National Institute for Health and Care Excellence

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Consultation

Chapter 34 Standardised systems of care for intra- and inter-hospital transfers

Emergency and acute medical care in over 16s: service delivery and organisation

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Chapter 35 Standardised systems of care for intra- and inter-hospital transfers

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34 Hospital transfers

34.1 Introduction

The transfer of critically ill patients is not at present standardised throughout the UK. There are some guidelines that have been published however they do cause some degree of inconsistency.

Currently there are large numbers of critically ill patients who require transfer between critical care units which does pose significant risks. It is also more than likely that these numbers will increase over the coming years and, there is data that shows transfers are poorly performed, we needed to look at all different ways this could be implemented and gather the evidence to make a strong enough recommendation to improve the transfer of these patients.

There are also many transfers of critically ill patients for therapeutic or diagnostic purposes within the same hospital which also needs to be looked at so that staff have some degree of instruction so that we have the best possible outcome for these patients.

Carefully planned transfers improve outcomes such as mortality and avoidance of adverse effects which the guideline group felt was of critical importance.

There is also some uncertainty as to how this should be standardised hence the reason the group looked at different comparisons including the possible use of mobile ICU transfers. However, this has to be cost effective and plausible. There can be significant differences throughout the country however it is said that "transfers should be standardised whether the travel is 100yards or 100 miles".

34.2 Review question: Do standardised systems of care for intra- and inter-hospital transfers of critically ill patients improve outcomes?

For full details see review protocol in Appendix A.

Table 1: PICO characteristics of review question

Population	Hospitalised adults and young people (16 years and over) with or at risk of critical illness undergoing intra- or inter-hospital transfer.
Intervention	Standardised system (including checklist of both staffing and equipment) for transfer.
Comparison	No standardised system for transfers.
Outcomes	Mortality (CRITICAL) Avoidable adverse events (CRITICAL) Quality of life (CRITICAL) Length of stay (CRITICAL) Patient and/or carer satisfaction (CRITICAL) Staff satisfaction (IMPORTANT)
Study design	Systematic reviews (SRs) of RCTs, RCTs, observational studies only to be included if no relevant SRs or RCTs are identified.

34.3 Clinical evidence

Six studies for inter-hospital transfer systems were included in the review (7 papers); 3 were non-randomised comparative studies and 3 were before-after studies[16,35,51,52,65,74,77]; these are summarised in Table 2 below. Evidence from these studies is summarised in the clinical evidence

summary below (Table 3, Table 4, Table 5 and Table 6). See also the study selection flow chart in Appendix B, forest plots in Appendix C, study evidence tables in Appendix D, GRADE tables in Appendix F and excluded studies list in Appendix G.

No RCTs were identified by the search and following the review strategy, observational studies were considered. The included observational studies pertain to standardised inter-hospital transfer systems only, as no studies on standardised intra-hospital transfer systems were identified. All included studies are non-randomised and the analyses un-adjusted.

Table 2: Summary of studies included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Bellingan 2000[16] Non-randomised comparative study	Transfer by: standardised system - UCLH specialist team using a mobile ICU (n=168). Versus Standard emergency ambulance with a medical escort provided by the referring hospital (n=91).	Retrospective review of all inter-hospital transfers (n=259) into University College London Hospital's (UCLH) intensive care unit, UK, over the course of 1 year in 1996/1997.	ICU mortality, mortality within 6 and 12 hours of admission and hazard ratio of survival.	Specialist team consisted of an ICU-trained doctor (senior SPR or consultant), nurse, driver, and medical physics technician, all trained in the transfer of ICU patients. The specialist team spent between 30 and 300 mins stabilising patients in the referral hospital before transfer. Unadjusted analysis.
Gallagher 2014B[36] Before and after study	Standardised checklist - introduction of a novel clinical pathway Heart Attack Centre-Extension (HAC-X) for the management of non-ST elevation acute coronary syndromes (NSTE-ACS). Before (n=391). Versus After (n=311).	Before and after study involving patients (n=702) treated at London Chest Hospital, UK, over the course of 1 year in 2009/2010.	Narrative results only: Length of stay (median, IQR), time to coronary angiography (median, IQR).	Before most patients with NSTE-ACS would present to their district general hospital (DGH) and await transfer to regional cardiac centre for angiography. The novel pathway was designed to rapidly identify patients with NSTE-ACS while in DGH emergency departments and facilitate transfer to the regional interventional centre for 'early' coronary angiography. Patients in post-HAC-X group were younger and more likely to have been smokers. Unadjusted analysis.
Malpass 2015[52] Before and	Introduction of a novel patient transfer standardised	Before and after study involving patients (n=211) admitted to the	48-hour mortality, ICU mortality, hospital mortality, adverse events	The novel patient transfer checklist covered: patient data, reason for transfer,

Study	Intervention and comparison	Population	Outcomes	Comments
after study	checklist. Before (n=134). Versus After (n=77).	medical ICU team of a single academic tertiary referral centre in Virginia, US, who were transferred from outside hospitals over the course of 1 year in 2009 (6 months) and 2011 (6 months).	(antibiotics changed on arrival, need for emergent intubation and need for emergent central line).	treatment recommendations, and condition on arrival. Adjusted analysis but only for APACHE score.
Reimer 2013[65] Non randomised comparative study	Transfer via: standardised checklist - streamlined inter-facility referral protocol (n=54) Versus Traditional referral process (n=79).	Retrospective database review of patients (n=133) undergoing inter-facility transport with a referring diagnosis of acute ST-segment elevation myocardial infarction (STEMI) to a tertiary care centre in Ohio, US, over the course of 1 year in 2009/2010.	Narrative results only: Time in ED (median, IQR; total time patient spent in referring department, including time for arrival of transport team), door-to-balloon time (median, IQR).	Non-randomised data; not before-and-after study. Unadjusted analysis. Both cohorts were evaluated ***after*** a streamlined inter-facility referral protocol to reduce door-to-balloon (D2B) times for patients experiencing acute STEMI had been implemented. The hospital operates a hospital-based critical care transport team consisting of 2 helicopters and 1 ground ambulance; the crews are staffed with an acute care nurse practitioner and critical care registered nurse and/or critical care paramedic.
Waddell 1975[74] Non randomised comparative study	Inter-hospital transfers via: standardised system - intensive therapy unit 'Flying squad' team in an ambulance of standard design (n=20). Versus Standard ambulance (n=46).	Before and after study involving critically ill patients (n=66) transferred to the intensive therapy unit of the Western Infirmary, Glasgow, UK. Data of ambulance transfers was collected retrospectively over 6 years. Data for the intensive therapy unit 'flying squad' was	Mortality within 24 hours of transfer, final mortality.	Unclear if before-and-after study ('retrospective' versus 'prospective' data collection). Time period of data collection for flying squad not mentioned. Six years for standard ambulance. Unadjusted analysis and flying squad patients considerably older. Team composition of

Study	Intervention and comparison	Population	Outcomes	Comments
		collected prospectively (time period unknown).		standard ambulance transfers not described. 'Flying squad' consisted of 1 or 2 members of a 'shock team', who travelled to transfer hospital set up equipment, started treatment and accompanied the patient in the ambulance.
Wiegersma 2011[77] Ligtenberg 2005[51] Before and after study	Inter-hospital transfers via: standardised system - mobile ICU with a specialised retrieval system (n=74). Versus Standard ambulance with staff provided by the referring hospital (n=100).	Before and after study involving critically ill patients (n=174) transferred to the University of Groningen affiliated ICU and the ICU of Scheper Hospital in Emmen, the Netherlands. Standard ambulance transfer data was collected over 14 months[51]; mobile ICU transfer data was collected over the course of 10 months in 2009[77].	Avoidable adverse incidents (technical failure; staff management issues and/or inadequate preparation), adverse events (delayed hypotension).	Direct comparison of 2 individual audits. Patients not comparable at baseline and no analysis and no adjustments made; for example, patients transferred via MICU had higher disease severity and were older.

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Table 3: Clinical evidence summary: Standardised system of transfer versus standard ambulance transfer

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Mobile ICU versus standard transfer (95% CI)
Adverse incidents (staff management issues or inadequate preparation)	174 (1 study)	⊕⊖⊖⊖ VERY LOW[a] due to risk of bias	Peto OR 0.13 (0.06 to 0.32)	Moderate	
				240 per 1000	201 fewer per 1000 (from 148 fewer to 221 fewer)
Adverse incidents (technical failures)	174 (1 study)	⊕⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	RR 1.22 (0.52 to 2.84)	Moderate	
				100 per 1000	22 more per 1000 (from 48 fewer to 184 more)
Adverse events (delayed hypotension)	66 (1 study)	⊕⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	RR 1.31 (0.43 to 3.99)	Moderate	
				152 per 1000	47 more per 1000 (from 87 fewer to 454 more)
Mortality HR	259 (1 study)	⊕⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	HR 0.56 (0.35 to 0.9)	Moderate	
				Control group risk not provided	Absolute effect cannot be calculated
Mortality - Overall ICU mortality	259 (1 study)	⊕⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	RR 0.8 (0.55 to 1.15)	Moderate	
				352 per 1000	70 fewer per 1000 (from 158 fewer to 53 more)
Mortality - 6 hour mortality	259 (1 study)	⊕⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	RR 0.14 (0.02 to 1.19)	Moderate	
				44 per 1000	38 fewer per 1000 (from 43 fewer to 8 more)
Mortality - 12 hour mortality	259 (1 study)	⊕⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	RR 0.39 (0.13 to 1.18)	Moderate	
				77 per 1000	47 fewer per 1000 (from 67 fewer to 14 more)

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with Mobile ICU versus standard transfer (95% CI)
Mortality - Final mortality	66 (1 study)	⊕⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	RR 1.15 (0.63 to 2.1)	Moderate	
				391 per 1000	59 more per 1000 (from 145 fewer to 430 more)
Mortality - Mortality within 24 hours of transfer	66 (1 study)	⊕⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	RR 0.77 (0.08 to 6.93)	Moderate	
				65 per 1000	15 fewer per 1000 (from 60 fewer to 385 more)

(a) All non-randomised studies automatically downgraded due to selection bias. Studies may be further downgraded by 1 increment if other factors suggest additional high risk of bias, or 2 increments if other factors suggest additional very high risk of bias.

