

Developing consensus-based outcome domains for trials in children and adolescents with chronic kidney disease: an international Delphi survey

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24
25
26
27 **Word count (Abstract):** 300

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29 **Word count (Body):** ~~3740~~4108

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32
33 **Short title:** Consensus-based outcomes for trials in children with CKD

1 **Abstract**

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3 **Rationale and Objective:** The inconsistency in outcomes reported and lack of patient-reported outcomes
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5 across trials in children with chronic kidney disease (CKD) limits shared decision-making. We aimed to
6
7 generate a consensus-based prioritized list of critically important outcomes to be reported in all trials in
8
9 children with CKD.
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13 **Study design:** An online two-round Delphi survey in English, French and Hindi languages
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16 **Settings and participants:** Patients (aged 8-21 years), caregivers/family and healthcare professionals
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18 (HCPs) rated the importance of outcomes using a 9-point Likert scale, (7-9 indicating critical importance)
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20 and completed a Best-Worst Scale.
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23 **Analytical approach:** We assessed the absolute and relative importance of outcomes. Comments were
24
25 analyzed thematically.
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28 **Results:** 557 participants (72 [13%] patients, 132 [24%] caregivers and 353 [63%] HCPs) from 48
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30 countries completed Round 1 and 312 (56%) participants (28 [40 %] patients, 64 [46%] caregivers and 220
31
32 [56%] HCP) completed Round 2. Five outcomes were common in the top 10 for each group: mortality,
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34 kidney function, life participation, blood pressure and infection. Caregivers and HCPs rated cardiovascular
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36 disease higher than patients. Patients gave lower ratings to all outcomes compared with caregivers/HCPs
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38 except they rated life participation (Round 2 mean difference 0.1), academic performance (0.1), mobility
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40 (0.4), and ability to travel (0.4) higher than caregivers; and rated ability to travel (0.4) higher than HCPs.
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42 We identified three themes: alleviating disease and treatment burden, focusing on the whole child, and
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44 resolving fluctuating and conflicting goals.
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50 **Limitations:** Most participants completed the survey in English.
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53 **Conclusions:** Mortality, life participation, kidney function and blood pressure were consistently highly
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55 prioritized by patients, caregivers, and health professionals. Patients gave higher priority to some lifestyle-
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57 related outcomes compared with caregivers/HCPs. Establishing critically important outcomes for all trials
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59 in children with CKD may improve consistent reporting of survival, kidney health, clinical and life impact
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61 outcomes that are meaningful for decision-making.
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Index words: chronic kidney disease, consensus, outcomes, patient-centered outcomes, pediatrics,

Plain language summary

This study uses an international online Delphi survey to achieve consensus among children with chronic kidney disease (CKD), family members, and health professionals on outcomes that are critically important for trials in children with CKD. Mortality, life participation, kidney function and blood pressure were consistently highly prioritized by patients, caregivers, and health professionals. Consistent reporting of these critically important outcomes in trials ensures that the evidence is relevant and useful for decision-making and care of children with CKD.

1 INTRODUCTION

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6 Children with chronic kidney disease (CKD) have an increased risk of mortality, cardiovascular events,
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8 cognitive impairment and worse quality of life compared with the general population¹⁻⁴. ~~Treatment~~
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10 ~~decision-making can be challenging for many reasons.~~ The potential impact upon growth, development,
11
12 quality of life, mental well-being, and survival of CKD and its treatments is often unclear in childhood,
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14 and the consequences through to adulthood are even more uncertain⁵⁻¹⁰. CKD can also have a profound
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16 impact on the patient's family⁵⁻¹⁰. Furthermore, there is the added complexity of balancing the competing
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18 priorities of patients, caregivers and health professionals, which can also change as the child matures^{11,12}.
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20 Finally, trials in CKD do not consistently report outcomes of critical importance to patients, caregivers and
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22 healthcare professionals (HCP)¹³.
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30 A recent systematic review of 200 randomized trials conducted in children with CKD, found that over
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32 5700 different outcome measures for 100 different outcome domains were reported¹⁴. The most frequently
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34 reported outcomes were blood pressure, relapse/remission of underlying disease, kidney function,
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36 infection, and growth, present in only 25% to 37% of trials. Quality of life, mental health, development,
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38 education, and cognition are common concerns in children with CKD and their caregivers, yet these
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40 outcomes were reported in less than one per cent of trials¹⁴. Patient-reported outcomes that reflect how
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42 patients feel and function such as these are largely absent from trials^{14,15}.
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50 The problems with the selection and reporting of outcomes indicate the need for a core outcome set. This is
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52 defined as an “agreed minimum set of outcomes to be reported in all trials”, which are critically important
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54 to all stakeholder groups¹⁶. Core outcome sets have been established for adults with CKD through the
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56 international Standardized Outcomes in Nephrology (SONG) initiative¹³. The SONG Initiative aims to
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58 establish consensus-based core outcomes that are critically important to patients, caregivers and health
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60 professionals, to be consistently reported in trials. Since 2014, three core outcome sets have been
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1 established for adults on dialysis and with a kidney transplant¹³. As part of the SONG-Kids initiative, this
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3 study aimed to gain consensus among children with CKD, caregivers and family members, and health
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5 professionals, on critically important outcomes for trials in children and adolescents with CKD. This will
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7 directly inform the development of a core outcome set to be reported in all trials in children with CKD, to
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9 better support informed decision-making ~~based on outcomes that are critically important to patients,~~
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11 ~~caregivers and health professionals.~~
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18 **METHODS**

23 **Study design**

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27 The Delphi survey has been used to generate consensus on core outcomes to be used in trials for different
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29 patient populations, including children with other medical conditions¹⁷⁻²². The SONG-Kids Delphi Survey
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31 was administered online with two rounds ~~completed by a panel of participants with lived experience or~~
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33 ~~expertise in childhood CKD~~. Participants ~~were asked to~~ prioritize outcomes for trials in children across all
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35 stages of CKD. ~~In Round 2, participants were able to view and reflect on their previous score, the~~
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37 ~~distribution of the group scores, and comments made by the participants.~~ The survey was conducted in
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39 three languages (English, French, Hindi). The English survey was translated into French and Hindi by a
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41 bilingual health professional and ~~independently~~ checked by a second bilingual professional. The SONG-
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43 Kids Delphi process is shown in Figure S1.
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52 **Participant selection and recruitment**

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57 Patients aged 8 to 21 years with any stage of CKD (including CKD Stage 5 not requiring kidney
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59 replacement therapy, on dialysis, or with a kidney transplant), caregivers of children aged 0 to 21 years
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61 with CKD (i.e. parents, other family members, guardians), and HCP with an interest in pediatric
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1 nephrology (including physicians, nurses, allied health professionals, researchers, policy makers,
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3 regulators and industry) with experience or expertise in childhood CKD were eligible.
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8 ~~We used different recruitment strategies to maximize diversity and inclusivity.~~ Patients were recruited
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10 from ~~inpatient and outpatient settings in~~ hospitals, consumer organizations, the SONG database, and social
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12 media (Table S1). Health professionals were recruited through the SONG database, investigator networks
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14 and professional organizations. Participants ~~were able to access~~ed the Delphi survey via the SONG website
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16 (www.songinitiative.org) or via standardized invitation emails. Ethics approval provided by the University
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18 of Sydney (2017-304) and participating institutions (Table S1).
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25 **Data collection**

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30 *Selection of outcome domains:* For Round 1, we included outcome domains based on a systematic review
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32 and a nominal group technique study with patient and caregivers^{14,23}. We designed two versions of the
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34 surveys with the same list of outcomes: one for adult participants (caregivers and health professionals), and
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36 one for children (patients) with a reading level of 8 years and included images and emojis to explain the
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38 outcomes visually. For both surveys, an age-appropriate plain language definition was given for each
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40 outcome (Table S2 and S3). The order the outcomes appeared in outcomes was randomized. The SONG-
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42 Kids Steering Group and investigators reviewed the list of outcomes and the survey was piloted among
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44 eight health professionals and five children and their families. The survey was programmed and
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46 administered online using Qualtrics (*Qualtrics software, Provo, UT, United States*) from June 2018 to
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48 November 2018.
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57 *Round 1:* Participants rated the importance of each of the 27 outcome domains using a 9-point Likert scale.
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59 Scores 1-3 indicated “limited importance” (adult version)/“not important” (child-version), 4-6 indicated
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61 “important but not critical”/“important” and 7-9 indicated “critical importance”/“very important”, based
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1 on the Grading of Recommendations Assessment, Development and Evaluation (GRADE)²⁴. An option of
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3 “don’t know” was provided. Participants could enter comments for each outcome in free-text boxes and
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5 could suggest new outcomes. New outcomes suggested by more than 10% of participants were eligible to
6
7 be included in the next round. Outcomes with a mean of less than 7 or median less than 8 across all groups
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9 were excluded from Round 2.

