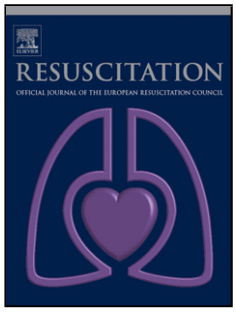

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PII: S0300-9572(16)00119-2
DOI: http://dx.doi.org/doi:10.1016/j.resuscitation.2016.03.004
Reference: RESUS 6721

To appear in: *Resuscitation*

Received date: 26-1-2016
Accepted date: 7-3-2016

Please cite this article as: Couper K, Yeung J, Nicholson T, Quinn T, Lall R, Perkins GD, Mechanical chest compression devices at in-hospital cardiac arrest: a systematic review and meta-analysis, *Resuscitation* (2016), http://dx.doi.org/10.1016/j.resuscitation.2016.03.004

Mechanical chest compression devices at in-hospital cardiac arrest: a systematic review and meta-analysis

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Funding: KC and JY are supported as NIHR post-doctoral research fellows. GDP is supported as an Intensive Care Foundation Director of Research and as an NIHR Senior Investigator.

Conflict of Interest: KC, TQ, RL and GDP have received funding to conduct a feasibility randomised controlled trial of mechanical devices for in-hospital cardiac arrest. The institutions of TQ, RL, and GDP have received funding from the National Institute for Health Research to evaluate the LUCAS-2 chest compression device for out-of-hospital cardiac arrest. GDP is editor for Resuscitation. JY and TN have no conflicts of interest to declare.

This article/paper/report presents independent research funded by the National Institute for Health Research (NIHR). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Word count: Abstract 250 words; Main paper: 3195.

Abstract

Aim: To summarise the evidence in relation to the routine use of mechanical chest compression devices during resuscitation from in-hospital cardiac arrest.

Methods: We conducted a systematic review of studies which compared the effect of the use of a mechanical chest compression device with manual chest compressions in adults that sustained an in-hospital cardiac arrest. Critical outcomes were survival with good neurological outcome, survival at hospital discharge or 30-days, and short-term survival (ROSC/ 1-hour survival). Important outcomes included physiological outcomes. We synthesised results in a random-effects meta-analysis or narrative synthesis, as appropriate. Evidence quality in relation to each outcome was assessed using the GRADE system.

Data sources: Studies were identified using electronic databases searches (Cochrane Central, MEDLINE, EMBASE, CINAHL), forward and backward citation searching, and review of reference lists of manufacturer documentation.

Results: Eight papers, containing nine studies [689 participants], were included. Three studies were randomised controlled trials. Meta-analyses showed an association between use of mechanical chest compression device and improved hospital or 30-day survival (odds ratio 2.36, 95% CI 1.44-3.89) and short-term survival (odds ratio 2.14, 95% CI 1.11-4.13). There was also evidence of improvements in physiological outcomes. Overall evidence quality in relation to all outcomes was very low.

Conclusions: Mechanical chest compression devices may improve patient outcome, when used at in-hospital cardiac arrest. However, the quality of current evidence is very low. There is a need for randomised trials to evaluate the effect of mechanical chest compression devices on survival for in-hospital cardiac arrest.

(PROSPERO registration number: CRD42015020220)

Introduction

Each year in the UK, approximately 35,000 patients sustain an in-hospital cardiac arrests, of which only 18.4% survive to hospital discharge.[1] The quality of chest compressions is an important modifiable determinant of survival following cardiac arrest.[2, 3] The challenge of delivering high-quality manual chest compressions has driven interest in the use mechanical chest compression devices, which provide chest compressions of consistent rate and depth.[4, 5] Potential ancillary benefits of such devices include the release of a rescuer to perform other interventions.[5]

