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Review

# Assessing health-related quality of life (HRQoL) in survivors of out-of-hospital cardiac arrest: A systematic review of patient-reported outcome measures

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ABSTRACT

*Aim:* High quality evidence of out-of-hospital cardiac arrest (OHCA) survivors' health-related quality of life (HRQoL) can measure the long-term impact of CA. The aim of this study was to critically appraise the evidence of psychometric quality and acceptability of measures used in the assessment of HRQoL in cardiac arrest survivors.
*Methods:* Systematic literature searches (2004–2017) and named author searches to identify articles pertaining to the measurement of HRQoL. Data on study quality, measurement and practical properties were extracted and assessed against international standards.
*Results:* From 356 reviewed abstracts, 69 articles were assessed in full. 25 provided evidence for 10 measures of HRQoL: one condition-specific; three generic profile measures; two generic index; and four utility measures. Although limited, evidence for measurement validity was strongest for the HUI3 and SF-36. However, evidence for reliability, content validity, responsiveness and interpretability and acceptability was generally limited or not available in the CA population for all measures.
*Conclusions:* This review has demonstrated that a measure of quality of life specific to OHCA survivors is not available. Limited evidence of validity exists for one utility measure – the HUI3 – and a generic profile – the SF-36. Robust evidence of the quality and acceptability of HRQoL measures in OHCA was limited or not available. Future collaborative research must seek to urgently establish the relevance and acceptability of these measures to OHCA survivors, to establish robust evidence of essential measurement and practical properties over the short and long-term, and to inform future HRQoL assessment in the OHCA population.



## Background

The importance of seeking to better understand and assess the long-term impact of cardiac arrest on survivors is evidenced by the recent inclusion of quality of life (QoL) and patient-reported outcomes (PRO) as supplementary outcomes in the standardised reporting frameworks for observational studies drawn from resuscitation registries [1]. However, historically, PROs and QoL have rarely been reported in resuscitation research [2], and assessment guidance for this population is lacking. Moreover, the concept of survival to a good QoL has been poorly explored from the perspective of survivors of out-of-hospital cardiac arrest (OHCA) and their care givers'.

Well-developed patient-reported outcome measures (PROMs) are questionnaires containing one or more items, designed to provide a structured assessment of an individual's health-related

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quality of life (HRQoL). PROMs may be generic – containing items reflective of the broad concepts of HRQoL and therefore applicable to the general population – or specific – to a condition (for example, traumatic brain injury), aspect or domain of health (for example, fatigue), or population (for example, children). Patient-derived, specific measures are expected to be both more relevant and responsive to important changes in health than their generic counterparts, with their combined use therefore recommended [3]. An earlier review of quality of life after cardiac arrest described significant heterogeneity in HRQoL reporting, listing more than 40 measures of either general HRQoL or specific health domains [4]. Although the quality and acceptability of these measures was not assessed – and hence assessment recommendations not made – recommendations included a need for greater standardisation in HRQoL measurement with which to support study comparison.

In this systematic review, we aim to critically appraise and summarise published evidence of the quality and acceptability of clearly defined, multi-item patient-reported measures of HRQoL following completion by OHCA survivors or appropriate proxy. The evidence synthesis will provide a transparent evaluation with which to inform measurement selection for future application in clinical research, cardiac arrest registries and audit, and routine practice.

## Methods

### *Identification of studies and measures: search strategy*

Medical subject headings (MeSH terms) and free text searching was used to develop terms reflective of: 1) population – cardiac arrest; 2) assessment type – including patient-reported outcome measures; HRQoL; and 3) measurement and practical properties (Appendix 1) [5–7].

Two databases were searched (MEDLINE, EMBASE ((OVID)); 2004 to March 2017) (Fig. 1). A named author search was also conducted. Citation lists of included articles and measurement reviews in resuscitation research were also reviewed [2,4,8].

### *Study inclusion/exclusion*

All study designs were included if they provided evidence of measurement and/or practical properties (summarised below; detailed Table X) for clearly defined and reproducible multi-item, patient or proxy completed measures of HRQoL, following completion in the target population of OHCA survivors.

Titles and abstracts of potential articles were assessed for eligibility by one experienced reviewer (KH). Full-text articles were retrieved and selected based on English Language, and publication in peer reviewed journal. Abstracts, conference proceedings and studies pertaining to domain specific, diagnostic and screening measures were excluded. The list of included studies was checked for completeness by the review co-authors.

HRQoL measures were categorised as: specific (condition or population) or generic (profile; utility).

### *Data extraction*

Data extractions were informed by established guidance for measurement evaluation [6,9,10], published reviews [7,11,12], and the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist [13,14]. Both study and PROM-specific information was extracted. Evidence on the following measurement properties was sought (Table 1): validity (content; construct – structural; convergent/divergent; discriminant); reliability (internal consistency; test-retest; measurement error); responsiveness; interpretation (including data quality (end-effects; change scores); smallest detectable difference (SDD), within-person (minimal important change (MIC)) and between-group (minimal important difference (MID)) [6,9,15].Although not included within the COSMIN framework, addition evidence of practical properties – acceptability (respondent burden; relevance) and feasibility (time, cost) [11,15,16] – and the involvement of patients as active research partners [11,16,17] was sought. Data were extracted by a single, experienced reviewer (KH).

To inform a comparative analysis of PROM content, individual questions (items) were considered as per the revised Wilson and Cleary HRQoL Model: that is, symptoms, functional status (physical, cognitive, psychological, and social/role) and general health perceptions [18,19].

### *Assessment of study methodological quality*

Study methodological quality was evaluated per measurement property on the 4-point COSMIN rating scale (excellent, good, fair, poor) and determined by the lowest rating in each assessment section [14].

### *Assessment of PROM quality*

Each measurement property was judged against an existing checklist (Table 1) [10–12]. Evidence was graded as: adequate (+) [reaches accepted standards]; conflicting (+/−); inadequate (−) [does not research accepted standards]; or indeterminate (?) [the results are difficult to define]. Whilst the 'quality' of evidence detailing practical properties was not determined, the extent of active patient engagement was graded (Table 1) [11,16,17].

### *Qualitative data synthesis*

The data synthesis combines four factors: 1) number of studies reporting evidence per measure; 2) the degree of consistency between evaluations; 3) the quality of the reported measurement property (Table 1); and 4s) tudy methodological quality (COSMIN scores) [11,20]. The final quality score has two elements: first, the overall quality of a measurement property is reported as: adequate (+), conflicting (+/−), inadequate (−), or indeterminate (?). Second, evidence is categorised: 'strong', 'moderate', 'limited', 'conflicting', or 'unknown' [20].

## Results

### *Identification of studies and measures*

Study and PROM identification is summarised as per PRISMA guidance (Fig. 1); www.prisma-statement.org). Twenty-five articles (Appendix 2) provided limited evidence for ten measures (Tables 2 [21–31] and 3 [32–56]): one condition-specific – the Quality of Life after Brain Injury questionnaire (QOLIBRI) [21] – and nine generic: three profile– the Short-Form 36-item Health Survey (SF-36 version 1 (v1)) [22], it's modification (SF-36 version 2 (v2)) [23], and the Short-Form 12-item version (SF-12v2) [24]; two index – the Life Satisfaction 11-item Checklist (LiSat-11) [25] and the Quality of Life Scale (QOLS) [26,27]; and four utility – the 15-dimension health-related quality of life instrument (15D) [28], EuroQol EQ-5D-3L [29], Health Utility Index version 3 (HUI3) [30], and the SF-6D [31] (Table 2). The SF-36 versions differ in the number of response options for seven role limitation items (Table 2); evidence suggests that v2 has improved reliability, validity and responsiveness [23]. Evidence for the two versions will be presented separately, but

**Table 1**
Assessment criteria for the quality of reported measurement properties [10,12,13],evidence of practical properties[15] and patient involvement in PROM development/evaluation [11,17].

