



## Developing a Set of Core Outcomes for Trials in Hemodialysis: An International Delphi Survey

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**Background:** Survival and quality of life for patients on hemodialysis therapy remain poor despite substantial research efforts. Existing trials often report surrogate outcomes that may not be relevant to patients and clinicians. The aim of this project was to generate a consensus-based prioritized list of core outcomes for trials in hemodialysis.

**Study Design:** In a Delphi survey, participants rated the importance of outcomes using a 9-point Likert scale in round 1 and then re-rated outcomes in rounds 2 and 3 after reviewing other respondents' scores. For each outcome, the median, mean, and proportion rating as 7 to 9 (critically important) were calculated.

**Setting & Participants:** 1,181 participants (202 [17%] patients/caregivers, 979 health professionals) from 73 countries completed round 1, with 838 (71%) completing round 3.

**Outcomes & Measurements:** Outcomes included in the potential core outcome set met the following criteria for both patients/caregivers and health professionals: median score  $\geq 8$ , mean score  $\geq 7.5$ , proportion rating the outcome as critically important  $\geq 75\%$ , and median score in the forced ranking question  $< 10$ .

**Results:** Patients/caregivers rated 4 outcomes higher than health professionals: ability to travel, dialysis-free time, dialysis adequacy, and washed out after dialysis (mean differences of 0.9, 0.5, 0.3, and 0.2, respectively). Health professionals gave a higher rating for mortality, hospitalization, decrease in blood pressure, vascular access complications, depression, cardiovascular disease, target weight, infection, and potassium (mean differences of 1.0, 1.0, 1.0, 0.9, 0.9, 0.8, 0.7, 0.4, and 0.4, respectively).

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\*A list of the SONG-HD initiative investigators is available at [www.songinitiative.org](http://www.songinitiative.org).

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**Limitations:** The Delphi survey was conducted online in English and excludes participants without access to a computer and internet connection.

**Conclusions:** Patients/caregivers gave higher priority to lifestyle-related outcomes than health professionals. The prioritized outcomes for both groups were vascular access problems, dialysis adequacy, fatigue, cardiovascular disease, and mortality. This process will inform a core outcome set that in turn will improve the relevance, efficiency, and comparability of trial evidence to facilitate treatment decisions.

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**INDEX WORDS:** Hemodialysis (HD); outcomes; Delphi survey; core outcome set; trials; outcome domains; research priorities; surrogate end points; Standardized Outcomes in Nephrology-Hemodialysis (SONG-HD); quality of life; lifestyle-related outcomes; well-being; biochemical end point; dialysis adequacy; cardiovascular disease (CVD); vascular access problems; mortality; patient-centered care.

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The enormous investment in biomedical research, particularly in randomized trials, may not have led to the improvements in health that were hoped for.<sup>1-3</sup> It has been estimated that 85% of the worldwide US \$240 billion invested in research annually is wasted.<sup>3</sup> In nephrology, there has been substantial research investment into hemodialysis (HD), yet survival rates have not improved correspondingly over the past 40 years and quality of life remains poor, even compared with patients with many cancers.<sup>4-7</sup> This may be partly attributable to what outcomes are selected and reported in trials, a challenge well recognized across medical specialties.<sup>1,8-10</sup>

Surrogate end points are frequently used in clinical trials because of feasibility, in preference to outcomes that are directly relevant to patients and clinicians.<sup>9,11,12</sup> In HD, biochemical markers such as serum phosphorus, calcium, and parathyroid hormone levels, are commonly reported but are not strongly and consistently associated with mortality, cardiovascular disease (CVD), or quality of life.<sup>13-17</sup> Patients on HD therapy prioritize outcomes relevant to their well-being and lifestyle—fatigue, ability to travel, ability to work, sleep, and anxiety/stress<sup>18,19</sup>—all of which are largely absent as outcomes reported by HD trials. In addition, the large heterogeneity of outcome measures and potential for outcome reporting bias (in which trials selectively report results for outcomes that favor the intervention) undermine the reliability of trial evidence to inform clinicians and patients about the relative effects of interventions.<sup>20</sup>

Engaging all stakeholders in establishing a core outcome set, an agreed minimum set of standardized outcomes to be measured and reported in all trials for a particular clinical area,<sup>21,22</sup> can increase the relevance, efficiency, and reliability of trials. Initiatives to develop core outcomes are seen in rheumatology and oncology and have demonstrated improvements in consistent reporting of relevant outcomes.<sup>10,23,24</sup> As part of the international Standardized Outcomes in Nephrology—Hemodialysis (SONG-HD) initiative, this study aimed to

generate a consensus-based prioritized list of outcome domains for people on HD therapy, which will be used to establish a core outcome set that reflects the shared priorities of patients, caregivers, and health professionals.

## METHODS

### Study Design

The Delphi method is a technique for achieving consensus among a panel of experts. This process involves sequential surveys, typically conducted over 3 rounds and answered anonymously, and gives equal influence to all who participate. It was first developed by the RAND Corporation in the 1950s<sup>25</sup> and has since been increasingly used as a valid approach to develop consensus-based core outcomes for clinical trials in various medical specialty areas.<sup>10,22,26-28</sup> The SONG-HD Delphi process is shown in [Figure S1](#) (provided as online supplementary material).

### Participant Selection and Recruitment

Stakeholders including patients, caregivers/family members, nephrologists, surgeons, nurses, social workers, psychologists, dietitians, pharmacists, policy makers, researchers, and industry with experience or interest in HD were invited to join the Delphi panel. Participants worldwide were eligible if they were older than 18 years and able to complete an online survey in English. All participants provided informed consent.

Using an opt-in snowballing sampling frame, we recruited patients/caregivers through participating hospitals, patient/consumer organizations, and social media listed in [Item S1](#). Health professionals were recruited via the investigators' networks and via e-mails and newsletters circulated by professional societies ([Item S1](#)). Participants registered their e-mail addresses on [www.songinitiative.org](http://www.songinitiative.org) prior to the survey launch. Ethics boards of the University of Sydney (2015/228), Baylor College of Medicine (H-37406), University of Calgary (REB15-0708), Monash Medical Centre (13082B), Salford Royal NHS (15/WM/0303), and Sydney West Area Health Service (HREC2009/6/4.15) approved this study.

### Data Collection

#### Overview

The 34 outcome domains for the 3-round Delphi survey were identified from a systematic review of outcomes reported in trials in HD therapy, stakeholder interviews, and nominal group technique conducted with patients on HD therapy and caregivers.<sup>29,30</sup> The ordering of outcomes was randomized and included a plain language definition ([Item S2](#)). The survey was reviewed by the SONG Executive Committee and SONG-HD investigators and piloted among 10 patients. The Delphi survey was completed online via LimeSurvey during September to November 2015. The online survey administration minimizes data entry error, allows for wider dissemination, and is more efficient compared to a paper survey.

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