WORKSHEET for Evidence-Based Review of Science for Emergency Cardiac Care

Worksheet author(s)

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Clinical question.

In adult and pediatric patients with out-of-hospital cardiac arrests (P), does transport to a specialist cardiac arrest centre (I) compared with no such directed transport (C), improve outcome (eg. survival) (O)?

Is this question addressing an intervention/therapy, prognosis or diagnosis? INTERVENTION
State if this is a proposed new topic or revision of existing worksheet: NEW

Conflict of interest specific to this question No

Do any of the authors listed above have conflict of interest disclosures relevant to this worksheet?

JS - No relevant conflicts

GN -

NHLBI Betheseda, MD Grantee, co-PI, Resuscitation Outcomes Consortium Data Coordinating Center
Canadian Institutes of Health Research, Medtronic Inc. Ottawa, Canada, and Minneapolis, MN
Grantee, Coinvestigator, Resynchronization in Advanced Failure Trial (RAFT)
Asmund S Laerdal Foundation for Acute Medicine Stavanger, NO
Principal Investigator, Randomized Trial of CPR Training Aid in Community
Laerdal Inc. Equipment donation of training aids for overseas medical mission (2006)
Physio-Control Inc. Equipment donation of monitors/defibrillators for overseas medical mission (2007)
Channing-Bete Inc. Equipment donation of training materials for overseas medical mission (2007)
Northfield Laboratories Evanston, IL Consultant (2008)
Paracor Medical Inc. Sunnyvale, CA Consultant (2007)
Innercool Therapies Inc. Travel expenses (Single trip, 2006)
Radiant Medical Inc. Travel expenses (Single trip, 2006)
Medic One Foundation, Seattle, WA. Member of Board of Directors
Member of the AHA Writing Group on Regional Systems of Care for Cardiac Arrest

Search strategy (including electronic databases searched).

GN:

Cardiac Arrest:(("Regional Medical Programs"[Mesh] OR regionalization[tiab] OR "regional systems"[tiab]) AND ("heart arrest"[MeSH Terms] OR("heart"[All Fields] AND "arrest"[All Fields]) OR "heart arrest"[All Fields] OR ("cardiac"[All Fields] AND "arrest"[All Fields]) OR "cardiac arrest"[All Fields]) AND ("Program Development"[Mesh] OR "Models, Organizational"[Mesh] OR feasibility[tiab] OR implementation[tiab] OR "health facilities"[mh]) AND ("Quality of Health Care"[Mesh] OR assessment[tiab] OR evaluation[tiab])

JS:

Search term:

Cardiac arrest centers OR cardiac arrest centres

Looked at key papers

(Langhelle, Tyvold et al. 2003; Lurie, Idris et al. 2005; Sunde, Pytte et al. 2007; Nichol, Thomas et al. 2008) and who had cited them in Scopus

Look at related articles and references

Search Medline, Embase, PsychINFO, CINAHL
Cochrane, Google Scholar, AHA EndNote Library, Science Direct, Scopus

GN also looked at Trauma/MI/Stroke care papers

Trauma
(("Regional Medical Programs"[Mesh] OR regionalization[tiab] OR "regional systems"[tiab]) AND ("Trauma Centers"[Mesh] OR
trauma systems"[tiab] OR triage[tiab])) AND ("Program Development"[Mesh] OR "Models, Organizational"[Mesh] OR feasibility[tiab] OR implementation[tiab] OR "health facilities"[mh]) AND ("Quality of Health Care"[Mesh] OR assessment[tiab] OR evaluation[tiab])

Stroke
("Regional Medical Programs"[Mesh] OR regionalization[tiab] OR "regional systems"[tiab]) AND ("stroke"[MeSH Terms] OR
"stroke"[All Fields]) AND ("Program Development"[Mesh] OR "Models, Organizational"[Mesh] OR feasibility[tiab] OR implementation[tiab] OR "health facilities"[mh]) AND ("Quality of Health Care"[Mesh] OR assessment[tiab] OR evaluation[tiab])

Myocardial Infarction
("Regional Medical Programs"[Mesh] OR regionalization[tiab] OR "regional systems"[tiab]) AND ("myocardial infarction"[MeSH Terms] OR ("myocardial"[All Fields] AND "infarction"[All Fields]) OR "myocardial infarction"[All Fields]) AND ("Program
Development"[Mesh] OR "Models, Organizational"[Mesh] OR feasibility[tiab] OR implementation[tiab] OR "health facilities"[mh])
AND ("Quality of Health Care"[Mesh] OR assessment[tiab] OR evaluation[tiab])

- **State inclusion and exclusion criteria**

Inclusion:

Any study that has looked at indicators of regionalization of care
All age groups

Regionalisation for Trauma, MI and Stroke studies also included for extrapolation

Exclusion

As this is a new topic with few relevant studies no exclusion

Abstract only studies

- **Number of articles/sources meeting criteria for further review:**

JS

12 Jan 2009

Cochrane – No relevant reviews

Medline, Embase, PsychINFO, CINAHL

(cardiac AND arrest AND center).ti,ab 790
(cardiac AND arrest AND centre).ti,ab 233

Combined with duplicates 1015

((cardiac arrest center*) OR (cardiac arrest centre*)).ti 36

Without duplicates 20

1 Lurie et al 2005

The Lurie paper (Lurie, Idris et al. 2005) is an editorial about cardiac arrest centres.

Search Scopus citation manager to find papers referencing Lurie et al 2005 gave 6 further papers

Searching through reference lists of key papers identified 6 further articles

Review of AHA ReSS 2008 identified 2 abstract only presentations

AHA EndNote library did not identify any new papers

14 papers including the 2 ReSS 2008 abstracts included in review – 1 (Callaway 2010 e published) subsequently published

Update after Osaka ILCOR discussion:

Identified 4 additional papers regarding package of post resuscitation care

Removal of 1 study (Nichol G et al. 2008)

GN

CA 5 five LOE 3 (retrospective controls)
T 20 LOE 5 (extrapolation from another clinical disorder- 2 prospective controls, 18 retrospective controls)
MI 10 LOE 5 (extrapolation from another clinical disorder- 6 RCTs, 3 prospective controls, 1 retrospective controls)
S 2 LOE 5 (extrapolation from another clinical disorder- 1 systematic review,1 retrospective controls)

<u>SEARCHES UPDATED for CARDIAC ARREST STUDIES 20 Jan 2010</u>

1 new study – Callaway 2010 epub
Receiving hospital characteristics associated with survival after out-of-hospital cardiac arrest. Resuscitation. 2010 Jan 11. [Epub ahead of print]

2 position papers (these were not included in evidence review but were checked for source of other studies)

Nichol 2010
Regional Systems of Care for Out-of-Hospital Cardiac Arrest. A Policy Statement From the American Heart Association. Circulation. Epub.

Mechem 2010
Resuscitation center designation: recommendations for emergency medical services practices. Prehosp Emerg Care. 2010 Jan-Mar;14(1):51-61

5 additional trauma centre studies also identified from AHA policy statement.