Research to-date has focussed mainly on the use of the mechanical devices in the pre-hospital setting.[5] Three large randomised controlled trials of mechanical devices in the pre-hospital setting have recently been published.[6-8] Meta-analysis of data from these trials has shown that the routine use of mechanical chest compression devices, compared with manual chest compressions, does not improve survival for out-of-hospital cardiac arrest.[9, 10] In 2015, on the basis of published evidence the International Liaison Committee for Resuscitation recommended against the routine use of mechanical chest compression devices in out-of-hospital cardiac arrest. [11]

In contrast, the routine deployment of mechanical devices in the in-hospital setting has received limited attention.[5] In out-of-hospital cardiac arrest, devices are typically deployed more than 15 minutes after cardiac arrest due to the inherent delays in EMS teams reaching the scene of the collapse.[7] Resuscitation is attempted by small teams who often have infrequent exposure to cardiac arrest, which may lead to harmful unrecognised prolonged interruptions in chest compressions.[12-16] By contrast, the hospital setting allows for earlier deployment of devices by larger teams, who are likely to have greater exposure to cardiac arrest events, and so may deploy devices more effectively.

To date, systematic reviews of mechanical devices have tended to include both in-hospital and pre-hospital studies, or focussed solely on pre-hospital studies.[9, 10, 17-19] A single systematic review of mechanical devices for in-hospital cardiac arrests has been published but the value of its findings are limited by its narrow approach to study identification and inclusion of both case reports and case series.[20] The aim of our review is to summarise evidence in relation to the use of mechanical chest compression devices for in-hospital cardiac arrest.

Methods

We undertook this review in accordance with a protocol which was registered with the PROSPERO database on 14th May 2015 (registration number: CRD42015020220).

Search strategy

We conducted searches of the following databases using a combination of keywords and MeSH terms: Cochrane Central Register of Controlled Trials; Ovid MEDLINE; Ovid EMBASE; and CINAHL. The search strategy, modelled on that used in the Cochrane review, included terms for the condition (e.g. cardiac arrest), the treatment (e.g. chest compression$) and intervention (compression$ ADJ9 device$).[19] An example search strategy is included in the electronic supplement. In addition, we interrogated trial registries, reference lists of worksheets produced as part of the 2010 and 2015 ILCOR evidence evaluation process, and resources provided on manufacturer's websites. Forward

and backward citation searching of included studies and key systematic reviews was also undertaken.

Following duplicate removal, titles were screened independently by two authors and obviously irrelevant results removed. This process was then repeated for abstract screening. The full-text of potentially relevant titles was obtained, and assessed independently by the same two authors in an unblinded manner against pre-determined eligibility criteria using a proforma.

Inclusion/ Exclusion criteria

We included all published primary research studies which compared the use of a mechanical chest compression device with manual chest compressions in human adults (≥ 16 years of age) that suffered an in-hospital cardiac arrest. Studies were included if they reported quantitative outcome data for each treatment group for at least one of the pre-determined outcome measures. Studies undertaken in the emergency department were excluded. No restriction on study design, publication date or language was imposed. Studies published only as abstracts were eligible for inclusion.

Outcomes

The following outcomes were defined as critical outcomes in accordance with GRADE: survival with good neurological outcome; patient survival to hospital discharge or at 30-days; short term survival (e.g. return of spontaneous circulation (ROSC), survival to 1 hour after ROSC). CPR quality and physiological outcomes (e.g. chest compression rate, coronary perfusion pressure), and safety outcomes (e.g. visceral organ damage) were considered important outcomes. Outcomes were defined in accordance with Utstein consensus definitions.[21]

Quality assessment

The risk of bias in individual studies were independently reviewed by two authors using the Cochrane risk of bias assessment for randomised controlled trials or the Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment tool for observational studies.[22, 23] For each outcome, we used the GRADE system and associated software (GRADEpro. [Computer program]. Version 3.2 for Windows. Jan Brozek, Andrew Oxman, Holger Schünemann, 2008) to assess overall evidence quality in relation to each outcome or outcome group.[24]

