your views are in the minority compared to others within the group it is important to continue as the final results may overestimate the consensus.

The each survey will take between 15 - 25 minutes to complete and a certificate to evidence research participation will be sent on completion of all rounds.

If you are unable to participate or have physiotherapy and occupational therapy who would like to take part I would be grateful if you could forward this invite. My email address is below; please contact me directly and I will send out a personal invite.

A full summary of the study and instructions for completion is available in this document attached.

You can access the first round by clicking the link here.

I would like to thank you in advance of you taking part.

AHP and patient invitation email

Dear Participant,

A study to find out what outcomes best show how well rib fracture surgery works

I am a Trauma and Orthopaedic Trainee surgeon undertaking an MD project at the University of York with funding from Orthopaedic Research UK.

To help patients, doctors and other health professionals make decisions about treatments; we need evidence about what works best. To do this researchers need to look at the effects those treatments have on patients. Researchers do this by measuring an 'outcome'. For example, in a study of how well rib fracture surgery treatment works, 'outcomes' might include

- A measure of how fast you can blow air out of your lungs
- How long you stayed in hospital
- Quality of life

I am inviting you to take part in a study in which we are bringing together clinicians, allied health professionals, rib fracture patients and carers. The aim of the study is to develop a consensus on the minimum recommended outcomes we should measure to investigate how well rib fracture surgery works.

The consensus process will follow the 'Delphi method' completed as an anonymous online survey. You will be asked to 'rate' on a scale of 1 to 9 how much you agree with the outcomes that are listed. Each outcome will be scored at the end of the round and a summary will be given as feedback during the next round. You will get to reflect how other groups have scored before rescoring them. A maximum of three rounds will take place.

All results will be confidential. Each survey (round) will take less than 15 minutes to complete.

A full summary of the study and instruction for completion is available in this document attached.

You can access the first round by clicking the link here.

I would like to thank you for taking part.

Participant Information sheet for medical panel

UNIVERSITY of York
The Department of Health Sciences

Developing a Core Outcome Set and a Consensus Statement on Indications and Timing for Surgical Rib Fracture Fixation Trials

A Delphi Study
Participant Information Sheet

What is a Delphi Consensus? – A general overview of the process

A consensus on the **indications** and **timing of surgical fixation** of rib fractures is not well established or evidenced and has not been undertaken with a consensus panel of multiple clinical specialties. If considering further trial work on rib fracture surgical fixation then clear evidence for the indication and timing of surgery needs agreement.

How are health care treatments developed?

To help patients, doctors and other health professionals make decisions about treatments, we need evidence about what works best. Treatments are developed and tested by researchers to make sure they work and are safe. To do this researchers need to look at the effects those treatments have on patients. Researchers do this by measuring an '**outcome**'. For example, in a study of how well rib fracture surgery treatment works, 'outcomes' might include:

- A measure of how fast you can blow air out of your lungs
- How long you stayed in hospital
- Quality of life measure

How do researchers decide on the indications for surgery and what outcomes are important to measure in research studies?

When researchers design research studies to investigate treatments for health conditions they need to know what are the indications for that health intervention and what outcome measures are important and relevant to those people affected by the condition. To decide which outcomes are important researchers need to get everyone's opinion and try to reach agreement, or "consensus", on the most important outcomes. In order to do this, researchers carry out a 'consensus exercise'. One way of doing this is by using something called a 'Delphi' study. In a Delphi study researchers identify groups of people who are "experts" in the health condition they are interested in. "Experts" are:

- People with personal experience of the condition, for example, patients, carers and service users (it doesn't matter how long the person has had the condition for, their opinion is incredibly valuable).
- Health professionals with expertise in treating and caring for people with the condition.

Experts taking part in a Delphi study are asked to give their opinion on what outcomes are most important. The study is anonymous to make sure everyone has an equal say. Patients and allied health professionals will be asked their opinions on outcomes however only clinicians will be asked to rate statements on indications and timing of surgical fixation to a consensus statement.

What happens early on in a Delphi Study?

The research team has developed a long list of possible outcomes that they want to ask the experts about. This list has been created after looking at research papers.

What happens next?

You have been sent the list in the form of a questionnaire by email link and asked to score the importance of each statement and outcome. If, in your opinion, there are key outcomes or statements missing from the list, they you are encouraged to add these to the list. We refer to this as "Round 1" of the Delphi study. Your ratings will be returned back to the research team, we will then summarise the responses from the group as a whole and send this summary back to each expert in what we refer to

as Round 2 of the Delphi process. At this stage each expert is given the range of scores of the rest of the group. No-one in the group can see your score; and you can only see the overall results for the group as a whole. Using this information you are asked to reflect on your own view and on the view of the group and to decide whether you stick with your original rating or change it. Through the whole process no-one is under any pressure to change their rating if they don't want to. It is perfectly fine for you to stick with your original rating even if you rated the outcome or statement differently to the rest of the group. Your responses are then sent back again to the research team who again collate the information.

Every time the researchers ask the experts for their opinions we call this a 'round' of the Delphi. Each time the idea is that the experts review their previous score based on what the group rated in their last round. At the end of this process the research team produce a report on what the experts have agreed as the most important outcomes. These are called the 'core outcomes' for a particular health condition.

Aim of this study

The aim of the study is to develop a consensus on the **indications** and **timing of fixation** of rib fractures which will undertaken by **clinicians**. In addition a consensus will be undertaken to develop a **core outcome set** for surgical rib fracture fixation this part of the Delphi consensus will bring together **clinicians** in the field of rib fracture surgery and chest trauma care with **allied health professionals** and **patients**. The consensus process will follow the Delphi method and will be completed as anonymous online questionnaires with up to three rounds. Each round will be open for four weeks at a time.

It is encourged that you complete all rounds as the reliability of the results could be compromised if you drop out. Even if you feel your views are in the minority compared to others within the group it is important to continue as the final results may overestimate the consensus.

Who is doing the study?

The Chief Investigator is Dr Helen Ingoe who is an Orthopaedic Surgeon in Training based at the University of York Trials Unit. The York Trials Unit is sponsored by the British Orthopaedic Association to develop and expand the portfolio of trials in the UK related to trauma and orthopaedics. This work is being completed as part of an MD project and is sponsored by Orthopaedic Research UK.

orthopaedic research UK

Who is being asked to participate? *or* Why have I been asked to participate?

You are being asked to participate, as you have experienced a blunt chest trauma injury with rib fractures or you care for someone who has had this injury.

Do I have to take part?

The questionnaires are voluntary, you will be asked to consent to take part by accepting the terms at the beginning of the questionnaire.

What will be involved if I take part in this study?

The study will involve up to three online questionnaires each will take 15 minutes to complete online.

Delphi Consensus

Method

Round One

The first part of the questionnaire will ask you about **your thoughts** on indications for surgery, timing of surgery and outcomes you feel are important to measure. The second part comprises of a list of outcomes that has been compiled following a review of the research studies. You will be asked to score on a scale of 1 to 9

important the statement on indications and timing or the outcome measure is, one being not important and nine being critically important. There will be a free text box for you to add any comments. Comments could include if you think that a statement or outcome is already covered within another statement or if you feel the outcome needs further explanation, expansion or clarity. We would strongly recommend you provide feedback on items such that we can incorporate your thoughts and ideas into the second round. If you are unable to comment on the outcome then please select unable to comment.

Scoring

Statement and outcome scores will be reviewed by the research team, outcomes that have a some level of agreement will be submitted into a second round in which you will be asked to rescore. Statements that did not have agreement will be dropped from the consensus process.

Round Two

All new statements and statements that had agreement will be rescored in the second round. You will be able to see the range of scores from each of the groups to compare. Using this information each expert is asked to reflect on their own view and on the view of the group. No one will be able to see individual scores.

Round Three

The research team will undertake another scoring process and further outcomes may be dropped. With the feedback from round two, you will rescore all the outcomes that had agreement. The aim of the third round is to finalise the core outcome set.

A maximum of 3 rounds will take place and a core outcome set will be formed after this round.

What are the advantages/benefits and disadvantages/risks of taking part?

Research into rib fracture fixation is lacking in the UK and it is vital that clinical trials in this area should be valid, robust and efficient. Providing a clear consensus statement on the outcome measures will inform future trial work. A certificate to evidence research participation will be sent on completion of all rounds.

Can I withdraw from the study at any time?

You can withdraw at any point up until the questionnaire is submitted. It is regrettable but data can't be withdrawn following questionnaire completion as all the data is anonymised and we will not be able to identify the data to withdraw.

Will the information I give be kept confidential?

All storage and archiving will be conducted in line with the York Trials Unit Standard Operating Procedure. All study data will be stored on a secure server accessed via a password protected computer at the University of York. No identifiable data will be collected and email addresses will not be linked to the data. We will only collect your email address if you submit it within the form and only to provide you with a certificate or report of the findings.

What will happen to the results of the study?

A summary report of the study will be available. If you would like a copy of this then please enter your email within the questionnaire and a copy of the findings will be sent to you.

Who has reviewed this study?

The research has been approved by the Department of Health Sciences' Research Governance Committee at the University of York and the Research and Ethics Committee (REC) and Health Research Authority (HRA).

Who do I contact in the event of a complaint?

If you have any concerns please contact Dr Catriona McDaid (Senior Research Fellow and Research Supervisor) Tel: +44 (0)1904 321371 Email: catriona.mcdaid@york.ac.uk

If you agree to take part, would like more information or have any questions or concerns about the study please contact

Patient and AHP information leaflet

UNIVERSITY of York
The Department of Health Sciences

A Core Outcome Set for Surgical Rib Fracture Fixation Trials

A Delphi Study

Participant Information Sheet

What is a Delphi Consensus? – A general overview of the process

How are health care treatments developed?

To help patients, doctors and other health professionals make decisions about treatments, we need evidence about what works best. Treatments are developed and tested by researchers to make sure they work and are safe. To do this researchers need to look at the effects those treatments have on patients. Researchers do this by measuring an 'outcome'. For example, in a study of how well rib fracture surgery treatment works, 'outcomes' might include:

- A measure of how fast you can blow air out of your lungs
- How long you stayed in hospital
- Quality of life measure

How do researchers decide on what outcomes are important to measure in research studies?

When researchers design research studies to investigate treatments for health conditions they need to measure outcomes that are important and relevant to those people affected by the condition. To decide which outcomes are important researchers need to get everyone's opinion and try to reach agreement, or "consensus", on the most important outcomes. In order to do this, researchers carry out a 'consensus exercise'. One way of doing this is by using something called a 'Delphi' study. In a Delphi study researchers identify groups of people who are "experts" in the health condition they are interested in. "Experts" are:

- People with personal experience of the condition, for example, patients, carers and service users (it doesn't matter how long the person has had the condition for, their opinion is incredibly valuable).
- Health professionals with expertise in treating and caring for people with the condition.

Experts taking part in a Delphi study are asked to give their opinion on what outcomes are most important. The study is anonymous to make sure everyone has an equal say.

What happens early on in a Delphi Study?

The research team will have developed a long list of possible outcomes that they want to ask the experts about. This list is likely to have been created after looking at research papers, and sometimes after interviewing patients (see the flowchart)

What happens next?

You have been sent the list in the form of a questionnaire by email link and asked to score the importance of each statement and outcome. If, in your opinion, there are key outcomes or statements missing from the list, they you are encouraged to add these to the list. We refer to this as "**Round 1**" of the Delphi study. Your ratings will be returned back to the research team, we will then summarise the responses from the group as a whole and send this summary back to each expert in what we refer to as **Round 2** of the Delphi process. At this stage each expert is given the range of scores of the rest of the group. No-one in the group can see your score; and you can only see the overall results for the group as a whole. Using this information you are asked to reflect on your own view and on the view of the group and to decide whether you stick with your original rating or change it. Through the whole process, you are not under any pressure to change your rating if you do not want to. It is perfectly fine for you to stick with your original rating even if you rated the outcome or statement differently to the rest of the group. Your responses are then sent back again to the research team who again collate the information.

