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ILCOR Advisory Statement

P-COSCA (Pediatric Core Outcome Set for Cardiac Arrest) in Children:

An Advisory Statement From the International Liaison Committee on Resuscitation

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[H1]Abstract

Studies of pediatric cardiac arrest use inconsistent outcomes, including return of spontaneous circulation and short-term survival, and basic assessments of functional and neurological status. In 2018, the International Liaison Committee on Resuscitation sponsored the COSCA initiative (Core Outcome Set After Cardiac Arrest) to improve consistency in reported outcomes of clinical trials of adult cardiac arrest survivors and supported this P-COSCA initiative (pediatric COSCA). The P-COSCA Steering Committee generated a list of potential survival, life impact, and economic impact outcomes and assessment time points that were prioritized by a multidisciplinary group of healthcare providers, researchers, and parents/caregivers of children who survived cardiac arrest. Then, expert panel discussions achieved consensus regarding the core outcomes, the methods to measure those core outcomes, and the timing of the measurements. The P-COSCA includes assessment of survival, brain function, cognitive function, physical function, and basic daily life skills. Survival and brain function were assessed at discharge or 30 days (or both if possible) and between 6 and 12 months postarrest. Cognitive function, physical function, and basic daily life skills were assessed between 6 and 12 months after cardiac arrest. Because many children have prearrest comorbidities, the P-COSCA also includes documentation of baseline (ie, prearrest) brain function and calculation of changes after cardiac arrest. Supplementary outcomes of survival, brain function, cognitive function, physical function, and basic daily life skills are assessed at 3 months and beyond 1 year after cardiac arrest if resources are available.

[H1]Background

Cardiac arrest occurs in >20 000 children annually in the United States.[1-7] Overall survival after in-hospital cardiac arrest increased from 14.3% in 2000 to 39.4% in 2009[8] most recent survival rates at 48.0%[1] in the United States and from 25.9% to 41% in Spain,[1,9] while survival after out-of-hospital cardiac arrest remains low at 8.3%[10] to 11.1%.[1]

Survivors of cardiac arrest are at significant risk for both short-term and long-term morbidity.[8,9,11-15] Children who survive out-of-hospital cardiac arrest can demonstrate decline in neurobehavioral function that is often severe.[14] Many who survive cardiac arrest with a grossly "favorable outcome" have more subtle and sustained neuropsychological impairment.[16] Furthermore, assessment of neurodevelopmental impact of cardiac arrest is complicated by the presence of preexisting neurological compromise in many children who have a cardiac arrest.[17] These challenges highlight the importance of research that can precisely define, compare, and improve patient outcomes.[18]

Outcomes reported in studies of children surviving cardiac arrest vary and include return of spontaneous circulation, short-term mortality, and basic assessment of functional and neurological outcome.[19] Lack of uniformity in reported outcome assessment methods and follow-up intervals prevents pooling of data for meta-analyses, limits generalizability of study conclusions, and impedes development of clinical recommendations to improve care.

A more contemporary approach to outcomes in research studies includes clinical, clinician-reported, and patient-/caregiver-/family-centered outcomes, neuropsychological testing, and evaluation and quantification of resource use and socioeconomic impact. In light of these developments, in 2015, the International Liaison Committee on Resuscitation (ILCOR), a council of the world's resuscitation councils, expanded its recommendations for uniform

reporting of outcomes of adult cardiac arrest to include both core and supplementary outcomes, acknowledging the need to add assessment of morbidities, patient-reported outcomes, and quality of life (QoL) measures.[20]

In 2018, to further improve consistency in reporting of outcomes of adult cardiac arrest, ILCOR sponsored the development of a core outcome set (COS) for adult cardiac arrest (COSCA).[21,22] A COS is a standardized minimal set of outcomes to be reported in all effectiveness trials in a specialty, designed to foster consistent reporting of outcomes.[23] To enhance the relevance of outcome assessment for policy and practice, COS development should incorporate the views of key stakeholders, including providers and patients. A COS constitutes the minimum reporting elements but does not limit the reporting of other outcomes.[23] Implementation of standardized assessment and outcome reporting reduces heterogeneity and outcome reporting bias, improves comparability across studies, and enables the pooling of data for meta-analyses.

The development of the adult COSCA included a consensus process involving the participation of key international stakeholders, including survivors and their partners, healthcare providers, and researchers who identified the key elements, tools, and the intervals for assessment. The COSCA includes assessment of survival and neurological function (using the modified Rankin Scale) at discharge or 30 days after cardiac arrest (or both if possible) and assessment of HRQoL (using 1 of 3 generic measures) at 90 days, with periodic reassessments through the first year if resources allow.

The ILCOR P-COSCA initiative (Pediatric COSCA) sought to develop a COS specific for pediatric cardiac arrest studies. The design and methods of this initiative were closely aligned with the COSCA design and methods, including use of a Delphi process to develop consensus regarding a core domain set. There are important differences between pediatric cardiac arrest and

adult cardiac arrest in causes, treatment, and survival rates. C hildren are still developing and are normally dependent on care providers before a cardiac arrest as well as during recovery and ongoing development. Thus, although there may be similarities in the outcomes that are critical to both children and adults, there are likely important differences that should be considered in pediatric outcome assessment.

[H1]Methods

Both the COSCA and the P-COSCA initiatives used approaches from OMERACT (Outcome Measures in Rheumatology)[24-26] and COMET (Core Outcome Measures in Effectiveness Trials)[27] initiatives.[21,22] The project was registered with the COMET initiative.[28] A pproval for survey distribution was obtained from the Children's Hospital of Philadelphia Institutional Review Board.