The GRADE system categorises evidence quality for each outcome as either very low, low, moderate, or high.[25] Initially, the quality of evidence for outcome is initially rated as high (for randomised controlled trials) or low (for observational studies). The rating may then downgraded or upgraded. Reasons for downgrading include risk of bias or indirectness, whilst reasons for upgrading include evidence of a dose-response or where the effect-size is large. The GRADE system was the approach used in the 2015 International Liaison Committee on Resuscitation evidence evaluation process.[26]

Data extraction and analysis

Data were extracted from index studies using a generic form that captured key study methodological information, intervention details, baseline group characteristics, and study results. Data were extracted by one reviewer, and then checked for accuracy by another reviewer. We undertook meta-analyses in Revman software using a random-effects model (Review Manager (RevMan) [Computer program]. Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). Meta-analysis results are presented as odds ratio (OR) and 95% confidence interval (95% CI) for dichotomous outcomes. Meta-analyses report the overall effect size, as well as the separate effect sizes for randomised controlled trials and observational studies. The Higgins I^2 statistic is used to measure consistency of results between trials and for any sub-group differences.[27] Where a meta-analysis is not appropriate, results are described in a narrative synthesis.

Results

Electronic database searches identified 2659 citations. A further 481 citations were identified through citation tracking, searches of trial registries, and review of manufacturer and ILCOR resources. Following duplicate removal and screening of titles and abstracts, we reviewed the full-text of 84 citations. Eight papers were identified as meeting inclusion criteria (figure one).[28-35] Despite the large number of citations identified through other sources, all included papers were identified through electronic database searches. The paper by Halperin et al describes two distinct studies (a crossover trial and a randomised controlled trial), so for clarity it is treated as two distinct studies in this review.[30] The paper by Lu et al was translated by one of the authors to facilitate inclusion in this review.[31]

Of the nine included studies, three were randomised controlled studies[28, 30, 31] and the remainder were observational studies[29, 30, 32-35]. Sample size ranged from 16 to 285 participants. Six studies were conducted in North America[28, 30, 33-35], with one each of the remaining three being conducted in the UK,[32] China,[31], and Brazil.[29]. Studies used a range of mechanical devices, including load-distributing band devices (n=2),[29, 32] pneumatic vest devices (n=2),[30] piston-type devices (n=3),[28, 31, 35] the LUCAS device (n=1),[34] and one study where the type of device is not reported.[33] Key characteristics of included studies are summarised in table one.

The overall quality of studies was low. Risk of bias summary tables are included as tables two and three for randomised controlled trials and observational studies respectively. Randomised controlled trials typically gave limited information about key methodological elements, such as allocation generation, concealment and the blinding of assessors. Observational studies were typically subject to a high risk of bias due to the measurement of exposure and outcome, and the risk of confounding. Of particular note was the study by Spiro et al, where treatment with a mechanical device was restricted to cardiology patients, but survival was compared with all other in-hospital cardiac arrest patients, irrespective of cardiac arrest aetiology.[32]

Critical outcomes:

For the critical outcome of neurological outcome at hospital discharge, none of the included studies report data.

Five studies (two randomised controlled trials [200 participants], three observational studies [401 participants]) report the critical outcome of survival at hospital discharge or 30-days.[28, 31-34] A

very-low quality of evidence (downgraded for risk of bias and indirectness) showed an association between the use of a mechanical chest compression device and improved hospital survival (OR 2.36, 95% CI 1.44-3.89, p<0.001) (figure two/ table four). Overall, study heterogeneity was low (I^2=0%). The estimate of treatment effect was similar between randomised controlled trials and observational studies (OR 2.53, 95% CI 1.21-5.29 v OR 2.23, 95% CI 1.14-4.37, p=0.80, I^2=0%).