Every time the researchers ask the experts for their opinions we call this a 'round' of the Delphi. Each time the idea is that the experts review their previous score based on what the group rated in their last round. At the end of this process the research team produce a report on what the experts have agreed as the most important outcomes. These are called the 'core outcomes' for a particular health condition.

Aim of this study

The aim of the study is to develop a core outcome set for surgical rib fracture fixation a clinical study. The Delphi consensus in will bring together doctors, allied health professionals, patients and carers. The consensus process will follow the 'Delphi method' completed as an anonymous online survey with up to three rounds. Each round will be open for four weeks at a time.

It is important that you complete all rounds as the reliability of the results could be compromised if you drop out. Even if you feel your views are in the minority compared to others within the group it is important to continue as the final results may overestimate the consensus.

Who is doing the study?

The Chief Investigator is Dr Helen Ingoe who is an Orthopaedic Surgeon in Training based at the University of York Trials Unit. The York Trials Unit is sponsored by the British Orthopaedic Association to develop and expand the portfolio of trials in the UK related to trauma and orthopaedics. This work is being completed as part of an MD project.

Who is being asked to participate? *or* Why have I been asked to participate?

You are being asked to participate, as you have experienced a blunt chest trauma injury with rib fractures or you care for someone who has had this injury.

Do I have to take part?

The questionnaires are voluntary, you will be asked to consent to take part by accepting the terms at the beginning of the questionnaire.

What will be involved if I take part in this study?

The study will involve up to three online questionnaires each will take less than 30 minutes to complete online.

Delphi Consensus Method

Round One

The first part of the questionnaire will ask you about **your thoughts** on what outcomes you feel are important to measure. The second part comprises of a list of outcomes that has been compiled following a review of the research studies. You will be asked to score on a scale of 1 to 9 how important is the outcome, one being not important and nine being critically important. There will be a free text box for you to add any comments. Comments could include if you think that an outcome is already covered within another statement or if you feel the outcome needs further explanation, expansion or clarity. We would strongly recommend you provide feedback on items such that we can take your thoughts and ideas into the second round. If you are unable to comment on the outcome then please select unable to comment.

Scoring

Outcome scores will be reviewed by the research team, outcomes that have a high level of agreement will be submitted into a second round in which you will be asked to rescore. Statements that did not have agreement will be dropped from the consensus process.

Round Two

All new statements and statements that had agreement will be rescored in the second round. You will be able to see the range of scores from the rest of the groups to compare. Using this information each expert is asked to reflect on their own view and on the view of the group. No one will be able to see individual scores.

Round Three

The research team will undertake another scoring process and further outcomes may be dropped. With the feedback from round two, you will rescore all the outcomes that had agreement. The aim of the third round is to finalise the core outcome set.

A maximum of 3 rounds will take place and a core outcome set will be formed after this round.

What are the advantages/benefits and disadvantages/risks of taking part?

Research into rib fracture fixation is lacking in the UK and it is vital that clinical trials in this area should be valid, robust and efficient. Providing a clear consensus statement on the outcome measures will inform future trial work.

Can I withdraw from the study at any time?

You can withdraw at any point up until the questionnaire is submitted. It is regrettable but data can't be withdrawn following questionnaire completion as all the data is anonymised and we will not be able to identify the data to withdraw.

Will the information I give be kept confidential?

All storage and archiving will be conducted in line with the York Trials Unit Standard Operating Procedure. All study data will be stored on a secure server accessed via a password protected computer at the University of York. No identifiable data will be collected and email addresses will not be linked to the data. We will only collect your email address if you submit it within the form and only to provide you with a certificate or report of the findings.

What will happen to the results of the study?

A summary report of the study will be available. If you would like a copy of this then please enter your email within the questionnaire and a copy of the findings will be sent to you.

Who has reviewed this study?

The research has been approved by the Department of Health Sciences' Research Governance Committee at the University of York.

Who do I contact in the event of a complaint?

If you have any concerns please contact Dr Catriona McDaid (Senior Research Fellow and Research Supervisor) Tel: +44 (0)1904 321371 Email: catriona.mcdaid@york.ac.uk

If you agree to take part, would like more information or have any questions or concerns about the study please contact

Miss Helen Ingoe MBBS, MSc, MRCS Ed, ORUK Research Fellow and Orthopaedic Registrar in Training

ARRC Building, York Trials Unit, Department of Health Sciences, University of York, Heslington, YO10 5DD. helen.ingoe@york.ac.uk, 01905 321830

Thank you for taking the time to read this information sheet.

Appendix C2 Electronic Delphi Survey

UNIVERSITY of York
The Department of Health Sciences

The Delphi Technique: Developing a Consensus on Indications, Timing and Core Outcome Measures for Rib Fracture Surgical Fixation

Consent

This question confirms your consent to participate in the study.

The decision to complete this consensus questionnaire is voluntary. If you do complete the questionnaire, information you provide will be included in our analysis along with anonymised direct quotes.

- I confirm I have read an understood the information provided above and in the participant information sheet – click here
- I understand that the completion of this questionnaire is voluntary
- I agree to the use of anonymised quotes in publications
- I agree that my data gathered in this study will be kept and stored confidentially
- I understand I can drop out at anytime

It is encouraged that you complete all rounds as the reliability of the results could be compromised if you drop out. Even if you feel your views are in the minority compared to others within the group it is important to continue as the final results may overestimate the degree of consensus.

Do you agree with all of these statements and agree to take part in this study?

Yes

No

Are you an **allied health professional**, **clinician**, **patient** or **carer**? – Drop down box

Patient or Carer	**(takes the participant only to the outcome questions)**
Allied Health Professional	**(takes the participant only to the outcome questions)**
Clinician	**(takes participant through the full survey)**

If clinician box is selected a further question will be asked

What is your **specialty?**

Emergency Medicine	General Surgery
Cardiothoracic Surgery	Intensive Care Medicine
Trauma and Orthopaedics	Other with free text box

Questionnaire Page 1

Medical panel only

In your **own words**, list up to **five INDICATIONS** in which you would offer surgery to fix any type of adult rib fracture. (Could include a certain injury pattern, patient demographic or a particular sign or symptom)

- Indication 1
- Indication 2
- Indication 3
- Indication 4
- Indication 5

In your **own words**, what would be the **EARLIEST** you would operate on adult patient?

- Earliest Timing 1
- Earliest Timing 2
- Earliest Timing 3

In your **own words**, what would be the **LATEST** you would operate on adult patient?

- Latest Timing 1
- Latest Timing 2
- Latest Timing 3

In your **own words**, how long would you **TRIAL WEANING** from a ventilator before considering rib fracture fixation?

- Wean Time 1
- Wean Time 2
- Wean Time 3

All participants will answer this question

In your **own words**, what do you believe are the most important **OUTCOMES** to measure following rib fracture surgery in adults? Please list up to **five** outcome measures.

- Outcome 1
- Outcome 2
- Outcome 3
- Outcome 4
- Outcome 5

Please click here to access the information leaflet

Questionnaire Page 2

Medical panel only

The second part of the questionnaire will ask you to rate the importance of each statement based on your experience. Statements are in three groups including indications for surgery, timing of surgery and outcome measures.

Indications for surgery

In this section, each statement describes an indication for surgical fixation of rib fractures. We would like you to rate, which you feel are important and should inform a list of recommendations on rib fracture surgery.

If you feel unable to comment based on your experience, please select 'unable to score'. **Please rate on the scale**

1 – 3 Not important
4 - 6 Important but not critical
7 - 9 Critically important.

If you would like clarification on any of the statements or further instructions, please click the link here

A list of the statements is provided but will be formatted as below with a rating scale for each statement.

Definitions

Flail SEGMENT – A radiological diagnosis of a segmental rib fracture in 2 or more adjacent ribs

Flail CHEST – A clinical diagnosis of a flail segment with paradoxical movement

A patient should be **routinely offered** surgical rib fixation for the following injury patterns:

Segmental fractures

1. Any **Flail SEGMENT** – no paradoxical movement
2. Any **Flail SEGMENT** with paradoxical movement (flail chest)
3. **Flail CHEST** with respiratory compromise
4. **Flail CHEST** and patient requiring invasive ventilation
5. **Flail CHEST** and intractable pain despite regional and epidural anaestheia
6. **Flail CHEST** and failure to wean from ventilation within 48 hours
7. **Flail CHEST** with deformity
8. **Flail CHEST** requiring tracheostomy placement
9. **Flail CHEST** and haemodynamic instability
10. **Flail CHEST** and pulmonary contusion
11. **Flail CHEST** and traumatic brain injury
12. **Flail CHEST** and underlying chronic lung disease

Simple Rib Fractures

13. **FOUR** or more **unilateral** adjacent rib fractures (non-flail chest)
14. **TWO** or **THREE unilateral** adjacent rib fractures (non-flail chest)
15. **ONE unilateral** rib fracture (non-flail chest)
16. **MULTIPLE** adjacent rib fractures with displacement of more than 1 rib width
17. **MULTIPLE** adjacent rib fractures with paradoxical movement
18. **MULTIPLE** adjacent rib fractures with respiratory compromise
19. **MULTIPLE** adjacent rib fractures and patient requiring invasive ventilation
20. **MULTIPLE** adjacent rib fractures and intractable pain despite regional and epidural anaestheia
21. **MULTIPLE** adjacent rib fractures and failure to wean from ventilation within 48 hours
22. **MULTIPLE** adjacent rib fractures with deformity
23. **MULTIPLE** adjacent rib fractures requiring tracheostomy placement
24. **MULTIPLE** adjacent rib fractures and haemodynamic instability
25. **MULTIPLE** adjacent rib fractures and pulmonary contusion
26. **MULTIPLE** adjacent rib fractures and traumatic brain injury
27. **MULTIPLE** adjacent rib fractures and underlying chronic lung disease

Other indications

28. **ANY chest wall injury** requiring a thoracic operation for another indication (fix on retreat)
29. **ANY chest wall injury** with more than 30% volume loss of hemithorax
30. **ANY rib fracture** with anticipated non-union

Please write any comments you have on the above statements. Comments could include if you think that a statement is already covered within another or if you feel the statement needs further explanation, expansion or clarity. We would **strongly recommend** you provide feedback on items such that we can incorporate your thoughts and ideas into the second round.

Questionnaire Page 3

Timing of surgery

In this section, each statement describes a scenario in which you are asked on your opinion on the timing of surgical fixation of rib fractures. We would like you to rate, which you feel are important and should inform a list of recommendations on timing of rib fracture surgery.

If you feel unable to comment based on your experience, please select 'unable to score'. **Please rate on the scale**

1 – 3 Not important
4 - 6 Important but not critical
7 - 9 Critically important.

If you would like clarification on any of the statements or further instructions, please click the link here

In the **first** scenario, your patient satisfies the indications for surgery. Having decided that your patient **requires surgery** in your opinion what would be the **EARLIEST** you would surgically fix any patient regardless of the **ventilation state** or **the injury morphology**?

1. The **EARLIEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **within 24 hours** after injury
2. The **EARLIEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **between 24 and 48 hours** after injury
3. The **EARLIEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **between 48 and 72 hours** after injury
4. The **EARLIEST** time a patient (independent of ventilation status or injury morphology should have fracture fixation is **between 3 and 5 days** after injury
5. The **EARLIEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **between 5 and 7 days** after injury
6. The **EARLIEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation **is between 7 and 14 days** after injury
7. The **EARLIEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation **is more than 14 days** after injury

n the **second** scenario, your patient satisfies the indications for surgery. Having decided that your patient **requires surgery** in your opinion what would be the **LATEST** you would surgically fix any patient regardless of the **ventilation state** or **the injury morphology**?