ILCOR appointed the P-COSCA international steering committee (SC). The SC consisted of 18 healthcare providers, including specialists in pediatric critical care medicine, pediatric emergency medicine, neuropsychology, physical medicine and rehabilitation, pediatric nursing, clinical trials, and outcome methodology. These experts reviewed the literature, drafted the survey, conducted the Delphi process, reached consensus, and served as the writing group for this consensus statement. The American Heart Association manuscript oversight committee reviewed all conflicts of interest statements by the SC members before approving their participation. The final manuscript has been endorsed by ILCOR member councils and the American Heart Association's Emergency Cardiovascular Care Science Subcommittee and Science Advisory and Coordinating Committee (SACC).

There were 2 major steps in the development of the P-COSCA:

- **Step 1: Defining the COS** (ie, what—at a minimum—should be measured): The SC used the OMERACT framework to identify 3 core areas of health to evaluate: survival, life impact, and resource use/economic impact (see Figure 1). Although a fourth area (pathophysiological manifestations) is also proposed in the OMERACT framework, this was not included. An international Delphi process was used to refine and prioritize outcome domains within each core. Then, the SC identified the minimum number of outcomes to include in the P-COSCA.
- **Step 2: Identifying the core measurement set** (ie, how and when the core outcomes should be measured): The SC debated the strengths and weaknesses of measurement tools appropriate for each selected outcome until consensus was reached. The SC then determined by consensus the time points for assessment.

[h2]Step 1: Defining the COS

[h3]Generating an Extensive List of Potential Outcomes

At an in-person meeting in November 2018, the SC used the COSCA[21,22] and SC suggestions to generate a comprehensive list of potential outcomes to serve as a starting point for this process. P otential outcomes were considered in light of the wide-ranging HRQoL needs and experiences of children,[12] longer-term impact of cardiac arrest on childhood growth and development,[29] and potential effects of cardiac arrest on family.[30] The list of outcomes and time points for consideration in step 2 are listed in Figure 2.

[h3]International Delphi Process to Refine and Prioritize Outcomes

The SC defined 2 panels: (1) healthcare providers experienced in the care of pediatric survivors of cardiac arrest and (2) parents/caregivers of survivors, with a goal of 100 healthcare providers (based on COSCA enrollment) and 20 parents/caregivers of survivors.

Each SC member (n=18) invited at least 5 healthcare providers to participate in the surveys. The survey was only in English. To provide a multidisciplinary view, prehospital providers, nurses, respiratory therapists, rehabilitation service providers, psychologists, social workers, and physicians were included.

To include parents/caregivers of children who survived cardiac arrest, surveys were distributed via survival networks in the United States and the United Kingdom (see Box) and, with institutional internal review board approval, at a US medical center that cares for pediatric cardiac arrest survivors and their families. To reach survival networks, an email was sent to the foundation or network contact with an attached introductory email and survey link and a request to forward the letter and link to parents and caregivers of survivors in the network. At the US institution that surveyed survivors, providers contacted eligible parents and caregivers of their own patients to request voluntary participation.

The first online survey (see Appendix 1) included a list of potential outcomes and time points for assessment (REDCap).[31] After the SC piloted the survey to ensure comprehensiveness, clarity, and face validity, the survey was then completed by both panels (ie, healthcare providers and parents/caregivers) and members of the SC.

The Delphi process consisted of 2 sequential rounds. Respondents who completed the survey in round 1 were eligible to complete a survey in round 2. The group decided a priori to analyze the combined responses of healthcare providers and parents/caregivers. In round 1, respondents rated the relative importance of outcomes for inclusion in future pediatric cardiac arrest research studies on a 9-point numerical rating scale, ranging from a low of 1 (ie, not at all important) to a high of 9 (ie, very important). Respondents were asked to rate the importance of each outcome at 3 distinct time points that were selected by SC consensus: (1) at discharge, (2) within the first

year after the cardiac arrest, and (3) >1 year after the cardiac arrest. Respondents could comment on their decisions and suggest additional important outcomes. Outcomes rated as most important (ie, a score of 8 or 9) by >75% of respondents were advanced to round 2 (see Figure 2).

In round 2 (see Appendix 2), respondents first prioritized all outcomes ranging from a low of 1 (ie, not a priority) to a high of 5 (ie, absolute priority) for assessment at each time point (ie, discharge, within the first year after cardiac arrest, and >1 year after cardiac arrest). Next, respondents ranked their top 7 highest priority outcomes at each time point (ie, outcome/time point combinations). Finally, respondents were asked to select the single most important assessment time point within the first year after the cardiac arrest and the single most important assessment time point >1 year after cardiac arrest.

Results were analyzed by summarizing the scores for the top 7 prioritized outcome/time point combinations. Round 2 mean and standard deviation (SD) rating scores for each outcome were compared with the top 7 prioritized outcome/time point combinations by rank score for healthcare providers and parents/caregivers. The SC identified and discussed the rank score and mean and SD rating for all outcomes for both healthcare providers and parents/caregivers. The top 7 outcome/time point combinations for healthcare providers and the top 7 outcome/time point combinations for parents/caregivers were identified and discussed by the SC in step 2. The SC also considered the outcome measures as well as the respondents' prioritization of time points independently.

[h2]Step 2: Identifying the Core Measurement Set

After the COS was identified in step 1, members of the SC then identified the core measurement tools and timing of those measurements (step 2) and reached consensus to create the final P-

COSCA. This group met by webinar on 22 occasions. A final vote of approval was conducted with unanimity required.

The SC first discussed the summarized survey results, including additional comments, acknowledging that the final COS needed to be valid, feasible, and acceptable. The SC reviewed measurement tools appropriate for children 0 to 18 years of age that were used in peer-reviewed published studies of pediatric cardiac arrest or in other relevant pediatric populations (eg, critical illness, neurological injury). Consensus was reached through repeated discussions, and unanimous agreement was achieved for final wording.