Four studies (three randomised controlled trials [234 participants], one observational study [16 participants]) report the critical outcome of short-term survival.[28, 30, 31, 33] Three studies reported this as return of spontaneous circulation and one study reported it as one-hour survival. Evidence quality was very low (downgraded for risk of bias and indirectness) (table four). There was evidence of an association between use of a mechanical chest compression device and improved short-term survival (OR 2.14, 95% CI 1.11-4.13, p=0.02) (figure three). Overall, there was low study heterogeneity (I^2=19%). The estimate of treatment of treatment effect was markedly different between the three randomised controlled trials and the single observational study, although this did not reach statistical significance (OR 1.94, 95% CI 1.14-3.30 v OR 18.33, 95% CI 0.81-416.04, p=0.16, I^2=48.2%).

Important outcomes:

Four studies reported the important outcome of physiological outcome.[29, 30, 35] Overall, evidence quality was very low (downgraded for risk of bias and indirectness) (table four). Included outcomes were blood gas values (2 studies), haemodynamic pressures (2 studies), and cerebral oxygenation (one study).

Blood gas values (pH, partial pressure of carbon dioxide, partial pressure of oxygen) were reported in both the crossover study and randomised controlled trial reported by Halperin et al.[30] In neither study was there evidence of a statistically significant difference in any value between groups, although data were collected for only approximately one-third of participants in each study.

Haemodynamic measurements, notably coronary perfusion pressure, were recorded in two crossover studies.[29, 30] Halperin et al reported an association between use of a mechanical device and improved coronary perfusion pressure (manual: 15 $\pm$ 8 mmHg v mechanical: 23 $\pm$ 11 mmHg, p<0.003).[30] A similar effect was reported by Timerman et al (manual: 15 $\pm$ 11 mmHg v mechanical: 20 $\pm$ 12 mmHg, p<0.015).[29]

Parnia et al examined the association between use of a mechanical chest compression device and cerebral oxygenation.[35] Cerebral oxygenation describes frontal cortex haemoglobin oxygen saturation as a percentage value. Parnia et al reported higher cerebral oxygenation in the group treated with a mechanical chest compression device, compared with manual chest compressions (53.1% ± 23.4 v 24% ± 25, p = 0.002).

No study reported data on the important outcome of CPR quality.

Two studies included the important outcome of patient safety outcomes.[28, 30] Overall, evidence quality was very low (downgraded for very serious risk of bias and indirectness). A broad range of specific injuries were examined across the two studies, including rib fractures (two studies), sternal fracture (one study), and liver laceration (one study). Both studies collected injury data through autopsy. Broadly, injury patterns were similar between patients treated with manual and mechanical chest compressions.

Discussion

In this systematic review and meta-analysis, we included data from nine studies. None of the papers reported neurological outcomes amongst survivors at any time point. In relation to the critical outcome of survival at hospital discharge or 30-days, there was evidence of an association between use of a mechanical chest compression device and improved survival (OR 2.36, 95% CI 1.44-3.89, p<0.001). We also found evidence of improved short-term survival and physiological outcomes. Patient safety outcomes were infrequently reported.

Evidence quality, as assessed using the GRADE framework, was categorised as very low in relation to all outcomes. As such, there is considerable uncertainty about the treatment effects described and the results of this review should be interpreted with significant caution.[24] The very low categorisation of evidence quality results from the high risk of bias of most included studies and indirectness of evidence. This indirectness stems from: the variety of mechanical devices used, of which some are no longer marketed; the 35-year period over which studies were undertaken, such that the resuscitation practice in some studies was markedly different to resuscitation practice of today; and the focus in some studies on patients in the cardiac catheter laboratory.

Taken at face value, however, the findings of this review differ markedly from systematic reviews of mechanical devices for out-of-hospital cardiac arrest. Gates et al meta-analysed data from five randomised controlled trials, which enrolled a total of 12,206 participants, and found that use of a mechanical device did not improve hospital or 30-day survival (odds ratio 0.89, 95% CI 0.77 - 1.02), or any other outcome.[9] Bonnes et al undertook a broader review that combined the same five randomised controlled trials with 15 observational studies (n=9,157).[10] In the review, data from observational studies showed an association between the use of a mechanical device and improved short-term outcome (ROSC, hospital admission), but this apparent benefit was not observed in analyses of longer-term outcomes to hospital discharge, or in analyses of randomised controlled trials.