8. The **LATEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **within 24 hours** after injury
9. The **LATEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **between 24 and 48 hours** after injury
10. The **LATEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation **is between 48 and 72 hours** after injury
11. The **LATEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **between 3 and 5 days** after injury
12. The **LATEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **between 5 and 7 days** after injury
13. The **LATEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **between 7 and 14 days** after injury
14. The **LATEST** time a patient (independent of ventilation status or injury morphology) should have fracture fixation is **more than 14 days** after injury

For a rib fracture patient who is **ventilated**, the **ABILITY TO WEAN** from a ventilator may influence decision making.

In the **third** scenario, your rib fracture patient is ventilated. How long would you use a **TRIAL OF WEANING** from a ventilator **BEFORE** considering surgical fixation?

15. In a patient that requires invasive ventilation, they should **NOT** have a **TRIAL OF WEANING** from a ventilator before considering surgical fixation
16. In a patient that requires invasive ventilation, they should have a **TRIAL OF WEANING** from a ventilator for **at least 24 hours** before considering surgical fixation
17. In a patient that requires invasive ventilation, they should have a **TRIAL OF WEANING** from a ventilator **between 24 and 48 hours** before considering surgical fixation
18. In a patient that requires invasive ventilation they should have a **TRIAL OF WEANING** from a ventilator **between 48 hours and 72 hours** before considering surgical fixation
19. In a patient that requires invasive ventilation they should have a **TRIAL OF WEANING** from a ventilator **between 3 and 5 days** before considering surgical fixation
20. In a patient that requires invasive ventilation they should have a **TRIAL OF WEANING** from a ventilator **between 5 and 7 days** before considering surgical fixation
21. In a patient that requires invasive ventilation should have a **TRIAL OF WEANING** from a ventilator **between 7 and 14 days** before considering surgical fixation
22. In a patient that requires invasive ventilation should have **A TRIAL OF WEANING** from a ventilator **more than 14 days** before considering surgical fixation

The **forth** scenario describes in what time frame after a **decision** has been made on treatment should patients be **transferred**, **referred** or **operated** on.

23. Patients should be **REFERRED** to a **multidisciplinary trauma unit** within **24 hours** for consideration of surgical rib fracture fixation
24. Patients should be **REFERRED** to a **multidisciplinary trauma unit** within **48 hours** for consideration of surgical rib fracture fixation
25. Patients should be **TRANSFERRED** to a **multidisciplinary trauma unit** for rib fracture fixation within **24 hours** of the decision to transfer or the patient becoming fit for transfer.
26. Patients should be **TRANSFERRED** to a **multidisciplinary trauma unit** for rib fracture fixation within **48 hours** of the decision to transfer or the patient becoming fit for transfer.
27. Patients with rib fractures (independent of ventilation status or type of injury) should have surgical fixation **within 24 hours** of the **DECISION to operate** unless patient becomes unwell or there are complications
28. Patients with rib fractures (independent of ventilation status or type of injury) should have surgical fixation **within 48 hours** of the **DECISION to operate** unless patient becomes unwell or there are complications

Please write any comments you have on the above statements. Comments could include if you think that a statement is already covered within another or if you feel the statement needs further explanation, expansion or clarity. We would strongly recommend you provide feedback on items such that we can incorporate your thoughts and ideas into the second round.

Questionnaire Page 4

All participants will answer the following questions

Outcomes

In this section, each statement describes a type of outcome. We would like you to rate, which you feel are important and should inform a list of recommendations for a core outcome set on rib fracture surgery.

It is the expectation that the core outcome set will always be collected and reported as a minimum within future trials making it easier for trials to be compared and contrasted. Other particular outcomes of relevance may be included within trial but may not form part of the 'core' outcome set.

If you feel unable to comment based on your experience, please select 'unable to score'. **Please rate on the scale**

1 – 3 Not important
4 - 6 Important but not critical
7 - 9 Critically important.

If you would like clarification on any of the statements or further instructions, please click the link here

Adverse events

How important are the following **adverse events** (a complication) for the evaluation rib fracture surgery effectiveness?

1. Overall adverse events (a complication)
    a. **Acute Respiratory Distress Syndrome** (not able to get enough oxygen into the body due to inflammation in the lungs in critically ill patients)
    b. **Barotrauma** (pressure damage to lungs following using a machine to help you breathe)
    c. **Empyema** (a collection of pus in the lining of the lung and the lining or the ribcage)
    d. **Mediastinitis** (inflammation or infection of the lining surrounding the heart)
    e. **Metal work failure** (broken metal plates within the body)
    f. **Multi Organ Failure** (a life threatening illness that causes the organs (lungs, liver, kidneys, heart) of the body to stop working)
    g. **Pleural effusion** (fluid between the lining of the lung and the lining or the ribcage)
    h. **Pneumonia** (an infection within the lung)
    i. **Pulmonary embolism** (clot of material (an embolus) that blocks blood from getting to the lungs)
    j. **Reintubation or Failed extubation** (having a tube reinserted into the windpipe to help breathing after removal of a previous tube)
    k. **Re-operation** (needing a further operation)
    l. **Respiratory failure** (not able to get enough oxygen into the body)
    m. **Retained Haemothorax** (blood that stays between the lining of the lung and the lining or the ribcage)
    n. **Sepsis** (a life-threatening illness that can occur when the whole body reacts to an infection)
    o. **Wound Infection** (redness and pain over the surgical site)
2. Overall perioperative adverse events (a complication during surgery)
    a. **Iatrogenic mediastinal injury** (an injury to the cavity containing the heart during surgery)
    b. **Iatrogenic nerve injury** (an injury to a nerve caused by surgery)
    c. **Iatrogenic thoracic injury** (an injury to the cavity containing the lungs during surgery)
    d. **Iatrogenic vascular injury** (an injury to a blood vessel caused by surgery)
3. Rib fracture non-union (rib fractures that do not heal)

Death

How important is the following **mortality** outcome for the evaluation rib fracture surgery effectiveness?

4. **Mortality**

Physiological or clinical

How important are the following **physiological and clinical** outcomes for the evaluation rib fracture surgery effectiveness?

5. **Acute pain** (sudden pain)
6. **Breathing movements** (the movement of the rib cage during breathing)
7. **Chest discomfort/ tightness**
8. **Chest wall deformity** (the shape of the rib cage)
9. **Chronic Pain** (ongoing pain)
10. **Dysopnea** (shortness of breath)
11. **Fracture healing** (how much the fracture has healed or united)
12. **Kinesiophobia** (fear of moving)
13. **Lung Function** (how well air is blow out of the lungs)
14. **Movement of the thorax** (how well the rib cage moves)
15. **Oxygen saturations** (how much oxygen in the blood)
16. **Scoliosis** (curvature of the spine)
17. **Shoulder function** (how well the shoulder works)
18. **Ventilation** (how well air can move between the lungs and outside the body)

Life impact

How important are the following **life impact** outcomes for the evaluation rib fracture surgery effectiveness?

19. **Disability** (a limit to a person's movements, senses, or activities)
20. **Discharge Destination** (where a patient lives after leaving hospital)
21. **Home Oxygen Therapy** (using a mask connected to a cylinder of oxygen to help with breathing)
22. **Mental health** (person's emotional well-being)
23. **Physical function** (performing tasks)
24. **Quality of life** (the standard of health, comfort, and happiness experienced by an individual)
25. **Return to Activities**
26. **Return to Work**
27. **Satisfaction** (whether the service met your requirements)

Resource use

How important are the following **resource use** outcomes for the evaluation rib fracture surgery effectiveness?

28. **Antibiotic requirements** (whether antibiotic medicine is needed)
29. **Chest drain** (a tube that is inserted into the chest to get rid of air or fluid)
30. **Cost of treatment**
31. **Epidural** (an injection in the back to stop feeling pain in a part of the body)
32. **Hospital readmission** (If you need to come back to hospital after leaving the hospital following your treatment)
33. **Hospital stay** (how long someone stays in hospital)
34. **Intensive care unit (ICU) stay** (a specialised ward in a hospital that cares for patients who are critically ill and requires specialist medical equipment and nursing care)
35. **Intensive care unit (ICU) readmission** (the need to come back to ICU after leaving the ICU following treatment)
36. **Invasive mechanical ventilation** (a tube inserted into the windpipe and attached to a machine that assists breathing)
37. **Non-invasive ventilation** (through a mask or a hood a machine helps supports a patient's own breathing)
38. **Plasma Transfusion requirements** (receiving the part of the blood that contains factors that help the blood clot and take away used products from a donor by injection)
39. **Red Cell Transfusion requirements** (receiving the part of the blood that contain red cells (red cells carry oxygen) from a donor by injection
40. **Tracheostomy** (a cut in the wind pipe replaced with a tube that helps reduce the work of breathing)

Please write any comments you have on the above statements. Comments could include if you think that a statement is already covered within another or if you feel the statement needs further explanation, expansion or clarity. We would strongly recommend you provide feedback on items such that we can incorporate your thoughts and ideas into the second round.

Questionnaire Page 5

Are there any statements relating to indications for rib fracture fixation surgery that you think have not been covered in this questionnaire?

Are there any statements relating to timing of surgery for rib fracture fixation that you think have not been covered in this questionnaire?

Are there any statements on outcome measures for rib fracture fixation that you think have not been covered in this questionnaire?

Appendix C3 Delphi scoring results Tables

Table 111 Indications and timing scoring for Rounds 1 to 3

Indications and timing of surgery	Percentage for each score category in Round 1				Percentage for each score category in Round 2				Percentage for each score category in Round 3			
	Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9	
Any Flail SEGMENT No paradoxical movement	25.8	58.1	16.1	N	-	-	-	-	-	-	-	-
Any Flail SEGMENT with paradoxical movement (flail chest)	0	25.8	74.2	Y	5.3	10.5	84.2	Y	0	6.3	93.8	Y
Flail CHEST with respiratory compromise	0	0	100	Y	5.3	0	94.7	Y	0	0	100	Y
Flail CHEST and patient requiring invasive ventilation	0	0	100	Y	0	0	100	Y	0	0	100	Y
Flail CHEST and intractable pain despite regional and epidural anaestheia	0	18.8	81.3	Y	5.3	10.5	84.2	Y	0	0	100	Y
Flail CHEST and failure to wean from ventilation within 48 hours	0	0	100	Y	5.3	0	94.7	Y	0	0	100	Y
Flail CHEST with deformity	0	28.1	71.9	Y	0	31.6	68.4	N	-	-	-	-
Flail CHEST requiring tracheostomy placement	0	25.8	74.2	Y	0	26.3	73.7	Y	0	25	75	Y
Flail CHEST and haemodynamic instability	16.7	33.3	50	Y	10.5	26.3	63.2		-	-	-	
Flail CHEST and pulmonary contusion	16.1	51.6	32.2	N	-	-	-	N	-	-	-	-
Flail CHEST and traumatic brain injury	15.2	32.3	22.6	N	-	-	-		-	-	-	-
Flail CHEST and underlying chronic lung disease	12.9	25.8	61.3	Y	0	26.3	73.7	Y	0	12.5	87.5	Y
One unilateral unifocal rib fracture	18.2	40.9	11.4	N	-	-	-		-	-	-	
TWO or THREE unilateral adjacent rib fractures (non-flail chest)	66.7	33.3	0	N	-	-	-	-	-	-	-	-
ONE unilateral rib fracture (non-flail chest)	96.7	3.3	0	N	-	-	-	-	-	-	-	-
MULTIPLE adjacent rib fractures with displacement of more than 1 rib width	22.6	41.9	35.5	N	-	-	-	-	-	-	-	-
MULTIPLE adjacent rib fractures with paradoxical movement	9.7	2.9	61.3	y	5.6	11.1	83.3	-	0	6.3	93.8	Y

