Safety and efficacy of exercise training in children and adolescents with congenital heart disease: A systematic review and descriptive analysis

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Background While exercise training is beneficial in the prevention and management of many chronic diseases, the role of exercise training in children and adolescents with congenital heart disease is less understood. We sought to determine the safety and efficacy of exercise training in children and adolescents with congenital heart disease.

Methods We conducted a systematic search of the following databases: PubMed, CINAHL, EMBASE, Web of Science and SportDiscus. We included randomised controlled trials that incorporated an exercise intervention compared with a non-exercising comparator group and examined safety and efficacy in children and adolescents with congenital heart disease. A descriptive analysis of the included trials was then conducted.

Results A total of 9 articles from 6 trials (642 participants with varying conditions and disease severity) were included. Significant variability of study participants and outcomes were observed across the trials. No adverse events linked to the exercise interventions were stated. The articles reported numerous positive changes to clinically relevant fitness measures. Exercise capacity improved with exercise training in 3 of 4 trials in which it was measured. Cardiorespiratory fitness showed improvements in 3 of 4 trials. Neuromuscular fitness increased in 1 of 2 trials. Physiological and metabolic parameters were improved, and negative changes were not observed to several clinically important measures (e.g. muscular oxygenation, cardiac measures) in 2 of 2 trials. Physical activity increased in 1 of 3 trials. No articles reported on changes in measures of body composition. Outcomes are varied with little consensus on measurements or assessment methods.

Conclusions Exercise training appears to be safe and efficacious for improving physical fitness in children and adolescents with congenital heart disease who have been appropriately screened by their medical team. However, the certainty of the evidence for these findings is low to moderate. (Am Heart J 2022;253:1–19.)

Congenital heart disease (CHD) is one of the most commonly diagnosed congenital disorders, affecting approximately 0.8% to 1.8% of live births worldwide (1787.6 cases per 100,000 babies).[1-3] A CHD condition typically results in greater morbidity and mortality and lesser physical fitness and quality of life than in the general population.[4-7] However, recent advances in surgical and critical care, more thorough prenatal testing, and earlier interventions mean that even those with severe CHD can live well into adulthood; the percentage of people with CHD aged 15 years and over increased globally from 23% in 1990 to over 28% in 2017.[2,8,9]

Historical opinion was that children and adolescents with a CHD are likely to be less physically active than their peers,[10] though this has recently been called into question.[11] A recent systematic review identified that the percentage of adolescents with CHD who reach recommended physical activity levels (typically 60 minutes of moderate-to-vigorous physical activity per day) varies greatly between studies – ranging from 7% to 76%.[11] This suggests that CHD children often have activity

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levels comparable to, or higher than, their healthy peers (only 19% of whom reach the recommended levels[12]) and are typically not more sedentary.[11] Though CHD children and adolescents may not be less active than their peers, they are typically still vulnerable to a hypoactive lifestyle. This occurs despite current recommendations that every child with CHD should be encouraged to engage in sports and recreational physical activity during leisure time, including at school.[11] A sedentary lifestyle exposes CHD populations to an increased risk of developing chronic conditions such as type 2 diabetes, depression, anxiety, and obesity (though some of these relationships may be bidirectional, e.g. exercise and mental health).[12] This increased risk stems from inherent physiological limitations from the disease and any associated corrective techniques (such as a Fontan circulation), perceptions around safety of exercise training and low exercise related self-efficacy, and potential overprotective attitudes from parents and carers.[13,14] Children with CHD have traditionally been held back from doing the same physical activity as their peers due to unwarranted (though well-intentioned) anxiety from parents, educators, and healthcare providers that exercise would increase the risk of adverse events.[10,15,16] Further, children and adolescents with CHD will likely develop excessive self-protective mechanisms from exercise, experience physiological anxiety over engaging in exercise training, have difficulty "keeping up" with their healthy peers or participating in team sports, and may not develop the foundational movement skills required to engage in lifelong physical activity.[17,18]

Clinicians are often unable to combat these issues as they lack clarity on the appropriateness of exercise for managing symptoms and improving clinical outcomes in CHD populations.[19] A recent systematic review found that cardiac rehabilitation programmes in paediatric populations were greatly underutilised, and it has been frequently reported that optimal programme structure and efficacy is still unclear.[20-22] This is also reflective of the relative paucity of high-quality evidence to inform clinical care and generate guidelines on the optimal types or quantity of physical activity and exercise training in children and adolescents with CHD (though expert opinion-based recommendations do exist[23]), and recommendations have recently been made for adult CHD populations.[16,24,25]

Because of these internal and external restrictions around exercise, many children and adolescents with CHD may miss out on potential improvements to exercise capacity, neuromuscular fitness, cardiorespiratory fitness, body composition, and metabolic parameters. These measurable benefits have been well-researched in adults with CHD and associated with positive health outcomes. Whilst there are also several published systematic reviews and meta-analyses (including a recent Cochrane review) on the effects of exercise in adolescents and adults with CHD, these have been specific to only a few categories of fitness, physical activity behaviors, or quality of life, and have included articles with a wide range of study designs.[6,20-22,26-29] Further, whilst the risks of adverse events are well-detailed in adult CHD populations,[29,30] no review has documented the risks associated with exercise training in paediatric CHD. Thus, the present study aimed to systematically review randomised controlled trials (RCTs) and summarise the safety and efficacy of exercise training for children and adolescents with CHD. Efficacy was determined using a physical fitness model that separates exercise capacity from cardiorespiratory fitness (CRF).[31] In agreement with contemporary exercise science teaching, exercise capacity is usually measured as time-on-test (treadmill) or peak power output (cycle ergometer), whereas CRF is a physiological measure representing maximal or peak oxygen consumption.[32] Importantly, the physiological factors that influence the 2 are different, albeit related. CRF is primarily dependent on stroke volume/cardiac output and to a lesser extent oxygen transport and then uptake at the working muscles. Whereas exercise capacity is also dependent on movement efficiency at sub-maximal workloads and the psychological motivation to continue exercising when approaching volitional fatigue. Historically, CRF and exercise capacity have often been used interchangeably, however the 2 measures have been shown to be independently affected by an exercise intervention.[33] Whilst prognostically oxygen consumption values from a cardiopulmonary exercise test (CPET) reflect disease status in CHD very well,[34] exercise capacity in certain individuals (e.g. limited capacity to improve maximal cardiac output) may be a better indicator of the effectiveness of an exercise intervention. The improvement in exercise capacity could be due to increased efficiency at sub-maximal workloads that does not require an increase in maximal cardiac output.

Methods

Protocol and registration

This systematic review was registered with the International Prospective Register of Systematic Reviews (Registration no. CRD42021225061, https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=225061) and undertaken according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. Article screening and data extraction was completed using Covidence (Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org)

Eligibility criteria

Articles were selected if they met the following criteria: randomised controlled trial with a control group receiving no outcome-affecting intervention, included

children and adolescents predominantly (over 50% total sample size) under the age of 18 with CHD, excluded participants with other diseases (e.g. Down's Syndrome), utilised any kind of exercise intervention (such as face to face coached sessions, telehealth sessions, home exercise prescription, or physical activity education and promotion), described outcome measures related to the fitness domains of exercise capacity (test duration and peak power output during cardiopulmonary exercise testing), CRF (oxygen uptake data during the test), neuromuscular fitness, physiological and metabolic parameters, body composition, and/or physical activity behaviors. The search was run from earliest record on each database until April 15, 2021. There was no restriction for language. The search was re-run on February 25, 2022.