[H1]Results

[h2]Step1: Defining the COS

[h3]Generating an Extensive List of Potential Outcome Domains

The initial survey questionnaire included 18 outcomes across the 3 core areas of health: survival (1 outcome), life impact (16 outcomes), and resource use/economic impact (1 outcome). In contrast to the COSCA outcomes,[21,22] the SC expanded the P-COSCA core area of life impact into more granular outcomes. Because children are raised by parents/caregivers, the impact of the child's cardiac arrest on the family was considered in more depth, and the economic impact domain was refocused on the family in the P-COSCA. The SC included assessment time points consistent with the COSCA's time points of at discharge and within the first year after cardiac arrest[21,22] and also chose to include >1 year after cardiac arrest as a potential outcome measurement because of children's longitudinal development (see Figure 2).

[h3]International Delphi Process to Refine and Prioritize Outcomes

[h4]Round 1

In total, 89 participants completed round 1: 83 healthcare providers (50 physicians, 7 psychologists, 11 nurses, 7 therapists [speech, physical, occupational], 4 social workers, 1 paramedic, and 3 not identified); and 6 parents/caregivers of children who survived cardiac arrest (median age of child at arrest was 11 years; median time since arrest, 3 years). Participants represented 12 countries (United States, United Kingdom, New Zealand, Peru, Singapore, Netherlands, Brazil, Canada, Belgium, Tunisia, South Africa, and Denmark).

The SC reviewed results of round 1 and identified 22 outcome/time point combinations and 11 unique outcomes to include in round 2 based on the combined input of healthcare providers and parents/caregivers (see Supplementary Table 1 and Figure 2). The respondents highly prioritized survival at all 3 time points (ie, hospital discharge, within the first year after cardiac arrest, and >1 year after cardiac arrest). Healthcare providers and parents/caregivers agreed on 10 of the outcome/time point combinations. Survival and brain function were the only 2 discharge outcomes that were ranked highly enough to be included in round 2. Parents/caregivers prioritized the assessment of survival, fatigue, and sleep >1 year after cardiac arrest and family relationships and economic impacts on the family at discharge and within the first year after cardiac arrest (see Supplementary Table 1).

[h4]Round 2

Seventy-four respondents completed round 2 (68 healthcare providers [82% response rate]; 6 parents/caregivers [100% response rate]). The top 7 outcome/time point combinations were identified. Both healthcare providers and parents/caregivers prioritized survival at discharge, survival within the first year after cardiac arrest, brain function at discharge, and brain function

and cognitive function within the first year after cardiac arrest (see Supplementary Table 2). Healthcare providers also highly ranked cognitive function >1 year after cardiac arrest and basic daily life skills within the first year after cardiac arrest. Parents/caregivers also included physical functioning within the first year. All 8 outcome domain time point combinations were considered in the consensus meeting (see Figure 2).

Hospital discharge was ranked as the highest priority time point for assessment when compared with the time points of within the first year and >1 year. To further identify time points for assessments within the first year, respondents prioritized assessments at 6 months (52%) and 1 year (35%) higher than assessments at 3 months (13%). For time points after 1 year, the majority of respondents (63%) selected 2 years as the most important time point, compared with 5 years (34%) and 10 years (3%). Survey comments identified concerns about the feasibility and practicality of collecting longer-term outcomes (ie, >1 year after cardiac arrest) and noted the critical importance of incorporating a baseline precardiac arrest assessment of the child's neurological function to better identify the impact of the cardiac arrest.

[h2]Step 2: Identifying the Core Measurement Set

[h3]Measuring Survival

The SC agreed that the core outcomes should include measurement of survival to discharge from an acute care facility or survival at 30 days (see Table 1). The P-COSCA suggests that researchers report both measures if possible, documenting assessments at each time point rather than as a composite score, to avoid loss of granularity regarding how time impacts outcomes.

The SC agreed to define the *discharge time point* as the time of discharge from the acute care facility associated with the hospitalization for the cardiac arrest because children surviving cardiac arrest may be transferred to and discharged from multiple facilities and the use of such

facilities may vary substantially across healthcare systems and countries. Additional variability is introduced by limitations of healthcare systems finances and the family's capability to care for the child at home. In addition, many children with cardiac arrest have chronic medical conditions, preexisting comorbidities, or postarrest complications and can remain hospitalized for prolonged periods.[17] For all these reasons, the 30-day survival outcome assessment time point is preferred for consistency; however, for patients who are discharged before 30 days, follow-up at 30 days may not be feasible due to the need for consent and loss to follow-up. As a result, the SC included assessment of survival at discharge or 30 days, or both if possible. The Delphi process also prioritized measuring survival within the first year after cardiac arrest.

[h3]Measuring Brain Function

In the Delphi survey, brain function was described as consciousness or awareness of surroundings. When considering methods to evaluate brain function, the SC discussed the relative merits and limitations of 2 healthcare provider-completed measures—the Pediatric Cerebral Performance Category (PCPC)[32,33] and the Glasgow Outcome Scale–Extended Pediatric Revision (GOS-E Peds).[34] Characteristics of these tools are listed in Table 2. The Functional Status Scale (FSS) was considered as a measure of brain function but not included for 3 reasons: (1) It does not include death in its scoring; (2) it has multiple domains not all related to brain function; and (3) the domains associated with brain function are too broad to capture the granularity of injury after cardiac arrest. The SC proposes the PCPC as the core outcome measure for brain function, noting that studies can use the GOS-E Peds as an additional measure. The SC considered several issues important in evaluation of post–cardiac arrest brain function, including validity and reliability in children with and without neurological deficits after cardiac arrest and ease of use. Both the PCPC and GOS-E Peds are tools for qualitative assessments of

performance that provide categorical outcome scores based on the GOS.[32-34] Although similar in design, these tools have not been compared directly in the same patient populations. Both the PCPC and GOS-E Peds include death in the scaling, which the SC considered to be important because survey respondents prioritized assessment of survival at multiple time points. The PCPC was included in the 1995 Pediatric Utstein template of recommended guidelines for reporting outcomes of pediatric advanced life support,[19,35] and it has been used extensively to measure cardiac arrest outcomes since that time.[36-38] The GOS-E Peds has been used to measure outcomes after pediatric traumatic brain injury[34,39] but has not yet been validated in the pediatric cardiac arrest population.

