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Cardiovascular Risk Factors and Activity Promotion in Children and Adolescents with Congenital Heart Disease

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"Action is movement with intelligence. The world is filled with movement. What the world needs in more conscious movement, more action."

B.K.S. IYENGAR

Summary

Congenital heart disease (CHD) is the most common organ malformation worldwide. Due to multiple achievements in cardiovascular diagnostics, interventional treatment, and cardiothoracic surgery over the past century, life expectancy of CHD patients has increased substantially. Currently around 97% of children with CHD reach adulthood in the industrialized world. With these increased survival rates, the medical and scientific focus has shifted from short-term morbidity and mortality to long-term physical functioning and quality of life. Cardiovascular risk factor assessment and health promotion are becoming a centerpiece in the aftercare of CHD patients and should begin as early as possible in childhood.
This thesis provides an overview of modifiable lifestyle-related risk factors in the long-term course of children and adolescents with CHD. The first study, a systematic literature review, revealed that the prevalence of overweight and obesity in CHD patients is comparable to the general population and increases particularly in adolescence. Concluding that the increasing obesity pandemic is also affecting CHD patients. The second study, a cross-sectional study, showed that there was no association between physical activity (PA) and arterial stiffness in physically active children with CHD. However, in physically inactive children and older CHD patients with prolonged exposure to physical inactivity, this association remains unclear. Therefore, early promotion of PA in the CHD population is nevertheless indicated.

Based on the results of these scientific studies, a target population was identified and subsequently a randomized controlled trial, *Digital Health Nudging,* was conducted for adolescents with CHD. The new concept of nudging, which originated in behavioral economics, was applied for the first time to adolescents with CHD and investigated for its effectiveness in increasing PA, activity-related self-efficacy, and health-related quality of life. Over a 12-week period, study participants received daily smartphone messages about PA based on Bandura's social cognitive theory. *Digital Health Nudging* did not increase PA, but improved feelings of emotional well-being. Changing behavior and building habits towards a physically active lifestyle is highly complex and requires multifactorial approaches. Digital behavior change interventions and the concept of nudging still seem to be a promising approach for PA promotion. Prevention programs of the future should therefore take advantage of the enormous potential offered by new technologies such as Artificial Intelligence and Big Data.

Zusammenfassung

Angeborene Herzfehler (AHF) sind weltweit die häufigste Organfehlbildung. Dank enormer Fortschritte in der kardiovaskulären Diagnostik und Therapie hat sich die Lebenserwartung von AHF-Patienten deutlich erhöht, so dass derzeit etwa 97% der Kinder mit AHF in Industrieländern das Erwachsenenalter erreichen. Aufgrund der gestiegenen Überlebensrate hat sich der medizinische und wissenschaftliche Fokus auf die langfristige, körperliche Funktionsfähigkeit sowie Lebensqualität verlagert. Modifizierbare lebensstilbezogene kardiovaskuläre Risikofaktoren und Gesundheitsförderung stehen nun im Fokus der Nachsorge von AHF-Patienten. Gesundheitsförderung sollte dabei frühestmöglich im Kindesalter beginnen.
Diese Dissertation gibt einen Überblick über lebensstilbezogene Risikofaktoren im Langzeitverlauf von Kindern und Jugendlichen mit AHF. Die erste Studie dieser Dissertation, eine systematische Literaturübersicht, zeigte, dass die Prävalenz von Übergewicht und Adipositas bei Patienten mit AHF ähnlich hoch ist wie in der Allgemeinbevölkerung und insbesondere im Jugendalter deutlich zunimmt. Somit betrifft die wachsende Pandemie der Übergewichtigkeit auch die AHF-Population. Die zweite Studie, eine Querschnittsstudie, zeigte, dass bei körperlich aktiven Kindern mit AHF kein Zusammenhang zwischen körperlicher Aktivität und arterieller Steifigkeit besteht. Bei körperlich inaktiven Kindern und Patienten mit längerer körperlicher Inaktivität bleibt dieser Zusammenhang jedoch unklar. Aktivitätsförderung beginnend im frühen Kindesalter ist in der AHF-Population dennoch von immenser Bedeutung.

Auf der Grundlage der Ergebnisse dieser wissenschaftlichen Studien wurde eine Zielpopulation ermittelt und anschließend wurde eine randomisierte kontrollierte Interventionsstudie, *Digital Health Nudging*, für Jugendliche mit AHF entwickelt und durchgeführt. Das neue und ursprünglich aus der Verhaltensökonomie stammende Konzept „Nudging“ wurde dabei erstmals bei Jugendlichen mit AHF angewandt und auf seine Wirksamkeit zur Steigerung der körperlichen Aktivität, der aktivitätsbezogenen Selbstwirksamkeit und der gesundheitsbezogenen Lebensqualität untersucht. Über einen Zeitraum von 12 Wochen erhielten die Studienteilnehmer täglich Smartphone-Nachrichten zum Thema körperliche Aktivität basierend auf der sozial kognitiven Lerntheorie von Bandura. *Digital Health Nudging* führte zwar nicht zu einer Steigerung der körperlichen Aktivität, verbesserte aber das emotionale

Wohlbefinden von Jugendlichen mit AHF. Die Änderung von Verhalten und der Aufbau von Gewohnheiten in Richtung eines körperlich aktiven Lebensstils ist hochkomplex und erfordert multifaktorielle Ansätze. Digitale Interventionen zur Verhaltensänderung und das Konzept „Nudging“ scheinen nach wie vor ein vielversprechender Ansatz für die Aktivitätsförderung zu sein. Präventionsprogramme der Zukunft sollten das enorme Potenzial nutzen, die neue Technologien wie künstliche Intelligenz und Big Data bieten.

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Abbreviations

ACC	American College of Cardiology
ACHD	Adults with Congenital Heart Disease
ArSE	Activity-Related Self Efficacy
AS	Aortic Stenosis
ASD	Atrial Septal Defect
AVSD	Atrioventricular Septal Defect
BMI	Body Mass Index
CHD	Congenital Heart Disease
CoA	Coarctation of the Aorta
cSBP	Central Systolic Blood Pressure
DBP	Diastolic Blood Pressure
HrQoL	Health-Related Quality of Life
EBS	Ebstein's Anomaly
eHealth	Electronic Health
mHealth	Mobile Health
MVPA	Moderate-to-vigorous Physical Activity
NHLBI	National Heart, Lung and Blood Institute
NYHA	New York Heart Association
PA	Physical Activity
PDA	Patent Ductus Arteriosus
PS	Pulmonary Stenosis
PWV	Pulse Wave Velocity
RCT	Randomized Controlled Trial
SBP	Systolic Blood Pressure
TAC	Truncus Arteriosus Communis
TCPC	Total Cavopulmonary Connection
TGA	Transposition of the Great Arteries
ToF	Tetralogy of Fallot
UVH	Univentricular Heart
VSD	Ventricular Septal Defect
WHO	World Health Organization

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1. Clinical Background of Congenital Heart Disease

Congenital heart disease (CHD) is defined as a structural abnormality of heart and/or great vessels that is present at birth [1]. The embryonic heart development is a complex developmental process of the embryogenesis and consists of numerous sophisticated steps, with the first rhythmical contractions of the heart being apparent as early as the 22nd day of pregnancy. Deviations from these crucial steps during the embryonic heart development lead to malformations resulting in CHD [2]. CHD is the most common birth defect in humans, affecting about 1% of live births in Europe and the United States [3]. The global prevalence of CHD at birth is higher with around 1.9 cases per 100 live births [4]. There are regional differences in the CHD prevalence, with lowest reported prevalence in Africa and highest reported prevalence in Asia [1]. In Germany, CHD affected 107 per 10,000 live births in 2007 [5]. In the last decades, the reported birth prevalence of CHD is increasing globally, see *Figure 1*. In particular the prevalence of mild lesions has increased, which also reflects the improved disease detection [1].

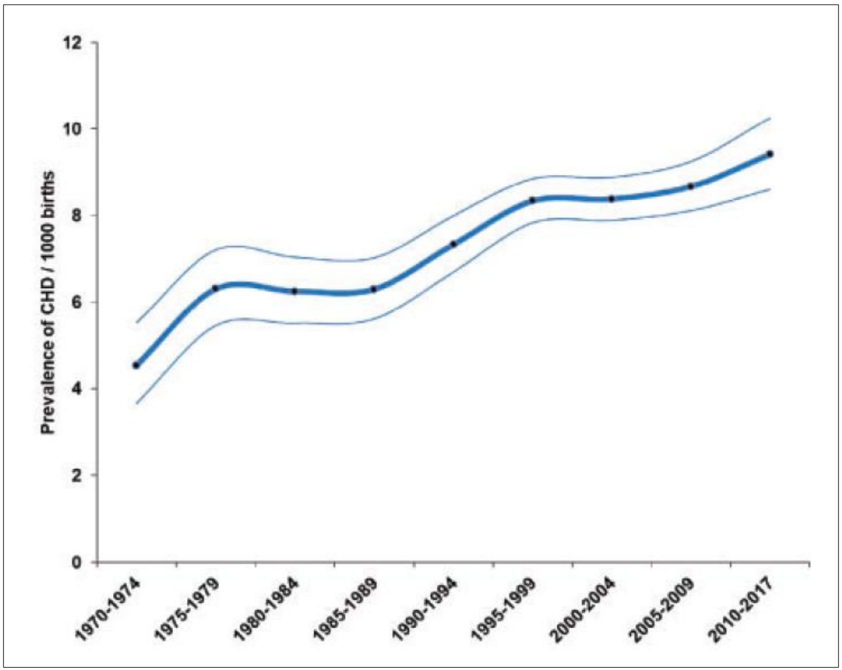
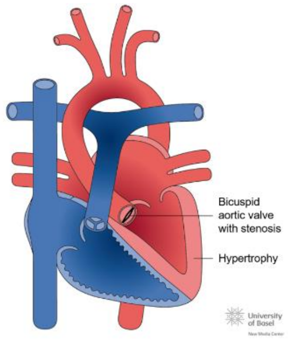
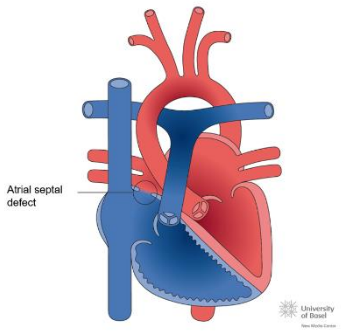
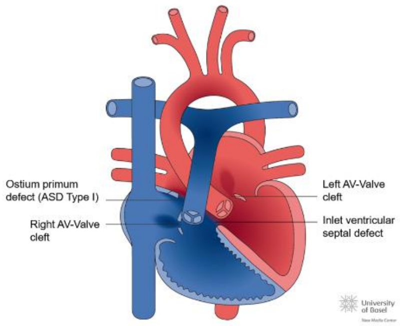


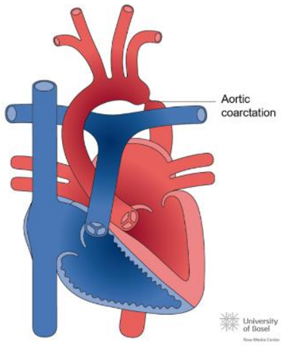
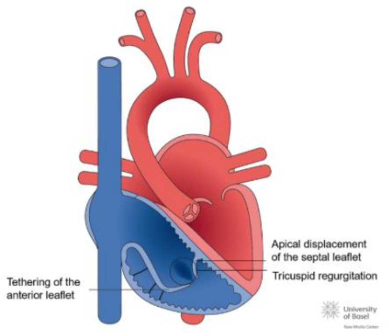
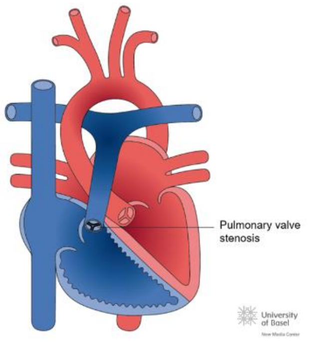
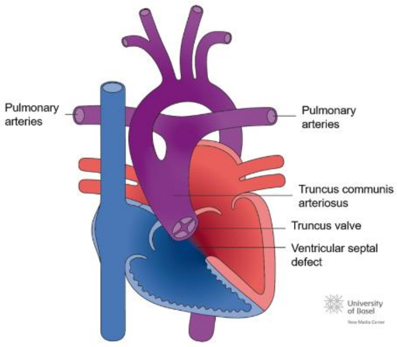
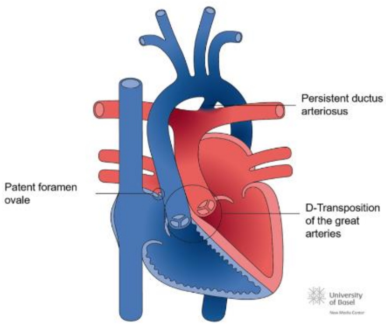
Figure 1: *Birth prevalence of CHD from 1970 – 2017 [1].* The thick line shows the estimated overall prevalence, thin lines represent 95% CI.

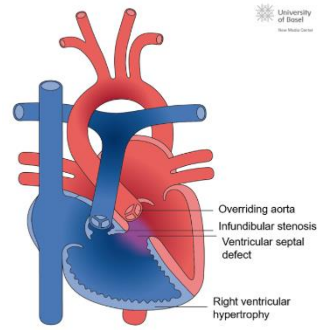
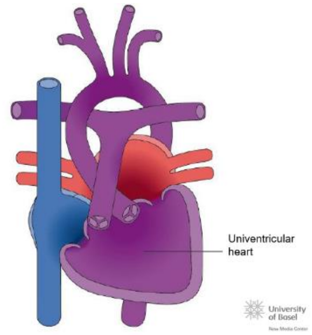
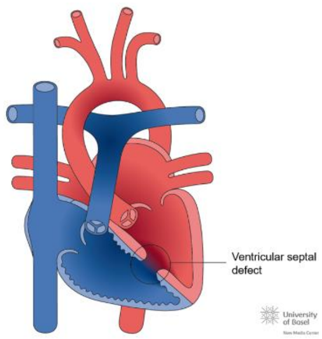
CHD can either occur isolated or as a combination of multiple defects, with varying effects on oxygen saturation. Thereby, CHDs can be differentiated in cyanotic and acyanotic heart defects based on the level of oxygen saturation [2].

Based on type and localization, CHDs can be classified into six major subgroups, which are used throughout this thesis: '*isolated shunts'*, including atrial/ventricular /atrioventricular septal defects; '*left heart obstruction',* including aortic stenosis and coarctation of the aorta; '*right heart obstruction',* including pulmonary stenosis and Tetralogy of Fallot; '*Transposition of the Great Arteries (TGA) after switch'*, children with '*Fontan circulation'* after total cavopulmonary connection in patients with functional univentricular hearts and '*miscellaneous defects'* including amongst others truncus arteriosus communis and Ebstein anomaly. *Table 1* gives an overview of the most common CHDs and their prevalence.

Table 1: *Overview of most common congenital heart diseases*

CHD	**Description** [2]	**Prevalence** [1] per 1,000 live births (% of all CHD)	**Visualization**
AS	Blood flow between the left ventricle and the aortic arch is obstructed (within the ventricle, the heart valve, or the ascending aorta). The left ventricle must exert additional force to overcome the obstruction, and its myo-cardium hypertrophies.	0.19 (2.3%)	
ASD	A wall defect in the atrial septum, the atria communicate with each other. The left atrium releases only part of the arterial blood into the left ventricle. Due to the pressure gradient between the atria, arterial blood leaks into the right atrium, right ventricle and pulmonary artery.	1.44 (15.4%)	
AVSD	A combination of ASD and VSD. Oxygen-rich blood from the lungs mixed with oxygen-poor blood from the body, resulting in in-creased workload for the heart.	0.29 (3.6%)	

CoA	The aortic isthmus is significantly narrowed or constricted. The left ventricle must exert more force and its myocardium hyper-trophies. The arterial blood pressure of the upper body half is higher than below.	0.29 (3.6%)	
EBS	EBS is a malformed tricuspid valve that does not properly close to keep the blood flow moving. Blood possibly leaks from the lower right to upper right chamber.	0.04 (0.5%)	
PS	Between the right ventricle and the pulmonary circulation is an obstruction. The ventricle has to exert more force to perfuse the pulmonary circulation and the strength of its wall musculature increases.	0.55 (6.2%)	
TAC	One arterial trunk arises from the heart, very often in combination with a VSD. Oxygen-rich blood mixes with oxygen-poor blood, leading to reduced oxygen saturation.	0.08 (1.0%)	
TGA	Aorta and pulmonary artery are connected to the wrong cardiac chambers. Venous blood re-circulates in the systemic circulation and arterial blood recirculates in the pulmonary circulation.	0.30 (3.8%)	

ToF	Combination of four defects: 1. ventricular septal defect 2. pulmonary stenosis 3. overriding aorta above the ventricular septal defect 4. hypertrophy of the right ventricle	0.36 (4.4%)	
UVH	A common ventricle pumps mixed venous and arterial blood with the systolic pressure of the systemic circuit into both circuits. A second ventricle is absent or sits as a small cavity inside the large ventricle.	0.09 (1.1%)	
VSD	A wall defect in the ventricular septum; the ventricles communicate with each other. The left ventricle pumps only part of the arterial blood into the systemic circulation. Because of the pressure gradient between the ventricles, arterial blood leaks into the right ventricle and the pulmonary artery.	3.07 (35.6%)	

AS: Aortic stenosis; ASD: Atrial septal defect; AVSD: Atrioventricular septal defect; CoA: Coarctation of the aorta; EBS: Ebstein anomaly; PS: Pulmonary stenosis; TGA: Transpositin of the great arteries; TAC: Truncus arteriosus communis; ToF: Tetralogy of Fallot; UVH: Univentricular Heart; VSD: Ventricular septal defect.
Illustrations from: http://www.chd-diagrams.com. These illustrations are licensed under the Creative Com-mons Attribution-NonCommercial-NoDerivatives 4.0 International License by the New Media Center of the University of Basel.

The American College of Cardiology (ACC) classifies CHDs according to the disease severity [6]. *Table 2* shows an overview of the ACC criteria with CHD diagnosis mostly used throughout this thesis. In Germany, 12.0% of CHDs are classified as complex, 27.4% as moderate, and 60.6% as simple [5].

Over the past century, multiple achievements have been made in cardiovascular diagnostics and cardiothoracic surgery, resulting in increased survival rates of new-borns with CHD. Consequently, life expectancy of CHD patients has increased substantially, with currently around 97% of CHD children reaching adulthood [7] creating a new and ever-growing patient population of adults with CHD [8]. Even though the majority of CHD patients will have had surgical or catheter interventions, patients are not considered cured but rather palliated. Throughout the lifespan, most CHD patients are affected by residuals, sequelae, and complications, as well as (acquired) cardiac and non-cardiac comorbidities, all of which can adversely affect morbidity and mortality [9]. They therefore live with a chronic disease and require life-long surveillance [10].

Table 2: *CHD diagnosis mostly used throughout this thesis classified by disease severity according to ACC criteria [6]*

Mild lesion	Moderate lesion	Complex lesion
- ASD/VSD, isolated or repaired without residua - PS, mild isolated	- ASD/VSD with associated abnormalities - AS - AVSD - CoA - EBS - PS, moderate or severe - ToF	- Cyanotic CHD - Fontan procedure - Mitral/Tricuspid atresia - TAC - TGA - UVH

AS: Aortic stenosis; ASD: Atrial septal defect; AVSD: Atrioventricular septal defect; CHD: congenital heart defect; CoA: Coarctation of the aorta; EBS: Ebstein anomaly; PS: Pulmonary stenosis; TGA: Transpositin of the great arteries; TAC: Truncus arteriosus communis; ToF: Tetralogy of Fallot; UVH: Univentricular Heart; VSD: Ventricular septal defect.

With the increased survival rates in children with CHD, the medical and scientific focus has shifted from short-term morbidity and mortality due to the primary cardiac disease to long-term physical functioning and quality of life. However, physical function, mental health, and quality of life continue to be compromised in the CHD population [11]. Individual risk stratification and early preventative interventions should become a priority in the aftercare of CHD patients [12]. Until now, health behavior has received little attention despite the impact it can have on health status and quality of life in the CHD population [13].

The group of CHD patients is very heterogeneous due to the interaction between genome, phenome and environment. As a consequence, each CHD patient remains an individual case, which makes a patient-specific therapeutic and preventive approach inevitable.

2. Cardiovascular Risk Factors in Children with Congenital Heart Disease

Globally, 74% of all deaths are attributed to non-communicable diseases, most of them cardiovascular diseases followed by cancer, chronic respiratory disease, and diabetes [14]. Thereby, leading risk factors for mortality worldwide and across all income groups are high blood pressure, tobacco use, high blood glucose, physical inactivity, as well as overweight and obesity [15]. As the life expectancy of CHD patients increases, they are exposed to the same modern lifestyle risks as the general population [16].

Even though the survival of patients with CHD has improved, CHD patients still have a higher risk of premature mortality compared to the general population across all forms of CHDs [17]. This long-term risk of premature mortality is mostly related to the residual CHD pathology, heart failure, and arrhythmias, but is also related to non-cardiac conditions [18]. The vast majority of patients with CHD die from cardiovascular causes, mainly heart failure and sudden death [19]. As a consequence of the congenital condition, patients are at high cardiovascular risk [16].

As most of the patients with CHD are not cured but palliated, appropriate and specialized CHD care as well as lifestyle-oriented prevention during their entire lifespan is essential and should begin as early in life as possible [20]. Risk factors and clinical markers for cardiovascular disease arise already during childhood [21]. As known from the famous Bogalusa Heart Study of 1994, there is a tracking of cardiovascular risk factors from childhood into adulthood. Therefore, prevention aimed at developing healthy lifestyles needs to begin early in life and has a special importance in CHD patients [22].

The first part of this thesis focuses on lifestyle-related risk factors in children and adolescents with CHD, including overweight and obesity, as well as physical inactivity and its association with arterial stiffness.

2.1 Overweight and Obesity

Overweight and obesity are referred to a global pandemic [23]. Among children and adolescents, the prevalence of overweight and obesity has risen dramatically from around 4% in 1975 to over 18% in 2016, and rates of overweight are expected to continue to increase in all countries worldwide [15]. This is particularly alarming in children, as overweight and obese children are likely to remain obese into adulthood and are more likely to develop non-communicable diseases [24]. The fundamental cause of the overweight and obesity pandemic are the increased intake of energy-dense food and physical inactivity associated with modern lifestyle [25]. Adolescents in particular consume a lot of sugar-sweetened beverages and junk food [26]. This excess energy intake often goes in hand with a decline in physical activity (PA) and increase of sedentary behavior during the transition from childhood to adulthood [27, 28]. During Covid-19 and the associated restrictions, overweight and obesity prevalence has increased additionally in school-aged children and worsened the burden of childhood overweight [29].

Overweight and obesity are associated with risk of coronary heart disease, ischemic stroke, and risk of breast, colon, prostate cancers, among others [30]. In the population of patients with CHD this is particularly concerning as they are prone to cardiovascular events. A previous study on children with CHD showed, that body weight has a huge impact on arterial stiffness, even more than measures of cardiorespiratory fitness. Therefore, prevention of overweight and obesity during childhood and adolescence is extremely important in CHD patients, to reduce arterial stiffness and delay the onset of cardiovascular disease [31]. First, however, the prevalence must be accurately determined, which is why a systematic literature review on overweight and obesity in CHD patients was conducted in this thesis.

2.2 Arterial Stiffness

Arterial stiffness is a generic term for functional and structural properties of the vessels. Independently and in interaction, vascular structure, function, and arterial pressure affect changes in arterial stiffness. Arterial stiffness is one of the earliest detectable manifestations of adverse structural and functional changes in the vascular wall. It is a marker of vascular damage and a strong predictor for cardiovascular disease such as myocardial infarction, hypertension, heart failure, and stroke [32].

The arterial wall mainly consists of collagen, elastin, and smooth muscles. Central arteries have relatively high elasticity which decreases towards the peripheral vessels [33]. Degenerative changes related to age in the intima of the large elastic arteries lead to a loss of arterial elastin and subsequently increases arterial stiffness [34].

Besides the transport function, the large arteries have a damping function for the pressure fluctuations caused by the pulsating heart. The so-called 'Windkessel function', describes the compliance and elasticity of the arteries that induce a reversible distensibilty and thereby convert the cyclic pulsatile blood flow into a continuous-phasic flow [35]. An impairment of this 'Windkessel function' through an increase of arterial stiffness results in an elevated afterload of the heart through increased pulse pressure leading to left ventricular hypertension. This elevated workload leads to left ventricular hypertrophy and, in addition, impaired myocardial perfusion, which can lead to heart failure in the long term [36].

Pulse Wave Velocity and Central Systolic Blood Pressure

This thesis focuses on the functional parameters of arterial stiffness including pulse wave velocity (PWV) and central systolic blood pressure (cSBP). PWV was first described by Bramwell and Hill [37] and describes the speed of the arterial pressure wave generated during ventricular ejection that is travelling along the aorta and the large arteries. Thereby, PWV reflects the vessel elasticity [35] and is the most validated method to noninvasively quantify arterial stiffness. PWV is considered as the gold standard for measuring arterial stiffness [22]. It can either be measured directly or estimated by special algorithms [36], which has the advantage that measurement with blood pressure cuffs is possible and thus fast and easy [34].

Arterial stiffness directly increases the blood pressure. Systolic blood pressure is a surrogate measure of arterial stiffness [38]. CSBP characterizes the vascular function for cushioning forward and, reflected from the periphery, backward traveling pulse wave [39]. CSBP is strongly associated with atherosclerosis and end-organ damage [40] and outperforms peripheral systolic blood pressure in predicting cardiovascular events and all-cause mortality [39]. The arterial pressure varies over the cardiac cycle, but in routine clinical practice mostly peripheral systolic and diastolic pressure are reported [39]. Whilst the diastolic pressure is relatively constant, systolic blood pressure was shown to be up to 40mmHg lower central than in the brachial artery [41].