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 4: Clinical evidence summary: ICU transfer checklist versus no transfer checklist

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ICU transfer checklist versus no transfer checklist (95% CI)
Adverse events - adjusted OR - Need for emergent central line	211 (1 study)	⊕⊖⊖⊖ VERY LOW due to risk of bias[a]	OR 0.09 (0.02 to 0.36)	Moderate	
				Control group risk not provided	Absolute effect cannot be calculated
Adverse events - adjusted OR - Need for emergent intubation	211 (1 study)	⊕⊖⊖⊖ VERY LOW[a,b] due to risk of bias, imprecision	OR 0.18 (0.02 to 1.46)	Moderate	
				Control group risk not provided	Absolute effect cannot be calculated
Adverse events - adjusted OR - Antibiotics changed on arrival	211 (1 study)	⊕⊖⊖⊖ VERY LOW[a, b] due to risk of bias,	OR 0.48 (0.27 to 0.86)	Moderate	
				Control group risk not	Absolute effect cannot be calculated

Outcomes	No of Participants (studies) Follow up	Quality of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects	
				Risk with Control	Risk difference with ICU transfer checklist versus no transfer checklist (95% CI)
		imprecision		provided	
Mortality - adjusted OR - Hospital mortality	211 (1 study)	⨁⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	OR 0.85 (0.46 to 1.61)	Moderate	
				Control group risk not provided	Absolute effect cannot be calculated
Mortality - adjusted OR - ICU mortality	211 (1 study)	⨁⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	OR 0.77 (0.39 to 1.51)	Moderate	
				Control group risk not provided	Absolute effect cannot be calculated
Mortality - adjusted OR - 48-hour mortality	211 (1 study)	⨁⊖⊖⊖ VERY LOW[a, b] due to risk of bias, imprecision	OR 0.74 (0.19 to 2.93)	Moderate	
				Control group risk not provided	Absolute effect cannot be calculated

(a) All non-randomised studies automatically downgraded due to selection bias. Studies may be further downgraded by 1 increment if other factors suggest additional high risk of bias, or 2 increments if other factors suggest additional very high risk of bias.

(b) Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Narrative results

A retrospective database review[65] compared the introduction of a streamlined transfer protocol with the traditional transfer protocol and found that it reduced transfer times of patients experiencing ST-segment myocardial infarction (see Table 5 below). The authors also comment that door-to-balloon times of 90 minutes or less were achieved in 13% of the traditional referral patients and in 30% of the streamlined protocol group (OR=2.9; 95% CI 1.2-7.0).

Table 5: Summary: Before and after introduction of a streamlined transfer

	Traditional transfer (n=79)	Streamlined transfer (n=54)	P

	Traditional transfer (n=79)	Streamlined transfer (n=54)	P
Emergency department	60 (45-84)	55 (44-67)	0.07
Door-to-balloon time	122 (99-157)	101 (88-128)	0.001

Data reported in minutes as median (25-75% interquartile range). Emergency department time is total time patient spent in referring department, including time waiting for arrival of transport team. Door-to-balloon time is total time from presentation at outside ED to percutaneous coronary intervention[65].

A prospective observational study[36] assessed a novel clinical pathway for the management of patients with non-ST elevation acute coronary syndromes and found the direct transfer protocol reduced length of hospital stay and time to coronary angiography (see Table 6 below).

Table 6: Summary: Before and after introduction of a clinical pathway for patients with suspected acute coronary syndromes

	Pre-HAC-X pathway (n=391)	Post-HAC-X pathway (n=311)	P
Time to coronary angiography	7.2 (5.1-10.2)	1.0 (0.7-2.0)	<0.001
Length of hospital stay	9.0 (6.0-14.0)	3.0 (2.0-6.0)	<0.001

Data reported in days as median (25-75% interquartile range).

34.4 Economic evidence

Published literature

No relevant health economic studies were identified.

The economic article selection protocol and flow chart for the whole guideline can found in the guideline's Appendix 41A and Appendix 41B.

Cost analysis

It is likely that the use of standardised systems for transfer will require more staff time for the implementation of the relevant checklists or protocols.

Of the studies included in the clinical review, 3 were UK studies[16,36,74]. It was possible to attach unit costs to resource use described in 1 of these studies, Bellingan 2000[16], which compared transferring ICU patients using a UCLH specialist transfer team and a mobile ICU with transfer by standard emergency ambulance with a medical escort (junior doctor with training in anaesthesia).

In Bellingan, the specialist transfer team consisted of an ICU-trained doctor (specialist registrar or consultant), nurse, driver and medical physics technician all trained in transfer of ICU patients. The mobile ICU is equipped to ICU standards with all-round stretcher access, piped oxygen and air, nitric oxide, mechanical ventilation, suction 220-V power supply and multi-channel monitoring. The specialist team spent between 30 and 300 minutes (mean 70 minutes) stabilising patients in the referring hospital before transfer.

The mean cost per patient in the intervention and the control arms has been calculated using information regarding the team composition and current unit costs. These costs are included in Table 7 for the intervention and in Table 8 for the comparator arms.

Table 7: Mean cost of staff time per patient in the intervention arm (mobile ICU)

	cost per hour(a)	Mean cost of patient stabilisation time at referring hospital(b)	mean cost of actual transfer (c)	Mean cost of patient stabilisation time at receiving hospital(d)	Weight (e)	Mean total cost
Consultant ICU	£140	£163.33	£26.83	£70.00	0.5	£130
Specialist registrar ICU	£61	£71.17	£11.69	£30.50	0.5	£57
Nurse	£49	£57.17	£9.39	£24.50	1	£91
medical physics technician	£38	£44.33	£7.28	£19.00	1	£71
Mean cost per patient						**£348**

(a) Source: PSSRU 2014 costs for a medical consultant, registrar, Nurse, 24---hour ward (includes staff nurse, registered nurse and registered practitioner) and science, technical and therapeutic staff: allied health professional (qualified), respectively, including qualifications[28].
(b) Based on a mean of 70 minutes as reported in the paper.
(c) Based on a mean travel distance of 12 miles, as reported in the paper, and 60 miles per hour.
(d) Assuming 30 minutes of stabilisation time in the receiving hospital.
(e) A weight of 0.5 assigned to both a consultant and a specialist registrar as the team could include either.

Table 8: Mean cost of staff time per patient in the control arm (standard ambulance)

	cost per hour(a)	Mean cost of patient stabilisation time at referring hospital(b)	mean cost of actual transfer (c)	Mean cost of patient stabilisation time at receiving hospital(d)	Weight (e)	Mean total cost
Paramedic (qualified)	£33	£16.50	£6.33	£16.50	1	£39
Specialist registrar	£61	£30.50	£11.69	£30.50	1	£73
Mean cost per patient						**£112**

(a) Source: PSSRU 2014[28].
(b) Based on a mean of 30 minutes stabilisation time at referring hospital (assumed).
(c) Based on a mean travel distance of 12 miles, as reported in the paper, and 60 miles per hour.
(d) Based on a mean of 30 minutes stabilisation time at referring hospital (assumed).
(e) One paramedic (assumed) and 1 junior doctor (reported in the paper) are considered to be present in each journey.

Other costs not included here are the costs of the standard ambulance and the mobile ICU journey, including the drivers' time, as it was not possible to locate these costs. The transfer service is usually provided by private providers with prices subject to locally negotiated contracts. Additionally, training costs for members of the specialist transfer team were not included. Hence, costs of the mobile ICU and specialist team intervention and its incremental cost compared to the standard ambulance transfer are likely to be underestimated. Additionally, we have not included any time required for the ambulance deployment and return to base.

Based on the study's mortality data reported in the clinical review, the use of mobile ICU and specialist transfer team was associated with lower overall ICU mortality (70 fewer per 1000, that is, 0.07 deaths averted per patient). Based on this, the incremental cost effective ratio could be calculated as:

ICER= (£348-£112)/0.07=£3,377 per death averted.

For this intervention to be cost-effective at a cost-effectiveness threshold of £20,000 per QALY gained, it has to generate a number of QALYs per patient equivalent to ΔQALYs where:

£20,000= ΔC/ΔQALYs = £3,377 /ΔQALYs.

Thus, ΔQALYs could be calculated to be 0.17 QALYs. This means the intervention will need to result in at least 0.17 QALYs gained per patient to be cost-effective at a threshold of £20,000 per QALY gained.

As explained earlier, the calculated incremental cost is likely to be an underestimate due to the possibly higher incremental cost when the cost of the transport vehicle is included. Additionally, if the routine use of the mobile ICU for transfers would require extra staffing to provide cover in the referring ICU, then the incremental cost of using the mobile ICU would be considerably higher. The quality of the clinical evidence that informed this analysis should also be taken into account when interpreting it. Furthermore, possible benefits from using a mobile ICU, other than mortality, have not been included in this analysis.

34.5 Evidence statements

Clinical

Specialist transport systems versus standard ambulance transfer

- Five studies compromising 1334 people evaluated the role of standardised systems of care for intra- and inter-hospital transfers of critically ill patients for improving outcomes in secondary care in adults and young people at risk of an AME, or with suspected or confirmed AME. The evidence suggested that transfer via specialist transport systems may provide a benefit in reduced adverse incidents expressed as staff management issues or inadequate preparation (1 study, very low quality) and mortality at 6 hours, 12 hours and ICU overall mortality (1 study, very low quality) and mortality within 24 hours of transfer (1 study, very low quality). However, there was a possible increase in adverse incidents technical failures (1 study, very low quality) and adverse events delayed hypotension (1 study, very low quality) and final mortality (1 study, very low quality).

