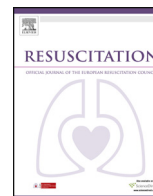




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## Review article

A systematic review of the outcomes reported in cardiac arrest clinical trials: The need for a core outcome set<sup>☆</sup>L. Whitehead<sup>a,b</sup>, G.D. Perkins<sup>a,b</sup>, A. Clarey<sup>c</sup>, K.L. Haywood<sup>d,\*</sup><sup>a</sup> Warwick Medical School, University of Warwick, Gibbet Hill Road, Coventry, CV4 7AL, UK<sup>b</sup> Heart of England NHS Foundation Trust, Bordesley Green East, Birmingham, B9 5SS, UK<sup>c</sup> Royal Victoria Hospital, 274 Grosvenor Rd, Belfast, BT12 6BA, UK<sup>d</sup> Royal College of Nursing Research Institute, Warwick Medical School, University of Warwick, Coventry, CV4 7AL, UK

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## ABSTRACT

**Background:** There is a limited guidance for outcome reporting for cardiac arrest trials. This review was conducted to explore the degree of variation and identify trends in outcome reporting.

**Methods:** Randomised controlled trials enrolling patients with cardiac arrest (2002–2012) were identified by applying a search strategy to four databases. Titles, abstracts and short-listed studies were independently assessed for eligibility. Data on the primary and secondary outcome measures, details of outcome reporting and reproducibility were extracted.

**Results:** 61 studies matched the inclusion criteria. There was wide variation in the focus, method and timing of assessment. Outcomes most commonly reported across studies were: survival (85.2%), activities (52.5%), body structure or function (41.0%), and processes of care (26.2%). Over 160 individual outcomes were reported including 39 different reports of survival measures of which 11 were measurements of ROSC (return of spontaneous circulation). Twenty different assessments of activity limitation were reported; only one was patient-reported. Many assessments were poorly defined or non-reproducible. The majority of outcomes were assessed up to hospital discharge (89.3%). There was no one outcome measure that was assessed across all trials.

**Conclusions:** Outcome reporting in cardiac arrest RCTs lacks consistency and transparency. Guidance for improved outcome reporting is urgently required to reduce this heterogeneity in reporting, improve the quality of assessment in clinical trials, and to support the synthesis of trial data. The results highlight the importance of working towards a core outcome set for cardiac arrest clinical trials to maximise the utility of future research.

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## 1. Introduction

Out of hospital cardiac arrest is one of the leading cause of deaths across Europe and America.<sup>1</sup> It has been estimated that somewhere between 350,000 and 700,000 out of hospital cardiac arrests occur in Europe each year.<sup>2</sup> Internationally survival rates are typically around 9% but can be as low as 2.2%.<sup>3,4</sup> Survival rates from in-hospital cardiac arrest are marginally higher usually ranging between 15 and 20%.<sup>5</sup> Both the low and variable survival rates

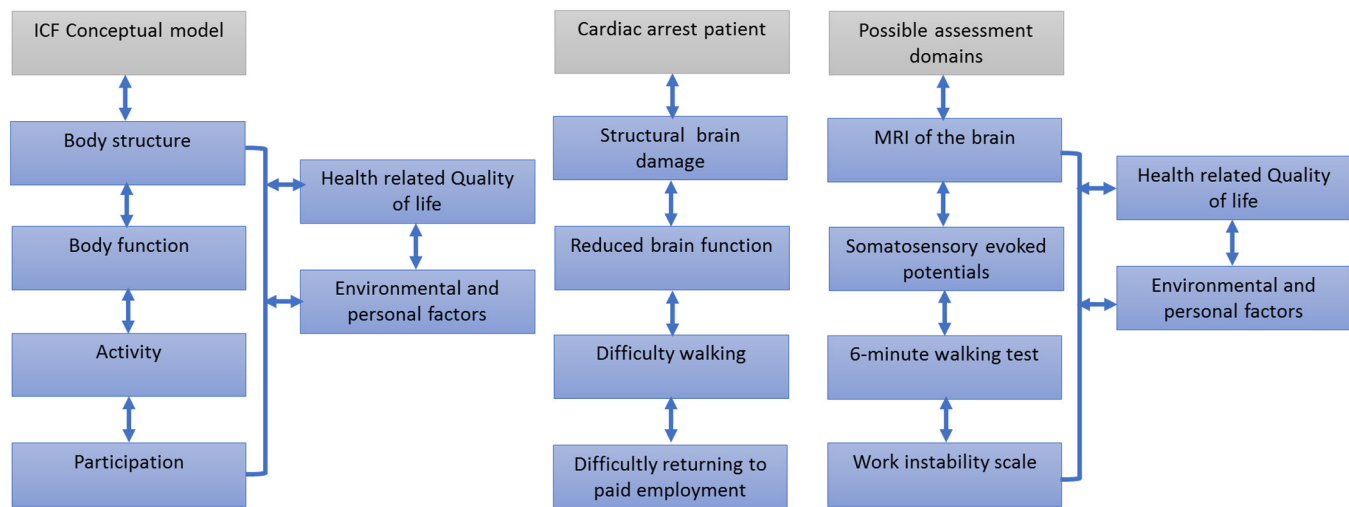
from cardiac arrest are a cause for concern and indicate a need for high quality research in this field.