There are two possible reasons to explain this apparent difference in findings between this review of in-hospital cardiac arrest studies and previous reviews of out-of-hospital cardiac arrest studies. Firstly, as per the GRADE process, treatment effects for very low quality evidence should be considered to be uncertain.[24] Data from other disease areas shows that studies at increased risk of bias may over-estimate or under-estimate treatment the treatment effect.[36-38]

As such, further high-quality research might show that, as is the case of out-of-hospital cardiac arrest, the routine deployment of mechanical chest compression devices for in-hospital cardiac arrest does not improve patient outcomes, compared with manual chest compressions.

The second explanation is that mechanical devices are more effective than manual chest compressions in the hospital setting. The ability to deploy devices earlier during the cardiac arrest by a larger team with greater exposure to cardiac arrest events may result in more effective deployment. Interestingly, a meta-regression in the review by Bonnes et al suggests that mechanical devices are more effective in the pre-hospital setting when they are deployed earlier during the cardiac arrest event.[10] Importantly, data on chest compression pauses associated with device deployment are rarely reported in studies of mechanical devices, but there is evidence from observational studies that well-trained teams deploy devices more effectively.[32, 39, 40] Furthermore, manual chest compressions in the hospital setting are often challenging to deliver effectively as the patient is typically positioned on a compressible mattress which absorbs up to 40%

of compression force.[41] In this setting, mechanical devices enable consistent high-quality chest compressions to be delivered, irrespective of the underlying surface.

Prior to this review, a single systematic review of the use of mechanical devices specifically for in-hospital cardiac arrest had been published.[20] This review, published in 2015, included 14 papers, of which nine were case reports or case series. Furthermore, the review adopted a relatively limited search strategy, with only 141 papers identified in electronic database searches, and narrow inclusion criteria. A single paper overlaps both that review and this review. Overall, survival following treatment with a mechanical chest compression device was reported to be 39%. However, the nature of included studies meant that no manual chest compression comparator could be reported and the reported survival for the mechanical chest compression group is likely to be subject to a very high risk of selection bias.

In this review, we excluded emergency department (ED) studies. There were two key reasons for this decision. Firstly, emergency department studies typically include out-of-hospital cardiac arrest patients that are transported in cardiac arrest. This patient group typically has a poor outcome and deployment of a mechanical device on ED admission will likely be too late to have a measurable effect on outcome.[42] Secondly, we have suggested that one reason for mechanical devices being more effective for in-hospital cardiac arrest is the compressibility of underlying mattress. However, ED cardiac arrest patients are usually treated on a trolley stretcher that absorbs less compression force than a mattress.[43]

This exclusion of emergency department studies meant that some informative studies were not included. Ong et al undertook a large before/ after study (n=1011) which found improved survival with good neurological outcome following the introduction of a mechanical chest compression device in the ED.[44] However, the increased incidence of ED, rather than out-of-hospital, cardiac arrest in the second phase of the study together with other significant baseline differences makes it difficult to reliably interpret these data. Another important excluded paper was the report of Koster et al's two parallel non-inferiority randomised controlled trials, which had the primary outcome of visceral injury.[45] The study found that the LUCAS device (Physio-control/Jolife AB, Lund, Sweden) did not cause more injury than the manual chest control, but an increase in injury could not be ruled out in relation to the AUTOPULSE device (Zoll Medical Corporation, Chelmsford, Massachusetts).