As many as 56.9% of children who experience in-hospital cardiac arrest have preexisting neurological deficits.[17] The SC agreed that it is important to include a baseline prearrest measure of brain function by using the same tool used for postarrest measurement to identify changes in neurological function after the cardiac arrest.

Both the PCPC and GOS-E Peds have limitations. While the PCPC has been used extensively in pediatric cardiac arrest research, its broad category descriptions are vague and the scoring criteria are subjective. In comparison, the GOS-E Peds has more categorical designations than the PCPC, and the descriptions within each category are more detailed, but as of the time of this publication, there have been no published studies using the GOS-E Peds in children after cardiac arrest. The PCPC is currently used to retrospectively retrieve assessment information regarding prearrest baseline brain function through review of medical records or through interview of parents/caregivers. Although the GOS-E Peds incorporates baseline function in the postinjury assessment, it has not been validated to assess baseline brain function retrospectively or independently of postevent outcome. The SC proposes the use of the PCPC to assess pediatric

brain function after cardiac arrest because of its demonstrated utility and validity in studies of children after cardiac arrest and the ability to document prearrest function.

When following older children who may be transitioning to adult care soon after cardiac arrest, clinicians and researchers should be aware that the Cerebral Performance Category (CPC) used in adults is scored differently than the PCPC.

[h4]Timing

Both healthcare providers and parents/caregivers identified evaluation of brain function within the first year after cardiac arrest as a high priority. For healthcare providers, it was the highest priority across all potential outcome measures and time points; for parents/caregivers, it was identified as the second-highest priority (second only to survival to discharge). The P-COSCA includes evaluation of brain function at either discharge from an acute care facility or at 30 days (or both) and between 6 and 12 months after cardiac arrest.

To achieve consensus regarding the timing of assessment of brain function, the SC considered feasibility as well as potential influences of the child's neurological development over time. Assessment of brain function within the first year allows for time to pass to enable more time for recovery, including potential improvement associated with rehabilitation interventions (which, depending on child's age, setting, and stability, may take time to assess); reintroduction of age-appropriate activities, such as schooling; and additional expected development in the youngest children, so that an expanded repertoire of skills can be assessed. However, assessment within 1 year creates a substantial burden for investigators, with impact on study timelines, cost, and risk of patients lost to follow-up. The SC also acknowledged that it is reasonable to designate an interval rather than a discrete time point for follow-up assessments because it often takes time to schedule follow-up telephone calls.

Given recent findings from the THAPCA (Therapeutic Hypothermia After Pediatric Cardiac Arrest) trials indicating that 3-month outcomes are predictive of outcomes at 1 year,[40] 3 months appears to be the earliest possible time point for evaluation of brain function within the first year after cardiac arrest. Based on these studies, correlation between 3- and 12-month outcomes differed between in-hospital and out-of-hospital cardiac arrest. T he SC agreed that there are insufficient data to confidently use 3-month outcomes as representative of later outcomes of cardiac arrest but agreed that this issue should be reassessed over time as more data become available. Thus, 3 months postarrest was identified as a supplementary time point in assessment of brain function, in part to encourage the development of evidence regarding the utility of this earlier outcome assessment.

Assessment time points beyond 1 year after cardiac arrest were determined to be impractical or overly burdensome at this time. The SC unanimously agreed that it is important to understand the impact of pediatric cardiac arrest on long-term education and on functional and developmental needs as children grow into adolescence and adulthood. While assessment at later time points allows more time for development and recovery, particularly in the youngest children, such extended follow-up also places significant burden on investigators. .

[h4]How to Complete

The PCPC and GOS-E Peds can be completed in approximately 10 minutes based on information obtained through direct observation of the child, a caregiver report, or a review of medical records.[41] Providers must obtain a parent's report of the child's baseline pre-injury level of functioning as soon as possible after study enrollment to minimize recall bias.[42]

[h4]What to Report

A primary goal of the P-COSCA is to standardize the reporting of study outcomes so that comparisons can be made across studies over time. Availability of baseline PCPC enables comparison of populations, and documentation of changes from baseline facilitates measurement of the impact of the cardiac arrest or interventions on each child and on the study population overall. Therefore, the P-COSCA includes both the prearrest PCPC and PCPC scores at each of the core time points (see Table 1), with reporting to include the percent of patients in each PCPC category as well as change in PCPC between post arrest time points and prearrest (a range of 0 to 4 in postarrest survivors). As noted below, there are many ways that change has been incorporated into outcome definitions. The SC considered both how to report the PCPC as well as how to address definitions of *favorable* and *unfavorable outcomes*. Pediatric cardiac arrest studies have historically dichotomized outcomes into favorable and unfavorable categories using the PCPC at discharge.[38,43] To include patients who have prearrest developmental delays, some studies have used *change from baseline*, defined as the difference between the postarrest and prearrest PCPC[38,43]; however, the method of incorporation of the PCPC and a change in PCPC have varied widely. Definitions of *favorable outcome* have included PCPC of 1, 2, or no change from baseline, as well as a PCPC of 1, 2, 3, or no change from baseline.[37] Furthermore, many studies have included a PCPC score of 6, death, in the definition of *unfavorable outcome*, thus combining patients who die with those who survive with significant neurological morbidity. When considering the definition of *favorable* and *unfavorable outcome*, the SC could not reach consensus regarding the optimal definitions of these outcomes and noted that the view of *favorable* may vary among families and even across cultures.

[h3]Measuring Cognitive Function, Physical Function, and Basic Daily Life Skills

Cognitive function was defined as ability to think, concentrate, or pay attention or to think clearly and remember things. *Compromise in physical function* was defined as difficulty with eyesight; loss of muscle strength or mobility, such as crawling or walking; chronic headaches; or seizures. *Basic daily life skills* were defined as age appropriate eating, washing, dressing, toileting, personal hygiene, and getting out of bed. While these domains are unique, they are presented together in this section because they can often be measured by using the same tools.