| Measurement properties [10,12,13] | Rating | Assessment of quality |
|---|---|---|
| Validity | | |
| *Content validity* | + | Authors provide a clear description of the measurement aim, target population, concept(s) measured and process of item selection. Members of the target population and experts in the field were clearly identified as being involved in development. For measures applied for the first time in a new population, evidence that the views of members of the target population (and experts in the field) have been sought to determine relevance, comprehension and comprehensiveness. |
| *the extent to which the item content of a measure is an adequate reflection of the construct being measured* | ? | Insufficient evidence available |
| | – | No detail re measurement aim, target population, concept(s) measured, process of item selection; members of the target population or experts were not specifically involved in development.<br>For measures applied for the first time in a new population, evidence whereby the relevance and acceptability of the measure with members of the target audience or experts was not provided. |
| *Construct validity – Structural validity* | + | Factors should explain 50% of the variance |
| *the extent to which PROM scores adequately reflect the dimensionality of the construct being measured.* | ? | Explained variance not reported |
| | – | Factors explain < 50% of the variance |
| *Construct validity – Hypothesis testing* | + | Correlations with measures of the same construct should be >0.50 OR at least 75% of the results in accordance with hypothesized associations AND correlations with related constructs should be higher than with those reported with unrelated constructs |
| *convergent (the extent to which measures of related constructs are related to each other)* | ? | Only report correlations with unrelated constructs OR the extent to which between group differences are expected is not described/justified |
| | – | Correlations with measures of the same construct are <0.50 OR < 75% of the results in accordance with hypothesized associations OR correlations with related constructs are lower than those reported with unrelated constructs |
| *Construct validity – Hypothesis testing: Known-groups validity (not included in COSMIN checklist)* | + | Hypothesized between group differences are supported (or can be assumed) AND between group differences are statistically significant |
| *discriminant (the extent to which a measure can demonstrate differences between groups known to differ on important variables)* | ? | Between group differences are poorly hypothesized, but between group differences are statistically significant |
| | – | Expected between group difference poorly defined or justified AND the statistical significance of between group differences not reported. |
| Reliability | | |
| *Internal consistency* | + | Cronbach's alpha(s) > 0.70 |
| *the extent to which items within a measure are internally consistent* | ? | Cronbach's alpha not evaluated or dimensionality unknown |
| | – | Cronbach's alpha(s) < 0.70 |
| Reliability *(test-retest/inter-rater/inter-rater)* | + | Intra-class Correlation Coefficient (ICC)/weighted Kappa >0.70 OR Pearson's r > 0.80 |
| the *extent to which a measure provides the same results on repeated completions, assuming no change in the underlying health state* | ? | Neither ICC/weighted Kappa, not Pearson's r evaluated |
| | – | ICC/weighted Kappa <0.70 OR Pearson's r < 0.80 |
| Reliability – *measurement error* | N/A | Descriptive (not rated) |
| The systematic and random error of a score that cannot be attributed to the true change in the construct being measured | | |
| Responsiveness | + | Change-score correlations with measures of the same construct are >0.50 OR at least 75% of the results are in accordance with hypothesized associations OR the Area Under the Curve (AUC) is >0.70 AND change-score correlations with measures of related constructs are higher than those reported with unrelated constructs |
| *the ability to detect important change over time in the construct being measured (criterion/construct-based assessment)* | ? | Solely correlations with unrelated constructs |
| | – | Change-score correlations with measure of the same construct <0.50 OR < 75% of the results are in accordance with hypothesized associations OR AUC is <0.70 AND change-score correlations with related constructs are lower than those reported with unrelated constructs |
| Interpretability | *N/A* | Descriptive (not rated) – requires evidence that the minimal important (within-person) change (MIC) and/or minimal importance (between group) difference (MID) exceeds evidence of the smallest detectable difference (SDD). Supported by evidence of acceptable data quality (that is, score distribution, absence of end effects (Floor/Ceiling) |
| *the degree to which qualitative meaning can be assigned to PROM scores or change in scores – that is, clinical or commonly understood implications can be linked with the score/change* | | |
| *includes consideration of completion rates and data quality (end effects; change in scores)* | | |
| Practical properties [15] | | |
| Acceptability | N/A | Descriptive (not rated) – evidence of respondent burden and relevance |
| is the PROM acceptable to patients? | | |
| Feasibility | N/A | Descriptive (not rated) – time and cost to administer and score |
| Is the PROM easy to administer and process? | | |
| Patient Engagement [11,17] | | |
| Patient and Public Involvement/Engagement in PROM development/evaluation [11,17] | ++ | User-led – broadly interpreted, patients control, direct and manage the PROM development/evaluation |
| *the extent of active involvement/collaboration in PROM development/evaluation assessed at 3-levels* | + | Collaboration – involves active engagement. Ongoing partnership between researchers and patients in PROM development/evaluation. Patients may be members of a research team or advisory group and collaborate on design, development and/or dissemination. |
| | – | Consultation – patients are consulted for their views, for example, through focus group, but these views are not necessarily adopted. |

**Table 2**
Summary and item content of the reviewed HRQoL measures (n = 10).

| PROM | Origin | Conceptual focus | Domains of HRQoL Ferrans et al., [18,19][a] (items per domain) | | | | | | How to score |
|---|---|---|---|---|---|---|---|---|---|
| Developer | | Response options; Recall period Completion format | *Functional Status* | | | | | | |
| Web-link | | Language versions | Symptoms | Physical | Cognition | Psychological | Social/Role | General Health perception | |
| Cost (license) *Time to complete* | | | | | | | | | |
| Condition-specific (n1) | | | | | | | | | |
| Quality of Life after Brain Injury | USA | HRQOL for individuals after traumatic brain injury | Pain – *included in 'physical problems'* | Physical problems (5) – includes movement problems, pain, vision/hearing, | Cognition (7) – concentrate, express self, remember, problem solve, decisions, navigate, thinking | View of self (7) – energy, motivation, self-esteem, looks, achievements, self-perception, future | Daily life & autonomy (7) – independence, getting out, domestic, finances, work, social, feeling in charge. | Satisfaction and view of oneself included in 'emotions and view of self' | Item responses are summed and divided by the number of responses to give a mean value. |
| (QOLIBRI) | | Designed to capture changes in HRQOL in areas commonly affected by brain injury. Development guided by a HRQoL assessment model: a person's perspective on his or her subjective health condition, functioning and wellbeing in the domains of physical, psychological (emotional and cognitive), social and daily life. | Energy – *included in 'view of self'* | | | Emotions (5) –anxiety, depression, ager/aggression, loneliness, boredom. | Social relationships (6) – family, friends, partner, sex life, affection, attitudes of others | | (Score cannot be calculated if > one third of responses (per domain or in total) are missing). |
| Bullinger et al., [21] | | 37 items across 6-domains of health – domains explore: | | | | | | | 6 sub-scales can be used separately or combined to provide a HRQOL profile; or summed to produce an Index score. |
| http://www.qolibrinet.com/index.htm | | a.'Satisfaction with key aspects of life' (4 domains): Cognition (7 items); Self (7 items); Daily life and autonomy (7); Social relationships (6 items); | | | | | | | Scores converted to a 0–100 scale, where 0 = worst possible HRQOL and 100 = best. |
| *License:* No license fee – free to use for researchers, clinicians and non-profit organizations. | | b.Feeling bothered with key aspects of life (2 domains); Emotions (5 items) and Physical problems (5 items). | | | | | | | http://www.qolibrinet.com/scoring.htm |
| Developers request that users register use of the QOLIBRI on the website | | *Response options* | | | | | | | |
| *Completion time:* | | Satisfaction items on a 1–5 scale – where 1 = npt at all satisfied ad 5 = very satisfied. | | | | | | | |
| *Self-complete approx. 7–10 mins* | | Feeling bothered items on a 1–5 scale – where 1 = very bothered and 5 = not at all bothered. | | | | | | | |
| *User guide:* see weblink | | *Recall period:* The past week Completion: Self- or interview-administered. *Language:* > 10 language versions: http://www.qolibrinet.com/registration.htm | | | | | | | |
| *Generic – profile measures (n3)* | | | | | | | | | |
| Short Form 36-item Health Survey – version 1 and version 2 | USA | Functional health and well-being from the patient's perspective – underpinned by 8 health domains across both physical (4) and mental (4) aspects of health | Bodily Pain (BP) (2) | Physical functioning (PF) (10) | – | Mental health (MH) (5); | Social functioning (SF) (2) | General health (GH) (5) – perceived well-being | 2-ways of presenting the data: |
| (SF-36 v1/SF-36 v2) | | Total 35 items plus one health transition item | Vitality (VT) – fatigue/tiredness (2) | Role limitation (RP) (4) | | Role limitation (RE) (3) | | | 2.1 8-domain profile 2.2 Two component summary scales: Physical Component Summary (PCS); |
| Ware & Sherbourne, [22]; Jenkinson et al., [23] | | *Response options:* Between 3 and 6-level categorical response options per item | | | | | | | |