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15 *Round 2:* Round 2 included 20 outcomes, none of which resulted from free text suggestions in round 1.
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17 Participants were shown their own scores from Round 1, the distribution of scores by patients, caregivers
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19 and health professionals and the total sample combined displayed in a column graph. Instructions on how
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21 to read the graph were provided to both adult and children participants. Participants could read de-
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23 identified comments provided in Round 1, which were grouped by patients, caregivers and health
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25 professionals. Participants re-rated the outcomes using the 9-point Likert scale and could again enter
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27 comments. To assess the importance of the outcomes relative to each other, participants also completed a
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29 Best-Worst Scale (BWS) Survey. The BWS survey is used to elicit preferences that involves less cognitive
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31 burden and provides better discrimination between outcomes, which helps demonstrate relative importance
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33 in addition to the nominal Likert scale²⁵. Participants were presented with five best-worst choice sets each
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35 consisting of six of the 16 outcomes. The outcomes included in each set were determined using a balanced,
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37 incomplete block design^{26,27}. The participants selected the most important and least important from each
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39 set.
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50 **Data analysis**

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54 *Quantitative analysis:* For both rounds, we calculated the mean score, median score and proportion of
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56 participants who rated the outcome as critically important (~~from~~ 7 to 9) for each outcome. Given that the
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58 three measures are fairly consistent, we chose to present the means in the text. However, the three
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60 measures are available the supplementary tables. We calculated the scores separately for patients,
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1 caregivers and health professionals, and then compared the family and health care professional groups with
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3 the patient group. Although we present the mean differences between the groups, we chose not to rely on
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5 the normality assumption and use a Mann-Whitney *U* test to compare the groups. The relative importance
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7 was estimated using a multinomial logistic regression model. Utility functions containing all outcomes and
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9 interaction terms for participant characteristics were constructed for the Best-Worst Survey. Following this
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11 approach, the mean regression coefficients of this function provided the relative importance scores for each
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13 outcome²⁷. The regression coefficients have the same underlying scale, therefore for ease of interpretation
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15 we used a scale of 1 (least important) to 9 (most important). Statistical analyses were undertaken using
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17 SPSS (*IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY*) and NLOGIT 6 (Econometric
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19 Software, Plainview, NY, USA). A p-value of less than 0.05 was considered statistically significant.
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28 *Definition of consensus for core outcomes:* The distribution of scores for the outcomes was unknown prior
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30 to data collection so the criteria for consensus for core outcome domains could not be defined *a priori*.
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32 “Consensus” to determine the top 3 to 5 outcomes (as recommended to ensure feasibility of
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34 implementation in all trials^{13,21}) was based on patient, caregiver and HCP having mean scores of more than
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36 7, median scores of equal to or greater than 8 and proportions rating the outcomes as ‘critically important’
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38 being greater than 75%. The thresholds were approved by the SONG-Kids Steering Group and the BWS
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40 scores were used to examine relative differences in preference scores across the stakeholders.
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47 *Qualitative analysis:* All comments from the survey were imported into Hyper RESEARCH (*Version 3.7,*
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49 *Randolph, MA, United States*) software for data analysis. Investigator (CL) used thematic analysis to code
50
51 the text and inductively identify themes to explain the reasons for prioritizing outcomes among stakeholder
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53 groups and changing in ratings across rounds. To enhance the analytical framework and to ensure the
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55 themes reflected the full range and depth of data collected²⁸, a second investigator (AT) read the open text
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57 responses, reviewed and discussed the themes with CL until consensus was reached.
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RESULTS

Participant characteristics

In Round 1, 557 participants across 48 countries completed the survey, of whom 72 (13%) were patients, 132 (24%) were family members/caregivers, and 353 (63%) were HCPs. By language, 533 (96%) (71 patients, 123 caregivers, 339 HCPs) completed the English survey, 23 (4%) (1 patient, 8 caregivers, 14 HCPs) completed the French survey, and 1 (0.1%) (1 caregiver) completed the survey in Hindi language. In Round 2, 312 (56% overall retention rate) participants from 48 countries completed the survey, of whom 28 (9% [40% retention]) were patients, 64 (20% [46% retention]) were caregivers, and 220 (71% [63% retention]) were HCPs. By language, 299 (96%) (29 patients, 57 caregivers, 213 HCPs) completed the English survey, 12 (4%) (0 patients, 4 caregivers, 8 HCPs) completed the French survey, and no participants completed the survey in Hindi language. Participant characteristics are provided in Tables 1 and 2.

Of the 28 patients who completed both rounds, 15 (54%) had a kidney transplant, six (21%) were on peritoneal dialysis, three (11%) were on hemodialysis, and 4 (14%) were not receiving kidney replacement therapy. The 337 patients and caregivers/family who completed both rounds were from 11 countries, ~~including the United States (25, 28%), Australia (16, 18%), Canada (11, 12%) and New Zealand (10, 11%) and Singapore (10, 11%).~~ Of the 220 health professionals who completed both rounds, 122 (55%) were nephrologists, 41 (18%) were nurses and 16 (7%) were researchers. Others included dieticians, pharmacists, policy makers, psychologists, social workers, and surgeons. Health professionals were from 39 countries, ~~with most from the United States (74, 34%), the United Kingdom (30, 14%), Australia (24, 11%) and Canada (18, 8%).~~

Delphi scores

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3 The mean scores across all groups for Rounds 1 and 2 are shown in Figures 1 and 2.
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8 *Round 1:* The mean and median scores and the proportion of participants scoring the outcomes from 7-9
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10 for each of the 29 outcome domains in Round 1 are shown in Table S3. The top ~~three five~~ outcomes for
11 patients were life participation (mean 7.8), blood pressure (7.5) ~~and~~, impact of the disease on family and
12 friends (7.5), ~~self-esteem (7.3) and ability to travel (7.3)~~. For caregivers the top ~~three five outcomes~~ were
13 kidney function (8.2), mortality (7.8) ~~and~~, life participation (7.7), ~~blood pressure (7.7), and infection (7.7)~~.
14
15 For health professionals, the top ~~three five~~ were mortality (8.1), kidney function (7.8) ~~and~~, cardiovascular
16 disease (7.8), ~~depression (7.8) and growth (7.8)~~. ~~Seven outcomes had a mean of less than 7 and a median~~
17 ~~of less than 8 across all groups and were not included in Round 2 (Table S3)~~. None of the new outcomes
18 (Table S4) were suggested by >10% of participants and were thus not included in Round 2.
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32 *Round 2:* The mean and median scores and the proportion of participants scoring the outcomes from 7-9
33 for each of the ~~20~~ outcome domains in Round 2 are provided in Table S5. The top ~~three five~~ outcomes for
34 patients were mortality (8.0), life participation (8.0) ~~and~~, kidney function (7.9), ~~blood pressure (7.5) and~~
35 ~~infection (7.4)~~; for caregivers: mortality (8.3), kidney function (8.3) ~~and~~, cardiovascular disease (8.1), ~~self-~~
36 ~~esteem (8.0), life participation (7.9)~~. The top ~~three five~~ for health professionals were mortality (8.4), kidney
37 function (8.3) ~~and~~, cardiovascular disease (8.2), ~~life participation (8.2), and depression (8.1)~~.
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50 **Differences between stakeholder groups**

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54 The differences in mean scores between patients and each of the other two stakeholder groups are shown in
55 Figure 3. In Round 2, patients rated the following five outcomes lower than caregivers on the Likert scale:
56 cardiovascular disease (mean difference 1.4, p= 0.01), self-esteem (0.8, p= 0.04), bone health (0.9,
57 p=0.05), anxiety (1.5, p= 0.004) and pain (1.3, p=0.005). Patients rated nine outcomes lower than health
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1 professionals: fatigue (0.8, p=0.04), cardiovascular disease (1.5, p=0.002), cognition (1.0, p=0.04), growth
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3 (0.3, p=0.002), hospitalization (0.9, p=0.02), bone health (1.1, p=0.02), anxiety (1.4, p<0.001), depression
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5 (1.7, p= 0.002), and pain (1.3, p=0.001). ~~Patients did not rate any outcome significantly higher than~~
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7 ~~caregivers and health professionals~~
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10 11 12 13 **Ranking of Outcomes** 14

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18 Table 3 and Figure S2 show the relative importance of outcomes on a scale of 1 (least important) to 9
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20 (most important). For patients, the top five most important outcomes were kidney function, mortality, life
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22 participation, blood pressure and cardiovascular disease with preference scores ranging from 8.5 (95% CI
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24 7.2 to 9.8) to 7.0 (5.7 to 8.2). Families and health professionals had similar preferences to patients with the
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26 exception of blood pressure which was of lower importance with preference scores of 4.9 (2.8 to 6.9) and
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28 6.5 (5.8 to 7.2) respectively compared to 7.4 (6.1 to 8.7) for patients. ~~Other differences in preferences~~
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30 ~~between patients and families were impact on family and friends with preference score of 6.3 (6.1 to 7.6)~~
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32 ~~for patients and 3.1 (1.3 to 5.0) for family, and hospitalization with preference scores of 4.3 (3 to 5.5) and~~
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34 ~~2.1 (0.2 to 4.1) for patients and family respectively.~~
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42 **Themes from comments** 43

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47 We identified three themes: alleviating disease and treatment burden, focusing on the whole child, and
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49 resolving fluctuating and conflicting goals. The subthemes are described below and encompass the
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51 perspectives of patients, caregivers and HCPs unless otherwise specified. Illustrative quotations are
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53 provided in Box 1.
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59 **Alleviating disease and treatment burden** 60 61 62 63 64 65