The SC prioritized review of the FSS[44]; the Pediatric Quality of Life Inventory (PedsQL)[45]; the Vineland Adaptive Behavior Scales, Second Edition (VABS-II)[46]; the Vineland Adaptive Behavior Scales, Third Edition (Vineland-3)[47]; and the Adaptive Behavior Assessment System, Third Edition (ABAS-3).[48] Aspects of each of these tools are highlighted in Table 3. Other tools to assess these skills (eg, PROMIS [Patient-Reported Outcomes Measurement Information System], Health Utilities Index) were not examined because they did not include assessment information for the full pediatric age range.

The FSS[44] was developed to provide a more granular assessment of outcome than the combined outcomes obtained by using the PCPC.[32] It includes categorical ratings within 6 functional domains (mental status, sensory function, communication, motor function, feeding, and respiratory function). The PCPC and the FSS are closely associated in pediatric intensive care unit patients, and relationships were even stronger when a subset of the FSS that focuses on neurological functioning (a composite of the mental status and communication domains) was compared with the PCPC.[49]

The PedsQL 4.0 Generic Core Scales and the extension for young children, the PedsQL Infant Scales, are HRQoL measures.[45,50] The PedsQL 4.0 Generic Core Scales,[45] a caregiver-proxy

measure for children 2 to 18 years of age, consists of 4 outcome sections, including Physical, Emotional, Social, and School Functioning. It is a reliable and valid tool to assess children with numerous health conditions, including cardiac disease[51,52] and acquired neurological conditions.[53] The PedsQL Infant Scales[50] consist of 5 scales, including Physical, Emotional, Social, and Cognitive Functioning as well as Physical Symptoms and is designed for caregiver-proxy rating of children from 1 month to 24 months of age. Both generic and the infant versions have good reliability and validity in children receiving inpatient care.[54] In addition to the core scales, condition-specific modules/scales that can be used to complement the Generic Core Scales for specific clinical populations. Because the PedsQL Generic Core and Infant Scales do not include a scale specifically measuring cognitive functioning and basic daily life skills for all age groups, several other PedsQL condition-specific scales were reviewed. The PedsQL Cognitive Functioning Scale has been validated in children with acquired neurological conditions,[53] neurodevelopmental disabilities,[55] and chronic health conditions.[56] The Daily Activities Scale from the Cerebral Palsy (CP) Module of the PedsQL has been validated in children with CP, but only for those ≥2 years of age.[57] Normative data have been published for healthy children for all scales, and the scales have been translated into many languages.[45,50,51,58] The ABAS-3 is a caregiver-report measure of functional skills.[48] There is one form for children 0 to 5 years of age and another for those 5 to 21 years of age. Key skills areas include communication, functional academics (pre-academics for younger children), self-direction, leisure, social, community use, home living, health and safety, and self-care. Scores are calculated for each area, and the user also calculates 3 composite scores (Conceptual, Social, Practical) and an overall Global Adaptive Composite score. Only the form for children ages 0 to 5 years includes a motor scale. Both forms take approximately 15 to 20 minutes to complete. The

ABAS-3 is sensitive to impairment in children with acquired neurological injury.[59] Standardized age-corrected scores are available.

The VABS-II and recently updated Vineland-3 are caregiver-report measures that assess adaptive functioning in detail in individuals with neurodevelopmental disabilities. These measures provide scores for an overall adaptive behavior composite and 4 domains (communication, daily living, socialization, motor skills). Each domain includes subdomains that are developmentally sequenced items, starting with skills typical of infancy. Both measures have demonstrated high reliability and validity.[46,60] Normative data obtained in a large sample of children from the United States are used to yield standardized age-corrected scores for the overall composite and for each domain. The VABS-II has been used as a primary outcome assessment tool in pediatric cardiac arrest studies.[42,61]

The SC discussed these measures at length and evaluated each measure in relation to cognitive, physical, and basic daily life skills as defined above. Although use of the FSS is highly feasible in a pediatric intensive care unit population, it is not included in the P-COSCA because it does not report cognitive function, physical function, or basic daily life skills at as granular a level as some alternative scoring systems that have been applied to cardiac arrest survivors. The ABAS-3 was also thought to lack feasibility because it takes up to 20 minutes to administer, and physical functioning is only measured in the youngest children. The VABS-II and Vineland-3 assess cognition, physical function, and basic daily life skills, but these measures lacked feasibility because they can take up to 45 minutes to administer.

The P-COSCA proposes the Physical Functioning Scale from the PedsQL Generic Core and Infant Scales to measure physical functioning and the PedsQL Cognitive Functioning Scale[58] for children ≥2 years of age, along with the Cognitive Functioning Scale of the PedsQL Infant

Scales for children <2 years of age (see Table 1). There were no feasible measures to assess basic daily life skills for all age groups. Therefore, the Daily Activities Scale from the PedsQL CP Module for children ≥2 years of age is included in the P-COSCA.[57] The VABS-II, Vineland-3, and ABAS-3 are included as supplementary outcome measurement tools for cardiac arrest studies.

[h3]Timing

The SC agreed that it is important to measure cognitive function, physical function, and basic daily life skills between 6 and 12 months after the cardiac arrest, at the same time that brain function is assessed. The P-COSCA includes assessments at 3 months and 12 months post–cardiac arrest as supplementary.

[h3]How to Complete

The PedsQL Generic Core, Infant, Cognitive Functioning Scales, and CP Module Daily Activities Scale are questionnaires that were developed to be completed directly by the caregiver. P aper and pencil, online, and telephone administration yield highly consistent in pediatric populations.[62] Telephone administration has been used to determine pre-injury baseline functioning and outcomes in children with neurological injury over the first year after injury.[53]

[h3]What to Report

The P-COSCA includes assessment of PedsQL physical function scale and cognitive function scale. Since the physical function scale is part of the Generic Core Scales, researchers may choose to use the full age-appropriate core measure and report the complete PedsQL total summary score and psychosocial health summary score in addition to the physical functioning

scale. Additionally, given that basic daily life skills were identified as a key outcome, researchers can use the Daily Activities Scale of the CP Module for children ≥2 years of age.