| PROM | Origin | Conceptual focus | Domains of HRQoL Ferrans et al., [18,19][a] (items per domain) | | | | | | How to score |
|---|---|---|---|---|---|---|---|---|---|
| Developer | | Response options; Recall period Completion format | *Functional Status* | | | | | | |
| Web-link | | Language versions | Symptoms | Physical | Cognition | Psychological | Social/Role | General Health perception | |
| Cost (license) *Time to complete* | | | | | | | | | |
| https://campaign.optum.com/content/optum/en/optum-outcomes/what-we-do/health-surveys.html | | *Revision of the SF-36v1 to v2:* | | | | | | | Mental Component Summary (MCS |
| License for use per project; minimum fee $USA | | 5-level response options replaced dichotomous options for 7 items in the role function items. Other modifications improved content and layout [23]. | | | | | | | Scoring requires SF-36 specific algorithm. |
| *Survey license request:* | | *Recall period:* Standard recall 4-weeks; Acute recall 1-week | | | | | | | Norm-based scoring: score transformed to 0–100 (mean 50 (SD 10)) |
| https://www.optum.com/campaign/ls/outcomes-survey-request.html | | *Completion:* Self, Interview (in person; telephone) or proxy supported | | | | | | | Population-based norms available |
| Completion time: *Range 5–30 minutes (not reported in Cardiac Arrest population)* | | *Language:* > 170 language versions: https://campaign.optum.com/optum-outcomes/what-we-do/health-survey-translation/surveys-translation-tables.html | | | | | | | |
| http://www.qolibrinet.com/scoring.htm | | The IQOLA project supported the development of conceptually equivalent and culturally appropriate translations (see http://www.iqola.org/ *NOTE:* Utility values A preference-based utility index – the SF-6D – can be calculated following completion of the SF-36 to inform economic analyses https://www.shef.ac.uk/scharr/sections/heds/mvh/sf-6d | | | | | | | |
| Short Form 12-item Health Survey – version 2 | USA | Functional health and well-being from the patient's perspective – underpinned by 8 health domains across both physical (4) and mental (4) aspects of health | Bodily Pain (BP) (1) | Physical functioning (PF) (2) | – | Mental health (MH) (2); | Social Functioning (SF) (1) | General health (GH) (5) – perceived well-being (1) | Scores presented as two component summary scales only: |
| (SF-12 v2) | | Total 11 items plus one health transition item | Vitality (VT) – fatigue/tiredness(1) | Role limitation (RP) (2) | | Role limitation (RE) (2) | | | Physical Component Summary (PCS); |
| Ware et al.,[24] | | *Response options:* Between 3 and 6-level categorical response options per item | | | | | | | Mental Component Summary (MCS |
| https://campaign.optum.com/content/optum/en/optum-outcomes/what-we-do/health-surveys.html | | *Recall period:* Standard recall 4-weeks; Acute recall 1-week | | | | | | | Scoring requires SF-12 specific algorithm. |
| *License for use per project; minimum fee $USA* | | *Completion:* Self, Interview (in person; telephone) or proxy supported | | | | | | | Norm-based scoring: score transformed to 0–100 (mean 50 (SD 10)) |
| *Survey license request:* | | *Language:* > 170 language versions: | | | | | | | Population-based norms available |
| https://www.optum.com/campaign/ls/outcomes-survey-request.html | | https://campaign.optum.com/optum-outcomes/what-we-do/health-survey-translation/surveys-translation-tables.html The IQOLA project supported the development of conceptually equivalent and culturally appropriate translations (see http://www.iqola.org/ NOTE: Utility values | | | | | | | Summary scores: Physical (PCS), Mental (MCS) (mean 50, sd 10) |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | A preference-based utility index – the SF-6D – can be calculated following completion of the SF-36 to inform economic analyses https://www.shef.ac.uk/scharr/sections/heds/mvh/sf-6d | | | | | | |
| *Generic – Index (n2/10)* | | | | | | | | |
| Life Satisfaction Checklist | Sweden | Generic self-report checklist of Life Satisfaction (aspiration – achievements gap) across 10 domains of life plus life as a whole). | – | (ADL) Ability to manage my self-care (1) | – | Psychological health (1) | My vocational situation (1) | My life as a whole (1) | Developers describe 4factors: |
| LiSat-11 | | Developed in Swedish population (aged 18–64yrs). LiSat-11 is an extension of the LiSat-9: addition of i) somatic and ii) psychological health. | | (Somatic) Physical health (1) | | | My financial situation (1) | | Closeness (3 items) |
| *License:* Not clear | | Factor analysis of original measure described a 4-factor solution | | | | | My leisure situation (1) | | Health (3 items) |
| *Completion time:* approx. 5 min (not reported in CA population) | | *Response options:* 6-grade ordinal scale from 1 (very dissatisfied) to 6 (very satisfied) | | | | | My contact with friends and acquaintances (1) | | Spare time (2 items) |
| *Users-guide:* – | | *Recall period:* Not clear | | | | | My sex life (1) | | Provision (2 items) |
| *No active web-site identified* | | *Completion:* Interview or self-administered. For use with adults (aged 18 years and older). | | | | | My family life (1) | | But – alpha levels were low; therefore, index score supported. |
| | | *Formats:* Unclear | | | | | My partner relationship (1) | | Item summation. Index score reported. |
| | | *Language: Unclear* | | | | | | | |
| Quality of Life Scale | USA | Generic self-report measure of quality of life for use across patient groups and culture – 16-items across 6 conceptual domains: material and physical well-being; relationships with other people; social, community and civic activities; personal development and fulfillment; recreation; independence (1 item). | – | Health – being physically fit and vigorous (1) | – | Understanding yourself (1) | Material comforts (1) | Independence – doing for yourself (1) | Item summation to give a total index score: range from 16 to 112; where higher scores indicate better QoL. |
| QOLS | | *Response options*: 7-point 'delighted (7)-terrible (1)' scale OR 7-point satisfaction scale (anchored 'very satisfied (7)' to 'very dissatisfied (1)' | | Participating in active recreation (1) | | | Relationships (1) | | Average total score for healthy population is approx. 90 see Burckhardt & Anderson, [27] |
| Flanagan, [26]; Burckhardt & Anderson, [27] | | *Recall period:* At this time | | | | | Having and rearing children (1) | | |
| *License:* QOLS is copyrighted by Carol Burckhardt. Contact burckhac@ohsu.edu for a free copy of the English language version. | | *Completion:* Interview or self-administered. For use with adults (aged 18 years and older). Requires approximately 5 min. | | | | | Close relationships (1) | | |
| *Completion time:* approx. 5 min (not reported in CA population) | | *Formats:* Unclear | | | | | Close friends (1) | | |
| *Users-guide:* see Burckhardt & Anderson, [27] | | *Language:* At least 16 – include English, Swedish, Norwegian, and Hebrew translations. | | | | | Helping others (1) | | |
| *No active web-site identified* | | | | | | | Participation-organizations (1)<br>Learning (1)<br>Work – job or home (1)<br>Expressing yourself – creatively (1)<br>Socializing (1)<br>Reading, music etc (1) | | |

Table 2 (*Continued*)

| PROM | Origin | Conceptual focus | Domains of HRQoL Ferrans et al., [18,19][a] (items per domain) | | | | | | How to score |
|---|---|---|---|---|---|---|---|---|---|
| Developer | | Response options; Recall period Completion format | *Functional Status* | | | | | | |
| Web-link | | Language versions | Symptoms | Physical | Cognition | Psychological | Social/Role | General Health perception | |
| Cost (license)<br>*Time to complete* | | | | | | | | | |
| *Generic – preference-based utility measures (n4)* | | | | | | | | | |
| The 15-dimension Health-Related Quality of Life Instrument | Finland | *Conceptual underpinning not clearly reported.* | Discomfort and symptoms (disco) (1) | Mobility (move)(1) | – | Mental function *(cognition and memory)(1)* | Usual activities (uact) (1) | – | Utility index score (multiattribute utility theory)): algorithm to score: http://www.15d-instrument.net/valuation-system/ |
| 15D | | *Descriptive system – 'health-related quality of life of adults' described across 15 dimensions.* | Vitality (vital) (1) | Sleeping (sleep)(1) | | Depression (dep)(1)<br>Distress (distr)(1) | Sexual activity (sex)(1) | | 15D single index on a scale 0.11–1.00; where 0 is dead and 1.00 is perfect health *(0.0162 is unconscious or comatose)* |
| Sintonen,[28] | | *Response options: 5-ordinal level response options (more/less of an attribute)* | | Body function – Breathing (breath)(1) | | | | | |
| http://www.15d-instrument.net/15d/ | | *Recall period: present health status.* | | Eating (eat)(1) | | | | | |
| *License:* | | *Completion: Primarily self-administered. For use with adults (aged 16years and older). Interview and proxy also supported.* | | Elimination/excretion (excret)(1) | | | | | |
| *Completion time:* less than 10-min (but not reported in CA population) | | ** Version for Adolescents – 16D (for children aged 12–15yrs) and for younger children – 17D (aged 8–11yrs) also available.* | | Senses – Vision (see)(1) | | | | | |
| *User guide: see web-site* | | *Formats:* | | Hearing (hear)(1) | | | | | |
| *Originally developed in 1981; revised in 1986 and 1993* | | *Language: Original Finnish for Finland; now >30 language versions.* http://www.15d-instrument.net/15d/languages/ | | Speech (speech)(1) (8) | | | | | |
| EuroQoL EQ-5D-3L | Multiple | Standardized, preference-based measure of health status for use in clinical and economic appraisal *d* | Pain/discomfort (1) | Mobility Self-care (2) | – | Anxiety/depression (1) | Usual activities *(including work, study, housework, family or leisure activities)* (1) | – | 2-ways of presenting the data: |
| EuroQoL Group, [29] | | EQ-5D descriptive system: 5 items across '5 domains' *(2/5 reflect physical functional status)* | | | | | | | 1. EQ-5D-5L Index value |
| http://www.euroqol.org/home.html | | *(EQ VAS – self-rated health on a 20 cm vertical visual analogue scale (VAS))* | | | | | | | EuroQoL-specific coding algorithms to support calculation of Utility Score (Index): |
| *License for use per project; Free.* | | *Response options:* 3-level categorical response options per item (no problems (1) to extreme problems (3) | | | | | | | Crosswalk values sets from EQ-5D-3L support calculation of EQ-5D-5L utility score. |
| *But use must be registered on EuroQol website* | | *Completion of all items will produce a 5-digit number describing the respondent's health state (but the numerals 1–5 have no inherent arithmetic properties and should not be used as a cardinal score)* | | | | | | | Index range –0.59 to 1.00; |
| http://www.euroqol.org/register-to-use-eq-5d.html | | *Recall period:* Today | | | | | | | where 1.00 is perfect quality of life, 0 is death, and <0 is a health state worse than death |
| *Completion time:* | | *Completion:* Self, Interview (in person; telephone) or proxy (two proxy versions) supported | | | | | | | Country-specific value sets and population-based norms available |
| *Less than 5 minutes (not reported in Cardiac Arrest population)* | | http://www.euroqol.org/about-eq-5d/modes-of-administration.html | | | | | | | Report both measure of central tendency and a measure of dispersion: eg, mean and SD; median and percentiles. |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| *User guide: free at the following link –*<br><br>http://www.euroqol.org/fileadmin/user_upload/Documenten/PDF/Folders_Flyers/EQ-5D-5L_UserGuide_2015.pdf | | *Formats:* PDA; pen and paper; proxy paper; tablet; telephone; web.<br><br>http://www.euroqol.org/eq-5d-products/eq-5d-5l.html<br>Language: > 120 language versions (see www.euroqol.org/) | | | | | | 2. EQ-5D-5L descriptive system as a health profile – reflects individual item scores. 2.1 Report as the frequency or proportion of reported problems for each level for each dimension<br>2.2 Dichotomise into 'No problems' (1) and 'Problems' (2–5) – report frequencies of reported problems. |
| Health Utility Index – 3<br><br>(HUI-3)<br><br>Feeney et al,[30]<br><br>http://www.healthutilities.com/<br><br>*License for use per project; minimum fee $USA 3k [Horsman, 2003]*<br>*Completion time:*<br><br>*Approx. 8mins self-completion*<br>*Approx 3mins interview completion (not reported in Cardiac Arrest population)*<br>*User guide: available once HUI3 is purchased* | Canada | *Preference-based, comprehensive system for measuring health status and HRQoL and for producing utility scores. Applicable for all persons aged 5years and older.*<br>*HUI3 classification system: describes the comprehensive health state of an individual across 8 attributes of general health (6/8 items reflect physical functional status)*<br>*Response options: Between 4 and 6 descriptive response options (ability/disability)*<br>*Recall periodl: 'Current' or 'Usual' – 'Usual' recommended for clinical studies. Choice of 1-week, 2-week or 4-week recall available.*<br>*Language: 16 versions – including English, Chinese, Dutch, French, German, Italian, Japanese, Portuguese, Russian, Spanish, Swedish* | Pain – severity (1) | Ambulation – *ability to walk (distances)*<br><br>Dexterity – ability to use hands and fingers<br><br>Senses – Vision<br><br>Senses – Hearing<br><br>Speech – *ability to be understood* (5) | Cognition – *ability to solve day to day problems* (1) | Emotion – *happiness and interest in life* (1) | – | – | 2-ways of presenting the data:<br><br>1.HUI3 utility index: scored using single and multi-attribute utility functions.<br><br>HUI-specific coding algorithms to support calculation of single-attribute Utility Score (Index); Index range –0.36 to 1.00;<br><br>Where 1.00 is perfect health, 0 is dead, <0 is a health state worse than death<br>Population-based norms available<br>2. Multi-attribute descriptive system – 'Classification system' – reflects individual item scores. |
| Short Form 6-dimensions SF-6D<br><br>*NOTE: Scoring of the SF-6D requires completion of the SF-36or SF-12*<br>Brazier et al., [31]<br>https://www.shef.ac.uk/scharr/sections/heds/mvh/sf-6d<br>*License – as per SF-36/12*<br>*Completion time* – as per SF-36/12 | UK | Generic, preference-based single index measure.<br>Produces 6-dimension scores (6D), a 6-digit health state and a utility value.<br>If from SF-36: 11 (of 36) items; | Bodily Pain (BP) (1)<br><br>Vitality (VT) – fatigue/tiredness (1) | Physical functioning (PF) (1)<br>Role limitation (RP) (1) | – | Mental health (1) | Social functioning (1) | – | 0.46 to 1.00; where 0 is dead and 1.00 is perfect health |

