


# BMJ Open The Australian and New Zealand Fontan Registry Quality of Life Study: Protocol for a population-based assessment of quality of life among people with a Fontan circulation, their parents, and siblings

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## ABSTRACT

**Introduction** Advances in the care of patients with single-ventricle congenital heart disease have led to a new generation of individuals living with a Fontan circulation. For people with Fontan physiology, physical, psychological and neurodevelopmental challenges are common. The objective of this study is to describe and develop a deeper understanding of the factors that contribute to quality of life (QOL) among children, adolescents and adults living with a Fontan circulation across Australia and New Zealand, their parents and siblings.

**Methods and Analysis** This article presents the protocol for the Australian and New Zealand Fontan Registry (ANZFR) QOL Study, a cross-sectional, population-based study designed to examine QOL among people of all ages with a Fontan circulation, their parents and siblings. Study eligibility criteria includes (1) individuals with a Fontan circulation aged ≥6 years, at least 12 months post-Fontan procedure and enrolled in the ANZFR; (2) parents of individuals enrolled in the ANZFR; and (3) siblings aged ≥6 years of an individual enrolled in the ANZFR. A novel, online research platform is used to distribute personalised assessments tailored to participant age and developmental stage. A suite of validated psychometric self-report and parent-proxy report instruments capture potential correlates and predictors of QOL, including symptoms of psychological distress, personality attributes, coping and cognitive appraisals, family functioning, healthcare experiences and costs, access to emotional support and socioeconomic factors. Clinical characteristics are captured via self-report and parent-proxy report, as well as the ANZFR. Descriptive analyses and multilevel models will be used to examine QOL across groups and to investigate potential explanatory variables.

**Ethics and Dissemination** Approval has been obtained from all relevant Human Research Ethics Committees (HRECs), including the Sydney Children's Hospitals Network and the Royal Children's Hospital Melbourne HRECs. Study findings will be published in peer-reviewed journals and presented at national and international meetings and seminars.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study uses population-based data captured via the Australian and New Zealand Fontan Registry to explore the sociodemographic, clinical and psychological factors that contribute to quality of life (QOL) among children, adolescents and adults living with a Fontan circulation, their parents and siblings.
- ⇒ Our conceptually driven approach to study design and methodology is a significant advance and ensures the complexity of QOL in the Fontan population is appropriately assessed.
- ⇒ Use of multiple informants (ie, self-report, parent-proxy report) across a range of participant ages (≥6years) is a novel addition to the literature, as is the collection of outcomes data for siblings.
- ⇒ The primary limitation of this study is the cross-sectional design, which precludes causal inference.

## INTRODUCTION

Designed to palliate single-ventricle congenital heart disease (CHD), the Fontan procedure is the last in a series of open-heart surgeries occurring in early childhood. It is now estimated that up to 70 000 individuals are living with a Fontan circulation worldwide.<sup>1</sup> People with Fontan physiology report physical, psychological and neurodevelopmental challenges across their lifespan.<sup>2 3</sup> These stressors place individuals and their families at risk of poorer health and well-being.

Quality of life (QOL) is typically defined as overall subjectively perceived well-being and life satisfaction,<sup>4-6</sup> encompassing all aspects of life, including health-related factors. Health-related QOL is a multidimensional concept, including domains related to physical, psychological, social and occupational