Measuring Arterial Stiffness

Pulse wave velocity measurement has been recommended by European professional societies (ESH and ESC) since 2007 for quantification of cardiovascular risk profile and estimation of potential end-organ damage [42, 43].
Non-invasive and relatively easy to obtain measures of arterial function have shown to be clinically useful in screening and diagnostics in pediatric patients as they allow to get an inside view of arterial health and endothelial function [35].
Throughout this thesis, cSBP and PWV were measured with the Mobil-O-Graph® device (I.E.M.,Stolberg Germany) at the A. brachialis [35]. The Mobil-O-Graph®, see *Figure 2*, is a blood pressure monitor with additional pulse wave analysis capability by oscillometric measurement. The data are recorded (peripheral blood pressure) and calculated (central blood pressure) with the Hypertension Management Software (HMS, CS5.1, I.E.M. GmbH). The PWV is filtered and averaged from a total of ten pulse waves. It has shown good validity and reliability in several studies and is regularly used in the pediatric population [44, 45]. A recently published study reported excellent accuracy of the Mobil-O-Graph® in children and adolescents [46]. The measurement procedure will be described in the scientific publication, see *2.6*.

Figure 2: *Mobil-O-Graph® device of I.E.M. (Germany)*

Arterial Stiffness in Children with Congenital Heart Disease

There is consistent evidence of early and/or accelerated arterial stiffening in adult CHD patients, contributing to the increased risk of adverse cardiovascular and cerebrovascular events in the CHD population [47]. Already children with CHD were found to have significantly higher cSBP compared with healthy peers, suggesting early signs of atherosclerosis and structural vessel wall changes already at a young age [48]. As arterial stiffness is strongly associated with aging [38], its occurrence already in young CHD patients is worrisome and needs to be investigated intensively. In particular, possible factors that positively counteract the development of arterial stiffness need to be investigated. Therefore, this thesis investigates the association between PA and arterial stiffness in children with CHD.

2.3 Physical Activity

Physical Activity Recommendation

International guidelines and consensus statements strongly recommend PA and exercise in pediatric CHD patients [49, 50]. According to the American Heart Association there is no need for PA restrictions in CHD patients [49] and all children with CHD can participate and benefit from PA. Patients with certain lesions or complications may need counseling on precautions and recommendations [50].

PA is important for optimal physical, emotional and psychosocial development in children with CHD just as much as in the general population [12, 50]. The European Society of Cardiology suggests that CHD children should accumulate a minimum of 60 min moderate-to-vigorous physical activity (MVPA) every day, thereby reaching the WHO recommendation for healthy children from 2010 [50]. According to the WHO recommendation from 2020, children and adolescents should accumulate at least an average of 60 minutes per day of moderate-to-vigorous-intensity, mostly aerobic, PA across the week. Additionally, vigorous-intensity aerobic, as well as strengthening muscle and bone should be incorporated at least three days a week. The recommendations highlight that some PA is better than none [51]. There was one notable update from the 2010 Global Recommendations on Physical Activity for Health [52] that changed from "at least 60 minutes" to "at least an average of 60 minutes" MVPA per day throughout the week [53]. Even though the statement from the European Society of Cardiology for CHD children referred to the 2010 WHO recommendation, it can still be considered for the updated recommendation.

Benefits of Physical Activity

According to WHO recommendations, PA leads to improved physical fitness, cardiometabolic health, bone health, cognitive outcomes, mental health, and reduced obesity [51]. Therefore in children with CHD, PA is just as much necessary for best physical, emotional, and psychosocial development as in healthy children [50]. PA is positively associated with exercise capacity and studies in adults with CHD showed that reduced exercise capacity is associated with increased risk of morbidity and mortality [54-56]. Besides the functional health benefits, PA is positively associated with health-related quality of life [57] and self-efficacy in children with CHD [58]. Activity restriction, on the other hand, was shown to be the strongest predictor of overweight and obesity in children with CHD [59].

Barriers for Physical Activity

There are multifactorial reasons why PA can be reduced in the CHD population. Uncertainty and fear concerning the congenital condition, as well as parental overprotection persist until today, fostering a vicious cycle of the CHD condition and physical inactivity [60]. Physical inactivity in CHD children was shown to be associated with heart-focused anxiety [61], parental overprotection as well as doctors restrictions [62]. Fear and exclusion from exercise and sports additionally affect activity-related self-efficacy, which was reported to be already reduced in children with CHD. However, it is one of the strongest predictors for PA behavior [63]. In addition to these disease-specific barriers to a physically active lifestyle, patients must also overcome the same obstacles faced by the healthy population. Lack of motivation, or the lack of time due to other priorities, is often more than enough to keep healthy people from being active and therefore need to be considered in the CHD population as well [64]. Similar to healthy children, children with CHD also experienced a significant decrease in PA during the Covid-19 pandemic, emphasizing that this issue is more urgent today than ever before [65].

For these reasons, activity promotion is particularly important in this patient cohort. Efforts to increase PA are substantial to ensure the beneficial effects on health and quality of life in the CHD population and PA counseling should be a priority in the aftercare of patients [50]. PA counseling as well as exercise prescriptions have to start early in young patients and should be a core component of patient care [12]. A recently published Cochrane statement showed that PA interventions for people with CHD have an overall positive, albeit small, effect on MVPA. Although level of evidence was low, it indicated that PA intervention programs are efficient in the CHD population [66]. Despite the disease burden, physical inactivity is responsible for a substantial economic burden worldwide including direct health-care costs and productivity losses [67].

Physical Activity Level

Physical inactivity is the fourth leading cause of death worldwide and referred to a global pandemic [68]. According to pooled analysis including 1.6 million healthy adolescents aged 11-17 years, 81% of healthy adolescents are insufficiently physically active. Across countries and income groups, adolescent girls were less active than boys [69]. The still-ongoing Covid-19 pandemic and its associated restrictions have further exacerbated physical inactivity among adolescents. PA level declined by 20% from before to during Covid-19 corresponding to a 17-minute reduction of daily MVPA in healthy adolescents [30].

In children with CHD, the reported PA levels vary widely between different studies. However, these inconsistent results are also due to different measurement methods, with subjective PA measurements often not providing an accurate picture [70]. A nationwide survey in Germany of 1,198 pediatric CHD patients published in 2020, found that children with CHD had lower subjectively assessed levels of PA compared with healthy peers. Children with complex CHD exhibited the lowest activity behaviors. A major contributor to the reduced activity behavior in the CHD population was the unexpected high rate of PA restrictions by physicians [71]. Brudy et al. assessed PA levels of children and adolescents with CHD objectively with wearables in the German Heart Center Munich in 2019. From 162 pediatric patients, 76% achieved the by the WHO recommended 60 minutes MVPA on a weekly average and thereby PA levels did not differ from healthy peers. They showed that children with higher age, overweight and obesity as well as patients with complex CHD severity were at higher risk for physical inactivity [72].

Measuring Physical Activity

According to recommendations in the CHD population, PA should be assessed routinely as part of the ongoing clinical care. PA counseling and exercise prescriptions should be facilitated accordingly [50]. However, PA is a complex health behavior and accurate measurement is challenging particularly in children [73]. There are subjective and objective ways to track PA. Subjective measurements include questionnaires, diaries and logbooks, and interviews and can be assessed via self-report or proxy-report. Self-reported measurements are not recommended for children below the age of 10 [74]. Objective measurements include, among others, direct observation, accelerometers, pedometers, and wearables. While all these measurements have advantages and disadvantages, commercially available wearables were used to assess PA in this study. Wrist-based activity trackers present an exciting opportunity for clinical monitoring and research. Due to the modern design of the devices and direct activity feedback, they also provide an appealing user experience, which was shown to be especially important in adolescents [73, 75].

A previous study from the German Heart Center Munich compared subjectively estimated and objectively measured PA in children with CHD. They reported, that half of the CHD children overestimated or underestimated their MVPA level, concluding that objective measurement should definitely be the measurement method of choice [72]. The ability to monitor real-time PA online is of particular interest in the clinical care of CHD children, where access to specialized care is often centralized and therefore may be infrequent. Assessing PA data remotely offers new approaches for PA monitoring, counseling, and health promotion in the ongoing care [73]. Tracking habitual PA with wearables is thereby of special interest.

In 2016, the Garmin vivofit jr.® was the first wearable device exclusively developed and designed for children. The Garmin vivofit jr.2® for children and adolescents, aged four years and older, by Garmin Inc. (Olathe, KS, USA), was used to measure PA in MVPA and step count throughout the projects of the thesis, see *Figure 3*.

Figure 3: *Garmin vivofit jr 2®*

The wearable has a child-friendly and appealing design, which is a crucial factor for long-term usage. The device is waterproof, and its battery lasts around one year. The Garmin vivofit jr.2® was shown to be a feasible device for measuring PA in children [76] and showed acceptable validity in measuring PA in children [77]. For data collection, the Garmin wearable was connected to the Garmin jr. APP on the smartphone where daily activity data was stored, see *Figure 4*.

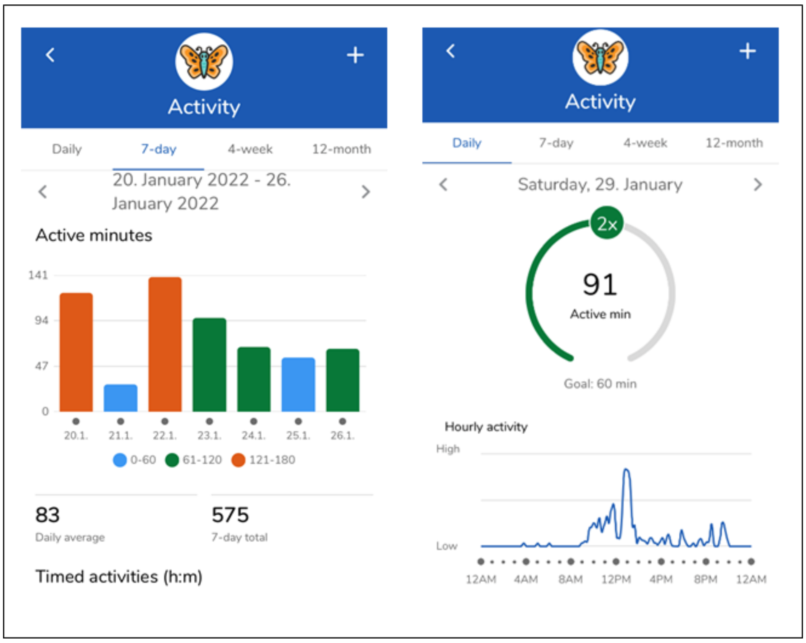


Figure 4: *Garmin jr. ® APP to collect physical activity data*

2.4 Purpose of the Thesis

The primary goal of this thesis was to assess lifestyle-related cardiovascular risk factors in children and adolescents with CHD. One systematic review and one observational study were conducted in the first part of this thesis, underlining the main objectives of this project:

1. Give an overview of overweight and obesity prevalence in children and adults with CHD (*Scientific Publication I, page 16*).
2. Determine the association between PA and arterial stiffness in children with CHD (*Scientific Publication II, page 38*).

Based on the results of these scientific studies, a target group was identified and subsequently a randomized controlled trial with a digital intervention was conducted for adolescents with CHD. Finally, the last objective of this thesis was to:

3. Elaborate the potential to increase PA, activity-related self-efficacy and health-related quality of life through *Digital Health Nudging* over the period of 12-weeks in adolescents with CHD (*Scientific Publication III, page 61*).

2.5 Overweight and Obesity in Patients with Congenital Heart Disease: A Systematic Review (Scientific Publication I)

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Conflicts of Interest:

The authors declare no conflict of interest.

Individual contribution:

The PhD candidate is the principal author of this paper. She developed and carried out the systematic search strategy. Along with the Co-Authors Leon Brudy and Michael Meyer, she screened and assessed the literature search results. Laura Willinger finally drafted the manuscript, which was revised by Jan Müller. Renate Oberhoffer-Fritz and Peter Ewert gave important feedback for further improvement of the manuscript. Laura Willinger under supervision of Jan Müller handled the submission process until final publication.

Abstract

Background: Overweight and obesity have become a major public health concern in recent decades, particularly in patients with chronic health conditions like congenital heart disease (CHD). This systematic review elaborates on the prevalence and the longitudinal development of overweight and obesity in children and adults with CHD.

Methods: A systematic literature search was conducted in PubMed, Cochrane, and Scopus from January 2010 to December 2020 on overweight and obesity prevalence in children and adults with CHD.

Results: Of 30 included studies, 15 studies evaluated 5680 pediatric patients with CHD, 9 studies evaluated 6657 adults with CHD (ACHD) and 6 studies examined 9273 both pediatric patients and ACHD. Fifteen studies received the quality rating "good", nine studies "fair", and six studies "poor". In children with CHD, overweight prevalence was between 9.5–31.5%, and obesity prevalence was between 9.5–26%; in ACHD, overweight prevalence was between 22–53%, and obesity was between 7–26%. The prevalence of overweight and obesity was thereby similar to the general population. Overweight and obesity have been shown to increase with age.

Conclusion: The prevalence of overweight and obesity in children and adults with CHD is similar to the general population, demonstrating that the growing obesity pandemic is also affecting the CHD population.

Introduction

Overweight and obesity have become major public health concerns in recent decades [1] and are referred to as a global pandemic [2]. The prevalence of childhood obesity has more than doubled in the last three decades [68], which is particularly concerning as childhood obesity tracks into adulthood [4]. Overweight and obesity, in particular, are independent risk factors for cardiovascular diseases and are associated with increased risk of morbidity and mortality in the general population [5]. As the majority of children with congenital heart disease (CHD) nowadays survive into adulthood [6], environmental and behavioral health risk factors are also of concern in this patient cohort [7, 8]. As patients with preexisting heart conditions are prone to cardiovascular events [9] due to underlying anatomic and functional abnormalities [10], overweight and obesity need to be considered here too. At first glance, one would assume that patients with CHD are at increased risk for overweight and obesity because, as cardiac patients, physical activity may be reduced due to exercise restriction or overprotection, and patients participate less in leisure and competitive sports [11]. On the other hand, surgeries, hospitalization, and rehabilitation early in life affect the development of children with CHD, which can be linked to underweight and malnutrition [12]. Additionally, many CHD patients have a very strong health awareness and maintain a mindful lifestyle, including a healthy body weight [13].

So far, only limited and conflicting data exist on the prevalence of overweight and obesity in the population with CHD [14]. Therefore, this systematic review elaborates on the prevalence and longitudinal development of overweight and obesity in children and adults with CHD.

Materials and Methods

Search Strategy

A systematic literature search was conducted in the electronic databases PubMed, Cochrane, and Scopus that referred to articles from January 2010 to December 2020. Relevant observational studies in the English language were identified by two independent reviewers.

A standard protocol with search terms was developed according to the population, intervention, comparison, outcome, and context (PICO–C) [15] method and applied in the following combination:

1. “congenital heart disease” OR “congenital heart defect” AND
2. “overweight” OR “obesity” OR “adiposity” OR “body constitution”

Medical Subject Headings terms and filters (published in the previous 10 years, humans, preschool child: 2–5 years, child: 6–12 years, adolescent: 13–18 years, adult: 19+ years) were used and appropriately adapted if necessary.

Data Collection

Two reviewers screened the relevant articles for title and abstract that had to fulfill the basic inclusion criteria: diagnosed CHD and the measurement of overweight and obesity. At least one of the reviewers had to consider a reference eligible; in case of disagreement, a third reviewer was consulted for a majority decision before full-text analysis.

Documenting critical appraisal of the included literature, reviewers used the “Study Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies” of the National Heart, Lung and Blood Institute (NHLBI), consisting of a 14-item list assessing potential risk for bias. Accordingly, included studies were categorized as good, fair, or poor [16].

Results

Study Inclusion

In total, 982 potential studies were identified in the initial search, of which 905 remained after duplicates had been removed. After screening titles and abstracts, 51 potential studies were retrieved for full-text analysis, of which 21 studies were excluded due to: main focus on the impact of overweight and obesity (n=12), lacking focus on overweight and obesity (n=5), focus on underweight (n=1) and not exclusively assessing patients with CHD (n=3). Finally, 30 studies with a total of 21,610 CHD patients met the inclusion criteria for this systematic review. The search algorithm and selection process is displayed in *Figure 1*.

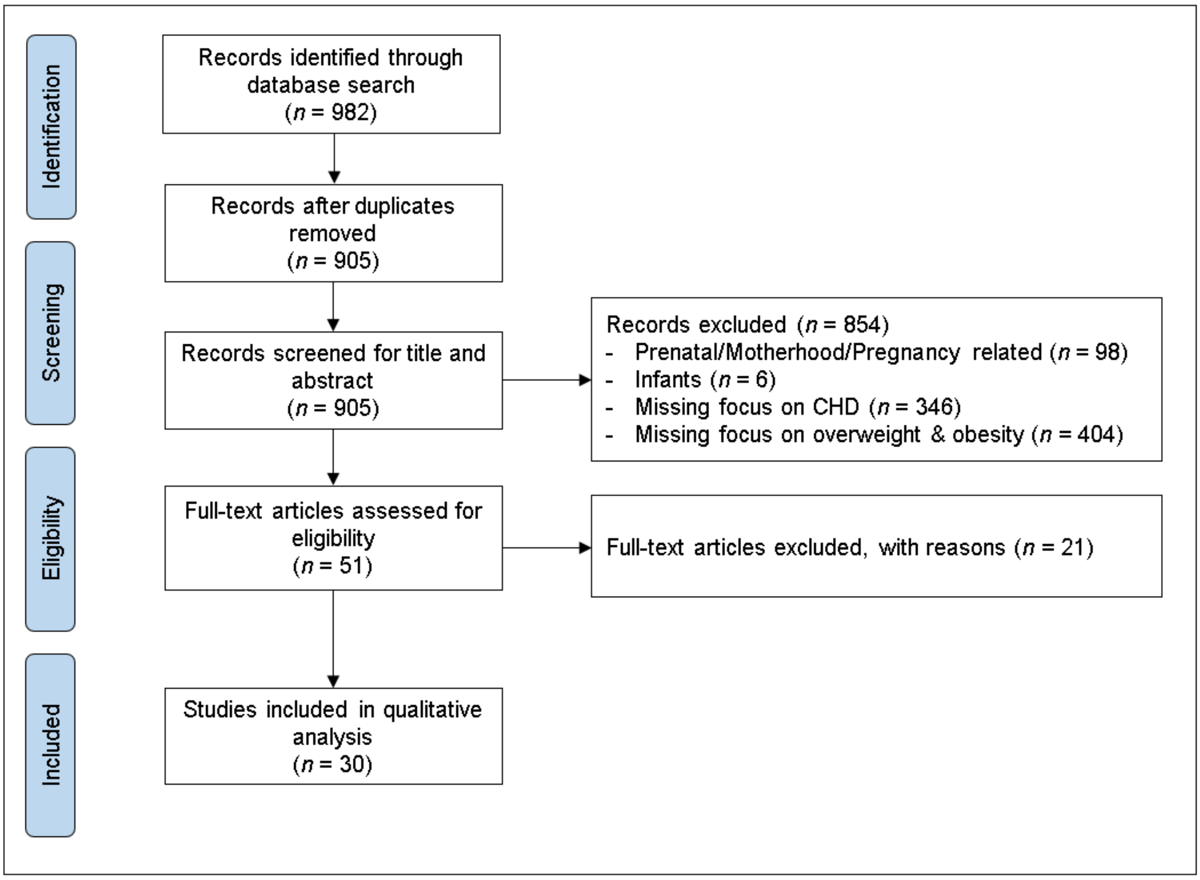

Figure 1: *Search and selection process for systematic review according to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISAM)*

Study Characteristics

Of the included studies, 15 studies evaluated 5680 pediatric patients with CHD (range 32–1080 patients) aged 2–18 years, 9 studies evaluated 6657 ACHD (range 54–2424 patients) aged 18–71 years, and 6 studies examined 9273 both pediatric and ACHD (range 50–4496 patients) aged 2–48 years.

Twenty-six of the included studies were cross-sectional studies that examined the prevalence of overweight and obesity in patients with CHD [17–42], and four were cohort studies that investigated the longitudinal change of the prevalence across the lifespan [10,43–45]. The body composition of patients with CHD was compared to a healthy reference cohort in 13 of the included studies [20–24,28–30,33,35,40,41,45], whereas 9 studies merely investigated the prevalence of overweight and obesity in patients with CHD [10,17–19,24,32,36,38,39]. *Table 1* provides further information on the study characteristics and outcomes of the included studies.

Table 1: *Study characteristics and outcomes*

Study	CHD, n (♀)	Control group, n (♀)	CHD Diagnosis or severity (n)	Age ± SD (range), y	Reference	Body constitution	Prevalence (%) Overweight/ Obesity (Both)	Results
PEDIATRIC CHD (n=15)								
Tamayo et al. 2015 [44]	725 (319)	-	ASD (116), VSD (152), AVSD (116), TGA (138), UVH (73), ToF/DORV (130)	Median age at complete repair 0.6	Center of Disease Control Atlanta	*	28 / 17	Proportion of overweight & obesity increased over time (p=.02). Patients with TGA showed higher BMI at any time point compared with other cardiac diagnoses (p<.001).
Wellnitz et al. 2015 [10]	84 (40)	-	undergoing Fontan palliation	At Fontan surgery: 4.72 (IQR: 3.51-5.14)	Centers for Disease Control	*	(*Fontan:* 10.7 *1y after*: 20.3 *5y after*: 30)	*Time of Fontan*: lower percentage of overweight/obesity compared with US children (10.7% versus 30.4%). *1y after Fontan*: overweight/obese children increased to 20.3%. *5y after Fontan:* increased to 30%. Increase in BMI after Fontan significantly associated with Hispanic ethnicity (p<.001).
Powell et al. 2020 [35]	47 (22)	165 (86) age-matched	Fontan circulation	15.0 ± 3.1	-	BIA	23 / -	Patients with Fontan had similar BMI as normal controls, but had higher body fat percentage (p=.03), lower lean muscle mass (p=.005) and skeletal muscle mass (p=.004).
O'Byrne et al. 2018 [32]	253 (106)	-	ToF (78), TGA (20), Fontan (74)	13.1 ± 2.9	United States Centers for Disease Control	*	15 / 11	Increasing exercise duration was associated with lower BMI (p=.01). Restriction to mild exertion and participation in low-intensity exercise were both associated with increased BMI.
Aguilar et al. 2015 [17]	551 (251)	-	CoA (79), VSD (281), ToF (66), TGA (65), SV (34), HLHS (26)	Median 7.5	Center for Disease Control & Prevention Growth Chart	-		*2-7y:* BMI Z-score increased during early childhood in VSD, and ♀ patients with CoA or HLHS. *8-15y:* BMI Z-score increased in those with CoA and ToF. *2-20y:* BMI Z-score gain between 2-20y was increased in CoA (♀ only), HLHS (♀ only) VSD, and decreased in SV (♀only) and TGA.

Barbour-Tuck et al. 2020 [20]	32 (12)	23 (10) age- and sex matched	Fontan (7), ToF (5), HT (4), TGA (3), ASD (2), PS (2), VSD (1), CoA (2), AS (1), TA (1), CM (2), DORF(2)	10.9 ± 2.6	-	WC & DXA	Mean BMI 18.9 ± 4.7 kg/m^2	CHD participants had a significantly greater waist circumference than controls when controlling for sex, birthweight, physical activity, and total lean mass. CHD and control groups were similar in BMI, total fat mass, total lean mass, percent fat mass, percent lean mass.
Welisch et al. 2013 [40]	1,080 (483)	1,083 (472)	VSD, ASD, PDA (146); Fallot, TGA, TAC, VD, AVSD, CoA (369); VD (271), F&M&S (40), Shunt (227), other (27)	9.0 ± 4.7	Center for Disease Control and Prevention BMI curve	*	(18.2)	No significant difference concerning weight category between CHD and healthy controls. No difference in overweight/obesity prevalence between operated and non-operated CHD. Age and gender no risk factor for being overweight/obese.
Barbiero et al. 2014 [19]	316 (140)	-	VSD (76), ASD (61), ToF (43), PA (6), others (130)	2-5y: 67 6-11y: 138 12-18y: 111	according to the WHO-2006/07	*	17.4 / 9.5	Excess weight was more common among ♂ (60%). Family history of obesity was associated with excess weight (p=.001). In patients with cyanotic lesions overweight less frequent than in acyanotic (23.3% vs. 27.7%).
Briston et al. 2017 [21]	137 (66)	1:1 age-matched controls	ToF	NR	-	**	19 / 19	In the first 5y of age and in the first 5y postoperatively the ToF cohort had a significantly lower BMI compared with the control group (p=0.042 and p =0.028). Afterwards no sig. difference between CHD & healthy controls (p =0.079).
Chen et al. 2012 [23]	*Child:* 705 (368) *Adoles-cent:* 219 (192)	*Child:* 18,753 (7798) *Adoles-cent:* 15,014 (7,666)	VSD (319), ASD II (209), PVD(99), PDA(72), AVD (38), CAVF(15), ToF(65) ECD(17), TGA(14), VSD with CoA (13), CoA (12), VSD with R (12), PA (7), EBS (8), Other (22)	*Child:* 6.4±0.5 *Adolescent:* 15.5±0.6	Nutrition and Health Survey in Taiwan	*	(Child: 14.5, Adolescent: 26.5%)	The prevalence of overweight/obesity in CHD adolescents close to controls. In ♀ fewer CHD children were overweight/obese (12.2% vs. 18.7%, p=0.002). ♂ with moderate to severe CHD had lower prevalence of overweight/obesity (p=.025). Children with cyanotic CHD had significantly lower prevalence of overweight/ obesity (1.5% vs. 15.5%, *P* = 0.003) than those with non-cyanotic.