Information sources and search terms

The following electronic databases were used to identify potential articles: PubMed, CINAHL, EMBASE, Web of Science, SportDiscus. Reference lists of included papers were hand searched for additional articles.

Search strategies for each database comprised of 3 topics: children or adolescents, physical activity or exercise, and congenital heart disease. These search strings were adapted for each database, with key words searched as full text and Medical Subject Headings. Additional filters were applied where possible for RCTs.

Study selection and data extraction

Results of the searches were exported to a web-based systematic review screening system (Covidence) for removal of duplicates, screening, quality assessment and data extraction. Titles and abstracts were screened by 1 author (C.A.), and full-text versions were screened and agreed upon by 2 authors (C.A. and J.S.). Data extraction included information on study design, participant characteristics, dropouts, inclusion criteria, exclusion criteria, outcome measures, intervention (including setting, type of exercises, duration, frequency, intensity, monitoring, compliance, and length of follow-up), excluded results, and control group monitoring. If relevant data were not included in the publication, efforts were made to contact the authors of the work seeking these details.

Risk of bias in individual studies

In exercise training intervention studies, some traditional study quality criteria (such as blinding of the participant and the researcher to the intervention) are difficult to implement. We therefore used a methodological quality assessment tool designed specifically for use in exercise training studies; Tool for the assEssment of Study qualiTy and reporting in EXercise (TESTEX).[35] This includes a checklist of 12 items for 15 points. Five of the 15 possible points are related to study quality and 10 to study reporting. One point is awarded for the following study quality criteria: eligibility criteria, randomization, allocation concealment, groups similar at baseline, and blinding of assessor for at least 1 key outcome. For study reporting, the remaining 10 points are distributed between 6 items. Points are awarded if adherence was >85%; adverse effects were reported; exercise attendance was reported; intention to-treat analysis was performed; between-group statistical comparisons were reported for the primary outcome measure and for the secondary outcome measure; point estimates were reported; there was activity monitoring in control groups; exercise load was adjusted to keep relative intensity constant; and exercise volume and energy expenditure could be calculated. Higher scores reflect better study quality and reporting.

Two researchers (C.A. and J.S.) independently evaluated the methodological quality of the included articles. Where there were disagreements, discussion occurred with a third author until a consensus was drawn.

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Results

Study selection and characteristics

Details of the search and screening process are shown in the PRISMA flow diagram (Figure 1). The initial search retrieved 3679 articles. The later search retrieved 162 articles. Of these, 9 articles from 6 trials met the inclusion criteria and were included in this narrative review. Three articles were from 1 trial,[36-38] and 2 were from another trial.[39,40] All 6 trials were undertaken in European countries, with 2 in Ireland, 1 in France, 1 in Germany, 1 in Denmark, and 1 in the Netherlands.

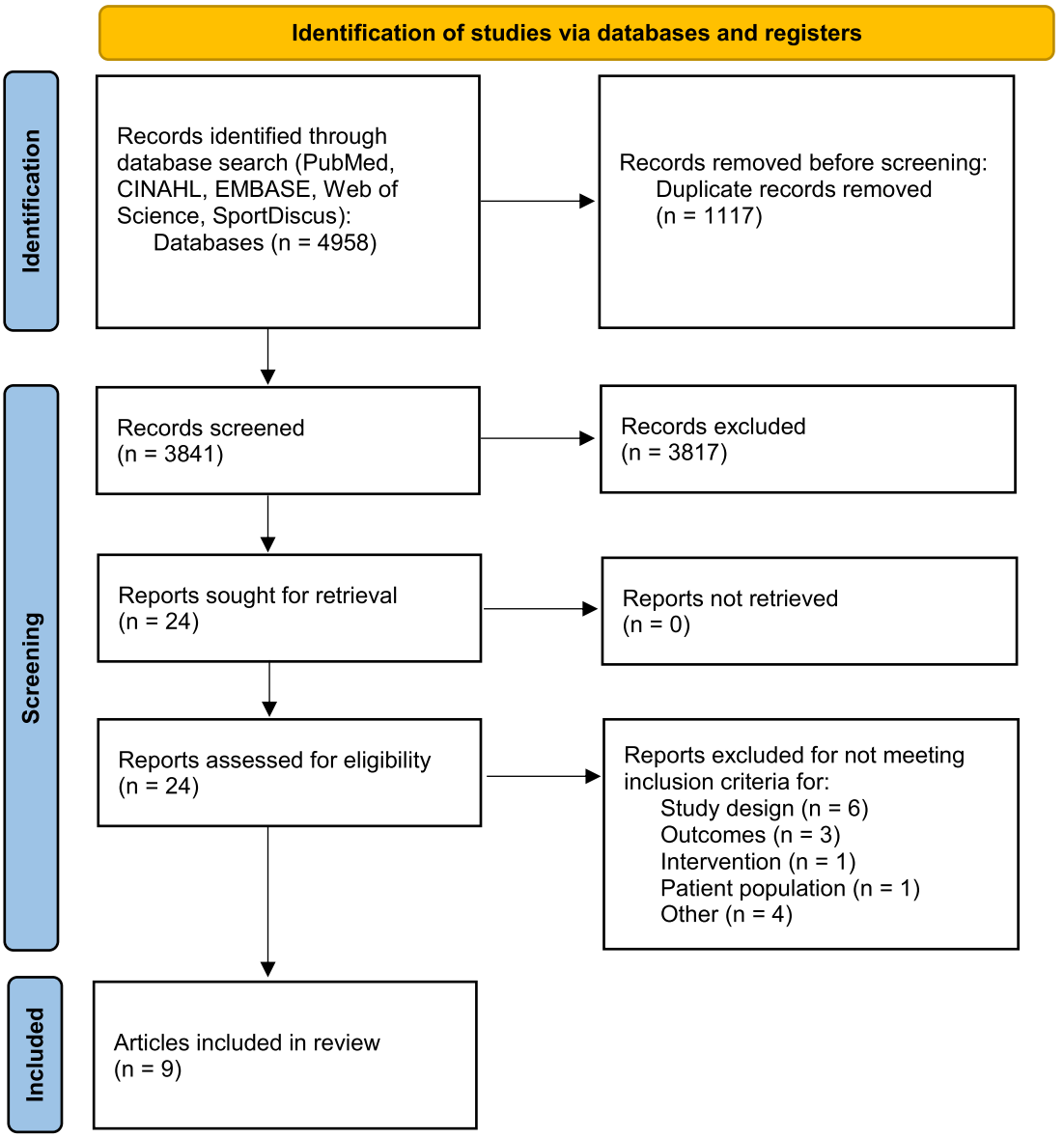
Description of participants

A total of 642 unique participants were reported across all trials. The age of participants ranged from 10 to 25, with the average age being 13.7 ± 2.1 years. Only 15 participants from 1 trial were over the age of 18.[36-38] There were 380 males, 244 females and 18 unreported. One article included participants only with corrected Tetralogy of Fallot (ToF),[37] and 2 articles included participants only with either corrected ToF or a Fontan circulation,[36,38] The remaining 6 articles included participants with a range of congenital heart defects and did not restrict participant inclusion based upon correction type. Of the 642 participants, 333 received an exercise intervention (52%). The diagnosis or severity of the conditions within the participants can be seen in Table I.