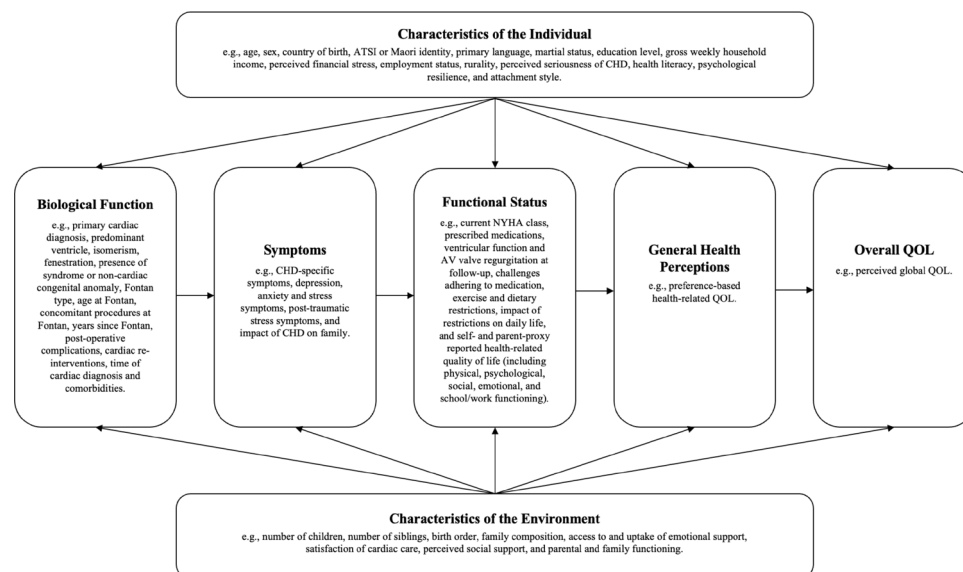
functioning potentially influenced by an individual's disease or treatment.<sup>7,8</sup> Adults with a Fontan circulation report lower QOL compared with patients with biventricular CHD,<sup>9</sup> although it is unclear whether these findings are similar in children and adolescents. Individuals with a Fontan circulation report poorer mean outcomes across all health-related QOL domains compared with the general community.<sup>10</sup> Families of people with complex CHD may also experience considerable physical, psychological, social, practical and financial challenges,<sup>11</sup> placing parents and siblings at heightened risk of poorer health-related QOL.<sup>12–15</sup>

Efforts to identify factors that influence health-related QOL among people with a Fontan circulation have focused on demographic and clinical variables; yet, the direction and strength of these relationships vary across studies.<sup>10</sup> Evidence suggests that psychological and social constructs, such as greater psychological stress, fewer social supports and lower socioeconomic resources, may play a potent role in determining QOL outcomes among people with complex CHD<sup>16–22</sup> and their parents.<sup>21, 23, 24</sup> Qualitative studies also highlight the role of illness perceptions and coping skills in fostering well-being among Fontan patients<sup>25, 26</sup> and their parents<sup>27</sup>; however, the extent to which these variables influence sibling QOL is not yet known. Additionally, QOL data are increasingly needed to determine the benefit-burden ratio of advances in clinical care. Patient and family perceptions of current health services and the extent to which QOL is influenced by healthcare practices remain unclear.<sup>10</sup> Given the potential for psychological factors to influence well-being among patients and parents, integrated approaches to psychological care are recommended.<sup>28, 29</sup> Characterising health service use and QOL, including access to mental health services, will help identify priorities for optimal care practices.

With the Fontan population predicted to double over the next 20 years,<sup>1</sup> there is an imperative to better understand the factors that may bolster individual and family resilience and well-being. Published research does not yet provide the necessary evidence to determine which factors have greatest influence on patient, parent and sibling QOL. Moreover, the majority of available studies do not examine QOL or health-related QOL in the Fontan population using a theoretical model to guide study design and methodology,<sup>10</sup> limiting replication and the implementation of findings into clinical practice. Without comprehensive investigation of multiple and inter-related demographic, clinical, psychological and social factors using evidence-based, theoretical frameworks, it is unclear which variables are best targeted in intervention design and clinical care for people with a Fontan circulation and their families.

### Theoretical Framework

This study uses the revised Wilson and Cleary model of health-related QOL<sup>7, 30</sup> to generate research questions, guide measurement selection and inform analyses and interpretation of results (figure 1). The revised Wilson and Cleary model has demonstrated utility evaluating predictors of health-related QOL among people with chronic illnesses.<sup>31</sup> It is recommended over existing models of health-related QOL as it is widely used, allowing for comparison and replication across studies and populations.<sup>32</sup> The framework identifies elements and determinants of health-related QOL, including biological and physiological factors (eg, cardiac diagnosis, comorbidities), symptoms (eg, pain, fatigue, psychological distress), functional status (eg, difficulties with physical, emotional, social and cognitive function), health perceptions (eg, perceived overall health) and overall QOL (eg, satisfaction with life). Individual (eg, age, sex, education level) and environmental (eg, family functioning,



**Figure 1** Revised Wilson and Cleary model of health-related quality of life (QOL). CHD, congenital heart disease.

social support, health service use) factors are posited as overarching constructs, influencing each domain and each other. Dominant causal associations between each domain as well as individual, and environmental factors are depicted in the model, and reciprocal or bidirectional relationships are implied.<sup>7</sup>