Perin et al. 2019 [33]	220 (95)	220 (93)	No residual defect(142), residual defects(58), UVH(20)	11.4±2.8	2007 World Health Organization growth charts	*	(35.4)	Higher prevalence of obesity in CHD patients (22.7%) compared to 15.5% in healthy subjects (p=.015). Higher proportion of obese children in the age 6-11 subgroup (28.6%) compared to the age 12-17 subgroup (16%, p=.006).
Ray et al. 2011 [36]	84 (33)	-	Mild (21.5%), Moderate (16.7%), Surgically (40.5%), Complex (21.4%)	12±1.4	Centers for Disease Control and Prevention	*	9.5 / 26.2	% of children who were overweight/obese ranged from 22% to 44%; with the lowest incidence in those with moderate disease or that were surgically corrected and the highest incidence in those with mild disease.
Steele et al. 2019 [39]	968 (419)	-	Cyanotic (232), Repaired or palliated (719), Acyanotic (217), Electrophysiologic (184)	13.3 (8.8-16.4)	Center for Disease Control	*	31.5 / 16.4	Children with overweight/obesity were older (p<.001), had lower median household income (p=.031), and more often complex CHD (p=.008). Children with CHD have increased risk of becoming overweight & obese in early childhood.
Yang et al. 2020 [41]	97 (45)	-	ASD (33), VSD (30), PDA (9), TGA (9), ToF (12), Endocardial cushion defect (4)	9.7±1.5	50th-percentile BMI for Taiwanese children	*	(14.4)	BMI did not differ between CHD and children in the general population. Greater obesity in children with mild heart disease (p=.04). Sedentary behaviors, cardiomegaly, and the NYHA class II-IV were associated with being overweight/obese.
Smith-Parris et al. 2014 [38]	160 (59)	Adult with AS, PS or ASD	Underwent CoA repair	median age at follow-up of 14y (range, 4.6-36.7y)	National Health & Nutrition Examination Survey	*	(47)	At age 5y, patients with CoA had significantly greater BMI z-scores compared with age-sex matched normal data (p<.001). The proportion of excess weight in COA significantly increased over time (p<.001). Adults with repaired COA developed obesity at a greater rate than those with either AS (p=.004) or with PS or ASD (p<.001).

CHILDREN & ADULTS (n=6)								
Chung et al. 2016 [24]	Child: 395 Adult: 129 (58)	-	Fontan circulation	*Child:* 2-5y: 401 6-11y: 333 12-19y:217 *Adult:* 27.8±6.8	Center for Disease Control	*	*Adults:* 22 / 17 (*Children:* 15)	Likelihood of being overweight/obese as an adult was three times higher if there was a BMI ≥85th percentile in childhood (p<.01). Pediatric rates of overweight/obesity comparable to healthy controls. No race or gender differences between overweight/ obese. Overweight/obesity in adulthood associated with lower heart failure rates (4 vs.19%, p=0.03).
Avitabile et al. 2014 [18]	50 (24)	992 healthy controls	Fontan Median 9.3 years from Fontan	Median: 11.5 (5.1-33.5)	2000 National Center for Health growth statistics	DXA	BMI z-Score: 0.15 ± 0.98	BMI Z-scores did not differ between Fontan and healthy controls (0.15 ±0.98 vs 0.35±1.02, p=0.18). Whole body lean mass Z-scores were lower in the Fontan participants compared with reference (p=0.003).
Jackson et al. 2019 [28]	4,496 (2,158)	-	36% simple, 50% moderate, 14% complex	6-12y: 1327 13-18y:1005 19-39y:1312 40+y: 842	Centers for Disease Control and Prevention	**	*White&Black:* <u>*6-12y:*</u> 15/19 & 18/15 <u>13-18y</u>: 18/20 & 21/27 <u>19-39y:</u> 31/27 & 28/42 <u>40+:</u> 34/40 & 32/52	White children with CHD had a higher prevalence of obesity (18.6%) compared to healthy controls (13.8%) (p<0.01). White young adults with CHD had a lower prevalence of obesity (27.4%) as compared with white young controls (31.1%) (p<0.01). No differences between white CHD & healthy adolescents (19.8% vs 20.8%), as well as black CHD survivors of all ages. Blacks with CHD had 58% increased risk of obesity in young adulthood and 33% in late adulthood.
Harris et al. 2018 [26]	*Youth:* 88 (36) *Adult:* 102 (47)	-	*Youth:* 32% mild, 40% moderate, 28% complex *Adult:* 30% mild, 47% moderate, 23% complex	Youth: 17.2±1.1 Adults: 35.4±12.9	International Obesity Task Force criteria	**	*Youth:* 10/ 11 *Adults:* 30/ 22	More adults than youth overweight/obese (52% vs. 22%, p<.001). Group mean BMI and prevalence of weight categories was not different by sex in adults, but in youth, more ♀ than ♂ were overweight/ obese (33% vs 13%, p=.026).

Weinreb et al. 2019 [45]	223 (97)	223 1:1 age, sex & race matched controls	34% simple, 32% moderate, 34% complex	5-11y 95 11-15y: 64 16-20y: 64	Commission for Disease Control BMI	*	(25)	Mean BMI% did not differ between CHD sample and paired controls over a 5y period. Significant increased BMI% change in the age cohort of 5–10y (p=.04), in ♂ sex (p=.01) and status-post surgery (p=.02).
Jackson et al. 2020 [27]	3,790 (1,868)	-	36% simple, 50% moderate, 14% severe	6-18y: 1927 19-39y: 1139 40+y: 724	Center for Disease Control & Prevention	*	*Youth:* 17/ 18 *Young adults:* 30/30 *Adult:* 33/40	Proportion of individuals with overweight/obesity increased with age (p<.001). Higher proportion of individuals with moderate lesion severity (29%) have obesity compared to simple (24%) and complex (18%, p<.001) lesion severity
				ADULTS (n=9)				
Lerman et al. 2017 [29]	1,451 (719)	1,451 (719) age, gender & race-matched	Simple (1,007), Complex (299), Unclassified (145)	52±20	-	**	33.5/25.6	ACHD were equally as likely to be overweight/obese as controls, ACHD decreased prevalence of morbid obesity. Age correlated with increased BMI in ACHD and controls (p<.001). BMI similar across all disease severity groupings. Hispanic patients were more likely to be obese than white patients (p=.02) & controls (p=.01).
Buys et al. 2013 [22]	103 (33)	-	CoA	28.7±6.3	Belgian health survey	**	♂: 27/7 ♀:18/12	Weight status was similar to the overall Belgian population, with a tendency toward higher BMI. Tendency towards higher incidence in obesity in ♀ patients.
Lui et al. 2017 [8]	178 (87)	-	Fallot (26%), TGA (20%), Fontan with UVH (15%)	37.1±12.6	-	**	53/21	Excess adiposity was the most common risk factor for developing atherosclerotic cardiovascular disease in ACHD.
Pike et al. 2012 [34]	54 (28)	66 age, family, ethnicity, region, sex, education	Fontan	26±9	Center for Disease Control	*	(21)	No sex differences in BMI in the SVCHD group. Patients >21y higher BMI compared with patients ≤ 21 years of age (p=.01).
Fedchenko et al. 2019 [25]	72 (30)	-	CoA	median 43.5 (20-71)	-	**	38.9/9.7	Cardiovascular risk factors are prevalent among patients with CoA.

Zaqout et al. 2019 [42]	539 (248)	1,737 (896) from Belgium	VSD(78), ASD(54), VPS (30), PDA (14), MVD (9), AS/AR (86), CoA/VSD (73), TOF (74), AVSD (34), TGA (14), TGA/ ASO (16), TCPC (30), TrA (6), PA/DORV (21)	32.0±9.3	-	**	23.7/10	ACHD patients had lower BMI than healthy controls (p=.012). BMI was positively associated with age (*p*<.001). Men in the mild & severe group (p=.007; p=.023) and women in the severe group (*p*<.001) had lower BMI compared to the reference group. Men with VSD, CoA and Fontan and women with Fontan had lower BMI than controls.
Deen et al. 2016 [43]	448 (230)	448 sex & age matched	ToF (95), VD (86), AAA (77), TGA (51), Fontan (43), VSD (21), AVSD (21), CAA (8), ccTGA(20), APVR (20), EBS (16), ASD (11), TAC (7), EM (8), PA (8), other (51)	32.4±11.3	International Diabetes Foundation Criteria	**	- /16.1	Obesity rate was similar between matched ACHD and healthy controls. Metabolic syndrome was more common in ACHD patients than in controls (15.0% versus 7.4%). Obese ACHD patients more likely to have metabolic syndrome than obese controls (93.1% vs. 44%).
Sandberg et al. 2015 [37]	2,424 (1,021)	4,605 age-stratified	Fontan (97), AS (122), ToF (238), PA/DORV (81), CoA (414), VSD (497), ASD (414), AS/AR (561)	18-50y	-	**	*Simple:* 24.0 ± 4.6 kg/m^2 *Complex:* 22.6 ± 4.2 kg/m^2	Men with PA/DORV, AS/AR and Fontan/TCPC had a lower prevalence of overweight/obesity (p<.001) than healthy controls. No differences in BMI in CoA, VSD, ASD or AS/AR and intervention vs. no intervention. *Complex lesions:* age & cardiovascular medication associated with a lower BMI. *Simple lesion*: age, impaired NYHA class and cardiovascular medication associated with higher BMI.
Malavazos et al. 2019 [31]	1,388 (776)	145,992 sex & age-stratified	Septal heart defects & left-to-right shunt (864), conotruncal heart disease (209), valve defects & aortic defects (247), UVH (68)	41.5±13.2	-	**	26.7/ 9.6	Lower prevalence of overweight in ACHD (27%) and in great complexity class (16%) compared to Italian reference (32%). In great complexity class prevalence of obesity significantly lower (3.1%). Men more likely to be overweight than women in ACHD population (34.64% vs 20.49%). Overweight/Obesity increased with age.

AAA, aortic arch anomalies; APVR, Anomalous pulmonary venous return; AS, aortic valve stenosis; AS/AR, aortic regurgitation or Ross procedure; ASD, atrial septal defect; ASO, arterial switch operation; AVD, aortic valve disease; AVSD, atrioventricular septal defect; BIA, bioelectrical impedance analysis; BMI, body mass index; CAA, coronary artery anomaly; CAVF, Coronary arterio-venous fistula; CHD, congenital heart disease; CM, cardiomyophathy; CoA, coarctation of the aorta; DORV, double outlet right ventricle; DXA, Dual energy X-ray absorptiometry; EBS; Ebstein; EM, Eisenmenger; F&M&S, Fontan & Mustard & Senning; HLHS, hypoplastic left heart syndrome; HT, heart transplantation; IQR, interquartile range; MVP, mitral valve disease; NR, not reported; PA, pulmonary atresia; PDA, patent ductus arteriosus; perc., percentile; PS, pulmonary valve stenosis; PVD, pulmonary valve disease; R, regurgitation; SD, standard deviation; SV, single ventricle physiology; TA, tricuspid atresia; TGA, transposition of the great arteries; ToF, tetralogy of Fallot; TrA, truncus arteriosus; UVH, uni-ventricular heart; VD, valvar disease; VPS, valvular pulmonary stenosis; VSD, ventricular septal defect; WC, waist circumference; y, year; *: Overweight: BMI ≥85th-95th perc.; Obesity: BMI ≥95th perc.; **: Overweight: BMI 25–29.9 kg/m^2; Obesity: BMI ⩾30 kg/m^2; Morbidly obese: BMI ≥ 40 kg/m^2.

Measuring Overweight & Obesity

All included studies assessed overweight and obesity with the body mass index (BMI), while two studies additionally performed dual x-ray absorptiometry [18,20], one study performed impedance measurement [35], and one study assessed waist circumference [20]. Based on the BMI, patients were classified as underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2), obese (≥30 kg/m^2) and severe obese (≥35 kg/m^2). BMI values were converted into age and gender-specific z-Scores in a subset of studies [10,17,18,38,40]. Fourteen studies converted the BMI into percentiles based on various growth charts, classifying patients with BMI ≥85th–<95th percentile as overweight and those with BMI ≥95th percentile as obese [10,19,23,24,32–34,36,38–41,43,45].

Study Quality

According to the NHLBI study quality assessment tool [16], 15 studies received the quality rating "good", while 9 studies were rated as "fair". Six studies showed a substantial risk of bias and were rated as "poor". Various contributing factors have an impact on weight status and should therefore be considered when investigating the prevalence of overweight and obesity. The included studies in this review controlled for age [21,24,35,37,39], age and lesion severity [27], age and sex [10,17,18,20,23,28,31,33,36,38,40,41,43,44], race/ethnicity [29,45], family history, parent's nutritional status [19], marital status, educational level, and geographic region [34]. Six studies did not take confounders into account and were therefore rated as "poor" [8,22,25,26,37,42]. Comprehensive information on the quality rating can be found in *Table 2*.

Table 2: *Quality assessment according to the NHLBI Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies*

Study	Type	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Quality
							Pediatric CHD (n=15)									
Barbour-Tuck et al. 2020 [20]	CSS	✓	✓	CD	-	-	-	-	✓	-	-	✓	-	NA	✓	Fair
Powell et al. 2020 [35]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	-	✓	-	NA	✓	Good
Yang et al. 2020 [41]	CSS	✓	✓	-	✓	-	-	-	✓	✓	-	✓	-	NA	✓	Fair
Perin et al. 2019 [33]	CSS	✓	✓	✓	-	-	-	-	✓	✓	-	✓	-	NA	✓	Fair
Steele et al. 2019 [39]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	✓	✓	-	NA	✓	Good
O'Byrne et al. 2018 [32]	CSS	✓	✓	✓	✓	✓	-	-	-	✓	-	✓	-	NA	✓	Fair
Briston et al. 2017 [21]	CSS	✓	✓	CD	✓	-	-	-	✓	✓	-	✓	-	NA	✓	Good
Aguilar et al. 2015 [17]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	✓	✓	-	NA	✓	Good
Tamayo et al. 2015 [44]	CS	✓	✓	CD	✓	-	✓	✓	✓	✓	✓	✓	-	NA	✓	Good
Wellniz et al. 2015 [10]	CS	✓	✓	-	✓	-	✓	✓	-	✓	✓	✓	-	NR	✓	Fair
Barbiero et al. 2014 [19]	CSS	✓	✓	CD	✓	✓	-	-	-	✓	-	✓	-	NA	✓	Fair
Smith-Parrish et al. 2014 [38]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	✓	✓	-	NA	✓	Good
Welisch et al. 2013 [40]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	NA	✓	-	NA	✓	Good
Chen et al. 2012 [23]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	-	✓	-	NA	✓	Good
Ray et al. 2011 [36]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	-	✓	-	NA	✓	Fair
							Pediatric & ACHD (n=6)									
Jackson et al. 2020 [27]	CSS	✓	-	CD	✓	-	-	-	-	✓	NA	✓	-	NA	✓	Fair
Jackson et al. 2019 [28]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	-	✓	-	NA	✓	Good
Weinreb et al. 2019 [45]	CS	✓	✓	✓	✓	-	✓	✓	✓	✓	✓	✓	-	NA	✓	Good
Harris et al. 2018 [26]	CSS	✓	✓	CD	✓	-	-	-	✓	✓	NA	✓	-	NA	-	Poor
Chung et al. 2016 [24]	CSS	✓	✓	CD	✓	-	-	-	✓	✓	✓	✓	-	NA	✓	Good
Avitabile et al. 2014 [18]	CSS	✓	✓	CD	✓	-	-	-	✓	✓	-	✓	-	NA	✓	Fair
							ACHD (n=9)									
Fedchenko et al. 2019 [25]	CSS	✓	✓	-	✓	-	-	-	-	✓	-	✓	-	NA	-	Poor
Malavazoz et al. 2019 [31]	CSS	✓	✓	CD	✓	-	-	-	✓	✓	NA	✓	-	NA	✓	Good
Zaqout et al. 2019 [42]	CSS	✓	✓	✓	-	-	-	-	✓	✓	-	✓	-	NA	-	Poor
Lerman et al. 2017 [29]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	NA	✓	-	NA	✓	Good

Lui et al. 2017 [8]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	-	✓	-	NA	-	Poor
Deen et al. 2016 [43]	CS	✓	✓	✓	-	-	✓	NA	✓	✓	NA	✓	-	NA	✓	Good
Sandberg et al. 2015 [37]	CSS	✓	✓	✓	✓	-	-	-	✓	✓	NA	✓	-	NA	-	Poor
Buys et al. 2013 [22]	CSS	✓	✓	✓	✓	-	-	-	NA	✓	NA	✓	-	✓	-	Poor
Pike et al. 2012 [34]	CSS	✓	✓	CD	✓	-	-	-	✓	✓	-	✓	-	NA	✓	Good

ACHD: adults with congenital heart disease, CD: cannot determine, CHD: congenital heart disease, CS: cohort study, CSS: cross-sectional study, NA: not applicable, NR: not reported, ✓ denotes “Yes”, - denotes “No”

Overweight and Obesity in Children with CHD

In children with CHD, the prevalence of overweight ranged from 9.5% [36] to 31.5% [39] and the prevalence of obesity ranged from 9.5% [19] to 26.2% [36]. Studies comparing children with CHD to healthy controls reported similar overweight and obesity prevalence in both groups [18,20,21,24,33,35,40,41,45], whereby controls were age-matched [21,35], age and sex matched [20], and age, sex and race/ethnicity matched [45]. One study reported decreased BMI in CHD children [23], whereas another study reported increased obesity rates in CHD children compared to healthy controls [33]. CHD participants had a significantly greater waist circumference than controls when controlling for sex, birth weight, physical activity score, and total lean mass [20]. Overweight and obesity occurred more frequently in CHD boys than in girls [19,23]. There was no association between overweight and obesity prevalence and CHD severity or surgical status in CHD children [26,40]. Children with cyanotic CHD had a lower prevalence of overweight and obesity than those with non-cyanotic CHD [19,23]. Significantly lower BMI values were found in children with tetralogy of Fallot five years after surgery compared to age-matched controls [21]. Patients with Transposition of the Great Arteries and Coarctation of the Aorta showed significantly higher BMI compared with norm data and other cardiac diagnoses [38,44]. Studies on Fontan children reported a lower prevalence of overweight and obesity at the time of Fontan procedure, which increased to 30% five years post-surgery [10], but showed no significant difference to healthy controls [35].

Overweight and Obesity in Adults with CHD

In adults with CHD, overweight prevalence was found in a range from 22% [24] to 53% [30], while obesity was reported in a range between 7% [22] and 26% [29]. Studies comparing overweight and obesity prevalence with healthy controls found either similar overweight and obesity rates [22,29,43] or lower prevalence compared to the reference cohort [31,42]. However, ACHD showed a decreased prevalence of morbid obesity compared to matched controls [29]. Two studies found no association between CHD severity and prevalence of overweight and obesity [26,29], whereas two other studies reported a reduced prevalence in the more complex classes like total cavopulmonary connection compared to the reference population [31,42]. One study on ACHD reported men being more overweight than women [31], while another study found no sex differences [34]. Hispanic patients were more likely to be obese than white ACHD after adjusting for age and gender [29]. Non-Hispanic Blacks with CHD had a 58% increased risk of obesity in young adulthood and 33% in late adulthood compared to white CHD [28]. BMI was positively associated with impaired NYHA class and cardiovascular medication intake [42]. Metabolic syndrome was more common in ACHD patients than in controls, and obese ACHD patients were more likely to have metabolic syndrome than obese controls [43].

Longitudinal Development of Overweight and Obesity

The number of overweight and obese children increased during adolescence [27,44]. Also, in adults with CHD, age correlated with increased BMI [29,31,34,42], with similar results found in the general population [29,31]. Generally, adults had significantly higher BMI scores and were more likely to be overweight or obese compared with younger samples [26]. The odds of being overweight or obese as an adult were found to be three times higher if their childhood BMI was already above the 85th percentile [24].

Discussion

This systematic review shows that the overall distribution of overweight and obesity is consistent with the prevalence in the general population, in which overweight and obesity rates have increased dramatically in recent decades [37]. Particularly, CHD patients with increasing age, male gender, and Hispanic origin are at risk for overweight and adiposity.

These findings are worrisome, as the CHD population is at higher risk of developing metabolic syndrome and premature morbidity and mortality compared to their healthy peers [43]. Obesity is associated with an increased risk of cardiovascular diseases, like heart failure and coronary artery disease [46]. Excessive body adipose tissue impacts the vessel wall by changes in blood pressure, glucose level, lipid metabolism, and systemic inflammation [47]. In children and adults with CHD, overweight and obesity were shown to be associated with cardiac comorbidities, increased cardiac medication intake, and higher systolic and diastolic blood pressure compared to normal-weight patients. According to this recently published study, the elevated risk of morbidity and mortality in the CHD population is exacerbated by obesity [27]. Obesity has been associated with adverse perioperative outcomes [48] as well as adverse short-term outcomes after cardiothoracic surgery in patients with CHD [49]. In contrast, another study on ACHD reported that overweight and moderate obesity were associated with reduced mortality rates, especially in symptomatic ACHD patients and those with complex underlying cardiac defects, replicating the so-called “obesity paradox” in the general population [14]. It was also shown that overweight and obesity are associated with lower heart failure rates in ACHD [24]. In the elderly, this may indeed be true, as a slightly elevated weight above normal BMI can be a resource to build upon when facing surgical procedures or beginning aggressive drug therapy. However, overweight and obesity are among the most significant contributors to illness and adverse health outcomes and should be prevented or reduced at all costs, at least in younger patients with CHD.

Underlying causes and effects of the high overweight and obesity prevalence in the CHD population are multifactorial. Heart failure-associated reasons such as medication intake were identified along with the already mentioned behavioral factors. Two major factors influencing the CHD population are physical inactivity due to restrictions or overprotection by physicians and parents, as well as weight gain interventions in infancy, which can develop into excess weight later in life [17]. Part of the included studies examined the association between overweight and obesity and contributing factors. Yang et al. reported an association between sedentary behavior and increased overweight and obesity prevalence in CHD children [41]. BMI has been shown to be negatively associated with exercise duration [32] and exercise capacity in the CHD population [42]. Continuous monitoring of weight status and interventions to reduce the prevalence of overweight and obesity are required in this patient cohort at high risk for acquired cardiovascular disease [37]. Interventions such as lifestyle and nutritional counseling to reduce risk factors for obesity should begin in early childhood and include parental education.

Limitations and Further Research

The classification of overweight and obesity in the majority of included studies refers to the BMI, which, however, does not analyze fat distribution and body composition. Abdominal fat, in particular, has been associated with various pathologies [45]. Therefore, further studies should specifically address abdominal fat in order to quantify the visceral component of adipose tissue [31]. Moreover, BMI is based on both fat mass and lean mass and therefore carries the risk of classifying muscular patients as overweight [37]. The majority of included studies have not considered race and ethnicity as potential confounders, even though their influence on weight status is well established [44].

Conclusions

The prevalence of overweight and obesity in children and adults with CHD reflects that of the general population, demonstrating that the growing obesity pandemic is also affecting the CHD population. Such a high prevalence of overweight and obesity is particularly worrying in the context of CHD. We hope that these results will raise awareness of this issue and encourage appropriate health-promoting interventions and individual consultation.

References

[1] Ng, M.; Fleming, T.; Robinson, M.; Thomson, B.; Graetz, N.; Margono, C.; Mullany, E.C.; Biryukov, S.; Abbafati, C.; Abera, S.F.; et al. Global, regional, and national prevalence of over-weight and obesity in children and adults during 1980–2013: A systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014, 384, 766–781.

[2] Swinburn, B.A.; Sacks, G.; Hall, K.D.; McPherson, K.; Finegood, D.T.; Moodie, M.; Gortmaker, S.L. The global obesity pandemic: Shaped by global drivers and local environments. Lancet 2011, 378, 804–814.

[3] Ogden, C.L.; Carroll, M.D.; Lawman, H.G.; Fryar, C.D.; Kruszon-Moran, D.; Kit, B.K.; Flegal, K.M. Trends in obesity prevalence among chil-dren and adolescents in the United States, 1988–1994 through 2013–2014. JAMA 2016, 315, 2292–2299.

[4] Suchindran, C.; North, K.E.; Popkin, B.M.; Gordon-Larsen, P. Association of Adolescent Obesity With Risk of Severe Obesity in Adulthood. JAMA 2010, 304, 2042–2047.

[5] Lim, S.S.; Vos, T.; Flaxman, A.D.; Danaei, G.; Shibuya, K.; Adair-Rohani, H.; AlMazroa, M.A.; Amann, M.; Anderson, H.R.; Andrews, K.G. A comparative risk assessment of burden of dis-ease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: A systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012, 380, 2224–2260.

[6] Khairy, P.; Ionescu-Ittu, R.; Mackie, A.; Abrahamowicz, M.; Pilote, L.; Marelli, A.J. Changing Mortality in Congenital Heart Disease. J. Am. Coll. Cardiol. 2010, 56, 1149–1157.

[7] St-Pierre, J.; Poirier, P. What Nature Used to Allow to Die, Don’t Let Modern Habits Damage After Repair: Preventable Obesity Risk in Congenital Heart Disease. Can. J. Cardiol. 2015, 31, 109–111.

[8] Lui, G.K.; Fernandes, S.; McElhinney, D.B. Management of Cardiovascular Risk Factors in Adults With Congenital Heart Disease. J. Am. Hear. Assoc. 2014, 3, e001076.

