

Psychological functioning in paediatric patients with single ventricle heart disease: a systematic review



Review

Cite this article: McCormick AD, Wilde MM, Charpie CE, Saylor KM, Yu S, Schumacher KR, and Cousino MK (2022) Psychological functioning in paediatric patients with single ventricle heart disease: a systematic review. *Cardiology in the Young* **32**: 173–184. doi: [10.1017/S1047951122000063](https://doi.org/10.1017/S1047951122000063)

Received: 29 November 2021
Revised: 22 December 2021
Accepted: 3 January 2022
First published online: 20 January 2022

Author for correspondence:

Amanda D. McCormick, MD, Department of Pediatrics, Michigan Medicine, University of Michigan, 1500 E Medical Center Dr., Ann Arbor, MI 48109, USA. Tel: +1 330-289-4871. E-mail: acdelong@med.umich.edu

Amanda D. McCormick¹ , Megan M. Wilde¹, Christine E. Charpie², Kate M. Saylor³, Sunkyung Yu¹, Kurt R. Schumacher¹ and Melissa K. Cousino¹ 

¹Department of Pediatrics, Michigan Medicine, University of Michigan, Ann Arbor, MI, USA; ²College of Literature, Science and the Arts, University of Michigan, Ann Arbor, MI, USA and ³Taubman Health Sciences Library, University of Michigan, Ann Arbor, MI, USA

Abstract

Background: Patients with single ventricle heart disease are living into adulthood due to medical and surgical advancements but have significant physical comorbidities and an increased risk for psychological comorbidities compared to healthy subjects or those with other CHD diagnoses. This study aimed to systematically review psychological functioning in paediatric single ventricle heart disease. **Methods:** Literature was searched using PubMed, Embase, PsycInfo, CINAHL Complete and Scopus. Peer-reviewed articles that included patients ages 0–25 years with single ventricle heart disease, and quantitative measures of psychological outcomes were included. Meta-analysis using a fixed-effect model was conducted for internalising and externalising t-scores, utilised by the Achenbach Child Behavior Checklist. **Results:** Twenty-nine records met the criteria for inclusion. 13/24 studies demonstrated increased risk for internalising disorders, such as anxiety/depression; 16/22 studies demonstrated risk for externalising disorders, such as attention or behavioural problems. Meta-analysis of four studies revealed that paediatric single ventricle heart disease patients had no significant difference in internalising and externalising t-scores compared to normative values. **Conclusions:** The current review demonstrates the need for further studies to better understand psychological functioning in patients with single ventricle heart disease, with a majority of studies showing increased risk for psychological problems despite no difference seen in a small meta-analysis. This summary of the literature underscores the need for regular psychological screening, earlier intervention and integrated mental health therapies in paediatric single ventricle heart disease.

Single ventricle heart disease is a heterogeneous group of diagnoses that until 50 years ago was almost universally fatal. Since the description of the Fontan palliation in 1971 by Francis Fontan,¹ staged palliation for single ventricle heart disease culminating in the Fontan palliation has evolved in surgical technique, perioperative and outpatient care,^{2,3} and now allows the majority patients with single ventricle heart disease to survive well into adolescence and adulthood. Recent studies based on multi-centre data estimate 20-year post-Fontan survival at 75–85%⁴, while more modern era survival estimates approach 90%.⁵ However, Fontan palliation survivors experience a myriad of comorbidities related to their cardiac condition and face the possibility of Fontan circulatory failure, with even the most optimistic reports estimating that 10% of survivors will die or require heart transplant by early adulthood.⁶ Physical and neurodevelopmental comorbidities affect not only the physical health status of patients with single ventricle heart disease but also their well-being, quality of life⁷ and mental health.⁸

This growing population of patients with single ventricle heart disease seeks primary care from paediatricians as well as routine care from paediatric cardiology providers.⁹ It is well known that many children who would benefit from treatment of mental health conditions do not receive appropriate care,¹⁰ and the American Academy of Pediatrics has focused on preparedness of physicians to address mental health appropriately in their patients.¹¹ Despite this, literature on psychological functioning in the single ventricle heart disease population has not been synthesised. The research gap regarding psychological outcomes in the paediatric single ventricle heart disease population has been identified as a priority for exploration.^{12,13} Given the known association between poor psychological health and cardiovascular risk in adult patients,¹⁴ better characterisation of psychological functioning and outcomes in the paediatric single ventricle heart disease population is of utmost importance.

Building upon the current literature in adult cardiovascular disease and paediatric and adult CHD, this study aimed to review and summarise the existing literature on psychological functioning and outcomes in paediatric single ventricle heart disease patients guided by the following questions: (1) what is the impact of paediatric single ventricle heart disease on psychological

functioning? and (2) what variables, if any, have been identified as risk factors for adverse psychological sequelae in the single ventricle heart disease population? This systematic review will provide targets for intervention and underscore future research directions in this critical area for the single ventricle heart disease paediatric and emerging adult population.

Materials and methods

This systematic review followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement.¹⁵ The protocol is available in the University of Michigan's institutional repository Deep Blue and is accessible here: <https://doi.org/10.7302/1165>.

Search strategy

The review team met with health informationist (KMS) in early 2020. After discussion of included patients and outcomes, a search strategy was crafted to inform the selection of potential databases, concepts and search terms. The databases selected for this project include MEDLINE via PubMed, Embase (Elsevier), PsycInfo (EBSCO), CINAHL Complete (EBSCO) and Scopus (Elsevier). When available, publication limits were applied to exclude commentaries and book chapters. Reviews were included in the initial search for evaluation of additional articles through the ancestry method but were not included in manuscript review. The final searches were run on 21 April, 2020 and 15 June, 2020, with an additional search update to identify more recent articles on 10 May, 2021. EndNoteX9 was used to manage citations and to identify and remove duplicates. The deduplicated set of records was imported into Rayyan for screening where a few additional citations were identified as duplicates.

The searches were built around three main concepts: single ventricle heart disease, paediatrics and psychological functioning. Each search consisted of a combination of controlled terms appropriate for the selected databases and keywords limited to relevant fields. The PubMed search strategy is included in Appendix A and all reproducible search strategies and associated search files are available at <https://doi.org/10.7302/087c-9g95>. The ancestry method was also utilised, in which authors examined reference sections of studies meeting the review's predefined inclusion criteria for additional studies examining psychological functioning among paediatric patients with single ventricle heart disease.

Inclusion criteria

The following inclusion criteria were established prior to conducting the search: (1) study included a sample majority of paediatric patients between 0 and 25 years of age with single ventricle heart disease, (2) contained a quantitative measure of patient psychological functioning (e.g., measurement of symptomatology via self or parent report form, or participant reported diagnosis by a clinician) (3) published in a peer-reviewed journal and (4) published in English. Studies that primarily evaluated neurodevelopmental outcomes (e.g., cognitive development, motor development) or quality of life/health-related quality of life were included in the full-text article review, but only findings specific to patient psychological functioning were extracted for analysis.

Data extraction and study coding

Titles and abstracts of all search results were reviewed by one of two authors (AM and MW), with 20% of articles reviewed by both reviewers for reliability. Full articles were selected based on the inclusion criteria above and reviewed for inclusion by at least two reviewers (AM, MW, CC/MC). Reviewers extracted data from each study including sample characteristics (sample size, mean/median age/range, sex, CHD diagnosis/% of sample with single ventricle heart disease, presence of control group), measures of psychological functioning and reporter of measure and results.