### Study Objective and Aims

The objective of this study is to develop a deeper understanding of the factors that contribute to health and well-being among children, adolescents and adults living with a Fontan circulation across Australia and New Zealand, their parents and siblings. To achieve this, our study has the following aims:

1. To characterise self-reported QOL and health-related QOL among children, adolescents and adults living with a Fontan circulation, their parents and siblings, and to compare each group with published normative data where available.
2. To assess parent-proxy reported health-related QOL among individuals living with a Fontan circulation, and their siblings and compare each group with published normative data where available.
3. To identify demographic, clinical, psychological and social correlates, and predictors of self-reported QOL and self-reported and parent-proxy reported health-related QOL among people with a Fontan circulation, their parents and siblings.

## METHODS AND ANALYSIS

### The Australian and New Zealand Fontan Registry

The Australian and New Zealand Fontan Registry (ANZFR) was established in 2011<sup>33</sup> and captures data on clinical encounters and health outcomes for over 1650 individuals with a Fontan circulation from all congenital cardiac centres across Australia and New Zealand.<sup>34</sup> Patients undergoing the Fontan operation are automatically enrolled into the ANZFR unless they or their parent opt out.<sup>33</sup> Demographic (eg, age, sex, country of birth) and preoperative and postoperative characteristics (eg, Fontan type, postoperative complications) are recorded at enrolment following the Fontan operation. Once enrolled, patients consent to yearly collection of clinical correspondence and echocardiogram reports from their treating cardiac team. Data extracted include functional assessment findings, medications, comorbidities and physical complications.<sup>33</sup>

Overall, 82% of individuals with a Fontan circulation in Australia and New Zealand are consented to participate in the ANZFR.<sup>34</sup> The average age of ANZFR participants is 19 years (range 2–56 years; 55% aged ≤18 years and 45% aged ≥19 years), more than half are male (58%) and the average age at Fontan procedure is 5.6 years.<sup>34</sup> The most common primary diagnoses are tricuspid atresia (22%), double inlet left ventricle (16%), double outlet right ventricle (14%) and hypoplastic left heart syndrome (13%). Extracardiac conduit is the most common Fontan

procedure performed among ANZFR participants (69%) and more than one-third have fenestration (38%).<sup>34</sup> One-hundred and forty-four Australian patients have provided consent to the ANZFR to access their Medicare data.<sup>35</sup> Medicare Australia is the publicly funded universal health-care insurance scheme in Australia and provides subsidies for hospital, primary and secondary care services.

### Patient and Public Involvement

Fontan patients and families are engaged as ongoing partners within our research team. Key patient and parent contributions to study development and design include identifying areas of greatest research need, generating research questions and reviewing proposals, study materials and recruitment processes. In addition to study meetings, researchers also engaged with patients and families at the ANZFR Steering Committee meetings and via presentations and workshops during ANZFR Education Days to facilitate communication about the study and engage the Fontan patient, family and clinician community in the research. ANZFR Education Days are held annually online or at a congenital cardiac centre (in Australia or New Zealand) and is a symposium designed for Fontan patients, families, clinicians, allied health professionals and researchers. These efforts serve to improve the relevance and applicability of research outcomes to the needs and values of Fontan patients and families.<sup>36</sup>

### Participants

The present study includes three participant groups:

1. *Children, adolescents and adults with a Fontan circulation:* Patients aged ≥6 years, at least 12 months post-Fontan procedure, enrolled in the ANZFR and consented for approach for research.
2. *Parents:* Parent, primary caregiver or legal guardian of a child, adolescent or adult who is at least 12 months post-Fontan procedure and enrolled in the ANZFR. The term ‘parent’ in this context refers broadly to all primary caregivers. Where possible, both parents are invited to participate.
3. *Siblings:* Siblings (including biological, non-biological or stepsiblings) of a child, adolescent or adult who is at least 12 months post-Fontan procedure and enrolled in the ANZFR.

Patients are not eligible if they have undergone heart transplantation or had a Fontan takedown. Participants in all groups are not eligible if they meet any of the following criteria: (1) a history of severe chronic psychiatric illness or intellectual disability; (2) limited reading fluency in English, as translation services were unavailable for this study; and (3) inability to give informed consent or assent. To minimise participant burden, individuals identified by the research team as critically unwell are not contacted.