[9] Verheugt, C.L.; Uiterwaal, C.S.P.M.; Van Der Velde, E.T.; Meijboom, F.J.; Pieper, P.G.; van Dijk, A.; Vliegen, H.W.; Grobbee, D.E.; Mulder, B.J. Mortality in adult congenital heart disease. Eur. Hear. J. 2010, 31, 1220–1229.

[10] Wellnitz, K.; Harris, I.S.; Sapru, A.; Fineman, J.R.; Radman, M. Longitudinal development of obesity in the post-Fontan population. Eur. J. Clin. Nutr. 2015, 69, 1105–1108.

[11] Diller, G.-P.; Kempny, A.; Alonso-Gonzalez, R.; Swan, L.; Uebing, A.; Li, W.; Babu-Narayan, S.; Wort, S.J.; Dimopoulos, K.; Gatzoulis, M.A. Survival Prospects and Circumstances of Death in Contemporary Adult Congenital Heart Disease Patients Under Follow-Up at a Large Tertiary Centre. Circulation 2015, 132, 2118–2125.

[12] Costello, C.L.; Gellatly, M.; Daniel, J.; Justo, R.N.;Weir, K. Growth Restriction in Infants and Young Children with Congenital Heart Disease. Congenit. Hear. Dis. 2015, 10, 447–456.

[13] Zomer, A.C.; Vaartjes, I.; Uiterwaal, C.S.; van der Velde, E.T.; Sieswerda, G.-J.T.; Wajon, E.M.; Plomp, K.; van Bergen, P.F.; Verheugt, C.L.; Krivka, E.; et al. Social Burden and Lifestyle in Adults With Congenital Heart Disease. Am. J. Cardiol. 2012, 109, 1657–1663.

[14] Brida, M.; Dimopoulos, K.; Kempny, A.; Liodakis, E.; Alonso-Gonzalez, R.; Swan, L.; Uebing, A.; Baumgartner, H.; Gatzoulis, M.A.; Diller, G.-P. Body mass index in adult congenital heart disease. Heart 2017, 103, 1250–1257.
[15] Uman, L.S. Systematic reviews and meta-analyses. J. Can. Acad. Child. Adolesc. Psychiatry 2011, 20, 57.
[16] National Heart, Lung, and Blood Institute. Quality Assessment Tool for Observational Cohort and Cross-Sectional Studies 2014. Available online: https://www.nhlbi.nih.gov/health-topics/study-quality-assessment-tools (accessed on 1 June 2021).
[17] Aguilar, D.C.; Raff, G.W.; Tancredi, D.; Griffin, I.J. Childhood growth patterns following congenital heart disease. Cardiol. Young 2015, 25, 1044–1053.
[18] Avitabile, C.M.; Leonard, M.B.; Zemel, B.S.; Brodsky, J.L.; Lee, D.; Dodds, K.; Hayden-Rush, C.; Whitehead, K.K.; Goldmuntz, E.; Paridon, S.M.; et al. Lean mass deficits, vitamin D status and exercise capacity in children and young adults after Fontan palliation. Heart 2014, 100, 1702–1707.
[19] Barbiero, S.M.; D'Azevedo Sica, C.; Schuh, D.S.; Cesa, C.C.; de Oliveira Petkowicz, R.; Pellanda, L.C. Overweight and obesity in children with congenital heart disease: Combination of risks for the future? BMC Pediatrics 2014, 14, 1–6.
[20] Barbour-Tuck, E.; Boyes, N.G.; Tomczak, C.R.; Lahti, D.S.; Baril, C.L.; Pockett, C.; Runalls, S.; Kakadekar, A.; Pharis, S.; Bradley, T.J.; et al. A cardiovascular disease risk factor in chil-dren with congenital heart disease: Unmasking elevated waist circumference-a CHAMPS* study *CHAMPS: Children's Healthy-Heart Activity Monitoring Program in Saskatchewan. BMC Cardiovasc. Disord. 2020, 20, 1–10.
[21] Briston, D.A.; Sabanayagam, A.; Zaidi, A.N. Observations on obesity patterns in tetralogy of Fallot patients from childhood to adulthood. Cardiol. Young 2017, 27, 890–894.
[22] Buys, R.; Budts, W.; Delecluse, C.; Vanhees, L. Exercise Capacity, Physical Activity, and Obesity in AdultsWith Repaired Aortic Coarctation. J. Cardiovasc. Nurs. 2013, 28, 66–73.
[23] Chen, C.-A.; Wang, J.-K.; Lue, H.-C.; Hua, Y.-C.; Chang, M.-H.; Wu, M.-H. A Shift from Underweight to Overweight and Obesity in Asian Children and Adolescents with Congenital Heart Disease. Paediatr. Périnat. Epidemiol. 2012, 26, 336–343.
[24] Chung, S.T.; Hong, B.; Patterson, L.; Petit, C.J.; Ham, J.N. High Overweight and Obesity in Fontan Patients: A 20-Year History. Pediatr. Cardiol. 2016, 37, 192–200.
[25] Fedchenko, M.; Mandalenakis, Z.; Dellborg, H.; Hultsberg-Olsson, G.; Björk, A.; Eriksson, P.; Dellborg, M. Cardiovascular risk factors in adults with coarctation of the aorta. Congenit. Hear. Dis. 2019, 14, 549–558.
[26] Harris, K.C.; Voss, C.; Rankin, K.; Aminzadah, B.; Gardner, R.; Mackie, A.S. Modifiable cardiovascular risk factors in adolescents and adults with congenital heart disease. Congenit. Hear. Dis. 2018, 13, 563–570.
[27] Jackson, J.L.; Fox, K.R.; Cotto, J.; Harrison, T.M.; Tran, A.H.; Keim, S.A. Obesity across the lifespan in congenital heart disease survivors: Prevalence and correlates. Heart Lung 2020, 49, 788–794.
[28] Jackson, J.L.; Harrison, T.; Keim, S. Differences in Obesity Among Black and White Children, Adolescents, and Adults With Congenital Heart Disease. J. Cardiovasc. Nurs. 2019, 34, 71–75.

[29] Lerman, J.B.; Parness, I.A.; Shenoy, R.U. Body Weights in Adults With Congenital Heart Disease and the Obesity Frequency. Am. J. Cardiol. 2017, 119, 638–642.

[30] Lui, G.K.; Rogers, I.S.; Ding, V.Y.; Hedlin, H.K.; MacMillen, K.; Maron, D.J.; Sillman, C.; Romfh, A.; Dade, T.C.; Haeffele, C.; et al. Risk Estimates for Atherosclerotic Cardiovascular Disease in AdultsWith Congenital Heart Disease. Am. J. Cardiol. 2017, 119, 112–118.

[31] Malavazos, A.; Capitanio, G.; Chessa, M.; Matelloni, I.A.; Milani, V.; Stella, E.; Al Kassem, L.; Sironi, F.; Boveri, S.; Giamberti, A.; et al. Body mass index stratification in hospitalized Italian adults with congenital heart disease in relation to complexity, diagnosis, sex and age. Nutr. Metab. Cardiovasc. Dis. 2019, 29, 367–377.

[32] O'Byrne, M.L.; McBride, M.G.; Paridon, S.; Goldmuntz, E. Association of Habitual Activity and Body Mass Index in Survivors of Congenital Heart Surgery: A Study of Children and AdolescentsWith Tetralogy of Fallot, Transposition of the Great Arteries, and Fontan Palliation. World J. Pediatr. Congenit. Hear. Surg. 2018, 9, 177–184.

[33] Perin, F.; Blesa, C.C.; Cobo, I.; Maldonado, J. Overweight and obesity in children treated for congenital heart disease. An. de Pediatría 2018, 90, 102–108.

[34] Pike, N.A.; Evangelista, L.; Doering, L.V.; Eastwood, J.-A.; Lewis, A.B.; Child, J.S. Sex and Age Differences in Body-Image, Self-Esteem, and Body Mass Index in Adolescents and Adults After Single-Ventricle Palliation. Pediatr. Cardiol. 2012, 33, 705–712.

[35] Powell, A.W.; Wittekind, S.G.; Alsaied, T.; Lubert, A.M.; Chin, C.; Veldtman, G.R.; Cordina, R.; Katz, D.A.; Mays, W.A.; Knecht, S.K.; et al. Body Composition and Exercise Performance in Youth With a Fontan Circulation: A Bio-Impedance Based Study. J. Am. Hear. Assoc. 2020, 9, e018345.

[36] Ray, T.D.; Green, A.; Henry, K. Physical activity and obesity in children with congenital cardiac disease. Cardiol. Young 2011, 21, 603–607.

[37] Sandberg, C.; Rinnström, D.; Dellborg, M.; Thilén, U.; Sörensson, P.; Nielsen, N.E.; Christersson, C.; Wadell, K.; Johansson, B. Height, weight and body mass index in adults with congenital heart disease. Int. J. Cardiol. 2015, 187, 219–226.

[38] Smith-Parrish, M.; Yu, S.; Rocchini, A. Obesity and Elevated Blood Pressure following Repair of Coarctation of the Aorta. J. Pediatr. 2014, 164, 1074–1078.e1.

[39] Steele, J.M.; Preminger, T.J.; Erenberg, F.G.;Wang, L.; Dell, K.; Alsaied, Zahka, K.G. Obesity trends in children, adolescents, and young adults with congenital heart disease. Congenit. Hear. Dis. 2019, 14, 517–524.

[40] Welisch, E.; Rauch, R.; Seabrook, J.A.; Filler, M.G.; Norozi, K. Are the children and adolescents with congenital heart disease living in Southwestern Ontario really overweight and obese? Cardiol. Young 2013, 24, 848–853.

[41] Yang, F.-L.; Gau, B.-S.; Yang, H.-L.; Lin, M.-T.; Moons, P. Energy Balance-Related Behaviors and Body Mass Index in Asian School-Aged ChildrenWith Congenital Heart Disease. J. Cardiovasc. Nurs. 2020, 35, 291–299.

[42] Zaqout, M.; Vandekerckhove, K.; Michels, N.; Demulier, L.; Bove, T.; François, K.; de Backer, J.; de Henauw, S.; de Wolf, D. Body mass index in adults with congenital heart disease. Congenit. Hear. Dis. 2019, 14, 479–486.

[43] Deen, J.F.; Krieger, E.; Slee, A.E.; Arslan, A.; Arterburn, D.; Stout, K.K.; Portman, M.A. Metabolic Syndrome in Adults With Congenital Heart Disease. J. Am. Hear. Assoc. 2016, 5, e001132.
[44] Tamayo, C.; Manlhiot, C.; Patterson, K.; Lalani, S.; McCrindle, B.W. Longitudinal evaluation of the prevalence of overweight/obesity in children with congenital heart disease. Can. J. Cardiol. 2015, 31, 117–123.
[45] Weinreb, S.J.; Pianelli, A.J.; Tanga, S.R.; Parness, I.A.; Shenoy, R.U. Risk factors for development of obesity in an ethnically diverse CHD population. Cardiol. Young 2019, 29, 123–127.
[46] Aune, D.; Sen, A.; Norat, T.; Janszky, I.; Romundstad, P.; Tonstad, S.; Vatten, L.J. Body mass index, abdominal fatness, and heart failure incidence and mortality: A systematic review and dose-response meta-analysis of prospective studies. Circulation 2016, 133, 639–649.
[47] Fantuzzi, G.; Mazzone, T. Adipose tissue and atherosclerosis: Exploring the connection. Arterioscler. Thromb. Vasc. Biol. 2007, 27, 996–1003.
[48] O'Byrne, M.L.; Kim, S.; Hornik, C.P.; Yerokun, B.A.; Matsouaka, R.A.; Jacobs, J.P.; Jacobs, M.L.; Jonas, R.A. Effect of obesity and underweight status on perioperative outcomes of congenital heart operations in children, adolescents, and young adults: An analysis of data from the society of thoracic surgeons database. Circulation 2017, 136, 704–718.
[49] Garcia, R.U.; Balakrishnan, P.L.; Aggarwal, S. Does obesity affect the short-term outcomes after cardiothoracic surgery in adolescents with congenital heart disease? Cardiol. Young 2020, 30, 372–376.

2.6 Association between Objectively Measured Physical Activity and Arterial Stiffness in Children with Congenital Heart Disease (Scientific Publication II)

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The authors declare no conflict of interest.

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The PhD candidate is the principal author of this paper. Along with Leon Brudy she sampled the data at the German Heart Center Munich. Under the supervision of Jan Müller, she was responsible for the data analyses and drafted the manuscript. Renate Oberhoffer-Fritz and Peter Ewert gave important feedback for further improvement of the manuscript. Laura Willinger under supervision of Jan Müller handled the submission process until final publication.

Abstract

Background: The association between physical activity (PA) and arterial stiffness is particularly important in children with congenital heart disease (CHD) who are at risk for arterial stiffening. The aim of this study was to examine the association between objectively measured PA and arterial stiffness in children and adolescents with CHD.

Methods: In 387 children and adolescents with various CHD (12.2 ± 3.3 years; 162 girls) moderate-to-vigorous PA (MVPA) was assessed with the "Garmin vivofit jr." for 7 consecutive days. Arterial stiffness parameters including pulse wave velocity (PWV) and central systolic blood pressure (cSBP) were non-invasively assessed by oscillometric measurement via Mobil-O-Graph®.

Results: MVPA was not associated with PWV (ß=−0.025, $p=0.446$) and cSBP (ß=−0.020, $p=0.552$) in children with CHD after adjusting for age, sex, BMI z-score, peripheral systolic blood pressure, heart rate and hypertensive agents. Children with CHD were remarkably active with 80% of the study population reaching the WHO recommendation of average 60 min of MVPA per day. Arterial stiffness did not differ between low-active and high-active CHD group after adjusting for age, sex, BMI z-score, peripheral systolic blood pressure, heart rate and hypertensive agents (PWV: $F=0.530$, $p=0.467$; cSBP: $F=0.843$, $p=0.359$).

Conclusion: In this active cohort, no association between PA and arterial stiffness was found. Longer exposure to the respective risk factors of physical inactivity might be necessary to determine an impact of PA on the vascular system.

Introduction

Children with congenital heart disease (CHD) are at high cardiovascular risk as a consequence of their congenital condition. Hence, risk stratification and the identification of modifiable risk factors is particularly important [1]. Pulse wave velocity (PWV) and central systolic blood pressure (cSBP) are surrogate measures of arterial stiffness [2] and strong predictors for cardiovascular and all-cause morbidity and mortality [3–5]. Measures of arterial stiffness were shown to be increased already in children with CHD, predisposing this patient cohort to premature heart failure [6,7]. Physical activity (PA) is a clinically important modifiable risk factor for preventing arterial stiffening of the vessels and for determining risk of cardiovascular disease in children with CHD. The importance of PA in children and adolescents with CHD has been emphasized frequently in the recent years [8,9], yet the actual level of PA in children with CHD remains uncertain as the reported PA levels vary considerably between different studies [10–13].

In healthy children, the interplay of arterial stiffness and PA has provided contradictory findings [14–19]. Studies investigating the effect of PA on arterial stiffness in children and adolescents with CHD are rare. One study reported of increased arterial stiffness in low-active children with CHD compared to high-active children with CHD and healthy controls [20]. Another study reported of an inverse association between high levels of MVPA and lower aortic PWV in children with CHD [21]. This association is particularly important in the way of preventing cardiovascular disease in this patient cohort who showed reduced elasticity of the vascular system already in childhood [6,7]. Therefore, this study aimed to analyze the association between objectively measured PA and arterial stiffness in a large cohort of children and adolescents with CHD.

Materials and Methods

Study Participants

In a cross-sectional design, objectively measured PA and surrogates of arterial stiffness were assessed in 387 children and adolescents with various CHD (12.2 ± 3.3 years; 162 girls). Study participants were recruited during their routine outpatient visit at the German Heart Center Munich from March 2016 to January 2021. Study participants were free of acute infections or any neurologic diseases and without restriction to sports and exercise. Various CHDs were categorized into five major subgroups. Detailed information on the characteristics of the study population is given in *Table 1*. Part of the data have already been published in a cross-sectional comparison of PA levels with healthy controls [10].

Assessment of Arterial Stiffness

Aortic PWV and cSBP was obtained by a single measurement recording brachial oscillometric blood pressure waves using an automated Mobil-o-Graph® device (I.E.M, Stolberg, Germany) as previously described [22,23]. HMS software version 4.7 with C1 calibration was used. The Mobil-o-Graph® device is non-invasive and has shown good validity and reliability in several studies and is regularly used in the pediatric population [24–27]. PWV and cSBP were calculated by a proprietary algorithm of the device [28,29]. Measurements were performed at the left upper arm in a supine position after 5 minutes of rest with cuff size adjusted for individual arm circumference

Objective Assessment of Physical Activity

PA was objectively assessed with the “Garmin vivofit jr.” device (Garmin Ltd., Olathe, KS, USA), which children wore on their wrist for 7 consecutive days. The “Garmin vivofit jr.” is a wearable that tracks every single minute of moderate-to-vigorous PA (MVPA) and steps throughout the day. The physical activity wearable was shown to be accurate is assessing MVPA and step count [30,31]. Participants and their guardians were asked to transfer the data from the device to a report sheet at the end of each day. Overall, 329 children (85%) provided complete and valid data for objective PA on 7 consecutive days. Data of at least 3 weekdays and 1 weekend day were considered the minimum to calculate a weekly average and were available for another 58 children (15%). According to the WHO guidelines on PA and sedentary behavior published 2020, children and adolescents should do at least an average of 60 min per day of MVPA across the week [32].

Table 1: *Population characteristic of children with congenital heart disease*

Subgroup CHD	n	Sex ♀	Age (years)	BMI z-score	PWV (m/s)	cSBP (mmHg)	MVPA (min/day)	Steps/Day
Total	387	162 (42)	12.2 ± 3.3	-0.32 ± 1.19	4.60 ± 0.44	99.3 ± 10.8	83.3 ± 28.1	9,386 ± 3,090
CHD Diagnosis								
Left heart obstruction	69	21 (30)	12.3 ± 3.3	-0.58 ± 1.18	4.55 ± 0.46	101 ± 13.8	89.2 ± 29.8	9,976 ± 3,387
Right heart obstruction	89	35 (39)	12.1 ± 3.0	-0.44 ± 1.43	4.58 ± 0.42	98.1 ± 10.1	77.2 ± 29.1	9,233 ± 3,084
Isolated shunts	57	31 (54)	12.3 ± 3.5	-0.02 ± 1.05	4.58 ± 0.42	99.8 ± 11.1	83.8 ± 26.0	9,309 ± 2,905
TGA after switch	37	9 (24)	11.8 ± 3.1	-0.12 ± 0.97	4.60 ± 0.38	98.7 ± 10.9	98.3 ± 29.7	11,260 ± 3,460
TCPC	57	19 (33)	12.9 ± 3.5	-0.18 ± 1.03	4.66 ± 0.47	100 ± 10.4	98.3 ± 29.7	9,043 ± 2,768
Miscellaneous	78	47 (60)	11.9 ± 3.6	-0.39 ± 1.17	4.55 ± 0.32	98.4 ± 7.9	79.2 ± 23.4	8,456 ± 2,560
Surgical status								
Native CHD	112	51 (46)	11.8 ± 3.4	-0.26 ± 1.09	4.49 ± 0.37	98.2 ± 10.8	83.1 ± 28.8	9,383 ± 3,061
Heart surgery	275	111 (40)	12.4 ± 3.3	-0.35 ± 1.23	4.62 ± 0.42	99.8 ± 10.8	83.3 ± 27.8	9,387 ± 3,107
CHD severity*								
Simple	74	36 (49)	12.3 ± 3.6	-0.07 ± 1.12	4.57 ± 0.41	99.7 ± 11.1	85.4 ± 26.9	9,653 ± 3,034
Moderate	119	46 (39)	11.7 ± 3.1	-0.39 ± 1.16	4.57 ± 0.47	100.3 ± 13.1	81.7 ± 28.6	9,365 ± 3,161
Complex	171	65 (38)	12.4 ± 3.3	-0.42 ± 1.26	4.61 ± 0.38	98.7 ± 9.1	84.8 ± 28.7	9,551 ± 3,083

*23 patients could not be classified by the ACC criteria
Values are number (%) or mean ± SD.
BMI = body mass index, CHD = congenital heart disease, cSBP = central systolic blood pressure, MVPA = moderate to vigorous physical activity, PWV = pulse wave velocity, TGA = transposition of the great arteries, TCPC = total cavopulmonary connection.

Data Analysis

Descriptive data of the children with CHD are shown in mean values, standard deviations (mean ± SD) and total numbers (%) if appropriate. MVPA and steps were analyzed for every single day and computed to weekly averages for statistical purposes. The association between PA, in the form of MVPA and step count, and surrogates of arterial stiffness was analyzed using multivariate linear regression analyses adjusted for age, sex, zscore of the body mass index (BMI), peripheral systolic blood pressure (pSBP) heart rate and intake of hypertensive agents (yes/no) as in our previous analysis on this topic [22,23]. The activity level of CHD subgroups was compared to the WHO recommendation of average 60 min per day with one-sample t-test. The study population was categorized as high-active and low-active based on whether children met the WHO recommendations [32]. In addition, 10,000 steps on a daily average were identified as a cut-off for low-active and high-active CHD-groups. Differences in anthropometric data were analyzed with chi-square test and t-test for unpaired samples. General linear models adjusted for age, sex, z-score BMI, pSBP, heart rate and intake of hypertensive agents were calculated to detect differences between the high-active and low-active CHD group in PWV and cSBP. All analyses were performed with RStudio (version 1.3.1093) and SPSS (V25.0, IBM Corporation) with the level of significance set to two-sided p-values < 0.050 for all tests.

Results

Daily MVPA was not associated with PWV (ß=-0.025, p=0.446) and cSBP (ß=- 0.020, p=0.552) after adjusting for age, sex, BMI z-score, pSBP, heart rate and hypertensive agents in 387 children with CHD, (*Table 2*).

Table 2: *Association between arterial stiffness and MVPA adjusted for age, sex, BMI z-score, peripheral mean arterial pressure, heart rate and hypertensive agents*

	Adjusted R^2	**ß**	**95%CI**	**p-value**
PWV (m/s)	0.608	-0.031	[-0.002; 0.001]	0.470
cSBP (mmHg)	0.671	-0.016	[-0.039; 0.026]	0.692

cSBP=central systolic blood pressure, MVPA= moderate to vigorous physical activity, PWV = pulse wave velocity

This multivariate model explained 74.8% of the variance of PWV and of cSBP. There were no associations between daily step count and surrogates of arterial stiffness.

Separate analysis for patients with and without antihypertensive treatment can be found in *Supplementary Table S1*. Overall, children with CHD were remarkably active with a weekly average of 83.3 ± 28.1 min MVPA per day. In total, 80% of the study population (309 participants) accumulated at least 60 min of MVPA per day on a weekly average and thus met the WHO recommendations [32], (*Table 1* and *Figure 1*). Physical activity level did not significantly differ in the CHD severity groups (p=0.313, *Supplementary Table S2*).

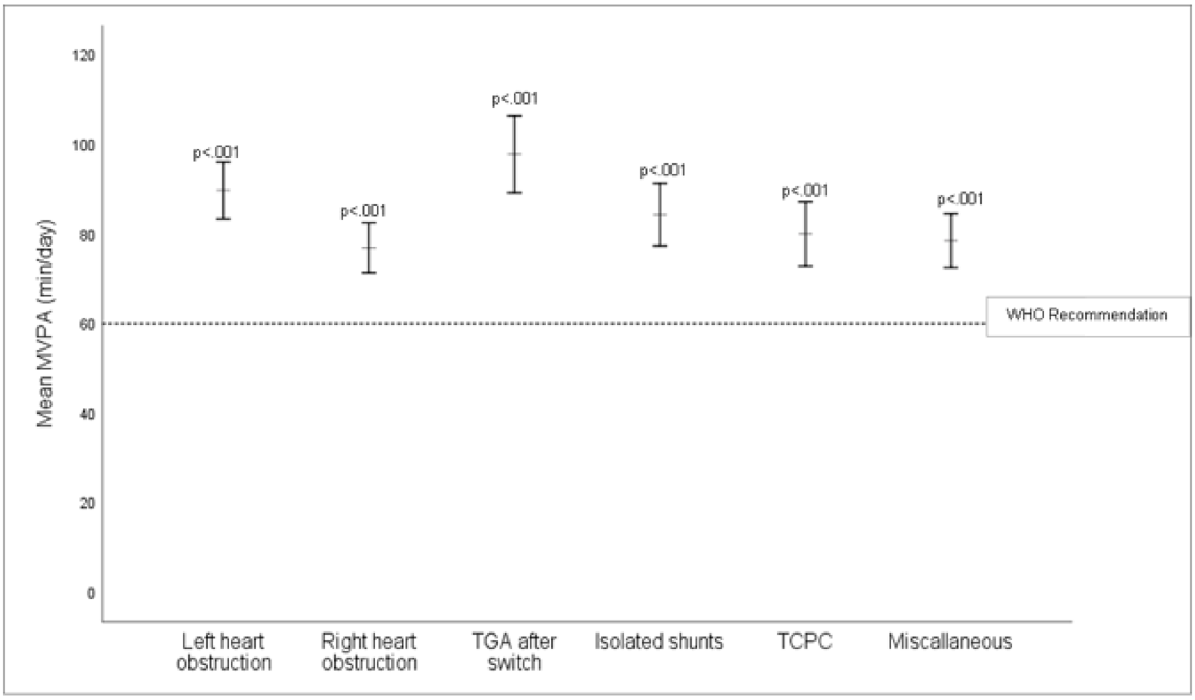

Figure 1: *Mean values of MVPA (min/day) between CHD subgroups corrected for age, sex and BMI z-score. All CHD subgroups significantly exceeded the minimum 60 min MVPA per day recommended by the WHO. TCPC = total cavopulmonary connection, TGA = transposition of the great arteries*

PWV z-Scores based on age, body height and sex were calculated according to Elemenhorst et al. 2015 [28], with an overall PWV z-score of 0.098 ± 1.76 m/s in our study population.