International and national resuscitation guidelines for the effective care of cardiac arrest patients are underpinned by results from clinical trials and systematic reviews that collate research evidence from trials.<sup>6</sup> Current cardiac arrest research focuses on the different stages of the chain of survival: early recognition and call for help, early cardiopulmonary resuscitation, early defibrillation and post-resuscitation care.<sup>7</sup> However, as reported in other clinical arenas,<sup>8</sup> clinical trials in the cardiac arrest population face major design challenges including recruitment, interventions and standardisation of the range of outcomes assessed. Heterogeneity in outcome reporting is a problem across many health areas<sup>8</sup> including cardiac arrest,<sup>9,10</sup> which can create challenges when completing systematic reviews and meta-analyses with the result that studies may be excluded from data syntheses.<sup>11</sup>

<sup>☆</sup> A Spanish translated version of the abstract of this article appears as Appendix in the final online version at <http://dx.doi.org/10.1016/j.resuscitation.2014.11.013>.

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**Fig. 1.** The International Classification of Function (ICF) conceptual model: illustrated with an example of possible assessment domains for a with the application to a cardiac arrest patient.

52 Researchers are required to pre-define primary and secondary  
53 study outcomes with the primary outcome essential to the trial  
54 sample size calculation.<sup>12</sup> A wide range of approaches to categorising  
55 health outcomes exist including the simple distinction of  
56 clinical (such as death, or impaired cardiac function) or patient-  
57 reported (such as, severity of pain or fatigue).<sup>13,14</sup> The International  
58 Classification of Functioning, Disability and Health (ICF) provides  
59 a useful biopsychosocial model which focuses on health as the  
60 result of an interaction between bodily structure and function,  
61 individual, social and environmental factors<sup>15</sup>. Whilst not an outcome  
62 measure, the ICF framework can be used to provide an  
63 external structure to understanding ‘what’ is measured in clinical  
64 trials and is increasingly recommended in supporting a consistency  
65 in language and reporting in the development of core outcome  
66 sets for clinical trials.<sup>16</sup> Fig. 1 (adapted from [17]) applies the  
67 ICF framework in the context of assessment following a cardiac  
68 arrest, providing an illustration of the wide ranging impact of  
69 cardiac arrest, suggestions of ‘what to assess’ in clinical trials  
70 (core domains) and ‘how’ these assessment might be undertaken  
71 (possible outcome measures). However, guidance for outcome  
72 assessment in cardiac arrest trials does not exist, standards of  
73 outcome reporting have not previously been explored, and the  
74 extent of reporting inconsistencies is unknown. This review aims  
75 to explore the degree of variation and identify trends in outcome  
76 reporting in cardiac arrest randomised controlled trials  
77 (RCTs).

## 78 2. Methods

### 79 2.1. Search strategy

80 An expert librarian was consulted to support the development  
81 of a search strategy to identify all randomised controlled trials  
82 (published between 2002 and 2012) of patients who had sustained  
83 a cardiac arrest. The search strategy key terms are listed in the  
84 electronic Supplementary material (Appendix 1). Four key  
85 databases were searched (January 2013): Medline Ovid, EMBASE  
86 Ovid, CINAHL and The Cochrane Library. Inclusion criteria were:  
87 randomised controlled trials in the adult cardiac arrest population,  
88 irrespective of location, published between 2002 and 2012.  
89 Pilot studies were included where the full trial was not yet published.  
90 Trials were excluded if cardiac arrest patients were not exclusively  
91 the primary population (e.g. ST elevation myocardial

92 infarction (STEMI)). Searches were limited to the English  
93 language.

### 94 2.2. Study selection

95 Titles, abstracts and full text articles were independently  
96 screened for eligibility by two reviewers (LW and AC). Where  
97 disagreement was encountered, a third reviewer (KH), provided the  
98 deciding vote for inclusion.