<u>Final studies included in WS based on 20 January 2010 search</u>

16 Cardiac arrest studies

And extrapolation from :

27 Trauma studies
10 MI studies
2 Stroke studies

Summary of evidence

Evidence Supporting Clinical Question

Good			**Oddo 2006 1865 D** **Sunde 2007 29 D E3 E6**	**Callaway 2010 epub C**	**MI** **Vermeer 1999 426 C** **Widimsky 2000 823 C** **Widimsky 2003 94 C** **Trauma** **Culica 2007 SR9 C** **Mackenzie 2006 366 C** **Sampalis 1995 232 C** **Sampalis 1997 288 C**
Fair			**Knafelj 2007 227 D**	**Carr 2009 30 C E4** **Carr 2009 505 C E4**	**MI** **Le May 2008 231 C** **Stroke** **Lamonte 2008 319 C** **Stroke Unit Trials Collaboration 2007 C** **Trauma** **Liberman 2004 1330 C** **Mann 2001 1111 C** **Mullins 1996 536 C** **Mullins 1998 609 C** **Mullins 1994 1919 C** **Nathens 2000 25 C** **Nicholl 1997 1349 C**
Poor				**Davis 2007 44 C E1** **Engdahl 2000 201 C E5 E6** **Herlitz 2006 25 E2** **Liu 2008 339 C** **Keenan 2007 836 C, E7** **Langhelle 2003 247 D E3** **Spaite 2008 61 C E1** **Spaite 2009 248 C E1**	**Trauma** **Abernathy 2002 182 C** **Clemmer 1985 861 C** **Hannan 2005 584 C** **Harrington 2005 961 C** **Mullner 1978 140 C** **Mullner 1978 103 C** **Nathens 2003 444C** **Potoka 2000 237 C -children**
	1	**2**	**3**	**4**	**5**
Level of evidence					

A = Return of spontaneous circulation C = Survival to hospital discharge

B = Survival of event D = Intact neurological survival
E=other endpoints:
E1 = Transport interval/mode E2 = 1-month survival E3 = 1 year survival
E4 = Hospital type/Patient Volume E5 = Socioeconomic status E6 = Post resuscitation interventions
E7 = length of ICU stay

Evidence Neutral to Clinical question

Good					**<u>MI</u>** **Andersen 2003 773C** **Bonnefoy 2002 825 C** **Grines 2002 1713 C** **<u>Trauma</u>** **De Jongh 2008 1007 C**
Fair			**Gaieski 2009 418 D** **Wolfrum 2008 1780 D**		**<u>MI</u>** **Henry 2007 721 C** **Ting 2007 729 C** **<u>Trauma</u>** **Boyd1975 25 C** **Goldberg 1981 547 C** **Hulka 1997 514 C (children)** **Kane 1992 576 C** **Norwood 1995 240 C** **Young 1998 88 C**
Poor					**<u>MI</u>** **Jollis 2007 2371 C**
	1	**2**	**3**	**4**	**5**
Level of evidence					

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival

Evidence Opposing Clinical Question

Good					
Fair					**<u>Trauma</u>** **Reilly2004 C**
Poor					
	1	**2**	**3**	**4**	**5**
Level of evidence					

A = Return of spontaneous circulation C = Survival to hospital discharge E = Other endpoint
B = Survival of event D = Intact neurological survival *Italics = Animal studies*

REVIEWER'S FINAL COMMENTS AND ASSESSMENT OF BENEFIT / RISK:

The rationale for cardiac arrest centres and regionalization of care for cardiac arrest centres is the subject of a recent supportive AHA policy statement (Nichol 2010 epub Circulation)

There are no randomised studies to test this and it is unlikely they will take place. Therefore we need to look at studies that we can extrapolate data from:

1. Is there variation in outcomes between hospitals served by the same EMS systems?
2. Transport interval from scene to resuscitation centre – i.e. is it safe to by bypass closer hospitals to go to a designated cardiac arrest centre?
3. Effect of patient volume or hospital characteristics on survival of OHCA patients admitted to the centre.
4. Specific post resuscitation care interventions offered by centre (e.g. therapeutic hypothermia, percutaneous coronary intervention).
5. Can we extrapolate from other emergencies i.e., Trauma, MI and stroke systems of care where specialist centres and regionalization are already an established?

<u>Transport interval (scene to hospital)/Transport mode</u>

Three LOE 4 Studies:

Davis DP et al (Davis, Fisher et al. 2007) showed in an observational study that for urban OHCA in one US city EMS, nearly all survivors had ROSC at scene and transport time to hospital did not impact survival to hospital discharge. Study carried out in 2001-2002. Mean transport times from scene to ED were similar for those who died in ED (8.3 min) died after admission (7.8 min) and survived to discharge (8.5 min). The ranges are not reported. This suggests feasible to take all ROSC patients to single urban centre. These transport times are relatively short. The high scene ROSC rate will depend on the EMS system, time at scene. It is not clear how many hospitals were involved and how hospital factors influenced outcome

Spaite DW et al (Spaite, Bobrow et al. 2008) showed in an observational study that in a number of EMS in Arizona during 2004-2006 transport time did not impact survival to hospital discharge in patients with ROSC in the field. Mean transport time 6.9 min (95% CI 6.7-7.1 min). Transport time data was missing in 38% of cases. It is not clear how hospital factors influenced these outcomes. It is difficult to interpret the results of this study since response times were missing in a high proportion of patients.

Spaite DW et al (Spaite, Stiell et al. 2009) studied observational data for 15,559 patients from the Ontario Prehospital Advanced Life Support Study (OPALS) collected between 1991 and 2002. The mean transport interval was 4 min for survivors and 4.2 min for non-survivors to hospital discharge. 19% of the data is missing. Transport interval with a multisystem EMS did not impact survival. It is difficult to extrapolate the results of this study to other settings since the overall survival was low.

The above studies with very short transport times [median (25 to 75 quartile); Davis = 7 (5 to 11) min; Spaite 2008 = 6 (4 to 9) min; Spaite 2009 = 4.2 (3.0 to 6.2) min] suggest it is feasible to bypass a hospital after ROSC achieved but not how long a safe journey time is. This requires further study.

<u>Variation between hospitals/regions</u>

Engdahl J et al (Engdahl, Abrahamsson et al. 2000) in an observational study in Goteberg, Sweden showed that hospital interventions impact survival. They studied approximately a 1000 patients with ROSC after OHCA between 1980 and 1996. There was a difference in survival to discharge between two hospitals served by the same EMS (44% versus 33%, P<001) despite pre-hospital and patient factors being similar. Patients in the hospital with better outcomes had a higher rate of interventions (coronary angiography, echocardiography, exercise testing, cardiac electrophysiology, Holter recording, and coronary angioplasty. The hospital with worse outcomes had patients of a lower socio-economic status. This is a relatively small study, there is a lot of missing information and there may be unmeasured confounders.

Langhelle A et al (Langhelle, Tyvold et al. 2003) observed outcomes in OHCA patients with ROSC (459 patients) admitted to Hospitals in 4 regions in Norway between 1995 and 1999. This study showed variation in hospital factors (after correcting for other factors) that effected survival and neurological status up to 1 year. This study did not however compare specific in hospital interventions.

Herlitz J et al (Herlitz, Engdahl et al. 2006) using data from the Swedish OHCA registry showed 1 month survival in OHCA patients served by 21 EMS systems and admitted to 21 hospitals after ROSC varied between 14 and 42%. Differences between hospitals remained after correcting for patient and pre-hospital factors. It was speculated that some of this difference was due to differences in post resuscitation care although hospital care was not formally assessed.

Keenan SP et al (Keenan, Dodek et al. 2007) studied 31 Canadian ICUs showed a large variation in ICU length of stay in non-survivors that was independent of hospital size. This study cannot specify what factors influenced this.

Carr BG et al (Carr, Goyal et al. 2008) studied 109, 739 hospital patients resuscitated after cardiac arrest in the US between 2000 and 2004. This includes both in and out of hospital cardiac arrests. In hospital mortality was lowest for urban, teaching and large hospitals (OR 0.58, 0.63, 0.55 respectively). This study did not adjust for case mix and cannot say which factors in hospital influenced outcome. Does support the fact that the hospital makes a difference for patients with OHCA or IHCA.

Liu JM et al (Liu, Yang et al. 2008) observed variation in OHCA survival to discharge between hospitals (29-42%) served by the Milwaukee County EMS (1995-2005). The main correlating factor for survival was beds to nurse ratio.