Our review has a number of limitations. Firstly, as noted above, the risk of bias of index studies meant that evidence quality in relation to all outcomes was categorised as very low. Secondly, the size of index studies was small, producing an overall sample size of 689 participants. In contrast, the review by Gates et al of out-of-hospital cardiac arrest included data from over 12,000 participants.[9] Thirdly, our decision to meta-analyse data may be questioned, given marked clinical heterogeneity between index studies. However, we noted overall statistical heterogeneity for each meta-analysis, as measured by the I^2 statistic, was low or moderate and we chose a random-effects model to account for differences in effect size between studies.[27, 46] The authors of the Cochrane review on mechanical chest compression devices chose not to meta-analyse studies due to concerns about clinical heterogeneity, although that review included both out-of-hospital and in-hospital studies.[19] Finally, it is important that none of the included studies reported data on important outcomes, such as survival beyond hospital discharge and survival with good neurological outcome. Survival with good neurological outcome is often not reported in cardiac arrest trials, but is considered an important outcome by both clinicians and patients.[47-49] Importantly, two pre-hospital mechanical chest compression studies have reported worse neurological outcome in groups treated with a mechanical chest compression device, so recording this important outcome should be considered essential in future trials.[8, 50]

Conclusion

In this review, our meta-analysis found an association between improved hospital or 30-day survival and treatment with a mechanical chest compression device for in-hospital cardiac arrest. We also found evidence of improved short-term survival and improved physiological outcomes when a mechanical device was used. However, no study included data on survival with good neurological outcome and evidence quality for each outcome was very low. This review suggests a potential role for mechanical chest compression devices for in-hospital cardiac arrest, but there is an urgent need for high-quality research, particularly adequately powered randomised trials, to further examine this role.

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Table one: summary of included studies

Study	Study design	Study setting	Mechanical device	Population	Key outcomes	Industry funding/ support
Taylor 1978	RCT	USA	Thumper (piston) device	50 IHCA patients. CA duration < 10 minutes.	Survival (1-hour/ 24-hour/ discharge); patient safety	Manufacturer supplied device
Halperin 1993a	Crossover study	USA	Pneumatic vest device	15 IHCA patients. CA duration >20 minutes.	Blood gas; haemodynamic pressures	9 authors report equity interest in company with device patent
Halperin 1993b	RCT	USA	Pneumatic vest device	34 IHCA patients. CA duration < 20 minutes.	Survival (ROSC/ 6-hour/ 24-hour); blood gas; patient safety	As Halperin 1993a
Timerman 2004	Crossover study	Brazil	Load-distributing band device	16 IHCA patients. CA duration > 10 minutes.	Haemodynamic pressures	Study financial support by device manufacturer. One authors reports financial interest in device manufacturer.
Lu 2010	RCT	China	Thumper (piston) device	150 IHCA paptient	Survival (ROSC/ discharge)	No
Gutteridge 2012	Cohort study	USA	LUCAS	89 IHCA patients	Survival (discharge)	No
Parnia 2014	Cohort study	USA	Lifestat (piston)	34 IHCA patients	Cerebral oxygenation	No
Retzer 2015	Cohort study	USA	Not stated	16 patients with CA in CCL	Survival (ROSC/ discharge)	One author is employed by a device manufacturer
Spiro 2015	Cohort study	UK	Autopulse	285 IHCA patients	Survival (discharge)	No

RCT- randomised controlled trial; IHCA- in-hospital cardiac arrest; CA- cardiac arrest; ROSC- return of spontaneous circulation; COI- conflict of interest

Table two: risk of bias- randomised controlled studies

Study	Allocation: Generation	Allocation: Concealment	Blinding: Participants[GP1][CK2]	Blinding: Assessors	Outcome: Complete	Outcome: Selective	Other Bias
Taylor 1978	Unclear	Unclear	High	Unclear	High	Unclear	High
Halperin 1993(b)	Unclear	Unclear	High	Unclear	Low	Unclear	High
Lu 2010	Unclear	High	High	High	Low	Unclear	Unclear