### 99 2.3. Data extraction

100 A template for data extraction was developed which included,  
101 study specific information: author, year of publication, title, the  
102 location of arrest, the number of patients, study intervention, and  
103 reference to the Utstein template.<sup>22,23</sup> Information about the  
104 primary and secondary outcomes were recorded based on what was  
105 assessed (domain of health), how they were assessed (methods),  
106 when they were assessed and whether the described method was  
107 reproducible (that is, supported by an appropriate citation or sufficient  
108 text to allow reproduction).<sup>24</sup> Data extraction was conducted  
109 by a single reviewer (LW) and independently checked on a random  
110 sample of 10 articles by two further reviewers (GDP, KLH).

111 Outcomes were categorised into six pre-determined assessment  
112 domains. Three categories were informed by the core ICF  
113 framework: (1) body structure and body function (including physiological  
114 and biochemical assessment); (2) activities, and (3) participation.<sup>15,17</sup>  
115 The three additional categories describe outcomes known to be  
116 frequently assessed in cardiac arrest trials, but not included in the  
117 ICF framework—that is, survival and processes of care; and those  
118 that would capture health-related information more widely (that is,  
119 health-related quality of life (HRQL)). Additional sub-domains were  
120 described during data-extraction.

### 121 2.4. Data analysis

122 Patterns of outcome reporting were examined including: the  
123 number of studies and frequency with which outcomes were  
124 assessed, categorisation of outcomes assessed (what was assessed),  
125 reported methods of assessment (how were outcomes assessed),  
126 time frame of reporting and reproducibility.

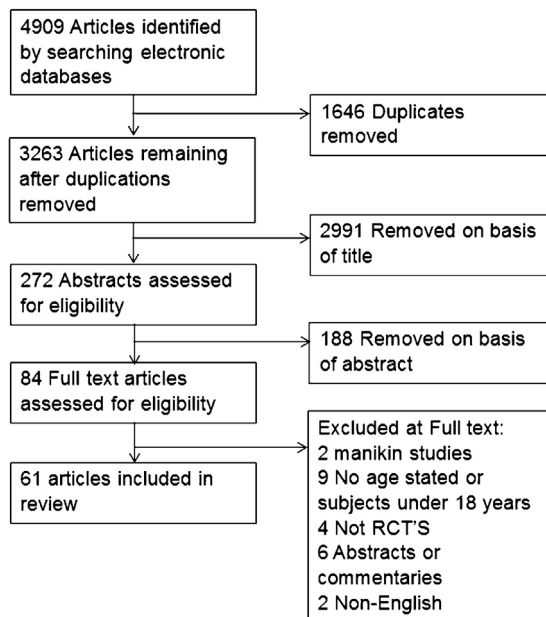


Fig. 2. PRISMA flow chart of study selection.

### 3. Results

#### 3.1. Search strategy

Once duplicates were removed, 3263 articles were identified (Fig. 2). Screening for eligibility resulted in 84 articles which initially met study inclusion criteria. Following full text assessment 23 articles were excluded, resulting in 61 articles meeting the inclusion criteria (Fig. 2). Studies were included from Europe (35), North America (19), Australia (4) and Asia (3).

#### 3.2. Included studies

The number of patients included in the studies ranged from 13 to 9933 (Table 1). The majority of studies ( $n=44$ ; 72.1%) made reference to the Utstein Template and recommendations for outcome reporting.<sup>22,23</sup> Only 3 out of the 61 studies included

Table 1  
Summary of studies included in the review ( $n=61$ ).

Included studies		
Number of participants	1–50	10
	51–100	11
	101–500	27
	501–1000	5
	Over 1000	8
Location of arrest population	In hospital	2 (3.3%)
	Out of hospital	58 (95.1%)
	Either	1 (1.6%)
Type of intervention	Pharmacological	20 (32.8%)
	Therapeutic hypothermia	12 (19.7%)
	Defibrillation techniques (shock delivery, waveforms, patterns)	7 (11.5%)
	Impedance threshold devices	7 (11.5%)
	Monitoring and feed back	4 (6.6%)
	Mechanical CPR	3 (4.9%)
	Other	8 (13.1%)
Reference to the Utstein Template [15,16]	Yes	44 (72.1%)

patients who had experienced a cardiac arrest in the hospital setting. Studies most commonly investigated: pharmacological interventions (32.8%); therapeutic hypothermia (19.7%); defibrillation techniques (11.5%) and Impedance Threshold Devices (11.5%). Distinguishing between primary and secondary outcomes was difficult in seven (11.5%) studies.