Indications and timing of surgery	Percentage for each score category in Round 1				Percentage for each score category in Round 2				Percentage for each score category in Round 3			
	Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9	
MULTIPLE adjacent rib fractures with respiratory compromise	0	19.4	80.6	Y	0	11.1	88.9	Y	0	6.3	93.8	Y
MULTIPLE adjacent rib fractures and patient requiring invasive ventilation	3.2	6.5	90.3	Y	0	5.6	94.4	Y	0	6.3	93.8	Y
MULTIPLE adjacent rib fractures and intractable pain despite regional and epidural anesthesia	6.5	9.7	83.9	Y	0	5.6	94.4	Y	0	0	100	Y
MULTIPLE adjacent rib fractures and failure to wean from ventilation within 48 hours	3.2	12.9	83.9	Y	0	5.9	94.4	Y	0	6.3	93.8	Y
MULTIPLE adjacent rib fractures with deformity	9.7	29	61.3	Y	5.6	22.2	72.2	Y	0	25	75	Y
MULTIPLE adjacent rib fractures requiring tracheostomy placement	3.2	22.6	74.2	Y	0	27.8	72.2	Y	0	18.8	81.3	Y
MULTIPLE adjacent rib fractures and haemodynamic instability	20	40	40	N	-	-	-	-	-	-	-	-
MULTIPLE adjacent rib fractures and pulmonary contusion	25.8	38.7	35.5	N	-	-	-	-	-	-	-	-
MULTIPLE adjacent rib fractures and traumatic brain injury	45.2	41.9	12.9	N	-	-	-	-	-	-	-	-
MULTIPLE adjacent rib fractures and underlying chronic lung disease	12.9	48.4	38.7	N	-	-	-	-	-	-	-	-
ANY chest wall injury requiring a thoracic operation for another indication (fix on retreat)	26.7	43.3	30	N	-	-	-	-	-	-	-	-
ANY chest wall injury with more than 30% volume loss of hemithorax	26.7	43.3	30	N	-	-	-	-	-	-	-	-
ANY rib fracture with anticipated non-union	32.3	32.3	35.5	N	-	-	-	-	-	-	-	-
The EARLIEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is within 24 hours after injury	21.4	35.7	42.9	N	-	-	-	-	-	-	-	-
The EARLIEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 24 and 48 hours after injury	14.8	25.9	59.3	Y	5.9	5.9	88.2	Y	0	12.5	87.5	Y

Indications and timing of surgery	Percentage for each score category in Round 1				Percentage for each score category in Round 2				Percentage for each score category in Round 3			
	Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9	
The EARLIEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 48 and 72 hours after injury	11.1	40.7	48.1	N	-	-	-	-	-	-	-	-
The EARLIEST time a patient (independent of ventilation status or injury morphology should have fracture fixation is between 3 and 5 days after injury	23.1	53.8	23.1	N	-	-	-	-	-	-	-	-
The EARLIEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 5 and 7 days after injury	38.5	42.3	19.2	N	-	-	-	-	-	-	-	-
The EARLIEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 7 and 14 days after injury	57.7	26.9	15.4	N	-	-	-	-	-	-	-	-
The EARLIEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is more than 14 days after injury	65.4	19.2	15.4	N	-	-	-	-	-	-	-	-
The LATEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is within 24 hours after injury	66.7	18.5	14.8	N	-	-	-	-	-	-	-	-
The LATEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 24 and 48 hours after injury	55.6	29.6	14.8	N	-	-	-	-	-	-	-	-
The LATEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 48 and 72 hours after injury	44.4	29.6	25.9	N	-	-	-	-	-	-	-	-
The LATEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 3 and 5 days after injury	30.8	46.2	23.1	N	-	-	-	-	-	-	-	-
The LATEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 5 and 7 days after injury	26.9	46.2	26.9	N	-	-	-	-	-	-	-	-

Indications and timing of surgery	Percentage for each score category in Round 1				Percentage for each score category in Round 2				Percentage for each score category in Round 3			
	Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9	
The LATEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is between 7 and 14 days after injury	44.4	33.3	22.2	N	-	-	-	-	-	-	-	-
The LATEST time a patient (independent of ventilation status or injury morphology) should have fracture fixation is more than 14 days after injury	51.9	22.2	25.9	N	-	-	-	-	-	-	-	-
In a patient that requires invasive ventilation, they should NOT have a TRIAL OF WEANING from a ventilator before considering surgical fixation	55.2	17.2	27.6	N	-	-	-	-	-	-	-	-
In a patient that requires invasive ventilation, they should have a TRIAL OF WEANING from a ventilator for at least 24 hours before considering surgical fixation	21.4	46.4	32.1	N	-	-	-	-	-	-	-	-
In a patient that requires invasive ventilation, they should have a TRIAL OF WEANING from a ventilator between 24 and 48 hours before considering surgical fixation	26.9	34.6	38.5	N	-	-	-	-	-	-	-	-
In a patient that requires invasive ventilation they should have a TRIAL OF WEANING from a ventilator between 48 hours and 72 hours before considering surgical fixation	36	28	36	N	-	-	-	-	-	-	-	-
In a patient that requires invasive ventilation they should have a TRIAL OF WEANING from a ventilator between 3 and 5 days before considering surgical fixation	60	20	20	N	-	-	-	-	-	-	-	-
In a patient that requires invasive ventilation they should have a TRIAL OF WEANING from a ventilator between 5 and 7 days before considering surgical fixation	64	20	16	N	-	-	-	-	-	-	-	-
In a patient that requires invasive ventilation should have a TRIAL OF WEANING from a ventilator between 7 and 14 days before considering surgical fixation	68	24	8	N	-	-	-	-	-	-	-	-
In a patient that requires invasive ventilation should have A TRIAL OF WEANING from a ventilator more than 14 days before considering surgical fixation	76	12	12	N	-	-	-	-	-	-	-	-

Indications and timing of surgery	Percentage for each score category in Round 1				Percentage for each score category in Round 2				Percentage for each score category in Round 3			
	Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9		Score 1-3	Score 4-6	Score 7-9	
Patients should be REFERRED to a multidisciplinary trauma unit within 24 hours for consideration of surgical rib fracture fixation	9.7	16.1	74.2	Y	0	29.4	70.6	Y	6.3	18.8	75	Y
Patients should be REFERRED to a multidisciplinary trauma unit within 48 hours for consideration of surgical rib fracture fixation	0	30	70	Y	0	17.6	82.4	Y	0	12.5	87.5	Y
Patients should be TRANSFERRED to a multidisciplinary trauma unit for rib fracture fixation within 24 hours of the decision to transfer or the patient becoming fit for transfer.	7.1	21.4	71.4	Y	0	17.6	82.4	Y	0	18.8	81.3	Y
Patients should be TRANSFERRED to a multidisciplinary trauma unit for rib fracture fixation within 48 hours of the decision to transfer or the patient becoming fit for transfer.	6.9	17.2	75.9	Y	0	5.9	94.1	Y	0	81.3	87.5	Y
Patients with rib fractures (independent of ventilation status or type of injury) should have surgical fixation within 24 hours of the DECISION to operate unless patient becomes unwell or there are complications	10	26.7	63.3	Y	5.9	17.6	76.5	Y	0	18.8	81.3	Y
Patients with rib fractures (independent of ventilation status or type of injury) should have surgical fixation within 48 hours of the DECISION to operate unless patient becomes unwell or there are complications	6.9	20.7	72.4	Y	5.9	5.9	88.2	Y	0	6.3	93.8	Y
FLAIL Chest with concomitant sternal fracture	-	-	-	-		17.6	82.4	Y	0	12.5	87.5	Y
MULTIPLE rib fractures with concomitant sternal fracture	-	-	-	-	5.9	29.4	64.7		0	25	75	Y
Bilateral FLAIL Chest	-	-	-	-	5.9		94.1	Y	0	0	100	Y
Bilateral MULTIPLE rib fractures	-	-	-	-	5.9	23.5	70.6	Y	0	18.8	81.3	Y
Any rib frature with intrusion into underlying lung	-	-	-	-	11.8	17.6	70.6	Y	0	25	75	Y
Any rib fracture with concern for diaphragm laceration	-	-	-	-	5.9	17.6	76.5	Y	0	31.3	68.8	N
MULTIPLE rib fractures with haemothorax	-	-	-	-	11.8	35.3	52.9	N	6.3	31.3	62.5	N
FLAIL Chest With Haemothorax	-	-	-	-	5.9	5.9	88.2	Y	0	6.3	93.8	Y

Table 112 Outcome measure scoring Round 1

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
Adverse events																
a. Acute Respiratory Distress Syndrome (not able to get enough oxygen into the body due to inflammation in the lungs in critically ill patients)	0	11.1	88.9	Y		25	75	Y	6.7	40	53.3	Y	4.7	32.6	62.8	Y
b. Barotrauma (pressure damage to lungs following using a machine to help you breathe)	11.1	22.2	66.7	Y	0	50	50	Y	18.5	33.3	48.1	N	15	32.5	52.5	Y
c. Empyema (a collection of pus in the lining of the lung and the lining or the ribcage	11.1	22.2	66.7	Y	0	25	75	Y	3.4	10.3	86.2	Y	4.8	14.3	81	Y
d. Mediastinitis (inflammation or infection of the lining surrounding the heart	22.2	44.4	33.3	N	0	66.7	33.3	N	14.3	21.4	64.3	Y	15	30	55	Y
e. Metal work failure (broken metal plates within the body)	0	33.3	66.7	Y	0	100	0	N	0	24.1	75.9	Y	0	33.3	66.7	Y
f. Multi Organ Failure (a life threatening illness that causes the organs (lungs, liver, kidneys, heart) of the body to stop working)	11.1	0	88.9	Y	0	0	100	Y	13.8	27.6	58.6	Y	11.9	19	69	Y
g. Pleural effusion (fluid between the lining of the lung and the lining or the ribcage)	11.1	44.4	44.4	N	0	75	25	N	6.9	37.9	55.2	Y	7.1	42.9	50	Y
h. Pneumonia (an infection within the lung)		22.2	77.8	Y	0	25	75	Y	10.3	27.6	62.1	Y	7.1	26.2	66.7	Y
i. Pulmonary embolism (clot of material (an embolus) that blocks blood from getting to the lungs)	11.1	0	88.9	Y	0	0	100	Y	10.3	41.4	48.3	N	9.5	28.6	61.9	Y
j. Reintubation or Failed extubation (having a tube reinserted into the windpipe to help breathing after removal of a previous tube)	0	33.3	66.7	Y	0	75	25	N	3.4	31	65.5	Y	2.4	35.7	61.9	Y
k. Re-operation (needing a further operation)	11.1	11.1	77.8	Y	0	100	0	N		20.7	79.3	Y	2.4	26.2	71.4	Y
l. Respiratory failure (not able to get enough oxygen into the body)	0	11.1	88.9	Y	0	50	50	Y	3.4	20.7	75.9	Y	2.4	21.4	76.2	Y
m. Retained Haemothorax (blood that stays between the lining of the lung and the lining or the ribcage)	0	22.2	77.8	Y	20	80	0	N	6.9	37.9	55.2	Y	7	39.5	53.5	Y
n. Sepsis (a life-threatening illness that can occur when the whole body reacts to an infection)	0	11.1	88.9	Y	0	0	100	Y	10.3	27.6	62.1	Y	7.1	21.4	71.4	Y