1 *Cause and effect of non-adherence:* HCPs considered adherence in prioritizing outcomes. Adherence was
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3 ~~regarded as a challenge because of the high burden of treatment.~~ For example, they attributed non-
4
5 adherence to depression and anxiety in patients: “kids who feel sad and hopeless are not going to look after
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7 themselves” (health professional), and were concerned about side-effects impacting on adherence: “~~often~~
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9 the side effects of the medication can change a child’s appearance and sometimes to the point of the child
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11 not taking them” (health professional). They considered bone health and cardiovascular disease important
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13 because they believed that medications and dietary interventions targeting these outcomes could be better
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15 explained to patients and thus potentially improve adherence.
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23 *Family support strengthening resilience:* Participants emphasized the ~~critical~~ role of social and family
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25 support to improve coping and better outcomes in children with CKD. Some patients prioritized mortality
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27 because of their family, “I want to live longer to be with my mum and sis.” (patient). Health professionals
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29 gave high priority to outcomes they believed would impact on the wellbeing of the family, such as
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31 infection, hospitalization, depression, anxiety, and reduced life participation.
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38 *Tensions between short and long-term risks:* Health professionals felt that the multiple trade-offs and
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40 uncertainty of risks was challenging. Some gave higher priority to immediate outcomes (e.g. life
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42 participation, kidney function, pain and blood pressure), because they could disrupt daily living – “the risk
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44 to die is smaller than the risk of being bothered by one of these patient-related outcomes” (health
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46 professional). Patients and caregivers also gave higher priority to immediate outcomes (e.g. fatigue, self-
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48 esteem, depression and anxiety and blood pressure) because it affected their lifestyle, required changes to
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50 treatment, and added burdens, “I did rate [blood pressure] highly as my daughter had fluctuating blood
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52 pressure which necessitated constant changes to medication type and dosages causing physical symptoms.”
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54 (caregiver). Patients commented that “steroids” changed their appearance and “gave them nightmares” and
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56 thus prioritized self-esteem and depression: “certain drugs, namely steroids, cause side effects in the way
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1 you look and can make it even harder to deal with a diagnosis because you don't even look the same"

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3 (patient).
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8 **Focusing on the whole child** 9

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13 *Striving for normalcy in childhood:* Participants prioritized outcomes that would enable some semblance of
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15 normality, "it is important to the child as well as their family that they lead the most normal life possible to
16
17 contribute to overall health and well-being" (health professional). ~~P-As such,~~ participants rated life
18
19 participation, ability to travel, fatigue and pain highly, as these related to having the capacity to live well.
20
21 Caregivers believed that "maximizing participation in day-to-day activities, to remind them (and us) that
22
23 they are part of the human race" (caregiver) was important. Patients also gave high priority to the outcome
24
25 of life participation so they could "be themselves" (patient).
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33 *Helping to reach full potential:* Participants considered patients' long-term life plans and prioritized d highly
34
35 outcomes that would enable patients to reach their potential in adulthood, particularly in terms of
36
37 educational and vocational opportunities. Some were adamant that CKD should not "stop [patients] from
38
39 accomplishing what they want." (caregiver). Patients were concerned that the time needed to manage their
40
41 CKD and being unable to attend and perform at school took away from their future success, and thus gave
42
43 higher priority to cognition and academic performance. Caregivers and HCPs did not want patients to "feel
44
45 left behind their peers" or unable to reach "educational attainment and [have] future employment
46
47 prospects." (health professional).
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54 **Resolving fluctuating and conflicting goals** 55 56 57 58

59 *Achieving wellbeing through to adulthood:* Patients and caregivers were concerned with immediate
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61 outcomes of CKD (e.g. academic performance, life participation ~~and other patient-reported outcomes~~).
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1 Some found it too “overwhelming” to think about long-term outcomes, “there are too many short-term
2 concerns for us to focus on mortality” (family member). ~~In contrast, health professionals~~ HCPs were
3 focused on outcomes that could have implications in adulthood (e.g. mortality, cardiovascular disease,
4 kidney function, growth and cognition) because their medical decisions could have long-term impacts ~~on~~
5 ~~the child~~ — “I am conscious that the treatments we give in childhood and what we accept to keep the child
6 well may have an impact on their future cardiovascular risk” (health professional). Health professionals
7 rated life participation highly so patients could “remain active and engaged with peers and to grow into
8 contributing members of society” (health professional).
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23 *Responding to shifting health:* Participants prioritized outcomes based on the stability of the patients’
24 health and debilitating symptoms. Outcomes such as infection impaired their health, and subsequently
25 limited life participation, and academic performance: “school goes on the backburner when you get super
26 sick” (patient). They recognized that changes in the patient’s health status could, ~~which were sometimes~~
27 unpredictable or sudden, which meant the way they valued outcomes could also change.
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37 **DISCUSSION**

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42 Mortality, kidney function, life participation, blood pressure, cardiovascular disease and infection were the
43 outcomes of highest priority to children with CKD, their caregivers and HCPs. The top four outcomes
44 (mortality, kidney function, life participation and blood pressure) were consistently within the top five
45 across all three stakeholder groups. For patients, infection was in the top five, and self-esteem and
46 depression were in the top five for caregivers and HCPs, respectively. Collectively these reflect a focus on
47 survival and meaningfully participating in life, whilst maintaining health and minimizing the risk of short-
48 term and long-term complications. While caregivers and HCPs gave highest priority to clinical outcomes,
49 life participation was the most important patient-reported outcome for all stakeholder groups. Other
50 patient-reported outcomes of importance included self-esteem, anxiety, depression, impact on
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1 family/friends ~~and f, fatigue, academic performance, cognition, mobility, and ability to travel. In~~
2
3 ~~comparison, O~~utcomes including growth, bone health, hospitalization, and anemia were of relatively
4
5 lower importance. ~~This e-prioritization of these outcomes~~ reflects a focus on alleviating the burden of
6
7 disease and treatment, a comprehensive and holistic consideration of the child and family, and ~~the need to~~
8
9 recognizing~~ze~~ and address~~ing~~ different treatment goals.
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15 Mortality and kidney function were of critical importance to ~~patients, caregivers and health~~
16
17 ~~professionals~~ all stakeholders. ~~The mortality rates of children with kidney failure are 30 times that of their~~
18
19 ~~age-matched general population~~⁴. ~~In adulthood, cardiovascular disease, infection and cancer are major~~
20
21 ~~drivers of morbidity and mortality~~²⁹. The high priority given to mortality by all subgroups suggests that
22
23 patients and caregivers may be cognizant of the higher mortality rates of children with CKD~~this~~, and want
24
25 children to be able to reach their potential in adulthood. Kidney function was considered critical to
26
27 monitoring disease progression and planning for dialysis or transplantation, a similar concern in adults
28
29 with CKD²³. ~~This may also be because declining kidney function has been found to be associated with~~
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31 ~~worsening overall health~~³⁰.
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40 Other outcomes that were thought to be potentially life-threatening or with a high burden of treatment,
41
42 such as infection, cardiovascular disease, or blood pressure problems, were also prioritized highly by all
43
44 groups. ~~This may also relate to awareness among clinicians that infections and cardiovascular disease are~~
45
46 ~~the main causes of mortality in adult patients who commenced kidney replacement therapy in childhood~~³¹.
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50 Infection is also the most frequent cause of hospitalization in patients requiring kidney replacement
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52 therapy³²⁻³⁵, which may explain the higher prioritization of this outcome. Other outcomes such as anemia,
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54 bone health, growth and pain, may have been indicated to be of relatively lower priority as they were
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56 perceived to be less life-threatening or because patient did not experience related symptoms.
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1 ~~In general, the priorities for outcomes were similar across all three groups. Notably, T~~the highest
2
3 prioritized patient-reported outcome across all groups was life participation. ~~This finding reinforces that~~
4 ~~CKD and the treatment burden can severely limit the patient's ability to do their daily activities and~~
5 ~~accomplish their goals.~~ Studies have shown that children with CKD feel restricted in social activities,
6
7 physical abilities, and overall life participation^{36,37}. ~~Life participation has also been highly prioritized by~~
8 ~~adults with CKD^{17,21,38,39}.~~ Of note, caregivers and HCPs tended to rate anxiety, depression, cognition and
9
10 pain higher than patients. Some studies have shown differences in how patients and caregivers rate the
11
12 child's quality of life and symptoms burden⁴⁰⁻⁴². ~~It is possible that P~~patients may perceived they are able to
13
14 adapt to their illness^{43,44} ~~or . Another explanation may be that children~~ focus on their immediate
15
16 circumstances and view their life more positively whereas their parents consider the ~~uncertainty and~~
17
18 potential difficulties in their child's longer-term future⁴². ~~Some children with CKD report their own quality~~
19
20 ~~of life as being no different than their healthy peers⁴⁵.~~
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33 Patients gave higher priority to impact on family and friends, compared with caregivers. This is consistent
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35 with family functioning being closely related to their overall well-being⁴⁶. Having direct experience with
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37 CKD in the school-setting, patients placed greater emphasis on self-esteem and cognition⁴⁷. For patients,
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39 growth appeared to be of lower priority compared with caregivers and HCPs. This may be because HCPs
40
41 believe that growth is associated with better quality of life^{48,49}, and CVD/vascular disease.
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47 Our Delphi survey included participants from 48 countries, ~~which indicates the breadth and diversity of the~~
48 ~~participants. We and we~~ achieved a reasonably high retention rate of 56% from Round 1 and 2. The
49
50 survey was available in multiple languages to enable a wider reach ~~and was available in two versions— for~~
51
52 ~~children and adults.~~ However, there are some potential limitations. Most ~~of the~~ participants were English-
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54 speaking and from high-income countries. Very few participants completed the survey in Hindi (n=1) and
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56 French (n=23) languages, ~~and we are unable to ascertain the reason.~~ There were also relatively few
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58 children who completed both rounds, though we note the number of children engaged in the process is
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1 higher than other initiatives to develop core outcomes sets for children. There were also small participant
2 numbers by stages of CKD and age. Approximately 70% of patients/caregivers had direct experience with
3 kidney replacement therapy and may have a different perspective regarding the importance of issues in
4 earlier CKD than those who have not yet experienced kidney replacement therapy. While health
5 professionals comprised the majority of participants in this survey (63%, round 1), this is lower compared
6 with the proportion of health professionals in the Delphi surveys to prioritize outcomes for adults receiving
7 kidney replacement therapy (72%)^{17,21,38}. The Delphi was administered using an online platform to
8 maximize participation and ~~this reduce errors in data entry, however this~~ would have prohibited
9 involvement from those without access to internet or limited computer literacy. ~~Nonetheless, the top~~
10 ~~prioritized outcomes in this study were similar to those identified in focus groups studies with children~~
11 ~~with CKD,~~^{11,23};

12 The most critically important outcomes to patients, caregivers and HCPs were mortality, kidney function,
13 life participation, blood pressure, cardiovascular disease and infection. Life participation was the most
14 highly prioritized patient-reported outcome. These will be considered for the core outcome set to be
15 reported in all trials in children with CKD, which will involve consensus workshops and public
16 consultation. Once the core outcome domains are established, further work will involve identifying or
17 developing feasible and valid core outcome measures for each outcome. Establishing and implementing a
18 core outcome set will help to improve the relevance and consistency of evidence to better inform shared
19 decision-making for children and adolescents with CKD.