Description of interventions

Details of each included trial can be found in Table II. Two trials included three 1-hourly exercise training

Figure 1



PRISMA flow chart. *PRISMA*, preferred reporting items for systematic reviews and meta-analyses.

sessions per week for 12 weeks.[36-40] Neither trial reported methods for progressive overload of their exercise intervention intensity during the program. One trial had their intervention completed by participants at home,[39,40] and the other was supervised by physiotherapists.[36-38] Two trials used a web-based exercise intervention, motivating participants to increase their exercise levels each day for several months.[41,42] Two trials involved attendance to an "activity" or "education" day which applied models of behavior change individually and in small group sessions, followed by exercise education and the provision of a written exercise training program to implement at home.[43,44] Five trials instructed their control participants to go about their daily routine as usual or allowed them to receive their usual standard of care, and 1 trial had their control group receive the same 45-minute group education and 15-minute individual counselling session that the intervention group

Table I. Conditions, and severity of conditions in all patients

Condition	Total ($n = 336$)	Intervention ($n = 179$)	Control ($n = 157$)
Tetralogy of fallot	73	38	35
Coarctation of the aorta	52	31	21
Transposition of the great arteries	48	26	22
Fontan circulation	43	26	17
"Right Heart Obstruction"	23	10	13
Total cavopulmonary connection	22	13	9
Atrioventricular septal defect	9	5	4
"Left Heart Obstruction"	9	1	8
Double-outlet right ventricle	7	4	3
Atrial septal defect	4	3	1
Pulmonary atresia	4	1	3
Truncus arteriosus	4	3	1
Isolated shunt	4	2	2
"Miscellaneous/Other"	34	16	18
Severity	**Total ($n = 306$)**	**Intervention ($n = 144$)**	**Control ($n = 152$)**
Minor/Acyanotic with no intervention (e.g. secundum atrial septal defect, aortic stenosis, pulmonary stenosis)	69	36	33
Acyanotic corrected (e.g. primum atrial septal defect, patent ductus arteriosus, atrioventricular septal defect)	122	57	65
Cyanotic corrected (e.g. transposition of the great arteries, truncus arteriosus, tetralogy of fallot)	75	35	40
Cyanotic palliated (e,g, hypoplastic left heart syndrome, triscuspid atresia, right ventricular hypoplasia)	40	26	14

Note: some trials reported their participants by condition and some by severity.

received, followed by no further outcome-affecting intervention.[42] No study carried out a follow-up assessment after the end of trial to assess sustainability of the intervention.

Risk of bias and quality assessment within articles

Results of the assessment of quality for the RCTs using the 15-point tool are in Supplementary Table I. The lowest score was 7,[39,40,43] and the highest was 10.[41,44] All articles were assessed as average quality with the median score 9.0.

All articles reported eligibility criteria for participants. Four out of the 9 articles reported the method of randomisation for the intervention and control groups.[41-44] One article did not specify that it was randomized,[39] but a later publication specified that the trial was randomized.[40] Only 1 article did not describe whether the group allocation was concealed from participants (e.g. consent was given before randomization).[37] In terms of participant allocation and similarity of the groups at baseline, only 2 articles failed to meet the criteria for 1 point.[42,43] Only 2 articles addressed the blinding of outcome assessors.[36,42] No articles scored the full 3 points for participant adherence over 85% and reporting of adverse events and reporting of exercise attendance, though 5 articles did report two of these criteria and were given 2 out of 3 points.[36-38,41,44] All the articles scored the full 2 points for between-groups statistical analysis. Three articles did not report statistical comparisons and point measures of variability for all outcomes.[36,39,40] Four articles used intention-to-treat analysis.[41-44] No articles scored points for activity monitoring in control groups, or for keeping relative exercise intensity constant throughout the intervention. Five articles provided sufficient detail of the intervention (including session and programme duration, session frequency, exercise training intensity and modality) to calculate exercise volume or energy expenditure.[36-40]

One TESTEX criteria requires articles to present the percentage of participants completing the study in both groups, any adverse events or lack thereof, and indicate if the training adherence was greater than 85%. Three articles reported the training adherence to be greater than 85%, but they specify that this was assessed by reviewing a random sample of recorded heart rates during exercise training (22% of the exercise group, $n = 11$), in addition to monitoring during the sessions by a local physiotherapist.[36,37]

Outcomes

Meta-analyses were not possible given the small number of trials and large variability in data and methodology;

Table II. Randomised controlled trials investigating the effects of exercise training in children and adolescents with congenital heart disease.

Study	Participants	Intervention and control groups	Dropouts (% of all participants)	Intervention	Control	Adverse events
Duppen Trial (Predominantly aerobic exercise)						
Duppen et al[36], Duppen et al[37], Duppen et al[38], Netherlands	Average age 15.5 ± 3.1 Total *n* = 90 Male *n* = 66 Female *n* = 34 ToF *n* = 47 Fontan *n* = 43	Exercise (*n* = 54) Control (*n* = 37)	Exercise group (Fontan) *n* = 1 (1%)	3 training sessions completed under supervision of a physiotherapist per week for 12 wks. Protocol was 10 mins of warmup, followed by 40 mins of aerobic dynamic cardiovascular training (e.g. cycling), ending with 10 mins cooldown. Intensity was set at resting HR plus 60% to 70% of HR reserve calculated during CPET.	Instructed to go about daily routine as usual.	One participant experienced a collapse whilst walking on the street, unrelated to the study protocol.
Moalla Trial (Predominantly aerobic exercise)						
Moalla et al[39], Moalla et al[40], France	Average age 12.9 ± 1.35 Total *n* = 18 Male *n* = NS Female *n* = NS ToF *n* = 5 TGA *n* = 5 ASD *n* = 4 PA *n* = 4	Training (*n* = 10) Control (*n* = 8)	NS	3 training sessions of home-based aerobic training per week for 12 wks. Protocol was 10 mins warmup, followed by 45 mins of alternating 10 mins work and 5 mins activity recovery on an ergocycle, ending with 5 mins unloaded cycling to cool down. Intensity was set at HR corresponding to VT calculated during CPET.	NS	NS
Single articles (predominantly exercise promotion/behavior change)						
Klausen et al[42], Denmark	Average age 14.6 ± 1.3 Total *n* = 158 Male *n* = 92 Female *n* = 66 Coarc *n* = 52 TGA *n* = 35 ToF *n* = 21 DORV *n* = 7 Truncus Arteriosus *n* = 4 AVSD *n* = 9 TCPC *n* = 6	eHealth (*n* = 81) Control (*n* = 77)	eHealth *n* = 35 (43%) Control *n* = 16 (21%)	One session consisting of 45-mins of group health education and 15 mins of individual counselling. Followed up by a 52-wk internet, mobile application, and SMS-based program delivering individually tailored text messages to encourage exercise. Participants recorded exercise duration and type in a mobile application that translated intensity into virtual points, with a goal to achieve bronze, silver, or gold level of points on a weekly basis.	One session consisting of 45-mins of group education and 15 mins of individual counselling.	NS

(*continued on next page*)

Table II. (*continued*)