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
o. Wound Infection (redness and pain over the surgical site)	11.1	33.3	55.6	Y	25	75	0	N	6.9	27.6	65.5	Y	9.5	33.3	57.1	Y
a. Iatrogenic mediastinal injury (an injury to the cavity containing the heart during surgery)	0	33.3	66.7	Y	0	50	50	Y	3.7	29.6	66.7	Y	2.5	32.5	65	Y
b. Iatrogenic nerve injury (an injury to a nerve caused by surgery)	11.1	22.2	66.7	Y	0	75	25	N	7.4	25.9	66.7	Y	7.5	30	62.5	Y
c. Iatrogenic thoracic injury (an injury to the cavity containing the lungs during surgery)	0	44.4	55.6	Y	0	50	50	Y	3.7	25.9	70.4	Y	2.5	32.5	65	Y
d. Iatrogenic vascular injury (an injury to a blood vessel caused by surgery)	0	44.4	55.6	Y	0	75	25	N	3.7	14.8	81.5	Y	2.5	27.5	70	Y
e. Rib fracture non-union (rib fractures that do not heal)	0	33.3	66.7	Y	0	75	25	N	10.3	34.5	55.2	Y	7.1	38.1	54.8	Y
Mortality																
Mortality (overall)	0	22.2	77.8	Y	0	0	100	Y	0	19.4	80.6	Y	0	18.6	81.4	Y
7 Day Mortality	0	11.1	88.9	Y	0	0	100	Y	10	13.3	76.7	Y	7.1	11.9	81	Y
30 Day Mortality	22.6	22.6	54.8	N	0	0	100	Y	9.7	19.4	71	Y	7	18.6	74.4	Y
90 Day Mortality	0	22.2	77.8	Y	0	0	100	Y	22.6	22.6	54.8	N	16.3	20.9	62.8	Y
Physiological or clinical																
a. Acute pain (sudden pain)	0	37.5	62.5	Y	0	80	20	N	3.3	20	76.7	Y	2.3	30.2	67.4	Y
b. Breathing movements (the movement of the rib cage during breathing)	0	37.5	62.5	Y	0	80	20	N	6.5	32.3	61.3	Y	4.5	38.6	56.8	Y
c. Chest discomfort/ tightness	0	37.5	62.5	Y	25	50	25	N	10	36.7	53.3	Y	9.5	38.1	52.4	Y
d. Chest wall deformity (the shape of the rib cage)	12.5	50	37.5	N	25	75	0	N	13.3	36.7	50	Y	14.3	42.9	42.9	N
e. Chronic Pain (ongoing pain)	0	25	75	Y	0	40	60	Y	3.2	32.3	64.5	Y	2.3	31.8	65.9	Y
f. Dyspnoea (shortness of breath)	0	50	50	Y	0	75	25	N	3.2	25.8	71	Y	2.3	34.9	62.8	Y
g. Fracture healing (how much the fracture has healed or united)	0	37.5	62.5	Y	0	100	0	N	12.9	38.7	48.4	N	9.1	45.5	45.5	N
h. Kinesiophobia (fear of moving)	12.5	37.5	50	Y	0	100	0	N	20	33.3	46.7	N	16.7	40.5	42.9	N
i. Lung Function (how well air is blow out of the lungs)	0	25	75	Y	0	80	20	N	6.5	32.3	61.3	Y	4.5	36.4	59.1	Y
j. Movement of the thorax (how well the rib cage moves)	0	50	50	Y	0	100	0	N	10	46.7	43.3	N	7.1	52.4	40.5	N

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
k. Oxygen saturations (how much oxygen in the blood)	0	12.5	87.5	Y	0	75	25	N	6.5	35.5	58.1	Y	4.7	34.9	60.5	Y
l. Scoliosis (curvature of the spine)	12.5	50	37.5	N	0	80	20	N	24.1	55.2	20.7	N	19	57.1	23.8	N
m. Shoulder function (how well the shoulder works)	0	62.5	37.5	N	0	80	20	N	23.3	53.3	23.3	N	16.3	58.1	25.6	N
n. Ventilation (how well air can move between the lungs and outside the body)	0	12.5	87.5	Y	0	75	25	N	6.9	17.2	75.9	Y	4.9	22	73.2	Y
Life impact																
a. Disability (a limit to a person's movements, senses, or activities)	0	12.5	87.5	Y	0	20	80	Y	6.5	19.4	74.2	Y	4.5	18.2	77.3	Y
b. Discharge Destination (where a patient lives after leaving hospital)	0	50	50	Y	0	20	80	Y	3.2	41.9	54.8	Y	4.5	47.7	47.7	N
c. Home Oxygen Therapy (using a mask connected to a cylinder of oxygen to help with breathing)	0	37.5	62.5	Y	25	75	0	N	10	30	60	Y	9.5	35.7	54.8	Y
d. Mental health (personâ€™s emotional well-being)	0	62.5	37.5	N	20	0	80	Y	6.5	48.4	45.2	N	6.8	45.5	47.7	N
e. Physical function (performing tasks)	0	12.5	87.5	Y	0	20	80	Y	3.2	19.4	77.4	Y	2.3	18.2	79.5	Y
f. Quality of life (the standard of health, comfort, and happiness experienced by an individual)	0	0	100	Y	0	20	80	Y	3.2	9.7	87.1	Y	2.3	9.1	88.6	Y
g. Return to Activities	0	0	100	Y	0	40	60	Y	3.2	12.9	83.9	Y	2.3	13.6	84.1	Y
h. Return to Work	0	0	100	Y	0	40	60	Y	3.2	12.9	83.9	Y	2.3	13.6	84.1	Y
i. Satisfaction (whether the service met your requirements)	0	12.5	87.5	Y	0	40	60	Y	6.5	25.8	67.7	Y	4.5	25	70.5	Y
Resource use																
a. Antibiotic requirements (whether antibiotic medicine is needed)	25	62.5	12.5	N	0	100	0	N	35.5	35.5	29	N	30.2	46.5	23.3	N
b. Chest drain (a tube that is inserted into the chest to get rid of air or fluid)	25	50	25	N	0	100	0	N	35.5	35.5	29	N	30.2	44.2	25.6	N
c. Cost of treatment	12.5	75	12.5	N	40	60	0	N	9.7	45.2	45.2	N	13.6	52.3	34.1	N
d. Epidural (an injection in the back to stop feeling pain in a part of the body)	25	37.5	37.5	N	25	75	0	N	19.4	61.3	19.4	N	20.9	58.1	20.9	N

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
e. Hospital readmission (If you need to come back to hospital after leaving the hospital following your treatment)	0	50	50	Y	0	80	20	N	0	29	71	Y	0	38.6	61.4	Y
f. Hospital stay (how long someone stays in hospital)	12.5	25	62.5	Y	20	80	0	N	3.2	19.4	77.4	Y	6.8	27.3	65.9	Y
g. Intensive care unit (ICU) stay (a specialised ward in a hospital that cares for patients who are critically ill and requires specialist medical equipment and nursing care)	12.5	12.5	75	Y	0	80	20	N	0	25.8	74.2	Y	2.3	29.5	68.2	Y
h. Intensive care unit (ICU) readmission (the need to come back to ICU after leaving the ICU following treatment)	0	37.5	62.5	Y	0	75	25	N	0	22.6	77.4	Y	0	30.2	69.8	Y
i. Invasive mechanical ventilation (a tube inserted into the windpipe and attached to a machine that assists breathing)	0	25	75	Y	0	75	25	N	6.5	9.7	83.9	Y	4.7	18.6	76.7	Y
j. Non-invasive ventilation (through a mask or a hood a machine helps supports a patientâ€™s own breathing)	12.5	12.5	75	Y	0	100	0	N	6.5	25.8	67.7	Y	7	30.2	62.8	Y
k. Plasma Transfusion requirements (receiving the part of the blood that contains factors that help the blood clot and take away used products from a donor by injection)	25	50	25	N	0	100	0	N	19.4	64.5	16.1	N	18.6	65.1	16.3	N
l. Red Cell Transfusion requirements (receiving the part of the blood that contain red cells (red cells carry oxygen) from a donor by injection	25	50	25	N	0	100	0	N	22.6	54.8	22.6	N	20.9	58.1	20.9	N
m. Tracheostomy (a cut in the wind pipe replaced with a tube that helps reduce the work of breathing)	0	37.5	62.5	Y	0	75	25	N	0	38.7	61.3	Y	0	41.9	58.1	Y

Table 113 Outcome measure scoring Round 2

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
Adverse Events																
a. Acute Respiratory Distress Syndrome (not able to get enough oxygen into the body due to inflammation in the lungs in critically ill patients)	0	0	100	Y	0	0	100	Y	0	35.3	64.7	N	0	24	76	Y

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
b. Ventilator induced Barotrauma (pressure damage to lungs following using a machine to help you breathe)	0	16.7	83.3	Y	0	0	0	N	5.9	41.2	52.9	N	4.3	34.8	60.9	N
c. Empyema (a collection of pus in the lining of the lung and the lining or the ribcage	0	0	100	Y	0	0	100	Y	0	23.5	76.5	Y	0	16.7	83.3	Y
d. Mediastinitis (inflammation or infection of the lining surrounding the heart	0	50	50	N	0	100	0	N	5.9	41.2	52.9	N	4.2	45.8	50	N
e. Metal work failure (broken metal plates within the body)	0	0	100	Y	50		50	N	5.9	35.3	58.8	N	8	24	68	N
f. Multi Organ Failure (a life threatening illness that causes the organs (lungs, liver, kidneys, heart) of the body to stop working)	0	0	100	Y	0	0	100	Y	5.9	29.4	64.7	N	4.2	20.8	75	N
g. Pleural effusion (fluid between the lining of the lung and the lining or the ribcage)	0	50	50	N	50	0	50	N	23.5	41.2	35.3	N	20	40	40	N
h. Pneumonia (an infection within the lung)	0	0	100	Y	0	0	100	Y	11.8	17.6	70.6	Y	8.3	12.5	79.2	Y
i. Pulmonary embolism (clot of material (embolus) that blocks blood from getting to the lungs)	0	16.7	83.3	Y	0	50	50	N	29.4	23.5	47.1	N	20	24	56	N
j. Reintubation or Failed extubation (having a tube reinserted into the windpipe to help breathing after removal of a previous tube)	0	0	100	Y	0	0	100	Y	18.8	12.5	68.8	N	13.6	9.1	77.3	Y
k. Re-operation (needing a further operation)	0	0	100	Y	50	0	50	N	17.6	23.5	58.8	N	16	16	68	N
l. Respiratory failure (not able to get enough oxygen into the body)	0	0	100	Y	0	0	100	Y	0	11.8	88.2	Y	0	8	92	Y
m. Retained Haemothorax (blood that stays between the lining of the lung and the lining or the ribcage)	0	16.7	83.3	Y	0	50	50	N	17.6	23.5	58.8	N	12	24	64	N
n. Sepsis (a life-threatening illness that can occur when the whole body reacts to an infection)	0	0	100	Y	0	0	100	Y	0	41.2	58.8	N	0	28	72	Y
o. Wound Infection (redness and pain over the surgical site)	0	50	50	N	50	50	0	N	11.8	23.5	64.7	N	12	32	56	N

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
a. Iatrogenic mediastinal injury (an injury to the cavity containing the heart during surgery)	0	16.7	83.3	Y	50	50	0	N	11.8	11.8	76.5	Y	12	16	72	Y
c. Iatrogenic thoracic injury (an injury to the cavity containing the lungs during surgery)	0	16.7	83.3	Y	50	50	0	N	5.9	0	94.1	Y	8	8	84	Y
d. Iatrogenic vascular injury (an injury to a blood vessel caused by surgery)	0	16.7	83.3	Y	50	50	0	N	5.9	11.8	82.4	Y	8	16	76	Y
e. Rib fracture non-union (rib fractures that do not heal)	0	0	100	Y	0	50	50	N	11.8	47.1	41.2	N	8	36	56	N
Mortality																
Mortality (overall)	0	0	100	Y	0	33.3	66.7	N	0	5.9	94.1	Y	0	7.7	92.3	Y
7 Day Mortality	0	16.7	83.3	Y	0	66.7	33.3	N	5.9	11.8	82.4	Y	3.8	19.2	76.9	Y
30 Day Mortality	0	0	100	Y	0	66.7	33.3	N	0	11.8	88.2	Y	0	15.4	84.6	Y
90 Day Mortality	0	16.7	83.3	Y	0	66.7	33.3	Y	0	29.4	70.6	Y	0	30.8	69.2	N
Physiological or clinical																
a. Acute pain (sudden pain)	0	0	100	Y	0	66.7	33.3	N	5.9	29.4	64.7	N	3.8	26.9	69.2	N
b. Breathing movements (the movement of the rib cage during breathing)	0	16.7	83.3	Y	0	100	0	N	5.9	29.4	64.7	N	3.8	34.6	61.5	N
c. Chest discomfort/ tightness	0	33.3	66.7	N	0	100	0	N	5.9	41.2	52.9	N	3.8	46.2	50	N
e. Chronic Pain (ongoing pain)	0	0	100	Y	0	0	100	Y	5.9	29.4	64.7	N	3.8	19.2	76.9	Y
f. Dyspnoea (shortness of breath)	0	16.7	83.3	Y	0	50	50	N	5.9	17.6	76.5	Y	4	20	76	Y
i. Lung Function (how well air is blow out of the lungs)	0	0	100	Y	0	0	100	Y	0	17.6	82.4	Y	0	12	88	Y
k. Oxygen saturations (how much oxygen in the blood)	0	33.3	66.7	N	0	50	50	N	5.9	41.2	52.9	N	4	40	56	N
n. Ventilation (how well air can move between the lungs and outside the body)	0	0	100	Y	0	0	100	Y	0	29.4	70.6	Y	0	20	80	Y
Life Impact																