Carr BG et al (Carr, Kahn et al. 2009) showed in an observational study of 39 US hospitals that ICUs dealing with higher patient volumes had improved survival to hospital discharge. The study could not say if the 44% of the 4674 ICU admissions from the ED were out of hospital cardiac arrests or not. Age and illness adjusted survival varied between 46 and 68%. Hospitals that treated more than 50 cardiac arrests/year had a lower mortality than those who treated less than 20/year (OR 0.62, 95% CI 0.45-0.86). This study supports there is variation between hospitals. It is difficult to extrapolate the results of this study to management of OOHCA since inclusion of ICU patients only is subject to selection bias, and the study included patients with OOHCA as well as IHCA.

Callaway C et al 2010 observed a risk unadjusted improved survival to discharge, after OHCA in 9 US and Canadian regions (254 hospitals, 3644 OHCA, 2005-2007), in large hospitals with cardiac catheter facilities compared with smaller hospitals with no cardiac catheter facilities. Large hospital (>400 beds) with cardiac catheter facilities had fewer deaths (OR 0.71, 95% CI 054-0.93). The study did not show any significant differences between CATH and Non–CATH hospitals or high/low volume (40 cut-off) after risk adjustment. The study does not list whether patients actually had cardiac catheterization and volume of patients attending hospitals. The hospital size and presence of catheter facilities is inferred to be a surrogate marker for improved post resuscitation care.

These studies show variation in survival from cardiac arrest between hospitals and regions.

<u>Hospital treatments – 5 LOE 3 studies comparing with historical controls summarised in Table 1</u>

Studies of systems for Trauma and MI are summarized in Table 2 and 3. These Tables based on Nichol at al. Regional Systems of Care for Out-of-Hospital Cardiac Arrest. A Policy Statement From the American Heart Association. Circulation. Epub.

Author Design	Population	Intervention	Comparator
Oddo 2006 Historical case-control LOE3	Proportion VF 79%	Hypothermia, PPCI, Goal directed therapy; glucose control not stated (n=55) CPC 1 or 2 at discharge 20 (37%)	Standard care (n=54) CPC 1 or 2 at discharge 6 (11%) p=0.004
Sunde 2007 Historical case-control LOE3	Prop. VF 90%	Hypothermia, PPCI, Goal directed therapy; glucose control (n=61) CPC 1 or 2 at discharge 56%	Standard care (n=58) CPC 1 or 2 at discharge 26% p=0.001
Knafelj 2007 Historical case-control LOE3	ST-elevation MI Prop. VF 100%	Hypothermia, PPCI; Goal directed therapy, glucose control not stated (n=40) CPC 1 or 2 at discharge 53%	Standard care (n=32) CPC 1 or 2 at discharge 19% p=0.001
Wolfrum 2008 Historical case-control LOE3	ST-elevation MI Prop. VF 100%	Hypothermia, PPCI; Goal directed therapy, glucose control not stated (n=16) CPC 1 or 2 at discharge 69%	Standard care (n=17) CPC 1 or 2 at discharge 47% p=0.3
Gaieski 2009 Historical case-control LOE3	Prop. VF 50%	Hypothermia, PPCI, Goal directed therapy; glucose control (n=20) CPC 1 or 2 at discharge 8 (40%)*	Standard care (n=18) CPC 1 or 2 at discharge 4 (22%) p=0.12

Table 1 – Hospital treatments

TABLE 2: EFFECT OF REGIONALIZATION OF CARE FOR PATIENTS WITH TRAUMATIC INJURY – ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Abernathy 2002 Retrospective cohort study of administrative data	Patients from 6 counties in Alabama transported by EMS and admitted to level 1 trauma center from April 1995 to March 1998	Implementation of voluntary regional trauma system n=1 718 Mortality 65 (3.8%) ISS ≥16 342 (20%) Adjusted OR or RR not reported	Before implementation n=1 306 Mortality 77 (5.9%), *P*=0.0002 ISS ≥16 276 (21%)	N/A	N/A
Boyd 1975 Retrospective cohort study of hospital-based trauma registries	Patients with motor vehicle–related injuries from 14 counties in Region 13A, Illinois, from July 1970 to December 1972	Implementation of regional trauma program n=15 061 ISS not reported Mortality 2.5% Adjusted OR or RR not reported	Before implementation n=13 459 ISS not reported Mortality 2.7%	N/A	N/A
Culica 2007 Retrospective cohort study of administrative data	Injured patients hospitalized in trauma centers in Texas from 1999 to 2000	Admitted to level 1 (n=35 878) Mortality 1514 (57.4%) Adjusted OR[a] 0.31 (95% CI 0.27, 0.36)	Admitted to level 2 (n=15 300) Mortality 603 (22.9%) Adjusted OR[a] 0.47 (95% CI 0.4, 0.55)	Admitted to level 3/4 (n=31 669) Mortality 520 (19.7%) Reference group, *P*<0.0001	N/A
de Jongh 2008 Retrospective cohort study of regional trauma registry	Trauma admissions, dead on arrival, or died in ED at 12 EDs in Netherlands from 2000 to 2006	Transferred from another hospital to trauma center (n=69) ISS, median (IQR) 25 (17, 26) Mortality 21.7% Referent group	Direct admissions to nontrauma center (n=448) ISS, median (IQR) 19 (16, 25) Mortality 13.6% Adjusted OR[b] 1.5 (95% CI 0.7, 3.4)	Direct admissions to trauma center (n=382) ISS, median (IQR) 25 (17, 30) Mortality 28.8% Adjusted OR[b] 1.9 (95% CI 0.9, 4.1)	N/A

EMS indicates emergency medical services; ISS, Injury Severity Score; N/A, not applicable; ED, emergency department; IQR, interquartile range; ICD, implantable cardioverter-defibrillator; FARS, Fatality Analysis Reporting System; MVC, motor vehicle collision; CRAMS, Circulation, Respiration, Abdomen, Motor, Speech; and ICD-9, International Classification of Diseases version 9.
[a]Adjusted for age, race, insurance status, hospital stay >1 wk, emergency admission, severity of injury, and risk of mortality.

[b]Adjusted for age, ISS, Glasgow Coma Scale score, and severe neurological trauma.

Table 2 – Trauma Studies continued - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Hannan 2005 Retrospective cohort study of state trauma registry	Injured, age >13 y identified in prehospital care reports, >1 trauma triage criterion, transported directly to hospital Excluded patients with flat vital signs on arrival at ED. From 1996 to 1998	Level 1 trauma center (n=2 218) ISS not reported Mortality 46.8% Referent group Unadjusted OR 0.79 (95% CI 0.65, 0.95)	Level 2 trauma center or nontrauma center (n=2 525) ISS not reported Mortality 53.2% Referent group	N/A	N/A
Harrington 2005 Retrospective cohort study of hospital trauma registry	Trauma patients admitted to single level 1 trauma hospital from 2001 to 2003	Direct transfer from field (n=3 227) ISS 11 ± 0.2 Mortality 7% OR or RR not reported	Transfer from nontrauma center (n=280) ISS 17.5 ± 0.8 Mortality 10%	N/A	N/A
Liberman 2004 Retrospective cohort study of provincial trauma registry	Major trauma treated at hospital, including ≥1 death as result of injury, admission with hospital stay ≥3 d, admission to intensive care or interhospital transfer during 1992-1993 (before) and 2001-2002 (after)	After designation of level 1 trauma centers, triage, and transfer protocols (n=1 884) ISS not reported Mortality 8.6% OR or RR not reported	Before implementation of regional trauma care (n=3 823) ISS not reported Mortality 51.8%	N/A	N/A
MacKenzie Prospective stratified sample of cases and controls using medical record review and patient interview	Injured patients age 18 to 84 y with ISS >15 treated at hospital in 15 contiguous Metropolitan Statistical Areas (n=5 191) Excluded patients dead on arrival or within 30 min	Level 1 trauma centers Observed in-hospital mortality 8% Adjusted mortality within 1 y 10.4% Adjusted RR 0.75 (95% CI 0.6, 0.95)	Nontrauma centers that treated >25 patients with trauma annually Observed in-hospital mortality 5.9% Adjusted mortality within 1 y 13.8%	N/A	N/A
Mann 2001 Retrospective cohort	Age >65 y discharged from acute care hospital who had ≥1 injury-related ICD-9 discharge diagnosis in Washington from	After implementation of statewide trauma system (n=46 424) ISS 7.1 ± 4.2	Before implementation (n=30 712) ISS 6.8 ± 4.4	N/A	N/A

study of hospital discharge data linked with death index	1988 to 1995	Mortality within 60 d 10.4% Adjusted mortality 5.1% lower among patients with ISS >15[c]	Mortality within 60 d 10.1%		

[c]Adjusted for age, gender, injury severity, and comorbidity.