Study quality was evaluated independently by two reviewers. The National Institutes of Health National Heart, Lung and Blood Institute Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies¹⁶ was adapted based on applicable criteria for the current literature. Assessment items included reference to an established research objective or study aim, description of study population including time period and geographical location of recruitment, participation rate of greater than or equal to 50%, established selection criteria and procedure, consideration of sample size, statistical power or effect sizes in interpretation, defined and validated outcome measures and consideration of potential confounding variables in analyses. Each study was assessed for all items and received a "yes" when quality indicators were met and a "no" when quality indicators were not met. Additional responses included "not applicable (NA)", "not reported (NR)" and "cannot determine (CD)". Based on these indicators, studies received a rating of "good", "fair" or "poor" quality. Discrepancies in ratings were discussed between the two rating authors and an agreement was made. Quality assessment is reported in Results section.

Defining psychological functioning and outcomes can methodologically be a challenge due to the wide range of metrics used. For the purpose of this review, analyses were divided into two large groups: studies that measured internalising problems (e.g., mood problems and symptoms of anxiety and depression) and studies that measured externalising problems (e.g., behavioural problems and symptoms of attention-deficit/hyperactivity disorder). Some studies also evaluated for symptoms of schizophrenia and autism spectrum disorder which were considered separately. While important, quality of life and neurodevelopmental outcomes are considered elsewhere in the literature and not included in this review.

Meta-analysis

The articles that provided adequate (t-score) data of the Achenbach Child Behavior Checklist, which is widely used to detect behavioural and emotional problems in children and adolescents,¹⁷ were included in the meta-analysis for evaluation of total t-score, internalising t-score and externalising t-score compared to the Child Behavior Checklist normative t-value of mean 50 with 10 SD. The effect sizes were estimated by Hedges' g ¹⁸ for the Child Behavior Checklist t-scores across each domain (total, internalising and externalising). The equal sample size of the articles included in the meta-analysis was used for the sample size of the Child Behavior Checklist norms. For the article in which the SD of the t-score was not reported, a pooled SD was used. All meta-analyses across the three Child Behavior Checklist domains were conducted using a fixed-effect model, assessing heterogeneity between studies. Heterogeneity between studies was examined using Cochran's Q ¹⁹ and I^2 statistic²⁰ with $I^2 \geq 50\%$ indicating substantial heterogeneity.²¹ Considering that the numbers of the

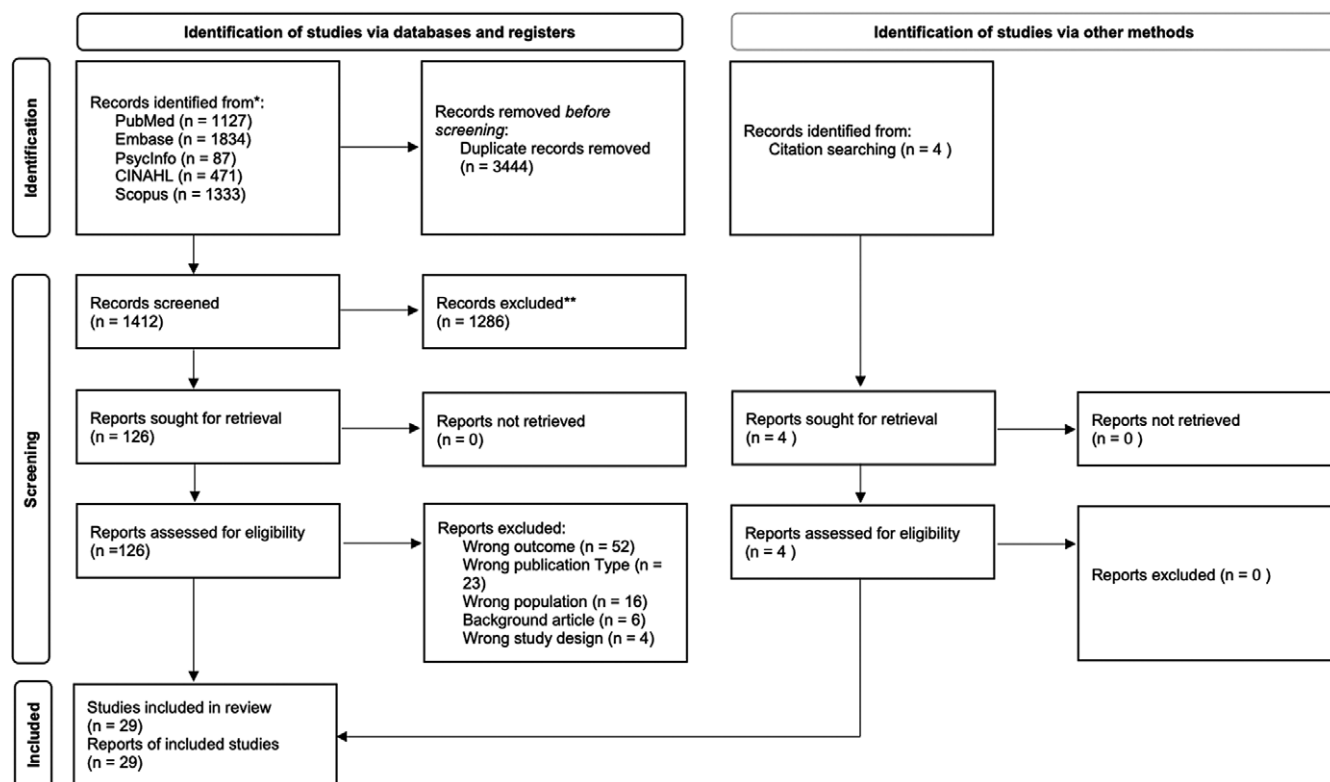


Figure 1. PRISMA diagram.

studies included were relatively small (five studies for total scale and four studies for both internalising and externalising scales) and the studies included in the meta-analysis were homogeneous based on Cochran's Q and I² statistics (Table 2), a random-effect model was not performed.

Results

Study characteristics

The searches yielded 1416 studies after the removal of duplicate results. See Figure 1 for the PRISMA flow diagram. After title and abstract screening, 130 articles were included for full-text article review. Of the studies excluded at the full-text review, the majority did not include a quantitative measure of psychological functioning (e.g., did not include measurement of symptomatology via self or parent report form, or participant reported diagnosis by a clinician, n = 52) or were the wrong publication type (n = 23). The remaining 29 articles met the criteria. For a full summary of study results, see Table 1. Within these 29 studies, approximately 30% were published in the last 5e years. Study sample sizes ranged from 12 to 1164 participants. Participate age ranges were vast, ranging from 1 year to adulthood. In paediatric patients with single ventricle heart disease, 24 studies assessed risk for internalising disorders and 22 studies assessed risk for externalising disorders.

Study quality assessment

Across included studies, all (n = 29, 100%) explicitly defined the research objective or study aim. All studies established inclusion criteria and consistent selection procedures (n = 29, 100%), defined the study population, including time period and geographical location of recruitment, and utilised defined outcomes

with validated measures (n = 29, 100%). Nineteen (66%) studies reported a participation rate of greater than 50%. Thirteen studies (45%) justified sample size or utilised effect sizes, and 18 (62%) statistically considered potential confounding variables in analyses. Based on the results of this quality assessment, 90% of included studies were rated as "good" quality (n = 26) and 10% of included studies were rated as "fair" quality (n = 3). No studies were excluded from the current literature review based on the quality assessment.

What is the impact of single ventricle heart disease on patient psychological outcomes?