ICU transfer checklists versus no transfer checklist

- One study compromising 211 people evaluated the role of ICU transfer checklist versus no transfer checklist for intra- and inter-hospital transfers of critically ill patients for improving outcomes in secondary care in adults and young people at risk of an AME, or with suspected or confirmed AME. The evidence suggested that transfer checklists and protocols may provide a benefit in reduced adverse events and mortality. The evidence was graded very low for all outcomes.

Economic

- No relevant economic evaluations were identified.

34.6 Recommendations and link to evidence

Recommendations	**20. Use standardised systems of care (including checklists, staffing and equipment) when transferring critically ill patients within or between hospitals.**
Research recommendations	**-**
Relative values of different outcomes	The guideline committee considered mortality, avoidable adverse events as reported by study, quality of life, and carer/family satisfaction to be critical outcomes. Length of stay, and staff satisfaction were considered important outcomes.
Trade-off between benefits and harms	Six observational studies were identified for inter-hospital transfers. No evidence from randomised trials was identified. The evidence was presented across separate intervention types: ***Standardised specialist transport systems versus standard ambulance transfer*** Specialist transport systems include mobile intensive care units and standard transport augmented by specialist retrieval. Mobile intensive care systems were primarily focused on secondary transfers of critically ill patients from a referring hospital to a major centre. Five studies were identified. The evidence suggested that specialist transport systems may provide a benefit in reduced adverse incidents (staff management issues or inadequate preparation) and mortality (overall ICU, 6 hour, within 24 hours of transfer). However, in these observational and before-and-after studies there was a possible increase in adverse incidents (technical failures and episodes of delayed hypotension) and a higher final mortality. These trends, associated with mobile intensive care unit transfers, are very likely to be a consequence of unmeasured case mix differences and more effective monitoring: specialist transport permits transfer of sicker patients. The committee noted that other studies have shown physiological stability during specialist transfer[18,19]. Whilst the evidence was not conclusive, the committee felt that elements of standardised specialist transport systems were likely to be effective in improving care including the use of specialist staff and equipment. ***ICU transfer checklist versus no transfer checklist*** One study evaluated the role of ICU transfer checklist versus no transfer checklist for critically ill patients. The evidence suggested that transfer checklists and protocols may provide a benefit in reduced adverse events upon arrival at the receiving hospital (that is, reduced need for emergent central venous cannulation, emergent intubation, and changes to antibiotics at the time of arrival) and mortality (48-hour, ICU and overall hospital mortality). No evidence was found for length of stay, quality of life, carer/family satisfaction, and staff satisfaction for either specialist transport systems or the transfer checklist sections. The committee felt that the benefits of a reduction in mortality and reduction of adverse events was strong enough to make a recommendation to use standardised systems of care for the transfer of critically ill patients, including standardised protocols, skilled staff, specialised equipment and checklists for the secondary transfer of critically ill patients. The decision to make a strong recommendation based on weak evidence represents the unanimous view of the committee based on extensive clinical experience, the widespread adoption of standardised processes by industry and by the military, and the promotion by the World Health Organisation of standardised care processes such as the WHO checklist. Paediatric critical care has long provided specialist critical

Recommendations	**20. Use standardised systems of care (including checklists, staffing and equipment) when transferring critically ill patients within or between hospitals.**
Research recommendations	-
	care regional retrieval services, demonstrated to be effective[64] and now funded by NHS England as part of specialised commissioning.
Trade-off between net effects and costs	No economic evaluations were identified. It was possible to attach UK-specific unit costs to resource use described in 1 of the UK studies that compared transferring critically ill patients using mobile ICU with transfer using standard ambulance. The analysis showed that transferring patients using mobile ICU would be more costly, with an incremental cost of £236 per patient. Combining this estimate of the incremental cost with the effectiveness estimate from the systematic review of the clinical evidence, which estimated that the use of mobile ICU would be associated with a reduced overall ICU mortality (70 fewer per 1000), it was possible to calculate an incremental cost ratio of £3,200 per death averted for the mobile ICU intervention. A threshold analysis was also presented where the minimum number of QALYs gained required in order to make the use of mobile ICU cost effective at a threshold of £20,000 per QALY gained was calculated and was found to be 0.17 QALYs gained per patient. The committee highlighted that this could be considered a plausible QALY gain to achieve, however, it has to be taken into account that these are critically ill patients. It was also highlighted that the study on which this analysis is based was a small observational study conducted in a single hospital in London and the generalisability of its findings to the rest of the UK might be limited. Additionally, the committee acknowledged that a mobile ICU might not always be available, especially in rural areas, and it was important therefore to focus not on the ambulance as the mobile ICU, but on the specialist staff and transport equipment which constitute the basis of mobile intensive care. There are arguments for having regional transport teams so that existing staff are not diverted away from delivering care in the ICU. The cost-effectiveness of such a service is difficult to estimate and will depend on local demand and travel times. The results of the clinical review showed a benefit in terms of mortality and adverse events for the use of standardised transfer systems using checklists, protocols and skilled staff. Given the limited resources required for use, the committee believed that these are likely to be cost-effective. Based on their collective experience, and evidence from other clinical areas (for example, surgery), the committee believed that there is clear evidence of benefit when using standardised systems. The committee felt that there should not be a cost impact from the use of checklists and protocols. For more high-risk transfers, for example transfer between ICUs, specialist staff might be required, which could require investment in some parts of the country.
Quality of evidence	Six observational studies for inter-hospital transfer systems were included in the review. No RCTs were identified by the search. The included observational studies pertain to standardised inter-hospital transfer systems only, as no studies on standardised intra-hospital transfer systems were identified. All included studies are non-randomised and most of the analyses un-adjusted, leading to very high risk of bias for most of the evidence. Also, before-and-after studies do not control for an effect of time on the outcome. The evidence for mortality and avoidable adverse events in both sections, mobile ICU transfers and ICU transfer checklist, was of very low quality due to the study design, risk of bias

Recommendations	**20. Use standardised systems of care (including checklists, staffing and equipment) when transferring critically ill patients within or between hospitals.**
Research recommendations	-
	and imprecision. In addition, data of 2 of the 6 studies (those that were in a cardiac population) could only be presented in narrative form (medians and interquartile range). Three of the studies were from the UK. The committee considered the study demonstrating reduced hazards of death through transport via a mobile ICU particularly relevant to the current UK context. However, they also highlighted 1 other UK study on mobile ICU transfers as being old and at high risk of bias.
Other considerations	The committee recognised that despite expansion of critical care services in England, ICU transfers still occur in situations when 1 unit has reached capacity. The practice may vary widely across the country depending on geography as well as local funding of services (for example, urban versus rural locations). As transfer of critically ill patients for non-clinical reasons is undesirable, if the practice persists because of resource constraints, then standardising processes of care to assure patient safety needs little justification. Paediatric retrieval teams were established precisely for this reason. Two of the studies focused on inter-hospital transfers to more specialist cardiology units. The committee felt that hospital transfers involving highly specialist units are important. They noted that there is already NICE guidance available about the use of standardised systems of care for hospital transfer for specific indications. The NICE service delivery guideline on Major Trauma published in 2016[57] recommends: 1.5 Transfer between emergency departments. 1.5.1 Provide a protocol for the safe and rapid transfer of patients who need definitive specialist intervention. 1.5.2 Train clinical staff involved in the care of patients with major trauma in the transfer protocol. 1.5.3 Review the transfer protocol regularly. The committee noted that professional guidance exists for standardised transfers, including equipment, personnel, training and communication[34,45,48]. Adequate training in inter- and intra-hospital transfers is delivered uniformly in the NHS. With the increasing move to integrated care, transfers between hospitals are likely to be more common place. Training in the transfer of patients should be embedded into the curricular of both medical and non-medical practitioners.