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
a. Disability (a limit to a person's movements, senses, or activities)	0	0	100	Y	0	0	100	Y	5.9	17.6	76.5	Y	3.8	11.5	84.6	Y
c. Home Oxygen Therapy (using a mask connected to a cylinder of oxygen to help with breathing)	0	66.7	33.3	Y	0	50	50	N	5.9	29.4	46.7	N	4	40	56	N
e. Physical function (performing tasks)	0	0	100	Y	0	0	100	Y	5.9	23.5	70.6	Y	3.8	15.4	80.8	Y
f. Quality of life (the standard of health, comfort, and happiness experienced by an individual)	0	0	100	Y	0	0	100	Y	5.9	11.8	82.4	Y	3.8	7.7	88.5	Y
g. Return to Activities	0	0	100	Y	0	33.9	66.7	N	0	23.5	76.5	Y	0	19.2	80.8	Y
h. Return to Work	0	0	100	Y	33.3	66.7	0	N	0	23.5	76.5	Y	3.8	23.1	73.1	Y
i. Satisfaction (whether the service met your requirements)	0	33.3	66.7	N	0	100	0	N	0	29.4	70.6	Y	0	38.5	61.5	N
Resource Use																
e. Hospital readmission (If you need to come back to hospital after leaving the hospital following your treatment)	0	16.7	83.3	Y	0	50	50	N	5.9	23.5	70.6	Y	4	24	72	Y
f. Hospital stay (how long someone stays in hospital)	0	16.7	83.3	Y	33.3	66.7	0	N	5.9	29.4	64.7	N	7.7	30.8	61.5	N
g. Intensive care unit (ICU) stay (a specialised ward in a hospital that cares for patients who are critically ill and requires specialist medical equipment and nursing care)	0	16.7	83.3	Y	0	66.7	33.3	N	5.9	29.4	64.7	N	3.8	30.8	65.4	N
h. Intensive care unit (ICU) readmission (the need to come back to ICU after leaving the ICU following treatment)	0	16.7	83.3	Y	0	66.7	33.3	N	5.9	29.4	64.7	N	4.2	33.3	62.5	N
i. Invasive mechanical ventilation (a tube inserted into the windpipe and attached to a machine that assists breathing)	0	0	100	Y	0	100	0	N	0	5.9	94.1	Y	0	12	88	Y
j. Non-invasive ventilation (through a mask or a hood a machine helps supports a patientâ€™s own breathing)	0	50	50	N	0	100	0	N	5.9	23.5	70.6	Y	4.2	33.3	62.5	N
m. Tracheostomy (a cut in the wind pipe replaced with a tube that helps reduce the work of breathing)	0	33.3	66.7	N	0	100	0	N	0	35.3	64.7	N	0	37.5	62.5	N
Health related quality of life (the standard of health, comfort, and happiness experienced by an individual related specifically to their health	0	16.7	83.3	Y	0	0	100	Y	0	5.9	94.1	Y	0	7.7	92.3	Y

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
Pulmonary toilet (the ability to clear lung secretions	0	16.7	83.3	Y	0	7.7	92.3	Y	0	5.9	94.1	Y	0	7.7	92.3	Y
Narcotic addiction (whether someone is dependent on using pain medication such as morphine)	16.7	33.3	50	Y	0	100	0	Y	0	35.3	64.7	N	4	40	56	Y
Cosmetic look of the chest (the shape of the chest)	16.7	50	33.3	N	0	100	0	N	23.5	23.5	52.9	Y	20	36	44	N

Table 114 Outcome measure scoring Round 3

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
Adverse events																
a. Acute Respiratory Distress Syndrome (not able to get enough oxygen into the body due to inflammation in the lungs in critically ill patients)	0	0	100	Y	0	0	100	Y	0	18.8	81.3	Y	0	13.6	86.4	Y
c. Empyema (a collection of pus in the lining of the lung and the lining or the ribcage	0	20	80	Y	0	0	100	Y	0	18.8	81.3	Y	0	18.2	81.8	Y
h. Pneumonia (an infection within the lung)	0	20	80	Y	0	0	100	Y	0	31.3	68.8		0	27.3	72.7	Y
j. Reintubation or Failed extubation (having a tube reinserted into the windpipe to help breathing after removal of a previous tube)	0	40	60	N	0	0	0	N	0	18.8	81.3	Y	0	23.8	76.2	Y
l. Respiratory failure (not able to get enough oxygen into the body)	0	0	100	Y	0	0	100	Y	0	37.5	62.5	N	0	27.3	72.7	Y
n. Sepsis (a life-threatening illness that can occur when the whole body reacts to an infection)	0	20	80	Y	0	0	100	Y	6.3	56.3	37.5	N	4.5	45.5	50	N
a. Iatrogenic mediastinal injury (an injury to the cavity containing the heart during surgery)	0	40	60	N	0	0	100	Y	0	25	75	Y	0	27.3	72.7	Y
c. Iatrogenic thoracic injury (an injury to the cavity containing the lungs during surgery)	0	40	60	N	0	0	100	Y	0	18.8	81.3	Y	0	22.7	77.3	Y
d. Iatrogenic vascular injury (an injury to a blood vessel caused by surgery)	0	40	60	N	0	100	0		0	18.8	81.3	Y	0	27.3	72.7	Y
Mortality																
Mortality (overall)	0	0	100	Y	0	0	100	Y	0	12.5	87.5	Y	0	9.1	90.9	Y
7 Day Mortality	0	20	80	Y	0	0	100	Y	6.3	6.3	87.5	Y	4.5	13.6	86.4	Y
30 Day Mortality	0	0	100	Y	0	50	50	N	6.3	6.3	87.5	Y	4.3	8.7	87	Y
Physiological or clinical																
e. Chronic Pain (ongoing pain)	0	0	100	Y	0	0	100	Y	6.3	31.3	62.5	N	4.3	21.7	73.9	Y
f. Dyspnoea (shortness of breath)	0	40	60	N	0	0	100	Y	6.3	12.5	81.3	Y	4.5	22.7	77.3	Y
i. Lung Function (how well air is blow out of the lungs)	0	20	80	Y	0	0	100	Y	6.3	12.5	81.3	Y	4.5	13.6	81.8	Y
n. Ventilation (how well air can move between the lungs and outside the body)	0	20	80	Y	0	0	100	Y	0	12.5	87.5	Y	0	13.6	86.4	Y

Outcome Measure	Allied Health Professionals				Patients				Clinicians				Overall			
	1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9		1-3	4-6	7-9	
Life impact																
a. Disability (a limit to a person's movements, senses, or activities)	0	20	80	Y	0	0	100	Y	6.3	6.3	87.5	Y	4.3	8.7	87	Y
e. Physical function (performing tasks)	0	20	80	Y	0	0	100	Y	0	12.5	87.5	Y	0	13	87	Y
f. Quality of life (the standard of health, comfort, and happiness experienced by an individual)	0	0	100	Y	0	0	100	Y	0	1.25	87.5	Y	0	8.7	91.3	Y
g. Return to Activities	0	0	100	Y	0	0	100	Y	0	25	75	Y	0	17.4	82.6	Y
h. Return to Work	0	0	100	Y	0	100	0	N	0	18.8	81.3	Y	0	21.7	78.3	Y
Resource use																
e. Hospital readmission (If you need to come back to hospital after leaving the hospital following your treatment)	0	40	60	N	0	50	50	N	0	37.5	62.5	N	0	39.1	60.9	N
i. Invasive mechanical ventilation (a tube inserted into the windpipe and attached to a machine that assists breathing)	0	0	100	Y	0	0	100	Y	0	18.8	81.3	Y	0	13.6	86.4	Y
New outcomes																
Health related quality of life (the standard of health, comfort, and happiness experienced by an individual related specifically to their health	0	0	100	Y	0	0	100	Y	0	6.3	93.8	Y	0	4.3	95.7	Y
Pulmonary toilet (the ability to clear lung secretions	0	0	100	Y	0	0	100	Y	0	18.8	81.3	Y	0	13.6	86.4	Y
Narcotic addiction (whether someone is dependent on using pain medication such as morphine)	0	60	40	N	0	50	50	N	0	50	50	N	0	52.2	47.8	N

Appendix D1 TARN Data cleaning and preparation

Table 115 Patient factor variables

Category	Raw data	Type	Original Covariate	Final Covariates
Patient factors				
Age (years)	Continuous	Ordinal	Range 0-106	Age (years) or 16-24, 25-49, 50-74, 75 and over
Sex	Categorical	Binary	Male, Female	Male Female
Charlson Index	Continuous	Ordinal	Range 0-29	Charlson Index 0-29 or 0 None, 1-2 Mild, 3-4 Moderate, 5< Severe
Injury Severity Score	Continuous	Ordinal	Range 0-75	Injury Severity Score 0-75 or ISS<15 ISS>15
Probability of Survival (PS14)	Continuous	Ordinal	0-100%	0-100% or 95% and above Less than 95%
Flail Chest	Categorical	Binary	Flail Chest, Non-Flail Chest	Flail Chest Non-Flail Chest
Mechanism of Injury	Categorical	Ordinal	Vehicle incident Fall less than 2m Fall more than 2m Shooting and Weapon Stabbing and Weapon Blast Burn Skeletal/organ/vessel destruction Blow Other Amputation	Fall less than 2m Vehicle incident Fall more than 2m Penetrating injury –shooting and stabbing with weapon Non-Penetrating Injury -Blast, Blow, Burn, Skeletal/organ/vessel destruction, amputation and Other
Lung Contusion			Lung contusion bilateral Lung contusion bilateral minor Lung contusion bilateral major Lung contusion NFS	Unilateral - Lung contusion NFS, Lung contusion unilateral, Lung contusion unilateral minor, Lung contusion unilateral major Bilateral - Lung contusion bilateral, Lung contusion bilateral minor, Lung contusion bilateral major

Category	Raw data	Type	Original Covariate	Final Covariates
Patient factors				
			Lung contusion unilateral Lung contusion unilateral minor Lung contusion unilateral major	
Injury description	Categorical	Ordinal	Fracture one rib Fracture two ribs Fracture greater than 3 ribs Multiple rib fractures NFS Fracture greater than 3 ribs on each side Fracture ribs with flail NFS Fracture ribs with unilateral flail Fracture ribs with 3-5 ribs fracture ribs with unilateral flail > 5 ribs Fracture ribs with bilateral flail Fracture ribs: complex Sternum fracture	Less than three rib fractures (non-flail)- Fracture one rib, Fracture two ribs 3 or more rib fractures (non-flail) - Fracture greater than 3 ribs, multiple rib fractures NFS, fracture greater than 3 ribs on each side Unilateral flail chest - Fracture ribs with flail NFS, fracture ribs with unilateral flail, fracture ribs with unilateral flail 3-5 ribs, fracture ribs with unilateral flail & gt; 5 ribs Bilateral flail chest or complex rib fractures with sternal fracture - Fracture ribs with bilateral flail, fracture ribs: complex, sternum fracture