### Recruitment

An invitation pack for the current study containing an invitation letter, participant information sheets, family

**Table 1** Australian and New Zealand Fontan Registry Quality of Life Study recruitment strategies

Strategy	Description
Study invitation pack	Posted by mail directly to eligible patients and families via the Central and Data Coordinating Centre, the Heart Centre for Children at The Children's Hospital at Westmead.
CHD clinic posters and postcards	Hardcopy colour posters and postcards distributed to paediatric and adult CHD clinics across Australia and New Zealand. Digital posters also created for display on televisions within clinic waiting areas.
Social media messages	Information about the study shared with the Fontan community via the ANZFR Facebook page, and researcher and key stakeholder Twitter accounts (eg, HeartKids).
Hospital and CHD advocacy organisation websites	Examples include notices and stories on the Heart Centre for Children at the Children's Hospital at Westmead, HeartKids and ANZFR websites.
Conferences and patient and family education days	Information about the study shared with the Fontan community, clinicians and research via the annual ANZFR Education Day.

ANZFR, Australian and New Zealand Fontan Registry; CHD, congenital heart disease; SCHN, Sydney Children's Hospital's Network.

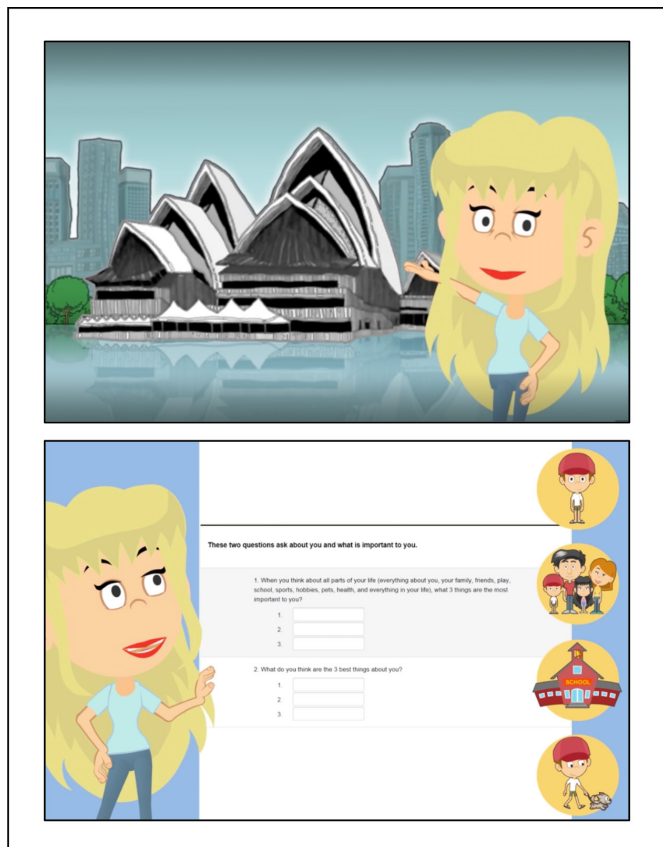
and individual consent and assent forms, and reply-paid envelope are sent to all eligible patients and families. The family consent form enables parents to provide consent for themselves, their child with a Fontan circulation and their siblings aged  $\leq 17$  years. Parents can also identify and provide the contact details of their child with a Fontan circulation and their siblings aged  $\geq 18$  years not currently living at home. Invitation packs are then sent directly to individuals aged  $\geq 18$  years. Individuals can opt into the study by returning the signed consent form or decline study participation by returning the non-participation section of the form. Individuals who do not return their consent form within 3 weeks receive an initial telephone call from the research team to gauge interest and provide an opportunity to ask questions about the study and participation. Three follow-up telephone calls are made after initial contact. To support enrolment, calls are made on different days and times. Individuals who are unable to be contacted via telephone (eg, wrong number, missing details), but have an email address recorded in the ANZFR, are sent an email to determine interest. All contacts and contact attempts are logged using a password-protected record.