Within each scale, all PedsQL items have 5 options, corresponding to scores of 0, 25, 50, 75, or 100. Higher scores indicate better HRQoL or better functioning. For each scale, the mean score is reported. The psychosocial health summary score is the mean score of all items within the emotional, social, and school functioning scales. The physical health summary score is the same as the physical functioning scale score. The total scale score is the mean score for all items on the entire scale. For all scores, means are calculated by including only completed items. If a scale has >50% missing items, the scale score should not be calculated.

[H1]Discussion

The P-COSCA Steering Committee identified a COS for research involving children surviving cardiac arrest. This COS includes 5 outcomes: survival, brain function, cognitive function, physical function, and basic daily life skills. The P-COSCA includes assessment of survival status and brain function by using the PCPC at discharge or 30 days after the cardiac arrest (or both if possible), and again between 6 and 12 months after cardiac arrest. In addition, assessment of prearrest baseline brain function is included. Other COS outcomes (cognitive function, physical function, and basic daily life skills) are also evaluated between 6 and 12 months after cardiac arrest by using the PedsQL and additional modules. If resources are available, investigators may also include other assessments at 3 months after cardiac arrest and >1 year after cardiac arrest. Lastly, the use of the GOS-E Peds to assess brain function and the PCPC and the VABS-II, Vineland-3, or ABAS-3 to assess adaptive function are supplementary outcomes measures, depending upon availability and feasibility.

With this consensus statement, the P-COSCA initiative broadens the descriptions of pediatric cardiac arrest outcomes in 3 key ways. First, the P-COSCA initiative provides a standardized platform of outcomes, measures, and time points for assessment that improves the ability to compare results across studies and to analyze results via meta-analyses and systematic reviews. Next, the P-COSCA improves the utility of future studies by including assessment of prearrest brain functioning and identification of a change in this function after cardiac arrest. This is of particular importance in pediatrics because a high percentage of children who develop cardiac arrest, particularly in the hospital, have preexisting conditions.[17] Previous studies that have explicitly excluded children with baseline neurological deficits are not representative of the cardiac arrest population and may not convey an accurate representation of the extent and scope of cardiac arrest outcomes in the pediatric population. Accounting for prearrest baseline function may reduce bias toward the appearance of poor post–cardiac arrest brain function that may be attributable to prearrest co-morbidities rather than to the cardiac arrest itself. Including this baseline measure of neurological function will enhance our understanding of the full scope of outcomes after pediatric cardiac arrest. The survey participants clearly conveyed that assessment of survival and brain function are not sufficient measures of the sequelae of cardiac arrest. They noted that measures of HRQoL, such as cognitive function, physical function, and basic daily life skills, are also important. Thus, inclusion of these outcomes in the P-COSCA may provide a more complete picture of the consequences of pediatric cardiac arrest and required interventions.

The P-COSCA was viewed as an extension of the COSCA, not a separate initiative; t herefore, the outcomes of the COSCA Delphi were considered when designing outcomes that should be considered for the P-COSCA. Both COSs included assessment of survival and

neurological function at discharge or 30 days (or both if possible). However, key differences emerged. The COSCA focused on HRQoL and provided 3 potential options for assessment after 90 days and then every year after, if feasible. The P-COSCA evaluated HRQoL with more granular subcomponents, and like the COSCA, the P-COSCA sought to evaluate longer term outcomes pending resource availability. However, in contrast to the COSCA, the P-COSCA includes assessment of neurological function between 6 and 12 months after cardiac arrest and beyond the first year after cardiac arrest, if possible. This focus on neurological assessment and the longer timeframe was intentional because children may have ongoing brain development occurring independent of the cardiac arrest that affects brain and cognitive function. The P-COSCA, unlike the COSCA, also included a baseline neurological function assessment because many children who have a cardiac arrest have developmental abnormalities even before their arrest.[17]

A recent American Heart Association scientific statement proposed guidelines for studies of neurological prognostication in comatose adult and pediatric survivors of cardiac arrest.[63] This statement noted the challenge in neurological prognostication created by ongoing brain development in infants and children (especially to the age of 6 years). Many of the follow-up assessment time points proposed in the neurological prognostication statement were taken into consideration and are consistent with the P-COSCA, such as the inclusion of assessment of neurological outcome at hospital discharge or 1 month; and both statements include additional assessments during the first year. The neurological prognostication statement proposes neurological and HRQoL assessments at 3 months, 6 months, and 1 year for all ages and additional annual neurodevelopmental assessments for children until 3 years of age. There are important differences between the purposes and methods of the neurological prognostication

statement and the P-COSCA statement that account for differences in the proposed timing of outcomes assessments. First, the neurological prognostication statement focuses on assessment of only those patients who are comatose after cardiac arrest, while the P-COSCA focuses on evaluation of core outcomes for all cardiac arrest studies involving all survivors. Second, development of the P-COSCA used a Delphi approach involving almost 100 healthcare providers and parent/caregivers to garner their input, so it reflects a wide scope of outcome priorities. Third, identification of the P-COSCA highly weighted feasibility when selecting outcome measures and assessment time points. Although the approaches of these 2 scientific statements differ, the intent of the 2 documents is similar, and they are designed for distinct but complementary study populations.