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Appendices

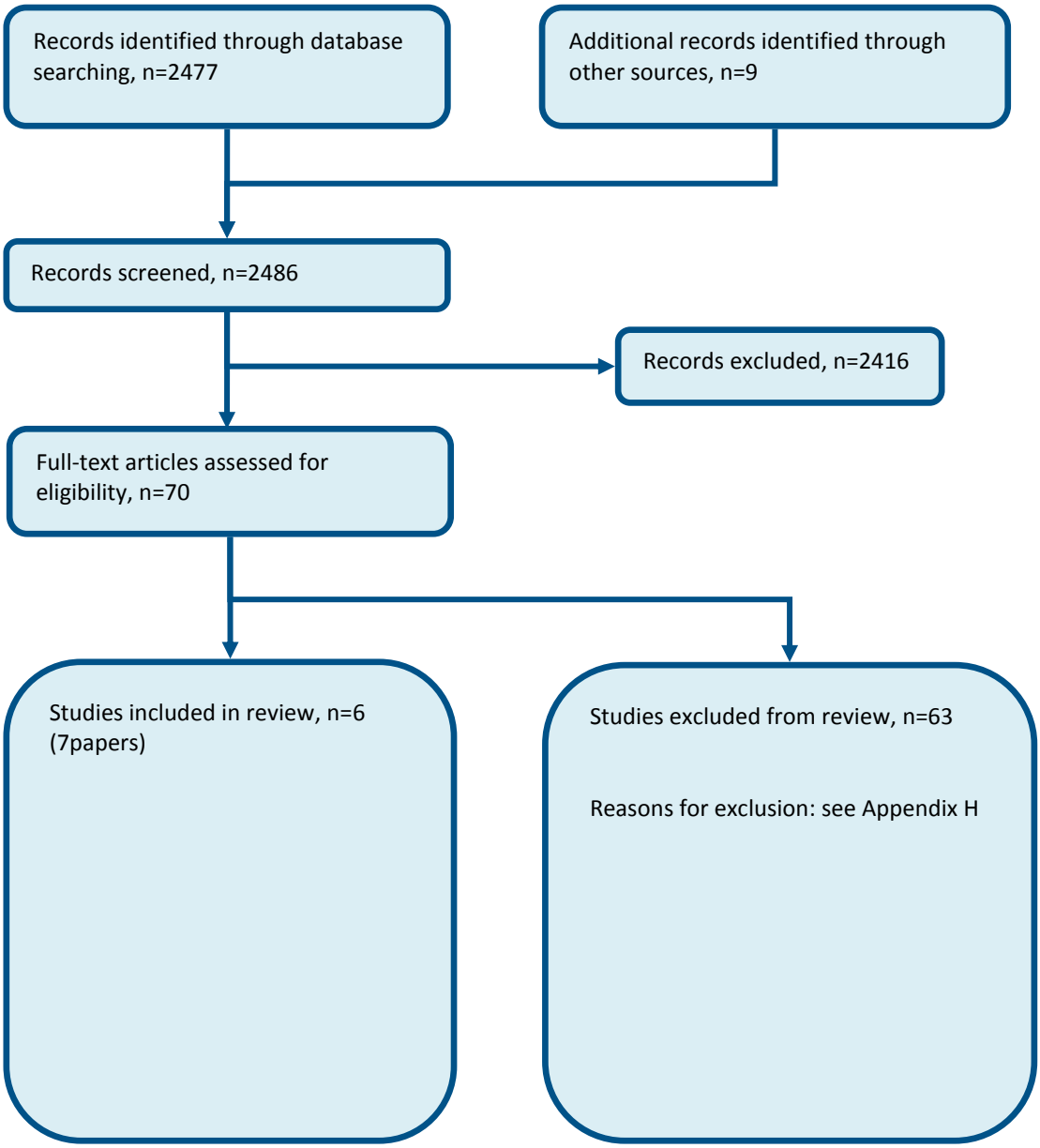
Appendix A: Review protocol

Table 9: Review protocol: standardised systems for intra- and inter-hospital transfers

Review question: Do standardised systems of care for intra- and inter-hospital transfers of critically ill patients improve outcomes? **(Please note this is allocated as 2 questions as the criteria includes protocols, documentation and equipment).**	
Rationale	Systems for transferring critically ill patients within or between hospitals vary widely. Standardised systems for planning and conducting transfers, and for quality assurance through audit, may reduce risks in this highly dependent patient population.
Topic code	T6-12.
Population	Hospitalised adults and young people (16 years and over) with or at risk of critical illness undergoing intra- or inter-hospital transfer.
Intervention	Standardised system (including checklist of both staffing and equipment) for transfer.
Comparison	No standardised system for transfers.
Outcomes	Patient outcomes; Mortality (CRITICAL) Avoidable adverse events (CRITICAL) Quality of life (CRITICAL) Length of stay (CRITICAL) Carer outcomes; Carer/family satisfaction Staff satisfaction
Exclusion	Non-OECD countries.
Search criteria	The databases to be searched are: Medline, Embase, the Cochrane Library. Date limits for search: None. Language: English.
The review strategy	Systematic reviews (SRs) of RCTs, RCTs, observational studies only to be included if no relevant SRs or RCTs are identified.
Analysis	Data synthesis of RCT data. Meta-analysis where appropriate will be conducted. Studies in the following subgroup populations will be included in subgroup analysis: • Inter versus intra-hospital. In addition, if studies have pre-specified in their protocols that results for any of these subgroup populations will be analysed separately, then they will be included in the subgroup analysis. The methodological quality of each study will be assessed using the Evibase checklist and GRADE.

Appendix B: Clinical article selection

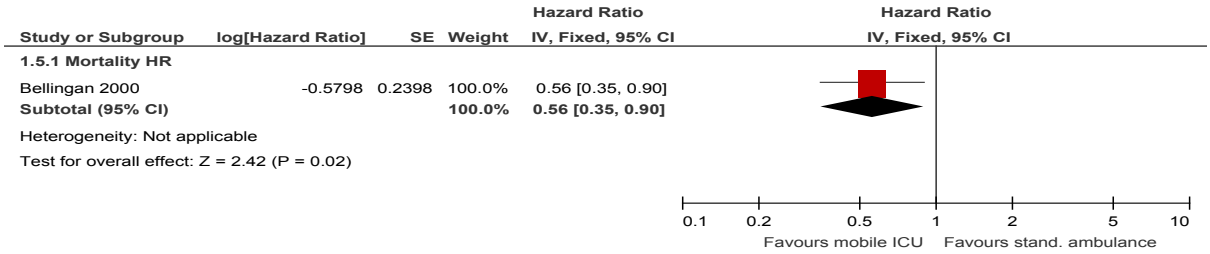
Figure 1: Flow chart of clinical article selection for the review of inter- and intra-hospital transfers



Appendix C: Forest plots

C.1 Standardised system versus standard ambulance transfer

Figure 2: Mortality (hazard ratio)



Extracted from the Kapplan-Meier plot in the paper.

Figure 3: Mortality (at different time points)

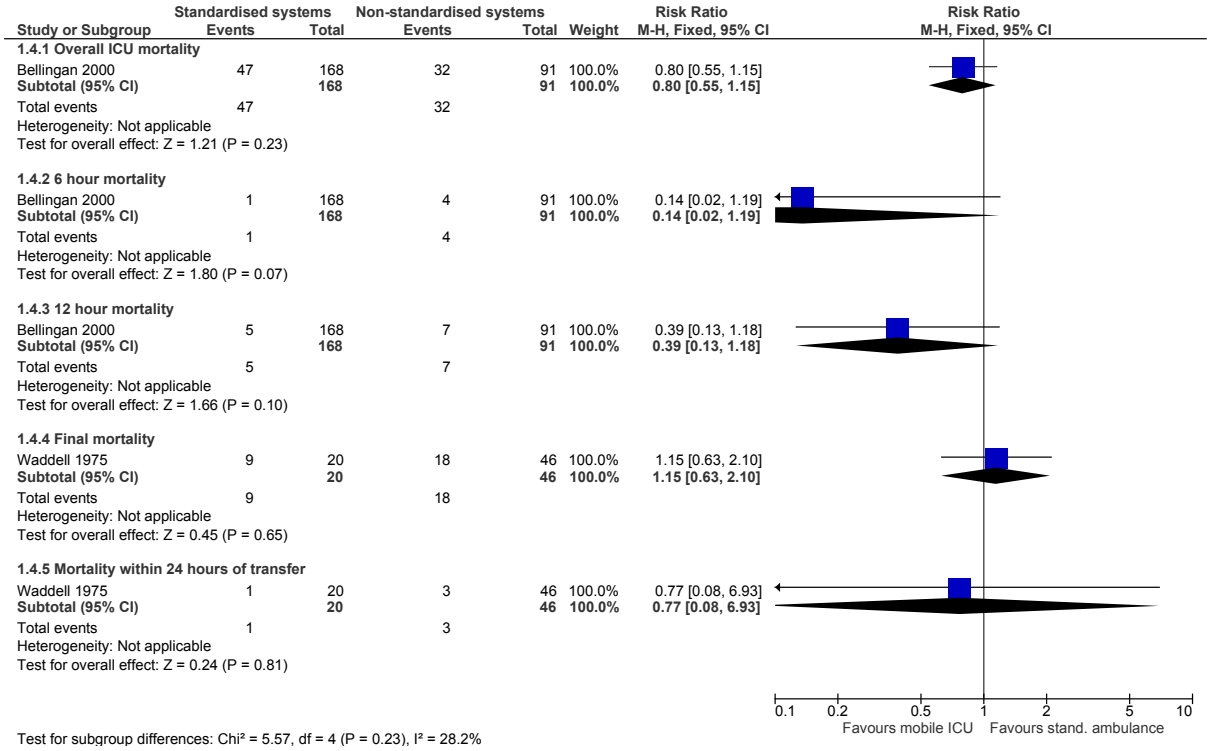


Figure 4: Adverse incidents (due to staff management issues or inadequate preparation)

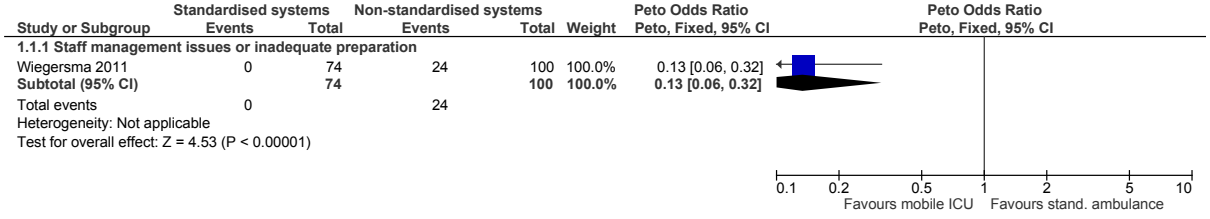
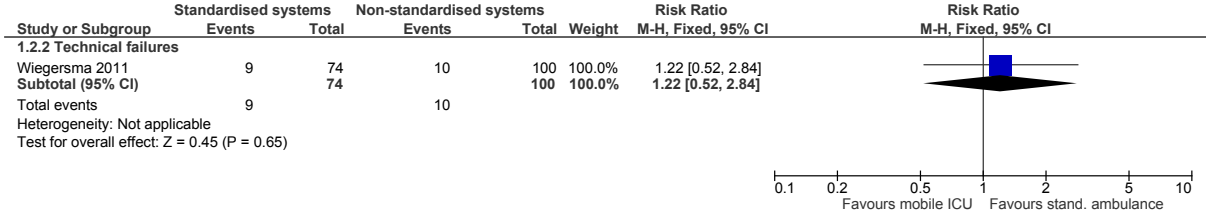
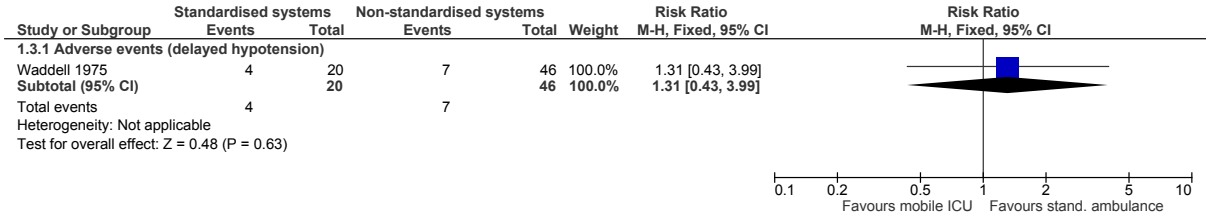