#### 3.3. Which outcomes are assessed in cardiac arrest clinical trials?

A total of 164 individual outcomes were reported (Table 2; and electronic Supplementary material Appendix 2). The number of individual outcomes reported within each assessment domain is summarised in Table 2. Sub-domains are listed to capture further variations in assessment. Looking at the total frequency of outcomes reported from each outcome, the majority focused on the assessment of survival ( $n=116$ ; 41.7%) body structure or body function ( $n=75$ ; 27.0%), activity ( $n=48$ ; 17.3%) and processes of care ( $n=39$ ; 14.0%) (Table 2).

#### 3.4. Survival

The majority of studies reported an assessment of survival ( $n=52$ , 85.2%), with 37 (60.7%) and 44 (72.1%) studies reporting a measure from this domain as a primary or secondary outcome, respectively (Tables 2 and 3). 39 individual reports of survival outcomes were assessed (Table 2, listed in electronic Supplementary material Appendix 2), which included 11 different measurement of return of spontaneous circulation (ROSC). The most frequently reported assessment of survival was 'survival to hospital discharge' reported in 30 (49.1%) of trials. This was followed by 'survival to hospital admission' ( $n=13$ , 21.3%). The most frequent assessment of ROSC was 'ROSC' which was assessed in 10 studies (16.3%), however definition between studies varied with some studies providing no details ( $n=3$ ). For full details of definition of ROSC assessments see the electronic Supplementary material Appendix 3). The majority of trials reported short-term survival, that is, up to and including hospital discharge (89.5%). Following hospital discharge, survival was most frequently assessed at 6 months ( $n=3$ ).

#### 3.5. Body structure and function

Almost half ( $n=25$ ; 41.0%) of studies reported at least one measure of body structure or function. (Table 2; electronic Supplementary material Appendix 2). A total of 72 individual (different) pathophysiological outcomes were reported; the majority provided an assessment of circulatory function (24), cerebral function (15), or 'other organ function' (12) (Table 2). Assessments of body structure or function were most commonly reported as secondary outcome measures (74.7%). The majority of these assessments were adequately reported, with 69.3% detailed sufficiently to allow reproduction. All assessments of body structure and function were completed before hospital discharge.

#### 3.6. Activities

Over half (52.5%) of trials reported an assessment of activity limitation. Where reported this was more often as a secondary outcomes ( $n=28$ , 45.9%) rather than a primary outcome ( $n=7$ , 11.5%) (Tables 2 and 4). The majority of activity limitation assessments were reported the short-term limitation in activity up to hospital discharge (68.8%) with only 31.2% of reports assessing activity limitation reporting a longer-term assessment (following hospital discharge).

Twenty individual (different) assessments of activity limitation were described (Table 4); ten focused on short-term outcome.

**Table 2**  
Outcome domains, definition and the number of individual (different)<sup>a</sup> outcomes categorised in each domain and reported in reviewed cardiac arrest RCTs (*n* = 61) (adapted from Whistance et al. [8]).

Outcome domains: <i>What was assessed?</i>	Definition	Number of individual (different) outcomes in each domain: <i>How were outcomes assessed?</i>	Included in cardiac arrest RCTs (total 61) (%)	Frequency of outcomes reported from this domain <sup>b</sup>
<i>Survival</i>	Outcomes related to short- and long-term survival/death rates and cause of death [8]	39	52 (85.2%)	116
<i>Body structure/function</i>	Body structure—anatomical structure. For example, organs, limbs and their components. Body function—physiological and psychological function of body systems. For example, heart function and circulation	72	25 (41.0%)	75
<i>Circulatory function</i>	Assessment of stability of the circulatory system. For example, blood pressure, heart rate, oxygen saturation	24	10	
<i>Cerebral function</i>	Measures of cerebral activity or damage. For example, biomarkers (NSE and S100), cerebral perfusion and intracranial pressure	15	5	
<i>Other organ function</i>	Biochemical markers of system function—other systems including renal and immune functions	12	3	
<i>Cardiac rhythm stability</i>	Any rhythm analysis, pharmacological use to control cardiac rhythm, unusual heart rhythm properties. For example, episodes of VT, premature beats	7	5	
<i>Respiratory function</i>	Indicators of functioning of the respiratory system. For example, intra-thoracic pressures and end tidal carbon dioxide	6	5	
<i>Adverse events</i>	Reporting of adverse events through time points, serious adverse events and any complications	5	5	
<i>Fluid regulation</i>	Assessment of fluid infusion or capillary leakage	3	2	
<i>Activities</i>	Ability of an individual to perform an activity or task. Includes assessment of basic and instrumental activities of daily life (e.g. washing, dressing) and walking. Examples of approaches to assessment include the Barthel Index, <sup>18</sup> Modified Rankin score <sup>25</sup> and cerebral performance category [26]	20	32 (52.5%)	48
<i>Participation</i>	Ability of an individual to participate in life and related activities, as influenced by their health (body structure, body function, activities, and contextual factors). Includes work stability, engaging with family life and usual social role. Examples of approaches to assessment include the Keele Assessment of Participation <sup>26</sup> and the Work Instability Scale [27]	0	0	0
<i>Health-related Quality of life (HRQL)</i>	Assessment of the quality of an individuals' life as influenced by their health—how they feel, what they can do, and how they live life. Assessment may include emotional well-being, symptoms (pain, sleep, fatigue), physical functioning, level of dependency, and social participation. Examples of approaches to assessment include the Short Form 36-item Health Survey (SF-36) [19]	0	0	0
<i>Process of care</i>	Outcomes related to a specific intervention received, also the flow of patients through the healthcare system (e.g., hospital stay, readmission). <sup>3</sup> Examples approaches to assessment in cardiac arrest include: the efficiency of therapeutic hypothermia, quality of CPR variables and the duration of stay in hospital	33	16 (26.2%)	39
<b>Total</b>		<b>164</b>		<b>278</b>