Table 2 – Trauma Studies continued - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Mullins 1996 Retrospective cohort study of hospital discharge data linked with death index	Patients discharged from acute care hospital who had ≥1 injury-related ICD-9 discharge diagnosis in Oregon (n=27 633) from 1985 to 1987 (before) and 1991 to 1993 (after)	After implementation of regional trauma system Adjusted OR for mortality[d] 0.82 (0.73, 0.92)	Before implementation	N/A	N/A
Mullins 1998 Retrospective cohort study of hospital discharge data linked with death index	Patients discharged from acute care hospital who had ≥1 injury-related ICD-9 discharge diagnosis in Oregon and Washington from 1990 to 1993	Regional trauma system in Oregon (n=11 879) Adjusted OR for mortality[e] 0.80 (0.70, 0.91)	Regional trauma system in Washington (n=17 369)	N/A	N/A
Mullins 1994 Retrospective cohort study of hospital discharge data and hospital trauma registry	Patients discharged from acute care hospital who had ≥1 injury-related ICD-9 discharge diagnosis in 4 counties in Oregon (n=27 633) from 1984 to 1985 (before), 1986 to 1987 (during), and 1990 to 1991 (after)	After implementation of regional trauma system Level 1 center (n=7 238) Applicant trauma hospitals (n=4815) Nontrauma hospitals (n=9 753) ISS not reported All hospitals adjusted OR for mortality[f] 0.94 (0.82, 1.07) compared with reference period	During implementation of regional trauma system Level 1 center (n=5017) Applicant trauma hospitals (n=6 691) Nontrauma hospitals (n=11 691) ISS not reported All hospitals adjusted OR for mortality[f] 1.01 (0.88, 1.16) compared with reference period	Before implementation of regional trauma system Level 1 center (n=4 239) Applicant trauma hospitals (n=6812) Nontrauma hospitals (n=14 094) ISS not reported Reference period	N/A

[d]Adjusted for age, gender, multiple injuries, AIS score, and preexisting conditions.

[e]Adjusted for age, gender, anatomic site, severity of injury, and preexisting conditions.

[f]Adjusted for age, gender, AIS score, and preexisting conditions.

Table 2 – Trauma Studies continued - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Mullner 1978 Retrospective cohort study of sample from Department of Transportation records of motor vehicle–related trauma	Patients with severe or fatal trauma in Region 5, Illinois, during and 1970 to 1973 (after)	Implementation of regional trauma system Regional trauma hospitals (n=958) ISS not reported Mortality 8.5% Nontrauma hospitals (n=1676) ISS not reported Mortality 11.4% OR or RR not reported	Before implementation Regional trauma hospitals (n=992) ISS not reported Mortality 11.5% Nontrauma hospitals (n=1866) ISS not reported Mortality 11.5%	Mullner(134) Retrospective cohort study of sample from Department of Transportation records of motor vehicle–related trauma	Patients with severe or fatal trauma in Region 5, Illinois, during and 1970 to 1973 (after)
Nathens 2000 Retrospective cohort study of National Center for Health Statistics data, FARS database, and census data	Deaths associated with unintentional injury or injury purposely inflicted by other persons FARS motor vehicle–related deaths during 1995	States with functional trauma systems Deaths per 100 000 population All injuries 26.5 $\pm$ 16.0 Incident rate ratio 0.91 (95% CI 0.89, 0.92) MVC-related injuries 17.3 $\pm$ 10.2 Incident rate ratio 0.82 (95% CI 0.81, 0.84)	States without functional trauma systems Deaths per 100 000 population All injuries 29.2 $\pm$ 17.2 MVC-related injuries 14.2 $\pm$ 8.8	Nathens(135) Retrospective cohort study of National Center for Health Statistics data, FARS database, and census data	Deaths associated with unintentional injury or injury purposely inflicted by other persons FARS motor vehicle–related deaths
Nathens 2003 Retrospective cohort study of regional trauma registry	Trauma patients age $\geq$16 y injured in King County, Wash, from 1995 to 1998 Included if length of stay >2 d; ICD injury-related code; dead on arrival or died in hospital; interhospital transfer; or trauma team activation	Field triage to level 1 trauma hospital by medics (n=4439) ISS 11.7 $\pm$ 12.9 Mortality 10%	Field triage to level 3 or 4 trauma hospital by medics, then transfer to level 1 hospital after initial assessment (n=281) ISS 8.9 $\pm$ 7.0 Mortality 5% Adjusted RR for mortality[f] 1.05 (0.61, 1.80) compared with reference period	N/A	N/A

[f]Adjusted for age, ISS, severity of head injury, maximum AIS score, shock, and payer status.

Table 2 – Trauma Studies continued - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Nicholl 1997 Prospective before-after study using individual patient data	Trauma patients with ISS >15 brought directly to ED by ambulance or other means, whether or not vital signs present on arrival from 1990 to 1993	Implementation of regional trauma system in northwest Midlands with 1 central hospital and on-site neurosurgery, 6 regional hospitals, 1 EMS agency Mortality Before (n=502) 35% After (n=409) 34% Adjusted difference in change in mortality between intervention and control per year[g] 0.8% (95% CI 3.6%, 2.2%)	No change in trauma care in Lancashire with 1 central hospital and on-site neurosurgery but not cardiothoracic surgery, 5 regional hospitals, 3 EMS agencies Mortality Before (n=620) 35% After (n=617) 33%	No change in trauma care in Humberside with 1 central hospital and on-site neurosurgery but not cardiothoracic surgery, 3 regional hospitals, 1 EMS agency Data combined with Lancashire	N/A
Potoka 2000 Retrospective cohort study of state trauma registry	Trauma patients age ≤16 y treated at accredited trauma center from 1993 to 1997 Excluded injuries due to burns	Transported to pediatric trauma center (n=5189) ISS >15 11.9% Mortality Blunt 11.3% Penetrating 21.3%	Transported to level 1 adult trauma center with additional qualifications (n=3636) ISS >15 12.4% Mortality Blunt 11.4% Penetrating 28.1%	Transported to level 1 adult trauma center (n=1207) ISS >15 21.6% Mortality Blunt 13.0% Penetrating 46.3%	Transported to level 2 adult trauma center (n=3319) ISS >15 16.2% Mortality Blunt 14.1% Penetrating 40.9%
Reilly 2004 Retrospective cohort study of hospital discharge data	Adult trauma patients discharged from New York City hospital from 1998 to 2000 (n=103 659) Excluded injuries due to burns	Hospitalized at level 1 trauma hospital (n=50 021) ISS not reported Mortality 2.6% Adjusted odds of mortality in trauma hospital[h] 1.8 (95% CI 1.7, 2.0)	Hospitalized at other hospitals (n=53704) ISS not reported Mortality 1.9%	N/A	N/A

[g]Adjusted for age, ISS, and Revised Trauma Score.

[h]Adjusted for age, gender, and severity of injury.