Figure 5: Adverse incidents (due to technical failures)



1

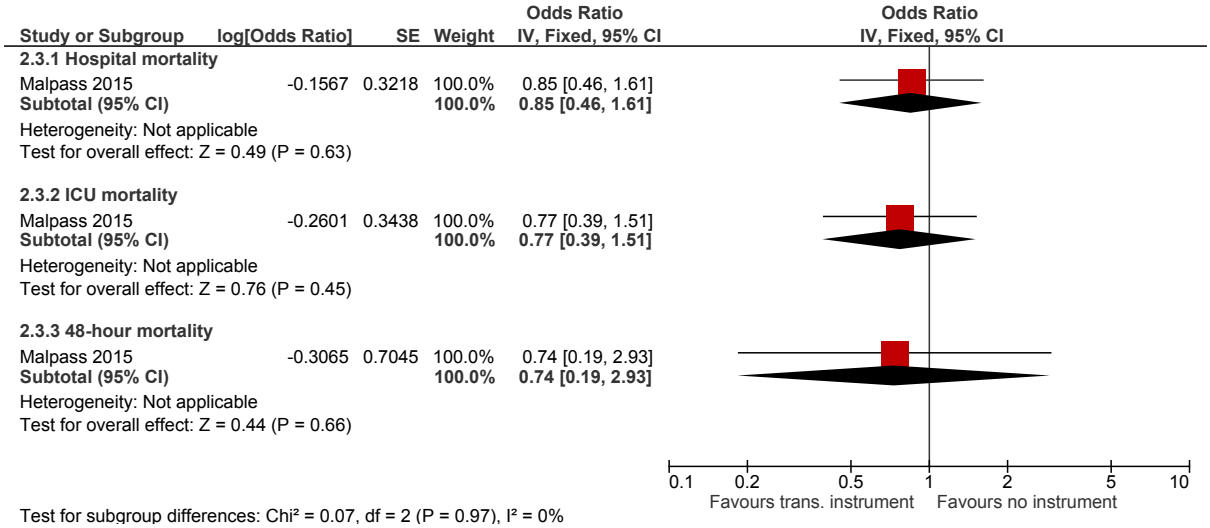
Figure 6: Adverse events (that is, delayed hypotension)



2

3 C.2 ICU transfer checklist versus no transfer checklist

Figure 7: Mortality (at different time points)

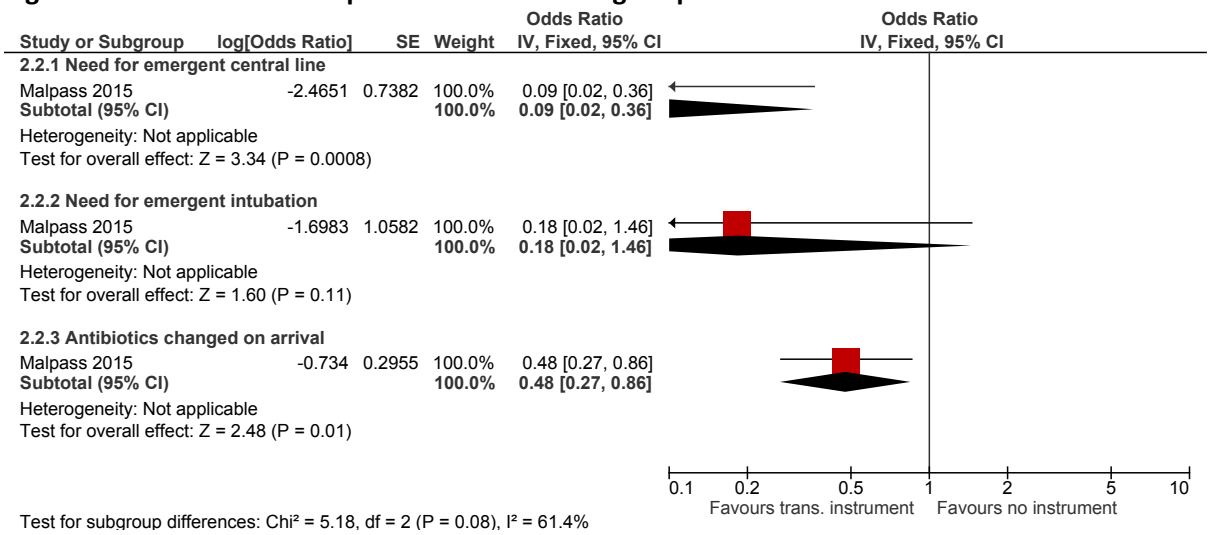


Analysis adjusted for APACHE score.

4

5

Figure 8: Adverse events upon arrival at receiving hospital



Analysis adjusted for APACHE score.

1

Appendix D: Clinical evidence tables

Study	Comparison of a specialist retrieval team with current UK practice trial: Bellingan 2000[16]
Study type	Non-randomised comparative study.
Number of studies (number of participants)	1 (n=259).
Countries and setting	Conducted in United Kingdom; setting: University College London Hospitals (UCLH), UK.
Line of therapy	1st line.
Duration of study	Other: retrospective review of all transfers over 1 year.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	All critically ill patients who were transferred into the UCLH intensive care unit (ICU) from 1st October 1996 to 30th September 1997.
Exclusion criteria	n/a.
Recruitment/selection of patients	Patients were transferred either by the UCLH specialist team using a mobile ICU (n=168, 64.9%) or by standard emergency ambulance with a medical escort provided by the referring hospital (n=91, 35.1%). Transfer by standard ambulance occurred when the specialist team was busy or unavailable owing to training or maintenance. There was no selection policy determining which mode of transfer was used.
Age, gender and ethnicity	Age - Mean (SD): mobile ICU: 54 (19); standard ambulance: 56 (19). Gender (M:F): mobile ICU: 1/1; standard ambulance: 3/2. Ethnicity: n/a.
Further population details	1. Inter versus Intra hospital: Inter hospital (transfer into ICU of UCLH from referring hospital).
Indirectness of population	No indirectness.
Interventions	(n=168) Intervention 1: Standardised system (including checklist of both staffing and equipment) for transfer - As defined by the study. Inter-hospital transfer by specialist team using a mobile ICU. The team consisted of an ICU-trained doctor (senior SPR or consultant), nurse, driver, and medical physics technician, all trained in the transfer of ICU patients. The mobile ICU is an ambulance equipped to ICU standards (all round stretcher access, piped oxygen and air, nitric oxide, mechanical ventilation, suction, 220V power supply and multi-channel monitoring). The specialist team spent between 30 and 300 min (mean 70 min) stabilising patients in the referring hospital before transfer. Duration: retrospective review of all transfers over the course of 1 year. Concurrent medication/care: n/a.

	(n=91) Intervention 2: No standardised system for transfers - As defined by the study. Inter-hospital transfer by standard ambulance with a medical escort provided by the referring hospital (when specialist team was busy or unavailable). Duration: retrospective review of all transfers over the course of 1 year. Concurrent medication/care: n/a.
Funding	Funding not stated.
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTER-HOSPITAL TRANSFER BY SPECIALIST TEAM USING A MOBILE ICU versus INTER-HOSPITAL TRANSFER BY STANDARD AMBULANCE. Protocol outcome 1: Mortality - Actual outcome: Mortality within 6 hours of admission; Group 1: 1/168, Group 2: 4/91; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no difference in baseline characteristics; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: overall ICU mortality within ICU stay; Group 1: 47/168, Group 2: 32/91; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no difference in baseline characteristics; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: Mortality- HR at 1000 hours; HR 0.56 (95%CI 0.35 to 0.9) Reported; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no difference in baseline characteristics; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: Mortality within 12 hours of admission; Group 1: 5/168, Group 2: 7/91; Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: no difference in baseline characteristics; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Avoidable adverse events; Quality of life; Length of stay; Carer/Family satisfaction; Staff satisfaction.

Study	Direct transfer protocol for patients with non-ST-elevation acute coronary syndromes trial: Gallagher 2014[36]
Study type	Before and after study.
Number of studies (number of participants)	1 (n=702).
Countries and setting	Conducted in United Kingdom; setting: London Chest Hospital, a 'stand-alone' regional interventional cardiac centre serving a population of about 1.8 Million in North East London, UK. Prospective observational study of the management of patients with non-ST elevation acute coronary syndrome (NSTE-ACS) treated at the institution between October 2009 and October 2010. The study period represents the last 6 months of the previous NSTE-ACS care model and the first 6 months of the new Heart Attack Centre Extension (HAC-X).
Line of therapy	1st line.
Duration of study	Other: 6 months before + 6 months after introduction of transfer protocol.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	Inclusion criteria were an admission diagnosis of NSTE-ACS with chest pain within 24 h of presentation plus either an elevated blood troponin T or troponin I concentration, or ECG changes compatible with ischaemia (defined asST-segment depression ≥1 mm or T-wave inversion ≥2 mm in 2 contiguous leads, or biphasic ST/T wave segments indicative of a critical stenosis in the left anterior descending artery).
Exclusion criteria	Patients were excluded if they had contraindication to early interventional management including major medical comorbidity, unexplained anaemia (haemoglobin concentration ≤10 g/dL), acute renal failure, recent traumatic injury or loss of consciousness (except when secondary to cardiac arrhythmia), overt epsis or unexplained hypoxia.
Recruitment/selection of patients	Patients were eligible for inclusion in the study if they presented to a district general hospital (DGH) ED participating in the HAC-X project and were subsequently transferred to the Chest Hospital for further management.
Age, gender and ethnicity	Age - Mean (SD): before: 65.2 (12.6); after: 57.0 (13.9). Gender (M:F): 7/3. Ethnicity: n/a.
Further population details	1. Inter versus Intra hospital: Inter hospital (transfer from district general hospital to this regional interventional cardiac centre).
Indirectness of population	No indirectness.
Interventions	(n=311) Intervention 1: Standardised system (including checklist of both staffing and equipment) for transfer - As defined by the study. Direct transfer protocol through Heart Attack Centre-Extension. After initiation of the HAC-X pathway patients diagnosed with NSTE-ACS in the DGH ED, and meeting the inclusion criteria received protocol driven evidence-based medical therapy [Aspirin 200mg, Clopidogrel 600mg, Fondaparinux 2.5mg, and Eptifibatide bolus (180 mg/kg) as long as no contraindications] and were transferred to the Chest Hospital directly within 1 h of diagnosis.