Study	Participants	Intervention and control groups	Dropouts (% of all participants)	Intervention	Control	Adverse events
Meyer et al[41], Germany	Average age 13.1 ± 2.6 Total *n* = 70 Male *n* = 46 Female *n* = 24 Left heart obstruction *n* = 9 Right heart obstruction *n* = 23 Isolated shunt *n* = 4 TGA after arterial switch *n* = 8 TCPC *n* = 16 Miscellaneous *n* = 10	E-Health (*n* = 35) Control (*n* = 35)	E-Health dropout *n* = 4 (6%) Control dropout *n* = 5 (7%)	Web-based intervention for 24 wks targeting 3 x 20 min home exercise sessions per week. The web app included child-friendly instructions and demonstration of different exercises. Exercise was performed simultaneously while watching the video demonstrations.	Instructed to go about daily routine as usual.	None
Morrison et al.[43], Ireland	Average age 15.6 ± 2.27 Total *n* = 143 Male *n* = 86 Female *n* = 57 Minor CHD (no intervention) *n* = 39 Acyanotic corrected *n* = 61 Cyanotic corrected *n* = 30 Cyanotic palliated *n* = 13	Education and exercise prescription (*n* = 72) Control (*n* = 71)	Education and exercise prescription dropout *n* = 10 (3%) Control dropout *n* = 23 (22%)	One activity day involving a motivational interview-style group session. Then provided a written home exercise training plan. Followed-up with a letter summarising the discussion from the activity day. Each participant contacted once a month to check on progress with exercise plan for the subsequent 6 mo.	Received usual level of care.	None
Callaghan et al[44], Ireland	Average age 8.45 ± 1.53 Total *n* = 163 Male *n* = 98 Female *n* = 65 Acyanotic no intervention *n* = 30 Acyanotic corrected *n* = 61 Cyanotic corrected *n* = 45 Cyanotic palliated *n* = 27	Education and exercise prescription (*n* = 82) Control (*n* = 81)	Education and exercise prescription *n* = 9 (6%) Control dropout *n* = 2 (1%)	One education day involving a motivational group session, a family meeting with a doctor to discuss increasing participation in exercise, and prescription of a home-exercise plan to be carried out over the subsequent 4 mo. Then provided an information pack included a letter of encouragement containing materials from the education day. The summarised exercise plan was also provided to primary school teacher to guide participation in activities during school hours.	Received usual level of care.	None

ASD, atrial septal defect; *AVSD*, atrioventricular septal defect; *Coarc*, coarctation of the aorta; *CPET*, cardiopulmonary exercise test; *DORV*, double-outlet right ventricle; *HR*, heart rate; *NS*, not stated; *PA*, pulmonary atresia; *TCPC*, total cavopulmonary connection; *TGA*, transposition of the great arteries; *ToF*, tetralogy of fallot; *VT*, ventilatory threshold.

Table III. Reported outcomes.

Study	Domains of fitness and physical activity behavior					
	Exercise capacity	Cardiorespiratory fitness	Neuromuscular fitness	Physiological & metabolic parameters	Body composition	Physical activity
Moalla et al[39]	√	√		√		
Moalla et al[40]			√	√		
Duppen et al[36]	√	√		√		√
Duppen et al[37]				√		
Duppen et al[38]				√		
Klausen et al[42]		√				
Meyer et al[41]			√			
Morrison et al[43]	√	√				√
Callaghan et al[44]	√					√

√: Article reports on measures within this category.

therefore, the results are described narratively. The outcomes from the 6 trials included in this review are shown in Tables III and IV separated into domains of fitness and physical activity levels. Exercise capacity and CRF are presented as 2 discrete outcomes as they fundamentally represent different physiological measures.[45] Little consensus on clinically relevant outcome measures and assessment methods was observed. Only 1 trial presented data from individual CHD presentations across all outcomes[36-38]; all others presented their data across CHD presentations without stratification. Where possible data for individual conditions are presented.

Exercise Capacity: 4 trials reported measures of exercise capacity from a CPET. Three reported significant changes: 2 trials reported significant between-group increases in maximum power,[36,44] and 2 trials reported significant between and within-group changes for test duration.[43,44] In 1 trial peak workload during a cycle CPET was reported to not change significantly in the Fontan group compared to the ToF group.[36]

Cardiorespiratory Fitness: 4 trials reported measures of cardiorespiratory fitness.[36,39,42,43] Only 1 found a significant between-group improvement in VO_2peak,[43] and 2 reported within-group improvements.[36,43] One trial reported significant improvements between-group and within-group in VO_2, VCO2, and PeakV_E when expressed as a percentage of peak exercise values at the first VT (first threshold assumed as is not specified in the article; the authors specify this was identified as the breakpoint of the linearity of the curve VO_2 versus VCO2).[39] One trial reported a significant change in oxygen uptake efficiency slope (OUES) and VO_2 at VT in the Fontan group, and a significant change in peak V_E in the ToF group.[36]

Neuromuscular Fitness: 2 trials reported measures of neuromuscular fitness,[40, 41] with one finding a significant between-group improvement in maximal voluntary contraction (MVC) of vastus lateralis and increased strength endurance at 50% MVC.[40]

Physiological and Metabolic Parameters: 2 trials reported measures of physiological and metabolic parameters.[36-40] One trial noted significant between-group improvements in muscle oxygenation values during isokinetic strength testing and CPET.[39,40] They also found a significant correlation at the VT between changes in respiratory muscle oxygenation and VO_2,[39] and significant relationships between changes in muscle oxygenation and maximal voluntary contraction ($r = 0.95$) and muscular endurance at 50% MVC ($r = 0.9$).[40] The other trial reported significant within-group improvements to peak oxygen pulse in the training group,[36] and a statistically significant between-group decrease in mitral valve peak velocity and increase in tricuspid valve peak E/A ratio within the control group.[38] One trial reported a significant change in mitral valve peak A and tricuspid valve peak E/A ratio in the ToF group.[38]

Body Composition: No articles reported on changes to measures of body composition.

Physical Activity: 3 trials reported on physical activity levels using daily moderate-to-vigorous physical activity collected using accelerometers,[36,43,44] with only 1 noting a significant between-group increase in the intervention group.[43]

Reported adverse events

Of the 6 trials, 4 reported on the incidence of adverse events.[38,41,43,44] Of the trials that did document adverse events, the only incident was a Fontan participant who experienced a collapse whilst walking on the street 1 month after starting the training program.[38] The authors reported: 'Further investigation did not clarify the reason for collapsing'. No other events were reported from the 305 participants who were randomised to exercise in the trials that reported adverse events.[38,41,43,44]

Discussion

The aim of this systematic review was to investigate the safety and efficacy of exercise interventions on physical fitness and physical activity in children and adolescents

Table IV. Summary of findings for exercise interventions in children and adolescents with congenital heart disease.