Table 2 – Trauma Studies continued - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Sampalis 1995 Retrospective cohort study of hospital discharge data	Trauma patients transported by EMS and admitted to hospital during 1987 and 1993	Designation of receiving hospitals as level 1 trauma center (n=288) ISS 15.5 $\pm$ 11.6 Mortality 10% Adjusted odds of mortality before designation[i] 3.3 (95% CI 1.6, 6.5)	Before designation (n=158) ISS 15.0 $\pm$ 12.3 Mortality 20%	N/A	N/A
Young 1998 Retrospective cohort study of hospital trauma registry	Adult trauma patients with ISS >15 admitted to trauma center	Direct transfer to level 1 trauma center (n=165) ISS 24 $\pm$ 8 Mortality before discharge 21% Adjusted odds of mortality not reported	Transfer from another hospital (n=151) ISS 23 $\pm$ 7 28 Mortality before discharge 18.5%	N/A	N/A
Clemmer 1985 Retrospective cohort study of regional trauma registry	Trauma patients transported by EMS with field CRAMS score $\leq$6 Excluded patients transported for >15 min or interfacility transports	Transported to level 1 trauma center (n=57) Mortality before discharge 46% Adjusted odds of mortality not reported	Transported to local hospital (n=33) Mortality before discharge 61%	N/A	N/A
Goldberg 1981 Retrospective cohort study of hospital discharge data	Trauma patients hospitalized in Illinois outside Chicago with selected injuries during 1973 and 1974	Hospitalized at trauma system hospitals (n=4 560) Mortality before discharge 2.9% Adjusted odds of mortality not reported	Hospitalized at nontrauma hospitals (n=5465) Mortality before discharge 2.7%	N/A	N/A

[i]Adjusted for age, ISS, and mechanism of injury

Table 2 – Trauma Studies continued - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Hulka 1997 Retrospective cohort study of hospital discharge data	Children age ≤18 y with acute injury hospitalized in Oregon from 1985 to 1993	Before (n=14 082, 1985 to 1987) and after (n=8981, 1991 to 1993) implementation of statewide trauma system in Oregon Mortality Before 0.96% After 1.2% Adjusted odds of mortality not reported	Before (n=18 525, 1985 to 1987) and after (n=12 991, 1991 to 1993) No implementation of statewide trauma system in Washington Mortality Before 0.93% After 1.2%	N/A	N/A
Kane 1992 Retrospective cohort study of hospital discharge data	Injured <48 h before ED admission, ISS >15, admitted to or died at acute hospital in Los Angeles County from 1982 to 1984 Excluded injuries limited to drowning, smothering, strangulation, choking, hanging, electrical shock, asphyxiation, or spontaneous pathological fracture	After (n=766, 1984) implementation of countywide trauma system Mortality 30.7% Adjusted odds of survival compared with before[j] 1.351 (95% CI 0.917, 1.988)	Before (n=658, 1982) implementation of countywide trauma system Mortality 29.5%	N/A	N/A
Mullner 1978 Retrospective cohort study of state trauma registry	Patients injured in motor vehicle collision in southern Illinois from 1970 to 1973	After implementation of regional trauma system at trauma hospitals (n=958) and other hospitals (n=1 676) Mortality trauma hospitals 8.5% Mortality other hospitals 11.4% Adjusted odds of mortality not reported	Before implementation of regional trauma system at trauma hospitals (n=992) and other hospitals (n=1 866) Mortality trauma hospitals 11.5% Mortality other hospitals 11.5%	N/A	N/A

[j]Adjusted for age, gender, hypotension, status of head injury, and mechanism of injury.

Table 2 – Trauma Studies continued - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator	Alternative Comparator
Norwood 1995 Retrospective cohort study of regional trauma registry	Injured patients who underwent surgery, died in ED, or were admitted to level 2 trauma hospital in east Texas from 1987 to 1992	After implementation of level 2 designation at trauma hospital (n=699) Mortality 7.7% Adjusted odds of mortality not reported	Before implementation of level 2 designation at trauma hospital (n=862) Mortality 8.0% Adjusted odds of mortality not reported	N/A	N/A
Sampalis 1997 Retrospective cohort study of hospital discharge data combined with census data	Patients with acute injury treated at tertiary trauma centers in Quebec from 1993 to 1995	Field transfer to tertiary trauma hospitals (n=2 756) Mortality 4.8%	Transfer from lower-level hospital to tertiary trauma hospital (n=1 608) Mortality 9.8% Adjusted odds of mortality[k] compared with field transfer 1.57 (95% CI 1.17, 2.11	N/A	N/A

Adjusted for age, head and injury status, status of extremity injury, and Injury Severity Sc

TABLE 3 : EFFECT OF REGIONALIZATION OF CARE FOR PATIENTS WITH ST-ELEVATION MYOCARDIAL INFARCTION - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator
Vermeer 1999 Individual randomized trial in 1 province, Netherlands	AMI, presenting at hospitals not capable of PPCI	Transfer for PPCI (n=75) Symptoms to therapy 240 ± NR Door to balloon NR Death[a] 5 (7) Recurrent infarct[a] 1 (1) Stroke[a] 2 (3)	Fibrinolytic in non-PCI hospital (n=75) Symptoms to therapy 135 ± NR Door to balloon NR Death[a] 5 (7) Recurrent infarct[a] 7 (9) Stroke[a] 2 (3)	Fibrinolytic with transfer; rescue PCI if indicated (n=74) Symptoms to therapy 255 ± NR Door to balloon NR Death[a] 6 (8) Recurrent infarct[a] 4 (5) Stroke[a] 3 (4)
Widimsky 2000 Individual randomized trial in 1 province, Czech Republic	AMI, presenting within 6 h of symptom onset at hospitals not capable of PPCI	Immediate transfer for PPCI (n=101) Symptoms to therapy 215 ± NR Door to balloon NR Death[b] (7) Recurrent infarct[b] (1) *P*<0.03 Stroke[b] (0)	Fibrinolytic therapy in non-PCI hospitals (n=99) Symptoms to therapy 132 ± NR Door to balloon NR Death[b] (14) Recurrent infarct[b] (10) Stroke[b] (1)	Fibrinolytic therapy during transport for PCI (n=100) Symptom to therapy 220 ± NR Door to balloon NR Death[b] (12) Recurrent infarct[b] (7) Stroke[b] (3)
Andersen 2003 Individual randomized trial in Denmark	AMI with ST elevation presenting at hospital not capable of PPCI	Transfer for angioplasty within 3 h (n=567) Symptoms to therapy 227± NR Door to balloon 26 Death[b] 37 (7) Recurrent infarct[b] 11 (2) Stroke[b] 16 (2)	Fibrinolysis at referral hospital (n=562) Symptoms to therapy 150 ± NR Door to therapy NR Death[b] 48 (9) Recurrent infarct[b] 35 (6) Stroke[b] 11 (2)	N/A
Grines 2002 Individual randomized trial in US and Europe	High-risk AMI with ST elevation or presumed new left bundle branch block <12 h	Transfer for PPCI (n=71) Symptoms to therapy NR Door to balloon 174 ± 80 Death[b] 6 (8) Recurrent infarct[b] 1 (1) Stroke[b] 0 (0)	Fibrinolytic therapy (n=66) Symptoms to therapy NR Door to therapy 63 ± 39 Death[b] 8 (12) Recurrent infarct[b] 0 (0) Stroke[b] 3 (4)	N/A

AMI indicates acute myocardial infarction; PPCI, primary percutaneous coronary intervention; and NR, Not reported.

[a]Outcomes at 42 d, not hospital discharge. [b] Outcomes at 30 d, not hospital discharge.