[a] Item content distribution according to the Ferrans et al revision to the Wilson and Cleary HRQOL model [18,19].

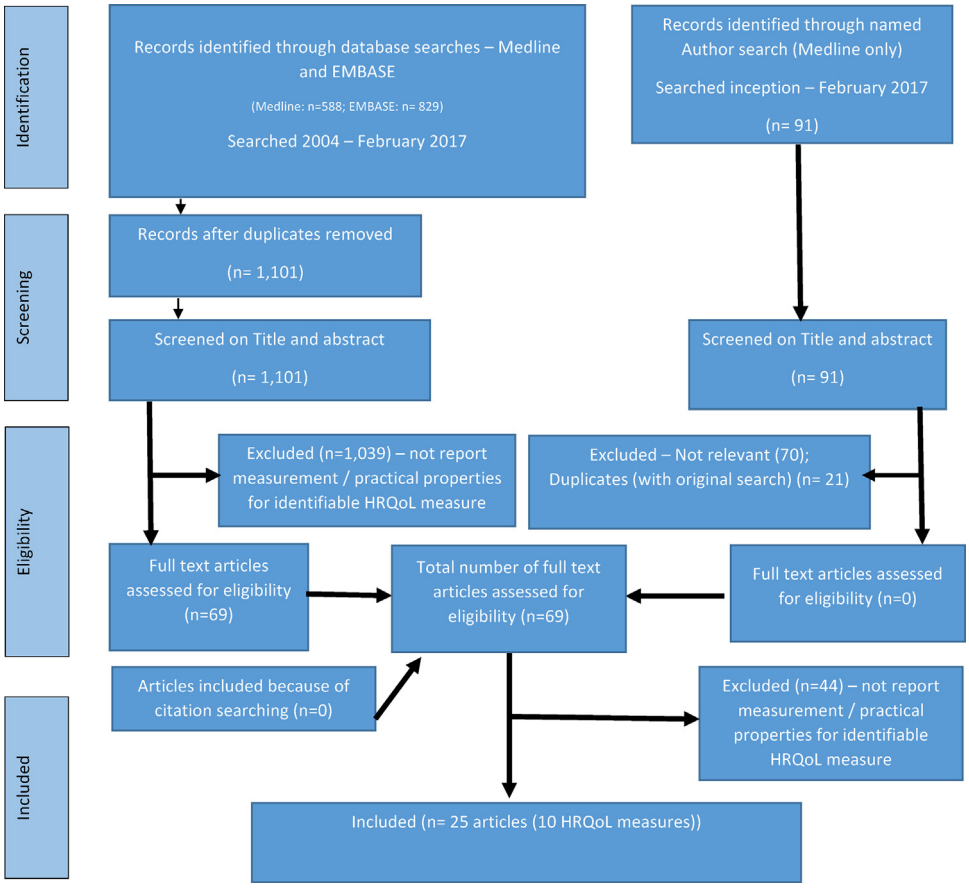


**Fig. 1.** Review of measures for Cardiac Arrest Clinical Trials – PRISMA flow-chart for article inclusion.

collectively appraised for the SF-36. The longest measure was the QOLIBRI (37-items); the shortest the EQ-5D-3L (5-items).

*Patient and study characteristics (Appendix 1)*

Sample sizes ranged from 20 to 1188; age ranged from 18 to more than 75 years. Studies were from international settings: mostly North America (n 7/25) and the Netherlands (n 7/25). Most were cross-sectional evaluations – trial sub-studies or cohort studies. Three were specific to PROM psychometric evaluations [46,52,23].

*Measurement properties and methodological quality*

Study methodological quality is reported per reported measurement property per PROM (Table 3) (data extraction in Appendix 2); the evidence synthesis is reported in Table 4 (detailed in Appendix 3).

*Validity – content validity*

The comparative analysis highlights similarities and discrepancies in PROM content and assessment focus (Table 2).

*Symptoms* – Except for the two generic index measures, all measures assess symptoms, including pain and/or discomfort. Most (6/10) assess fatigue – the SF-36 provides the most detailed assessment (2 items); most include just single items.

*Functional status – physical*

All measures assess physical function – the SF-36 and SF-12 include the greater number of items with this focus. Two of the five EQ-5D-3L items assess limitations in self-care and mobility, whilst 2/8 HUI3 items assess ambulation (walking distances) and dexterity. Several measures assess vision (QOLIBRI, 15D, HUI3), hearing (QOLIBRI, 15D, HUI3) and speech (15D, HUI3).

*Functional status – cognition:* Just 3/10 measures specifically assess cognitive impairment – the QOLIBRI includes 7 items, whilst the HUI3 and 15D include just single items.

*Functional status – psychological:* All measures assess mental or emotional well-being. The QOLIBRI includes several items that explore an individual's 'view of self' and concerns about anxiety, anger, depression and loneliness. The SF-36 and SF-12 also include multiple items to assess mental health concerns. The 15-D includes two items; the LiSat-11, QOLS, EQ-5D-3L and HUI3 include single items.

*Functional status – social/role:* Apart from the HUI3, all measures assess limitations in, or satisfaction with, social or role functioning. The QOLIBRI provides a detailed assessment of the impact of brain injury on daily life and autonomy. The SF-36 includes items relating to social function. The remaining measures provide a more limited assessment, including items that reflect changes in self-care and usual activities.

*General health perception:* Just five measures – the QOLIBRI, SF-36, SF-12, LiSat-11 and QOLS – include items pertaining to perceived well-being.

*Validity – construct validity (structural; construct)*

Evidence of construct validity was limited (Tables 3 and 4). Five studies reported acceptable evidence of convergent or known-groups validity for the HUI3 (Table 3). One good quality study demonstrated the ability of the HUI3 to discriminate between sur-

**Table 3**
Methodological quality (COSMIN[a]) of each study (n = 25) per HRQoL measure (n = 10) and quality of investigated measurement properties[b].