1 **Figure legends**
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6 **Figure 1.** Mean scores of patients, family/caregivers, and health professionals in Round 1
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8 **Figure 2.** Mean scores of patients, family/caregivers, and health professionals in Round 2
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10 **Figure 3.** Difference in mean scores among patients, caregivers and health professionals for rounds 1 and
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13 2. Patients is the referent group.
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15 The graph shows mean differences of scores. The patient group is the referent group. The red markers
16 show differences in mean ratings in round 1, and blue markers represent mean differences in ratings in
17 round 2. Square markers represent the difference between caregiver means and patient means of ratings.
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22 Diamond markers represent difference between HCP and patient mean ratings.
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24 Markers closer to the axis indicate ratings are closer to the patient group (consensus). E.g. for mortality,
25 the blue markers indicate that the caregivers (square marker) and the HCP (diamond marker) have smaller
26 difference in mean rating from patients in round 2 than in round 1 (red markers are further away from the
27 axis than the blue markers).
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1 **Supplementary files**
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6 **Table S1.** Institutional Ethics Review Boards of participating sites
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8 **Table S2.** Outcomes and definitions
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10 **Table S3.** Round 1 means, medians and proportion (rating 7-9) of patients/caregivers and health
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12 professionals for 27 outcomes.
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15 **Table S4.** Suggested outcomes by participants in round 1.
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18 **Table S5.** Round 2 means, medians and proportions (rating 7-9) of patients/caregivers and health
19
20 professionals for 20 outcomes.
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23 **Figure S1.** SONG-Kids Delphi process
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25 **Figure S2.** Mean relative importance scores of patients, caregivers and health professionals based on the
26
27 Best-Worst Scale. Ordered by the mean importance scores of patients (error bars are the 95% CI).
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1 **Article information**

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Acknowledgements:

We thank all the patients, caregivers and health professionals who gave their time to participate in the study.

Support and financial disclosure declaration:

The authors have no financial relationships relevant to this article to disclose. C.L is supported by the NHMRC Program Grant (ID1092957). C.S.H is supported by the NHMRC Program Grant (ID1092957). A.T. is supported by a NHMRC Fellowship (ID1106716). The study was funded by The University of Sydney Research Accelerator Grant and the NHMRC Program Grant Better Evidence and Translation in Chronic Kidney Disease (BEAT-CKD) (ID1092957). The funders had no role in the study design, data collection, analysis, reporting, or decision to submit for publication. The authors have no conflicts of interest relevant to this article to disclose.

Financial conflict of interest:

Charlotte Logeman	none
Chandana Guha	none
Martin Howell	none
Camilla S. Hanson	none
Jonathan C. Craig	none
Susan Samuel	none
Michael Zappitelli	none
Mina Matsuda-Abedini	none
Allison Dart	none

1	Susan Furth	none
2		
3	Allison Eddy	none
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5		
6	Jaap Groothoff	none
7		
8	Hui-Kim Yap	none
9		
10		
11	Detlef Bockenhauer	none
12		
13	Aditi Sinha	none
14		
15		
16	Stephen I. Alexander	none
17		
18	Stuart L. Goldstein	none
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21	Debbie S. Gipson	none
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23	Mini Michael	none
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25		
26	Amanda Walker	none
27		
28	Joshua Kausman	none
29		
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31	Segolene Gaillard	none
32		
33	Justine Bacchetta	none
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35		
36	Michelle N Rheault	none
37		
38	Bradley A Warady	none
39		
40		
41	Alicia Neu	none
42		
43	Martin Christian	none
44		
45	Steven McTaggart	none
46		
47		
48	Isaac Liu	none
49		
50		
51	Sharon Teo	none
52		
53		
54	Benedicte Sautenet	none
55		
56		
57	Talia Gutman	none
58		
59		
60	Simon Carter	none
61		
62	Armando Teixeira-Pinto	none
63		
64		
65	Allison Tong	none

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Contributions

Research idea and study design: All authors; data acquisition: CL, CSH, JCC, SS, MZ, MM, AD, SF, AE, HY, DB, AS, SIA, DSG, MM, AW, JK, SG, JB, MNR, BAW, AN, MC, SM, IL, ST, BS, TG, SC, AT ; data analysis/interpretation: CL, CG, MH, CSH, JCC, SS, MZ, AD, SF, AE, JG, HY, DB, AS, DSG, MM, AW, JK, MNR, BAW, AN, MC, SM, BS, TG, ATP, AT; supervision or mentorship: MH, AT, JCC. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual’s own contributions and to ensure that questions pertaining to the accuracy or integrity of any portion of the work, even one in which the author was not directly involved, are appropriately investigated and resolved, including with documentation in the literature if appropriate.

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1 **Table legends**

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3 **Table 1.** Characteristics of patients/caregivers

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5 **Table 2.** Characteristics of health professionals

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7 **Table 3.** Mean preference scores scaled from 1 least important to 9 most important from BWS survey with

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9 95% confidence interval.

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11 **Box 1.** Selected illustrative quotations

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Table 1. Characteristics of patients/caregivers.

Characteristic		Round 1, n (%) 204 participants	Round 2, n (%) 92 participants	
Role				
Patient		72 (35)	28 (30)	
Caregiver/family		132 (65)	64 (70)	
Sex				
Male		67 (33)	25 (27)	
Female		134 (66)	67 (73)	
Prefer not to say		3 (1)	0 (0)	
Age group (years)				
Child patient	8-14	24 (12)	7 (8)	
	15-18	25 (12)	11 (12)	
	19-21	16 (9)	7 (8)	
	Family/caregiver*	18-30	10 (5)	3 (3)
		31-40	48 (22)	22 (24)
		41-50	53 (26)	27 (29)
		51-60	22 (11)	12 (13)
	61-70	6 (3)	3 (3)	
71-80	0 (0)	0 (0)		
> 81	0 (0)	0 (0)		
Cause of kidney disease				
Congenital anomaly of the kidney and urinary tract		71 (35)	24 (26)	
Glomerular disease		43 (21)	27 (29)	
Cystic kidneys		17 (8)	9 (10)	
Hemolytic uremic syndrome		5 (2)	2 (2)	
Tumours		5 (2)	5 (5)	
Did not recover after severe acute kidney injury		6 (3)	3 (3)	
I don't know		20 (10)	7 (8)	
Other		37 (18)	15 (16)	
Current treatment				
Not on dialysis or transplant		59 (30)	27 (29)	
Haemodialysis (at home)		5 (2)	2 (2)	
Haemodialysis (hospital)		23 (11)	5 (5)	
Peritoneal dialysis		25 (12)	13 (14)	
Transplant (deceased donor)		37 (18)	14 (15)	
Transplant (living donor)		55 (27)	31 (34)	
Country**				
United States of America		69 (34)	25 (27)	
Australia		27 (13)	16 (17)	
United Kingdom		22 (11)	8 (9)	
Singapore		21 (10)	10 (11)	
Canada		17 (8)	11 (12)	
India		17 (8)	5 (5)	
New Zealand		15 (7)	10 (11)	
Other*		16 (8)	7 (8)	

*5 participants indicated their role as a "patient." **Other includes 8 countries (in descending order of number of participants in round 1): France, Morocco, Myanmar, Malaysia, Pakistan, Philippines, Portugal and Saudi Arabia. For those "not on dialysis or transplant" the stage of CKD was not collected.

Table 2. Characteristics of health professionals.

Characteristic	Round 1, n (%) 353 participants	Round 2, n (%) 220 participants
I am a:		
Adult nephrologist	42 (12)	35 (16)
Pediatric nephrologist	139 (39)	87 (40)
Surgeon	3 (1)	3 (1)
Nurse	79 (22)	41 (19)
Social worker	9 (3)	4 (2)
Psychologist	11 (3)	3 (1)
Dietician	18 (5)	10 (5)
Researcher	18 (5)	16 (7)
Pharmacist	5 (1)	3 (1)
Policy maker	1 (0)	1 (1)
Other	28 (8)	17 (8)
Gender		
Male	94 (27)	69 (31)
Female	258 (73)	151 (69)
Prefer not to say	1 (0)	0 (0)
Age group (years)		
18-30	28 (8)	15 (7)
31-40	99 (28)	44 (20)
41-50	113 (32)	76 (35)
51-60	82 (23)	60 (27)
61-70	27 (8)	22 (10)
71-80	4 (1)	3 (1)
Years of experience in paediatric kidney disease		
≤10	145 (41)	75 (34)
11-20	86 (24)	55 (25)
21-30	50 (14)	37 (17)
>30	30 (9)	22 (10)
None/not applicable	42 (12)	31 (14)
Number of trials as investigator		
0	190 (54)	110 (50)
1-5	91 (26)	56 (25)
6-10	40 (11)	29 (13)
11-15	12 (3)	8 (4)
>15	20 (6)	17 (8)
Country*		
United States of America	136 (39)	74 (34)
United Kingdom	44 (13)	30 (14)
Australia	31 (9)	24 (11)
Canada	25 (7)	18 (5)
Singapore	15 (4)	2 (1)
France	10 (3)	7 (3)
Germany	10 (3)	8 (4)
Other*	82 (23)	57 (26)

*Other includes 38 countries (in descending order of number of participants in round 1): Malaysia, Belgium, New Zealand, India, Italy, Poland, Brazil, Russian Federation, Argentina, Netherlands, Romania, Serbia, Turkey, Bolivia, China, Czech Republic, Egypt and Greece.