Study	Test	Outcome	Intervention group			Control group			
			n	Absolute change	% change	*n*	Absolute change	% change	*P* (between group difference)
Exercise Capacity									
Duppen et al[36]	Ergocycle CPET	Peak workload in all (W)	53	6.9 ± 3.5	3.9%†	37	1.0 ± 1.0	0.7%	*.047*
		Peak workload in ToF (W)	24	8.4 ± 3.0	5.2%	19	-0.1 ± 1.0	0.0%	*.048*
		Peak workload in Fontan (W)	19	5.0 ± 4.0	3.9%	11	3 ± 3	2.7%	NS
Morrison et al[43]	Treadmill CPET	Duration of CPET (seconds)	72	66 ± 36*	9.6%	71	-5 ± 12	0.7%	*<.05*
		METs from duration of CPET	72	2.7 ± 1.3	19.0%	71	-0.3 ± 0.4	2.1%	.1
Callaghan et al[44]	Ergocycle CPET	Duration of CPET (seconds)	82	42 ± 0.17*	11%†	81	0 ± 54	0.0%	*<.001*
		Peak workload (W)	82	5.78 ± 4.14*	8.1%	81	-0.19 ± 0.87	0.3%	*<.001*
Moalla et al[39]	Ergocycle CPET	Peak workload (W)	10	8.0 ± 4.0	7.3%†	8	2.0 ± 1.0	1.9%	NS
Cardiorespiratory fitness									
Moalla et al[39]	Ergocycle CPET	VO_2peak (mL/kg/min)	10	2.50 ± 0.50	7.9%	8	-0.30 ± 0.40	1.0%	NS
		VO_2 at VT (mL/kg/min)	10	4.80 ± 0.50*	22.6%	8	-0.50 ± 0.20	2.7%	*<.05*
		Peak VCO_2 (L/min)	10	0.12 ±0.06	6.6%	8	0.00 ± 0.03	0.0%	NS
		VCO_2 at VT (L/min)	10	0.24 ± 0.60*	24.2%	8	0.01 ± 0.02	1.2%	*<.05*
		PeakV_E (L/min)	10	7.60 ± 3.70	10.8%	8	-1.20 ± 0.80	1.8%	NS
		V_E at VT (L/min)	10	8.10 ± 1.90*	25.5%	8	-0.50 ± 0.30	1.8%	*<.05*
Duppen et al[36]	Ergocycle CPET	VO_2peak in all (mL/kg/min)	43	1.7 ± 1.0*	4.9%	30	0.9 ± 0.8	2.7%	.14
		Peak V_E in all (L/min)	43	7.7 ± 8.3	10.3%	30	-0.5 ± 2.1	0.7%	*.014*
		VO_2 at VT in all (mL/kg/min)	46	-1.3 ± 2.0	6.0%	31	0.0 ± 0.2	0.0%	NS
		V_E/V_{Co2} slope in all	46	0.7 ± 1.3	2.4%	31	-0.3 ± 0.1	1.0%	NS
		OUES in all	46	-16.0 ± 1.0	0.7%	31	126.0 ± 73.0	6.0%	NS
		VO_2peak $_k$ (mL/kg/min) in ToF	24	2.9 ± 0.9*	7.9%†	19	0.7 ± 0.3	2.0%	NS
		Peak V_E (L/min) in ToF	24	10.1 ± 9.2	12.4%	19	-1.9 ± 2.6	2.5%	*.008*
		VO_2 at VT (mL/kg/min) in ToF	24	1.6 ± 0.7	7.4%	19	-0.4 ± 0.1	2.0%	NS
		V_E/V_{Co2} slope in in ToF	24	1.2 ± 1.0	4.4%	19	0.1 ± 0.8	0.4%	NS
		OUES in ToF	24	82.0 ± 57.0	3.3%	19	109.0 ± 72.0	4.6%	NS
		VO_2peak (mL/kg/min) in Fontan	19	0.3 ± 0.6	0.9%	11	1.2 ± 3.8	3.8%	NS
		Peak V_E (L/min) in Fontan	19	4.7 ± 2.1	7.1%	11	2.0 ± 3.8	3.2%	NS
		VO_2 at VT (mL/kg/min) in Fontan	22	-4.5 ± 3.8	20.9%	12	0.7 ± 0.6	3.3%	*.038*
		V_E/V_{Co2} slope in Fontan	22	0.1 ± 2.2	0.3%	12	-1.8 ± 0.3	2.3%	NS
		OUES in Fontan	22	-123.0 ± 67.0	6.6%	12	153.0 ± 138.0	14.1%	*.009*
Klausen et al[42]	Ergocycle CPET	VO_2peak (mL/kg/min)	81	-0.5 ± 0.1	1.2%	77	2.9 ± 0.8	6.5%	.52

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Table IV. (*continued*)

Study	Test	Outcome	Intervention group			Control group			
			n	Absolute change	% change	*n*	Absolute change	% change	*P* (between group difference)
Morrison et al.[43]	Treadmill CPET	Predicted VO_2max (mL/kg/min)	72	2.4 ± 1.4*	6.6%	71	-0.3 ± 0.0	0.8	.02
Neuromuscular fitness									
Moalla et al.[40]	Isokinetic dynamometer, hip and knee at 90°	Knee extensor MVC (N.m)	10	18.6 ± 5.4*	16.8%	8	2.0 ± 0.8‡	1.9%	<.001
		Knee extensor T_{lim} (s)	10	19.8 ± 0.4*	26.0%	8	2.4 ± 0.3‡	3.5%	<.001
Meyer et al[41]	5 Task FITNESSGRAM: curl-ups, trunk-lifts, push-ups, shoulder stretch, sit-and-reach test	HRPF (total z score)§	31	0.15 ± 0.38	24.6%	30	0.09 ± 0.38	11.3%	.560
Physiological & metabolic parameters									
Moalla et al[40]	NIRS of Vastus Lateralis	$T_{1/2R}$ (s)	10	-6.40 ± 1.9*	26.7%	8	0.90 ± 0.2	3.1%	<.001
		R_s (s)	10	-12.8 ± 7.0*	22.6%	8	-1.8 ± 2.0	2.8%	<.001
		D_{mO2} (a.u.)	10	-0.05 ± 0.06*	28.6%	8	0.01 ± 002	4.9%	<.001
		Mean rate of decrease in MO_2 (%.s)	10	0.49 ± 0.33*	33.5%	8	-0.03 ± 0.22	2.5%	<.001
Moalla et al[39]	NIRS of serratus anterior (sixth intercostal space)	R_{mO2} at end of CPET (%)	10	11.48 ± 4.12*	11.5%	8	1.37 ± 1.37	1.4%	<.01
		R_{mO2} at VT (%)	10	12.1 ± 0.3*	12.1%	8	2.05 ± 0.41	2.05%	<.01
		FEV_1 (L)	10	0.20 ± 0.20	7.2%	8	-0.10 ± 0.2	3.6%	NS
		% predicted FEV_1 (%)	10	3.40 ± 6.50	4.1%	8	-0.30 ± 1.90	0.4%	NS
	Spirometer	FVC (L)	10	0.20 ± 0.10	6.1%	8	0.00 ± 0.10	0.0%	NS
		% predicted FVC (%)	10	2.40 ± 1.80	2.5%	8	0.20 ± 3.90	0.2%	NS
		TLC (L)	10	0.20 ± 0.90	4.2%	8	0.00 ± 0.10	0.0%	NS
		% predicted TLC (%)	10	2.40 ± 1.20	2.5%	8	-0.60 ± 1.00	0.6%	NS
		FEV_1/FVC ratio		0.01 ± 0.06	1.1%		0.00 ± 0.02	0.0%	NS
		MVV (L/min)		6.30 ± 10.50	5.6%		-0.70 ± 3.10	0.6%	NS

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Table IV. (*continued*)