Additional study recruitment and engagement strategies are summarised in [table 1](#), including posters and postcards, social media, notices and blogs on organisation and advocacy group websites, presentations at patient and family education days, and conference presentations. Hard-copy and digital colour posters and postcards are distributed to CHD clinics across Australia and New Zealand to display in waiting areas. Information about the study is shared with the Fontan patient and family community via the ANZFR Facebook page. Researcher and key stakeholder's Twitter accounts are also leveraged to share information to enhance recruitment, community engagement and dissemination of findings. Typical Facebook and Twitter posts include a brief description of the study and contact information for the research team.

### Assessment Procedures

An online research portal, developed specifically for the ANZFR QOL Study, is used to distribute surveys. Patients enrolled in the ANZFR are assigned a unique identification number (eg, NSW001) and this is used to link all family members, along with a unique, three-digit participant identifier. Participants who choose to receive their survey online receive a personalised weblink via the research portal. Participants can also choose to receive a hardcopy questionnaire which can be returned on completion via reply-paid envelope. A short, instructional animation is embedded into the online survey for children and adolescents aged  $\leq 17$  years ([figure 2](#)). The video is designed for children to watch with the support of their parents and aims to briefly explain the study, provide directions on how to complete the survey, and information on how participants can contact the research team to share any questions or concerns. Twenty-two versions of the survey have been created using developmentally appropriate psychometric measures to ensure comparable outcomes are captured for each participant and age group. Five age-specific surveys were created for people with a Fontan circulation (eg, 6–7, 8–11, 12–14, 15–17,  $\geq 18$  years). Twelve surveys were developed for parents based on (1) the age of their child with a Fontan circulation (eg, 6–7, 8–17,  $\geq 18$  years), and (2) the age of their siblings (eg, no siblings, 6–7, 8–17,  $\geq 18$  years). Five age-specific surveys were created to measure sibling outcomes (eg, 6–7, 8–11, 12–14, 15–17,  $\geq 18$  years). Participants who do not complete their survey within 2 weeks receive three reminder telephone calls. Email reminders are sent to participants who are unable to be contacted via telephone. Questionnaires will be continually monitored for signs of participant distress (eg, Depression, Anxiety and Stress Scales (DASS-21) scores in the at-risk range). Participants who express distress or a desire for support will be referred to appropriate psychological services, as indicated. For participants who consent to the present study, clinical characteristics will be extracted from the registry.





**Figure 2** Examples of images used in the instructional video designed to support child and adolescent study participation and engagement. Images are from original animation entitled, ‘Australian and New Zealand Fontan Registry Quality of Life Study Instructional Video’ created by N.A. Kasparian. Video is displayed via unique, online survey weblink (eg, <https://fromtheheart.fontanregistry.com/#/questionnaireID>).

## Measures

Psychometric measures were selected based on available validity and reliability data, and relevance to CHD and other chronic illness populations. Further detail is provided in the online supplemental table 1.

### Outcome Measures

#### *Overall quality of life (QOL)*

Aligned with best practices for the assessment of QOL,<sup>47</sup> a two-item, self-report measure has been purposely designed to assess perceived global QOL. Participants rate their QOL today and over the past month on a 10-centimetre, horizontal line graded with indicators from 0 (‘The worst it could be’) to 10 (‘The best it could be’).

#### *Health-related QOL*

Health-related QOL will be assessed among patients, parents and siblings using the Pediatric Quality of Life Inventory 4.0 Generic Core Scales (PedsQL).<sup>37</sup> The 23-item PedsQL core scales encompass physical, emotional, social and school/work functioning. Items are rated using a five-point scale, scores are reversed, transformed to a linear scale (0–100, with higher scores representing greater health-related QOL), and the

mean of each subscale is calculated. Parallel self-report and parent-proxy reported child, adolescent and adult versions of the PedsQL have been developed to facilitate evaluation between age groups and longitudinal tracking. The PedsQL enables comparison with a database of scores of individuals without chronic illness.<sup>37,38</sup> A cut-off of 1 SD below the normative mean is indicative of ‘at-risk’ status and a need for clinical assessment.<sup>38</sup>

### Potential Correlates and Predictors

The revised Wilson and Cleary model<sup>7,30</sup> was used as a conceptual framework to identify potential correlates and predictors of health-related QOL (figure 1). Concepts and measures assessed include the following (online supplemental table 1):