The cerebral performance category (CPC) scale at discharge was the most frequently reported (*n* = 14, 23%). Several CPC variants were described, most frequently the Glasgow Pittsburgh CPC score, reported in a further seven trials (11.4%) (Table 4). However, the reproducibility of all activity assessments was poor (33.3%) (Table 4). For many, terminology and concept definition was poorly defined and inconsistently applied; assessment was variably described as cerebral performance, neurological outcome or functional outcome. With the exception of one poorly defined and non-reproducible patient-reported outcome measure,<sup>28</sup> all assessments were clinician-completed. One study reported patient and family interviews to assist the assessment of activity limitation.<sup>29</sup>

### 3.7. Health-related quality of life and participation

None of the reviewed trials assessed the impact of cardiac arrest on an individual's health-related quality of life (HRQL) or their ability to participate in society.

### 3.8. Processes of care

A small number of studies (*n* = 16, 26.2%) reported assessments which reflected processes of care (Table 2; electronic Supplementary material Appendix 2); in 7 (11.4%) and 12 (19.7%) of the studies these were reported as primary or secondary outcomes, respectively.

**Table 3**Summary of reporting of survival in cardiac arrest RCTs ( $n = 61$ ), showing the top 10 most frequently reported terms used to describe short-<sup>a</sup> or long<sup>b</sup>-term survival.

Individual survival outcome	Number of studies reporting survival as a primary outcome ( $n = 61$ )	Number of studies reporting survival as a secondary outcome ( $n = 61$ )	Frequency reported	Frequency with which assessment was reproducible <sup>c</sup>
<b>Short term survival<sup>a</sup></b>				
Survival to hospital discharge	8	22	30	30
Survival to hospital admission	6	8	14	4
'ROSC <sup>d</sup> '	4	7	11	6
'ROSC <sup>d</sup> rate'	0	6	6	1
24 h Survival	1	3	4	4
Survival to ICU admission	2	1	3	3
Pre-hospital ROSC <sup>d</sup>	1	2	3	1
Any ROSC <sup>d</sup>	1	2	3	3
ROSC <sup>d</sup> at Emergency Department	0	3	3	2
Survival to the Emergency Department	2	0	2	2
<b>Long term survival<sup>b</sup></b>				
Death	0	4	4	3
3-Months survival	1	1	2	0
Mortality a 6-months	0	2	2	1
1 Year survival	0	2	2	0
Awakening at 3-months	1	0	1	1
6-Month survival	1	0	1	0
All-causes mortality 30 days after ROSC	1	0	1	0
3 Year survival	0	1	1	0
30 Day survival	0	1	1	0
Duration of survival	0	1	1	0

<sup>a</sup> Short term survival—defined as any measurement at or before hospital discharge.<sup>b</sup> Long term survival—defined as any measurement after hospital discharge.<sup>c</sup> Reproducible—appropriate citation or sufficient text to allow reproduction.<sup>d</sup> ROSC—return of spontaneous circulation. Various requirements were made in each study to obtain ROSC assessments, definitions for each ROSC measurement are detailed in the electronic Supplementary material Appendix 3.**Table 4**Summary of reporting of 'Activities<sup>a</sup>' in cardiac arrest RCTs ( $n = 61$ ), showing the top 10 most frequently reported methods of assessment used to describe short-<sup>b</sup> or long<sup>c</sup>-term activity limitation.