	There was no requirement for ECG review or prior notification of the patient's transfer to the centre but clinical advice could be sought in cases of diagnostic uncertainty. If admission diagnosis of NSTE-ACS was confirmed at the centre, coronary angiography was performed; unstable patients were taken directly for coronary angiography. Stable patients had coronary angiography scheduled for later the same day, or on next available routine list. All subsequent cardiac care was undertaken at the regional cardiac centre. Patients were aimed to be discharged within 48 hours of their admission. Patients requiring surgical revascularisation remained at the centre until surgery was performed. Duration: 6 months post-induction of the scheme. Concurrent medication/care: n/a. (n=391) Intervention 2: No standardised system for transfers - As defined by the study. Previous NSTE-ACS care model which involved admission of patients to their local DGH for 'medical stabilisation' pending availability of a bed at the regional interventional cardiac centre for transfer for coronary angiography (and/or PCI). Clinical instability prompted more urgent transfer and patients were usually transferred back to their local hospital for discharge following invasive cardiac treatment. Duration: 6 months pre-induction of the scheme. Concurrent medication/care: n/a.
Funding	Funding not stated.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: DIRECT TRANSFER PROTOCOL THROUGH HEART ATTACK CENTRE-EXTENSION versus PREVIOUS NSTE-ACS CARE MODEL.

Protocol outcome 1: Avoidable adverse events.
- Actual outcome: Time to coronary angiography (median) during study period; Indirectness of outcome: Serious indirectness, Comments: surrogate outcome for avoidable adverse events

Protocol outcome 2: Length of stay.
- Actual outcome: Length of hospital stay at time from registration at the DGH ED to final hospital discharge (median); Indirectness of outcome: No indirectness.

Narrative data only -

Before and after introduction of a clinical pathway for patients with suspected acute coronary syndromes.

Pre-HAC-X pathway (n=391)	Post-HAC-X pathway (n=311)	P	
Time to coronary angiography	7.2 (5.1-10.2)	1.0 (0.7-2.0)	<0.001
Length of hospital stay	9.0 (6.0-14.0)	3.0 (2.0-6.0)	<0.001

Data reported in days as median (25-75% interquartile range).

Protocol outcomes not reported by the study	Mortality; Quality of life; Carer/Family satisfaction; Staff satisfaction.

Study	Inter-hospital medical intensive care unit transfer instrument trial: Malpass 2015[52]
Study type	Before and after study.
Number of studies (number of participants)	1 (n=211).
Countries and setting	Conducted in USA; setting: development of ICU transfer instrument development, pilot testing of the ICU transfer instrument, and outcome ascertainment prior to and following the patient transfer instrument intervention by the University of Virginia, USA. Pilot testing initiated and done by physicians accepting outside hospital transfers to a closed medical ICU in a single academic tertiary referral centre. Pre-intervention data was collected over 6 months starting January 2009; post-intervention data was collected over 6 months starting January 2011. In both cases included all patients admitted to the medical ICU who were transferred from outside hospitals within the time period specified.
Line of therapy	1st line
Duration of study	Other: for 6 months before + for 6 months after induction 2 years later.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	The pre-intervention group included all patients admitted to the medical ICU team who were transferred from outside hospitals for 6 months starting in January 2009; the post-intervention group included all patients admitted to the medical ICU team transferred from outside hospitals for 6 months starting January 2011 (after implementation of the transfer instrument).
Exclusion criteria	n/a.
Recruitment/selection of patients	Pilot testing initiated and done by physicians accepting outside hospital transfers to a closed medical ICU in a single academic tertiary referral centre. Pre-intervention data was collected over 6 months starting January 2009; post-intervention data was collected over 6 months starting January 2011. In both cases included all patients admitted to the medical ICU who were transferred from outside hospitals within the time period specified.
Age, gender and ethnicity	Age - Mean (SD): 56.4 (16.4). Gender (M:F): 1/1. Ethnicity: n/a.
Further population details	1. Inter versus Intra hospital: Inter hospital (Inter-hospital transfer to a closed medical ICU at a tertiary referral centre).
Indirectness of population	No indirectness.
Interventions	(n=77) Intervention 1: Standardised system (including checklist of both staffing and equipment) for transfer - As defined by the study. Inter-hospital ICU transfer instrument was developed which consisted of 4 main sections: patient data, reason for transfer, treatment recommendations, and condition on arrival. It included physician and

	hospital contact info, past medical history, a history of present illness narrative highlighting complicating problems, the patient's current vital signs (e.g. airway, breathing, and circulation; notation of ventilator setting paired with the ABG, blood pressure paired with vasopressor, and vascular access), and essential test results. The second section prompted the user to notify key services that will be involved in the patient's care so that the full care team is ready to act when the patient arrives. The third section prompted and documented recommendations made to referring physician (including reasoning behind therapy choices to facilitate dialog and identify opportunities for intervention delivery before or during transport). The final section provided feedback to the process by collecting data on the patient's status on arrival to receiving hospital. The tool was to systematise communication between the units. Duration: 6 month after intervention implementation. Concurrent medication/care: n/a. (n=134) Intervention 2: No standardised system for transfers - As defined by the study. Pre-implementation of transfer instrument. No information given as to how transfers were arranged before the tool had been developed and implemented. Duration: 6 months before intervention implementation. Concurrent medication/care: n/a.
Funding	No funding.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INTER-HOSPITAL ICU TRANSFER INSTRUMENT versus PRE-IMPLEMENTATION OF TRANSFER INSTRUMENT.

Protocol outcome 1: Mortality
- Actual outcome: ICU mortality; OR 0.77 (95%CI 0.39 to 1.51); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: post-implementation group had higher predicted mortaity; Key confounders: unclear if adjusted for anything other than APACHE II score and predicted mortality; Group 1 Number missing: 0; Group 2 Number missing: 0

- Actual outcome: 48-hour mortality at 48 hours; OR 0.74 (95%CI 0.19 to 2.93); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: post-implementation group had higher predicted mortaity; Key confounders: unclear if adjusted for anything other than APACHE II score and predicted mortality; Group 1 Number missing: 0; Group 2 Number missing: 0- Actual outcome: hospital mortality; OR 0.85 (95%CI 0.46 to 1.61); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: post-implementation group had higher predicted mortaity; Key confounders: unclear if adjusted for anything other than APACHE II score and predicted mortality; Group 1 Number missing: 0; Group 2 Number missing: 0
Protocol outcome 2: Avoidable adverse events.
- Actual outcome: Need for emergent central line; OR 0.09 (95%CI 0.02 to 0.36); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: post-implementation group had higher predicted mortaity; Key confounders: unclear if adjusted for anything other than APACHE II score and predicted mortality; Group 1 Number missing:

0; Group 2 Number missing: 0 - Actual outcome: Need for emergent intubation; OR 0.18 (95%CI 0.02 to 1.46); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: post-implementation group had higher predicted mortaity; Key confounders: unclear if adjusted for anything other than APACHE II score and predicted mortality; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: Antibiotics changed on arrival; OR 0.48 (95%CI 0.27 to 0.86); Risk of bias: All domain - Very high, Selection - High, Blinding - High, Incomplete outcome data - Low, Outcome reporting - Low, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: post-implementation group had higher predicted mortaity; Key confounders: unclear if adjusted for anything other than APACHE II score and predicted mortality; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Quality of life; Length of stay; Carer/Family satisfaction; Staff satisfaction.

Study	**Decreasing door-to-balloon times through streamlined protocol trial: Reimer 2013[65]**
Study type	Non-randomised comparative study.
Number of studies (number of participants)	1 (n=133).
Countries and setting	Conducted in USA; setting was a 1300-bed Midwest tertiary care centre that serves as a regional referral centre in Northeast Ohio, USA. Two cohorts were analysed after implementation of a streamlined referral protocol to improve door-to-balloon times for patients with acute STEMI (ST segment elevation myocardial infarction): patients transferred using the streamlined protocol and patients referred through the traditional referral process. The cardiac catheterisation laboratory is fully staffed weekdays, with on-call staffing for nights and weekends. The hospital operates a hospital-based critical care transport (CCT) team consisting of 2 helicopters and 1 ground ambulance that operate 24 hours a day 7 days a week. All CCT crews are staffed with an acute care nurse practitioner and critical care registered nurse and/or critical care paramedic.
Line of therapy	1st line.
Duration of study	Intervention time: 1 year.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	All patients undergoing transport by helicopter or ground for acute STEMI to the Cleveland Clinic for emergent PCI by the hospital-based CCT team from July 2009 through to June of 2010 were eligible for the study.
Exclusion criteria	n/a.