#### *Demographic characteristics*

Age and sex are extracted for patients via ANZFR records, and parents and siblings’ data are captured using self-report. Child patient and sibling self-reported sociodemographic factors (6–11 years; four items) include number of siblings, birth order, family composition and education level. Adolescent (12–17 years) questionnaires assess the same factors plus employment status (one item). Parents, adult patients and siblings self-reported sociodemographic factors ( $\geq 18$  years; nine items) include country of birth, primary language, marital status, number of children, education level, gross weekly household income (compared with Australian<sup>39</sup> or New Zealand<sup>40</sup> average), perceived financial stress (from 0 ‘Not worried at all’ to 4 ‘Extremely worried’) and employment status. Rurality is determined using the Australian Statistical Geography Standard—Remoteness Classification<sup>41</sup> and the New Zealand Urban/Rural Profile Classification.<sup>42</sup> Regions are grouped as major urban, medium/large urban and small urban/rural.

#### *Clinical characteristics*

Factors extracted from ANZFR records (15 items) include primary cardiac diagnosis, predominant ventricle, isomerism, fenestration, presence of syndrome or non-cardiac congenital anomaly, Fontan type, age at Fontan, concomitant procedures at Fontan, years since Fontan, postoperative complications (eg, pleural effusions, mechanical support, arrhythmias, stroke, protein-losing enteropathy, plastic bronchitis), cardiac reinterventions (eg, atrioventricular (AV) valve replacement, pacemaker), current New York Heart Association Classification, prescribed medications (eg, anticoagulation, ACE inhibitors), ventricular function and AV valve regurgitation at follow-up. Patient clinical characteristics (25 items) measured via self-report and parent-proxy reports include cardiac abnormality (verified using ANZFR records), time of cardiac diagnosis (antenatal or postnatal), comorbidities (ie, presence of chronic health conditions), total length of hospital admission (consecutive and non-consecutive days) in the preceding 12 months, planned surgical or hospital admission(s) in the next 12 months, total consultations with

cardiologist in the preceding 2 years, current medication use, challenges adhering to medication, exercise and dietary restrictions, and impact of restrictions on daily life. Perceived seriousness of single-ventricle CHD (one item) assesses patients, parents and siblings' perception of the seriousness of their own, or family member's CHD (from 0 'Not at all serious' to 4 'Extremely serious').

#### *CHD-specific symptoms*

The Paediatric Quality of Life Inventory 3.0 Cardiac Module (PedsQL Cardiac Module; 27 items)<sup>43 44</sup> is a self-report and parent-proxy report, disease-specific measure for child (5–7, 8–12 years), adolescent (13–18 years) and adult ( $\geq 19$  years) patients measuring heart problems and treatment, treatment adherence, perceived physical appearance, treatment anxiety, cognitive difficulties and communication problems. Items are rated using a five-point scale, then scores are reversed, transformed to a linear scale (0–100, with higher scores representing less severe symptoms), and the mean of each subscale is calculated.

#### *Health literacy*

The Brief Health Literacy Screen (BHLS; two items)<sup>45</sup> is a self-report scale assessing parents, adult patients and siblings' need for assistance reading health-related materials (from 0 'Never' to 4 'Always') and level of confidence completing medical forms (from 0 'Not at all confident' to 4 'Extremely confident'). Item 2 is reversed and scores summed, with higher scores indicating greater health literacy.

#### *Access to and uptake of emotional support*

Nine self-report items assess whether patients, parents and siblings recall being offered emotional support from a health professional (eg, psychologist, cardiologist) during their, or their child's cardiac diagnosis or treatment, perceived helpfulness of the support, difficulties accessing support and anticipated responses to future offers of psychological referral by their cardiac team.

#### *Satisfaction with cardiac care*

Patient and family member satisfaction with cardiac care (1 'Not satisfied at all' to 5 'Extremely satisfied'; one item).

#### *Financial impact of cardiac condition*

Parents and adult patients will estimate out-of-pocket expenses related to cardiac diagnosis (eg, cardiac visits, medication, allied healthcare, accommodation, equipment; one item). School or work absenteeism and government assistance will also be assessed (six items).