Table 3 MI studies (Continued) - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator
Bonnefoy 2002 Individual randomized trial in France	Patients with STEMI presenting to EMS within 6 h of symptom onset	Primary PCI (n=421) Symptoms to therapy NR Death[b] 20 (5) Recurrent infarct[b] 7 (2) Stroke[b] 0 (0)	Prehospital fibrinolysis (n=419) Symptoms to therapy NR Death[b] 16 (4) Recurrent infarct[b] 15 (4) Stroke[b] 4 (1)	N/A
Widimsky 2003 Individual randomized trial in Czech Republic	Patients with STEMI within 12 h of symptom onset presenting to non–PCI-capable hospital	Immediate transfer for primary PCI (n=429) Symptoms to therapy 203 ± NR Death[b] 29 (7) Recurrent infarct[b] 6 (1) Stroke[b] 1 (0)	Fibrinolytic in community hospital (n=421) Symptoms to therapy 185 ± NR Death[b] 42 (10) Recurrent infarct[b] 13 (3) Stroke[b] 9 (2)	N/A
Ting 2007 Prospective cohort in 3 US states up to 150 mi from PCI-capable hospital	Patients with STEMI within 12 h of symptom onset	Presented at non-PCI capable hospital and transferred for PPCI (n=258) Symptoms to therapy 278 (171, 601) Door to balloon 116 (102, 137) In-hospital death 6 (5.7) Recurrent infarct 3 (2.9) Stroke 1 (1.0)	Presented at PCI-capable hospital and underwent PPCI (n=105) Symptoms to therapy 188 (124, 389) Door to balloon 71 (56, 90) In-hospital death 17 (6.6) Recurrent infarct 4 (1.6) Stroke 2 (0.8)	Presented at non-PCI hospital <3 h from symptom onset and given fibrinolytic (n=131) Symptoms to therapy 103 (61, 145) In-hospital death 4 (3.1) Recurrent infarct 8 (6.1) Stroke 2 (0.8)
Henry 2007 Prospective cohort in 3 US states	Patients with STEMI or new left bundle branch block within 24 h of symptom onset	Transfer for PCI at PCI-capable hospital (n=621) Symptoms to therapy 203 (147, 325) Door to balloon 95 min (82, 116) In-hospital death 24 (3.8) Recurrent infarct 5 (0.8) Stroke 6 (1.0)	Transfer for facilitated PCI at PCI-capable hospital[c] (n=421) Symptoms to therapy 214 (167, 326) Door to balloon 120 min (100, 145) In-hospital death 22 (5.2), *P*=0.48 Recurrent infarct 1 (0.2), *P*=0.02 Stroke 5 (1.2), *P*=0.84	Primary PCI at PCI-capable hospital (n=297) Symptoms to therapy 171 (118, 307) Door to balloon 65 min (47, 84) In-hospital death 11 (3.7) Recurrent infarct 7 (2.4) Stroke 4 (1.3)

[b]Outcomes at 30 d, not hospital discharge.

[c]Half-dose of tenecteplase given to fibrinolytic-eligible patient before transfer.

Table 3 MI studies (Continued) - ALL LOE 5 EXTRAPOLATIONS

Author/Reference Design	Population	Intervention	Comparator	Alternative Comparator
Jollis 2007 Before-after year-long implementation in 1 state	Patients with STEMI	After implementation of statewide system for reperfusion (n=404 non-PCI; n=585, PCI) Presentation to PCI hospital 74 Transferred to PCI hospital 128 Door-to-needle in non-PCI 29 Door-in door-out non-PCI 71 Nonreperfusion in non-PCI hospital 15% Nonreperfusion in PCI hospital 11% Death in PCI hospital 6.2%	Before implementation Control (n=518 non-PCI; n=579 PCI) Presentation to PCI hospital 85 (*P*<0.001) Transferred to PCI hospital 165 (*P*<0.001) Door-to-needle in non-PCI 35 (*P*=0.002) Door-in-door-out non-PCI 120 (*P*<0.001) Nonreperfusion in non-PCI hospital 15% (*P* not significant) Nonreperfusion in PCI hospital 23% (*P* not stated) Death in PCI hospital 7.5% (*P*=0.38)	N/A
Le May 2008 Prospective cohort study in 1 city	Patients with STEMI	Referral from field by paramedics for PPCI (n=135) Symptoms to balloon 158 (116, 207) Death 4 (3.0) Recurrent infarct 2 (1.5) Stroke 1 (0.7)	Referral from ED by physicians for PPCI after interhospital transfer (n=209) Symptoms to balloon 230 (173, 351) In-hospital death 12 (5.7) Recurrent infarct 2 (1.0) Stroke 3 (1.4)	N/A

Knowledge Gaps

What treatments should a cardiac arrest centre offer?

What is a safe journey time for a patient with ROSC at scene?

Is secondary transport from receiving hospital to a regional centre an option?

Should all cardiac arrests be taken to a cardiac arrest centre or are there specific criteria e.g. ROSC at scene?

Is it ethical to do a randomised controlled trial comparing standard care versus sending patients to a cardiac arrest centre? Observational work as part of quality improvement may show this as being beneficial rather than randomised studies.

Are cardiac arrest centres only worthwhile in areas where the other links in the chain of survival are optimized?

Cost effectiveness of intervention

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Citation List

Abstracts

Cardiac arrest studies

Carr, B. G., M. Goyal, et al. (2009). "A national analysis of the relationship between hospital factors and post-cardiac arrest mortality." Intensive Care Med. 2009 Mar;35(3):505-11

LOE 4, Fair, Supportive of large hospitals treating post cardiac arrest patients – retrospective cohort observational study using a large data set. Patients identified by diagnostic codes. How reliable these are is difficult to say. Mix of both in and out of hospital cardiac arrests. No case mix adjustment. If we believe larger hospitals (teaching, tertiary etc) have sickest patients this study may underestimate the improved survival in these hospitals. Patients transferred from other hospitals were excluded. The study can only speculate on what factors determine improved outcome.

Carr, B. G., J. M. Kahn, et al. (2009). "Inter-hospital variability in post-cardiac arrest mortality." Resuscitation 80(1): 30-34.

LOE4, Fair, Supportive of inter-hospital variability – retrospective cohort observational study of ICU APACHE IV database serving 39 hospitals. Both in and out of hospital cardiac arrests. Case mix adjusted outcomes reported. Excluded 215 patients in 18 very low volume hospitals, resulting in 39 hospitals in the final sample. The hospitals in the dataset are all committed to benchmarking – this may not be a true representation of all ICUs. The study cannot comment on which hospital interventions make a difference. The implication is large volume centres offer a more comprehensive package of care.

Callaway CW, et al. Receiving hospital characteristics associated with survival after out-of-hospital cardiac arrest. Resuscitation (2010), Epublished doi:10.1016/j.resuscitation.2009.12.006

LOE 4 good , weakly supporting good quality multicentre observational study from North America (ROC group). Shows improved survival to discharge in centers with cath labs and greater that 40 patients admitted per year had improved outcomes. There was however no difference in risk adjusted outcomes. WE also do not know what interventions the patient's actually had.

Davis, D. P., R. Fisher, et al. (2007). "The feasibility of a regional cardiac arrest receiving system." Resuscitation 74(1): 44-51.

LOE4, poor, supporting – prospective observational study. This study suggests that in patients with ROSC transport time does not influence survival – note the transport time is relatively short. Study implies that could bypass a closer hospital for a 'cardiac arrest centre'. Relatively old data - 18-month period from January 2001 through June 2002. Predates hypothermia studies. It is not clear how many hospitals were involved and how hospital factors influenced outcome.

Engdahl, J., P. Abrahamsson, et al. (2000). "Is hospital care of major importance for outcome after out-of-hospital cardiac arrest? Experience acquired from patients with out-of-hospital cardiac arrest resuscitated by the same Emergency Medical Service and admitted to one of two hospitals over a 16-year period in the municipality of Goteborg." Resuscitation 43(3): 201-11.

LOE4, poor, supporting differences between two hospitals served by the same EMS. Retrospective observational study of data from the EMS database and hospital records. Difference may be due to increased number of interventions available in more successful hospital. This hospital however had more patients needing ongoing CPR on arrival. Cannot rule out socio-economic factors. Relatively small numbers of patients. Large amount of missing data. Predate recent work on post resuscitation care, e.g., hypothermia.