Table 3. Mean preference scores scaled from 1 least important to 9 most important from BWS survey with 95% confidence interval.

Outcome	Patient	Family	Health Professionals
Kidney function	8.5 (7.2-9.8)	7.5 (5.6-9.5)	8.2 (7.5-8.9)
Mortality	8.3 (7-9.6)	8.9 (6.9-10.9)	9.0 (8.3-9.7)
Life participation	7.8 (6.5-9.1)	6.6 (4.7-8.6)	6.8 (6.1-7.4)
Blood pressure	7.4 (6.1-8.7)	4.9 (2.8-6.9)	6.5 (5.8-7.2)
Cardiovascular disease	7.0 (5.7-8.2)	8.2 (6.1-10.2)	7.9 (7.3-8.6)
Infection	6.5 (5.2-7.8)	7.0 (5.0-9.0)	6.5 (5.8-7.2)
Depressive symptoms	6.4 (5.1-7.6)	6.3 (4.3-8.3)	6.8 (6.1-7.5)
Impact on family/friends	6.3 (5.1-7.6)	3.1 (1.3-5.0)	4.1 (3.5-4.8)
Cognition	5.9 (4.6-7.1)	4.7 (2.8-6.7)	4.8 (4.2-5.5)
Self-esteem	5.8 (4.5-7.1)	5 (3.1-6.9)	4.8 (4.1-5.4)
Fatigue/energy	5.7 (4.3-7)	5.4 (3.4-7.3)	6.5 (5.8-7.2)
Anxiety/stress	5.5 (4.2-6.7)	6.6 (4.6-8.6)	5.9 (5.2-6.6)
Mobility/Physical activity	5.4 (4.1-6.7)	5.6 (3.7-7.6)	5.2 (4.5-5.8)
Growth	5.1 (3.8-6.4)	4.5 (2.6-6.4)	4.2 (3.5-4.8)
Pain	5.0 (3.7-6.2)	5.7 (3.9-7.5)	5.6 (5-6.3)
Bone health	4.9 (3.5-6.2)	4.2 (2.2-6.1)	4.3 (3.6-5.0)
Hospitalization	4.3 (3.0-5.5)	2.1 (0.2-4.1)	4.2 (3.6-4.9)
Anemia	4.1 (2.8-5.3)	4.6 (2.6-6.6)	4.3 (3.6-5.0)
Academic performance	3.7 (2.4-5.0)	3.1 (1.2-5.0)	3.1 (2.4-3.7)
Ability to travel (ref)	1 (Ref)	1 (Ref)	1 (Ref)

1 **Box 1. Selected illustrative quotations**

Theme	Illustrative Quotation
Alleviating disease and treatment burden	
Cause and effect of non-adherence	<p>An increasing problem in healthy young people, let alone those with a chronic disease. Evidence in young adults that mental health problems are common and linked with wellbeing and adherence. (Anxiety/stress; HCP)</p> <p>This is extremely important as the child's mental health will have an impact on the rest of their life & potentially their compliance/ concordance with treatment. (Self-esteem; HCP)</p> <p>Self-esteem is really affected by chronic disease, especially body image when a child is on peritoneal dialysis or post-transplant. Often the side effects of the medications can change a child's appearance and sometimes to the point of the child not taking them, so they do not have the side effects. (Self-esteem; HCP)</p> <p>Kids who feel sad and hopeless are not going to look after themselves. Staying "well" is hard work and so if they feel sad or hopeless, they cannot do the work. We need to be aware of all aspects of our patient's well-being. (Depression; HCP)</p> <p>This is something that we address but I don't think we emphasize it enough. There might be more compliance with diet and medications if we could emphasize the significance of cardiovascular disease. (CVD; HCP)</p>
Family support strengthening resilience	<p>I want to live longer to be with my mum and sis (Death; Patient)</p> <p>Huge upheaval, but ultimately, we got through and came out stronger. (Impact on family/friends; C/F)</p> <p>Social support is a multi-dimension concept. It depends on income, social circle, cultural background... Fortunately, we are lucky financially and we have a close family supporting each other. (Impact on family/friends; C/F)</p> <p>This outcome is not only important for wellbeing but is also important for resilience. Feeling positive and hopeful makes treatment, medication, food restrictions and lifestyle limitations easier to accept and comply with. Ability of parents and health professionals to help children with kidney disease manage their depressive symptoms also has a significant impact on the child's mental health status. (Depression; C/F)</p> <p>My daughter has a lot of pain when she wakes up in the mornings. I think it would be great to let parents have more awareness how the child would be feeling so we can know what to expect especially as a young child us parents try to figure out what is wrong with their children and end up doing a bit of research themselves to find these things out. (Pain; C/F)</p> <p>The family approach and attitudes can be a major influence on the success or otherwise of the child's life participation. (Life participation; HCP)</p>
Tensions between short and long term risks	<p>Certain drugs, namely steroids, cause side effects in the way you look and can make it even harder to deal with a diagnosis because you don't even look the same. (Self-esteem; Patient)</p> <p>I was flown to hospital because of high blood pressure. (Blood pressure; Patient)</p> <p>We had issues with acute severe steroid induced mood disorder, leading to adjustment disorder after suddenly becoming ill at the age of 10 having never had health issues previously. It has taken significant input from mental health professionals to assist with transition back to normal functioning. (Anxiety/stress; C/F)</p> <p>I didn't know about the impact of high blood pressure on kidney disease. But I did rate it highly as my daughter had fluctuating blood pressure which necessitated constant changes to medication type and dosages. Each of these changes resulted in physical symptoms such as dizziness, heart palpitations etc. Doctors and nurses who cared for my daughter placed different levels of importance on blood pressure levels which resulted in conflicting advice. I sometimes felt that I had to make a decision about an acceptable blood pressure level because there wasn't consensus between the two professions. (BP; C/F)</p> <p>Extremely important to treat. It is one of those outcomes that has a widespread impact on many other outcomes, clinical and psychosocial. (Depression; HCP)</p> <p>Under-appreciated and under-recognized across the spectrum for children and young people. Inadequate service provision can lead to it being pushed down the priority list into the "too difficult to deal with" box. Need to identify it measurably first and demonstrate effective interventions - including cost-effective - to change public policy approach to resourcing. (Depression; HCP)</p>
Focusing on the whole child	
Striving for normalcy in childhood	<p>I was always tired at the beginning and it created a lot of problems for me because then I wasn't socializing, or doing schoolwork, or being "myself." (Fatigue; Patient)</p> <p>Important to ensure that CKD/ESRF sufferers are able to maximize participation in day-to-day activities, to remind them (and us!) that they are part of the human race. (Life participation; C/F)</p> <p>My daughter is taking adult doses of blood pressure medications and is only 7 years old. It makes her tired and she can get cranky. (Blood pressure; C/F)</p> <p>We forget children need to be children, they do not know how to deal with the fear and worries about their own health. Kids are also very smart and know when they are not being told the whole truth</p>

1 because we are trying to protect them. We need to be more aware of what each child need so they
 2 are not living in fear because that fear will impact their entire well-being. (Anxiety/stress; HCP)
 3 Because expecting the child to perform well at school normalizes the situation the child is in. Not
 4 expecting the child to perform well is in a way emphasizing the part the disease plays in the child's
 5 life. (Academic performance; HCP)
 6 Kids are often placed in a "sick" role and we do not expect them to participate in physical activity,
 7 sometimes being on dialysis prevents them from taking part in some activities, but we need to
 8 emphasize total body health so that kids can keep involved in the activities they enjoy. They also
 9 will feel better overall not leading a sedentary lifestyle. (Physical ability; HCP)
 10 This is hugely important for the child and the family unit to be able to be in their own environment
 11 doing things as a family. It is important for the child to feel as normal as possible. (Ability to travel;
 12 HCP)
 13 This contributes to overall health and well-being; it is important to the child as well as their family that
 14 they lead the most normal life possible. We need to be more aware of how our medical
 15 interventions affect the child and family's overall lifestyle. (Life participation; HCP)

Helping to reach full potential

16 I hate staying in the hospital for treatment all the medical stuff not being able to go to school and
 17 social activities sometimes it affects school performance example: failing (Hospitalization; Patient)
 18 The child can miss multiple days and fall behind in class. Which will effect on how they perceive
 19 themselves being smart. (Academic performance; C/F)
 20 I try to instill in my child that even though they suffer from this disease that it won't stop her from
 21 accomplishing what she wants. It might be a harder goal, but she can do it. (Life participation; C/F)
 22 Again, this gives them the best start in life & for the future. It is also important for them not to feel left
 23 behind their peers, so they are keeping up with them. It is important that a child who is missing lots
 24 of school is given educational support when in for dialysis of hospital admissions if well enough.
 25 (Academic performance; HCP)
 26 Has a major impact on self-management and concordance with treatment as child moves to
 27 adulthood. Also impact on educational attainment and future employment prospects (Cognition;
 28 HCP)