Internalising disorders (anxiety, depression)

Twenty-four studies examined internalising problems (e.g., depression, anxiety) in the present review. Of these, 13 concluded that there was an increased risk of internalising problems in patients with single ventricle heart disease compared to healthy controls or other CHD patient populations.^{8,22-33} Eleven studies found no increase in risk of internalising problems as compared to controls.³⁴⁻⁴⁴

Anxiety symptoms were measured in 23 studies with 12 showing a higher risk of anxiety disorders compared to single ventricle heart disease compared to controls. One study showed as much as a fivefold increase in the rate of lifetime anxiety diagnosis in patients with single ventricle heart disease compared to referents (35% vs. 7%).⁸ Cassidy and colleagues found that patients with Fontan physiology had higher rates of anxiety than Transposition of the Great Arteries and Tetralogy of Fallot groups.²³ Twenty-four studies included measures of depressive symptoms. Results from 13 studies showed patients with single ventricle heart disease had a higher likelihood of developing depression or having a lifetime

Table 1. Included Study Characteristics and Results

Study	Sample Characteristics, n = # of SVHD patients	Comparison	Measures of Psychological Functioning	Category	Results
Bellinger et al 2015 ⁴⁵	N=156, M patient age: 14.5 ± 2.9 years	N=111 (healthy)	The Conners' Rating Scales Toronto Alexithymia Scale The Reading the Mind in the Eyes Test-Revised Autism Spectrum Quotient	Externalising, Autism	Externalising – SVHD patients had significantly worse scores on the measures of attention compared to controls ($p < 0.001$). 22% of SVHD patients had an ADHD diagnosis Autism – SVHD patients had significantly worse scores on all measures ($p = 0.02$, <0.001 , <0.001). Norwood group had higher but not significant scores than non-Norwood group on measures of attention and scored significantly worse than non-Norwood group on Reading the Mind in Eyes ($p = 0.02$) and Autism Spectrum Quotient ($p = 0.03$) tests, but not the Toronto Alexithymia scale
Brosig et al 2007 ³⁴	N=13, M patient age: 4.7 years	N=13 (DTGA)	CBCL	Internalising, Externalising	Internalising – No difference between SVHD and DTGA groups Externalising - HLHS group scored higher for attention ($p = 0.049$), externalising ($p = 0.026$), compared to TGA. 15% of patients in the HLHS group showed total and externalising problems scores in the clinical range, 23% of HLHS patients showed attention problems in the clinical range—not significant compared to DTGA, but may be clinically relevant Total problems - HLHS group scored higher than DTGA ($p = 0.42$) Internalising and total problems were significantly associated with minutes of circulatory arrest at time of surgery, with more minutes correlating with more behaviour problems
Brosig et al 2013 ³⁵	N=34, M patient age: 6.4 years	Compared to norms	CBCL The Conners' Rating Scales	Internalising, Externalising	Overall behavioural rating scale was normal. No significant findings in Internalising or Externalising total scores. Externalising – SVHD patients scored higher than norms on attention subscale of CBCL ($p = 0.0002$) although the scores were within the normal range. More likely to fall in the “at-risk” or “impaired” ranges on attention measures. No demographic or clinical variables were significant predictors of internalising or externalising scores, or Conners' scores
Calderon et al 2016 ³⁶	N=133, M patient age: 14.6 ± 3.0 years	SVHD patients born early term vs. full term	The Reading the Mind in the Eyes Test Revised, Autism Spectrum Quotient, Toronto Alexithymia Scale, K-SADS-PL Children's Depression Inventory Revised Children's Manifest Anxiety Scale The Conners' Rating Scales BPRS-C The Child Stress Disorder Checklist	Internalising, Externalising, Autism, PTSD	SVHD patients born early term were more likely than those born full term to have a lifetime ADHD diagnosis (55% vs. 26%) Early term SVHD patients scored significantly worse in both parent and self-report Conners' Rating Scales compared to full-term group. BPRS-C indicated greater severity of psychiatric symptoms in early term group. Those also born early term had greater posttraumatic stress symptoms on the Child Stress Disorder Checklist. No difference on measures of Autism, Depression, Anxiety Risk of ADHD diagnosis was lower for adolescents born early term who experienced a neurological event than those who had not ($p = 0.02$), full term adolescents who experienced a neurological event were at greater but not significantly increased risk than those who had not. Higher BPRS total scores, indicating greater psychiatric severity, were associated with longer circulatory arrest time, more catheterizations. Higher Conners' scores were associated with more total operative complications and female sex
Casey et al 1996 ²²	N=26, M patient age 8.78 ± 3.26 years	N=26 (Healthy)	CBCL	Internalising, Externalising	SVHD patients were rated higher on the Internalising scale ($p = 0.016$) but not the Externalising scale SVHD patients scored higher on the overall score ($p = 0.017$)

Table 1. (Continued)

Cassidy et al 2019 ²³	N=86, M patient age: 13.85 ± 2.86 years	N=134 (DTGA) N=58 (TOF)	K-SADS-PL	Internalising, Externalising	SVHD patients were more likely than DTGA or TOF to have a history of psychotherapy (p = 0.002), but were not significantly different on rates of current stimulant or psychotropic medications Prevalence of lifetime anxiety disorders (p < 0.001), ADHD (p = 0.01), and disruptive behaviour disorders (p = 0.01) was higher in SVHD group than DTGA group. Also had higher prevalence of lifetime anxiety disorders (p = 0.01) than TOF but did not differ in ADHD or disruptive behaviours.
d'Udekem et al 2009 ³⁷	N=36, M patient age: 21.6 ± 5 years	None	Hopkins Symptoms Checklist	Internalising	Hopkins symptoms Checklist scores were normal
Davidson et al 2015 ³⁸	N=58 (HLHS) M patient age: 12.3 years N=44 (nonHLHS SVHD) M patient age: 13.5 years	HLHS vs. non HLHS SVHD	Behavioral outcomes were measured by referrals to psychology services	Internalising, Externalising, Autism	23% of the population was referred to an educational psychologist or child psychiatrist at a higher rate in HLHS group. Higher incidence of formally diagnosed behavioural disorders in HLHS group compared with non-HLHS and healthy norms in local population (Autism 7% vs. 1-1.5%, ADHD 7% vs. 0.8%)
DeMaso et al 2017 ⁸	N=156, M patient age: 14.5 years	N=111 (Healthy)	K-SADS-PL BPRS-C Revised Children's Manifest Anxiety Scale Child Stress Disorders Checklist The Conners' Rating Scales Children's Depression Inventory	Internalising, Externalising, PTSD	SVHD patients had higher rates of lifetime psychiatric diagnosis (p < 0.001), anxiety (p < 0.001), ADHD (p < 0.001) BPRS-C scores indicated higher degree of psychiatric symptom severity for SVHD patients SVHD patients and parents reported significantly more symptoms of anxiety, disruptive behaviour, depression and PTSD Higher lifetime risk of anxiety disorder with lower birth weight and longer circulatory arrest duration. Higher risk of lifetime ADHD diagnosis associated with lower IQ scores and male gender
Denniss et al 2019 ⁴⁹	N=30, M patient age: 2.7 years	N=57 (Other CHD Diagnosis)	Short Temperament Scale for Children	"Other"	No differences on Short Temperament Scale
Fuller et al 2010 ⁴⁶	N=36, M patient age: 4 years	N=202 (Other CHD Diagnosis)	Impulsivity and Inattention Scales of the ADHD Rating Scale-IV Preschool Version.	Externalising	Patients with SVHD were more likely to have abnormal scores of inattention (p = 0.021)
Goldberg et al 2000 ³⁹	N=51, M patient age 4.8 years	Compared to norms	CBCL	Internalising, Externalising	1/51 patients was found to have abnormal behaviour per the CBCL
Goldberg et al 2019 ²⁴	N=291, M patient age: 6 years	Compared to norms	Behavior Assessment System for Children 2 (BASC-2)	Internalising, Externalising	Somatization was significantly worse for SVHD patients compared to normative sample For all other behaviour symptoms, no significant difference SVHD patients scored significantly worse internalising and externalising behaviour scales and adaptive skills composite
Gonzales et al 2021 ²⁵	N=63, Patient age: 4 to 17 years	N=1101 (Healthy)	N/A - Dx or Tx with anxiety, depression, ADHD	Internalising, Externalising	Patients with SVHD diagnoses were more likely to be diagnosed with anxiety/depression (p < 0.05) but not ADHD than their peers without CHD
Hagemo et al 1997 ⁴⁰	N=12, M patient age: 4 years	Compared to norms	CBCL	Internalising, Externalising	Mean scores below the norms for normative samples, but no evidence of clinical psychopathology