Study	Test	Outcome	Intervention group			Control group			
			n	Absolute change	% change	*n*	Absolute change	% change	*P* (between group difference)
Duppen et al[36]	Ergocycle CPET	Peak oxygen pulse (mL/beat) in all	43	1.0 ± 0.7*	8.8%	24	0.6 ± 0.0	5.6%	NS
		Peak oxygen pulse (mL/beat) in ToF	24	1.3 ± 0.6*	10.2%	19	0.5 ± 0.1	4.3%	NS
		Peak oxygen Pulse (mL/beat) in Fontan (mL/beat)	19	0.2 ± 0.1	2.1%	11	0.7 ± 0.7	7.8%	NS
Duppen et al[37]	Tissue-Doppler imaging	TDI Echocardiography in ToF	27			20			NS
	Magnetic resonance imaging	MRI in ToF	27			20			NS
Duppen et al[38]	Transthoracic echocardiography	Mitral valve peak A in ToF	27	0.04 (-0.02,	8.0%	20	-0.10 (-0.18,	18.9%	*.013*
		Tricuspid valve peak E/A ratio in ToF	27	0.10)	4.9%	20	-0.02)*	15.8%	*.020*
	Magnetic resonance imaging	Echocardiography§ in ToF	27	-0.08 (0.29,			0.33 (0.09,		
		MRI§ in ToF	27	0.13)		20	0.57)*		NS
	Blood samples	Neurohormonal§ in ToF	27			20			NS
		Echocardiography§ in Fontan	20			20			NS
		MRI§ in Fontan	20			15			NS
		Fontan neurohormonal§ in Fontan	20						
						15			NS
						15			NS
Physical activity									
Duppen et al[36]	Triaxial accelerometer	METs	28	0.0 ± 0.0	0.0%	18	0.0 ± 0.0	0.0%	NS
		Time spent sedentary (%)	28	2.0 ± 1.3	2.9%	18	0.0 ± 0.4	0.0%	NS
		MVPA (% of total measured time)	28	-2.1 ± 1.4	15.3%	18	0.0 ± 0.4	0.0%	NS
Morrison et al[43]	Dual-axis accelerometer	Average daily MVPA (minutes)	72	28.8 ± 12.1*	67.3%	71	-3.5 ± 1.4	11.3%	*<.001*
Callaghan et al[44]	Triaxial accelerometer	Average daily MVPA (minutes)	82	7.12 ± 2.36	15.5%	81	2.72 ± 1.02	5.8%	.314
		Average daily step count	82	1059.9 ± 392.0	11.3%	81	448.6 ± 433.2	4.9%	.23

Data presented as Mean ± Standard Deviation or Mean (95% Confidence Interval).

CPET, cardiopulmonary exercise test; D_{mO2}, fall in muscle oxygenation; FEV_1, forced expiratory volume in 1 second; *FVC*, forced vital capacity; *HRPF*, health-related physical fitness; *METs*, metabolic equivalents; *MRI*, magnetic resonance imaging; *MVC*, maximal voluntary contraction; *MVPA*, moderate-to-vigorous physical activity; *MVV*, maximum voluntary ventilation; *NS*, not significant; *OUES*, oxygen uptake efficiency slope; $Peak_{O2}Pulse$, Peak VO_2 divided by peak heart rate during exercise; *PeakVE*, peak minute ventilation; *% pred*, percentage of predicted values; R_{mO2}, oxygenation of respiratory muscles; R_S, recovery speed to maximal oxygenation; *TDI*, tissue-doppler imaging; *TLC*, total lung capacity; T_{lim}, time to exhaustion; *ToF*, tetralogy of fallot; $T_{1/2R}$, half time of recovery; VE/V_{Co2} *Slope*, minute ventilation to carbon dioxide production slope measured from start of exercise up until the respiratory compensation point; *VT*, ventilatory threshold; *W*, watts.

* within group analysis $P < .05$.

† Percentage change calculated by original author.

‡ Values measured using ruler from a bar graph.

§ multiple other non-significant results not reported.

Italicised significant between group differences.

with CHD. Nine articles from 6 RCTs were included. Data from these studies found positive effects of exercise on indicators of fitness and physical activity behaviors in children and adolescents with CHD. Although univentricular corrections and biventricular presentations may have fundamentally different responses to exercise, stratification of these subgroups for this narrative review was not possible due to data being mixed across studies. Meta-analyses were not possible given the small number of trials and heterogeneity in data and methodology. An improvement in exercise capacity (time-on-test and peak power output) was the most consistent finding, with 3 from 4 trials reporting a between-group difference. Cardiorespiratory fitness (peak oxygen uptake) was only found to have a between-group improvement in 1 from 4 trials and neuromuscular fitness (strength endurance) in 1 from 2 trials. Physiological and metabolic parameters were improved, and negative changes were not observed in 2 from 2 trials. Physical activity levels improved in 1 from 3 trials. There was only 1 adverse event reported across the studies, although it was unclear if it was related to exercise. Overall, certainty of evidence is low to moderate due to low sample sizes, increased potential for outcome reporting bias, and inconsistency in effects.

Attendance & adherence

Attendance and adherence rates must be considered as there were significantly higher drop-out rates and lower attendance and adherence rates in the exercise promotion interventions than the supervised exercise training programs. Attendance (presence during a session) and adherence (to specific exercise prescription during a session) are separated to reflect current practice.[46] The total participant dropout from supervised exercise training interventions was less than 1%,[36-40] whereas the total dropout from exercise promotion interventions was 19%.[41-44] Only 1 trial reported an adherence of greater than 85%.[36-38] Importantly, this reported adherence value may change across the literature depending on the criteria established within any given trial (e.g. an arbitrary analysis of 30% of the participants' heart rates during any intervention period). Further, behavior change programs are commonly reported to have low levels of adherence and high levels of attrition, though this may be due to improper methods of measuring adherence (or engagement) resulting in an inaccurate representation of the programs efficacy.[47] In our review, the greater attrition and lower adherence to exercise promotion interventions may be due to the larger sample sizes and longer durations of these interventions and not necessarily reflective of a less efficacious intervention. Nevertheless, the evidence included in this review highlights that both exercise training and physical activity promotion are beneficial for improving important clinical measures. Though to our knowledge there are no trials combining physical activity promotion with exercise interventions for children and adolescents with CHD. They would likely provide an efficacious and well adhered-to program given the evidence presented here and the recommendations made in other literature.[16,21,48,49]

Determinants of exercise capacity & cardiorespiratory fitness

The improvement in exercise capacity is similar to that found in other exercise-based interventions in cardiac populations.[50-54] It is noteworthy that both traditional aerobic exercise interventions and exercise promotion interventions achieved this result, suggesting that behavior change techniques may improve this measure as much as typical exercise regimes. The finding that exercise capacity was more responsive to exercise training than cardiorespiratory fitness in children with CHD is an important observation, and one that has been observed in other studies. A number of small exercise trials in CHD patients have reported significant changes to either exercise capacity (peak workload or endurance time) or cardiorespiratory fitness (peak VO_2),[53-55] or modest improvements in both.[56] Though, some trials will report only CRF measures and not exercise capacity outcomes, presenting only the peak VO_2 values (likely due to the prognostic significance of this measure). Exercise capacity is defined as the ability to complete a physical task (e.g. graded exercise test to voluntary exhaustion), which depends on a number of factors including CRF, movement efficiency and motivation.[31,45] A number of studies in clinical populations including people with kidney disease and diabetes, have shown that exercise capacity is more sensitive than CRF when assessing the efficacy of exercise training.[33,55,56] This likely reflects a diminished reserve in stroke volume/cardiac output in people with these chronic conditions and therefore a decreased ability to increase maximal oxygen uptake. Whereas other factors that contribute to exercise capacity such as movement efficiency at sub-maximal workloads and strength are more responsive to training. This may explain why there was a lack of improvement in VO_2peak within the included trials compared to exercise capacity.[36,39,42,43] The finding that exercise capacity may be a more sensitive measure of exercise-training induced physiological adaptations should not dissuade the use of CPET in this population, especially given the prognostic strength of the measures derived from the test.

Further, due to the inherent difficulties of conducting maximal exercise tests with children, improvements in exercise capacity may not be apparent due to low participant willingness or motivation; studies should attempt to verify achievement of a maximal exercise test based on attainment of a maximal heart rate (within 10 beats per minute).