Gaieski DF, Band RA, Abella BS, Neumar RW, Fuchs BD, Kolansky DM, et al. Early Goal-Directed Hemodynamic Optimization Combined with Therapeutic Hypothermia in Comatose Survivors of Out-of-Hospital Cardiac Arrest. Resuscitation 2009 Apr;80(4):418-24.

LOE 3, fair neutral, shows feasibility of goal directed therapy and care bundle but not powerful enough to show statistically significant improvement – small numbers.

Herlitz, J., J. Engdahl, et al. (2006). "Major differences in 1-month survival between hospitals in Sweden among initial survivors of out-of-hospital cardiac arrest." Resuscitation 70(3): 404-9.

LOE4, poor, supporting – retrospective observation study based on Swedish cardiac arrest registry data. Shows variation in survival between hospitals. Weaknesses - missing information. Cannot say which hospital factors make a difference. Predates hypothermia.

Keenan, S. P., P. Dodek, et al. (2007). "Variation in length of intensive care unit stay after cardiac arrest: where you are is as important as who you are." Crit Care Med 35(3): 836-41.

LOE4, poor, supporting. Observation study of ICU database (1998-2002. Thirty-one Canadian ICUs, all but one being members of the Critical Care Research Network. In and out of hospital cardiac arrests. Admitting hospital remained independently and strongly associated with length of ICU stay after controlling for age, gender, APACHE II score, GCS score (the latter two in separate analyses), and hospital size. Data suggest that decisions on how long to support these patients is determined, in part, by where patients are treated (hospital site), not solely by patient characteristics. Data from before when therapeutic hypothermia benefits known. Do not know what proportion of cardiac arrest survivors were not admitted to an ICU. Some ICUs may just no admit them.

Knafelj R, Radsel P, Ploj T, Noc M. Primary percutaneous coronary intervention and mild induced hypothermia in comatose survivors of ventricular fibrillation with ST-elevation acute myocardial infarction. Resuscitation. 2007 Aug;74(2):227-34.

LOE 3, fair supporting – shows benefit of post cardiac arrest care package V historical control.

Langhelle, A., S. S. Tyvold, et al. (2003). "In-hospital factors associated with improved outcome after out-of-hospital cardiac arrest. A comparison between four regions in Norway." Resuscitation 56(3): 247-63.

LOE4, poor, supporting- retrospective observation study showing difference in performance between hospitals. This study showed variation in hospital factors (after correcting for other factors) that effected survival and neurological status up to 1 year. This study did not however compare specific in hospital interventions. Predates work on hypothermia.

Liu, J. M., Q. Yang, et al. (2008). "Hospital variability of out-of-hospital cardiac arrest survival." Prehosp Emerg Care 12(3): 339-46.

LOE 4, poor, supporting – retrospective, observational study shows variability between hospitals –due to bed:nurse ratio? Is this the result of a data trawl or a real factor.

Lurie, K. G., A. Idris, et al. (2005). "Level 1 cardiac arrest centers: learning from the trauma surgeons." Acad Emerg Med 12(1): 79-80.

Editorial on need for cardiac arrest centres.

Oddo M, Schaller MD, Feihl F, Ribordy V, Liaudet L. From evidence to clinical practice: effective implementation of therapeutic hypothermia to improve patient outcome after cardiac arrest. Crit Care Med. 2006 Jul;34(7):1865-73.

LOE 3, good , supporting – Shows benefit of TH and other interventions after ROSC in single centre V historical control group. Does not directly answer PICO.

Spaite, D. W., B. J. Bobrow, et al. (2008). "The impact of prehospital transport interval on survival in out-of-hospital cardiac arrest: implications for regionalization of post-resuscitation care." Resuscitation 79(1): 61-6.

LOE 4, poor, supporting – prospective observational cohort study. Transport time data was missing in 38% of cases. The transport times were short. It is not clear how hospital factors influenced these outcomes. (October 2004 through December 2006).

Spaite, D. W., I. G. Stiell, et al. (2009). "Effect of Transport Interval on Out-of-Hospital Cardiac Arrest Survival in the OPALS Study: Implications for Triaging Patients to Specialized Cardiac Arrest Centers." Ann Emerg Med. ;54(2):248-55

LOE4, poor, supporting. Large data base but before therapeutic hypothermia. 19% of data missing. Short (4-5 min) transport times. Suggests transport time does not effect survival.

Sunde, K., M. Pytte, et al. (2007). "Implementation of a standardised treatment protocol for post resuscitation care after out-of-hospital cardiac arrest." Resuscitation 73(1): 29-39.

LOE3, good, supporting – observational study with historical control group showing improvement in outcomes with comprehensive post resuscitation care package. Small numbers. Supports concept of standardised care protocols improving survival

Wolfrum S, Pierau C, Radke PW, Schunkert H, Kurowski V. Mild therapeutic hypothermia in patients after out-of-hospital cardiac arrest due to acute ST-segment elevation myocardial infarction undergoing immediate percutaneous coronary intervention. Crit Care Med. 2008 Jun;36(6):1780-6.

LOE3, fair, neutral. Study shows improvement with care package V historical control group that is not statistically significant as underpowered- small numbers. LOE5 as not directly answering question.

Non – cardiac arrest studies all LOE 5

MI Studies

Anderson et al. A comparison of coronary angioplasty with fibrinolytic therapy in acute myocardial infarction. N Engl J Med. 2003 Aug 21;349(8):733-42

LOE5, neutral, good. Individual randomized trial in Denmark

Bonnefoy E et al. Primary angioplasty versus prehospital fibrinolysis in acute myocardial infarction: a randomised study. Lancet. 2002 Sep 14;360(9336):825-9.

LOE5, neutral, good. Individual randomized trial in France

Grines CL et al. A randomized trial of transfer for primary angioplasty versus on-site thrombolysis in patients with high-risk myocardial infarction: the Air Primary Angioplasty in Myocardial Infarction study. J Am Coll Cardiol. 2002 Jun 5;39(11):1713-9.

LOE5, neutral, good Individual randomized trial in US and Europe

Henry TD et al. A regional system to provide timely access to percutaneous coronary intervention for ST-elevation myocardial infarction. Circulation. 2007 Aug 14;116(7):721-8. Epub 2007 Aug 1.

LOE5, neutral, fair. Prospective cohort in 3 US states

Jollis JG et al. Implementation of a statewide system for coronary reperfusion for ST-segment elevation myocardial infarction. JAMA. 2007 Nov 28;298(20):2371-80. Epub 2007 Nov 4.

LOE5, neutral, poor. Before-after year-long implementation in 1 state

Le May MR et al. A citywide protocol for primary PCI in ST-segment elevation myocardial infarction. N Engl J Med. 2008 Jan 17;358(3):231-40.

LOE5, supporting, fair. Prospective cohort study in 1 city

Ting HH et al. Regional systems of care to optimize timeliness of reperfusion therapy for ST-elevation myocardial infarction: the Mayo Clinic STEMI Protocol. Circulation. 2007 Aug 14;116(7):729-36. Epub 2007 Aug 1.

LOE5, neutral, fair. Prospective cohort in 3 US states up to 150 mi from PCI-capable hospital

Vermeer F, Oude Ophuis AJ, vd Berg EJ, Brunninkhuis LG, Werter CJ, Boehmer AG, Lousberg AH, Dassen WR, Bär FW. Prospective randomised comparison between thrombolysis, rescue PTCA, and primary PTCA in patients with extensive myocardial infarction admitted to a hospital without PTCA facilities: a safety and feasibility study. Heart. 1999 Oct;82(4):426-31.

LOE5, supporting, good. Individual randomized trial in 1 province, Netherlands

Widimsky P et al. Multicentre randomized trial comparing transport to primary angioplasty vs immediate thrombolysis vs combined strategy for patients with acute myocardial infarction presenting to a community hospital without a catheterization laboratory. The PRAGUE study. Eur

Heart J. 2000 May;21(10):823-31.