(Continued)

Table 1. (Continued)

Study	Sample Characteristics, n = # of SVHD patients	Comparison	Measures of Psychological Functioning	Category	Results
Hagemo et al 2007 ⁴¹	N=15, Patient age 5 to 12 years	Compared to norms	CBCL	Internalising, Externalising	One parent scored their child above the normal range, indicated more total problems, for overall behaviour Three parents scored their child above the normal range for emotional problems
Hansen et al 2012 ⁴⁷	N=14, M patient age: 12.6 years	N=37 (Other CHD diagnosis)	SNAP-IV	Externalising	There appeared to be a statistically non-significant trend towards the SVHD patients having a greater prevalence of elevated inattention symptoms (21.43% vs. 5.41%, $p = 0.12$). This trend was not seen for the hyperactive/impulsivity symptoms (7.14% vs. 2.70%, $p = 0.48$)
Mahle et al 2000 ²⁶	N=28	Compared to norms	CBCL	Internalising, Externalising	14 (50%) of SVHD patients scored within the normal range for all 8 subtests, 5 (17.8%) met criteria for borderline or clinical behavioural problems on 2 or more subtests, the subtest most likely to be abnormal was attention (5 clinical, 2 borderline). 6 children (20.7%) were in the clinical range for anxious/depressed
McCusker et al 2007 ⁴²	N=12, M patient age: 4.6 years	N=78 (Other CHD diagnosis)	CBCL	Internalising, Externalising	The percentage of SVHD patients with abnormal total scores was twice as many as the control group Poor parental control skills, single parent status, high maternal worry, and maternal psychological symptoms were associated with worse behavioural outcomes. Surgical procedure and bypass time were not.
Mellander et al 2007 ²⁷	N=14, Patient age: 2.7 to 10.6 years	N=180 (Healthy)	Model of Lindstrom	Internalising	SVHD patients had lower self-esteem ($p < 0.05$), basic mood lower with more psychosomatic symptoms ($p < 0.001$)
Noorani et al 2020 ²⁸	N=23, M Patient Age 15.9 ± 1.3 years	N=37 (Healthy)	PHQ9 Beck Anxiety Inventory WRAML2	Externalising Internalising	Attention/concentration subscale of WRAML2 was significantly lower in SVHD patients ($p < 0.001$) PHQ9 scores were significantly higher in SVHD patients ($p = 0.001$) Beck Anxiety Inventory scores were significantly higher in SVHD patients ($p = 0.001$)
Overgaard et al 2011 ⁴³	N=62, M patient age: 22 years	N=142 (Healthy)	Hospital Anxiety and Depression Scale	Internalising	SVHD patients experienced only few symptoms of anxiety or depression, the median score was 5 for anxiety and 2 for depression. Anxiety was not related to functional class
Pike et al 2018 ²⁹	N=9, M patient age: 15.8 years	N=36 (Healthy)	Beck Anxiety Inventory Patient Health Questionnaire-9 (PHQ-9)	Internalising	The PHQ-9 and Beck Anxiety Inventory scores were significantly higher in SVHD patients over controls (PHQ-9, $p = 0.004$; Beck Anxiety Inventory, $p = 0.006$).
Puosi et al 2011 ³⁰	N=36, M patient age: 29.7 months	N=41 (Healthy)	CBCL	Internalising, Externalising	No significant difference in total, internalising, or externalising scores between SVHD patients and controls, however t-scores suggest more internalising problems in SVHD patients ($p < 0.05$) No difference in HLHS vs. other SVHD patients in total, externalising or internalising problems
Saliba et al 2001 ⁴⁴	N=49, M patient age: 22.7 years	Compared to norms	Duke Health Profile	Internalising	The Duke scores SVHD patients were similar to the normal population.
Sarajuuri et al 2012 ³¹	N=37, M patient age: 18.3 months	N=46 (Healthy)	CBCL	Internalising, Externalising	The parents of the SVHD patients reported significantly more total (mean 49.8 versus 45.0, $p = 0.009$) and internalising (48.6 versus 40.8, $p = 0.001$) behaviour problems than those of the controls, but not externalising problems. Among the syndrome scales, a significant difference was only found in somatic complaints. No difference in HLHS and other SVHD patients in total, internalising or externalising problems

Table 1. (Continued)

Sarrechia et al 2016 ³²	N=17, M patient age 9.1 ± 2.2 years	N=17 (healthy)	CBCL	Internalising, Externalising	Parents of SVHD patients reported significantly more externalising and total behaviour problems, and there was a trend towards more internalising problems No significant correlations between patient characteristics and total, internalising or externalising problems.
Sistino et al 2014 ⁴⁸	N=33, M patient age: 9 years	Compared to norms	ADHD-IV survey	Externalising	9/33 SVHD patients (23.7%) had ADHD
Vahsen et al 2018 ³³	N=104, M patient age: 8.6 years	Compared to norms	CBCL	Internalising, Externalising	Parents reported significantly more total behavioural problems, internalising behaviour problems and externalising behaviour problems

Abbreviations: SVHD = Single Ventricle Heart Disease, DTGA = D-Transposition of the Great Arteries, CBCL = Child Behavior Checklist, K-SADS-PL = Schedule for Affective Disorders and Schizophrenia for School-Aged Children, BRPS-C = Brief Psychiatric Rating Scale for Children, TOF = Tetralogy of Fallot, PTSD = Post Traumatic Stress Disorder, CHD = Congenital Heart Disease, ADHD = Attention Deficit/Hyperactivity Disorder, WRAML2 = Wide Range Assessment of Memory and Learning, Second Edition, PHQ-9 = Patient Health Questionnaire-9 HLHS = Hypoplastic Left Heart Syndrome.

depression diagnosis compared to normed samples or other CHD groups. Gonzales and colleagues reported a 7x higher odds of diagnosis or treatment of anxiety and/or depression in patients with single ventricle heart disease compared to controls.²⁵ One study found that patients with single ventricle heart disease reported lower self-esteem and mood than healthy peers.²⁷

Health-related correlates of anxiety and depressive symptoms were examined across some studies. Deep hypothermic arrest time was found to be associated with greater total internalising problems³⁴ and a higher likelihood for lifetime anxiety disorder⁸ in patients with single ventricle heart disease. Lower birth weight was also found to be associated with greater likelihood for lifetime anxiety disorder diagnosis.⁸ Overgaard and colleagues detected a significant positive correlation between impairment of physical abilities and depression, whereas anxiety was not observed to be correlated.⁴³

Externalising disorders (disruptive behaviors, attention-deficit/hyperactivity disorder)

Twenty-two studies examined externalising problems in the present review, with 16 studies concluding that single ventricle heart disease patients had increased risk or a trend towards increased risk of externalising problems. Ten studies included measures looking broadly at externalising problems. Of these, four found that patients with single ventricle heart disease demonstrated greater risk of externalising problems than healthy controls,^{24,32-34} and six found no statistical difference in externalising problems.^{22,30,31,39-41}

Seven studies evaluated symptoms of inattention, which are sometimes used as proxy for attention-deficit/hyperactivity disorder assessment. Four studies showed that patients with single ventricle heart disease performed significantly worse on measures of attention than healthy control groups.^{28,34,45,46} An additional three studies showed trends towards increased attention deficits between patients with single ventricle heart disease and controls.^{26,35,47}

In addition to symptoms, multiple studies showed that patients with single ventricle heart disease have an increased rate of diagnosis of attention-deficit/hyperactivity disorder as compared to healthy control groups and local prevalence data. Two studies showed higher rates of lifetime attention-deficit/hyperactivity disorder diagnosis in patients with single ventricle heart disease when compared with patients with other forms of CHD.^{8,23} Rates of attention-deficit/hyperactivity disorder diagnosis within study-specific cohorts of patients with single ventricle heart disease widely ranged from 5.1% to 23.7% among four different studies.^{25,38,45,48}