Whilst other reviews have reported improvements to peak oxygen uptake after exercise training in children

and adolescents with CHD, these results are mostly from cohort studies or a studies with a control group, not high-quality RCTs.[16,26] Additionally, the presentation of submaximal CPET measures is valuable, as parameters such as VT, VE/VCO2 slope, work efficiency (VO_2/work rate) slope, and OUES can be useful measures for tests in severely debilitated or unmotivated patients who may not be able to provide a peak/maximal effort.[16,57] Further, higher levels of submaximal outcomes (such as VT) have been associated with a reduced risk of major adverse cardiovascular events, indicating reporting them is valuable.[58] Submaximal values may be more specific measurements for the aerobic capacity required for daily life and recreational activities. Even if an intervention results in no change to VO_2peak values, a change in VT would indicate an improvement in exercise tolerance and agree with the improvements in exercise capacity. Of note is the presentation of CPET measures at the VT reported by Moalla et al., (2006), where clinically relevant improvements to cardiorespiratory fitness would have gone unreported if submaximal values were absent.[39]

With the diverse measures reported in the included articles, it is difficult to identify a clear hierarchy of outcomes. Though, at this stage of research, it may be appropriate for trials conducting CPETs on children and adolescents with CHD to report all data recorded during these tests. As new research indicates novel correlations with important clinical outcomes, clinicians need to be able to revisit these trials and understand the implications of the intervention not just for the reported data, but for what it means at the patient level. For instance, the reporting of a VE/VCO2 slope is only present in 1 trial of the 4 that report on CRF outcomes; recent research has indicated that the VE/VCO2 slope may be a useful tool for evaluating physiological status of children and adolescents with CHD.[59] To this end, it may be appropriate that there is no obvious hierarchy of outcome measures for CPETs in children and adolescent with CHD. Whilst peak VO_2 is considered the reference method for CRF due to its reported associations with many clinical variables and disease severity,[60-63] it may be that another less-reported variable has more prognostic implications.

Neuromuscular fitness

Regarding neuromuscular fitness, both interventions and outcomes from the 2 included articles are dissimilar. The traditional at-home aerobic training program improved knee extensor strength and endurance, but the exercise promotion program found no change from a battery of other neuromuscular tests. It was reported that the exercise intervention was not direct enough in its encouragement of training volume or intensity, nor was the training protocol specific and individualized, resulting in a training stimulus that was insufficient to achieve any effect.[41] The authors acknowledged that "…our flexible approach might have led to laziness and carelessness" regarding participation in their prescribed exercise regime.[41] Improved strength measures after the 12-week at-home aerobic training intervention were attributed to increased muscular perfusion and oxygenation as an adaptation to individualised cycling training.[40] The findings of these 2 studies limit the ability to conclude the appropriate characteristics of an exercise or fitness intervention for children and adolescents with CHD to undergo neuromuscular fitness improvement.

Physiological and metabolic parameters

In regards to the findings with physiological and metabolic parameters; traditional aerobic training improved muscular oxygenation and did not lead to clinically relevant adverse cardiac remodeling.[38] Two articles reported improved muscular oxygenation in children with CHD as a result of their intervention, demonstrating the value of exercise training for improving oxygen supply to the muscle.[39,40] Muscular oxygenation is often reported in CHD populations to be lower than that of their healthy age-matched peers in youth and in adulthood, and improving this measure is integral to enhancing exercise capacity in these groups.[39,64,65] Further, the significant relationships between muscular oxygenation and cardiorespiratory fitness indicate improvements to one will strongly influence the other, increasing overall exercise tolerance.[39] Exercise training also appears to improve some measures of diastolic performance of the heart in ToF patients (potentially resulting in enhanced stroke volume), though no significant changes were reported in many other echocardiographic parameters.[37,38] It is noteworthy that the use of echocardiography has questionable validity and reliability in this setting, especially when considering atypical/mixed chamber geometries and preload deprivation; a more appropriate measure may be cardiac MRI and exercise cardiac MRI. The same trial reported no significant changes to neurohormonal assessments after the exercise intervention. It was postulated that this was a result of the trial participants being in relatively good health, without clinical signs typically associated with impaired long term prognosis in CHD.[38] Echoing a systematic review from 2013, it is remarkable that hardly any RCTs have investigated exercise-induced changes to cardiac measures in children and adolescents with CHD, aside from the 1 trial included here,[37,38] given the physiology of CHD.[26]

Physical activity behaviors

Only 1 study found an effect on physical activity levels resulting from their intervention.[43] However, the articles that did not find any significant changes indicated that their study populations were already highly active and most were meeting recommended levels of daily activity at baseline.[36,44] These articles indicated that their participant pool was likely meeting these thresholds due to environmental factors such as their countries population

using bicycles as a primary mode of transport, even in youth. As they identified, whilst adolescents with CHD can significantly increase daily activity levels following exercise training, many of these participants are already likely as active as their condition allows, offering less room for improvement. However, it was highlighted in one of the articles that the participants may not have reached the point in their lives where the functional restrictions of their conditions become apparent and inhibit physical activity.[43] Overall, the literature reflects the difficulty in changing lifestyle measures with only an exercise program and no behavioral modification. Further, a recent systematic review indicated that most of the literature on assessment of physical activity in CHD populations was fair at best, and that no clear answer on how active CHD patients really are can be currently given[66]; though other reviews suggest that children with CHD may be as active as their healthy counterparts and are not more sedentary.[11]

Comparison to other reviews of studies and non-RCT interventions

As stated earlier, a number of other literature reviews into the efficacy and safety of exercise training for children and adolescents with CHD have been published.[20-22,26,27] Though these reviews were either not systematic, nor restricted to randomised controlled trials, or specific to 1 presentation of CHD, it would be prudent to compare their findings alongside ours in the context of presenting the contours of the literature and the current gaps in research.

Our finding that exercise training is efficacious for improving aerobic fitness is echoed across other studies, provided the exercise is performed at sufficient intensities.[21] Though, it should be noted these findings tend to be from studies with small sample sizes and potential bias due to heterogenous cohorts, absence of healthy controls, and insufficient exercise volume. Regarding exercise capacity, other studies report similar increases to time on test[54,67,68] and distance covered after exercise interventions, even in groups where there was no significant change to maximum cardiorespiratory fitness.[69] Though, an improvement to exercise capacity or cardiorespiratory fitness is not always observed with exercise training: 1 study with participants training using a dyspnoea-based intensity observed no changes to either of these measures after a 2-month training program.[70] Still, with appropriate exercise prescription the evidence strongly supports exercise training for improvements to exercise capacity and cardiorespiratory fitness, though not necessarily both at the same time.

Neuromuscular fitness is not a frequently reported outcome across exercise training and paediatric CHD literature, as most interventions incorporate a traditional cardiovascular exercise training model focussed on elevating heart rate rather than promoting muscular development. This is in spite of research suggesting skeletal muscle function is closely tied to exercise tolerance and cardiorespiratory fitness in CHD populations.[71,72] This is especially relevant to Fontan patients, where endurance training (by far the most common type of exercise intervention) may not result in similar changes to cardiorespiratory fitness as observed in other CHD types.[36] Therefore, other exercise training types may be more advisable for improvements to these important clinical measures, such as combined aerobic and resistance training, resistance training alone, or inspiratory muscle training.[73]

We reported that the exercise interventions in the included studies largely did not present a significant change in physical activity measures. This is similar to reported findings in other recent systematic reviews which included sport-based or game-based interventions in addition to structured interventions (such as the ones included in this review).[74]

Though the included trials in this review were not limited to a specific CHD cohort, other reviews specific to Fontan patients report largely similar findings to the ones presented here: that exercise training can be safely implemented with this population, and that it can effectively improve exercise-related outcomes.[75]

Adverse events

Only 1 adverse event was reported in 305 participants randomised to an exercise intervention in the trials that reported adverse events. However, it is important to note all participants passed a pre-screening protocol and had medical clearance prior to engaging in an exercise intervention. Therefore, these results are not necessarily generalisable to all those with a CHD diagnosis. Rather, exercise interventions have been indicated to be safe for children and adolescents with clinical situations compatible with exercise training. Still, for those who have no contraindications for exercise, the research supports their participation.