Comparing the high-active and low-active group, both groups did not differ in regard to surrogates of arterial stiffness after adjusting for age, sex, BMI z-score, pSBP, heart rate and hypertensive agents for PWV (high-active: 4.55 ± 0.4 m/s vs. low-active: 4.70 ± 0.4 m/s, F=0.53, p=0.467) and cSBP (high-active: 98.9 ± 11.0 mmHg vs. low-active: 101.1 ± 9.9 mmHg, F=0.843, p=0.359), (*Table 3*). The results remain unchanged when evaluating 10,000 steps on a daily average as a cut-off for low-active and high-active CHD-groups.

Table 3: *Population characteristic of high-active and low-active children with congenital heart disease*

	Low-active CHD (n = 78)	High-active CHD (n = 309)	p-value
Sex, female	40 (51%)	122 (40%)	0.079
Age, years	13.3 ± 3.3	11.9 ± 3.3	**0.002**†
BMI, z-score	-0.20 ± 1.6	-0.36 ± 1.1	0.298†
MVPA, min/day	47.8 ± 11.8	92.1 ± 23.6	**<0.001**†
Steps/day	6,150 ± 2,014	10,203 ± 2,762	**<0.001**†
PWV, m/s	4.70 ± 0.4	4.55 ± 0.4	0.265‡
cSBP, mmHg	101.1 ± 9.9	98.9 ± 11.0	0.491‡

Values are number (%) or mean ± SD.
†: Student's t-test for independent sample
‡: General linear model adjusted for age, sex, BMI z-score, peripheral mean arterial pressure, heart rate and hypertensive agents
BMI = body mass index, CHD = congenital heart disease, cSBP = central systolic blood pressure, MVPA = moderate to vigorous physical activity, PWV = pulse wave velocity.

Discussion

The main finding of the present study is that objectively measured PA was not related to arterial stiffness measures in a largely active cohort of children with CHD.

In healthy children, the relationship between PA and arterial stiffness remains unclear [14], as only half of the included studies in a recently published review reported of improved vascular function in physically active healthy children. In particular, the type of vascular measurement and the type of PA assessment has a considerable influence on reported outcomes [19].

Compared to healthy children, several diagnostic subgroups of patients with CHD show increased arterial stiffness already in the childhood [6,7]. Arterial stiffening in children with CHD has anatomic, histologic, and surgical reasons. Underlying factors are great arterial medial abnormalities of smooth muscle, elastic fibers, collagen and ground substance, impairing the natural buffering function of the vessels in children with CHD [33]. Additionally, surgical scars and resulting fibrotic tissue, implanted patches or conduits as well as pharmacological treatment foster arterial stiffness [2,34]. Due to the pre-existing pathology in children with CHD, the influence of PA becomes particularly important and sufficient evidence is lacking.

In contrast to our results, a study by Boyes and colleagues [20] with a rather small sample size of 17 children reported of increased arterial stiffness in low-active children with CHD compared to high-active children with CHD based on objectively measured daily step-counts. However, this study did not take confounders into account even though several influencing factors on arterial stiffness are well known [68], especially age, obesity and hypertension [35]. When examining the association between PA and arterial stiffness it is therefore important to consider these confounders, as otherwise the impact of PA on arterial stiffness will be biased. Furthermore, our larger sample size might contribute to a clearer picture on the association.

Lopez and colleagues [21] reported of an inverse association between MVPA and aortic PWV after adjusting for sex, age and BMI in 104 children with CHD at a mean age of 12 years. In contrast to our study their patient cohort was rather inactive with an average of 46.7 ± 20.0 min MVPA per day and only 25% of the cohort meeting the WHO recommendation, which markedly differs from the 80% in our patient cohort [21]. In our specialized tertiary center children are encouraged to be physically active during their follow-up appointments which may result in our cohort being more active than the average CHD population. Previous studies investigating PA levels in children with CHD reported rather conflicting results, as some studies showed reduced PA [11,12]. Other studies found high PA levels in children with CHD [10] with no significant differences to healthy peers [10,13]. Overall, the disease-awareness of our patients and their families who attend the regular follow-up appointments is considerably high. In combination with the high activity level, this might have been the most explanatory factor for our results. However, these findings cannot be generalized as our findings largely depend on a large high-active and small low-active CHD group. Further studies are needed to explore and understand the association of arterial stiffness and PA in high-active and low-active children with CHD.

Limitation

As the exposure to risk factors is relatively short in studies with children it is often difficult to show correlations. In addition, when sampling patients from 8 to 18 years of age the time period is just 10 years. This narrow time window and the lack of exposure indicates the necessity for a huge sample size or a huge effect to yield significant results. As our institution is a specialized tertiary center, complex CHD might be overrepresented in this study population. Combined with the already mention encouragement of PA in our institution the novelty and excitement of wearing the “Garmin vivofit jr.” device might have additionally increased the PA level during the measurement period [36]. Therefore, PA levels in our study cohort might be overrepresented compared to reality. However, compared to recent research on PA level of children with CHD in our institution, the measured PA level seems rather normal [10]. A prior study has shown a systematic underestimation of the PWV in high PWV values with the Mobil-O-Graph® device [29], which might have influenced our results even in this young cohort. The algorithm used by the Mobil-O-Graph® yields only estimates of the PWV, whereby estimates of PWV were shown to be strongly dependent on age and systolic BP and less on the waveform characteristics [29,37]. Mobil-O-Graph® is nevertheless considered as a good and valid method for estimating PWV as it is easy to perform, operator-independent and reliable [29]. In children and adolescents, oscillometric noninvasive estimations using Mobil-O-Graph® were shown to be effective for evaluating cSBP in this age group [27].

Conclusions

No association between PA and arterial stiffness was found in this active cohort of children with CHD. The influence of PA on arterial stiffness in low-active children and patients with a longer exposure to respective risk factors needs further investigation. Nevertheless, PA promotion is indicated in patients with CHD, as its benefits are unquestionable.

Supplementary Table S1: *Association between arterial stiffness and MVPA adjusted for age, sex, BMI z-score, peripheral mean arterial pressure and heart rate, separated for patients treated with antihypertensive drugs and untreated patients*

	Adjusted R^2	**ß**	**95%CI**	**p-value**
		UNTREATED		
PWV (m/s)	0.586	-0.010	[-0.002; 0.001	0.823
cSBP (mmHg)	0.684	0.007	[-0.028; 0.033]	0.862
		TREATED		
PWV (m/s)	0.754	-0.177	[-0.006; 0.0001]	0.058
cSBP (mmHg)	0.537	-0.248	[-0.276; -0.0003]	**0.049**

cSBP=central systolic blood pressure, MVPA= moderate to vigorous physical activity, PWV = pulse wave velocity

Supplementary Table S2: *Physical activity level based on MVPA of different CHD severities after adjusting for age, sex and BMI z-score.*

CHD Severity	**Estimated marginal means MVPA (min/day)**	**Standard error**	**95%-CI**
Complex CHD	84.5	2.1	[80.4 – 88.7]
Moderate CHD	80.7	2.5	[75.8 – 85.6]
Simple CHD	86.7	3.2	[80.4 – 93.0]

Corrected for age, sex and BMI z-score. CHD = congenital heart disease, CI = confidence interval, MVPA= moderate to vigorous physical activity

References

[1] Bigras, J.-L. Cardiovascular Risk Factors in Patients with Congenital Heart Disease. Can. J. Cardiol. 2020, 36, 1458–1466.

[2] Laurent, S.; Cockcroft, J.; Van Bortel, L.; Boutouyrie, P.; Giannattasio, C.; Hayoz, D.; Pannier, B.; Vlachopoulos, C.;Wilkinson, I.; Struijker-Boudier, H.; et al. Expert consensus document on arterial stiffness: Methodological issues and clinical applications. Eur. Heart J. 2006, 27, 2588–2605.

[3] Laurent, S.; Boutouyrie, P.; Asmar, R.; Gautier, I.; Laloux, B.; Guize, L.; Ducimetiere, P.; Benetos, A. Aortic Stiffness Is an Independent Predictor of All-Cause and Cardiovascular Mortality in Hypertensive Patients. Hypertension 2001, 37, 1236–1241.

[4] McEniery, C.M.; Yasmin; McDonnell, B.; Munnery, M.; Wallace, S.M.; Rowe, C.V.; Cockcroft, J.R.; Wilkinson, I.B. Central pressure: Variability and impact of cardiovascular risk factors: The Anglo-Cardiff Collaborative Trial II. Hypertension 2008, 51, 1476–1482.

[5] Sharman, J.E.; Marwick, T.H.; Gilroy, D.; Otahal, P.; Abhayaratna, W.P.; Stowasser, M. Randomized trial of guiding hypertension management using central aortic blood pressure compared with best-practice care: Principal findings of the BP GUIDE study. Hypertension 2013, 62, 1138–1145.

[6] Häcker, A.-L.; Reiner, B.; Oberhoffer, R.; Hager, A.; Ewert, P.; Müller, J. Increased arterial stiffness in children with congenital heart disease. Eur. J. Prev. Cardiol. 2018, 25, 103–109.

[7] Müller, J.; Ewert, P.; Hager, A. Increased aortic blood pressure augmentation in patients with congenital heart defects—A cross-sectional study in 1125 patients and 322 controls. Int. J. Cardiol. 2015, 184, 225–229.

[8] Longmuir, P.E.; Brothers, J.A.; De Ferranti, S.D.; Hayman, L.L.; Van Hare, G.F.; Matherne, G.P.; Davis, C.K.; Joy, E.A.; McCrindle, B.W. Promotion of physical activity for children and adults with congenital heart disease: A scientific statement from the American Heart Association. Circulation 2013, 127, 2147–2159.

[9] Takken, T.; Giardini, A.; Reybrouck, T.; Gewillig, M.; Hövels-Gürich, H.; Longmuir, P.; McCrindle, B.; Paridon, S.; Hager, A. Recommendations for physical activity, recreation sport, and exercise training in paediatric patients with congenital heart disease: J. Clin. Med. 2021, 10, 3266 7 of 8 A report from the Exercise, Basic & Translational Research Section of the European Association of Cardiovascular Prevention and Rehabilitation, the European Congenital Heart and Lung Exercise Group, and the Association for European Paediatric Cardiology. Eur. J. Prev. Cardiol. 2012, 19, 1034–1065.

[10] Brudy, L.; Hock, J.; Häcker, A.-L.; Meyer, M.; Oberhoffer, R.; Hager, A.; Ewert, P.; Müller, J. Children with Congenital Heart Disease Are Active but Need to Keep Moving: A Cross-Sectional Study UsingWrist-Worn Physical Activity Trackers. J. Pediatr. 2020, 217, 13–19.

[11] Moola, F.; McCrindle, B.W.; Longmuir, P.E. Physical activity participation in youth with surgically corrected congenital heart disease: Devising guidelines so Johnny can participate. Paediatr. Child Health 2009, 14, 167–170.

[12] Siaplaouras, J.; Niessner, C.; Helm, P.C.; Jahn, A.; Flemming, M.; Urschitz, M.S.; Sticker, E.; Abdul-Khaliq, H.; Bauer, U.M.; Apitz, C. Physical Activity Among Children with Congenital Heart Defects in Germany: A Nationwide Survey. Front. Pediatr. 2020, 8.

[13] Ewalt, L.A.; Danduran, M.J.; Strath, S.J.; Moerchen, V.; Swartz, A.M. Objectively assessed physical activity and sedentary behaviour does not differ between children and adolescents with and without a congenital heart defect: A pilot examination. Cardiol. Young 2011, 22, 34–41.
[14] Böhm, B.; Oberhoffer, R. Vascular health determinants in children. Cardiovasc. Diagn. Ther. 2019, 9, S269–S280.
[15] Schack-Nielsen, L.; Mølgaard, C.; Larsen, D.; Martyn, C.; Michaelsen, K.F. Arterial stiffness in 10-year-old children: Current and early determinants. Br. J. Nutr. 2005, 94, 1004–1011.
[16] Sakuragi, S.; Abhayaratna, K.; Gravenmaker, K.J.; O'Reilly, C.; Srikusalanukul, W.; Budge, M.M.; Telford, R.D.; Abhayaratna, W.P. Influence of adiposity and physical activity on arterial stiffness in healthy children: The lifestyle of our kids study. Hypertension 2009, 53, 611–616.
[17] Heil, L.; Oberhoffer, R.; Böhm, B. Association Between Physical Activity Intensity Levels and Arterial Stiffness in Healthy Children. J. Phys. Act. Health 2020, 17, 1–7.
[18] Khadilkar, A.V.; Chiplonkar, S.A.; Khadilkar, V.V.; Kinare, A.S.; Pandit, D.S. Arterial stiffness in obese children: Role of adiposity and physical activity. Indian J. Endocrinol. Metab. 2014, 18, 70–76.
[19] Baumgartner, L.;Weberruß, H.; Oberhoffer-Fritz, R.; Schulz, T. Vascular Structure and Function in Children and Adolescents: What Impact Do Physical Activity, Health-Related Physical Fitness, and Exercise Have? Front. Pediatr. 2020, 8, 103.
[20] Boyes, N.G.; Stickland, M.K.; Fusnik, S.; Hogeweide, E.; Fries, J.T.; Haykowsky, M.J.; Baril, C.L.; Runalls, S.; Kakadekar, A.; Pharis, S.; et al. Physical activity modulates arterial stiffness in children with congenital heart disease: A CHAMPS cohort study. Congenit. Heart Dis. 2018, 13, 578–583.
[21] Lopez, J.R.; Voss, C.; Kuan, M.T.; Hemphill, N.M.; Sandor, G.G.; Harris, K.C. Physical activity is associated with better vascular function in children and adolescents with congenital heart disease. Can. J. Cardiol. 2020, 36, 1474–1481.
[22] Hock, J.; Häcker, A.-L.; Reiner, B.; Oberhoffer, R.; Hager, A.; Ewert, P.; Müller, J. Functional outcome in contemporary children and young adults with tetralogy of Fallot after repair. Arch. Dis. Child. 2018, 104, 129–133.
[23] Häcker, A.-L.; Reiner, B.; Oberhoffer, R.; Hager, A.; Ewert, P.; Müller, J. Functional outcomes in children with anatomically repaired transposition of the great arteries with regard to congenital ventricular septal defect and coronary pattern. Arch. Dis. Child. 2019, 104, 851–856.
[24] Hametner, B.;Wassertheurer, S.; Kropf, J.; Mayer, C.; Eber, B.;Weber, T. Oscillometric estimation of aortic pulse wave velocity: Comparison with intra-aortic catheter measurements. Blood Press. Monit. 2013, 18, 173–176.
[25] Weiss, W.; Gohlisch, C.; Zidek, W.; Van Der Giet, M. Oscillometric Estimation of Central Blood Pressure: Validation of the Mobil-O-Graph® in Comparison to the Sphygmocor® Device. J. Hypertens. 2011, 29, e1–e2.
[26] Sharman, J.E.; Avolio, A.P.; Baulmann, J.; Benetos, A.; Blacher, J.; Blizzard, C.L.; Boutouyrie, P.; Chen, C.-H.; Chowienczyk, P.; Cockcroft, J.R.; et al. Validation of non-invasive central blood pressure devices: ARTERY Society task force consensus statement on protocol standardization. Eur. Heart J. 2017, 38, 2805–2812.

[27] Shiraishi, M.; Murakami, T.; Higashi, K. The accuracy of central blood pressure obtained by oscillometric noninvasive method using Mobil-O-Graph in children and adolescents. J. Hypertens. 2020, 38, 813–820.

[28] Elmenhorst, J.; Hulpke-Wette, M.; Barta, C.; Pozza, R.D.; Springer, S.; Oberhoffer, R. Percentiles for central blood pressure and pulse wave velocity in children and adolescents recorded with an oscillometric device. Atherosclerosis 2015, 238, 9–16.

[29] Salvi, P.; Scalise, F.; Rovina, M.; Moretti, F.; Salvi, L.; Grillo, A.; Gao, L.; Baldi, C.; Faini, A.; Furlanis, G.; et al. Noninvasive estimation of aortic stiffness through different approaches: Comparison with intra-aortic recordings. Hypertension 2019, 74, 117–129.

[30] Alsubheen, S.A.; George, A.M.; Baker, A.; Rohr, L.E.; Basset, F.A. Accuracy of the vivofit activity tracker. J. Med. Eng. Technol. 2016, 40, 298–306.

[31] Price, K.; Bird, S.R.; Lythgo, N.; Raj, I.S.; Wong, J.Y.; Lynch, C. Validation of the Fitbit One, Garmin Vivofit and Jawbone UP activity tracker in estimation of energy expenditure during treadmill walking and running. J. Med. Eng. Technol. 2017, 41, 208–215.

[32] Bull, F.C.; Al-Ansari, S.S.; Biddle, S.; Borodulin, K.; Buman, M.P.; Cardon, G.; Carty, C.; Chaput, J.-P.; Chastin, S.; Chou, R.; et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. Br. J. Sports Med. 2020, 54, 1451–1462.

[33] Niwa, K.; Perloff, J.K.; Bhuta, S.M.; Laks, H.; Drinkwater, D.C.; Child, J.S.; Miner, P.D. Structural abnormalities of great arterial walls in congenital heart disease: Light and electron microscopic analyses. Circulation 2001, 103, 393–400.

[34] Murakami, T.; Tateno, S.; Kawasoe, Y.; Niwa, K. Aortic surgery is one of the risk factors for enhancement of pressure wave reflection in adult patients with congenital heart disease. Int. J. Cardiol. 2014, 175, 451–454.

[35] Giannattasio, C.; Mancia, G. Arterial distensibility in humans. Modulating mechanisms, alterations in diseases and effects of treatment. J. Hypertens. 2002, 20, 1889–1899.

[36] Lubans, D.R.; Morgan, P.J.; Callister, R.; Collins, C.E. Effects of Integrating Pedometers, Parental Materials, and E-mail Support Within an Extracurricular School Sport Intervention. J. Adolesc. Health 2009, 44, 176–183.

[37] Schwartz, J.E.; Feig, P.U.; Izzo, J.L., Jr. Pulse wave velocities derived from cuff ambulatory pulse wave analysis: Effects of age and systolic blood pressure. Hypertension 2019, 74, 111–116.

2.7 Discussion Cardiovascular Risk Factors in Children with CHD

The purpose of the first part of this thesis was to quantify cardiovascular risk factors in children and adolescents with CHD. The previously presented scientific publications have highlighted modifiable cardiovascular risk factors and the need for activity promotion and behavior change in the CHD population, particularly in adolescents.

The overweight and obesity prevalence is high in children with CHD and especially increases during adolescence, demonstrating that the growing obesity pandemic is also affecting the CHD population [78]. Similar to the general population, high overweight and obesity prevalences in CHD patients are a multifactorial problem, involving hereditary as well as traditional risk factors [79]. During the first years of life, children with CHD often face high prevalence of preoperative underweight and malnutrition, often associated with cyanosis and pulmonary hypertension [80]. Consequently, adequate growth and weight development is priority in treatment including excessive nutritional rehabilitation for weight gain in infancy with increased calorie consumption [81]. Although postoperative prevalence of malnutrition significantly decreases over time [80] and the nutritional status changes after successful surgery and throughout the lifespan of CHD patients, inappropriate dietary behavior and physical inactivity often persists into childhood and beyond [82]. Additionally, this effect can be amplified due to exercise restrictions and parental overprotection [60].

Therefore, childhood seems to be the time point were actions need to be taken, to help families understand that there happens a shift in the nutritional situation und to help them overcome their well-understandable fears and uncertainties. The results of the first scientific publication of this thesis also indicate that there is an urgent need for health promotion in the CHD population, especially in adolescents and boys. More knowledge and consideration on diet, nutrition, and associated factors are indicated in the holistic medical aftercare of CHD patients. Nutritional education and counseling should start early in childhood. As parents have a huge responsibility for the eating behavior of their children, education and counseling should include the entire families. Besides the focus on the nutrition, the results of the systematic review underline the importance of activity promotion in CHD patients.

As presented in the second scientific publication of this thesis, no association between PA and arterial stiffness was found in physically active children with CHD. However, this association remains unclear in physically inactive children and patients with longer exposure to physical inactivity. PA promotion starting early in life is nevertheless indicated [83].

Compared to healthy adolescents, where 81% were found to be insufficiently active [69], in our cohort of CHD children, 80% did reach the WHO recommendation. This is particularly positive, as several previous studies on CHD children, reported of reduced PA levels [71, 84]. It shows that PA encouragement in one of the most specialized centers, the German Heart Center, seems to be successful. However, also in Germany many CHD patients are not connected to specialized follow-up care [85]. These patients do not appear in our studies and might further influence the results. One week of measurement is comparably short, and the Hawthorn Effect might have affected the reported PA levels. The Hawthorn Effect implies that the awareness of being observed and studied, impacts people's behavior [86].

Similar studies in less active CHD children, did report of associations between arterial stiffness and PA. However, sample sizes were small and the adjusting for possible confounders insufficient [87, 88]. Assessing the association between arterial stiffness and PA in CHD children definitely needs further investigation especially in less-active patients. As the measures of arterial stiffness are of extreme importance, the identification of modifiable risk factors should be of high interest in research and medical aftercare. Not only PA, but also BMI and overweight/obesity have an influence on arterial stiffness. Several studies in healthy children have shown a positive association between BMI and arterial stiffness [89, 90].

In the holistic aftercare of children with CHD, this thesis supplies mosaic pieces to the great picture of cardiovascular risk factors. Based on the results of these studies, preventive measures or long-term behavior change starting already in early age are mandatory in the CHD population. PA is thereby a key factor to reconcile the discussed modifiable risk factors in patients with CHD. However, long-term behavior change and activity promotion is highly complex and different approaches failed to achieve the desired results. The following part of this thesis will explain and evaluate a possible concept for activity promotion in adolescents with CHD.

3. Activity Promotion in Adolescents with Congenital Heart Disease

The findings of the first part of this thesis, along with a study from the German Heart Center Munich, published by Brudy and colleagues [72], conclude that adolescents with CHD are in special need for health promotion. These previous results are the fundament for the randomized controlled trail *Digital Health Nudging*. In addition to this previous research, the Covid-19 pandemic has further exacerbated modifiable lifestyle-related risk factors including overweight and physical inactivity not only in the healthy population, but also in children with CHD [65]. Based on the previous results we were able to tailor the intervention very precisely to the patient cohort in need for activity promotion.

During adolescence, future patterns of adult health are established and health promotion during this time has the potential to impact lifelong wellbeing [91]. Adolescence is the transition period from childhood to adulthood and is characterized by the complex interplay of biological growth, cognitive development, and social role transition [92]. *Figure 5* shows the common developmental tasks of adolescents, developed by Moons and colleagues [93].

Figure 5: *Developmental tasks of adolescents, from [69]*

The health behavior of adolescents is influenced by the interactions between prenatal and childhood development and the specific biological and social role changes that accompany growing up [91]. Puberty is a biologically determined process affecting behavior, emotional well-being, and health in complex ways [91]. Many opportunities for the prevention of non-communicable diseases arise from focusing on risk processes that begin in adolescence or even earlier, when adolescents become responsible of their own health behaviors and choices [91]. It is thereby of extreme importance to acknowledge, that children and adolescents are not simply young adults. They need a special approach to health care, prevention, and health promotion. While adolescents with CHD have to master the same developmental tasks as healthy peers, dealing with the congenital condition in day-to-day life is an extra stressor [93].

While care over the entire lifespan is essential in patients with CHD, a special focus should be placed on the transition phase from pediatric to adult care. Studies have shown that patients growing out of the pediatric care are often lost to specialized cardiological follow-up, even patients with severe heart defects [94]. One possible explanation is that young patients want to live like their healthy peers and do not want to identify with the heart defect [95, 96]. To ensure early detection of acquired secondary diagnosis, the gap between specialized pediatric and adult cardiology has to be closed. Next to health promotion during this time period, a special focus on keeping adolescents with CHD in the aftercare has to be developed [97].

Another reason for the special focus on health promotion in adolescents is the tracking effect of PA behavior: PA during adolescence significantly predicts adult PA. Persistent PA at young age increases the probability of being active in adulthood [98]. Even higher is the likelihood of staying physically inactive once a person becomes inactive during adolescence [99]. Given the extreme burden of physical inactivity, it is extremely important to encourage patients to remain active throughout their youth, which will impact their lifelong health.

3.1 Behavior Change in Adolescents with CHD

Leading causes of chronic diseases are linked to health behaviors such as unhealthy diet, physical inactivity, tobacco or alcohol consumption [15]. Even though most people are aware of these lifestyle-related risk factors, most people nevertheless fail to maintain health-promoting behavior [100]. Human decision making is often irrational and biased, which may lead to suboptimal health behavior and outcome [101]. Key question in prevention and health promotion is therefore how people can be supported in making health-promoting choices and following a healthy lifestyle.

To successfully influence people's health behaviors, it is essential to understand the driving factors and cognitive approaches underlying human decision-making [102]. According to behavioral economics as well as cognitive and social psychology, human behavior and decision making is only partly rational, but rather habitual [103]. Human behavior is greatly influenced by the context or environment within which decisions are taken and are mostly led by emotions [104]. An example for that is the default effect, which describes the tendency of decision makers to stick with the default regardless of actual options they have [101]. However, these biases in human decision making can also be used to guide individual health behaviors in a positive direction [101]. If the healthy option is the easier choice, or even the default option, the likelihood that people will engage in health-promoting behaviors increases [102].