| Measure Study (n) | Country (language) | Subjects (n) | Reliability | | Validity | | | Responsivene | Interpretability Include score distribution – item/scale level |
|---|---|---|---|---|---|---|---|---|---|
| | | | Internal consistency | Temporal stability | Content | Construct | | | |
| | | | | | | Convergent/ divergent | Known-groups | | |
| *Health-related Quality of Life (n = 10)* | | | | | | | | | |
| *Condition-specific (n = 1/10)* | | | | | | | | | |
| QOLIBRI (2 studies) | | | | | | | | | |
| Middlekamp et al. [32] | NL<br>Dutch | 20 | | | | +<br>Poor | | | |
| Mak et al. [33] | NL<br>Dutch | 59 | | | | +<br>Good | | | |
| *Generic Profile (n = 3/10)* | | | | | | | | | |
| SF-36v1 (8 studies) | | | | | | | | | |
| Graf et al. [34] | Germany<br>German | 81 | +<br>Poor | | | | +<br>Poor | | |
| Bro-Jeppesen et al. [35] | Denmark<br>Danish | 156 | +<br>Poor | | | | +<br>Poor | | |
| Mouleart et al. [36] | NL<br>Dutch | 63 | | | | PCS + MCS +<br>Fair | PCS + MCS +<br>Fair | | 2/63 patients had >15% missing items for SF-36 (same as FAI, CIQ, CFQ, FSS) |
| Reinhard et al. [37] | Estonia | 44 | | | | | +<br>Poor | | |
| Kowalik et al. [38] | Poland<br>Polish | 65 | | | | +<br>Poor | +<br>Poor | | |
| Moulaert et al. [39] | NL<br>Dutch | 143 | | | | | +<br>Fair | | |
| Boyce-van der Wal et al. [40] | NL<br>Dutch | 77 | | | | +<br>Fair | +<br>Fair | | |
| SF-36v2 (2 studies) | | | | | | | | | |
| Cronberg et al. [41] | Sweden<br>Swedish | 946 | | | | | ?<br>Fair | | In-person (or telephone) interview (n455)(proxy 8%) completion equivalent to 'Two Simple Questions' rate – and higher than several other measures (MMSE, IQCODE) |
| Orbo et al. [42] | Norway<br>Norwegian | 33 | | | | PCS + MCS +<br>Fair | | ES: MCS −0.38; PCS 0.21 | *Reliable Change Index:*<br>Deterioration: MCS 5 (15%) of patients; PCS 0.<br>Improvement: MCS 0; PCS 4 (12%).<br>No change: MCS 28 (86%); PCS 29 (88%) |
| SF-12v2 (4 studies) | | | | | | | | | |
| Deasy et al. [43] | Australia<br>English | 56 | | | | | +<br>Fair | | Item/scale level data – no end effects<br>'Good' telephone interview completion rates; but 'challenges with loss to follow-up' |
| Beesems et al. [44] | NL<br>Danish | 220 | | | | | +<br>Fair | | |
| Smith et al. [45] | Australia<br>English | 687 | | | | | +<br>Fair | | 'Good' telephone completion rates |
| Andrews et al. [46] | Australia<br>English | 1188 | | | | PCS + MCS +<br>Fair | PCS + MCS +<br>Fair | | 79% of those known to be alive at 12/12) responded to interviews<br>Missing items at scale level: 3.4% (34/1188)<br>No end effects |
| *Generic Index (n = 2/10))* | | | | | | | | | |
| LiSat-11 (1 study) | | | | | | | | | |
| Wallin et al. [47] | Sweden<br>Swedish | 45 | +<br>Poor | | | | –<br>Poor | | |
| QOLS (1 study) | | | | | | | | | |
| Wilson et al. [48] | English<br>UK | 56 | | | | | –<br>Poor | | |

Table 3 (*Continued*)

| Measure Study (n) | Country (language) | Subjects (n) | Reliability | | Validity | | | Responsivene | Interpretability Include score distribution – item/scale level |
|---|---|---|---|---|---|---|---|---|---|
| | | | Internal consistency | Temporal stability | Content | Construct | | | |
| | | | | | | Convergent/ divergent | Known-groups | | |
| *Preference-based utility (n = 4/10)* | | | | | | | | | |
| 15D (1 study) | | | | | | | | | |
| Tainen et al. [49] | Finland Finish | 49 | | | | ? Poor | + Fair | | Interviews 1yr: 85.6% response rate |
| EQ-5D-3L (3 studies) | | | | | | | | | |
| Deasy et al. [43] | Australia English | 56 | | | | | | | Item level: At 1-year: >70% report 'No problems' with Mobility, Self-care, Pain |
| Smith et al. [45] | Australia English | 687 | | | | | | | Item level: At 1-year: >30% No problems in 5/5 domains: Self-care (87.6%); Pain (71.7%); Usual activities (67.8%); Mobility (66.4%); Anxiety (66.2%) |
| Andrews et al. [46] | Australia English | 1188 | | | | +/– Fair | + Fair | | Large ceiling effects and poor discrimination at higher levels of QoL/function 75th percentile is equal to a score of 1.00 for all GOSE categories above lower moderate disability |
| HUI3 (7 studies) | | | | | | | | | |
| Nichol et al. [50] | USA US-English | 86 | | | | ? Fair | + Good | | |
| Stiell et al. [51] | USA US-English | 268 | | | | | | | Score range −0.30 to 1.0 >0.80 134/316 (42%); <0.80 134/316 (42%); 0.60-0.80 56/316 (18%) <0.60 78/316 (25%) (Unknown n = 48 (Known survivors 316)) *(HUI3 > 25% have scores <0.60 at 12/12 (severe impairment))* (CPC at 12/12: Good 88%; Mod 9%; Severe 6%) |
| Raina et al. [52] | USA US-English | 21 | | + Poor | | +/– Poor | | | |
| Steill et al. [53] | USA US-English | 305 | | | | + Fair | + Fair | | HUI3 median 0.84 (IQR 0.61–0.97) *Approximate range −0.25 to 1.00. Skewed distribution – End effects? – unclear how many scored 1.00* |
| Longstretch et al. [54] | USA US-English | 32 | | | | | + Fair | | At 3/12: authors report that missing most often in those not reporting full recovery (so scores may overestimate QoL) |
| Raina et al. [55] | USA US-English | 29 | | | | +/– Poor | | ES 0.43 (1–6mth); 0.19 (6–12mth); 0.26 (1–12mth) | Mean scores at HD,1/6/12mths: HUI3 severe disability all time-points (all <0.68); vs. GOS-E (low mod disability) vs. CPC and mRS suggest 'good outcome' |
| Nichol et al. [56] | USA US-English | 644 | | | | ? Fair | + Fair | | Mean HUI3 (*scores <0.70 = severe impairment*): 3/12 0.75 (0.33); 6/12 0.74 (0.35); Worst 0.71 (0.35); Best 0.77 (0.33) *Range and end effects NR.?Skewed distribution towards better health.* Predictive model: Suggests that for every unit change in mRS, this predicts a change of −0.06 in the HUI3 |
| SF-6D (1) | | | | | | | | | |
| Andrews et al. [46] | Australia English | 1188 | | | | + Fair | + Fair | | No end effects*: strong evidence of variability in SF-6D score across GOSE categories (in patients reporting full health on EQ-5D-3L). SF-6D scores improved as GOSE scores improve* |

[a] COSMIN – Consensus on Standards for Measurement Instruments. Four-grade rating for study methodological quality: Excellent, Good, Fair Poor.

[b] Quality of Measurement property: Evidence is graded as: adequate (+) [reaches accepted standards]; conflicting (+/–); inadequate (–) [does not research accepted standards]; or indeterminate (?) [the results are difficult to define]. (Adapted from 10,12)(Table 1 for detail).

**Table 4**
Data synthesis, levels of evidence and overall quality of reviewed measures of HRQoL (n = 10)[a].

| PROM[b] | Number of evaluations | Reliability | | | Validity | | Construct Validity | | Responsiveness | Interpretation |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Internal consistency | Temporal stability | Measurement error | Content validity | Structural validity | Hypothesis testing | Known-groups | Responsiveness | |
| Condition-specific (1) | | | | | | | | | | |
| QOLIBRI | 2 | | | | | | + Moderate | | | |
| Generic measures (9) | | | | | | | | | | |
| Profile measures (3/9) | | | | | | | | | | |
| SF-36v1 | 8 | + Unknown | | | | | + Limited | + Moderate | | |
| SF-36v2 | 2 | | | | | | + Moderate | + Moderate | ES only (small) | + Unknown |
| SF-12 | 4 | | | | | | + Limited | + Limited | | + Moderate |
| Generic Index (2/9) | | | | | | | | | | |
| LiSat-11 | 1 | + Unknown | | | | | | + Unknown | | |
| QOLS | 1 | | | | | | | + Unknown | | |
| Preference-based Utility measures (4/9) | | | | | | | | | | |
| 15D | 1 | | | | | | ? Unknown | + Limited | | |
| EQ-5D-3L | 3 | | | | | | +/− Limited | +/− Limited | | - Moderate |
| HUI-3 | 7 | | − Unknown | | | | +/− Conflicting | + Moderate | ES only (small) | |
| SF-6D | 1 | | | | | | + Limited | + Limited | | + Moderate |

[a] Data synthesis: The data were qualitatively synthesized to determine the overall quality of measurement properties and acceptability of each reviewed HRQoL measure. The synthesis took the following factors into account: 1) methodological quality of the reviewed studies (COSMIN scores); 2) the number of studies reporting evidence of measurement properties per measure; 3) the results for each measurement property for each measure; and 4) the consistency of results between reviewed studies.
The data synthesis score has two elements [11,12,20].
First, the overall quality of a measurement property was reported as: adequate (+), not adequate (−), conflicting (+/−), or unclear/indeterminate (?).
Second, levels of evidence for the overall quality of each measurement property were further defined to indicate:
'strong' − consistent findings in multiple studies of good methodological quality OR in one study of excellent quality;
'moderate' − consistent findings in multiple studies of fair methodological quality OR in one study of good methodological quality;
'limited' − one study of fair methodological quality;
'conflicting' − conflicting findings; or
'unknown' evidence − only studies of poor methodological quality
Where the data entry box is left blank, this signifies no available evidence.
[b] PROM acronyms (detailed in text and Tables 1 and 2)

vivors per duration of resuscitation.[50] Two smaller studies reported the ability of the HUI3 to distinguish between survivors grouped per CPC scores at 1-year post-arrest [53], or when identified as 'fully recovered' versus 'dependent' [54]. Limited evidence also suggests that the 15D can discriminate between survivors grouped per CPC or mRS scores at 6-months [49]. Small levels of association between the HUI3 and measures of global disability such as the CPC (pre/at hospital discharge) [50,52], the GOS-E and mRS [52] have been reported. However, this association appears to increase when CPC is assessed post-discharge [52]. Similarly, small to moderate levels of association have also been reported between the 15D and the CPS and mRS at 6-months [49]. Despite the inclusion of a cognition-specific item, only small levels of association have been reported between the HUI3 and a cognition-specific measure (Telephone Interview of Cognitive Status (r = 0.37)); and small to moderate levels (range r = 0.23 to r = −0.45) with measures of psychological well-being [55]. More moderate associations have been reported with measures of self-care and reintegration into 'normal living' [55], suggesting a stronger focus on physical function.