Resolving fluctuating and conflicting goals

Achieving wellbeing through to adulthood

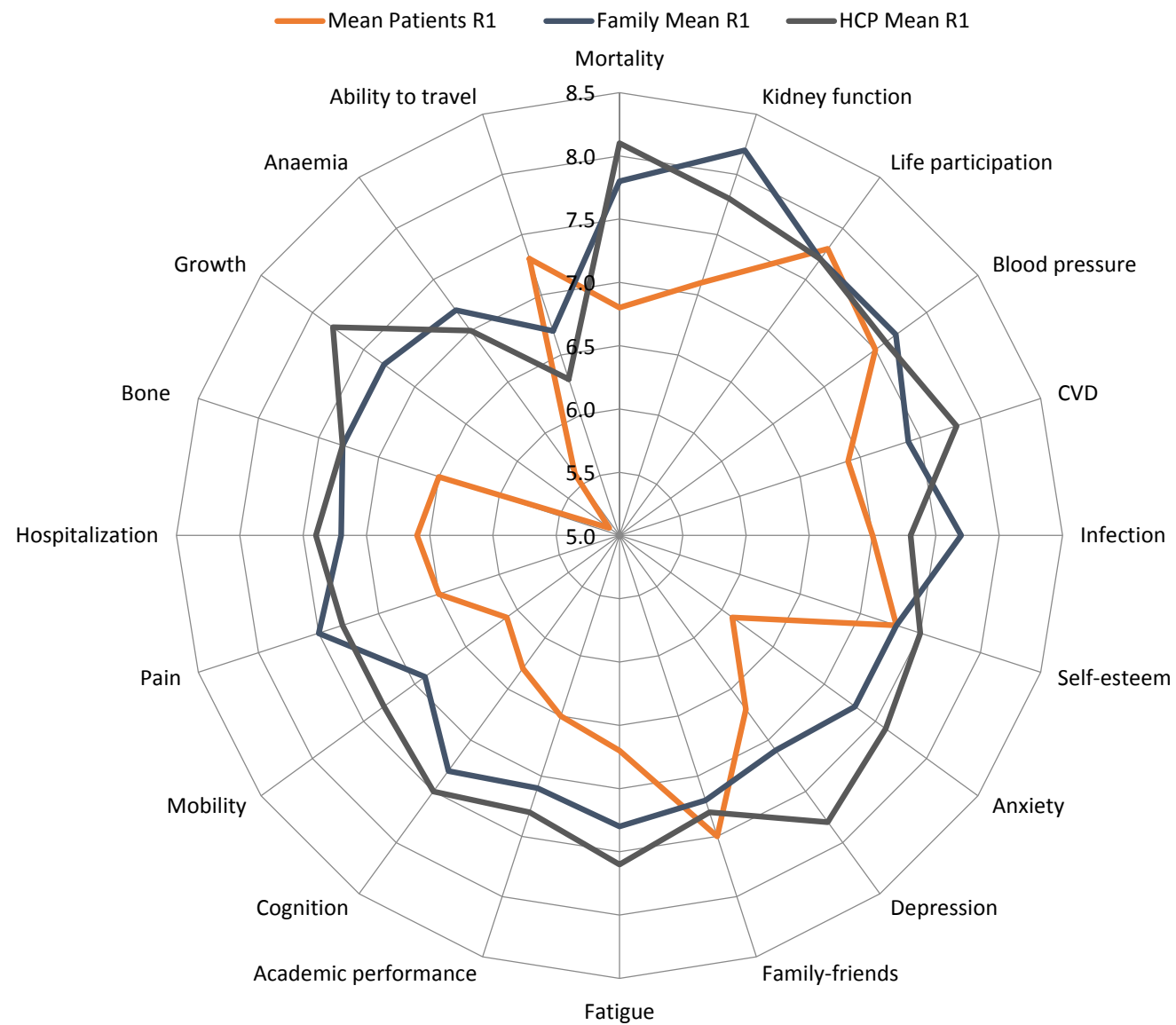
29 Likely duration of the transplanted kidney is a more immediate concern for us. There are too many
 30 short-term concerns for us to focus on mortality. It is also very overwhelming to think about
 31 mortality. (Death; C/F)
 32 I hope this will highlight the ways we can support academic performance to better their overall life
 33 chances for their future as adults. It is important to understand the affect chronic kidney disease has
 34 on this & the parent's perception/ intervention on this. (Academic performance; HCP)
 35 Achieving school potential is essential to growing up to be a productive and happy adult. (Academic
 36 performance; HCP)
 37 The immediate needs are always the most important, but we often do not let our families know about
 38 the long-term challenges that these kids will often face into adulthood. With kids we usually just
 39 want to get them well through the childhood phase. (Death; HCP)
 40 Risk of immediate death vs. death later indicates benefit in terms of longevity but the quality during
 41 that period is more important than the period of survival itself. That is to say 10-year survival but a
 42 very poor QoL would potentially be outweighed by shorter survival but a superior QoL - for some.
 43 Very individual as patient comments show. (Death; HCP)
 44 This is future proofing to allow the child the best chance as an adult as it most frequently the
 45 cardiovascular issues which cause the eventual mortality. Healthy diet & exercise advise is
 46 importance also post-transplant to give these children the best chance to improve their outcomes.
 47 (CVD; HCP)

Responding to shifting health

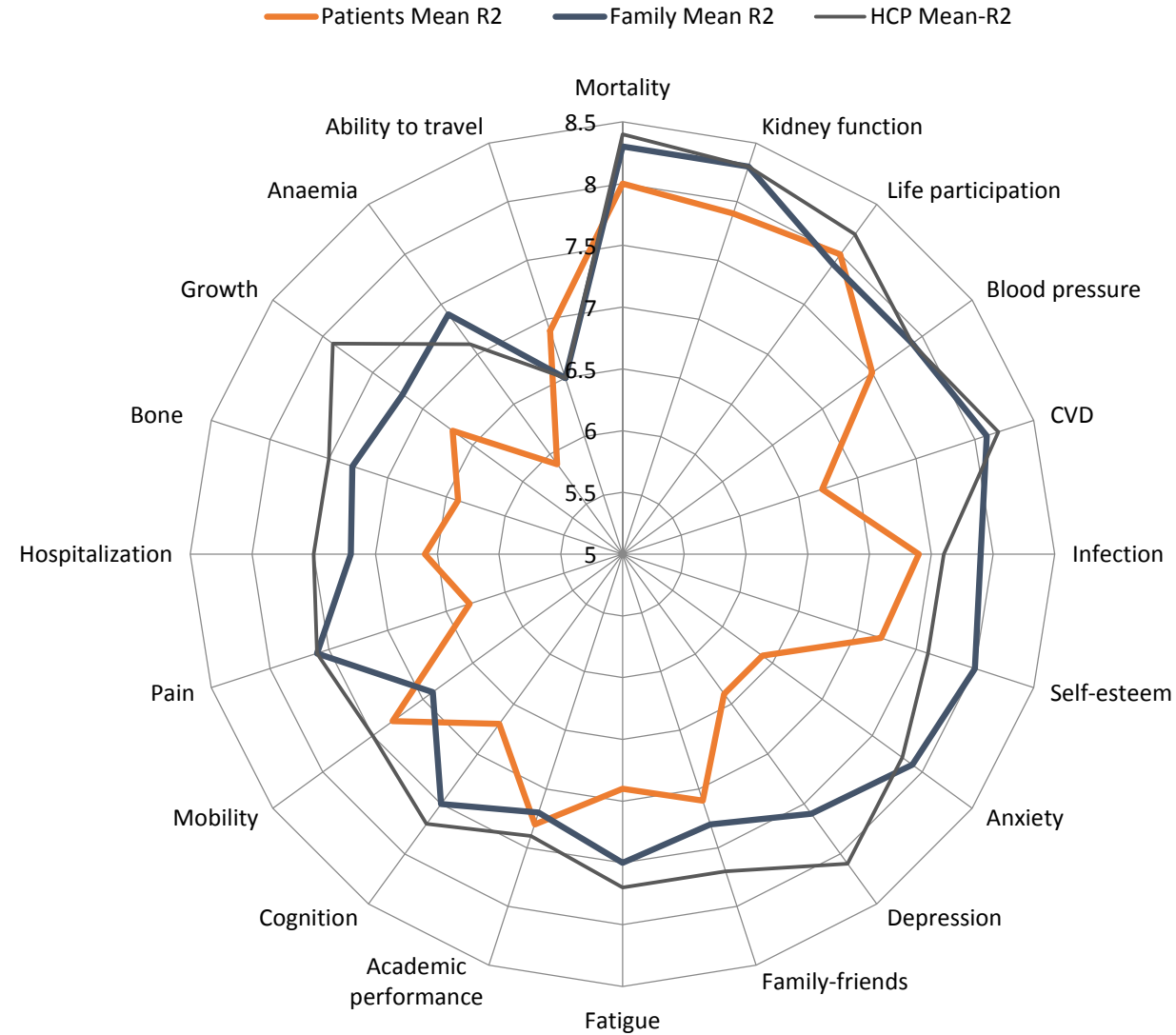
48 You have to know you are still working towards something. I will say though that school goes on the
 49 back burner when you get super sick. (Academic performance; Patient)
 50 I constantly get stress fractures in my feet from exercise. But I think it's a small price to pay for good
 51 general health (Bone health; Patient)
 52 It annoys me a lot seeing the health professional attitude of "don't focus on this, it's not as important
 53 as quality and you are fine now". Stop telling us what to be concerned about, this is a huge factor
 54 always in our minds. (Death; C/F)
 55 Longevity is affected by having continuously high blood pressure. It effects all organs. The
 56 challenging part is that there usually are no immediate symptoms of high blood pressure so the child
 57 and often family do not see it as important as many of the other things that they are dealing with.
 58 (BP; HCP)
 59 Because the effect of the bone disease is not immediately evident, we tend to put off dealing with it
 60 because usually we have more pressing health issues to worry about but we have seen a number of
 61 kids who as they become older teenager having chronic bone disease which really does affect their
 62 quality of life. (Bone health; HCP)