Recruitment/selection of patients	A hospital-based CCT log was used to track all streamlined cases for acute STEMI. The hospital also had an acute myocardial infarction (AMI) database to identify door-to-balloon times which includes only patients with a referring diagnosis of STEMI and a positive cardiac catheterisation defined as coronary artery occlusion deemed to be associated with an acute coronary syndrome by the interventional cardiologist. Only cases that had complete data entered into the CCT STEMI log and AMI database were included for analysis.
Age, gender and ethnicity	Age - Median (IQR): streamlined: 55 (49-64); traditional: 61 (50-72). Gender (M:F): 1/2. Ethnicity: White: streamlined (65%); traditional transfer (77%).
Further population details	1. Inter versus Intra hospital: Inter hospital (patients transferred for acute STEMI to the clinic for emergent PCI).
Indirectness of population	No indirectness.
Interventions	(n=54) Intervention 1: Standardised system (including checklist of both staffing and equipment) for transfer - As defined by the study. Streamlined referral protocol. The traditional protocol was reviewed to identify areas for improvement by the transport team and cardiology management team. The abbreviated streamlined protocol was then developed: Referring facilities were provided with a contact telephone number linked directly to a CCT coordinator via a hotline dedicated to streamlined referrals. Upon receiving a hotline request, to coordinator obtained patient information, location, and simultaneously dispatches the aircraft. The coordinator also instructs the referring hospital to fax the patient's electrocardiogram to the coronary care unit and a demographic sheet to the hospital transfer centre. The aircraft is dispatched without regard for bed availability and without accepting physician communication before dispatch. While the transport is taking place, the coordinator activates the catheterisation laboratory to reserve a table or to activate the on-call team and then contacts the on-call cardiologist to inform them of the referral and information regarding the referring facility. Duration: 1 year. Concurrent medication/care: n/a. (n=79) Intervention 2: No standardised system for transfers - As defined by the study. The traditional protocol processed time-sensitive patient transfer requests the same as all other transfer requests. It consisted of 21 steps with an average time to complete of 42 minutes, ranging from 23 to 64 minutes. Duration: 1 year. Concurrent medication/care: n/a.
Funding	Funding not stated.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: STREAMLINED REFERRAL PROTOCOL versus TRADITIONAL REFERRAL PROTOCOL.

Protocol outcome 1: Avoidable adverse events.
- Actual outcome: door-to-balloon time (as surrogate for avoidable adverse events); Indirectness of outcome: Serious indirectness.

Protocol outcome 2: Length of stay
- Actual outcome: total time patient spent in referring ED, including time for arrival of transport team; Indirectness of outcome: No indirectness.

Narrative data only.
Before and after introduction of a streamlined transfer.

	Traditional transfer (n=79)	Streamlined transfer (n=54)	P
Emergency department	60 (45-84)	55 (44-67)	0.07
Door-to-balloon time	122 (99-157)	101 (88-128)	0.001

Data reported in minutes as median (25-75% interquartile range). Emergency department time is total time patient spent in referring department, including time waiting for arrival of transport team. Door-to-balloon time is total time from presentation at outside ED to percutaneous coronary intervention.

Protocol outcomes not reported by the study	Mortality; Quality of life; Carer/Family satisfaction; Staff satisfaction.

Study	**Effects of ambulance transport trial: Waddell 1975[74]**
Study type	Non-randomised comparative study.
Number of studies (number of participants)	1 (n=66).
Countries and setting	Conducted in United Kingdom; setting: transfers of critically ill patients to the intensive therapy unit of the Western Infirmary in Glasgow, UK, via ambulance from other hospitals over the course of 6 years. Time period of data collection for intensive therapy unit 'flying squad' not reported.
Line of therapy	1st line.
Duration of study	Not clear: no information given.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	Retrospective review of ambulance transfers to the Western Infirmary ICU; only ‘adequate’ records reported. Prospective data collection of eligible patients for transfers via intensive therapy unit 'flying squad'.
Exclusion criteria	Patients for whom no adequate records were available or who were deemed unsuitable for transfer.
Recruitment/selection of patients	Retrospective review of ambulance transfers to the Western Infirmary ICU; only adequate records reported. Prospective data collection of eligible patients for transfers via intensive therapy unit 'flying squad'.
Age, gender and ethnicity	Age - Mean (SD): flying squad 57; standard ambulance 42 (SDs not provided). Gender (M:F): 3/2. Ethnicity: n/a.
Further population details	1. Inter versus Intra hospital: Inter hospital.

Indirectness of population	No indirectness.
Interventions	(n=20) Intervention 1: Standardised system (including checklist of both staffing and equipment) for transfer - As defined by the study. The intensive therapy unit 'flying squad' consisted of 1 or 2 members of a 'shock team'. When the intensive therapy unit received a request for a transfer the flying squad travelled to the referring hospital, set up monitoring equipment, and began treatment. They accompanied the patient in an ambulance of standard design and continued treatment on arrival at the unit. Average ambulance ride was 12 minutes and the total time from bed to bed 33 minutes. Duration: unclear. Concurrent medication/care: n/a. (n=46) Intervention 2: No standardised system for transfers - As defined by the study. Transfers by standard ambulance from other hospitals to ICU of Glasgow Western Infirmary. Duration: 6 years. Concurrent medication/care: n/a.
Funding	Funding not stated.

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: TRANSFERS VIA INTENSIVE THERAPY UNIT 'FLYING SQUAD' versus TRANSFERS VIA STANDARD AMBULANCE.

Protocol outcome 1: Mortality.
- Actual outcome: Mortality within 24 hours of transfer within 24 hours of transfer; Group 1: 1/20, Group 2: 3/46; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: flying squad patients much older and differences in clinical conditions; Key confounders: illness secerity, age etc.; Group 1 Number missing: 0; Group 2 Number missing: 0
- Actual outcome: Final mortality; Group 1: 9/20, Group 2: 18/46; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: flying squad patients much older and differences in clinical conditions; Key confounders: illness secerity, age etc.; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcome 2: Avoidable adverse events.
- Actual outcome: Delayed hypotension; Group 1: 4/20, Group 2: 7/46; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: flying squad patients much older and differences in clinical conditions; Key confounders: illness secerity, age etc.; Group 1 Number missing: 0; Group 2 Number missing: 0

Protocol outcomes not reported by the study	Quality of life; Length of stay; Carer/Family satisfaction; Staff satisfaction.

Study (subsidiary papers)	Inter-hospital transport via a mobile intensive care unit trial: Wiegersma 2011[77] (Ligtenberg 2005[51])
Study type	Before and after study.
Number of studies (number of participants)	2 (n=174).
Countries and setting	Conducted in Netherlands; setting: consecutive transfers via mobile ICU to the University of Groningen affiliated ICU and the ICU of the Scheper Hospital, Emmen, Netherlands, from 14 regional hospitals in the north-eastern region of the Netherlands between March and December 2009. These data were compared to consecutive transfers of ICU patients via standard ambulance to the same ICU from 18 regional hospitals in the north-eastern part of the Netherlands over a 14 month period (not specified but must be pre-2005).
Line of therapy	1st line
Duration of study	Other: 14 months standard transfer + 10 months mobile ICU.
Method of assessment of guideline condition	Adequate method of assessment/diagnosis.
Stratum	Overall.
Subgroup analysis within study	Not applicable.
Inclusion criteria	All consecutive transfers of ICU patients during the pre-defined study periods. Only patients admitted to the ICU are transferred by MICU.
Exclusion criteria	n/a.
Recruitment/selection of patients	Main indication for transfer was the need for higher intensity of care or advanced therapy; for example renal replacement therapy. Main diagnoses at transfer were respiratory problems, sepsis, and multi-organ failure. Shortage of ICU capacity was cited as the reason for transport on only a few occasions.
Age, gender and ethnicity	Age - Mean (SD): mobile ICU 59.8 (15.6); standard ambulance 54.7 (1.7). Gender (M:F): 1/1. Ethnicity: n/a.
Further population details	1. Inter versus Intra hospital: Inter hospital.
Indirectness of population	No indirectness.
Interventions	(n=74) Intervention 1: Standardised system (including checklist of both staffing and equipment) for transfer - As defined by the study. Mobile ICU transfer. A specifically designed large-volume mobile ICU and a specialised retrieval team were used to transfer critically ill patients. A stratified protocol clarification was sent to all referring ICUs in the region, explaining the procedure of transfer. Before working in the mobile ICU team all ICU nurses and intensivists completed a scenario-based training in skills-lab. Transfers between 8am and midnight 7 days a week. The referring intensivist had to consult the MICU-coordinator, who completes a MICU transport form with patient characteristics and study data. After authorisation of the transfer by the MICU-physician and the supervising staff member of the accepting ICU, the MICU sets out to transfer the critically ill patient. Upon arrival at the referring ICU, the MICU-team stabilises and prepares the patient for transfer. The APACHE II score (measure of severity of illness) was being

	determined for the patient. Duration: 10 months. Concurrent medication/care: n/a. (n=100) Intervention 2: No standardised system for transfers - as defined by the study. Standard ambulance transfer. Patients were transferred after telephone consultation with the supervising staff member of the receiving ICU, who authorised the admission. The referring hospital was advised to stabilise the patient as much as possible and to send a skilled physician with the patient. The transfer was done by standard ambulance of the referring hospital. The patient was accompanied by an ICU nurse in 23% and by a physician in 57% of transports. Duration: 14 months. Concurrent medication/care: n/a.
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: MOBILE ICU TRANSFER versus STANDARD AMBULANCE TRANSFER. Protocol outcome 1: Avoidable adverse events. - Actual outcome: Incidents during transfer (excluding technical failure - but including staff management or inadequate preparation) at 10 and 14 months; OR 0.13 (95%CI 0.06 to 0.32); Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: not matched; separate audit data compared; Group 1 Number missing: 0; Group 2 Number missing: 0 - Actual outcome: Incidents during transfer (technical failure) at 10 and 14 months; Group 1: 9/74, Group 2: 10/100; Risk of bias: All domain - Very high, Selection - Very high, Blinding - High, Incomplete outcome data - Low, Outcome reporting - High, Measurement - Low, Crossover - Low; Indirectness of outcome: No indirectness ; Baseline details: not matched; separate audit data compared; Group 1 Number missing: 0; Group 2 Number missing: 0	
Protocol outcomes not reported by the study	Mortality; Quality of life; Length of stay; Carer/Family satisfaction; Staff satisfaction.