Table 116 Admission factor variables

Admission factors				
Category	Raw data	Type	Original Covariate	Final Covariate
Admitting Specialty	Categorical	Ordinal	Orthopaedics	Orthopaedics
			Emergency Medicine	Emergency Medicine
			General Surgery	General Surgery
			General Medicine	General Medicine
			Major Trauma Service	Major Trauma Service
			'Thoracic Surgery	'Cardio thoracic Surgery'
			Neurosurgery	Thoracic Surgery
			Geriatric Medicine	Cardiac Surgery
			ITU	'Neurosurgery and Spinal'
			Spinal Surgery	Neurosurgery
			Urology	Spinal Surgery
			Vascular Surgery	Neurosurgical rehabilitation
			Paediatric Emergency Medicine	Spinal rehabilitation
			Paediatrics (Medical)	Geriatric Medicine
			Plastic Surgery	ITU
			Paediatric General Surgery	'Other Medicine'
			Paediatric Orthopaedics	Neurology
			Stroke Services	Stroke Services,
			Oral +Maxillo-Facial Surgery	'Other Surgery'
			Neurosurgical Rehabilitation	Urology
			Neurology	Vascular Surgery
			Gynaecology	Plastic Surgery
			Burns	Oral +Maxillo-Facial Surgery
			Cardiac Surgery	Gynaecology
			Spinal Rehabilitation	Burns
			ENT/Otolaryngology	ENT/Otolaryngology
			Hepatobiliary Surgery	Hepatobiliary Surgery
			Not Known	Excluded -Paediatric Emergency Medicine, Paediatrics (Medical), Paediatric
			Not applicable	General Surgery, Paediatric Orthopaedics, Not Known, Not applicable
Type of hospital	Categorical	Binary	MTC	MTC

Admission factors				
Category	Raw data	Type	Original Covariate	Final Covariate
			Non MTC	Non MTC
Transfer Type	Categorical	Ordinal	No Transfer	No Transfer
			Transfer In	Transfer In
			Tranfer Out	Tranfer Out
			Transfer In & Out	Transfer In & Out
Transfer time	Continuous	Continuous	Minutes	Time in days

ENT = Ear nose and throat, ITU= intensive therapy unit, MTC = Major Trauma Unit

Table 117 Treatment factor variables

Treatment factors				
Category	Raw data	Type	Original Covariate	Final Covariate
Rib fracture operation 1	Categorical	Binary	Yes	Any rib op
			No	or
Rib fracture operation 2			Yes	Yes in first procedure
			No	Yes in second procedure
				Two rib operations
				No rib fracture operation
Thoracic operation 1	Categorical	Binary	Yes	Any thoracic op
			No	or
Thoracic operation 2			Yes	Yes in first procedure
			No	Yes in second procedure
				Two thoracic operations
				No thoracic operation
Time to surgery	Continuous	Ordinal	Minutes	Time to surgery (days)
				Early fixation Less than 72 hours
				Late fixation More than 72 hours
Number of ribs fixed 1 Number of ribs fixed 2	Continuous	Ordinal	Days	Total number of ribs fixed
Rib plating 1	Categorical	Binary	Yes	Yes in first procedure
			No	Yes in second procedure

Treatment factors				
Category	Raw data	Type	Original Covariate	Final Covariate
Rib plating 2			Yes	Two rib plating procedures
			No	No rib plating
Type of plating 1	Categorical	Ordinal	Specific	Specific
			Generic	Generic
			Combination	Combination
Type of plating 2			Specific	No plating
			Generic	
			Combination	
Intramedullary splint 1	Categorical	Binary	Yes	Yes in first procedure
			No	Yes in second procedure
Intramedullary splint 2			Yes	Two Intramedullary procedures
			No	No
Lead surgeon specialty	Categorical	Ordinal	Orthopaedic Surgery	Orthopaedic Surgery
			Trauma Surgery	Trauma Surgery
			Thoracic Surgery	Thoracic Surgery
			General Surgery	General Surgery
			Other	Other
Intrathoracic viscera inspected 1	Categorical	Binary	Yes	First Intrathoracic viscera inspected
			No	Second Intrathoracic viscera inspected
Intrathoracic viscera inspected 2			Yes	Intrathoracic viscera inspected on both procedures
			No	No Intrathoracic viscera inspected
Method of inspection of Viscera 1	Categorical	Ordinal	VATS	VATS
			Thoracotomy	Thoracotomy
Method of inspection of Viscera 2			VATS	No inspection (if second inspection then Thoracotomy will be recorded as the most invasive over VATs)
			Thoracotomy	
Air leak 1	Categorical	Binary	Yes	First procedure air leak
			No	Second procedure air leak
Air leak 2			Yes	Air leaks in both procedures
			No	

Treatment factors				
Category	Raw data	Type	Original Covariate	Final Covariate
Air leak repaired 1	Categorical	Ordinal	Yes	First procedure air leak repaired
			No	Second procedure air leak repaired
Air leak repaired 2			Yes	Two air leaks repaired
			No	
Pleural tear 1	Categorical	Binary	Yes	First procedure pleural tear
			No	Second procedure pleural tear
Pleural tear 2			Yes	Pleural tears in both procedures
			No	
Pleural lavage 1	Categorical	Binary	Yes	First procedure pleural lavage
			No	Second procedure pleural lavage
Pleural lavage 2			Yes	Pleural lavages in both procedures
			No	
Method of repair 1	Categorical	Ordinal	Glue	Glue
			Sutures	Sutures
Method of repair 2			Staples	Staples
			Glue	(if second method of repair then staples will be recorded as the most invasive
			Sutures	over sutures then staples)
			Staples	
Reintubation 1	Categorical	Binary	Yes	First reintubation
			No	Second reintubation
Reintubation 2			Yes	No reintubation
			No	
Noninvasive ventilation 1	Categorical	Binary	Yes	First t noninvasive ventilation
			No	Second noninvasive ventilation
Noninvasive ventilation 2			Yes	No noninvasive ventilation
			No	
Tracheostomy 1	Categorical	Binary	Yes	First tracheostomy
			No	Second tracheostomy
Tracheostomy 2			Yes	No Tracheostomy
			No	
Tube Type 1			Single lumen	Single lumen

Treatment factors				
Category	Raw data	Type	Original Covariate	Final Covariate
Tube Type 2			Double lumen Single lumen Double lumen	Double lumen Single lumen Double lumen
Position for surgery 1			Prone Lateral Supine	Prone Lateral Supine
Position for surgery 2			Prone Lateral Supine	Prone Lateral Supine
Entonox	Categorical	Ordinal	Yes No	Entonox Intravenous paracetamol
Intravenous paracetamol			Yes No	Intravenous opioid PCA
Intravenous opioid			Yes No	LA patches Ketamine
PCA			Yes No	LA blockade Paravertebral block
Ketamine			Yes No	Epidural block
LA patches			Yes No	To also transform into highest level of analgesia used using this list as a hierarchy
LA blockade			Yes No	
Paravertebral block			Yes No	
Epidural block			Yes No	

PCA = Patient controlled analgesia, LA = Local anesthetic

Table 118 Treatment outcome variables

Treatment Outcomes				
Category	Raw data	Type	Original Covariate	Final Covariate
Glasgow Outcome Score	Categorical	Ordinal	Death Prolonged Disorder of Consciousness Severe Disability Moderate Disability Good Recovery	Death Prolonged Disorder of Consciousness Severe Disability Moderate Disability Good Recovery
Pre-operative ventilation time	Continuous	Ordinal	Minutes	Pre-operative ventilation time in days
Post-operative intubation time 1 Post-operative Intubation time 2 Post-operative Intubation time 3	Continuous	Ordinal	Days	Total intubation time in days
Length of stay 1 Length of stay 2 Length of stay 3 Length of stay 4	Continuous	Ordinal	Days	Total length of stay in days
Critical care length of stay 1 Critical care length of stay 2 Critical care length of stay 3 Critical care length of stay 4	Continuous	Ordinal	Days	Total critical care length of stay in days
Duration of Noninvasive ventilation 1 Duration of Noninvasive ventilation 2	Continuous	Ordinal	Days	Total noninvasive ventilation in days
Duration of Tracheostomy 1 Duration of Tracheostomy 2	Continuous	Ordinal	Days	Total tracheostomy in days

Table 119 Valid records after erroneous data removed, data recorded as 'not recorded and records with a blank response

Variable	Valid record with data	Recorded as 'Not recorded'	Non response (blank data field)	Percentage missing
Age	16638	0	0	-
Gender	16638	0	0	-
Charlson Index	15886	0	752 (values imputed)	4.5%
Mechanism Of Injury	16638	0	0	-
Probability Of Survival (PS14)	16075	0	563(values imputed)	3.4%
ISS	16638	0	0	-
Glasgow Outcome Score	13155	0	3483 (values imputed)	20.9%
Admitting Specialty	6320	0	10318	62.2%
Transfer Type	16637	0	1	-
Type of hospital	16638	0	0	-
Rib Operation	404	0	16234	97.8%
Thoracic Operation	1452	0	15186	91.2%
Time to Rib operation	376	0	16262	97.7%
Analgesia				
Entonox	966	0	15672	94.2
Intravenous paracetamol	5433	0	11205	67.3
Intravenous opioid	7948	0	8690	52.2
PCA	870	0	15768	94.8
Ketamine	475	0	16163	97.1
LA patches	141	0	16497	99.2
LA blockade	260	0	16378	98.4
Paravertebral block	178	0	16460	98.9
Epidural block	289	0	16349	98.3
Length Of Stay 1	16637	0	1	0.00%
Length Of Stay 2	1167	0	15471	92.9%
Length Of Stay 3	32	0	16606	99.8%
Length Of Stay 4	1	0	16637	99.9%
Total Length of Stay	16637	0	1 (value imputed)	0.00%
Critical Care Stay 1	16638	0	0	-
Critical Care Stay 2	1167	0	15471	92.9%
Critical Care Stay 3	321	0	16606	99.8%
Critical Care Stay 4	1	0	16637	99.9%
Total length of Critical Care Stay				
Transfer Time	1460	0	15178	91.2%
Intubation Time 1	15027	0	1611	1.00%
Intubation Time 2	1006	0	15632	94.0%
Intubation Time 3	30	0	16608	99.8%
Total Intubation time	4701		11937	28.3 %
Noninvasive ventilation duration 1	127	0	16511	99.2%
Noninvasive ventilation duration 2	32	0	16606	99.8%
Noninvasive ventilation 1	16149	480	9	0.05%
Noninvasive ventilation 2	1131	32	15475	93%
Pre op ventilation Time	930	0	15708	94.4%
Rib fixation 1	841	107	15690	94.3%
Rib fixation 2	139	5	16494	99.1%

Variable	Valid record with data	Recorded as 'Not recorded'	Non response (blank data field)	Percentage missing
Rib Plating 1	265	38	16335	98.2%
Rib Plating 2	8	6	16624	99.9%
Rib Plating Type 1	220	0	16418	99.6%
Rib Plating Type 2	69	0	16569	99.6%
Intramedullary splint 1	623	289	15726	94.5%
Intramedullary splint 2	113	27	16498	99.1%
Tracheostomy Duration 1	242	0	16396	98.5%
Tracheostomy Duration 2	43	0	16595	99.7%
Tracheostomy Present 1	16411	218	9	0.05%
Tracheostomy Present 2	1142	21	15475	93.0%
Number of ribs fixed 1	278	0	16360	98.3%
Number of ribs fixed 2	81	0	16557	99.5%
Intrathoracic viscera inspected 1	566	346	15726	94.5%
Intrathoracic viscera inspected 2	110	31	16497	99.1%
Method of inspection of Viscera 1	184	0	16454	98.9%
Method of inspection of Viscera 2	63	0	16575	99.6%
Reintubation 1	16354	275	9	0.05%
Reintubation 2	1143	20	15475	93%
Tube Type 1	164	0	16474	99.0%
Tube Type 2	53	0	16585	99.4%
Position for surgery 1	334	0	16304	98.0%
Position for surgery 2	92		16546	99.4%
Air leak 1	140	26	16472	99.0%
Air leak 2	54	8	16576	99.6%
Air leak repaired 1	16	0	16622	99.9%
Air leak repaired 2	6	0	16632	99.9%
Pleural tear 1	145	21	16472	99.0%
Pleural tear 2	58	3	16577	99.6%
Pleural lavage 1	139	26	16473	99.0%
Pleural lavage 2	59	4	16575	99.6%
Method of repair 1	11	0	16627	99.9%
Method of repair 2	4	0	16634	99.9%