Seven studies report acceptable (judged to be of at least 'fair' quality) evidence of validity for the SF-36, SF-12 and SF-6D (Table 3). As hypothesized, associations between the SF-12 summary scores and global measures of disability (GOSE with MCS r = 0.31; with PCS r = 0.44) were smaller than with other generic measures of health status (PCS with EQ-5D-3L r = 0.63; with SF-6D r = 0.69; MCS with SF-6D r = 0.56) [46]. Similar levels of association were reported between both SF-12 summary scores and the SF-6D – suggesting that the SF-6D has an equal focus on both physical and mental well-being. The significantly stronger association between the SF-12 PCS and EQ-5D-3L (r = 0.63) than with the MCS (r = 0.29) highlights the greater focus of the EQ-5D-3L on physical limitations. However, a moderate to strong association between the EQ-5D-3L and the SF-6D was reported (r = 0.65) suggesting that they assess similar, although not identical, aspects of health status. Similarly, the moderate association between the SF-6D and GOSE at 12-months following the arrest (r = 0.52), suggests that whilst there is assessment overlap, there is substantial divergence in measurement focus.

Moderate associations between both the SF-36 PCS and MCS and the Fatigue Severity Scale (range r = 0.57 to r = 0.61) highlight the multi-faceted nature of fatigue [36]. Strong associations between the SF-36 MCS and the Hospital Anxiety and Depression Scale (range r = −0.77 to −0.84) supports the ability of the MCS to capture aspects of emotional well-being in this population [36,42]. The moderate association between the SF-36 PCS and the Cognitive Failures Questionnaire (r = 0.55) suggests that, whilst not specifically including items about cognition, the PCS is influenced by aspects of cognitive impairment.

Acceptable evidence details the ability of the SF-12 MCS and PCS, the SF-6D, and EQ-5D-3L to discriminate between survivors of cardiac arrest who return to work at 12-months, and on gender (lower health state for females) [46]. Scores on the SF-12 PCS and SF-6D discriminate between survivors discharged to home or an alternative at 12-months. Scores across 6/8 SF-36 domains (not bodily pain or general health) discriminate between survivors with and without cognitive impairment, with unimpaired survivors reporting better levels of well-being [40]. However, scores on the QOLS were unable to discriminate between survivors with or without anoxic brain injury [48].

Several studies report the ability of measures to discriminate between the health status of OHCA survivors and that of the general population. Both SF-36 summary scales demonstrate worse health state in OHCA survivors at 3-years when compared to that of the Dutch general population [36], and at 5-years when compared to an age- and gender-matched German population [34]. At 12-months, evidence suggests that the SF-12 PCS for OHCA survivors is lower, but the MCS equivalent, to both the Australian [45] and Dutch [44] population norm. However, evidence suggests that the MCS is lower for younger Australian survivors at 12-months than age-matched members of the general population [43]. Similarly, a deteriorating state of mental well-being has been reported at 12-months (when compared to that reported at 3-months), with scores significantly lower than that of an age- and gender-matched 'norm' population [42]. However, non-statistically significant between group differences for OHCA survivors and the general population have also been reported on the SF-36 [41]. There was no difference in 15D utility scores for OHCA survivors at 6-months and the general Finnish population [49], although statistically significant differences in two single domains – usual activities and sexual activities – were reported.

Limited evidence of convergent validity was reported for the QOLIBRI following completion by a small group of survivors with neurological impairment referred for rehabilitation at 2-years [32], and a larger group at 6-months post arrest [33]. Although a small study, the strong association between the QOLIBRI and cognition (Cognitive Failures Questionnaire (range r = 0.77 to r = 0.86) and the moderate to strong association with a measure of participation and autonomy (range r = −0.44 to r = −0.86) supports the ability of the QOLIBRI to capture issues associated with cognitive impairment and participation in OHCA survivors with neurological impairment [32].

Limited evidence suggests that there are gender differences for psychological health when assessed with the LiSat-11, with more men reporting greater satisfaction with their health [47].

The structural validity of the reviewed measures was not reported.

*Reliability (internal consistency; test-retest; measurement error)*

Limited evidence of acceptable inter-rater reliability was reported for the HUI3 following completion by just ten patients [55]. Limited evidence of acceptable internal consistency reliability was reported for all domains of the SF-36 following completion by 81 patients [34]. Additionally, there is limited evidence of internal consistency for the LiSat-11 [47], and QOLS [48]. Evidence of measurement reliability and measurement error was not identified for the remaining measures (Tables 3 and 4).

*Responsiveness*

Statistically significant between group differences were reported for several SF-36 domains – role emotional, mental health and general health – at 12-months in favour of survivors who had participated in the active arm of a rehabilitation trial; of note, there was no between group difference at 3-months [39]. Responsiveness statistics were not reported. A statistically significant reduction in mental well-being (SF-36 MCS) was reported between 3 and 12-months, accompanied by a non-statistically significant improvement in physical well-being (PCS) [42]. Small effect size statistics, comparable to those reported for the Hospital Anxiety and Depression Scale (HADS), were also reported for both component scores. Small effect size statistics were reported for the HUI3 up to 12-months post-arrest in a small prospective cohort [55]. However, robust evidence of measurement responsiveness following completion with OHCA survivors was not reviewed for any measure.

*Interpretation (completion rates, data quality and meaning)*

For OHCA survivors who agreed to complete the reviewed measures, acceptable completion rates have been reported for all generic measures completed following interview-administration between 6 and 12-months post-arrest (range 73% to 92%) (Table 2). Most non-responders were reportedly 'lost to follow-up'. However, evidence suggests that non-responders are more likely to be those

with significant limitations, and hence scores may overestimate quality of life in survivors [54].

Acceptable postal self-completion rates (72%) have also been reported for the SF-36(v1) at 36-months post-arrest.[36] A missing item rate of greater than 15% was reported – a rate comparable to other self-completed measures in this population.

Good data quality, with no evidence of end-effects, and low levels of missing data (3.4%) was reported for the SF-12 and SF-6D [46]. However, although missing data was low (total 1.0%; patients 0.5%; proxy 2.7%), large ceiling effects were reported for the EQ-5D-3L – with more than 46% of patients (and 23% of proxy) achieving a maximum score of 1.00 (perfect health) at 12-months. However, for this group, scores on the SF-6D and GOSE suggested substantial variability in health, with concerns related to mental health and vitality (issues not addressed in detail by the EQ-5D-3L). Data quality was not evidenced for the remaining measures.

No studies have attempted to define the SDD, MIC or MID following completion with survivors of cardiac arrest. However, Orbo et al [42],calculated the Reliable Change Index (RCI) as a measure of the reliability of change scores on the SF-36 between 3 and 12-months post-OHCA. A reliable deterioration in mental well-being summary score (MCS) and improvement in physical well-being summary scores (PCS) was reported for fifteen percent and twelve percent of survivors, respectively, between 3 and 12-months. However, for most survivors, at the domain level, change in mental or physical well-being was not statistically significant, but remained below that of an age- and gender-matched population [42].

*Feasibility*

The feasibility of PROM completion has not been reported.

Where patients are very poorly or experience significant neurological deficit, proxy completion by a close relative or health professional is an option. However, there are few evaluations of proxy completion in this population. Acceptable SF-36 interview-administered, proxy-completion rates have been reported [41].A stronger association between proxy completed EQ-5D-3L and the GOSE (0.67), than with survivor self-report (0.47), has been reported at 12-months post-arrest [46]. Missing data was greater following EQ-5D-3L proxy-completion (2.7% versus 0.5% in patients) [46]. The associated cost, and concerns over loss to follow-up and associated reporting bias, have not been reported for PROM self- or proxy completion.

*Acceptability and patient involvement*

There is no evidence that OHCA survivors have been involved in the development or appraisal of PROM content for relevance or acceptability.

## Discussion

High quality and relevant HRQoL assessment provides essential survivor-derived evidence of the often profound, long-term impact of cardiac arrest. However, the survivors' perspective is not widely reflected in current resuscitation research, and a measure specific to cardiac-arrest does not exist. Apart from one utility measure – the HUI3–and a generic profile – the SF-36–for which limited, but acceptable evidence of measurement validity was reviewed, robust evidence of the quality and acceptability of HRQoL measures in this population was largely limited or not available.

This is the first systematic review of patient-reported measures of HRQoL following completion by OHCA survivors with which to inform measurement selection. The review is strengthened by a transparent assessment of both study and measurement methodological quality according to consensus-derived standards [7,13,14], and by reference to an established HRQoL framework with which to underpin a comparative evaluation of PROM content [18,19]. Although undertaken by one, experienced reviewer (KH), the study inclusion, data extraction and synthesis was discussed with an established working group of clinical academics, researchers and patients (as part of the Core Outcome Set for Cardiac Arrest (COSCA) initiative) [2,57], thus enhancing the transparency of the process and final recommendations. However, unlike other reviews of PROM quality [11,12,16], the primary purpose of most reviewed studies was often not PROM evaluation. Therefore, studies were often judged to be of limited quality per the COSMIN criteria.