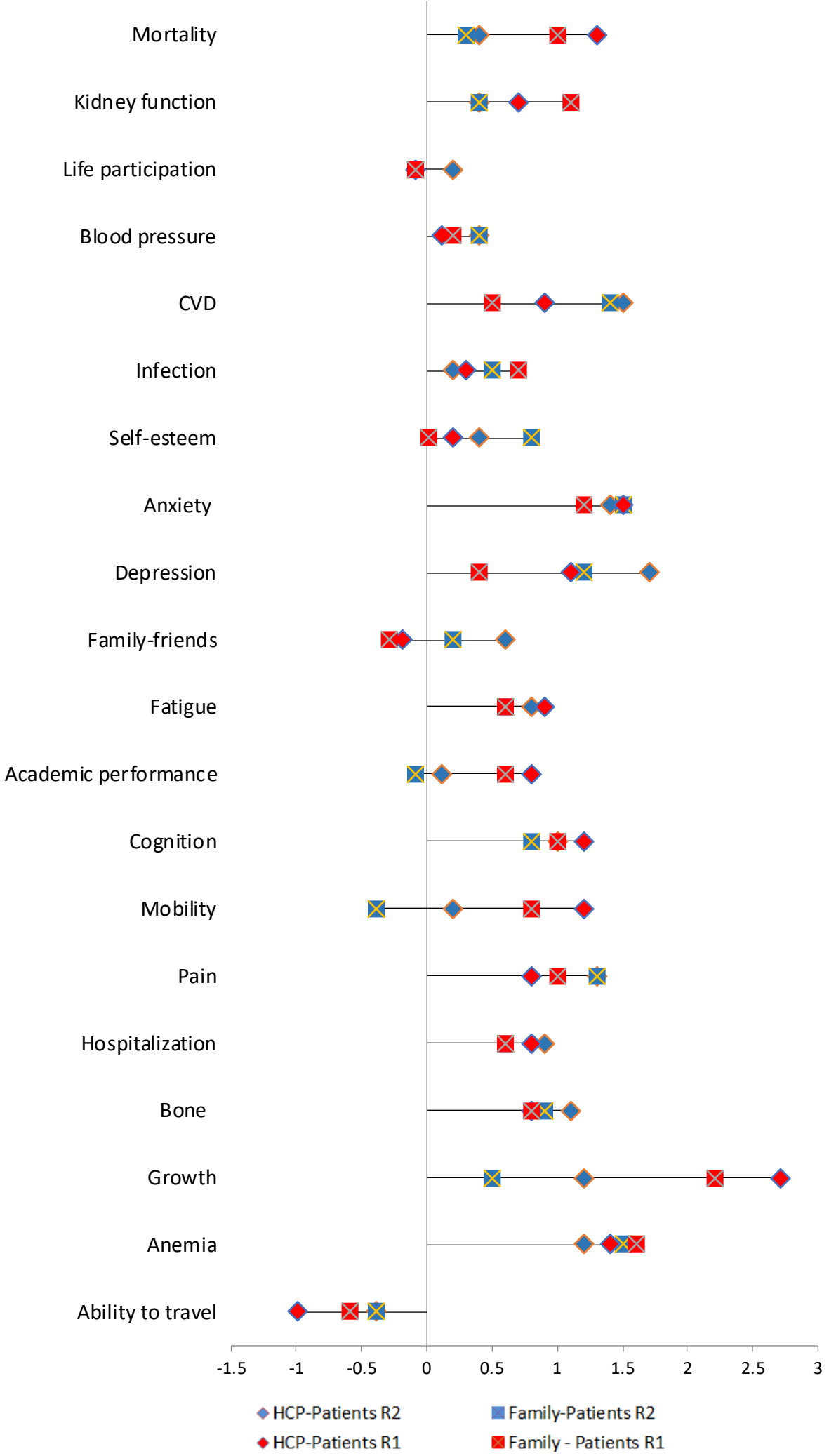
C/F, caregiver or family member, HCP, healthcare professional; CKD, chronic kidney disease; ESRF, end-stage renal failure; QoL, quality of life

Mean scores of Patients, Families and HCP in Round 1



Mean scores of Patients, Families and HCP in Round 2







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**Unmarked ("Clean") Revision | Note: must be .DOC(X)
or .RTF**

SONG-Kids_Delphi_vAJKD-D-19-01402R2-clean.docx

Supplementary Table 1. Institutional Ethics Review Boards of participating sites

The University of Sydney
Lady Cilento Children's Hospital
All India Institute of Medical Sciences
University of Michigan
University of British Columbia
University College London
National Healthcare Group Singapore
Emma Children's Hospital Academic Medical Centre
Toronto Hospital for Sick Children
The Children's Hospital at Westmead
University of Pennsylvania
University of Calgary
Texas Children's Hospital
University Hospital of Lyon
University of Minnesota
Children's Mercy Kansas City
Nottingham University Hospital
University of Melbourne

Informed consent was obtained from all participants.

Supplementary Table 2. Outcomes assessed during Round 1 and their definition (Adult version).

Adult version
Fatigue/energy: Child feels tired with no energy for weeks, for most of the time
Growth: Child has delayed growth due to kidney disease
Anxiety/stress: Child experiences intense, persistent worry, fear and anxious feelings
Self-esteem: Child likes themselves and the way they look
Academic performance: Child's ability to achieve potential at school
Appearance: How the child's face and body look e.g. swollen or round face, excessive hair growth or loss, skin disorders
Thirst and appetite: Child constantly feeling the need to drink water, lack of appetite, nutrition
Impact on family/friends: Impact of the child's kidney disease and treatment on family, caregivers, friends, including financial impact
Eye problems: Child having issues with blurry vision, unable to see clearly, clouding of the lens in the eye, cataracts
Death/mortality: The child's risk of death, how long the child or adolescent will live
Diabetes: Child's blood sugar problems, abnormally high levels of sugar in the blood because the body can't produce enough insulin
Depressive symptoms: Child experiencing strong feelings of sadness, hopelessness, despair for most of the time, over a long period
Sleep disturbance: Child having difficulty sleeping, poor quality sleep or needing more sleep than others
Mobility/Physical activity: Child's ability to physically move without assistance, to play and participate in sport
Cardiovascular disease: Disease of the child's heart and blood vessels in the future e.g. heart attack, stroke, blockage of blood vessels
Blood pressure: Child's blood pressure in the arteries being high or low (even when not on dialysis). High blood pressure can damage the heart. Low blood pressure can cause dizziness.
Hospitalisation: Child having to stay in hospital for a health problem or complication
Cognition: Child's ability to think clearly, remember things, solve problems
Bone health: Child's risk of osteoporosis, breaks/fractures, weakening of the bones
Gastrointestinal problems: Uneasy feeling in the stomach, wanting to throw up, diarrhoea, constipation
Pain: Any type of pain including; headache, pain in the back, arms, legs, hands, feet, bone, overall or general pain, etc.
Infection: Disease/harm caused by bacteria, viruses or parasites. Child easily getting a cold, flu, pneumonia, blood infections, etc.
Ability to travel: Time away from the hospital, time off dialysis, the ability to go on holiday
Anaemia: Low blood cell count; can make the patient feel tired, cold, dizzy, and irritable; or be short of breath or have a headache
Life participation: The ability to participate in key activities of daily living (e.g. work, study, family, hobbies, social activities)
Kidney function: Ability of the kidney to remove waste from the body and balance fluids (could be measured by creatinine in the blood)
Itching: Child having an irritating sensation that makes them want to scratch, known as pruritus
Child version (aged 8-21 years)
Tiredness: Feeling tired with no energy
Growth: Being short or small, not growing as fast as everyone else

Anxiety/stress: Feeling frightened and worried about something

Self-esteem: Liking yourself the way you are

School/study: How well you are doing at school or study

How I look: How your body and face look (like having lots of hair, puffy face, skin problems)

Drinking and eating: Being very thirsty or having to eat and drink differently to other people

Impact on family/friends: Impact of kidney problems on your family or friends (like your parent can't go to work because they have to go to the hospital)

Eyes: Having problems seeing clearly

Staying alive: Chance of dying, how long you will live for

Diabetes: Having too much sugar in the blood. This can hurt your kidneys

Depressive symptoms: Sadness that lasts longer than usual and can stop you from enjoying things you like doing

Sleeping: Finding it hard to sleep, or needing more sleep than other people

Physical activity: Being active and able to play sports

Heart and blood vessels: Problems with the heart and blood vessels when you're older

Blood pressure: How easy it is for your heart to pump blood through your body. High blood pressure can damage your heart. Low blood pressure can make you feel dizzy

Being in hospital: Staying in the hospital to get treatment

Thinking clearly: Being able to think clearly, remember things and solve problems

Bones: Bones not being as strong so they can't grow tall and you are more likely to break a bone

Stomach problems: Feeling sick in the stomach, needing to vomit, having gas, diarrhoea (runny poo) or being constipated (finding it hard to poo)

Pain: When any part of your body hurts (like a headache, arm pain or any other kind of pain)

Infection: Feeling sick because of a 'bug' or a germ that attacks your body like getting more colds than other people

Holidays and travel: The ability to go on holiday

Anaemia: Not enough red blood cells; can make you look pale and feel tired

Life participation: Being able to do the things you usually do like any hobbies, playing with your friends and going to school

Kidney function: The ability of your kidneys to remove waste and to keep your fluids in balance

Itching: Having an itchy feeling, wanting to scratch

Supplementary Table 3. Round 1 means, medians and proportion (rating 7-9) of patients/caregivers and health professionals for 27 outcomes.