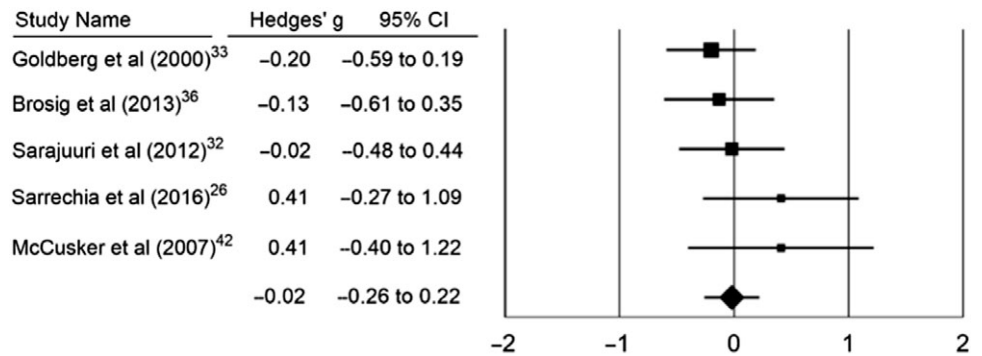
Five studies examined additional correlates of risk for externalising disorders in patients with single ventricle heart disease. One study evaluated single ventricle heart disease patients who were born at early term versus those that were born at full term. This study found that patients with single ventricle heart disease born early term (37-38 weeks gestation) were more likely than those born full term (39-40 weeks gestation) to have a lifetime attention-deficit/hyperactivity disorder diagnosis (55% vs. 26%). Additionally, higher scores on measures of attention-deficit/hyperactivity disorder were associated with more total operative complications and female sex.³⁶ A second study found higher risk of lifetime attention-deficit/hyperactivity disorder diagnosis was associated with lower IQ scores and male sex.⁸ Two additional studies found no significant correlations between patient characteristics and externalising problems.^{32,35}

Table 2. Meta-Analysis Results comparing CBCL t-scores in paediatric single ventricle heart disease patients to CBCL norms (mean t-score 50 with SD 10)

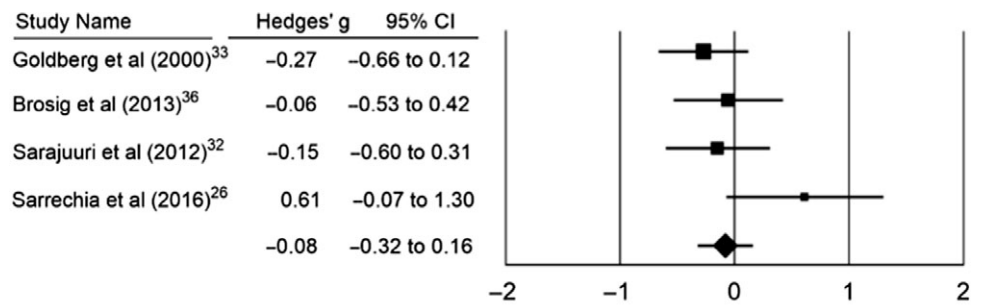
CBCL domain	Number of articles included	Number of patients with SVHD	Pooled effect size by Hedges' g	95% CI	P-value	Heterogeneity		
						Cochran's Q	P-value	I ²
Total	5	151	-0.02	-0.26 to 0.22	0.81	3.63	0.46	0.0%
Internalizing	4	139	-0.08	-0.32 to 0.16	0.50	4.89	0.18	38.6%
Externalizing	4	139	-0.20	-0.44 to 0.04	0.09	2.09	0.55	0.0%

Abbreviations: CBCL = Child Behavior Checklist, SVHD = Single Ventricle Heart Disease, CI, confidence interval.

(a) Total



(b) Internalizing



(c) Externalizing

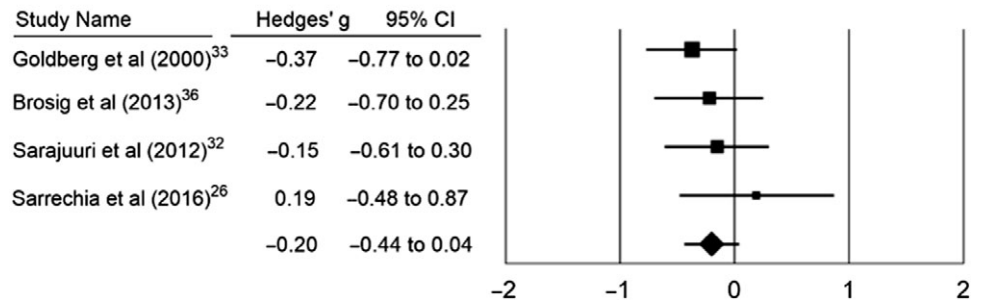


Figure 2. Forest plots from meta-analysis for CBCL total (A), internalising (B) and externalising (C) t-scores. Square sizes are proportional to the weight of each study's sample size in the analysis, and the lines represent their 95% CIs. The diamond represents the pooled effect size by Hedges' g with 95% CI.

Four studies examined type of single ventricle heart disease diagnosis as a risk factor for externalising problems. One study found that patients who underwent a Norwood palliation had higher but not significantly different scores than patients with other palliations on measures of attention.⁴⁵ A second study found an increased rate of

attention-deficit/hyperactivity disorder diagnosis in patients with hypoplastic left heart syndrome than other patients with single ventricle heart disease.³⁸ Two more studies found no difference in externalising problems between patients with hypoplastic left heart syndrome and other single ventricle heart disease diagnoses.^{30,31}

Other disorders (Autism spectrum disorders, schizophrenia spectrum disorders and post-traumatic stress disorders)

Three studies examined symptoms or diagnoses of autism spectrum disorder. One study found that patients with single ventricle heart disease had significantly worse scores on three measures of autism spectrum disorder as compared to healthy controls.⁴⁵ A second study found higher incidence of autism spectrum disorder diagnoses in patients with single ventricle heart disease compared with local prevalence rates (7% vs 1–1.5%).³⁸ Two studies evaluated symptoms of post-traumatic stress disorder with one study demonstrating that patients with single ventricle heart disease were more likely to report symptoms of post-traumatic stress disorder than healthy controls.⁸ Three studies evaluated measures of Schizophrenia symptoms with no significant findings.^{8,23,36} One study evaluated measures of temperament, with no significant findings.⁴⁹

Meta-analysis

Of 12 studies that utilised the CBCL, only five studies provided mean *t*-scores to allow for inclusion in the meta-analysis.^{31,32,35,39,42} One study only reported data for the total problems scale,⁴² and thus four studies were included in the externalising and internalising domain analyses. The pooled effect sizes for all three domains (total, internalising and externalising problems) were insignificant, suggesting no significant difference between mean *t*-scores of the studies and the mean *t*-scores for normative values. For a full summary of meta-analysis results, see Table 2 and Figure 2.

Discussion

Results of the current review present the first known synthesis of the literature regarding psychological functioning in the paediatric single ventricle heart disease population. Overall, review of results of individual studies underscores increased risk for psychological sequelae, including anxiety, depression and behavioural symptoms and disorders in paediatric patients with single ventricle heart disease. However, a small meta-analysis of 4–5 studies failed to show significant differences in total, internalising or externalising problems.

Of the 24 studies in the review that examined internalising problems, the majority found an increased risk of internalising problems in paediatric single ventricle heart disease patients when compared with control groups. This is consistent with the existing, albeit few, studies of the paediatric CHD population at large which show that children with CHD have increased incidence of depression when compared with their peers.^{50,51} Increased rates of internalising problems have been well described in the more robust adult CHD literature. Some studies estimate that over half of adult patients with CHD have significant symptoms of a mood or anxiety disorder,⁵² although it is also likely that these symptoms are underrecognized and this estimate does not fully capture the extent of psychological morbidity.