We acknowledge several limitations of the P-COSCA initiative. Given the difficulty in obtaining parental involvement despite multiple attempts to invite enrollment, these recommendations were disproportionately representative of the priorities of healthcare providers. However, the Delphi process, a priori, attempted to account for what was most important to each stakeholder group. Another limitation inherent to the P-COSCA initiative is related to feasibility challenges of longitudinal outcomes study design; multiple time points and assessments beyond 1 year after arrest pose significant practical challenges for obtaining data, with the potential for loss of patients to follow-up. The P-COSCA outcomes measures were selected with attention to the measures that are currently available and that are feasible and practical to administer.

This COS is the next step in defining standardized outcomes for pediatric cardiac arrest studies, building on the work of the Utstein publication over 20 years ago.[19] The SC envisions the P-COSCA as the start of a dynamic, iterative process in which current gaps can be addressed. The OMERACT Filter 2.0 framework includes the core area of resource use/economic impact,

which was not included in either the COSCA or P-COSCA. Similarly, the influence of the child's neurodevelopmental trajectory on outcomes and determination of the optimal time points to assess a child's recovery were not fully addressed. The P-COSCA acknowledges the importance of evaluating outcomes beyond the first year after the cardiac arrest. Because it is unclear how age at the time of cardiac arrest impacts longer-term outcomes and lifelong function and development, outcome should be evaluated at key milestones to understand which cardiac arrest survivors will eventually be able to live independently and work. Finally, the SC acknowledges the need to understand the impact of cardiac arrest from the perspective of the patient. A validation of the P-COSCA is warranted in a larger cohort of family *and* patients.

[H1]Conclusions

With the support of ILCOR, a multidisciplinary group of healthcare providers and group of parents/caregivers defined a P-COSCA, which includes assessment of survival and brain function, as measured by using the PCPC at discharge from acute-care hospitalization or 30 days after arrest or both if feasible. The P-COSCA also includes retrospective assessment of prearrest brain function obtained via PCPC as soon as possible after arrest. In addition, the P-COSCA includes assessment of brain function, cognitive function, and physical function for all children and basic daily life skills for those ≥2 years of age between 6 and 12 months after arrest by using the PCPC and specific PedsQL scales. Supplementary reporting of the GOS-E Peds, VABS-II, Vineland-3, and ABAS-3 can be included if resources are available. Future additions of outcomes assessment tools and time points beyond the first year after cardiac arrest, when feasible, will enhance our understanding of pediatric outcomes after cardiac arrest.

Box, Tables, and Figures

Box. Survivor networks in the United States and the United Kingdom that were contacted to distribute surveys to parents of children who survived cardiac arrest.

United States
Sudden Cardiac Arrest Foundation
Sudden Cardiac Arrest Association
Nick of Time Foundation
Adamsheart Foundation
Parent Heart Watch
Simon's Heart
Minnesota SCA Survivor Network
United Kingdom
Sudden Cardiac Arrest UK
https://www.suddencardiacarrestuk.org/

SCA indicates sudden cardiac arrest.

Table 1. Core Areas, Outcomes, Measures, Time Points, and Methods for Collection

Core Areas	Outcomes (Domains)	Measure	Time Point	Methods
Survival	Survival		Hospital discharge or 30 d after cardiac arrest (or both if possible)	Caregiver report Medical records Death registry
			Between 6–12 mo after cardiac arrest	
Life impact	Brain function	PCPC	Prearrest baseline	Caregiver report Medical records
			Hospital discharge or 30 d after cardiac arrest (or both if possible)	
			Between 6–12 mo after cardiac arrest	
	Cognitive function	PedsQL Infant Scales: cognitive		

		functioning scale (<2 y) PedsQL Cognitive Functioning Scale Module (>2 y)	Between 6–12 mo after cardiac arrest	Caregiver report
	Physical function	PedsQL Infant Scales (<2 y) PedsQL Core Scale (>2 y)		
	Basic daily life skills	PedsQL CP Module Daily Activities Scale (>2 y)		

CP indicates cerebral palsy; PCPC, Pediatric Cerebral Performance Category; PedsQL, Pediatric Quality of Life Inventory.

Table 2. Summary and Content of Tools to Measure Brain Function

Tools	Developer, Website, Cost	Conceptual Focus and Outcome Domains Assessed	Age Range	Can Be Used to Measure Baseline Prearrest Functioning	Ease of Administration/Who Administers	How to Score	Used in Published Cardiac Arrest Studies?
PCPC	Available for no cost via Fiser et al[37]	Developed to quantify global cognitive impairment; modified based on a similar adult scale	Birth–18 y	Yes, retrospectively	10 minutes Chart review or caregiver interview Administered by healthcare provider English	Score falls into 1 of 6 categories, including normal, mild disability, moderate disability, severe disability, coma or vegetative state, death.	Yes
GOS-E Peds	Available for no cost via Beers et al[39]	Developed to quantify global outcome in children following traumatic brain injury; modified based on a similar adult scale	Birth–18 y	Baseline functioning incorporated into postinjury assessment	10 minutes Chart review or caregiver interview Administered by healthcare provider or research assistant English	Score falls into 1 of 8 categories, including upper good recovery, lower good recovery, upper moderate disability, lower moderate disability, upper severe disability, lower severe disability, vegetative state, death.	No

GOS-E Peds indicates Glasgow Outcome Scale–Extended Pediatric Revision; PCPC, Pediatric Cerebral Performance Category.