Appendix E: Economic evidence tables

No studies were included.

Appendix F: GRADE tables

Table 10: Clinical evidence profile: Standardised system versus standard ambulance transfer

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Mobile ICU versus standard transfer	Control	Relative (95% CI)	Absolute		
Adverse incidents (staff management issues or inadequate preparation) - Staff management issues or inadequate preparation												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	no serious imprecision	None	0/74 (0%)	24%	Peto OR 0.13 (0.06 to 0.32)	201 fewer per 1000 (from 148 fewer to 221 fewer)	⊕OOO VERY LOW	CRITICAL
Adverse incidents (technical failures) - Technical failures												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	None	9/74 (12.2%)	10%	RR 1.22 (0.52 to 2.84)	22 more per 1000 (from 48 fewer to 184 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (delayed hypotension) - Adverse events (delayed hypotension)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	None	4/20 (20%)	15.2%	RR 1.31 (0.43 to 3.99)	47 more per 1000 (from 87 fewer to 454 more)	⊕OOO VERY LOW	CRITICAL
Mortality HR (over 1000 hours)												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	-	0%	HR 0.56 (0.35 to 0.9)	-	⊕OOO VERY LOW	CRITICAL
Mortality - Overall ICU mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	47/168 (28%)	35.2%	RR 0.8 (0.55 to 1.15)	70 fewer per 1000 (from 158 fewer to	⊕OOO VERY	CRITICAL

										53 more)	LOW	
Mortality - 6 hour mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	1/168 (0.6%)	4.4%	RR 0.14 (0.02 to 1.19)	38 fewer per 1000 (from 43 fewer to 8 more)	⊕OOO VERY LOW	CRITICAL
Mortality - 12 hour mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	None	5/168 (3%)	7.7%	RR 0.39 (0.13 to 1.18)	47 fewer per 1000 (from 67 fewer to 14 more)	⊕OOO VERY LOW	CRITICAL
Mortality - Final mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	None	9/20 (45%)	39.1%	RR 1.15 (0.63 to 2.1)	59 more per 1000 (from 145 fewer to 430 more)	⊕OOO VERY LOW	CRITICAL
Mortality - Mortality within 24 hours of transfer												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	None	1/20 (5%)	6.5%	RR 0.77 (0.08 to 6.93)	15 fewer per 1000 (from 60 fewer to 385 more)	⊕OOO VERY LOW	CRITICAL

[1] All non-randomised studies automatically downgraded due to selection bias. Studies may be further downgraded by 1 increment if other factors suggest additional high risk of bias, or 2 increments if other factors suggest additional very high risk of bias.
[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Table 11: Clinical evidence profile: ICU transfer checklist versus no transfer checklist

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**ICU transfer checklist versus no transfer checklist**	**Control**	**Relative (95% CI)**	**Absolute**		
Adverse events - adjusted OR - Need for emergent central line												
1	observational	very	no serious	no serious	no serious	none	-	0%	OR 0.09 (0.02	-	⊕OOO	CRITICAL

	studies	serious[1]	inconsistency	indirectness	imprecision				to 0.36)		VERY LOW	
Adverse events - adjusted OR - Need for emergent intubation												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	-	0%	OR 0.18 (0.02 to 1.46)	-	⊕OOO VERY LOW	CRITICAL
Adverse events - adjusted OR - Antibiotics changed on arrival												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	serious[2]	none	-	0%	OR 0.48 (0.27 to 0.86)	-	⊕OOO VERY LOW	CRITICAL
Mortality - adjusted OR - Hospital mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	-	0%	OR 0.85 (0.46 to 1.61)	-	⊕OOO VERY LOW	CRITICAL
Mortality - adjusted OR - ICU mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	-	0%	OR 0.77 (0.39 to 1.51)	-	⊕OOO VERY LOW	CRITICAL
Mortality - adjusted OR - 48-hour mortality												
1	observational studies	very serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	-	0%	OR 0.74 (0.19 to 2.93)	-	⊕OOO VERY LOW	CRITICAL

[1] All non-randomised studies automatically downgraded due to selection bias. Studies may be further downgraded by 1 increment if other factors suggest additional high risk of bias, or 2 increments if other factors suggest additional very high risk of bias

[2] Downgraded by 1 increment if the confidence interval crossed 1 MID or by 2 increments if the confidence interval crossed both MIDs.

Appendix G: Excluded clinical studies

Table 12: Studies excluded from the clinical review

Study	Exclusion reason
Aghababian 1991[7]	No comparison, no data Narrative review
Aguirre 2008[8]	No relevant comparison
Ailsby 1987[9]	No comparison, no data Description of guidelines for the transport of critically ill patients
Anonymous 1989[1]	No relevant comparison/intervention, no relevant outcomes Description of 4 physical patient transfer systems
Anonymous 1993[3]	No comparison, no data Commentary
Anonymous 1993A[2]	No comparison, no data Description of guidelines for the transfer of critically ill patients
Anonymous 2003F[4]	No comparison, no data Description of minimum standards for transfer
Anonymous 2011[5]	No comparison, no data Commentary
Anonymous 2013F[6]	No comparison, no data Narrative review
Ayers 2012[11]	No comparison, no data Commentary
Australasian College for Emergency Medicine 2003[10]	No comparison, no data Description of a standardised system/checklist for transfers
Bae 2010[12]	No relevant outcomes Effects of emergency medical service hospital notification on transfer and processing times
Barry 2006[13]	No comparison, no data Description of a transfer mattress
Baruch 2010[14]	Data not in analysable format Pilot study with very low patient numbers (n=19)
Beckmann 2004[15]	No comparison Description of the type of incidents and factors contributing to the incidents occurring during patient transfer
Belway 2006[17]	Systematic review
Boyko 1994[20]	No comparison, no data Description of guidelines
Brown 2015 [21]	No relevant extractable outcomes
Brunsveld-Reinders 2015[22]	No comparison, no data Description of the development and piloting of a checklist for transport
Burney 1995[23]	Not relevant comparison. Study compares aeromedical transport staffed with physician/nurse with nurse/nurse
Burney 1992[24]	Not relevant comparison. Study compares aeromedical transport staffed with physician/nurse with nurse/nurse

Study	Exclusion reason
Choi 2012[25]	Data cannot be extracted in a meaningful way Before and after study of implementation of transport checklist
Colardyn 1993[26]	No comparison, no data Narrative review
Comeau 2015 [27]	No relevant extractable outcomes
Dawkins 1983[29]	No comparison, no data Commentary
Dershin 1993[30]	No comparison, no relevant outcomes Case study only of a patient transportation system within a hospital
Etxebarria 1998[31]	No relevant comparison Study about the use of a scoring system rather than the standardisation of the transfer process
Fan 2006[32]	Systematic review
Fanara 2010[33]	Narrative review
Gore 1983[37]	No comparison Evaluation of a cardiac transport system
Gray 2004[38]	No comparison, no data Narrative review
Gupta 2004[39]	No comparison, no data Description of guidelines
Hamilton 1994[40]	No relevant comparison Narrative review presenting some data from other studies
Havill 1995[41]	No relevant comparison, incomplete data
Hendrich 2005[42]	No relevant outcomes, no comparison Study documents processes, labour, time and costs of transferring patients between nursing units in the hospital
Henry 2005[43]	No data Pilot study with very low numbers (n<250)
Hindmarsh 2012[44]	No comparison, no relevant data Description of a checklist and initial small audit
Iwashyna 2012[46]	No comparison, no data Description of a conceptual framework for transfer
Jarden 2010[47]	Narrative review and description of the development of a transfer tool No data, no comparison
Koppenberg 2002[49]	No data Narrative review
Kue 2011[50]	No relevant comparison/intervention Before and after study comparing aborted versus completed intra-hospital transfers by a specialised team
Manari [53]	No relevant comparison Retrospective study comparing directly admitted patients (i.e. no transfer) with transferred patients
Manataki 2016 [54]	Incorrect study design – narrative study
Martin 2012[55]	No comparison, no data Narrative review

Study	Exclusion reason
Mazza 2008[56]	No comparison Not from OECD country (Brazil)
Nerland 1978[58]	No comparison, no data Commentary
Newton 2015[59]	No data Description of an inter-hospital transfer centre model
Ohashi 2008[60]	No comparison, no data Description of an electronic vital sign-monitoring system for patient transfers
Ong 2011[61]	Review of failures in handoff communication during transfers
Petre 1989[62]	No relevant intervention/comparison, no data Description of a physical patient transport system
Pope 2003[63]	No comparison, no relevant data Narrative review including case study
Ridley 1989[66]	No relevant comparison Retrospective study comparing directly admitted patients (i.e. no transfer) with transferred patients
Roland 2010[67]	No comparison, no data Description of a physical transport system for critically ill obese patients
Russell 2015 [68]	Incorrect intervention
Sethi 2014[69]	No comparison, no data Not from OECD country (India)
Sivaram 1996[70]	No relevant outcomes, data cannot be extracted Establishment of a communication system for transfers between 2 specific hospitals
Steenson 1989[71]	No relevant comparison or data Description of a quality assured structured transport system
Swickard 2014[72]	No comparison, no data Description of adopting a triage model for patient care to critical care transport including 2 case studies
Uusaro 2002[73]	No relevant comparison and no relevant outcomes (compares vital signs before versus after the transport)
Watanabe 1991[76]	No comparison, no data Description of an intra-hospital transport service development
Warren 2004[75]	No comparison, no data Description of guidelines for safe transport
Wu 2007[78]	No comparison, no data Narrative review
Yamamoto 1988[79]	No data Description of an information system for patient transfer

1

Appendix H: Excluded health economic studies

No studies were excluded.