Individual activity outcome	Number of studies reporting activity as a primary outcome ( $n = 61$ )	Number of studies reporting activity as a secondary outcome ( $n = 61$ )	Frequency reported	Frequency with which assessment was reproducible <sup>d</sup>
<b>Short term outcome<sup>b</sup></b>				
CPC <sup>e</sup> at discharge	2	12	14	3
Glasgow Pittsburgh CPC <sup>f</sup> at discharge	0	7	7	2
Survival and mRS <sup>g</sup>	3	0	3	3
OPC <sup>h</sup> at discharge	0	3	3	1
Survival with location	1	0	1	1
CPC 1 week	0	1	1	0
CPC 24 h	0	1	1	0
Change in CPC	0	1	1	0
'Neurological outcome' assessment of notes	0	1	1	0
Survival to discharge with CPC	0	1	1	0
<b>Longer term outcome<sup>c</sup></b>				
CPC at 6-months	1	4	5	2
CPC at 3-months	0	2	2	0
Survival free from independence at 6 months (Barthel Index <sup>i</sup> )	1	0	1	1
Awake and independent at 3-months	0	1	1	1
Pittsburgh CPC <sup>j</sup> at 6-months	0	1	1	1
Survival at 1-year with CPC	0	1	1	1
CPC at 30-days	0	1	1	0
CPC at 3-years	0	1	1	0
GOS <sup>k</sup> at 3-months	0	1	1	0
HRQL adapted questionnaire at 1-year <sup>l</sup>	0	1	1	0

<sup>a</sup> Ability of an individual to perform an activity or task. Includes assessment of basic and instrumental activities of daily life (e.g. washing, dressing) and walking.<sup>b</sup> Short term survival—defined as any measurement at or before hospital discharge.<sup>c</sup> Long term survival—defined as any measurement after hospital discharge.<sup>d</sup> Reproducible—appropriate citation or sufficient text to allow reproduction.<sup>e</sup> CPC—cerebral performance category.<sup>26</sup><sup>f</sup> Glasgow Pittsburgh CPC score (GP CPC). No original author reference identified.<sup>g</sup> mRS—Modified Rankin Scale.<sup>25</sup><sup>h</sup> OPC—overall performance category.<sup>26</sup><sup>i</sup> Barthel Index [18].<sup>j</sup> Pittsburgh CPC No original author reference identified.<sup>k</sup> GOS—Glasgow Outcome Scale [30].<sup>l</sup> HRQL modification—a modification of the Minnesota Living with Heart Failure Questionnaire and Kansas City Cardiomyopathy Questionnaire. However, this was inadequately detailed and non-reproducible. The authors describe it as a measure of neurological function. The only patient-completed assessment (patient-reported outcome measure (PROM)).

A total of 33 individual (different) assessments were reported; these were assessed to reflect seven sub-domains. Most process measures related to cooling device efficiency which included 11 individual outcomes reported across six trials. Individual outcomes were often specific to an intervention, such as the quality of cardiopulmonary resuscitation, the effectiveness of defibrillation and the effectiveness of cooling devices. Reproducibility of these outcomes was generally high.

### 3.9. Timing of assessment

Although the timing of assessments ranged from pre-hospital care up to three years post-arrest (Fig. 3), assessments were most frequently reported before (64%) or at hospital discharge (25.3%). Long-term outcomes following hospital discharge were infrequently reported (10.7%).

Assessment of survival showed the greatest variation in timing of assessment, with a trajectory that ranged from pre-hospital, throughout the hospital journey and up to three years after hospital discharge. All assessments of body structure and function were reported before hospital discharge. The majority of activity measures were assessed at hospital discharge (66.6%) or after hospital discharge (31.2%). With the exception of one study which assessed Implantable cardioverter defibrillator (ICD) placement at 3 years,<sup>31</sup> all process-based assessments were reported before hospital discharge.

### 3.10. Reproducibility of outcome measures

The overall across all outcome domains the reproducibility of outcomes was 65.5%. The most clearly reported and hence reproducible assessments were the processes of care outcomes (82.1%). There was less clarity of reporting and hence lower levels of reproducibility rates were seen for assessments of survival (69.8%) (Table 3), body structure and function (69.3%). However assessments of activity were poorly reported and hence largely irreproducible (66.7%) (Table 4). Overall, fewer than 20% of reviewed studies (16.4%) included two or more non-reproducible outcome measure.