The review highlighted a lack of conceptual and empirical research regarding HRQoL assessment in this population – and evidence of measurement data quality, interpretability, reliability, construct validity and responsiveness was mostly unavailable. Moreover, PROM content validity and relevance to OHCA survivors was not specifically evaluated. Application of the HRQoL framework, suggests that the QOLIBRI – a traumatic brain-injury specific measure – was most reflective of the multi-dimensional nature of HRQoL, including many concerns identified as important by OHCA survivors [57–59]. The shorter utility measures – HUI3 and EQ-5D-3L – have a narrower focus and, as reported by others, may fail to include health concerns of relevance to specific patient populations [60–62].A consequence of using measures with limited content validity is that the impact of OHCA and associated healthcare is sub-optimally assessed – clinical trials may overestimate good outcome and fail to identify important differences between groups on the outcomes that really matter to patients.

Except for the two generic index measures, all assess pain or discomfort. Fatigue, another important consideration for CA survivors, was assessed by six measures – the QOLIBRI, SF-36, SF-12, 15D and SF-6D. Both the HUI3 and 15D include items about vision, hearing and speech; the 15D additionally includes items about eating and excretion. It is possible that items relating to vision and hearing are not relevant to CA survivors, and hence may result in an overestimation of utility scores and hinder the measures ability to detect meaningful change in this population [62]. However, speech, eating and excretion may be particularly relevant to survivors with more severe impairment and hence more likely to be completed by proxy respondents.

Just two measures (QOLIBRI, HUI3) assess cognition, but limited evidence suggests just a small association between the HUI3 and a cognition-specific measure [55]. In contrast, the QOLIBRI includes several items to explore a wide-range of issues associated with cognitive impairment, and a strong association with a cognition-specific measure has been reported [32]. Recognition of the importance of cognitive impairment in this population [8,42], suggests a more detailed assessment of cognitive impairment than can be afforded by a single item is recommended.

Despite the small number of items, two of the utility measures – the EQ-5D-3L and SF-6D – cover a comparable range of HRQoL concepts. However, whilst evidence of good data quality and discriminative ability has been reported for the SF-6D at 12-months post-arrest, large ceiling effects and poor discriminatory ability have been reported for the EQ-5D-3L, suggesting that it underestimates the significant impact of cardiac arrest and may not detect important change [46].A revised version – the EQ-5D-5L – has improved response options which may improve the data quality, but has yet to be evaluated in this population.

Proxy-completion – that is, by a significant other – has been evaluated following completion of the EQ-5D-3L[46] and the SF-36(v2) [41] in OHCA survivors. Whilst higher levels of missing data were reported following proxy completion of the EQ-5D-3L, there were significantly lower ceiling effects (23% versus 46%), possibly reflecting the inclusion of survivors with greater limitations.

HRQoL data are often missing or incomplete for patients with the poorest outcomes, which may result in systematic bias [63].

To enhance HRQoL data capture, standardised administration and routine screening for avoidable missing data is recommended [64], which should be detailed in study protocols and standard operating procedures (SOPs) [63,64].

Although all measures were developed to be self-completed, all were interview-administered – in person, via the telephone or both – in the OHCA studies reviewed, with acceptable interview completion rates reported up to 12-months post-arrest. Proxy-completion, by appropriate assessors, is advised to ensure that the perspective of survivors with the poorest outcomes are included in research and audit, and that HRQoL assessment does not underestimate the impact of OHCA survival. However, the logistical challenges of HRQoL assessment are not insignificant. Earlier guidance suggests that HRQoL should, as a minimum, be assessed up to 3-months post-arrest [65]. However, for many survivors, their HRQoL may continue to change [42] and a longer-term assessment of HRQoL is recommended [39,57]. Issues associated with the feasibility and acceptability of long-term PROM completion required urgent attention.

Most of the reviewed studies included HRQoL evaluations up to 12-months post-arrest – but no study commented on the ability of measures to detect real change. Demonstrating the ability of the measures to detect meaningful change – both within individual and between groups – over time is essential to enhancing confidence in data quality and interpretation.

Given the importance of HRQoL for future clinical trials, registries and cohort studies, and the paucity of conceptualisation and evidence of essential measurement and practical properties, further research is essential. Collaborative research with survivors of cardiac arrest and their partners or patient advocates is strongly recommended to improve the quality and acceptability of HRQoL assessment and to co-produce guidance informing the way in which HRQoL assessment can be applied in future research, registries and healthcare quality assessments.

Just a small number of mostly generic HRQoL measures have been evaluated with OHCA survivors. However, study methodological quality was poor and critical evidence of measurement properties and relevance to survivors was largely unavailable or at best limited. These significant limitations hinder clear assessment recommendations, whilst also limiting data interpretation when such measures are applied in research and healthcare quality assessment. A comparative evaluation of measurement content validity highlighted that few measures captured the multi-faceted nature of HRQoL and the outcomes that matter to OHCA survivors. Although providing a narrow, impairment-based assessment, limited evidence suggests that the HUI3 may be an acceptable, short, generic measure of HRQoL. Alternatively, the SF-36(v2) – for which evidence was also limited – may provide a more detailed assessment. Further comparative evaluations of widely-used generic measures – to include essential evidence of reliability, validity, responsiveness, interpretation and feasibility – is urgently required. Moreover, exploration of the relevance and acceptability of such measures with representative members of the OHCA survivors' community is urgently required to determine the need for a survivor-derived measure.

## Conflict of interest statement

none.

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## Authors contribution

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.resuscitation.2017.11.065.

## References

[1]. Perkins GD, Jacobs IG, Nadkarni VM, The Utstein Collaborators, et al. Cardiac arrest and cardiopulmonary resuscitation outcome reports: update of the Utstein resuscitation registry templates for out-of-hospital cardiac arrest. Resuscitation 2015;96:328–40.
[2]. Whitehead L, Perkins GD, Clarey A, Haywood KL. A systematic review of the outcomes reported in cardiac arrest clinical trials: the need for a core outcome set. Resuscitation 2015;88:150–7.
[3]. Devlin NJ, Appleby J. Getting the Most Out of PROMs: Putting health outcomes at the heart of NHS decision-making. London: The King's Fund; 2010.
[4]. Elliott VJ, Rodgers DL, Brett SJ. Systematic review of quality of life and other patient-centred outcomes after cardiac arrest survival. Resuscitation 2011;82:247–56.
[5]. Terwee CB, Jansma EP, Riphagen II, de Vet HC. Development of a methodological PubMed search filter for finding studies on measurement properties of measurement instruments. Qual Life Res 2009;18(October (8)):1115–23.
[6]. de Vet H, Terwee CB, Mokkink LB, Knol DL. Measurement in Medicine A Practical Guide. England: Cambridge University Press; 2011.
[7]. Terwee CB, Prinsen CA, Ricci Garotti MG, et al. The quality of systematic reviews of health-related outcome measurement instruments. Qual Life Res 2016;25(April (4)):767–79.
[8]. Moulaert VR, Verbunt JA, van Heugten CM, Wade DT. Cognitive impairments in survivors of out-of-hospital cardiac arrest: a systematic review. Resuscitation 2009;80(March (3)):297–305.
[9]. Streiner DL, Norman GR, Cairney J. Health measurement scales: a practical guide to their development and use. 5th edition USA: Oxford University Press; 2014.
[10]. Terwee CB, Bot SD, de Boer MR, et al. Quality criteria were proposed for measurement properties of health status questionnaires. J Clin Epidemiol 2007;60(January (1)):34–42.
[11]. Haywood KL, Mars TS, Potter R, Patel S, Matharu M, Underwood M. Assessing the impact of headaches and the outcomes of treatment: a systematic review of patient-reported outcome measures (PROMs). Cephalalgia 2017, http://dx.doi.org/10.1177/0333102417731348. Jan 1:333102417731348. [Epub ahead of print].
[12]. Conijn AP, Jens S, Terwee CB, Breek JC, Koelemay MJ. Assessing the quality of available patient reported outcome measures for intermittent claudication: a systematic review using the COSMIN checklist. Eur J Vasc Endovasc Surg 2015;49(March (3)):316–34.
[13]. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. J Clin Epidemiol 2010;63(July (7)):737–45.
[14]. Terwee CB, Mokkink LB, Knol DL, Ostelo RW, Bouter LM, de Vet HC. Rating the methodological quality in systematic reviews of studies on measurement properties: a scoring system for the COSMIN checklist. Qual Life Res 2012;21(May (4)):651–7.
[15]. Fitzpatrick R, Davey C, Buxton MJ, Jones DR. Evaluating patient-based outcome measures for use in clinical trials. Health Technol Assess 1998;2(14):1–74, i-iv.
[16]. Haywood KL, Staniszewska S, Chapman S. Quality and acceptability of patient-reported outcome measures used in chronic fatigue syndrome/myalgic encephalomyelitis (CFS/ME): a systematic review. Qual Life Res 2012;21(Febuary (1)):35–52.
[17]. Staniszewska S, Haywood KL, Brett J, Tutton L. Patient and public involvement in patient-reported outcome measures: evolution not revolution. Patient 2012;5(2):79–87.
[18]. Ferrans CE, Zerwic JJ, Wilbur JE, Larson JL. Conceptual model of health-related quality of life. J Nurs Scholarsh 2005;37(4):336–42.
[19]. Bakas T, McLennon SM, Carpenter JS, et al. Systematic review of health-related quality of life models. Health Qual Life Outcomes 2012;10(November (16)):134.
[20]. Elbers RG, Rietberg MB, van Wegen EE, et al. Self-report fatigue questionnaires in multiple sclerosis, Parkinson's disease and stroke: a systematic review of measurement properties. Qual Life Res 2012;21(Auguat (6)):925–44.
[21]. Bullinger M, The TBI Consensus Group. Quality of life in patients with traumatic brain injury–basic issues, assessment and recommendations. Restor Neurol Neurosci 2002;20:111–24.