Table 3. Characteristics of Tools Considered to Measure Cognitive Functioning, Physical Functioning, and Basic Daily Life Skills After Survival From Pediatric Cardiac Arrest

Tools	Developer, Website, Cost	Conceptual Focus and Domains Assessed	Age Range	Can Be Used to Measure Baseline Prearrest Functioning	Ease of Administration/ Who Administers	How to Score	Used in Published Cardiac Arrest Studies
FSS	Available for no cost via Pollack et al[51]	Developed to rapidly quantify functional status in 6 domains (mental status, sensory, communication, motor function, feeding, and respiratory)	38 wk gestation –<18 y	Yes, retrospectively	10 minutes Chart review or caregiver interview Administered by healthcare provider or research assistant English	Functional status for each domain is categorized from 1 (normal)–5 (very severe dysfunction). Overall score ranges from 6–30.	No

PedsQL 4.0 Generic Core PedsQL Infant Scales PedsQL Cognitive Functioning Scale PedsQL Daily Activities Scale from the CP Module	Available for purchase via pedsql.org	Developed as a modular approach for measuring HRQoL, Generic Core includes 4 core scales (physical, emotional, social, and school functioning) in children 2–18 y. The infant-toddler version, designed for children 1–24 mo, includes 5 domains (physical symptoms and physical, social, emotional, and cognitive functioning).	1 mo–18 y (for generic core and infant scales) 2–18 y for the cognitive functioning and Daily Activities Scales	Yes, retrospectively	10 minutes Caregiver and self-report versions Multiple languages	Scores range from 0–100 for individual scales, summary scores, and total score. Higher scores indicate better functioning. Generic Core and Infant Scales include psychosocial health summary, physical health summary, and total score. Healthy population norms available for benchmarking.	No
VABS-II	Available for purchase via Pearson.com (at least through December 2019); see publisher website for pricing	Developed to measure functional skills in 4 domains (communication, daily living, socialization, motor skills). Each domain includes subdomains that are developmentally sequenced items,	Birth through adulthood	Yes, retrospectively	30–60 minutes Caregiver-report and interview format versions; interview format administered by trained clinician Caregiver-report in English Interview in English and Spanish	Age-corrected standard scores for overall adaptive behavior composite and 4 domains based on normative data	Yes

		starting with skills typical of infancy.					
Vineland-3	Available for purchase via Pearson.com; see publisher website for pricing	Same as above with updated items	Birth through adulthood	Yes, retrospectively	30–60 minutes Caregiver-report and interview format versions; interview format administered by trained clinician English and Spanish	Age-corrected standard scores for overall adaptive behavior composite and 4 domains based on normative data	No
ABAS-3	Available for purchase via multiple publishers (eg, Pearson.com); see publisher website for pricing	Developed to measure 11 essential skills areas and 3 major adaptive domains	Birth through adulthood	Yes, retrospectively	15–20 minutes Caregiver-report English and Spanish	Age-corrected standard scores for overall composite, 3 areas, and all domains	No

ABAS-3 indicates Adaptive Behavior Assessment System, Third Edition; CP, cerebral palsy; FSS, Functional Status Scale; HRQoL, health-related quality of life; PedsQL, Pediatric Quality of Life Inventory; VABS-II, Vineland Adaptive Behavior Scales, Second Edition; Vineland-3, Vineland Adaptive Behavioral Scales, Third Edition.

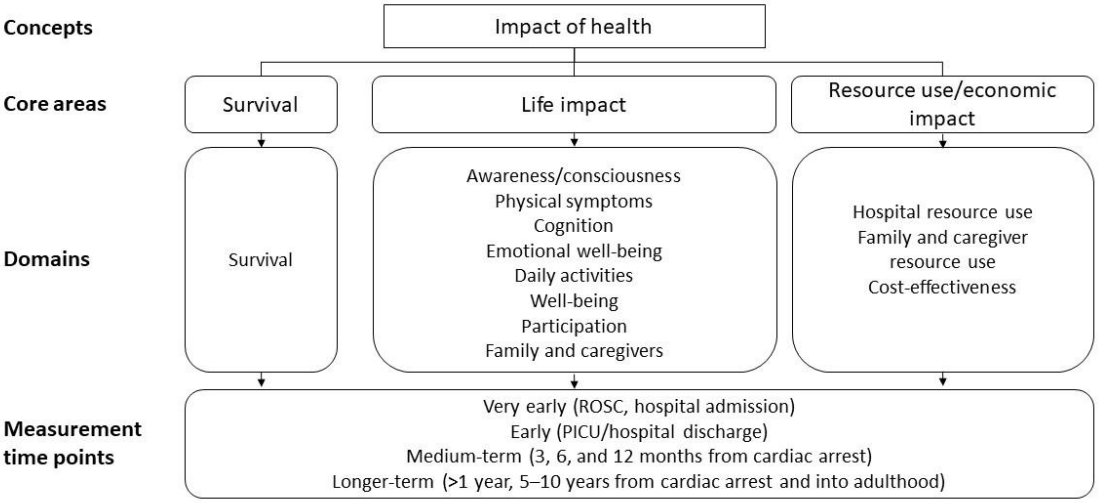

Figure 1. OMERACT Filter 2.0 framework modified for pediatric cardiac arrest. OMERACT indicates Outcome Measures in Rheumatology; PICU, pediatric intensive care unit; ROSC, return of spontaneous circulation. Reprinted from Boers et al.[72] Copyright © 2014, the authors. https://creativecommons.org/licenses/by-nc-nd/3.0/.

Core Area	Domains	Timing of Measurement		
		At hospital discharge	Within the first year after cardiac arrest	>1 y after cardiac arrest
Survival	Survival	●xo	●xo	●o
Life impact	Brain function	●x	●x	●xo
	Cognitive thinking function		●x	●xo
	Communication		●xo	●xo
	Physical function		●xo	●xo
	Fatigue			o
	Sleep			o
	Emotional well-being		●x	●xo
	Behavioral control			
	Basic daily life skills		●x	●x
	Activities			
	Education and school function			●x
	Social skills and relationships		●xo	●x
	Future potential			
	Daily family/household activities			
	Family participation in leisure and social activities			
	Family relationships	o	●x	●xo
Economic impact	Economic impact on the family	o	o	●x

Figure 2. Domains and time points presented in the initial survey were developed in step 1. An x indicates healthcare provider responses; o, parent/caregiver responses of >75% to round 1 of the survey; ●, outcomes and time points selected for round 2 of the survey based on >75% of responses of critical importance by healthcare providers and/or parents/caregivers. Gray boxes indicate domains and time points discussed at the SC consensus meeting to review results of survey.

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