This review also found increased risk of externalising problems in paediatric patients with single ventricle heart disease, with 16 of 22 studies that examined externalising problems describing increased risk compared to controls. The few existing studies in paediatric CHD show similar findings of increased risk of inattention symptoms and attention-deficit/hyperactivity disorder.^{51,53–55} There is minimal literature on adult CHD or adult cardiovascular disease and associations with attention-deficit/hyperactivity disorder, which could be an important area for further exploration given known associations with adult attention-deficit/hyperactivity

disorder and poor physical and mental health outcomes.⁵⁶ It is important to note that the broad category of externalising problems also includes aggression and conduct problems. It is possible that if children do not have aggression or conduct problems that their total externalising score may not be elevated, despite attention or self-regulation concerns. Further studies with more specific metrics can better identify the risk of attention-deficit/hyperactivity disorder in this patient population.

It is important to highlight that the meta-analysis of 4–5 studies did not show significant differences between single ventricle heart disease patients and normative values in total, externalising or internalising problems as measured by a well-validated metric of child emotional and behavioural problems. This non-significant finding amidst the broader literature review, which highlights a greater risk for adverse psychological sequelae for patients with single ventricle heart disease, should be interpreted with the following considerations in mind. First, only a small number of studies could be included in the meta-analysis due to the various measures of psychological functioning used across studies. Furthermore, it is possible that certain patients within the single ventricle heart disease population are at higher risk for poor psychological functioning than others. It is notable that in this small meta-analysis sample, four of the studies had a mean age of participant below age 5. Karsdorp et al previously found in their meta-analysis that older children and adolescents were at higher risk for poor psychological functioning.⁵¹ Likewise, Gonzalez et al found that the rate of diagnosis or medication for anxiety and depression increased as patients with CHD aged.²⁵ It is feasible that studies with older single ventricle heart disease patients may find more significant differences in rates of poor psychological functioning than those of younger patients. Lastly, a number of studies in the review noted normative sample mean scores in terms of psychological functioning but found percentage of patients with at-risk scores to be greater than population prevalence. As such, sample mean scores provide only a snapshot of psychological risk.

Several limitations to the current body of literature must be noted, which may direct future research in the field. First, few studies examined association of poor psychological functioning and health outcomes. It is known that in adults with CHD, depression is responsible for the variability of self-reported health status of patients, including physical functioning.⁵⁷ A recent study of adult patients with CHD found that major depression was associated with impaired functional status, heart failure and increased risk for adverse outcomes.⁵⁸ Mental health disease may also impact healthcare utilisation, as has been demonstrated in adult patients with CHD.⁵⁹ Further studies of associations of health outcomes and psychological functioning in paediatric patients with single ventricle heart disease are important to better understand the impact of mental health disorders in this population.

Five studies^{23,34,42,46,47} within the present review found increased risk of poor psychological functioning in patients with single ventricle heart disease when compared to patients with other forms of CHD. The findings presented here may suggest that patients with single ventricle heart disease have different risk for worse outcomes in psychological functioning, and thus should be considered separately from other patients with CHD. A previous systematic review and meta-analysis by Latal et al similarly looked at psychological functioning in the broader CHD population which found that psychological outcomes were worse for patients with more severe CHD.⁶⁰ A recent large international study of adult patients found worse psychological patient-related outcomes in patients with cyanotic heart disease compared to other

CHD.⁶¹ Future studies examining contributors of additive psychological burden in single ventricle heart disease are important next directions for the field.

This review highlights several important practice considerations. Mental health disorders are not reliably identified in the paediatrics population at large, and many children who would benefit from treatment of mental health conditions do not receive appropriate care.¹⁰ It is suspected that mental health disorders are under-identified and undertreated in children for a myriad of reasons. The integration of experienced social work and psychology clinicians into paediatric cardiology care is supported by international consensus statements.⁶² Screening for psychological functioning with brief, validated instruments at routine clinic visits may also help to identify those patients at highest need for referral and intervention. The Cardiac Neurodevelopmental Outcome Collaborative has made recent recommendations for a core battery of developmental testing including the Behavior Assessment System for Children, Third Edition⁶³ for consistent and validated screening methodologies across centres.^{64,65}

Notably, lack of preparedness by the paediatric provider to address mental health concerns in their patients has also been highlighted as a contributor to the under-identification of mental health concerns in children.¹¹ As a result, the American Board of Pediatrics and American Academy of Pediatrics have focused on preparedness of physicians to address mental health appropriately in their patients.¹¹ For this reason, mental health training in paediatric residency is a target of graduate medical education groups across paediatric care.^{11,66,67} To our knowledge, mental healthcare has not been a focus of education in paediatric cardiology fellowship. As it has been shown that some parents seek routine care from their cardiology providers,⁹ paediatric cardiology providers should also be comfortable with identifying patients who would benefit from referral for mental health services. While mental health assessments are taught in many paediatric residency programmes, this is not consistent across training programmes. Further education in addressing mental health concerns would better prepare paediatric cardiology trainees to meet the needs of their complex population. This education and training should also be expanded to all members of the multidisciplinary team providing cardiology specific care to this patient population, including nurses, social workers, therapists, psychologists, and developmental experts.

Mental health intervention design, implementation and effectiveness study are necessary next steps for research and practice.⁶⁸ A recent review of the literature identified only two published psychological intervention studies involving adolescents with CHD. Unfortunately, the interventions were not found to be highly efficacious,⁶⁹ but mental health interventions in adults with heart disease have demonstrated some successes to build upon.⁷⁰ Cognitive behavioural therapy and positive-psychology based interventions in particular have shown promise in adult heart disease populations.¹⁴ Therefore, examination of such intervention effects on both psychological and cardiovascular outcomes in paediatric single ventricle heart disease should be priorities for research study in the coming years.

The results of the current review must be interpreted in light of several limitations. Given the limited available research on psychological functioning in the paediatric single ventricle heart disease population, and the paediatric CHD population in general, studies for review were limited in number and often with varying methodology. A meta-analysis was conducted on studies utilising the same metric and methodology but given the wide range of

measures and methodologies available, a more comprehensive meta-analysis was not feasible. Further, studies in the current review widely varied in sample size with 18 of the 29 studies having sample sizes of 40 participants or fewer. While this is reflective of smaller populations of patients with single ventricle heart disease at some single centres, future research would continue to be improved by multi-site collaborations and registry-level studies to better understand psychological functioning in this population. While every effort was made to include all published studies on the presented topic, it is possible some studies were missed. Finally, qualitative studies were not included in the review given inconsistency in methodology but may add valuable insights into psychological functioning in this population.

This systematic review provides an important synthesis of the literature and a starting point for further research on risk factors and interventions for psychological functioning in patients with single ventricle heart disease. Results demonstrate that patients with single ventricle heart disease are at increased risk for poor psychological functioning when compared to healthy peers and to peers with other forms of CHD. Likely there are characteristics within the single ventricle heart disease population that put certain patients at even greater risk, potentially age and specific single ventricle heart disease diagnoses, however, these specific characteristics have yet to be well studied. The suggestion but lack of clear associations of single ventricle heart disease and psychological functioning through single centre studies supports the prospective integration of psychological outcomes into emerging registries like the Fontan Outcomes Network⁷¹ and the existing Cardiac Neurodevelopmental Outcome Collaborative,⁷² which in addition to neurodevelopmental outcomes is also collecting psychosocial outcomes data. Based on the findings of this systematic review and in keeping with the current American Heart Association statements,¹⁴ we would recommend that paediatric cardiologists prioritise mental health in their care of patients with single ventricle heart disease, with future research guiding best practices on screening techniques and intervention strategies.