Outcome	Mean			Median			Proportion scoring 7-9 (critically important)		
	Patients (combined)	Caregivers	HCP	Patients (combined)	Caregivers	HCP	Patients (combined)	Caregivers	HCP
Life participation	7.8	7.7	7.7	9	8	8	78	82	85
Blood pressure	7.5	7.7	7.6	8	8	8	56	81	78
Impact on family/friends	7.5	7.2	7.3	8	8	7	65	64	71
Infection	7	7.7	7.3	8	8	8	61	79	72
Mortality	6.8	7.8	8.1	8	9	9	57	80	86
Mobility	6.1	6.9	7.3	8	7	7	61	64	74
Bone health	6.5	7.3	7.3	7.5	7.5	7	53	71	71
Ability to travel	7.3	6.7	6.3	7	7	6	61	56	48
Self-esteem	7.3	7.3	7.5	7	8	8	51	67	76
Kidney function	7.1	8.2	7.8	7	9	8	53	88	82
CVD	6.9	7.4	7.8	7	8	8	49	70	85
Depression	6.7	7.1	7.8	7	8	8	47	68	84
Hospitalization	6.6	7.2	7.4	7	7	7	50	66	73
Itching	6.5	6.1	6.1	7	6	6	58	45	44
Academic performance	6.5	7.1	7.3	7	7	7	54	64	72
Pain	6.5	7.5	7.3	7	8	7	51	77	72
Thirst/appetite	6.4	6.9	7	7	7	7	53	64	63
Cognition	6.3	7.3	7.5	7	7	8	57	69	79
Fatigue	6.7	7.3	7.6	6	8	8	44	69	78
Sleep	6.6	6.5	7	6	7	7	47	55	64
Anxiety/stress	6.1	7.3	7.6	6	8	8	44	69	79
Gastro problems	6	7	6.5	6	7	6	42	65	48
Diabetes	5.7	6.3	6.9	6	7	7	36	52	62
Growth	5.1	7.3	7.8	6	8	8	43	67	83
Appearance	5.9	6.3	7	5	7	7	36	52	63
Anemia	5.6	7.2	7	5	7	7	25	70	64
Vision	4.8	6.3	6.7	5	7	7	32	47	54

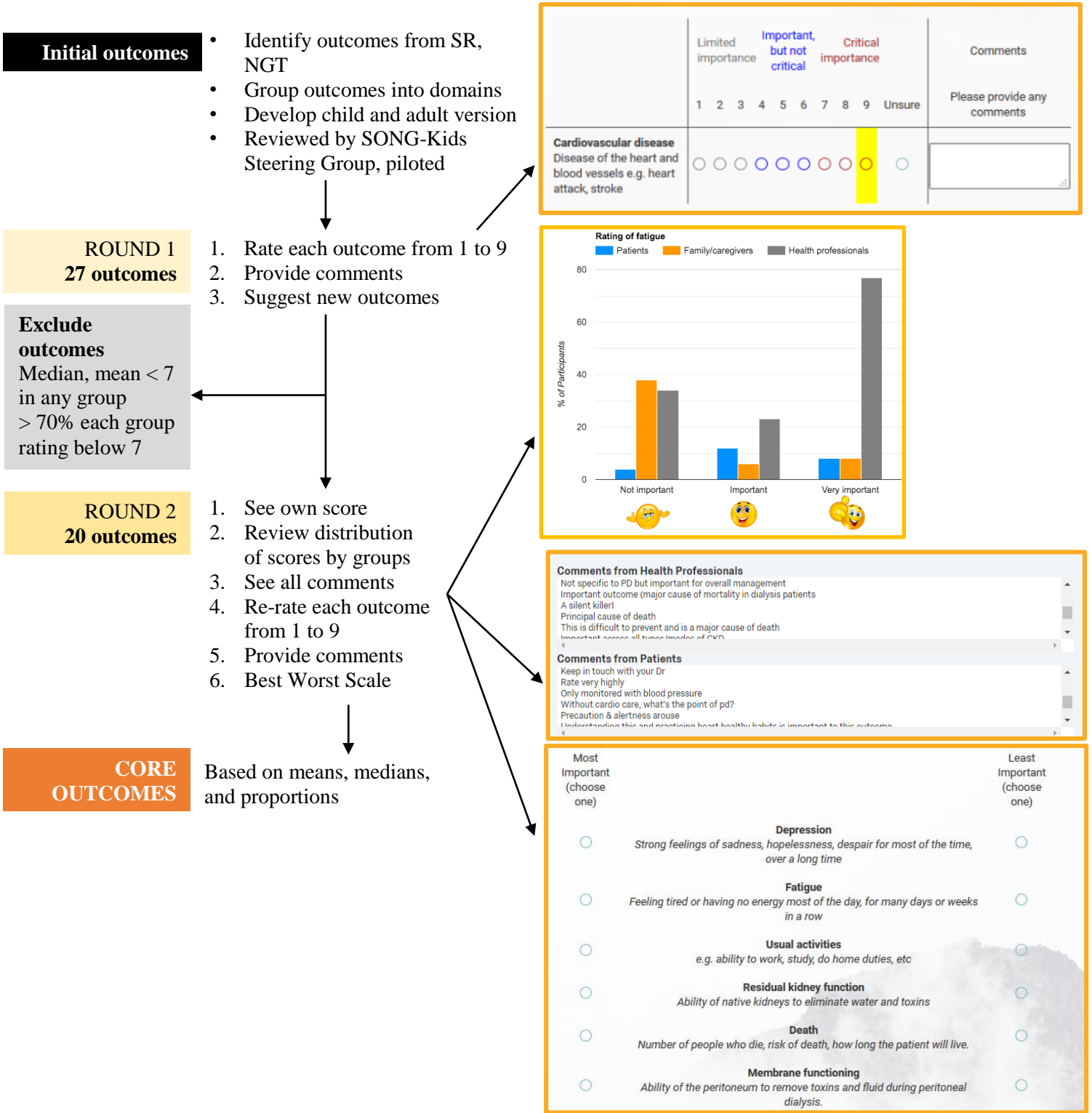
Supplementary Table 4. Suggested outcomes by participants in round 1.

New outcomes suggested	N (%)
Electrolytes	1 (0.1)
Brain complications	3 (0.4)
Nutrition/malnutrition	5 (0.5)
Adherence	10 (1.2)
Transition to adulthood	6 (0.7)
Vascular access	1 (0.1)
Hospitalization	1 (0.1)
Need for transplant	1 (0.1)
Amenorrhea	1 (0.1)
Dermatologic conditions	1 (0.1)
Parental support	4 (0.5)
Financial support	4 (0.5)
Post-transplant lymphoproliferative disorder	1 (0.1)
Fertility	4 (0.5)
Dyslipidemia	1 (0.1)
Vitamin D replete	1 (0.1)
Social integration/stable relationships with partners	10 (1.2)
Normal puberty	2 (0.2)
Proteinuria	5 (0.5)
Avoiding need for dialysis/transplant	3 (0.4)
Immunization	1 (0.1)
Impact on siblings	3 (0.4)
Nightmares	1 (0.1)
Sleep apnea	1 (0.1)
Body image	1 (0.1)
Water intake	1 (0.1)
Teeth/gum issues	1 (0.1)
Hypertension	1 (0.1)

Supplementary Table 5. Round 2 means, medians and proportions (rating 7-9) of patients/caregivers and health professionals for 20 outcomes.

Outcome	Mean			Median			Proportion scoring 7-9 (critically important)		
	Patients (combined)	Caregiver	HCP	Patients (combined)	Caregiver	HCP	Patients (combined)	Caregiver	HCP
Life participation	8.0	8.0	7.9	9.0	9.0	8.0	95.0	86.2	90.2
Mortality	8.0	8.0	8.3	9.0	9.0	9.0	92.8	82.8	85.2
Kidney function	7.9	7.9	8.3	8.0	8.0	9.0	95.0	96.6	95.1
Blood pressure	7.5	7.5	7.9	8.0	8.0	8.0	89.6	82.8	86.9
Infection	7.4	7.4	7.9	8.0	8.0	8.0	83.7	75.9	78.7
Academic performance	7.3	7.3	7.2	7.0	7.0	7.0	76.9	72.4	70.5
Mobility	7.3	7.3	6.9	8.0	8.0	7.0	81.4	69.0	67.2
Self-esteem	7.3	7.2	8.0	8.0	8.0	8.0	79.2	62.1	86.9
Impact on family/friends	7.1	7.1	7.3	8.0	8.0	8.0	84.2	65.5	62.3
Ability to travel	6.9	6.9	6.5	7.0	7.0	7.0	49.3	65.5	54.1
Fatigue	6.9	6.9	7.5	7.0	7.0	8.0	86.0	62.1	75.4
Cardiovascular disease	6.7	6.7	8.1	7.0	7.0	9.0	93.7	72.4	82.0
Cognition	6.7	6.7	7.5	7.0	7.0	7.0	89.6	55.2	78.7
Growth	6.7	6.7	7.2	7.0	7.0	7.0	90.5	58.6	70.5
Hospitalization	6.6	6.6	7.2	7.0	7.0	7.0	76.9	48.3	70.5
Anxiety/stress	6.4	6.4	7.9	7.0	7.0	9.0	85.5	51.7	78.7
Bone health	6.4	7.4	7.3	7.0	7.0	7.0	82.4	62.1	78.7
Depression	6.4	6.4	7.6	7.0	7.0	9.0	93.2	51.7	70.5
Pain	6.3	6.3	7.6	7.0	7.0	8.0	80.5	51.7	78.7
Anemia	5.9	5.9	7.4	6.0	6.0	8.0	70.6	41.4	75.4

Supplementary Figure 1. SONG-Kids Delphi process



Supplementary Figure 2. Mean relative importance scores of patients, caregivers and health professionals based on the Best-Worst Scale. Ordered by the mean importance scores of patients (error bars are the 95% CI).