#### *Depression, anxiety and stress symptoms*

The Spence Children's Anxiety Scale (SCAS; 38 items)<sup>46</sup> measures self-proxy and parent-proxy reported anxiety symptoms in child and adolescent (8–17 years) patients and siblings across six domains: general anxiety (six items), panic (nine items), social phobia (six items),

separation anxiety (six items), obsessive compulsive problems (six items), physical injury fears (five items). Response options range from 0 ('Never') to 3 ('Always') and summed to provide a total score. Scores  $>1$  SD below the normative mean indicate a need for clinical assessment.<sup>47 48</sup> The Short Mood and Feelings Questionnaire (SMFQ; 13 items)<sup>49</sup> assesses child and adolescent (8–17 years) self-report and parent-proxy reported symptoms of depression. Items are summed to provide a total score, with scores  $\geq 8$  warranting clinical investigation.<sup>49</sup> Depression, Anxiety and Stress Scales (DASS-21; 21 items)<sup>50</sup> measures depression, anxiety and stress experienced in the past 7 days in adult patients, siblings and parents. Items range from 0 ('Normal') to 3 ('Extremely severe') and normative data in non-clinical Australian adult samples are available.<sup>51–55</sup>

#### *Traumatic stress symptoms*

The Impact of Events Scale-Revised (IES-R; 22 items)<sup>56</sup> assesses post-traumatic stress symptoms associated with cardiac diagnosis and treatment. Parents and adult patients rate the frequency and severity of symptoms in the preceding week across three domains (intrusion, avoidance, hyperarousal) using a five-point scale ranging from 0 ('Not at all') to 4 ('Extremely'). Items are summed to provide a total score. The IES-R is not designed to provide clinical assessment; however, 'elevated' and 'probable' post-traumatic stress levels have previously been defined as IES-R total scores above 24 and 32, respectively.<sup>57</sup>

#### *Psychological resilience*

The Sense of Coherence (SOC; 13 items) scale<sup>58</sup> measures three, self-reported components of psychological resilience (comprehensibility, manageability and meaningfulness) in parents, adolescent ( $\geq 15$  years) and adult patients. Items are rated on a seven-point semantic differential scale ranging from 1 ('Very seldom or never') to 7 ('Very often'). Selected items are reversed, then summed to provide a total score (13–91, with higher scores indicating greater psychological resilience).

#### *Attachment style*

The Attachment Style Questionnaire Short Form (ASQ-SF; 29 items)<sup>59</sup> measures self-reported attachment avoidance (16 items) and anxiety (13 items) in parents, adolescent ( $\geq 15$  years) and adult patients and siblings. Response options range from 1 ('Totally disagree') to 6 ('Totally agree'). Selected items are reversed then averaged, creating two domain scores. Higher scores indicate greater attachment insecurity.

#### *Perceived social support*

The Multidimensional Scale of Perceived Social Support (MSPSS; 12 items)<sup>60</sup> assesses perceptions of available support from significant others (four items), family (four items) and friends (four items) in parents, adolescent ( $\geq 12$  years), and adult patients and siblings. Response options range from 1 ('Very strongly disagree') to 7 ('Very strongly agree'). Items are averaged to provide a

total score (12–48, with higher scores indicating greater perceived support).

#### *Parental reflective functioning*

The Parental Reflective Functioning Questionnaire (PRFQ; 18 items)<sup>61</sup> measures parents' ability to understand their child's behaviour using three subscales (prementalising modes, certainty of mental states, interest and curiosity in mental states). Response options range from 1 ('Strongly disagree') to 7 ('Strongly agree'), and the mean of each subscale is calculated. Higher scores indicating greater difficulty understanding their child's thoughts, feelings and intentions.

#### *Family functioning*

The General Functioning subscale (GF-12; 12 items) of the Family Assessment Device (FAD)<sup>62</sup> measures perceived healthy and unhealthy family functioning in parents, adolescent ( $\geq 12$  years), and adult patients and siblings. Response options range from 1 ('Strongly disagree') to 4 ('Strongly agree'). A total score is derived from the mean of all items (1–4, with  $\geq 2.0$  scores indicating potentially unhealthy family functioning).<sup>63</sup>

#### *Perceived impact of CHD on family*

The revised Impact on Family Scale<sup>64</sup> (IFS; 15 items) measures parents' perceptions of the impact of childhood chronic illness on family life. Responses range from 1 ('Strongly agree') to 4 ('Strongly disagree'). Items are summed to provide a total score (0–100, with higher scores indicating more negative the impact on family life).