LOE5, supporting good. Individual randomized trial in 1 province, Czech Republic

Widimsky P et al. Long distance transport for primary angioplasty vs immediate thrombolysis in acute myocardial infarction. Final results of the randomized national multicentre trial--PRAGUE-2. Eur Heart J. 2003 Jan;24(1):94-104.

LOE5 supporting, good. Individual randomized trial in Czech Republic

Stroke Studies

Lamonte MP et al. A regional system of stroke care provides thrombolytic outcomes comparable with the NINDS stroke trial. Ann Emerg Med. 2009 Sep;54(3):319-27. Epub 2008 Dec 19.

LOE5 – observational data from another study, supporting, fair.

Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke. Cochrane Database Syst Rev. 2007 Oct 17;(4):CD000197.

LOE5 – meta-analysis – supporting, fair

Trauma Studies

Abernathy JH, 3rd, McGwin G, Jr., Acker JE, 3rd, Rue LW, 3rd. Impact of a voluntary trauma system on mortality, length of stay, and cost at a level I trauma center. Am Surg. 2002 Feb;68(2):182-92.

LOE 5 Retrospective cohort study of administrative data, supporting poor.

Boyd DR, Pizzano WA, Romano TL, Van Stiegmann G, Nyhus LM. Regionalization of trauma patient care: the Illinois experience. Surg Annu. 1975;7:25-52.

LOE 5 Retrospective cohort study of hospital-based trauma registries, neutral fair.

Clemmer TP, Orme JF, Jr., Thomas FO, Brooks KA. Outcome of critically injured patients treated at Level I trauma centers versus full-service community hospitals. Crit Care Med. 1985 Oct;13(10):861-3.

LOE5 Retrospective cohort study of regional trauma registry, supporting, poor.

Culica D, Aday LA, Rohrer JE. Regionalized trauma care system in Texas: implications for redesigning trauma systems. Med Sci Monit. 2007 May;13(5):SR9-SR18.

LOE5 Retrospective cohort study of administrative data, supporting good.

de Jongh MA, Meeuwis JD, van Baar ME, van Stel HF, Schrijvers AJ. Evaluation of trauma care by comparing mortality risks and admission policy in a Dutch trauma region. Injury. 2008 Sep;39(9):1007-12.

LOE5 Retrospective cohort study of regional trauma registry, neutral, good,

Goldberg J, Levy PS, Gelfand HM, Mullner R, Iverson N, Lemeshow S, et al. Factors affecting trauma center utilization in Illinois. Med Care. 1981 May;19(5):547-66.

LOE5 Retrospective cohort study of hospital discharge data, neutral, fair.

Hannan EL, Farrell LS, Cooper A, Henry M, Simon B, Simon R. Physiologic trauma triage criteria in adult trauma patients: are they effective in saving lives by transporting patients to trauma centers? J Am Coll Surg. 2005 Apr;200(4):584-92.

LOE5 Retrospective cohort study of state trauma registry, supporting poor

Harrington DT, Connolly M, Biffl WL, Majercik SD, Cioffi WG. Transfer times to definitive care facilities are too long: a consequence of an immature trauma system. Ann Surg. 2005 Jun;241(6):961-6; discussion 6-8.

LOE5 Retrospective cohort study of hospital trauma registry, supporting, poor.

Hulka F, Mullins RJ, Mann NC, Hedges JR, Rowland D, Worrall WH, et al. Influence of a statewide trauma system on pediatric hospitalization and outcome. J Trauma. 1997 Mar;42(3):514-9.

LOE 5 Retrospective cohort study of hospital discharge data, neutral fair.

Kane G, Wheeler NC, Cook S, Englehardt R, Pavey B, Green K, et al. Impact of the Los Angeles County Trauma System on the survival of seriously injured patients. J Trauma. 1992 May;32(5):576-83.

LOE5 Retrospective cohort study of hospital discharge data, neutral fair.

Liberman M, Mulder DS, Lavoie A, Sampalis JS. Implementation of a trauma care system: evolution through evaluation. J Trauma. 2004 Jun;56(6):1330-5.

LOE5 Retrospective cohort study of hospital trauma registry, supporting, fair.

MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al. A national evaluation of the effect of trauma-center care on mortality. N Engl J Med. 2006 Jan 26;354(4):366-78.

LOE5 Prospective stratified sample of cases and controls using medical record review and patient interview, supporting good.

Mann NC, Cahn RM, Mullins RJ, Brand DM, Jurkovich GJ. Survival among injured geriatric patients during construction of a statewide trauma system. J Trauma. 2001 Jun;50(6):1111-6.

LOE5 Retrospective cohort study of hospital discharge data linked with death index, supporting, fair.

Mullins RJ, Veum-Stone J, Hedges JR, Zimmer-Gembeck MJ, Mann NC, Southard PA, et al. Influence of a statewide trauma system on location of hospitalization and outcome of injured patients. J Trauma. 1996 Apr;40(4):536-45; discussion 45-46.

LOE5 Retrospective cohort study of hospital discharge data linked with death index, supporting, fair.

Mullins RJ, Mann NC, Hedges JR, Worrall W, Jurkovich GJ. Preferential benefit of implementation of a statewide trauma system in one of two adjacent states. J Trauma. 1998 Apr;44(4):609-16; discussion 17.

LOE5 Retrospective cohort study of hospital discharge data linked with death index, supporting, fair.

Mullins RJ, Veum-Stone J, Helfand M, Zimmer-Gembeck M, Hedges JR, Southard PA, et al. Outcome of hospitalized injured patients after institution of a trauma system in an urban area. JAMA. 1994 Jun 22-29;271(24):1919-24.

LOE5 Retrospective cohort study of hospital discharge data and hospital trauma registry, supporting fair.

Mullner R, Goldberg J. An evaluation of the Illinois trauma system. Med Care. 1978 Feb;16(2):140-51.

LOE5 Retrospective cohort study of sample from Department of Transportation records of motor vehicle–related trauma, supporting, poor.

Mullner R, Goldberg J. Toward an outcome-oriented medical geography: an evaluation of the Illinois trauma/emergency medical services system. Soc Sci Med. 1978 Jun;12(2D):103-10.

LOE5 Retrospective cohort study of state trauma registry, supporting, poor.

Nathens AB, Jurkovich GJ, Rivara FP, Maier RV. Effectiveness of state trauma systems in reducing injury-related mortality: a national evaluation. J Trauma. 2000;48(1):25-30; discussion -1.

LOE5 Retrospective cohort study of National Center for Health Statistics data, FARS database, and census data, supporting, fair.

Nathens AB, Maier RV, Brundage SI, Jurkovich GJ, Grossman DC. The effect of interfacility transfer on outcome in an urban trauma system. J Trauma. 2003 Sep;55(3):444-9.

LOE5 Retrospective cohort study of regional trauma registry, supporting, poor.

Nicholl J, Turner J. Effectiveness of a regional trauma system in reducing mortality from major trauma: before and after study. BMJ. 1997;315(7119):1349-54.

LOE5 Prospective before-after study using individual patient data, supporting, fair.

Norwood S, Fernandez L, England J. The early effects of implementing American College of Surgeons level II criteria on transfer and survival rates at a rurally based community hospital. J Trauma. 1995 Aug;39(2):240-4; discussion 4-5.

LOE5 Retrospective cohort study of regional trauma registry, neutral, fair

Potoka DA, Schall LC, Gardner MJ, Stafford PW, Peitzman AB, Ford HR. Impact of pediatric trauma centers on mortality in a statewide system. J Trauma. 2000 Aug;49(2):237-45.

LOE5 Retrospective cohort study of state trauma registry, supporting, poor.

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LOE5 Retrospective cohort study of hospital discharge data, opposing, fair.

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