## 4. Discussion

This review is the first to demonstrate the heterogeneity and inconsistency in outcome reporting in cardiac arrest randomised controlled trials with regards to which outcomes are assessed, and how and when assessments are completed. This review demonstrates inconsistencies across the complete cardiac arrest patient journey, expanding on the work completed by Trzeciak and colleagues, who have previously highlighted the heterogeneity in outcome reporting focusing on post-ROSC interventions.<sup>32</sup>

The complexity of outcome assessment and the lack of guidance that exists for cardiac arrest clinical trials are evident. The current assessment focus on survival, body structure and function, and clinician-based assessment of activity limitation is important to understanding the clinical impact of cardiac arrest, but less helpful when seeking to understand the lived experience of survivors of cardiac arrest. Standardised assessment that captures the outcomes that matter to relevant stakeholders, including patients, is required.

The results of the review are strengthened by use of a transparent data extraction proforma which highlighted key challenges in outcome reporting in clinical trials.<sup>33</sup> The literature searching was extensive, including the four major medical and clinical trial databases. Although only English language publications were included, international publications were included and it is unlikely that any selection bias occurred. We only included trials of adults,

and hence the results are not applicable to the small numbers of trials of cardiac arrest in children. The review did not extend to an evaluation of the feasibility and quality of reported methods of assessment. Understanding the relative quality, in terms of essential measurement and practical properties, is an important requirement when selecting methods of assessment for inclusion in clinical trials.<sup>34</sup>

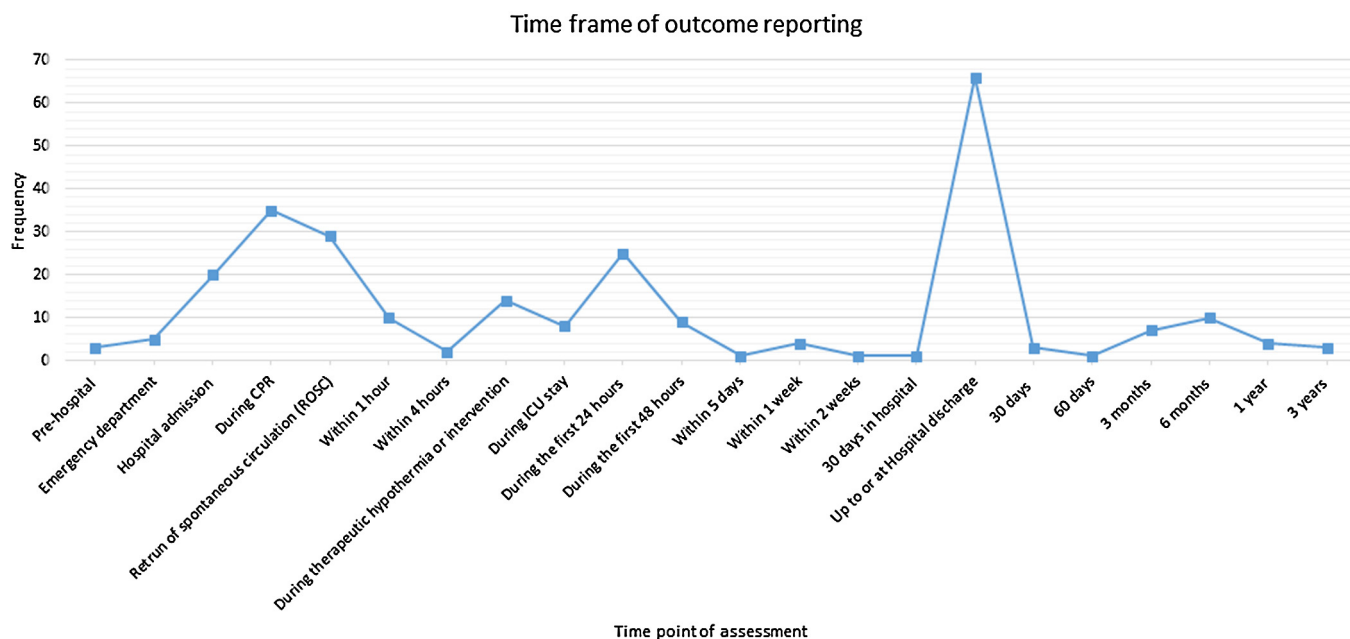
The review focused on outcome reporting in clinical trials and did not include alternative studies, such as observational or cohort studies. Alternative studies have highlighted a greater range of outcome reporting, in particular the assessment of cognitive impairment,<sup>9</sup> health-related quality of life or individual participation in society.<sup>10</sup> However, these studies do not provide specific guidance towards reducing the heterogeneity of outcome reporting in clinical trials. Moreover, the assessment period post cardiac-arrest may have differed in these studies, with a greater focus on the period following hospital discharge. The drivers for assessment focus may differ in these studies with a greater emphasis on understanding the perspective of survivors.<sup>35,36</sup> Well-developed patient reported outcome measures (PROMs) measure aspects of disease burden and ill-health which are important to patients but, as evidenced in this review, have received limited attention in resuscitation research and a PROM-specific to cardiac arrest survivors does not exist.<sup>10,37</sup>