Supplementary material. For supplementary material accompanying this paper visit <https://doi.org/10.1017/S1047951122000063>

Acknowledgements. The authors would like to acknowledge the Michigan Congenital Heart Outcomes Research and Discovery (MCHORD) group at the University of Michigan Congenital Heart Center, for their support in the development of this project.

Financial support. This research received no specific grant from any funding agency, commercial or not-for-profit sectors. Dr Cousino's research is supported by the National Heart, Lung, and Blood Institute (K23HL145096) of the National Institutes of Health.

Conflicts of interest. None.

References

1. Fontan F, Baudet E. Surgical repair of tricuspid atresia. *Thorax* 1971; 26: 240–248.
2. d'Udekem Y, Iyengar AJ, Cochrane AD, et al. The fontan procedure: contemporary techniques have improved long-term outcomes. *Circulation* 2007; 116: 1157–164.
3. Stewart RD, Pasquali SK, Jacobs JP, et al. Contemporary fontan operation: association between early outcome and type of cavopulmonary connection. *Ann Thorac Surg* 2012; 93: 1254–1260, discussion 1261.
4. Poh CL, d'Udekem Y. Life after surviving fontan surgery: a Meta-Analysis of the incidence and predictors of late death. *Heart Lung Circ* 2018; 27: 552–559.

5. Atz AM, Zak V, Mahony L, et al. Longitudinal outcomes of patients with single ventricle after the fontan procedure. *J Am Coll Cardiol* 2017; 69: 2735–2744.
6. McCormick AD, Schumacher KR. Transplantation of the failing fontan. *Transl Pediatr* 2019; 8: 290–301.
7. Marshall KH, D'Udekem Y, Sholler GF, et al. Health-Related quality of life in children, adolescents, and adults with a fontan circulation: a Meta-Analysis. *J Am Heart Assoc* 2020; 9: e014172.
8. DeMaso DR, Calderon J, Taylor GA, et al. Psychiatric disorders in adolescents with single ventricle congenital heart disease. *Pediatrics* 2017; 139: 319.
9. Luthy SK, Yu S, Donohue JE, Locco E, Goldberg CS, Lu JC. Parental preferences regarding outpatient management of children with congenital heart disease. *Pediatr Cardiol* 2016; 37: 151–159.
10. Jensen PS, Goldman E, Offord D, et al. Overlooked and underserved: "action signs" for identifying children with unmet mental health needs. *Pediatrics* 2011; 128: 970–979.
11. McMillan JA, Land M Jr., Tucker AE, Leslie LK. Preparing future pediatricians to meet the behavioral and mental health needs of children. *Pediatrics* 2020; 145: 1199.
12. Sanz JH, Anixt J, Bear L, et al. Characterisation of neurodevelopmental and psychological outcomes in CHD: a research agenda and recommendations from the cardiac neurodevelopmental outcome collaborative. *Cardiol Young* 2021; 31: 1–12.
13. Sood E, Jacobs JP, Marino BS. Optimising neurodevelopmental and psychosocial outcomes for survivors with CHD: a research agenda for the next decade. *Cardiol Young* 2021; 31: 1–3.
14. Levine GN, Cohen BE, Commodore-Mensah Y, et al. Psychological health, well-being, and the Mind-Heart-Body connection: a scientific statement from the american heart association. *Circulation* 2021; 143: e763–e783.
15. Moher D, Liberati A, Tetzlaff J, Altman DG, Group P. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009; 339: b2535–b2535.
16. National Institute of Health National Heart L, and Blood Institute. Study quality assessment tool for observational cohort and cross-sectional studies., <https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools>. Accessed.
17. Achenbach T. Manual for the Child Behavior Checklist/4-18 and 1991 Profile. University of Vermont, Department of Psychiatry, Burlington, VT, 1991.
18. Hedges L. Distribution theory for glass's estimator of effect size and related estimators. *J Educ Stat* 1981; 6: 101–128.
19. Borenstein M, Hedges L, Higgins J, Rothstein H. Introduction to Meta-Analysis. John Wiley & Sons, Ltd, Chichester, UK, 2009.
20. Borenstein M, Hedges L, Higgins J, Rothstein H. Comprehensive Meta-Analysis Version 3. Biostat. Englewood, NJ, 2013.
21. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ* 2003; 327: 557–560.
22. Casey FA, Sykes DH, Craig BG, Power R, Mulholland HC. Behavioral adjustment of children with surgically palliated complex congenital heart disease. *J Pediatr Psychol* 1996; 21: 335–352.
23. Cassidy AR, Bernstein JH, Bellinger DC, Newburger JW, DeMaso DR. Visual-spatial processing style is associated with psychopathology in adolescents with critical congenital heart disease. *Clin Neuropsychol* 2019; 33: 760–778.
24. Goldberg CS, Hu C, Brosig C, et al. Behavior and quality of life at 6 years for children with hypoplastic left heart syndrome. *Pediatrics* 2019; 144: 816.
25. Gonzalez VJ, Kimbro RT, Cutitta KE, et al. Mental health disorders in children with congenital heart disease. *Pediatrics* 2021; 147: 319.
26. Mahle WT, Clancy RR, Moss EM, Gerdes M, Jobs DR, Wernovsky G. Neurodevelopmental outcome and lifestyle assessment in school-aged and adolescent children with hypoplastic left heart syndrome. *Pediatrics* 2000; 105: 1082–1089.
27. Mellander M, Berntsson L, Nilsson B. Quality of life in children with hypoplastic left heart syndrome. *Acta Paediatr* 2007; 96: 53–57.
28. Noorani S, Roy B, Sahib AK, et al. Caudate nuclei volume alterations and cognition and mood dysfunctions in adolescents with single ventricle heart disease. *J Neurosci Res* 2020; 98: 1877–1888.
29. Pike NA, Roy B, Gupta R, et al. Brain abnormalities in cognition, anxiety, and depression regulatory regions in adolescents with single ventricle heart disease. *J Neurosci Res* 2018; 96: 1104–1118.
30. Puosi R, Korkman M, Sarajuuri A, et al. Neurocognitive development and behavioral outcome of 2-year-old children with univentricular heart. *J Int Neuropsychol Soc* 2011; 17: 1094–1103.
31. Sarajuuri A, Lonnqvist T, Schmitt F, Almqvist F, Jokinen E. Patients with univentricular heart in early childhood: parenting stress and child behaviour. *Acta Paediatr* 2012; 101: 252–257.
32. Sarrechia I, Miatton M, De Wolf D, et al. Neurocognitive development and behaviour in school-aged children after surgery for univentricular or biventricular congenital heart disease. *Eur J Cardiothorac Surg* 2016; 49: 167–174.
33. Vahsen N, Broder A, Hraska V, Schneider M. Neurodevelopmental outcome in children with single ventricle after total cavopulmonary connection. *Klin Padiatr* 2018; 230: 24–30.
34. Brosig CL, Mussatto KA, Kuhn EM, Tweddell JS. Neurodevelopmental outcome in preschool survivors of complex congenital heart disease: implications for clinical practice. *J Pediatr Health Care* 2007; 21: 3–12.
35. Brosig C, Mussatto K, Hoffman G, et al. Neurodevelopmental outcomes for children with hypoplastic left heart syndrome at the age of 5 years. *Pediatr Cardiol* 2013; 34: 1597–1604.
36. Calderon J, Stopp C, Wypij D, et al. Early-Term birth in single-Ventricle congenital heart disease after the fontan procedure: neurodevelopmental and psychiatric outcomes. *J Pediatr* 2016; 179: 96–103.
37. d'Udekem Y, Cheung MM, Setyapranata S, et al. How good is a good fontan? quality of life and exercise capacity of fontans without arrhythmias. *Ann Thorac Surg* 2009; 88: 1961–1969.
38. Davidson J, Gringras P, Fairhurst C, Simpson J. Physical and neurodevelopmental outcomes in children with single-ventricle circulation. *Arch Dis Child* 2015; 100: 449–453.
39. Goldberg CS, Schwartz EM, Brunberg JA, et al. Neurodevelopmental outcome of patients after the fontan operation: a comparison between children with hypoplastic left heart syndrome and other functional single ventricle lesions. *J Pediatr* 2000; 137: 646–652.
40. Hagemo PS, Rasmussen M, Bryhn G, Vandvik IH. Hypoplastic left heart syndrome: multiprofessional Follow-up in the Mid-term following palliative procedures. *Cardiol Young* 1997; 7: 248–253.
41. Hagemo PS, Skarbo AB, Rasmussen M, Fredriksen PM, Schage S. An extensive long term follow-up of a cohort of patients with hypoplasia of the left heart. *Cardiol Young* 2007; 17: 51–55.
42. McCusker CG, Doherty NN, Molloy B, et al. Determinants of neuropsychological and behavioural outcomes in early childhood survivors of congenital heart disease. *Arch Dis Child* 2007; 92: 137–141.
43. Overgaard D, Schrader AM, Lisby KH, et al. Patient-reported outcomes in adult survivors with single-ventricle physiology. *Cardiology* 2011; 120: 36–42.
44. Saliba Z, Butera G, Bonnet D, et al. Quality of life and perceived health status in surviving adults with univentricular heart. *Heart* 2001; 86: 69–73.
45. Bellinger DC, Watson CG, Rivkin MJ, et al. Neuropsychological status and structural brain imaging in adolescents with single ventricle who underwent the fontan procedure. *J Am Heart Assoc* 2015; 4: 216.
46. Fuller S, Rajagopalan R, Jarvik GP, et al. Maxwell chamberlain memorial paper for congenital heart surgery. deep hypothermic circulatory arrest does not impair neurodevelopmental outcome in school-age children after infant cardiac surgery. *Ann Thorac Surg* 2010; 90: 1985–1994, discussion 1994–1985.
47. Hansen E, Poole TA, Nguyen V, et al. Prevalence of ADHD symptoms in patients with congenital heart disease. *Pediatr Int* 2012; 54: 838–843.
48. Sistino JJ, Atz AM, Simpson KN, Ellis C, Ikonomidis JS, Bradley SM. The prevalence of attention-deficit/hyperactivity disorder following neonatal aortic arch repair. *Cardiol Young* 2015; 25: 663–669.
49. Denniss DL, Sholler GF, Costa DSJ, Winlaw DS, Kasparian NA. Need for routine screening of health-Related quality of life in families of young children with complex congenital heart disease. *J Pediatr* 2019; 205: 21–28 e22.
50. Luyckx K, Rassart J, Goossens E, Apers S, Oris L, Moons P. Development and persistence of depressive symptoms in adolescents with CHD. *Cardiol Young* 2016; 26: 1115–1122.