Constantine and colleagues created an overview of factors, that positively influence health behavior in patients with CHD, see *Figure 6*. They believe that health behavior has received too little attention in the CHD population and that there is still lot of need and potential to improve the health behavior of patients. Besides widely discussed factors in the CHD population like lifelong patient education, a structured transition phase for patients growing up, and specialized, structured follow-up care, they also highlight the use of technology-based approaches and thoughtful choice environments to empower patients in making healthy choices. They also point out to use nudges to revolutionize the way of interaction with the patients [13].

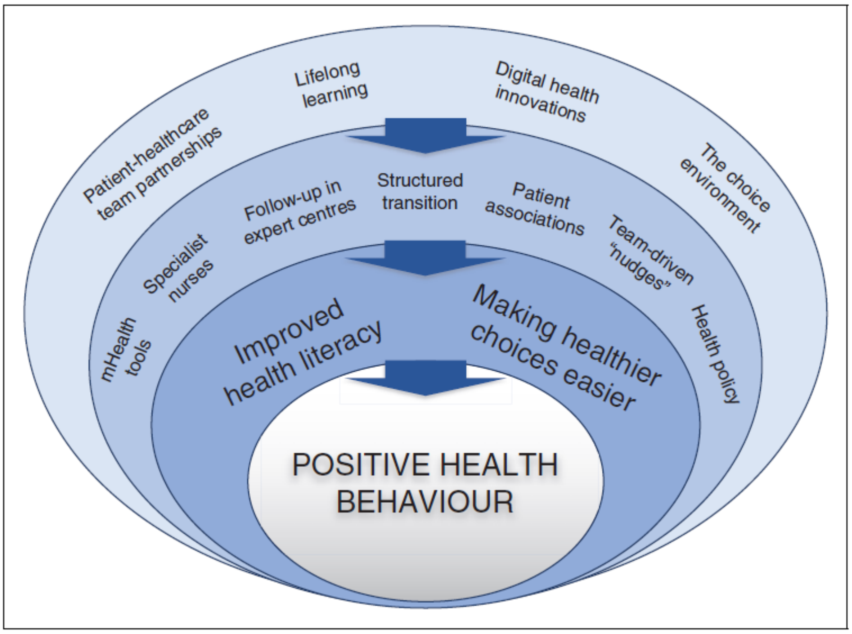

Figure 6: *Factors affecting health behaviors in patients with CHD, from [11]*

According to the research purpose of this thesis, the key question of prevention on how to encourage people to live a healthy life adapts to: How can adolescents with CHD be supported to develop a physically active lifestyle?

Long-term and sustainable behavior change toward a physically active lifestyle is highly complex and doesn't happen overnight. This becomes obvious when looking at the tremendous number of people who fail to be sufficiently physically active. Many different approaches of activity promotion have been made in the past, with more or less success. Thereby one of the biggest challenges was maintaining the adherence of the target group in the long term. To address this issue, the idea was to use the concept of nudging in a digital format and thereby reach young people in their every-day lives.

3.2 The Concept of Nudging

In recent years, the approach of nudging has emerged in behavioral science, targeting individual behaviors to prevent the rise of non-communicable diseases. The concept of nudging was originally developed by the lawyer Cass R. Sunstein and the economist Richard Thaler in 2008. Nudging originates from behavioral economics and utilizes psychological knowledge to influence human behavior through so-called nudges.

Nudging describes small changes or adaptations in the context, that influence the choices individuals make. Rather than restrictions or penalties, nudges encourage individuals to make healthier choices themselves [104].

In their book, *Nudge: Improving Decisions About Health, Wealth and Happiness,* Thaler and Sunstein explain that nudging aims at:

> *"alter[ing] people's behavior in a predictable way without forbidding any options or significantly changing their economic incentives. To count as a mere nudge, the intervention must be easy and cheap to avoid. Nudges are not mandates. Putting the fruit at eye level counts as a nudge. Banning junk food does not"* (Thaler & Sunstein, p.6) [104].

The so-called "choice architecture" describes the environment within which people make choices. Using the concept of nudging means that the decision architecture is designed in a way that beneficial or healthy options are facilitated. The decision architect tries to nudge the decision maker towards a particular option [104]. Nudges try to improve people's decisions by changing how options are presented to them and still respect freedom of choice [104]. In addition, the implementation of nudging in the health care setting is relatively easy and comparatively cheap [103].

3.3 Digital Health

The global strategy on digital health 2020-2025 from the WHO defines digital health as the field of knowledge and practice, that is associated with the development and use of digital technologies to improve health [105]. Digital health is an umbrella term for electronic health (eHealth), mobile health (mHealth), and evolving areas such as advanced computer science. eHealth is the use of information and communication technologies in support of health, mostly including health care services, health surveillance, health literature, and health education [105]. mHealth was defined as medical and public health practice, that is supported by mobile devices, personal digital assistants, or other wireless devices. It thereby includes text messages, smartphone apps, and other telecommunication systems. mHealth is providing enormous opportunities for healthcare delivery, with the possibility to deliver efficient and affordable healthcare services to widespread populations. Additionally, it offers new possibilities for prevention and patient education [106]. Digital approaches have the potential to transform our healthcare system to patient-centered and evidence-driven care, potentially improving outcomes and reducing costs [107]. Digital health including wearable and smartphone-connected devices allow remote real-time health measurement for individuals and health professionals [108].

Digital interventions to foster and support behavior change are increasingly popular, as they also give individuals the possibility to monitor and improve their health behavior. Digital behavior change interventions are services using digital technology such as websites, social media, text messages, smartphone apps, or wearable devices, to promote behavior change [109]. Digital interventions for behavior change addressing low PA levels, sedentary behavior, and unhealthy diet have received significant research attention [109]. Adolescents are high users of technology, which allows to reach adolescents in their personal environment and is therefore a good approach for addressing prevention and health promotion. Although reducing recreational screen time in children and adolescents is an urgent concern and is also strongly recommended by the WHO, the opportunity to make prevention and health promotion attractive and age-appropriate through the use of digital media should not be missed [51].

3.4 Social Cognitive Theory

Applying behavior change theories to health interventions, improves the applicability and increases the effectiveness of the intervention. Behavior change theories help to design interventions based on the understanding of human behavior [110]. Research has shown, that behavior change interventions are more effective when behavioral determinants are targeted [111]. The social cognitive theory was shown to be one of the most predominant approaches in PA interventions. The social cognitive theory is a behavior theory of human behavior and motivation invented by Albert Bandura in the 1970th. It explains the various internal and external processes that shape psychological functioning. The social cognitive theory is organized as a triadic reciprocal determinism, consisting of the dynamic interaction of cognitive, behavioral, and environmental determinants that shape human behavior [112]. In the field of PA and sports, typical examples for personal factors that shape human behavior are self-efficacy, self-regulation, and outcome expectations. Self-efficacy describes the belief of a person to be able to perform a certain behavior. Self-regulation refers to the control and management of one's behavior through planning, goal-setting, and self-monitoring. Outcome expectation describes the belief about the consequences of a behavior. Behavioral factors include information, motivation as well as skills and practice. Social and family support are examples for environmental factors [111], see *Figure 7*.

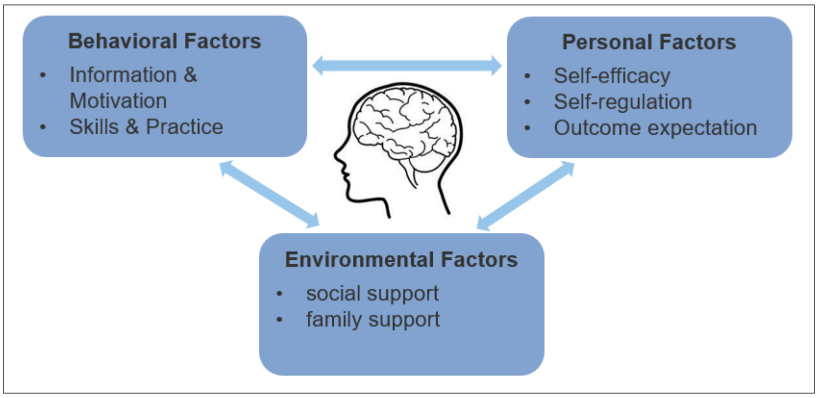

Figure 7: *Bandura's social cognitive theory [111]*

Previous studies have shown that the application of social cognitive theory has positive effects on activity promotion, with the strongest relationship being between self-efficacy and PA [111]. Based on the social cognitive theory the *Digital Health Nudging* intervention was created and structured, mostly focusing on behavioral and personal factors. An overview of the Nudges in German language can be found in the *Appendix I* of this thesis.

3.5 Digital Health Nudging to increase physical activity in pediatric patients with congenital heart disease: A randomized controlled trial (Scientific Publication III)

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Conflicts of Interest:

The authors declare no conflict of interest.

Individual contribution:

The PhD candidate is the principal author of this paper. She recruited the study participants at German Heart Center Munich, conducted the digital intervention and sampled the data. Laura Willinger finally drafted the manuscript. Jan Müller revised the manuscript and Renate Oberhoffer-Fritz and Peter Ewert gave important feedback for further improvement of the manuscript. Laura Willinger under supervision of Jan Müller handled the submission process of the paper until final publication.

Abstract

Objective: Digital nudging is a modern e-health approach to increase physical activity (PA) in younger age groups. As activity promotion is particularly important in adolescents with congenital heart disease (CHD) this randomized-controlled trail examines if *Digital Health Nudging* via daily smartphone messages increases PA, activity-related self-efficacy (ArSE) and health-related quality of life (HrQoL) in adolescents with CHD.

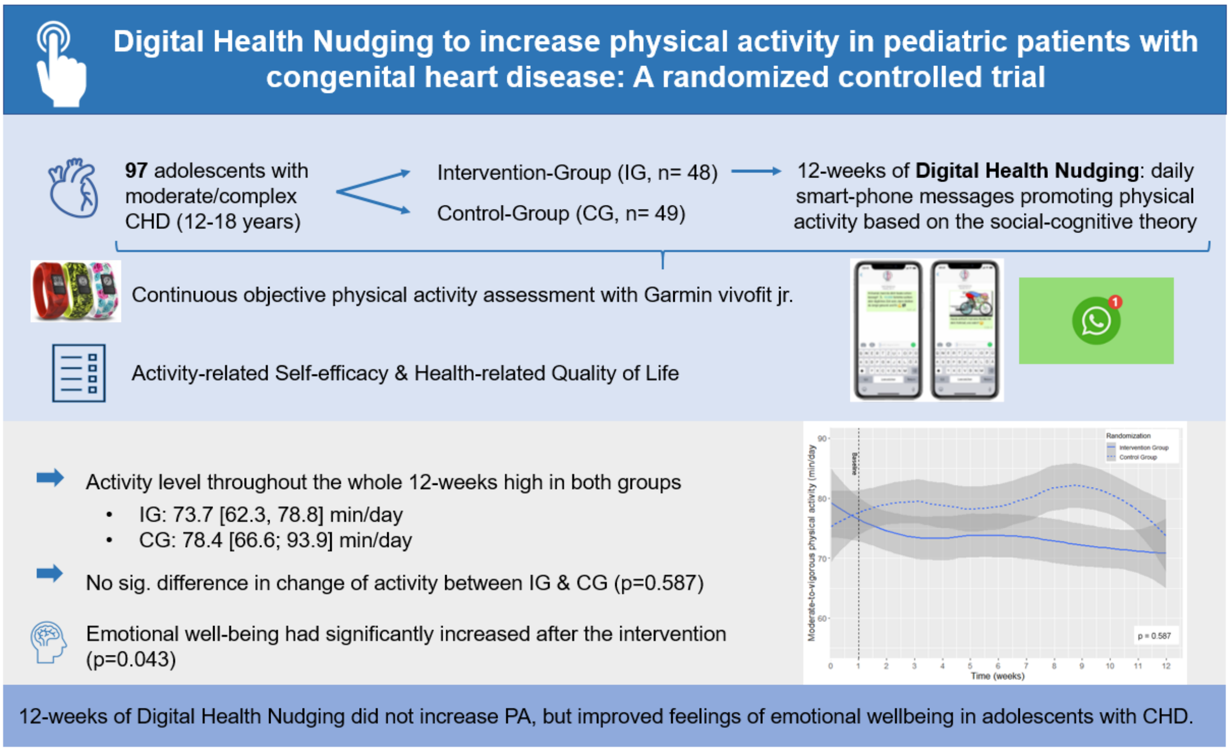
Methods: From May 2021 to April 2022, 97 patients (15.1 ± 2.0 years, 50% girls) with moderate or severe CHD were randomly allocated 1:1 to intervention (IG) or control group (CG). Daily PA was objectively assessed in minutes of moderate-to-vigorous PA (MVPA) by the wearable "Garmin Vivofit jr. 2®" over the entire study period. The IG received daily smartphone messages based on Bandura's social cognitive theory on the subject of PA over a period of 12-weeks.

Results: According to the linear mixed model, the change of MVPA over the study period did not significantly differ between IG and CG when taking baseline MVPA into account (b=0.136, 95%-CI [-0.355; 0.627], p=0.587). Activity level was comparably high and showed only minor variability in both groups with 73.7 [62.3; 78.8] min/day in IG and 78.4 [66.6; 93.9] min/day in CG throughout the whole 12-weeks. Emotional well-being significantly increased over the study period in the IG (IG: Δ1.60 [-0.2; 6.3] vs. CG: Δ0.0 [-12.5; 6.3], p=0.043), but not total HrQoL (p=0.518) and ArSE (p=0.305).

Conclusion: 12-weeks of *Digital Health Nudging* did not increase PA, but improved feelings of emotional well-being in adolescents with CHD.

Trial Registration: Clinical Trials Identifier NCT04933786

Graphical Abstract



Introduction

According to previous research, adolescents with more severe congenital heart disease (CHD) are particularly at risk to be physically inactive and in need of activity promotion [1-3]. International guidelines strongly recommend physical activity (PA) and exercise in patients with CHD [4, 5]. However, uncertainty and fear concerning the congenital condition, as well as parental overprotection persist until today, fostering a vicious cycle of the CHD condition and physical inactivity [6]. Additionally, adolescence is a crucial transition phase in which health habits such as an active lifestyle and future patterns of adult health are established [7]. This implies that there is a tracking effect of PA: the more active a person is in adolescence, the more likely this person will also be an active adult [8, 9]. To promote PA at this particularly important stage of life in adolescents with CHD, we developed a digital intervention approach that provides new opportunities to encourage and support PA. Digital Health Nudging is an age-appropriate, and modern e-health intervention to promote PA [10]. The concept of nudging originates from behavioral economics and aims to positively influence human decision making [11]. Through the use of innovative technology we are able to reach our young cardiac patients in their everyday lives. Previous studies on healthy children showed promising results concerning digital health interventions with SMS or text messages in facilitating PA in children and adolescents [10, 12, 13]. However, in adolescents with CHD such studies are still lacking, although particularly important in this vulnerable population where PA levels are already reduced. This randomized controlled trial (RCT) aimed to increase PA, health-related quality of life (HrQoL), as well as activity-related self-efficacy (ArSE) in adolescents with CHD by a 12-weeks Digital Health Nudging intervention.

Methods

Study design and participants

This study was a prospective, single center, RCT performed at the outpatient clinic of the German Heart Center of Munich. It was conducted in accordance with the Declaration of Helsinki and was approved by the local ethical board of the Technical University of Munich (project number: 265/21 S). It was registered at clinicaltrials.gov (NCT04933786). All participants and their guardians gave written informed consent before randomization. From June 2021 to April 2022, all patients at an age of 12-18 years, with moderate-to-complex CHD were screened for eligibility. For participation in the study, participants were required to have their own smartphone. Exclusion criteria were severe arrhythmias, chromosomal anomalies, genetic syndromes, and severe physical or cognitive impairments or developmental delays.

Estimated enrolment per G* power, was 98 participants (two-sided α of 0.05, effect size 0.52, Power 0.90). Because of a possible dropout, 100 patients have been recruited. Overall, 324 patients were identified in the daily routine of the outpatient clinic, of which 163 did not meet the inclusion criteria, 61 possible participants declined to participate, and 3 participants did not finish the one-week baseline measurement and were therefore excluded, see *Figure 1*. The 61 participants who declined to participate did not differ in age (p=0.426), however more boys (p=0.029) and more complex CHD (p=0.028) declined to participate compared to the included study participants. Eventually, 97 participants with CHD (15.1 ± 2.0 years, 50% girls) were randomly allocated 1:1 to either intervention group (IG) or control group (CG) stratified for sex and age using a sealed envelope.

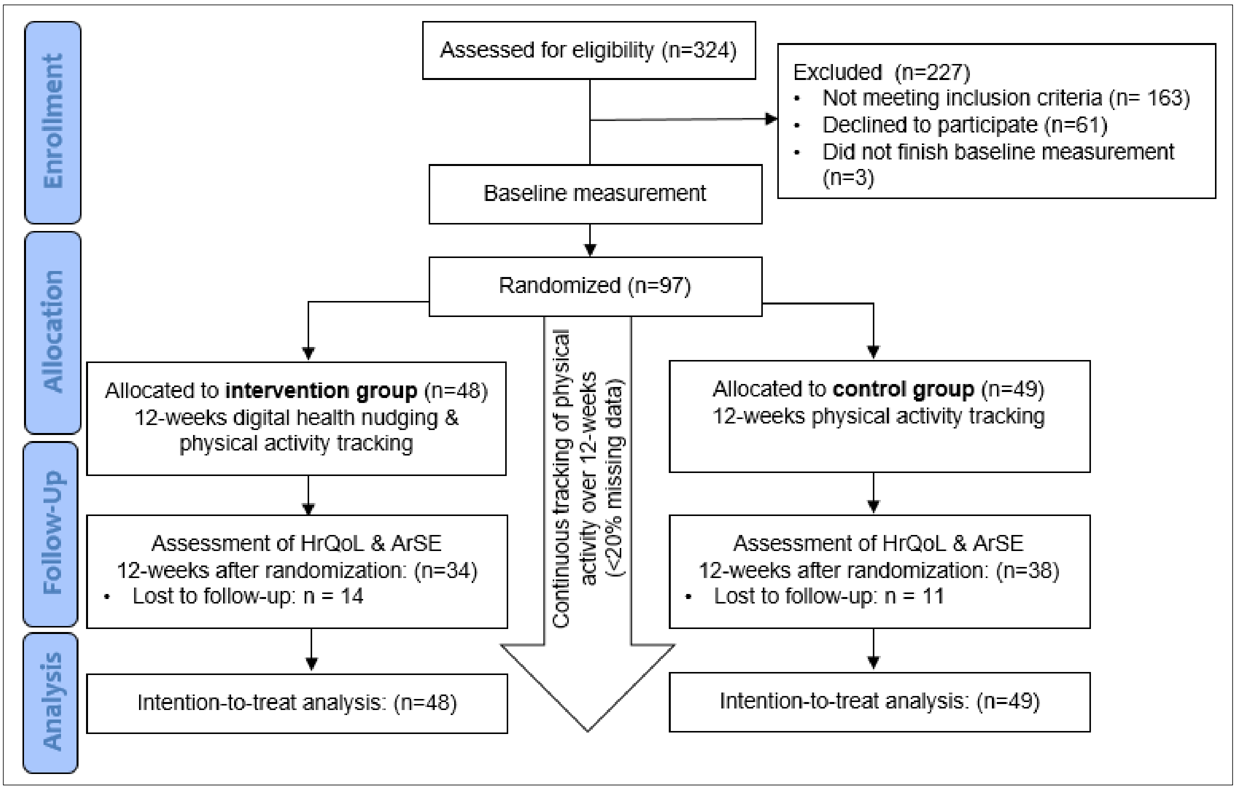


Figure 1: *CONSORT flowchart of enrolment and allocation of the study population*

Digital Health Nudging Intervention

In this study, the concept of information nudging was used to positively influence the activity behavior of our patients through skillful decision nudging [11]. Study participants received brief and informative text and video messages on their smartphone daily over a period of 12-weeks. Previous studies have shown that 12-weeks is an appropriate intervention duration to establish healthy habit formation [14, 15]. The Digital Nudges are on the subject of PA and based on Bandura's social cognitive theory. The social cognitive theory is organized as a triadic reciprocal determinism, describing the interaction of cognitive, behavioral, and environmental factors that shape human behavior [16]. The nudges addressed the behavioral determinant – skills, practice, information, and motivation – and the personal determinant – outcome expectation, self-regulation, and self-efficacy. Part of the nudges were adapted to the study period and included messages such as progress over time (e.g. half of the study time has passed, stick with it to reach your goals), season and weather-related nudges (e.g. it's cold and gray outside, go for a walk in the fresh air anyway, you will feel much better afterwards). Nudges regarding recommended activity levels were placed at the start of the intervention to give participants a certain goal (e.g. The WHO recommends that adolescents should be physically active for at least 60 minutes a day). In addition, activity challenges were advertised via the Nudges (e.g. try to take 10,000 steps every single day this week). These nudges were sent out in the early afternoon to avoid the time overlap with school [13]. With this lifestyle-oriented intervention, we were able to reach our patients regardless of location and time and tried to encourage them to adopt an active lifestyle. An overview of the nudges in German language can be found in the online supplements.

The CG was simply told to wear the wearable without receiving further instructions. After the 12-week intervention period, a cross-over took place to offer the nudging intervention to the control group as well and give them the opportunity to benefit from the intervention. In this manuscript only the 12-week intervention period of the RCT was investigated.

Assessment of Physical Activity

PA was objectively assessed with the “Garmin vivofit jr. 2®” (Garmin Ltd., Olathe, KS, USA), which children wore on their wrist for the entire study period. The “Garmin vivofit jr. 2®” is a wearable that tracks every single minute of moderate-to-vigorous PA (MVPA) throughout the day. The device is waterproof, and its battery lasts around one year, so study participants did not need to charge the device during the trial, which is a major advantage of the device to avoid missing data. Different wristband lengths were provided to ensure proper use of the device. Upon inclusion in the study, the wearable was fitted and its use was explained in detail. The accuracy has been proven in several evaluation studies [17, 18]. The wearable was connected with the APP “Garmin Junior”, where activity data was recorded. Once a week, participants transferred their daily activity data from the previous week to an online platform. For submitting activity data, study participants received a response from the study administration, either thanking them for submitting the data or, in the case of missing data, reminding them to wear the wearable again the following week. Prior to the start of the intervention, there was a one-week baseline measurement. According to the World Health Organization (WHO) guidelines on PA and sedentary behavior published 2020, children and adolescents should accumulate at least an average of 60 min per day of MVPA across the week [19].

Assessment of Health-related Quality of Life (HrQoL)

HrQoL was evaluated at baseline and follow-up with the KINDL® questionnaire [20]. The KINDL® is a generic instrument that comprises 24 items referring to the last week. The KINDL® relates to the six domains physical well-being, emotional well-being, self-esteem, family, friends, everyday functioning. Questions are answered on a 5-point Likert Scale and a total score ranging from 0 to 100 was calculated whereby higher values reflect better HrQoL. The KINDL® questionnaire shows good reliability and factorial validity for internal consistency [21, 22].

Assessment of Activity-Related Self-Efficacy (ArSE)

Youth ArSE is defined “as a youth’s belief in his/her capability to participate in PA and to choose PA despite existing barriers” [23]. ArSE was the only psychological factor consistently identified as a positive correlate and determinant of PA behavior in children and adolescents in several systematic reviews [24-26]. ArSE was assessed at baseline, and follow-up with the German version of the physical activity self-efficacy scale [27]. The scale consists of eight items and participants respond on a five point Likert-type scale ranging from 1 (“Disagree a lot”) to 5 (“Agree a lot”). The questionnaire shows good internal consistency on the individual level and excellent on the class level. Reliability and validity of the German version was shown in a study with 454 German school children [28].

Data Analysis

Patients’ characteristics are presented as median values, [25 quartile; 75 quartile], absolute numbers and percentage where appropriate. To evaluate the effectiveness of the intervention, analyses based on the intention-to-treat principle were conducted. Multiple imputation was used to replace missing data. Unbiased results can be obtained through multiple imputation even with extreme large proportions of missing data [29]. Missing values were imputed 5 times using the constraint method and consequently pooled to one dataset [30]. According to chi-squared test, the proportion of missing values did not differ between IG and CG ($p=0.787$). MVPA was calculated to weekly averages over the study period. To capture the longitudinal measurement of MVPA throughout the entire study period, a linear mixed model was used to compare the change of the MVPA behavior over time between IG and CG. The model was adjusted for baseline MVPA to account for small baseline difference. The linear mixed model allows both fixed and random effects. Analysis was performed using the lmer function from the lme4 R package in RStudio with the study participant modelled as random effect and time and randomization as fixed effects. Differences concerning activity level between moderate and complex CHDs were calculated with Mann-Whitney-U test. ArSE and HrQoL were compared between the groups with Mann-Whitney-U test. All analyses were performed with RStudio version 4.1.2 and SPSS (V28.0, IBM Corporation), with the level of significance set to two-sided p-values <0.05 for all tests.

Results

Patient characteristics of IG and CG are displayed in *Table 1*. Baseline PA was 79.3 [64.4; 93.1] min/day in the IG and 72.6 [53.4; 86.2] min/day in the CG. Activity level was comparably high in both groups throughout the 12-weeks with an average of 73.7 [62.3; 78.8] min/day in IG and 78.4 [66.6; 93.9] min/day in CG over the whole study period. Thereby 77% of the IG and 82% of the CG reached the PA recommendation of the WHO.