Key findings

These studies offer encouraging results on the benefits of exercise in this population; however, methodologies are mixed, particularly regarding the design of the interventions. The included articles provide an ambiguous answer toward which kinds of exercise interventions are most beneficial to children and adolescents with CHD for improving a range of fitness-related measures. In addition, no RCTs have reported on the effects of an exercise intervention on all domains of fitness, with none addressing body composition. This indicates there is still a need for further high quality RCTs to strengthen any conclusions on the most appropriate exercise-based intervention for children and adolescents with CHD. The lack of body composition reporting in the including RCTs is surprising, but not unexpected given the challenges

associated with its assessment in this population, particularly with long-term interventions where the natural process of growth and development may be a strong confounding variable. However, as this population is at increased risk of developing obesity-related comorbidities (due to a potentially sedentary lifestyle; though, the percentage of people with CHD with obesity or overweight is reportedly not greater than the general population[76]), it is interesting that no RCTs have investigated the effects of exercise training on anthropometric measures. Further, body composition anomalies may have significant implications for circulatory function and cardiovascular fitness, especially in Fontan populations.[77-79] Bioelectric impedance analysis is an alternative to body composition assessment to the superior dual-energy x-ray absorptiometry, and is quick, highly available, low cost, easy to perform, and simple to interpret without necessitating trained specialist staff[78]; though it has been reported to tend to underestimate measures of body fat.[80-83] Body mass index (BMI) may be an appropriate clinical measure of anthropometry (particularly for correlations to clinical outcomes[84]), though its use in research contexts must be taken with caution as the combination of elevated body adiposity and reduced lean mass common in CHD patients can result in an apparently "normal" BMI value.[77] Acknowledging that BMI is intended for primarily epidemiology, its reporting still gives insight into the changes to body mass that may be expected with exercise training. That none of the 6 trials included presented analyses on either of these measures is concerning given their apparent ease of use and the substantial benefit their values would provide as to the efficacy of the intervention on body composition status.

Strengths and limitations

This review adds to the body of literature on the effects of exercise training on domains of fitness and exercise behaviors in children and adolescents with CHD. Whilst other systematic reviews and meta-analyses have been published,[6,20-22,26-29] to our knowledge none of them have included exclusively high-quality RCTs. We also used a tool for the assessment of study quality specifically designed for exercise intervention trials, overcoming the limitations of the traditional tools to assess quality in these types of studies. Though, caution must be applied when interpreting our results due to the estimate of a low to moderate certainty in the findings. This is due to a small number of studies/sample sizes, increased potential for outcome reporting bias and inconsistency in the reported effects of the interventions. Further, this is a highly heterogenous cohort, and Fontan physiology in particular is likely to have unique adaptations to exercise.[85,86] Only one of the included trials presented data divided between Fontan physiology and others; though, the positive results reported are in line with other literature suggesting exercise training in Fontan patients is likely safe and efficacious.[73,87]

A key consideration when interpreting the results of this review is that the population were assessed as being safe to participate by a cardiologist. They were assessed as being safe to participate by a cardiologist who would likely be conservative given how little is known regarding exercise effects in people with CHD. As the field progresses it is likely we will see trials including higher risk CHD patients that will allow a deeper understanding of the safety and efficacy of exercise training in all children and adolescents with CHD. In addition, most of the studies here have small to very small populations and numerous outcomes. These trials may be better described as proof-of-concept or feasibility studies.

This review is limited in that the number of RCTs is not large enough to draw strong evidence-based conclusions from. Additionally, the RCTs that were included had significantly different study designs and interventions, which made it difficult to evaluate the true effects of exercise training on the outcomes of interest. Therefore, it is difficult to say whether any 1 type of exercise intervention is superior for improving any of the outcomes presented here, bar exercise capacity, which had somewhat consistent improvements after an exercise intervention. An important confounding variable is the specific diagnosis of CHD present within the participants. As mentioned, it is important to distinguish results of Fontan participants from other CHD subgroups due to their significantly different physiology and exercise response. Additionally, the lack of detail around exercise characteristics (frequency, intensity, mode, duration of session, type of exercises) make it unclear as to what exercises some of the interventions had their participants doing.[41-44] The methodological quality of the included studies had a median score of 9 out of 15 when assessed against the TESTEX criteria. The lack of consensus about outcomes is particularly problematic; it would be easier for clinicians and researchers to recommend exercise or physical activity if there were more agreement or standardised outcomes for exercise trials in this population.

The specific exercise programs within the physical activity education and promotion interventions are not well reported, and the prescribed home exercise regimes are not documented.[29,41,42,44] It is unclear how much of the exercise programs incorporated resistance training, aerobic training, or flexibility training. The lack of clarity around what the exercise protocol involved makes replication impossible. Additionally, at present there are no RCTs exclusively investigating resistance training in CHD children and adolescents, though there is substantial evidence supporting its inclusion in exercise programmes in other study designs.[16,88] There is also a limited research into high-intensity interval training modalities, which may be an appropriate exercise style that is

consistent with the sporadic and high-intensity activities that children seem to enjoy.[21,89]

Research recommendations

Well-designed and well-reported RCTs are needed to assess the efficacy of exercise interventions in these populations. To develop guidelines and recommendations for an optimal dose of exercise, studies comparing different types of interventions, or differing intensity or duration are needed. Researchers must be cautious to distinguish the results of the different subgroups of CHD, as not all conditions respond the same to a given exercise stimulus. The previous trials have involved either short term exercise delivery or a long-term exercise promotion intervention. Much larger, multicentre, long-term studies are required to see if the benefits of exercise interventions to cardiovascular wellbeing can be maintained. Additionally, it is essential that future research provide details on the presence of adverse events in their study population, so that clinicians treating these groups can present the safety of exercise training to CHD patients and their families. Future research directions should evaluate exercise impacts on other pathophysiology such as endothelial dysfunction, neurohormonal activation, ventricular remodelling via cardiac MRI, and other clinically relevant pathophysiology's associated with CHD.

Additionally, there is a need for researchers to prospectively determine adherence criteria so that adherence can be accurately recorded and reported, given the influence of adherence on prescription on outcomes. Recording and reporting adherence is traditionally very poor (and often limited to attendance rates) across exercise studies, and this may have implications for determining the treatment effect of the exercise interventions being compared.[46]

Conclusion

Exercise training is safe and efficacious for lower risk children and adolescents with CHD, though much remains unclear around the characteristics of the most appropriate intervention. Based on these trials it may be advised that certain children with CHD (e.g. categorised as low-risk) be encouraged to participate in exercise training similar to their age-matched peers, incorporating a wide mix of modalities and achieving recommended daily physical activity levels. However, there is currently insufficient evidence to make strong recommendations from, and the majority of existing trials have limitations in design with no clear consensus outcome measure.

Author's contributions

Christopher Anderson: Conceptualization, Methodology, Investigation, Data curation, Original draft preparation; Jessica Suna: Investigation, Data curation; Shelley Keating: Supervision, Writing – Reviewing and Editing; Rachael Cordina: Writing – Reviewing and Editing; Derek Tran: Writing – Reviewing and Editing; Julian Ayer: Writing – Reviewing and Editing; Jeff Coombes: Supervision, Writing – Reviewing and Editing.

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Conflicts of interest

The authors declare no conflicts of interest.

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