Table three: risk of bias- observational studies

Study	Eligibility Criteria	Exposure/ Outcome	Confounding	Follow up
Halperin 1993(a)	Unclear	High	High	Low
Timerman 2004	Low	High	High	Low
Gutteridge 2012	Low	High	Unclear	Low
Parnia 2014	Low	High	High	Low
Retzer 2015	Low	High	High	Low
Spiro 2015	High	High	High	Low

Table four: GRADE table

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Control	**Mechanical Chest Compressions v Manual chest compressions**				
Survival (hospital discharge/ 30-days)	**Study population**		**OR 2.36** (1.44 to 3.89)	601 (5 studies)	⊕⊖⊖⊖ **very low**[1,2]	
	119 per 1000	**242 per 1000** (163 to 345)				
	Moderate					
	108 per 1000	**222 per 1000** (148 to 320)				
Survival (ROSC/ 1-hour)	**Study population**		**OR 2.14** (1.11 to 4.13)	250 (4 studies)	⊕⊖⊖⊖ **very low**[1,2]	
	352 per 1000	**537 per 1000** (376 to 691)				
	Moderate					
	371 per 1000	**558 per 1000** (396 to 709)				
Physiological outcomes	**Study population**		Not estimable	(4 studies)	⊕⊖⊖⊖ **very low**[1,2]	Reported in four studies- three studies reported improvement in a physiological outcomes with the use of a mechanical device
	See comment	See comment				
Safety outcomes	**Study population**		Not estimable	(2 studies)	⊕⊖⊖⊖ **very low**[1,2]	Data from two other studies show broadly comparable injury patterns.
	See comment	See comment				

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk ratio; **OR:** Odds ratio;

[1] Combination of randomised controlled trials and observational studies- all studies associated with medium-high risk of bias
[2] Studies tended to use mechanical devices that are no longer marketed and/or used old resuscitation guidelines and/ or recruited predominantly cardiology patients