#### *Preference based health-related QOL*

The Child Health Utility 9D (CHU9D; nine items)<sup>65</sup> measures nine, self-reported dimensions of health-related QOL (worried, sad, pain, tired, annoyed, school-work, sleep, daily routine and ability to join activities) in children and adolescents (7–17 years). Response options range from 1 ('No Problems') to 5 ('Severe Problems') and scores are converted to single-index utility score using a reference weight scoring algorithm (ranging from  $-0.106$  (most severe health state) to  $1.0$  (best health state)).<sup>66</sup> The EuroQoL five-dimensions questionnaire (EQ-5D) measures five health-related QOL dimensions (mobility, self-care, usual activities, pain-discomfort and anxiety/depression) in adults ( $\geq 18$  years). Responses range from 1 ('No Problems') to 5 ('Extreme Problems') and scores are summed to create a five-digit value that can be compared with normative data.<sup>67</sup> The EQ-5D also includes a vertical visual analogue scale (EQ-VAS; one item) which provides a rating of self-perceived global health (ranging from 0 'the worst health you can imagine' to 100 'the best health you can imagine').

#### **Power and Sample Size Calculations**

Sample size calculation has been determined using G\*Power with a power set at 0.80 and a 0.05 significance level. Based on these values, to detect a medium effect

size of  $R^2=0.20$ , a sample size of at least 70 participants per age group is required for a regression analysis of five predictors.<sup>68</sup>

#### **Statistical Analyses**

Descriptive statistics will be computed for all dependent and independent variables. Data will be summarised as mean and SD or median and IQR for continuous variables and frequencies and proportions for categorical variables. Self-proxy and parent-proxy reported health-related QOL outcomes, assessed using the PedsQL total and summary scores, will be compared with normative data<sup>37 38</sup> using one-sample t-tests. Self-reported and parent-proxy reported psychological distress (eg, mean DASS-21, SCAS, SMFQ scores) will be compared with normative data using one-sample t-tests. Differences between (eg, self-reported vs parent-proxy report) and within (eg, mothers vs fathers) participant groups will be examined using independent samples t-tests or paired sample t-tests to account for the dependent nature of the comparison. Univariable associations between overall QOL and health-related QOL with predictor variables will be assessed with linear regression. A composite series of theory-driven hierarchical regression models will be used to examine whether sociodemographic, clinical and psychological variables (online supplemental table 1) explain a statistically significant proportion of the variance (as measured by the change in  $R^2$ ) for each of self-reported overall QOL and self-reported and parent-proxy reported health-related QOL. Outcome variables (eg, QOL, health-related QOL) with more than 50% of items incomplete will be excluded from analysis. Predictor variables captured via self-report and parent-report with missing data will be assumed missing at random. Analyses will be based on complete cases. Missing percentage values will be stated for each variable. For all analyses, a significance level of 0.05 will be applied and 95% CIs will be reported.

#### **ETHICS AND DISSEMINATION**

Ethics approval has been obtained from the Sydney Children's Hospitals Network Human Research Ethics Committee (LNR/14/SCHN/554) and the Royal Children's Hospital Melbourne Human Research Ethics Committee (HREC REF#35067A). The Heart Centre for Children at The Children's Hospital at Westmead in Sydney, Australia, serves as the coordinating centre for this research. Our dissemination plan includes publications in peer-reviewed scientific journals, academic presentations at conferences, and blog posts to CHD advocacy organisation websites. Reports will be developed for each recruiting site detailing results, and research and clinical practice recommendations. Results will also be shared with the Fontan community via the ANZFR Facebook page and key stakeholder Twitter accounts (eg, HeartKids). Findings will be shared with all participants and presented at the Australian and New Zealand Fontan



Registry Education Day. Selected publications related to this study will be included as part of a doctoral thesis (KM). Findings from this study will support the development of targeted preventive and intervention approaches to improve the health outcomes of people with a Fontan circulation and their families.

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**Contributors** NAK conceived the study, wrote the initial study protocol in collaboration with authors YD, DSW, KD, RB, GFS and the ANZFR Steering Committee, and secured IRB approvals with assistance from LM. DSJC and DZ designed the statistical analysis plan. KHM, LM and NAK are responsible for the acquisition of study data. KHM and NAK are responsible for project management. KHM drafted the manuscript and authors YD, DSW, KD, SRW, DZ, DSJC, DSC, GFS and NAK contributed to critical review. All authors have given approval for this version to be submitted for publication.

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