[22]. Ware JE, Sherbourne CD. The MOS 36-item short form health survey (SF-36): I.Conceptual framework and item selection. Med Care 1992;30:473–83.
[23]. Jenkinson C, Stewart-Brown S, Petersen S, Paice C. Assessment of the SF-36 version 2 in the United Kingdom. J Epidemiol Commun Health 1999;53(January (1)):46–50.
[24]. Ware J, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34(3):220–33.
[25]. Fugl-Meyer AR, Melin R, Fugl-Meyer KS. Life satisfaction in 18- to 64-year-old Swedes: in relation to gender, age, partner and immigrant status. J Rehabil Med 2002;34(September (5)):239–46.
[26]. Flanagan JC. A research approach to improving our quality of life. Am Psychol 1978;33:138–47.
[27]. Burckhardt CS, Anderson KL, Archenholtz B, Hagg O. The flanagan quality of life scale: evidence of construct validity. Health Qual Life Outcomes 2003;1:59.
[28]. Sintonen H. The 15D instrument of health-related quality of life: properties and applications. Ann Med 2001 Jul;33(5):328–36.
[29]. The EuroQol Group EuroQol–a new facility for the measurement of health-related quality of life. Health Policy 1990;16:199–208.
[30]. Feeny D, Furlong W, Torrance GW, et al. Multiattribute and single-attribute utility functions for the health utilities index mark 3 system. Med Care 2002 Feb;40(2):113–28.
[31]. Brazier J, Roberts J, Deverill M. The estimation of a preference-based measure of health from the SF-36. J Health Econ 2002 Mar;21(2):271–92.
[32]. Middelkamp W, Moulaert VR, Verbunt JA, et al. Life after survival: long-term daily life functioning and quality of life of patients with hypoxic brain injury as a result of a cardiac arrest. Clin Rehabil 2007;21(5):425–31.
[33]. Mak M, Moulaert VR, Pijls RW, Verbunt JA. Measuring outcome after cardiac arrest: construct validity of Cerebral Performance Category. Resuscitation 2016;100:6–10.
[34]. Graf J, Muhlohoff C, Doig GS, et al. Healthcare costs, long-term survival, and quality of life following intensive care unit admission after cardiac arrest. Crit Care 2008;12(4):R92.
[35]. Bro-Jeppesen J, Kjaergaard J, Horsted TI, et al. The impact of therapeutic hypothermia on neurological function and quality of life after cardiac arrest. Resuscitation 2009;80(2):171–6.
[36]. Moulaert VR, Wachelder EM, Verbunt JA, Wade DT, van Heugten CM. Determinants of quality of life in survivors of cardiac arrest. J Rehabil Med 2010;42(6):553–8.
[37]. Reinhard V, Parna K, Lang K, Pisarev H, Sipria A, Starkopf J. Long-term outcome of bystander-witnessed out-of-hospital cardiac arrest in Estonia from 1999 to 2002. Resuscitation 2009;80(1):73–8.
[38]. Kowalik R, Szczerba E, Koltowski L, et al. Cardiac arrest survivors treated with or without mild therapeutic hypothermia: performance status and quality of life assessment. Scand J Trauma Resusc Emerg Med 2014;22(December (12)):76.
[39]. Moulaert VR, van Heugten CM, Winkens B, et al. Early neurologically-focused follow-up after cardiac arrest improves quality of life at one year: a randomised controlled trial. Int J Cardiol 2015;193:8–16.
[40]. Boyce-van der Wal LW, Volker WG, Vliet Vlieland TP, van den Heuvel DM, van Exel HJ, Goossens PH. Cognitive problems in patients in a cardiac rehabilitation program after an OHCA. Resuscitation 2015;93:63–8. August.
[41]. Cronberg T, Lilja G, Horn J, The TTM Trial Investigators, et al. Neurologic function and health-related quality of life in patients following targeted temperature management at 33 °C vs 36 °C after out-of-hospital cardiac arrest: a randomized clinical trial. JAMA Neurol 2015;72:634–41.
[42]. Orbo M, Aslaksen PM, Larsby K, Schafer C, Tande PM, Anke A. Alterations in cognitive outcome between 3 and 12 months in survivors of out-of-hospital cardiac arrest. Resuscitation 2016;105:92–9.
[43]. Deasey C, Bray J, Smith K, et al. Functional outcomes and quality of life of young adults who survive out-of-hospital cardiac arrest. Emerg Med J 2013;30(7):532–7.
[44]. Beesems SG, Wittebrood KM, de Haan RJ, Koster RW. Cognitive function and quality of life after successful resuscitation from cardiac arrest. Resuscitation 2014;85:1269–74.
[45]. Smith K, Andrew E, Lijovic M, Nehme Z, Bernard S. Quality of life and functional outcomes 12 months after out-of-hospital cardiac arrest. Circulation 2015;131:174–81.
[46]. Andrew E, Nehme Z, Bernard S, Smith K. Comparison of health-related quality of life and functional recovery measurement tools in out-of-hospital cardiac arrest survivors. Resuscitation 2016;107:57–64.
[47]. Wallin E, Larsson IM, Rubertsson S, Kristofferzon ML. Cardiac arrest and hypothermia treatment–function and life satisfaction among survivors in the first 6 months. Resuscitation 2014;85(4):538–43.
[48]. Wilson M, Staniforth A, Till R, das Nair R, Vesey P. The psychosocial outcomes of anoxic brain injury following cardiac arrest. Resuscitation 2014;85(June (6)):795–800.
[49]. Tiainen M, Poutiainen E, Oksanen T, et al. Functional outcome, cognition and quality of life after out-of-hospital cardiac arrest and therapeutic hypothermia: data from a randomized controlled trial. Scand J Trauma Resusc Emerg Med 2015;23(Febuary 6):12.
[50]. Nichol G, Stiell IG, Hebert P, et al. What is the quality of life for survivors of cardiac arrest? A prospective study. Acad Emerg Med 1999;6(2):95–102.
[51]. Stiell I, Nichol G, Wells G, De Maio V, Nesbitt L, Blackburn J, et al. for the OPALS Study Group: health-related quality of life is better for cardiac arrest survivors who received citizen cardiopulmonary resuscitation. Circulation 2003;108:1939–44.
[52]. Raina KD, Callaway C, Rittenberger JC, Holm MB. Neurological and functional status following cardiac arrest: method and tool utility. Resuscitation 2008;79:249–56.
[53]. Stiell IG, Nesbitt LP, Nichol G, Maloney J, Dreyer J, Beaudoin T, et al. the OPALS Study Group: comparison of the Cerebral Performance Category score and the Health Utilities Index for survivors of cardiac arrest. Ann Emerg Med 2009;53:241–8.
[54]. Longstreth Jr WT, Nichol G, Van Ottingham L, Hallstrom AP. Two simple questions to assess neurologic outcomes at 3 months after out-of-hospital cardiac arrest: experience from the public access defibrillation trial. Resuscitation 2010;81:530–3.
[55]. Raina KD, Rittenberger JC, Holm MB, Callaway CW. Functional outcomes: one year after a cardiac arrest. Biomed Res Int 2015;2015:283608.
[56]. Nichol G, Guffey D, Stiell IG, et al. the Resuscitation Outcomes Consortium Investigators: post-discharge outcomes after resuscitation from out-of-hospital cardiac arrest: a ROC PRIMED substudy. Resuscitation 2015;93:74–81.
[57]. Haywood KL, Whitehead L, Nadkarni V, et al. Core outcome set for cardiac arrest (COSCA) in adults: an advisory statement from the international liaison committee on resuscitation. Circulation 2017, in press.
[58]. Whitehead LL. Identifying a Core Outcome Set for Cardiac Arrest Effectiveness Trials Doctoral Thesis. University of Warwick; 2017.
[59]. Haydon G, van der Riet P, Inder K. A systematic review and meta-synthesis of the qualitative literature exploring the experiences and quality of life of survivors of cardiac arrest. Eur J Cardiovasc Nurs 2017;16(August (6)):475–83.
[60]. Lim WC, Black N, Lamping D, Rowan K, Mays N. Conceptualizing and measuring health-related quality of life in critical care. J Crit Care 2016;31(Febuary (1)):183–93.
[61]. Pietersma S, de Vries M, van den Akker-van Marle ME. Domains of quality of life: results of a three-stage Delphi consensus procedure among patients, family of patients, clinicians, scientists and the general public. Qual Life Res 2014;23(June (5)):1543–56.
[62]. Kuspinar A, Mayo NE. A review of the psychometric properties of generic utility measures in multiple sclerosis. Pharmacoeconomics 2014;32(August (8)):759–73.
[63]. Fairclough DL, Peterson HF, Chang V. Why are missing quality of life data a problem in clinical trials of cancer therapy. Stat Med 1998;17:667–77.
[64]. Kyte D, Ives J, Draper H, Calvert M. Current practices in patient-reported outcome (PRO) data collection in clinical trials: a cross-sectional survey of UK trial staff and management. BMJ Open 2016;6(16):e012281. October 3.
[65]. Becker LB, Aufderheide TP, Geocadin RG, et al. American heart association emergency cardiovascular care committee; council on cardiopulmonary, critical care, critical care, perioperative and resuscitation. primary outcomes for resuscitation science studies: a consensus statement from the american heart association. Circulation 2011 Nov 8;124(19):2158–77.