Table 1: *Baseline characteristics of the study population*

Characteristics	Total (n = 97)	Intervention (n = 48)	Control (n = 49)
Female sex, n (%)	49 (51)	25 (52)	24 (49)
Age, y	15.1 ± 2.0	15.1 ± 2.0	15.0 ± 2.1
Height, cm	163.5 ± 12.0	163.9 ± 12.8	163.1 ± 11.3
Weight, kg	55.4 ± 15.2	53.3 ± 13.9	57.4 ± 16.2
BMI, km/m2	20.6 ± 5.3	19.6 ± 3.1	21.6 ± 6.7
Severity*, n (%)			
Moderate	48 (49)	21 (44)	27 (55)
Complex	49 (51)	27 (56)	22 (45)
Diagnosis, n (%)			
Left heart obstruction	22 (23)	11 (23)	11 (23)
Right heart obstruction	29 (30)	11 (23)	18 (37)
Isolated shunts	14 (14)	9 (19)	5 (10)
TGA after arterial switch	7 (7)	3 (6)	4 (8)
Fontan circulation	18 (19)	8 (17)	10 (20)
Miscellaneous	7 (7)	6 (12)	1 (2)
Number of heart surgery	1.4 ± 1.4	1.5 ± 1.6	1.3 ± 1.2
Number of catheter	1 ± 1.3	1.1 ± 1.4	1 ± 1.2
Hypertensive medication, n (%)	14 (14)	7 (15)	7 (14)

BMI: body mass index, TGA: transposition of the great arteries. *CHD Severity according to the American College of Cardiology.

There was no significant difference in the activity level between patients with moderate and complex CHDs (moderate 77.9 [66.2; 89.4] min/day vs. complex 74.4 [58.0; 86.9] min/day, p=0.251). Intention-to-treat analysis revealed a MVPA decreased from 78.1 [62.5; 86.5] min/day in the first two weeks to 72.9 [59.3; 74.8] min/day during the last two weeks in the IC and from 80.2 [64.7; 102.3] min/day to 73.8 [60.0; 87.5] min/day in the CG over the study period, see *Figure 2* and *Figure 3*.

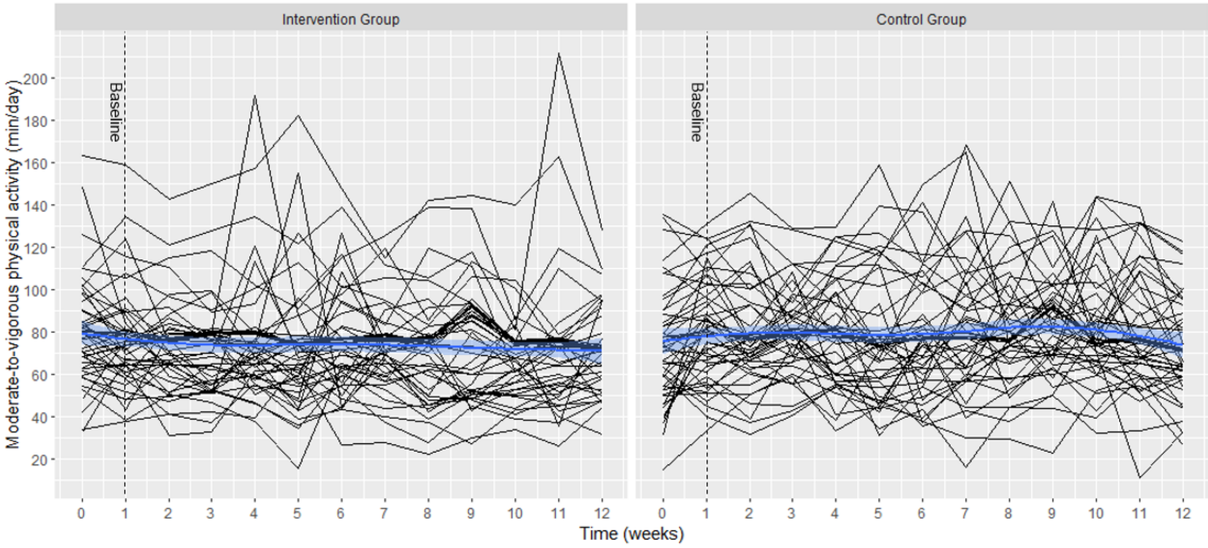


Figure 2: *Weekly average of minutes of moderate-to-vigorous physical activity over 12-week study period in intervention and control group with standard errors*

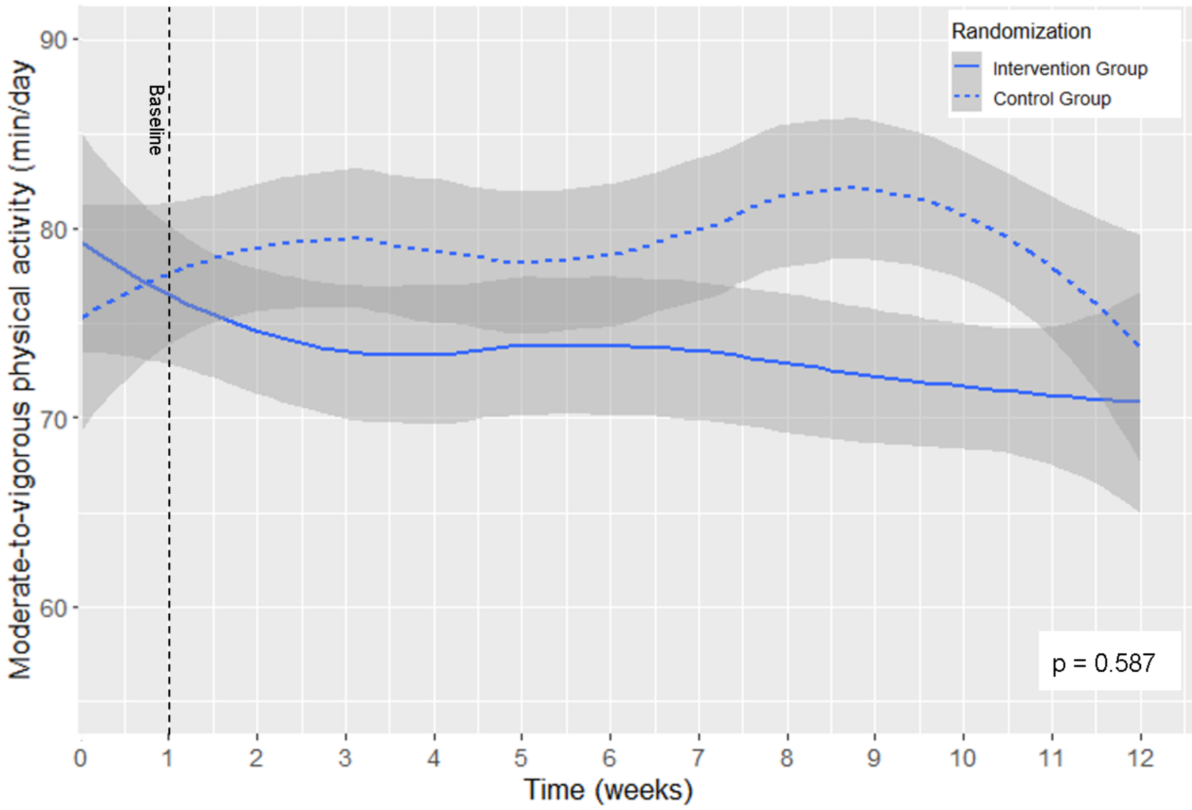


Figure 3: *Close-up of weekly average of minutes of moderate-to-vigorous physical activity over time in intervention and control group with standard errors. The p-value compares the change in MVPA over the 12-week period between the IG and CG with a linear mixed model.*

According to the linear mixed model, the change of MVPA over the study period did not significantly differ between IG and CG (b=0.136, 95%-CI [-0.355; 0.627], p=0.587), see *Table 2*.

Table 2: *Change of moderate-to-vigorous physical activity over the study period compared between intervention and control group*

	Mean MVPA (min/day) change/week	Standard error	p-value
Intercept	29.937	5.213	**<0.001**
Randomization: CG	9.836	3.401	**0.004**
Time	-0.343	0.178	0.054
Baseline MVPA	0.566	0.058	**<0.001**
Randomization: CG x Time	0.136	0.250	0.587

CG: Control group, MVPA: moderate-to-vigorous physical activity

In comparison to the CG, emotional well-being significantly increased over the study period (IG: Δ1.60 [-0.2; 6.3] vs. CG: Δ0.0 [-12.5; 6.3], p=0.043), but not the total HrQoL score (IG: Δ0.0 [-6.8; 5.4] vs. CG: Δ-1.0 [-8.9; 3.5], p=0.518), see *Table 3*. ArSE (IG: Δ-0.1 [-0.5; 0.1] vs. CG: Δ0.0 [-0.4; 0.3], p=0.305) did not change during the *Digital Health Nudging* intervention compared to the CG, see *Table 3* and *Table S1*.

Table 3: *Differences in health-related quality of life and activity-related self-efficacy between intervention and control group after 12-weeks digital health nudging*

	Intervention group (n=48)			**Control group** (n=49)			
	Baseline evaluation	12-weeks follow-up	Change	Baseline evaluation	12-weeks follow-up	Change	p-value*
Health-related quality of life							
Total score	79.7 [69.3; 84.1]	76.9 [71.9; 81.3]	0.0 [-6.8; 5.4]	76.1 [71.4; 83.9]	76.2 [70.3; 81.4]	-1.0 [-8.9; 3.5]	.518
Physical well-being	75.0 [62.5; 87.5]	78.0 [63.3; 87.5]	0.0 [-13.2; 11.3]	75.0 [68.8; 97.5]	75.0 [68.8; 81.4]	0.0 [-12,5; 6.6]	.986
Emotional well-being	81.3 [70.3; 87.5]	81.3 [75.0; 87.5]	1.6 [-0.2: 6.3]	81.3 [68.8; 93.8]	81.3 [65.4; 93.8]	0.0 [-12.5; 6.3]	**.043**
Self-esteem	68.8 [62.5; 81.3]	68.8 [62.5; 81.3]	-2.2 [-6.3; 5.7]	75.0 [62.5; 81.3]	68.8 [57.2; 79.5]	0.0 [-10.8; 6.3]	.876
Family	93.8 [81.3; 100]	91.4 [85.3; 99.6]	0.0 [-6.3; 5.7]	93.8 [81.3; 100]	93.8 [81.3; 100]	0.0 [-6.3; 6.3]	.965
Friends	81.3 [68.8; 87.5]	77.3 [68.8; 87.5]	0.0 [-6.3; 6.3]	75.0 [68.8; 87.5]	75.0 [62.5; 87.2]	-4.9 [-12.5; 11.2]	.381
School	75.0 [64.1; 87.5]	75.0 [62.5; 81.6]	0.0 [-6.25; 6.25]	68.8 [56.3; 84.4]	70.4 [67.2; 81.3]	0.0 [-6.3; 6.3]	.965
Activity-related self-efficacy							
Total score	3.9 [3.1; 4.2]	3.6 [2.9; 4.0]	-0.1 [-0.5; 0.1]	3.5 [2.8; 3.9]	3.4 [2.8; 3.7]	0.0 [-0.4; 0.3]	.305

**Mann-Whitney-U-Test comparing the mean change between intervention and control group with p<.05 considered significant.*

Discussion

This randomized control trial shows that 12-weeks of *Digital Health Nudging* did not increase PA and ArSE, but improved feelings of emotional well-being in adolescents with CHD. To the best of our knowledge, no digital nudging intervention has been conducted in the CDH population so far. In a RCT from Klausen et al., an individually tailored eHealth program to promote PA was implemented over a 52-week period in adolescents with complex CHD. The program consisted of three main approaches: health education, a personal exercise planning tool and, comparable to our intervention, tailored text encouragements sent out every week. Only 70% of the study participants used the eHealth application for at least two consecutive weeks. Similar to our RCT results, no increase in PA and HrQoL was observed. Overall their study participants were way less active compared to our study population with only around 40 min/day MVPA in both IG and CG [31]. Another technology-based approach is being implemented with a chat-based health platform to increase PA in CHD children. The "HeartFIT" intervention provides multilevel engagement, including health education, exercise prescriptions, and telephone follow-ups over a 12-week study period. However results are not published yet [15]. A previous RCT at our institution attempted to improve health-related fitness in pediatric CHD patients through a 24-week web-based exercise intervention. The e-Health intervention was safe but did not improve health-related fitness and HrQoL in children with moderate or complex CHD. A major concern of that intervention study was that adherence to the weekly exercise program was quite low with only 33% [32]. Generally, one of the key challenges of activity promotion is to maintain the adherence of the target group in the long run. Therefore, the idea of providing only a short, daily nudge with easy implementation in everyday-life was executed. The proportion of eligible participants who signed up to participate in our study was high with 60%, compared with only 38% in the previous RCT at our institution [32]. This may indicate that our intervention appeared attractive to study participants and their parents. In healthy children several studies have shown positive effects of nudging interventions. A scoping review from 2019 identified the efficacy of mHealth intervention strategies for facilitating PA among healthy adolescents and reported improved PA outcomes [12]. Another review from Ludwig and colleagues reported promising results for improving PA and sedentary behavior of SMS interventions in healthy youth [13]. Digital health interventions are easy accessible, low-cost to implement, and have the potential to reach people independent of location, time, and socioeconomic status [33]. Besides activity promotion, text message interventions also showed an increase in self-efficacy among healthy peers. A text message intervention on healthy children was not effective in increasing PA itself, but resulted in a significant improvement of self-efficacy. Thus, despite the lack of increase in PA itself, the intervention resulted in participants becoming more confident to be physically active, which could facilitate behavior change in the long-run [10]. Given that self-efficacy has been shown to be the strongest predictor of PA, digital nudges may need to focus even more on activity-related self-efficacy to give participants the confidence to become more active in the long-term [25]. A previous study showed, that children with CHD who move more appear to report better HrQoL [32]. The result of our study showed that the *Digital Health Nudging* had no effect on PA levels also did not improve overall HrQoL. This is consistent with other digital health interventions to increase PA in CHD children, which also failed to increase HrQoL [31, 32]. Fortunately, previous studies have shown that the quality of life of children with CHD is already at a high level, which may have made further improvement by digital nudging difficult. A study using the same questionnaire as in our study reported good HrQoL compared to healthy peers and thereby showed similar HrQoL values as in our study population [34]. However, *Digital Health Nudging* was able to increase emotional well-being in adolescents with CHD. Emotional well-being includes positive mood and high self-esteem [35], this might indicate that study participants had fun and enjoyed the *Digital Health Nudging* intervention. As enjoyment and fun increases the likelihood that PA becomes a routine, this might have long-term effects [36]. However, interpretation of these results must be considered with precaution, as it might as well be a spurious association.

The novelty effect of wearables

Wearables provide users with the ability to receive real-time feedback, self-monitor and compare their behavior, and potentially create internal motivation for PA [37]. A recent RCT investigated the effectiveness of wearables for increasing PA, reporting of mixed evidence that wearables increase MVPA and steps [38]. Thereby the so-called novelty effect of the wearable plays a major role in the increase of activity. Initially, the wearable leads to an increase in PA, but after the novelty period, PA declines again, resulting in only a short-term increase in PA. Previous studies reported of novelty periods of only about 2-4 weeks in adolescents [37, 39]. In contrast to our study, in these studies the wearable is used as the intervention itself and not as the outcome measure as in our study. Nevertheless, our results might indicate that although wearables and *Digital Health Nudging* initially have a positive influence on PA, activity declines over time in both groups and *Digital Health Nudging* apparently does not have the potential to stop or slow down this phenomenon.

Limitations and implications for upcoming PA promotion studies

All included patients are in regular tertiary care follow-up in our institution where PA is recommended, which might over-represent the activity level of adolescents with CHD. Combined with this encouragement of PA in our institution the novelty and excitement of wearing the “Garmin vivofit jr. 2®” device might have additionally increased the PA level in the beginning besides the nudging intervention [40]. As the sample size calculation was based on a medium effect size it might have been too optimistic and the overall sample size might have been too small after all. Further studies with greater sample size are needed. Partially low adherence to wearing the wearable and associated missing data may also have influenced the results. On days when activity data was available, we were unable to verify whether the participants wore the device at all times during the day.

Further projects might need to individualize the nudging intervention, as we speculate that our standardized nudges were not individual enough for our relatively wide age range of participants [32]. Nudges should also be tailored to the individual’s baseline PA level. Artificial intelligence or deep learning algorithms might be promising features in this context. Guidance and external supervision might play a larger role and should be included for example in the form of individual feedback in upcoming digital PA promotion programs [41]. Long-term and sustainable behavior change does not happen overnight. Therefore, an appropriate intervention period is required, also taking into account that the novelty effect of the wearable might affect the outcomes in the beginning. Adding gamification to the digital approach might optimize the intervention, as gamification has shown to be a promising way to leverage the effectiveness of digital interventions in adolescents [42]. Furthermore, this might make the PA promotion more fun and engaging [43], which was shown to be crucial in establishing sustainable habits [36]. In addition, the involvement of peers or family in the intervention could contribute to motivation and improve quality of life [44].

Conclusion

Digital Health Nudging over 12-weeks did not increase PA and ArSE, but improved emotional well-being in adolescents with moderate to complex CHD. Given the complexity of health interventions and interplay of factors influencing PA behavior, digital interventions might still play a role in activity promotion in the CHD population.

Supplementary Table S1: *Differences in activity-related self-efficacy between intervention and control group after 12-weeks digital health nudging*

	Intervention group (n=48)			**Control group** (n=49)			
Activity-related self-efficacy	Baseline evaluation	12-weeks follow-up	Change	Baseline evaluation	12-weeks follow-up	Change	p-value*
Total score	3.9 [3.1; 4.2]	3.6 [2.9; 4.0]	-0.1 [-0.5; 0.1]	3.5 [2.8; 3.9]	3.4 [2.8; 3.7]	0.0 [-0.4; 0.3]	.305
1. I can be physically active during my free time on most days.	4.0 [3.0; 5.0]	4.0 [3.0; 4.3]	0.0 [-1.0; 0.0]	4.0 [3.0; 5.0]	4.0 [2.1; 4.2]	0.0 [-0.9; 0.0]	.265
2. I can ask my parent or other adult to do physically active things with me.	4.0 [3.0; 5.0]	3.9 [3.0; 4.0]	0.0 [-1.0; 0.0]	4.0 [3.0; 5.0]	3.0 [2.0; 4.0]	-0.1 [-1.0; 0.0]	.440
3. I can be physically active during my free time on most days even if I could watch TV or play video games instead.	4.0 [3.0; 5.0]	3.7 [3.0; 4.0]	0.0 [-1.0; 0.0]	4.0 [3.0; 4.5]	4.0 [2.6; 4.1]	0.0 [-0.6; 1.0]	.146
4. I can be physically active during my free time on most days even if it is very hot or cold outside.	4.0 [3.0; 4.0]	3.2 [2.8; 4.0]	0.0 [-1.0; 1.0]	3.0 [2.0; 4.5]	3.1 [2.0; 4.0]	0.0 [-1.0; 1.0]	.548
5. I can ask my best friend to be physically active with me during my free time on most days.	3.0 [2.0; 4.0]	3.0 [2.2; 4.0]	0.0 [-0.9; 1.0]	3.0 [2.0; 4.0]	3.0 [2.0; 4.0]	0.0 [-0.6; 1.0]	.790
6. I can be physically active during my free time on most days even if I have a lot of homework.	4.0 [3.0; 5.0]	3.6 [2.8; 4.8]	0.0 [-1.0; 0.0]	3.0 [2.0; 5.0]	3.3 [2.6; 4.0]	0.0 [-1.0; 0.6]	.224
7. I have the coordination I need to be physically active during my free time on most days.	4.0 [3.0; 5.0]	3.2 [3.0; 4.0]	-0.5 [-1.0; 0.0]	4.0 [3.0; 4.0]	3.5 [3.0; 4.0]	0.0 [-1.0; 1.0]	.189
8. I can be physically active during my free time on most days no matter how busy my day is.	3.0 [2.3; 4.0]	3.3 [2.0; 4.0]	-0.0 [-0.6; 0.3]	3.0 [2.0; 4.0]	3.0 [2.0; 4.0]	0.0 [-1.0; 0.0]	.410

**Mann-Whitney-U-Test comparing the mean change between intervention and control group with p<.05 considered significant*

References

[1] Brudy L, Hock J, Häcker A-L, Meyer M, Oberhoffer R, Hager A, et al. Children with congenital heart disease are active but need to keep moving: A cross-sectional study using wrist-worn physical activity trackers. The Journal of pediatrics. 2020;217:13-9.

[2] Siaplaouras J, Niessner C, Helm PC, Jahn A, Flemming M, Urschitz MS, et al. Physical activity among children with congenital heart defects in Germany: a nationwide survey. Frontiers in Pediatrics. 2020;8:170.

[3] Voss C, Duncombe SL, Dean PH, de Souza AM, Harris KC. Physical activity and sedentary behavior in children with congenital heart disease. Journal of the American Heart Association. 2017;6(3):e004665.

[4] Longmuir PE, Brothers JA, De Ferranti SD, Hayman LL, Van Hare GF, Matherne GP, et al. Promotion of physical activity for children and adults with congenital heart disease: a scientific statement from the American Heart Association. Circulation. 2013;127(21):2147-59.

[5] Takken T, Giardini A, Reybrouck T, Gewillig M, Hövels-Gürich H, Longmuir P, et al. Recommendations for physical activity, recreation sport, and exercise training in paediatric patients with congenital heart disease: a report from the Exercise, Basic & Translational Research Section of the European Association of Cardiovascular Prevention and Rehabilitation, the European Congenital Heart and Lung Exercise Group, and the Association for European Paediatric Cardiology. European journal of preventive cardiology. 2012;19(5):1034-65.

[6] Longmuir PE, McCrindle BW. Physical activity restrictions for children after the Fontan operation: disagreement between parent, cardiologist, and medical record reports. American heart journal. 2009;157(5):853-9.

[7] Sawyer SM, Afifi RA, Bearinger LH, Blakemore S-J, Dick B, Ezeh AC, et al. Adolescence: a foundation for future health. The lancet. 2012;379(9826):1630-40.

[8] Telama R, Yang X, Viikari J, Välimäki I, Wanne O, Raitakari O. Physical activity from childhood to adulthood: a 21-year tracking study. American journal of preventive medicine. 2005;28(3):267-73.

[9] Hallal PC, Wells JC, Reichert FF, Anselmi L, Victora CG. Early determinants of physical activity in adolescence: prospective birth cohort study. Bmj. 2006;332(7548):1002-7.

[10] Schwerdtfeger AR, Schmitz C, Warken M. Using text messages to bridge the intention-behavior gap? A pilot study on the use of text message reminders to increase objectively assessed physical activity in daily life. Frontiers in psychology. 2012;3:270.

[11] Thaler RH, Sunstein CR. Nudge: Improving decisions about health, wealth, and happiness: Penguin; 2009.

[12] Lee AM, Chavez S, Bian J, Thompson LA, Gurka MJ, Williamson VG, et al. Efficacy and effectiveness of mobile health technologies for facilitating physical activity in adolescents: scoping review. JMIR mHealth and uHealth. 2019;7(2):e11847.

[13] Ludwig K, Arthur R, Sculthorpe N, Fountain H, Buchan DS. Text messaging interventions for improvement in physical activity and sedentary behavior in youth: systematic review. JMIR mHealth and uHealth. 2018;6(9):e10799.

[14] Gardner B, Lally P, Wardle J. Making health habitual: the psychology of ‘habit-formation’and general practice. British Journal of General Practice. 2012;62(605):664-6.
[15] Li Y, Zhou Y, Chen M, Fu MR, Luo B, Yu P, et al. A WeChat-Based Rehabilitation Platform for Children and Adolescents with Congenital Heart Disease to Promote Cardiac FITness (HeartFIT): Protocol for a Mixed-Methods Strategy from Evidence-Based Design to Pilot Study. Journal of Multidisciplinary Healthcare. 2022;15:907.
[16] Bandura A. Social foundations of thought and action. Englewood Cliffs, NJ. 1986;1986(23-28).
[17] Alsubheen SaA, George AM, Baker A, Rohr LE, Basset FA. Accuracy of the vivofit activity tracker. Journal of medical engineering & technology. 2016;40(6):298-306.
[18] Price K, Bird SR, Lythgo N, Raj IS, Wong JY, Lynch C. Validation of the Fitbit One, Garmin Vivofit and Jawbone UP activity tracker in estimation of energy expenditure during treadmill walking and running. Journal of medical engineering & technology. 2017;41(3):208-15.
[19] Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. British journal of sports medicine. 2020;54(24):1451-62.
[20] Ravens-Sieberer U, Bullinger M. Assessing health-related quality of life in chronically ill children with the German KINDL: first psychometric and content analytical results. Quality of life research. 1998;7(5):399-407.
[21] Ellert U, Ravens-Sieberer U, Erhart M, Kurth B-M. Determinants of agreement between self-reported and parent-assessed quality of life for children in Germany-results of the German Health Interview and Examination Survey for Children and Adolescents (KiGGS). Health and quality of life outcomes. 2011;9(1):1-11.
[22] Erhart M, Ellert U, Kurth B-M, Ravens-Sieberer U. Measuring adolescents' HRQoL via self reports and parent proxy reports: an evaluation of the psychometric properties of both versions of the KINDL-R instrument. Health and Quality of Life Outcomes. 2009;7(1):1-12.
[23] Voskuil VR, Robbins LB. Youth physical activity self-efficacy: A concept analysis. Journal of advanced nursing. 2015;71(9):2002-19.
[24] Bauman AE, Reis RS, Sallis JF, Wells JC, Loos RJ, Martin BW, et al. Correlates of physical activity: why are some people physically active and others not? The lancet. 2012;380(9838):258-71.
[25] Cortis C, Puggina A, Pesce C, Aleksovska K, Buck C, Burns C, et al. Psychological determinants of physical activity across the life course: A" DEterminants of DIet and Physical ACtivity"(DEDIPAC) umbrella systematic literature review. PloS one. 2017;12(8):e0182709.
[26] Craggs C, Corder K, van Sluijs EM, Griffin SJ. Determinants of change in physical activity in children and adolescents: a systematic review. American journal of preventive medicine. 2011;40(6):645-58.
[27] Dishman RK, Hales DP, Sallis JF, Saunders R, Dunn AL, Bedimo-Rung AL, et al. Validity of social-cognitive measures for physical activity in middle-school girls. Journal of pediatric psychology. 2010;35(1):72-88.
[28] Bachner J, Sturm DJ, Haug S, Demetriou Y. Multi-level validation of the German physical activity self-efficacy scale in a sample of female sixth-graders. BMC Public Health. 2020;20(1):1-10.