51. Karsdorp PA, Everaerd W, Kindt M, Mulder BJ. Psychological and cognitive functioning in children and adolescents with congenital heart disease: a meta-analysis. *J Pediatr Psychol* 2007; 32: 527–541.
52. Kovacs AH, Saidi AS, Kuhl EA, et al. Depression and anxiety in adult congenital heart disease: predictors and prevalence. *Int J Cardiol* 2009; 137: 158–164.
53. Wang CC, Weng WC, Chang LY, et al. Increased prevalence of inattention-related symptoms in a large cohort of patients with congenital heart disease. *Eur Child Adolesc Psychiatry* 2021; 30: 647–655.
54. Holland JE, Cassidy AR, Stopp C, et al. Psychiatric disorders and function in adolescents with tetralogy of fallot. *J Pediatr* 2017; 187: 165–173.
55. Yamada DC, Porter AA, Conway JL, et al. Early repair of congenital heart disease associated with increased rate of attention deficit hyperactivity disorder symptoms. *Can J Cardiol* 2013; 29: 1623–1628.
56. Cherkasova MV, Roy A, Molina BSG, et al. Review: adult outcome as seen through controlled prospective Follow-up studies of children with Attention-Deficit/Hyperactivity disorder followed into adulthood. *J Am Acad Child Adolesc Psychiatry* 2021. DOI [10.1016/j.jaac.2021.05.019](https://doi.org/10.1016/j.jaac.2021.05.019). [Online ahead of print].
57. Ko JM, Tecson KM, Rashida VA, et al. Clinical and psychological drivers of perceived health status in adults with congenital heart disease. *Am J Cardiol* 2018; 121: 377–381.
58. Carazo MR, Kolodziej MS, DeWitt ES, et al. Prevalence and prognostic association of a clinical diagnosis of depression in adult congenital heart disease: results of the boston adult congenital heart disease biobank. *J Am Heart Assoc* 2020; 9: e014820.
59. Desai R, Patel K, Dave H, et al. Nationwide Frequency. Sequential trends, and impact of Co-morbid mental health disorders on hospitalizations, outcomes, and healthcare resource utilization in adult congenital heart disease. *Am J Cardiol* 2020; 125: 1256–1262.
60. Latal B, Helfricht S, Fischer JE, Bauersfeld U, Landolt MA. Psychological adjustment and quality of life in children and adolescents following open-heart surgery for congenital heart disease: a systematic review. *BMC Pediatr* 2009; 9: 6.
61. Moons P, Luyckx K, Thomet C, et al. Physical Functioning, Mental health, and quality of life in different congenital heart defects: comparative analysis in 3538 patients from 15 countries. *Can J Cardiol* 2021; 37: 215–223.
62. Rychik J, Atz AM, Celermajer DS, et al. Evaluation and management of the child and adult with fontan circulation: a scientific statement from the american heart association. *Circulation* 2019; 140: CIR0000000000000696.
63. Reynolds CR, Kamphaus RW. Behavior assessment system for children—Third Edition (BASC-3). Pearson, Bloomington, MN, 2015.
64. Ware J, Butcher JL, Latal B, et al. Neurodevelopmental evaluation strategies for children with congenital heart disease aged birth through 5 years: recommendations from the cardiac neurodevelopmental outcome collaborative. *Cardiol Young* 2020; 30: 1609–1622.
65. Ilardi D, Sanz JH, Cassidy AR, et al. Neurodevelopmental evaluation for school-age children with congenital heart disease: recommendations from the cardiac neurodevelopmental outcome collaborative. *Cardiol Young* 2020; 30: 1623–1636.
66. Harris E, Bowden J, Greiner E, DUBY JC. Mental health training in pediatric residency: where can we go? *J Pediatr* 2019; 211: 4–6.
67. McMillan JA, Land M Jr., Leslie LK. Pediatric residency education and the behavioral and mental health crisis: a call to action. *Pediatrics* 2017; 139: 1199.
68. Cassidy AR, Butler SC, Briend J, et al. Neurodevelopmental and psychosocial interventions for individuals with CHD: a research agenda and recommendations from the cardiac neurodevelopmental outcome collaborative. *Cardiol Young* 2021; 31: 1–12.
69. Tesson S, Butow PN, Sholler GF, Sharpe L, Kovacs AH, Kasparian NA. Psychological interventions for people affected by childhood-onset heart disease: a systematic review. *Health Psychol* 2019; 38: 151–161.
70. Moon JR, Huh J, Kang I-S, Park SW, June T-G, Lee HJ. Relationship between depression and resilience in adolescents with congenital heart disease. *Am Heart Assoc*, in, 2006.
71. Alsaied T, Allen KY, Anderson JB, et al. The fontan outcomes network: first steps towards building a lifespan registry for individuals with fontan circulation in the United States. *Cardiol Young* 2020; 30: 1070–1075.
72. Sood E, Jacobs JP, Marino BS. The cardiac neurodevelopmental outcome collaborative: a new community improving outcomes for individuals with congenital heart disease. *Cardiol Young* 2020; 30: 1595–1596.