Figure one: PRISMA chart

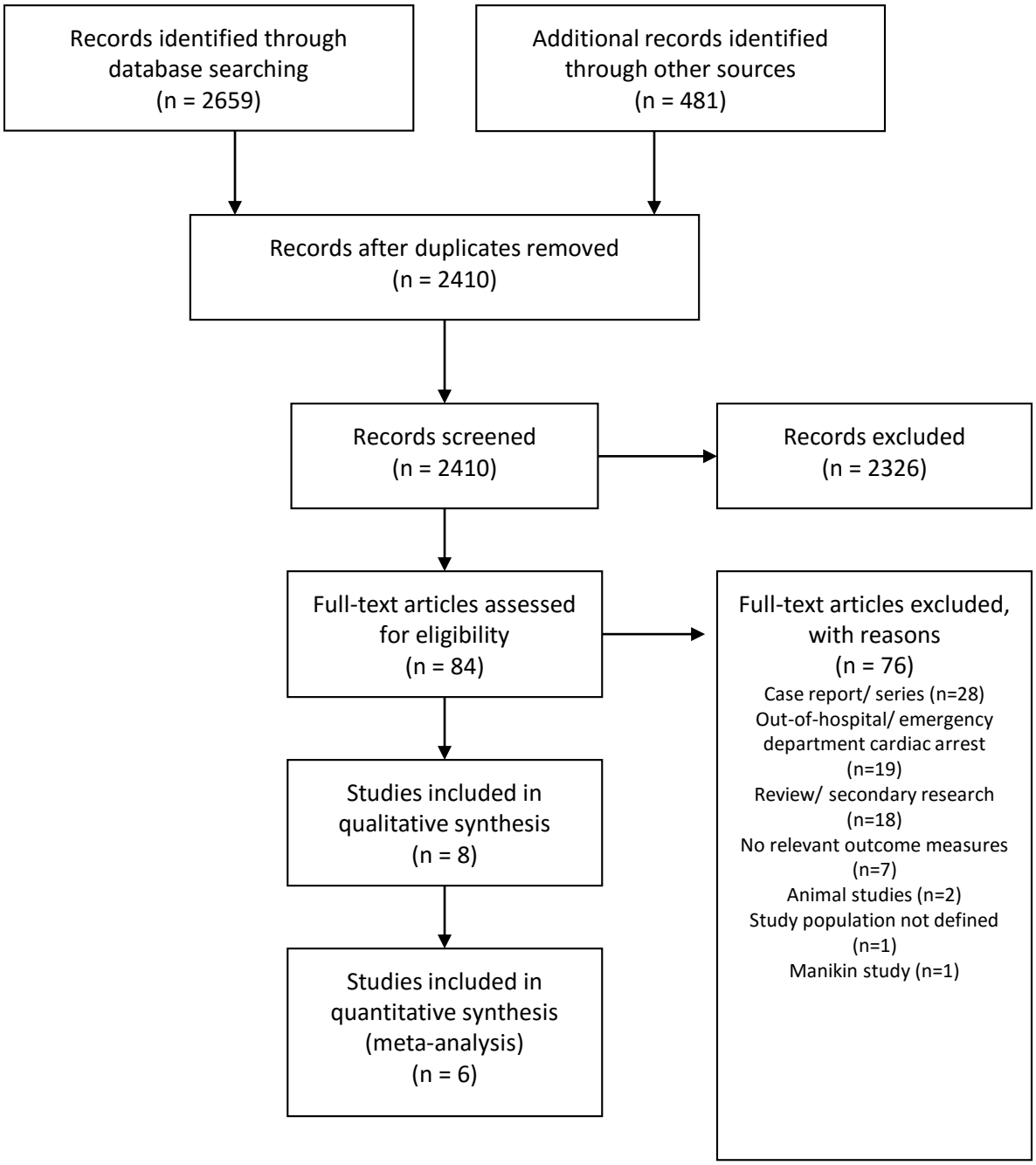

Figure two: Mechanical v manual chest compressions, outcome: survival to hospital discharge

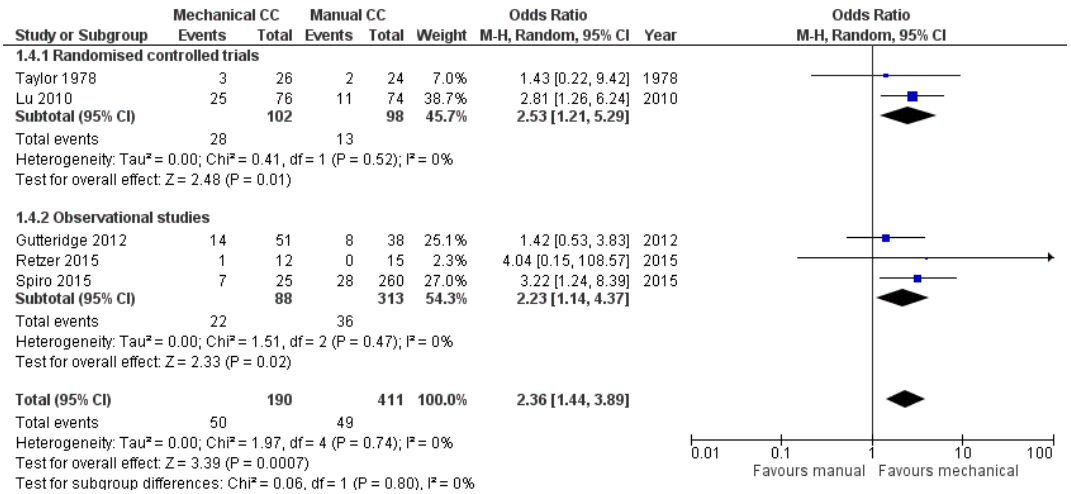

Figure three: Mechanical v manual chest compressions, outcome: Survival at one hour/ ROSC