The study has highlighted an important lack of clarity in reporting methods, with many potential assessment methods excluded due to inadequate detail or supporting reference. Similarly, it was often difficult to determine how an assessment had been administered—for example, clinician-completed, analysis of hospital notes, patient or proxy interview. Such concerns over data integrity and inadequate reporting have been reported by other authors.<sup>8,38–40</sup> Data completeness and transparency of reporting is essential to ensuring that trial data is appropriately utilised. The CONSORT (Consolidated Standards of Reporting Trials) statement,<sup>24,41</sup> and recent PRO (Patient Reported Outcome)-extension<sup>33</sup> aims to facilitate transparent and complete recording of clinician trials, including the optimal reporting of outcome data.

Reflecting the poor survival rates in this patient population,<sup>4</sup> survival is a critical outcome for clinical trials of cardiac arrest and was the most frequently assessed outcome. However, there was significant variation in the way in which survival was assessed: 39 different assessment of survival were identified, a result that is comparable to the multiple reports of mortality identified in other trials of critical care—for example, oesophagectomy.<sup>42</sup> Moreover, although 'survival to hospital discharge' was the most frequently assessed measure of survival, this was reported by fewer than 50% of studies. Similarly, ROSC was frequently reported, but 11 different approaches were identified: the most common was 'ROSC' for which only 27.3% included a definition similar to the Utstein recommendations.<sup>23</sup> The remaining studies included a range of definitions (45.4%) (listed in electronic Supplementary material, Appendix 3) or no detail at all (27.3%).

Similarly wide inconsistencies in the reporting activity assessments were reported. Reviews of outcome measurements used in critical care patients<sup>43</sup> and numerous surgical conditions – for example, oesophagectomy<sup>42</sup> breast reconstruction,<sup>44</sup> and colorectal cancer surgery<sup>8</sup> – have reported similar inconsistencies in outcome reporting, absent or wide variations in definitions of similar outcomes, and problems with reporting bias, thus reducing the possibility of data synthesis or case comparison.

The review has highlighted the lack of consistency in outcome reporting in clinical trials of cardiac arrest survivors over the short- and longer-term follow-up periods, the dominance of clinician-based assessment, and the limited attempts to capture the perspective of survivors or their close relatives/carers. A standardised approach towards outcome reporting for cardiac arrest trials,



**Fig. 3.** Timing of outcome assessment.

across the post-arrest trajectory, is required which will enhance cross-study comparisons and future data synthesis.

By seeking to develop a core outcome set, the COSCA (Core Outcome Set for Cardiac Arrest) initiative will provide guidance towards improving the standardisation of outcome reporting in future cardiac arrest clinical trials<sup>37</sup> (<http://www.comet-initiative.org/studies/details/284>). Whilst not intending to limit assessment, a core outcome set will seek to specify both the minimum number of outcomes (What to measure) and robust methods of assessment (How to measure) that should be reported for all clinical trials of a particular health condition.<sup>45,46</sup> Multiple stakeholders, including cardiac arrest survivors and their partners will be involved in this process to ensure that outcomes of relevance to the wider stakeholder group are considered, and methods of assessment that are relevant, comprehensive and robust are recommended.

The use of a core outcome set in future cardiac arrest clinical trials will reduce outcome reporting bias and support the future synthesis and meta-analysis of trial data. Moreover, the recommendation for high quality, comprehensive and relevant methods of assessment will provide sufficiently robust evidence to underpin future healthcare and health technology evaluations.<sup>8</sup>

## 5. Conclusion

This review highlights the wide variation, lack of consistency and poor descriptions of outcome reporting in clinical trials of cardiac arrest. It also highlights the dominance of clinical-based assessment with a limited focus on patient-reported outcomes. Guidance for improved outcome reporting is urgently required to reduce the heterogeneity in reporting, improve the quality and transparency of assessment in clinical trials, and to support the synthesis of trial data. The results highlight the importance of working towards a core outcome set for cardiac arrest clinical trials, to complement the Utstein template and maximise the utility of future research.

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## Conflict of interest statement

I can confirm that Laura Whitehead, Gavin Perkins, Andrew Clarey and Kirstie Haywood do not present any conflicts of interest related to this publication.

## Uncited references

Refs. [20,21].

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.resuscitation.2014.11.013>.

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