Table 120 Glasgow Outcome Score comparing original and imputed data

	Original data		Imputed data Frequency (valid percentage)					
Glasgow Outcome Score	**Frequency (valid percentage)**	**Percentage including missing values**	**1**	**2**	**3**	**4**	**5**	**Pooled (valid percentage)**
1 Death	1239 (9.4%)	7.4%	1569	1548	1557	1551	1567	1558 (9.4%)
2 Prolonged disorder of consciousness	13 (0.1%)	0.1%	17	17	14	16	16	16 (0.1%)
3 Severe disability	622 (4.7%)	3.7%	759	792	781	778	791	780 (4.7%)
4 Moderate disability	2422 (18.4%)	14.6%	3059	3053	3061	3036	3085	3059 (18.4%)
5 Good Recovery	8859 (67.3%)	53.2%	11234	11228	11225	11257	11179	11225 (67.5%)
Missing	3483	20.9%						

Table 121 PS-14, Charlson Index and total hospital length of stay comparing original and imputed data

PS-14 Original		**PS-14 Imputed**					
		1	**2**	**3**	**4**	**5**	**Pooled**
Minimum value	0.961	0.96	0.96	0.96	0.96	0.96	
Maximum value	99.85	99.98	99.97	99.95	99.99	99.94	
Mean	91.25	91.14	91.15	91.15	91.15	91.14	91.15
Standard deviation	15.30	15.17	15.16	15.15	15.16	15.17	
Charlson index Original		**Charlson Index Complete imputed data**					
		1	**2**	**3**	**4**	**5**	**Pooled**
Minimum value	0	0	0	0	0	0	
Maximum value	25	25	25	25	25	25	
Mean	2.40	2.45	2.44	2.44	2.45	2.45	2.45
Standard deviation	3.23	3.21	3.22	3.21	3.22	3.22	
Total hospital length of stay Original		**Total hospital length of stay Complete imputed data**					
		1	**2**	**3**	**4**	**5**	**Pooled**
Minimum value	1	1	1	1	1	1	
Maximum value	402	402	402	402	402	402	
Mean	15.75	15.75	15.75	15.75	15.75	15.75	15.75
Standard deviation	22.27	22.27	22.27	22.27	22.27	22.27	

Appendix E1 Survey participant documents

Invitation email

Blunt Chest Trauma Care – A nationwide survey of practice

Dear Participant,

You are invited to take part in a survey where you will be asked about the provision of care for patients with rib fractures within your hospital. We are surveying all trauma leads within all hospitals that undertake trauma care. The answers you provide will help us map the current provision for blunt chest trauma care in the UK as we believe this differs widely across trusts.

Rib fracture fixation is under researched in the UK and it is vital that the current care of these patients is understood before undertaking clinical trials in this area. You will be directly helping with this research.

We would be grateful if you could take 5-10 minutes of your time to complete a short survey of chest trauma care provision in your hospital. A certificate of undertaking this activity can be provided to show engagement with research for portfolio and revalidation purposes.

This survey is part of a larger piece of work involving researchers at the British Orthopaedic Association's Orthopaedic Research Centre embedded within York Trials Unit, University of York. Please contact helen.ingoe@york.ac.uk if you have any queries.

A participant information sheet can be accessed by clicking this link (link to information sheet)

Link to survey

If you would like to print this survey and return it by post please send it to the following address:

Dr Helen Ingoe, ARRC Building Ground Floor ,York Trials Unit, Department of Health Sciences, University of York, Heslington, YO10 5DD

Participant Information Sheet

UNIVERSITY of York
The Department of Health Sciences

BLUNT CHEST TRAUMA CARE – A NATIONWIDE SURVEY OF PRACTICE

Participant Information Sheet

What is the purpose of this study?

Blunt chest trauma and rib fractures are linked with high mortality and recent advances in rib fracture fixation has reinvigorated this as a priority topic. There is still a variety of specialities undertaking this care and no one specialty has been indicated to take these patients on a national level. It can be found in one district general hospital that patients are looked after by an A+E physician, trauma and orthopaedic surgeons (T&O), cardiothoracic surgeons or general surgery in another, intensivists or respiratory physicians in another. The knock on effect of multiple specialities is that not one specialty has taken a lead in research. Our objective is to map the current delivery of care within the UK to highlight similarities and disparities in practice with the aim to help design further research in this area. The questions relate to the current provision of care including ownership of patients within your trust we wish to gather facts rather than personal opinions.

Who is doing the study?

The Chief Investigator is Dr Helen Ingoe who is an Orthopaedic Surgeon in Training based at the University of York Trials Unit. The York Trials Unit is sponsored by the British Orthopaedic Association to develop and expand the portfolio of trials in the UK related to trauma and orthopaedics. This work is being completed as part of an MD project.

Who is being asked to participate? or Why have I been asked to participate?

You are receiving an invite as you are involved in the provision of chest trauma care in your hospital.

Do I have to take part?

This questionnaire is entirely voluntary and you will be asked to consent to take part by accepting the terms below.

What will be involved if I take part in this study?

The study will involve a 5-10 minute questionnaire completed on line.

What are the advantages/benefits and disadvantages/risks of taking part?

The answers you provide will help us map the current provision for blunt chest trauma care in the UK as we believe this is widely different within trusts. Research into rib fracture fixation is lacking in the UK and it is vital that the care of these patients is understood before undertaking clinical trials in this area.

Can I withdraw from the study at any time?

You can withdraw at any point up until the questionnaire is submitted. It is regrettable but data can't be withdrawn following questionnaire completion as all the data is anonymised and we will not be able to identify the data to withdraw.

Will the information I give be kept confidential?

All storage and archiving will be conducted in line with the York Trials Unit Standard Operating Procedure. All study data will be stored on a secure server accessed via a password protected computer at the University of York. No identifiable data will be collected and email addresses will not be linked to the data. We will only collect your email address if you submit it within the form and only to provide you with a certificate or report of the findings.

What will happen to the results of the study?

A summary report of the study will be available. If you would like a copy of this then please enter your email within the survey and a copy of the findings will be sent to you.

Who has reviewed this study?

The research has been approved by the Department of Health Sciences' Research Governance Committee at the University of York.

Who do I contact in the event of a complaint?

If you have any concerns please contact Dr Catriona McDaid (Senior Research Fellow and Research Supervisor) Tel: +44 (0)1904 321371
Email: catriona.mcdaid@york.ac.uk

If you agree to take part, would like more information or have any questions or concerns about the study please contact

Miss Helen Ingoe MBBS, MSc, MRCS Ed, ORUK Research Fellow and Orthopaedic Registrar in Training

ARRC Building,York Trials Unit, Department of Health Sciences, University of York, Heslington, YO10 5DD. helen.ingoe@york.ac.uk, 01905 321830

Thank you for taking the time to read this information sheet.

Appendix E2 Survey Questions

Consent

This question confirms your consent to participate in the study.

The decision to complete this survey is completely voluntary. If you do complete the survey, information you provide will be included in our analysis along with anonymised direct quotes.

I confirm I have read an understood the information provided above and in the cover letter

I understand that the completion of this questionnaire is voluntary

I agree to the use of anonymised quotes in publications

I agree that my data gathered in this study will be kept and stored confidentially

Do you agree with all of these statements and agree to take part in this study?

Yes

No

Survey

In what type of hospital are you based?

District General

Tertiary Centre

Is the hospital in which you are based a Major Trauma Centre?

Yes – will skip next two questions

No – will answer next question

How far are you from nearest Major Trauma Centre?

<10miles

10-29miles

30-49miles

49-74 miles

75miles +

Is your hospital part of a trauma network?

Yes

No

Don’t know

What size of population does your hospital serve?

<100,000 people

100,000-250,000,

250,000-500,000,

500,000-750,000,

750,000+

Don’t know

Does your hospital service incorporate mostly city, town or rural communities?

City

Town

Rural

How many Trauma and Orthopaedic Surgeons do you have delivering trauma care in your hospital?

5 or less

6-10

11-15

16-20

More than 20

Do you have a thoracic surgery service in your hospital?

Yes

No

Do you have a pathway or protocol for patients presenting to your A+E Department with rib fractures?

Yes

No – miss next question

Don’t know miss next question

Has this been developed by the Trust/Hospital or disseminated from regional trauma network?

Trust/Hospital level

Regional level

Don’t know

If in-patient care is required for a patient with isolated rib fractures (including flail) and does NOT require respiratory support, which speciality undertakes this care?

Accident and Emergency

Anaesthetics/Intensive Care

Cardiothoracic Surgery

General Surgery

Respiratory Medicine

Trauma and Orthopaedic Surgery

Other – Free text box

Who is the parent team if a patient with isolated rib fractures (including flail) that requires care following a chest drain?

Accident and Emergency

Anaesthetics/Intensive Care

Cardiothoracic Surgery

General Surgery

Respiratory Medicine

Trauma and Orthopaedic Surgery

Rehabilitation Medicine

Other – Free text box

Who is the parent team if a patient with isolated rib fractures (including flail) requires non-invasive ventilation?

Accident and Emergency

Anaesthetics/Intensive Care

Cardiothoracic Surgery

General Surgery

Respiratory Medicine

Rehabilitation Medicine

Trauma and Orthopaedic Surgery

Other – Free text box

Who is the parent team if a patient with isolated rib fractures (including flail) requires intubation?

Accident and Emergency

Anaesthetics/Intensive Care

Cardiothoracic Surgery

General Surgery

Respiratory Medicine

Rehabilitation Medicine

Trauma and Orthopaedic Surgery

Other – Free text box

Who would be the parent team for a patient with isolated rib fractures (including flail) who does NOT require respiratory support and is over 75 years old?

Accident and Emergency

Anaesthetics/Intensive Care

Cardiothoracic Surgery

Elderly Medicine

General Surgery

Respiratory Medicine

Rehabilitation Medicine

Trauma and Orthopaedic Surgery

Other – Free text box

Does anyone in your hospital undertake rib fracture fixation ?

Yes

No

Don’t know

Do you have a guideline/pathway for identifying which patients are suitable for rib fracture fixation?

Yes

No

Don’t know

Do you have a dedicated referral pathway for rib fracture fixation (either within hospital or between hospitals)?

Yes

No

Don’t know

Do you have a rehabilitation service led by a rehabilitation consultant to undertake care of patients with rib fractures?

Yes

No

Don’t know

Do you have a specialised respiratory physiotherapy service to undertake care of patients with rib fractures?

Yes

No

Don’t know

Would your centre be willing to take part or identify patients suitable for a randomised controlled trial of rib fracture fixation for FLAIL Chest?

Yes

No

Maybe

Would your centre be willing to take part or identify patients suitable for a randomised controlled trial of rib fracture fixation for simple rib fractures (non-flail)?

Yes

No

Maybe

Would you or someone you know be interested in undertaking consensus work relating to core outcome measures and indications for surgical fixation of rib fractures?

Yes >>>>> Please provide an email address so we can contact you further.

No

Do you have any comments on rib fracture care? E.g. further research questions, aspects not covered in this questionnaire

Free text box

Thank you for completing this survey.

Would like a summary report of the survey findings sent to you via email?

Yes

No

Would you like a certificate for your records?

Yes

No