[29] Madley-Dowd, P., Hughes, R., Tilling, K., & Heron, J. (2019). The proportion of missing data should not be used to guide decisions on multiple imputation. Journal of clinical epidemiology, 110, 63-73.
[30] Donders ART, Van Der Heijden GJ, Stijnen T, Moons KG. A gentle introduction to imputation of missing values. Journal of clinical epidemiology. 2006;59(10):1087-91.
[31] Klausen SH, Andersen LL, Søndergaard L, Jakobsen JC, Zoffmann V, Dideriksen K, et al. Effects of eHealth physical activity encouragement in adolescents with complex congenital heart disease: the PReVaiL randomized clinical trial. International journal of cardiology. 2016;221:1100-6.
[32] Meyer M, Brudy L, Fuertes-Moure A, Hager A, Oberhoffer-Fritz R, Ewert P, et al. E-health exercise intervention for pediatric patients with congenital heart disease: a randomized controlled trial. The Journal of Pediatrics. 2021;233:163-8.
[33] Hswen Y, Viswanath K. Beyond the hype: mobile technologies and opportunities to address health disparities. Journal Of Mobile Technology In Medicine. 2015;4(1):39-40.
[34] Reiner B, Oberhoffer R, Ewert P, Müller J. Quality of life in young people with congenital heart disease is better than expected. Archives of disease in childhood. 2019;104(2):124-8.
[35] Schutte NS, Malouff JM, Simunek M, McKenley J, Hollander S. Characteristic emotional intelligence and emotional well-being. Cognition & Emotion. 2002;16(6):769-85.
[36] Foster C, Moore J, Singletary C, Skelton J. Physical activity and family-based obesity treatment: a review of expert recommendations on physical activity in youth. Clinical obesity. 2018;8(1):68-79.
[37] Kerner C, Goodyear VA. The motivational impact of wearable healthy lifestyle technologies: a self-determination perspective on Fitbits with adolescents. American Journal of Health Education. 2017.
[38] Creaser AV, Clemes SA, Costa S, Hall J, Ridgers ND, Barber SE, et al. The acceptability, feasibility, and effectiveness of wearable activity trackers for increasing physical activity in children and adolescents: a systematic review. International journal of environmental research and public health. 2021;18(12):6211.
[39] Ridgers ND, Timperio A, Brown H, Ball K, Macfarlane S, Lai SK, et al. Wearable activity tracker use among Australian adolescents: usability and acceptability study. JMIR mHealth and uHealth. 2018;6(4):e9199.
[40] Lubans DR, Morgan PJ, Callister R, Collins CE. Effects of integrating pedometers, parental materials, and E-mail support within an extracurricular school sport intervention. Journal of Adolescent Health. 2009;44(2):176-83.
[41] Duppen N, Takken T, Hopman M, ten Harkel AD, Dulfer K, Utens EM, et al. Systematic review of the effects of physical exercise training programmes in children and young adults with congenital heart disease. International journal of cardiology. 2013;168(3):1779-87.
[42] Mazeas A, Duclos M, Pereira B, Chalabaev A. Evaluating the effectiveness of gamification on physical activity: systematic review and meta-analysis of randomized controlled trials. Journal of Medical Internet Research. 2022;24(1):e26779.
[43] Cugelman B. Gamification: what it is and why it matters to digital health behavior change developers. JMIR serious games. 2013;1(1):e3139.

[44] Morrissey JL, Janz KF, Letuchy EM, Francis SL, Levy SM. The effect of family and friend support on physical activity through adolescence: a longitudinal study. International Journal of Behavioral Nutrition and Physical Activity. 2015;12(1):1-9.

3.6 Discussion Digital Health Nudging

In this thesis, the new concept of nudging, originally developed in behavioral economics, was applied to adolescents with CHD for the first time and examined for its effectiveness in promoting PA. *Digital Health Nudging* via daily smartphone messages over a 12-week period did not increase PA, but did improve feelings of psychological well-being.

As digitalization has arrived in the medical field, there has also been a rapid increase of digital health behavior change interventions targeting PA in the healthy population and in different patient cohorts [113]. Digital text message interventions have led to positive changes in preventive health behaviors [114], including PA [115, 116] and body weight [117]. Especially in adolescents, text message interventions have shown to be an effective approach to increase PA [118, 119].

Despite the increased usage of digital text messaging interventions for promotion of PA in different target groups, several methodological and content related issues have emerged in previous studies and also during our *Digital Health Nudging* intervention. According to a meta-analysis of prevention-based text messaging interventions for behavior change, further research with high-quality design is needed to establish evidence-based best practices [114]. This is particularly relevant in the cohort of adolescents with CHD, as in the *Digital Health Nudging* trial digital text messaging was introduced for the first time in the CHD population. Based on previous research and the *Digital Health Nudging* trial, several advantages and disadvantages can be identified from which recommendations for future aspects of digital health interventions can be derived, in order to adopt evidence-based best practices in the future.

Outcome Measurement Procedure

1. Subjective/Objective Measurement

Roberts and colleagues conducted a meta-analysis on digital health behavior change interventions targeting PA and diet in cancer survivors. All of the fifteen included studies reported significant improvements of MVPA and BMI, concluding that digital technologies offer promising approaches to encourage health behavior change among cancer survivors [120]. Contrary to our findings, all studies included in this meta-analysis assessed PA level subjectively with self-reported questionnaires. In particular, when activity levels are measured after an activity promotion intervention, there is a high risk of social desirability bias and recall bias. Even the authors indicate that the results therefore need to be interpreted with caution. A previous study from the German Heart Center Munich showed, that also in children with CHD subjectively measured PA levels often deviate considerably from the objectively measured PA level [72]. Therefore, objective measurement throughout the 12-week study period is a major strength of the *Digital Health Nudging* trial, and further studies evaluating digital behavior change interventions should use objective PA measurement tools.

2. Measurement Period

Text messaging over a 12-week period to increase PA was also evaluated in a cohort of adolescents with type 1 diabetes. Similar to our study-design, PA was assessed objectively and participants did wear the wearable during the entire study period. No increase in PA was observed in this study either. However, only a four-day period before and after the intervention was used for the outcome measurement [121]. A similar measurement procedure was used in a text messaging intervention study in healthy adolescents, where PA was objectively assessed, but again only for a time period of one week [115]. However, thereby the already discussed Hawthorn Effect may have a considerable effect on the PA levels. There is no clear evidence on how long the Hawthorn Effect lasts. However, it can be assumed that it decreases the longer the measurement period lasts and that its effect may have decreased substantially during the 12-week period of the *Digital Health Nudging* intervention. The long measurement period of the *Digital Health Nudging* trial is an advantage, in which longitudinal data were evaluated over the entire study period. Additionally, the period of PA assessment has never been so long in the CHD population. Various studies have been published on PA levels itself, however measurement periods were only between some days to one week [70].

3. Blinding the Outcome Measurement

Newton and colleagues blinded their outcome measures in a text messaging intervention by taping the wearable [121]. This might also be an approach to reduce the effect of the wearable itself so that the results can be attributed exclusively to the digital intervention. However, it must also be taken into account that motivation is required to wear the wearables, especially over a longer period of time, which might be lost by blinding the activity values and restricting direct functions for the user.

4. Design of Measurement Device

User-friendly design and aesthetics were shown to play a significant role for acceptance and motivation in digital interventions [122]. The Garmin vivofit jr2.® has a very child-friendly design that seems to be appealing for younger children, however, may not have been age-appropriate for older adolescents. This might have reduced the engagement in the intervention and motivation to participate. For further digital health measures, emphasis should definitely be placed on user-friendliness and aesthetics of the intervention and the measurement device, suitable for corresponding age groups.

Digital Intervention Design

1. Intervention Frequency

A systematic review on text messaging interventions for improving PA reported of beneficial effects of studies with higher frequency of messages, so the daily text messages in our intervention seem to be advantageous [119]. Concerning intervention duration, which also varied widely between different text messaging interventions, intervention durations of around six months were associated with the greatest effects [114].

2. Intervention Modality

A previous study has shown, that digital behavior change approaches on the smartphone like APPs and text messages might be more effective than other digital approaches like websites due to the widespread usage and constant access to the smartphone [120]. Especially in adolescents we would therefore recommend, to implement further digital behavior change approaches via smartphone.

3. Population

Identifying high-risk groups was shown to be important for generating substantial health gains, for the least effort and hence for the lowest costs [123]. A huge advantage of the *Digital Health Nudging* intervention was that we were able to precisely tailor our target population based on previous research. Only the vulnerable group of adolescents with moderate and complex CHD diagnosis were included in the study.

However, the *Digital Health Nudging* trial included children independent of their activity level, which in our case meant that the cohort was comparatively active from the beginning. This may have made it difficult to further increase PA levels and thus show an effect of the intervention. Future studies on digital behavior change should therefore exclusively target an inactive cohort.

Content of the Digital Intervention

1. Social Comparison and Feedback-Loops

Different studies have shown that PA promotion programs were more efficient when participants received feedback on how they performed in comparison to other study participants [124, 125]. As people tend to compare their situation with that of others, social comparison can be used to encourage health behavior [102]. Further activity promotion studies might incorporate this, not only to promote the competitive approach, but also to connect patients.

In addition, upcoming studies should take advantage of the continuously collected PA data for providing individual feedback-loops during the digital intervention. Targeting feedback as part of the self-regulatory process via text messages was shown to be efficient in increasing PA in healthy adolescents [126, 127]. Part of the studies also examined interactivity in the form of responses to text messages and reported positive effects. Further studies should set individual goals and provide feedback based on individual goal-attainment [119].

2. Individualized Intervention

Last but not least, future digital behavior change measures should be designed to be as individualized and patient-centered as possible. For these content-related modifications, artificial intelligence, deep learning algorithms or chatbots as ChatGPT are promising features. At present, there is an underutilization of artificial intelligence in the clinical setting for diagnosis, prognosis, and management of patients with CHD [128].

New technologies should be widely applied in the aftercare of patients with CHD to increase quality and precision of health care delivery in a cost-effective way. Developing new “intelligent” patient-centered approaches is crucial in the aftercare of CHD and should also be implemented in prevention programs [129].

Digital Health Nudging in the Broader Context

All in all it needs to be recognized, that changing behavior and building habits towards a physically active lifestyle is highly complex and requires solutions and approaches across many sectors and at many levels [64]. According to the ecological model individual's PA behavior is affected by diverse factors including individual, interpersonal, environmental, regional, and global determinants of PA. Besides personal contributors like age, sex, health status, self-efficacy, and motivation also the social and physical environment were elaborated as contributors for PA behavior. Broader views of health behavior causation also include contributors outside the health sector like urban planning, transportation systems, and parks [130]. Previous studies did show that text messages used in combination with other approaches had larger effects [114, 119].

In the future, *Digital Health Nudging* might be implied as one of several approaches and could be used as a moderator or add-on in different settings. Taking into account all the factors discussed, the *Digital Health Nudging* intervention could potentially be adapted and transferred to other medical conditions or health promotion in the general population.

4. Overall Conclusion

This thesis identified cardiovascular risk factors that are already prevalent in children and adolescents with CHD. Modifiable, lifestyle-related risk factors, the main contributors for non-communicable diseases in the general population, also affect the vulnerable population of children with CHD. The growing pandemic of overweight and obesity as well as physical inactivity are prevalent in the CHD population as well. Although an association between PA and arterial stiffness has not been demonstrated in an active cohort of CHD children, the impact of PA on cardiovascular health is undeniable.

Therefore, preventive measures, long-term behavioral changes, and PA promotion starting at an early age is of extreme importance in children and adolescents with CHD. Based on the findings of the first two studies, the *Digital Health Nudging* randomized controlled trial was developed particularly for adolescents. Adolescents have not only been identified as being at particular risk for overweight, obesity, and physical inactivity, but are additionally at a crucial stage in which life-long health habits are developed.

Today, the application of *Digital Health Nudging* in the outpatient care of pediatric patients with CHD is unique. Its implementation worked well and received a lot of positive feedback of adolescents and parents. Behavior change toward a physically active lifestyle is extremely complex and multifactorial, especially in children and adolescents. Even though *Digital Health Nudging* alone did not increase PA in adolescents with a CHD, it may still have an impact when used in conjunction with other approaches. Efforts including digital health and the concept of nudging should be further intensified for its application in prevention and health promotion in patients with CHD.

Finally, for future preventive approaches, patient-centered and individualized programs are of particular importance in the very heterogeneous group of CHD. Therefore new technologies such as Artificial Intelligence and Big Data offer immense potential and should be implemented in the future aftercare of CHD patients.

5. References

[1] Liu Y, Chen S, Zühlke L, Black GC, Choy M-k, Li N, et al. Global birth prevalence of congenital heart defects 1970–2017: updated systematic review and meta-analysis of 260 studies. International journal of epidemiology. 2019;48(2):455-63.

[2] von Blum U, Meyer H, Beerbaum P, Peuster M. Kompendium angeborene Herzfehler bei Kindern - Diagnose und Behandlung Berlin, Heidelberg Springer; 2021.

[3] Dolk H, Loane M, Garne E, Group aESoCAW. Congenital heart defects in Europe: prevalence and perinatal mortality, 2000 to 2005. Circulation. 2011;123(8):841-9.

[4] Zimmerman MS, Smith AGC, Sable CA, Echko MM, Wilner LB, Olsen HE, et al. Global, regional, and national burden of congenital heart disease, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet Child & Adolescent Health. 2020;4(3):185-200.

[5] Schwedler G, Lindinger A, Lange PE, Sax U, Olchvary J, Peters B, et al. Frequency and spectrum of congenital heart defects among live births in Germany. Clinical Research in Cardiology. 2011;100(12):1111-7.

[6] Warnes CA, Liberthson R, Danielson GK, Dore A, Harris L, Hoffman JI, et al. Task force 1: the changing profile of congenital heart disease in adult life. Journal of the American College of Cardiology. 2001;37(5):1170-5.

[7] Mandalenakis Z, Giang KW, Eriksson P, Liden H, Synnergren M, Wåhlander H, et al. Survival in children with congenital heart disease: have we reached a peak at 97%? Journal of the American Heart Association. 2020;9(22):e017704.

[8] Van Der Linde D, Konings EE, Slager MA, Witsenburg M, Helbing WA, Takkenberg JJ, et al. Birth prevalence of congenital heart disease worldwide: a systematic review and meta-analysis. Journal of the American College of Cardiology. 2011;58(21):2241-7.

[9] Perloff JK, Warnes CA. Challenges posed by adults with repaired congenital heart disease. Circulation. 2001;103(21):2637-43.

[10] Baumgartner H, Budts W, Chessa M, Deanfield J, Eicken A, Holm J, et al. Recommendations for organization of care for adults with congenital heart disease and for training in the subspecialty of 'Grown-up Congenital Heart Disease'in Europe: a position paper of the Working Group on Grown-up Congenital Heart Disease of the European Society of Cardiology. European heart journal. 2014;35(11):686-90.

[11] Moons P, Luyckx K, Thomet C, Budts W, Enomoto J, Sluman MA, et al. Physical functioning, mental health, and quality of life in different congenital heart defects: comparative analysis in 3538 patients from 15 countries. Canadian Journal of Cardiology. 2021;37(2):215-23.

[12] Caterini JE, Campisi ES, Cifra B. Physical activity promotion in pediatric congenital heart disease: are we running late? Canadian Journal of Cardiology. 2020;36(9):1406-16.

[13] Constantine A, Barradas-Pires A, Dimopoulos K. Modifiable risk factors in congenital heart disease: Education, transition, digital health and choice architecture. European Journal of Preventive Cardiology. 2020;27(10):1074-6.

[14] World Health Organization (WHO). Noncommunicable diseases - Key facts. 2022. Available from: https://www.who.int/news-room/fact-sheets/detail/non communicable-diseases. [cited 01/2023].

[15] World Health Organization (WHO). Global health risks: mortality and burden of disease attributable to selected major risks. World Health Organization. 2009. Available from: https://apps.who.int/iris/handle/10665/44203. [cited 02/2023]

[16] Bigras J-L. Cardiovascular risk factors in patients with congenital heart disease. Canadian Journal of Cardiology. 2020;36(9):1458-66.

[17] Spector LG, Menk JS, Knight JH, McCracken C, Thomas AS, Vinocur JM, et al. Trends in long-term mortality after congenital heart surgery. Journal of the American College of Cardiology. 2018;71(21):2434-46.

[18] McCracken C, Spector LG, Menk JS, Knight JH, Vinocur JM, Thomas AS, et al. Mortality following pediatric congenital heart surgery: an analysis of the causes of death derived from the national death index. Journal of the American Heart Association. 2018;7(22):e010624.

[19] Verheugt CL, Uiterwaal CS, van der Velde ET, Meijboom FJ, Pieper PG, van Dijk AP, et al. Mortality in adult congenital heart disease. European heart journal. 2010;31(10):1220-9.

[20] Cardiology EbtAfEP, Members ATF, Baumgartner H, Bonhoeffer P, De Groot NM, de Haan F, et al. ESC Guidelines for the management of grown-up congenital heart disease (new version 2010) The Task Force on the Management of Grown-up Congenital Heart Disease of the European Society of Cardiology (ESC). European heart journal. 2010;31(23):2915-57.

[21] Magnussen CG, Smith KJ, Juonala M. When to prevent cardiovascular disease? As early as possible: lessons from prospective cohorts beginning in childhood. Current opinion in cardiology. 2013;28(5):561-8.

[22] Bao W, Srinivasan SR, Wattigney WA, Berenson GS. Persistence of multiple cardiovascular risk clustering related to syndrome X from childhood to young adulthood: the Bogalusa Heart Study. Archives of Internal Medicine. 1994;154(16):1842-7.

[23] Swinburn BA, Sacks G, Hall KD, McPherson K, Finegood DT, Moodie ML, et al. The global obesity pandemic: shaped by global drivers and local environments. The Lancet. 2011;378(9793):804-14.

[24] Nittari G, Scuri S, Petrelli F, Pirillo I, Di Luca N, Grappasonni I. Fighting obesity in children from European world health organization member states. Epidemiological data, medicalsocial aspects, and prevention programs. La Clinica Terapeutica. 2019;170(3):e223-e30.

[25] World Health Organization (WHO). Obesity and overweight - Key facts. 2021. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight. [cited 02/2023].

[26] Hardy LL, Mihrshahi S, Drayton B, Bauman A. NSW schools physical activity and nutrition survey (SPANS) 2015: Full Report. 2016 Sydney: NSW Department of Health.

[27] Pearson N, Braithwaite R, Biddle SJ, van Sluijs EM, Atkin AJ. Associations between sedentary behaviour and physical activity in children and adolescents: a meta-analysis. Obesity reviews. 2014;15(8):666-75.

[28] Partridge SR, Redfern J. Strategies to engage adolescents in digital health interventions for obesity prevention and management. Healthcare. 2018;6(3):70.

[29] Chang T-H, Chen Y-C, Chen W-Y, Chen C-Y, Hsu W-Y, Chou Y, et al. Weight gain associated with COVID-19 lockdown in children and adolescents: A systematic review and meta-analysis. Nutrients. 2021;13(10):3668.

[30] Neville RD, Lakes KD, Hopkins WG, Tarantino G, Draper CE, Beck R, et al. Global changes in child and adolescent physical activity during the COVID-19 pandemic: a systematic review and meta-analysis. JAMA pediatrics. 2022;176(9):886-94.

[31] Müller J, Meyer J, Elmenhorst J, Oberhoffer R. Body weight and not exercise capacity determines central systolic blood pressure, a surrogate for arterial stiffness, in children and adolescents. The Journal of Clinical Hypertension. 2016;18(8):762-5.

[32] Urbina EM, Williams RV, Alpert BS, Collins RT, Daniels SR, Hayman L, et al. Noninvasive assessment of subclinical atherosclerosis in children and adolescents: recommendations for standard assessment for clinical research: a scientific statement from the American Heart Association. Hypertension. 2009;54(5):919-50.

[33] Bank AJ, Wang H, Holte JE, Mullen K, Shammas R, Kubo SH. Contribution of collagen, elastin, and smooth muscle to in vivo human brachial artery wall stress and elastic modulus. Circulation. 1996;94(12):3263-70.

[34] Cavalcante JL, Lima JA, Redheuil A, Al-Mallah MH. Aortic stiffness: current understanding and future directions. Journal of the American College of Cardiology. 2011;57(14):1511-22.

[35] Böhm B, Oberhoffer R. Vascular health determinants in children. Cardiovascular diagnosis and therapy. 2019;9(Suppl 2):S269.

[36] Weber T, Auer J, O'Rourke MF, Kvas E, Lassnig E, Berent R, et al. Arterial stiffness, wave reflections, and the risk of coronary artery disease. Circulation. 2004;109(2):184-9.

[37] Bramwell JC, Hill AV. The velocity of pulse wave in man. Proceedings of the Royal Society of London Series B, Containing Papers of a Biological Character. 1922;93(652):298-306.

[38] Iurciuc S, Cimpean AM, Mitu F, Heredea R, Iurciuc M. Vascular aging and subclinical atherosclerosis: why such a “never ending” and challenging story in cardiology? Clinical interventions in aging. 2017;12:1339.

[39] McEniery CM, Cockcroft JR, Roman MJ, Franklin SS, Wilkinson IB. Central blood pressure: current evidence and clinical importance. European heart journal. 2014;35(26):1719-25.

[40] Sharman JE, Marwick TH, Gilroy D, Otahal P, Abhayaratna WP, Stowasser M. Randomized trial of guiding hypertension management using central aortic blood pressure compared with best-practice care: principal findings of the BP GUIDE study. Hypertension. 2013;62(6):1138-45.

[41] Ohte N, Saeki T, Miyabe H, Sakata S, Mukai S, Hayano J, et al. Relationship between blood pressure obtained from the upper arm with a cuff-type sphygmomanometer and central blood pressure measured with a catheter-tipped micromanometer. Heart and vessels. 2007;22(6):410-5.

[42] Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, et al. Expert consensus document on arterial stiffness: methodological issues and clinical applications. European heart journal. 2006;27(21):2588-605.

[43] Van Bortel LM, Laurent S, Boutouyrie P, Chowienczyk P, Cruickshank J, De Backer T, et al. Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. Journal of hypertension. 2012;30(3):445-8.

[44] Shiraishi M, Murakami T, Higashi K. The accuracy of central blood pressure obtained by oscillometric noninvasive method using Mobil-O-Graph in children and adolescents. Journal of Hypertension. 2020;38(5):813-20.

[45] Weiss W, Gohlisch C, Harsch-Gladisch C, Tölle M, Zidek W, van der Giet M. Oscillometric estimation of central blood pressure: validation of the Mobil-O-Graph in comparison with the SphygmoCor device. Blood pressure monitoring. 2012;17(3):128-31.

[46] Walser M, Schlichtiger J, Dalla-Pozza R, Mandilaras G, Tengler A, Ulrich S, et al. Oscillometric pulse wave velocity estimated via the Mobil-O-Graph shows excellent accuracy in children, adolescents and young adults: an invasive validation study. Journal of Hypertension. 2023;41(4):597-607.

[47] Sandhu K, Pepe S, Smolich JJ, Cheung MM, Mynard JP. Arterial stiffness in congenital heart disease. Heart, Lung and Circulation. 2021;30(11):1602-12.

[48] Häcker A-L, Reiner B, Oberhoffer R, Hager A, Ewert P, Müller J. Increased arterial stiffness in children with congenital heart disease. European journal of preventive cardiology. 2018;25(1):103-9.

[49] Longmuir PE, Brothers JA, De Ferranti SD, Hayman LL, Van Hare GF, Matherne GP, et al. Promotion of physical activity for children and adults with congenital heart disease: a scientific statement from the American Heart Association. Circulation. 2013;127(21):2147-59.

[50] Takken T, Giardini A, Reybrouck T, Gewillig M, Hövels-Gürich H, Longmuir P, et al. Recommendations for physical activity, recreation sport, and exercise training in paediatric patients with congenital heart disease: a report from the Exercise, Basic & Translational Research Section of the European Association of Cardiovascular Prevention and Rehabilitation, the European Congenital Heart and Lung Exercise Group, and the Association for European Paediatric Cardiology. European journal of preventive cardiology. 2012;19(5):1034-65.

[51] World Health Organization (WHO). WHO guidelines on physical activity and sedentary behaviour. Geneva: World Health Organization. 2020. Licence: CC BY-NC-SA 3.0 IO.

[52] World Health Organization (WHO). Global recommendations on physical activity for health. Geneva: World Health Organization. 2010.

[53] Bull FC, Al-Ansari SS, Biddle S, Borodulin K, Buman MP, Cardon G, et al. World Health Organization 2020 guidelines on physical activity and sedentary behaviour. British journal of sports medicine. 2020;54(24):1451-62.

[54] Buys R, Van De Bruaene A, Müller J, Hager A, Khambadkone S, Giardini A, et al. Usefulness of cardiopulmonary exercise testing to predict the development of arterial hypertension in adult patients with repaired isolated coarctation of the aorta. International journal of cardiology. 2013;168(3):2037-41.

[55] Diller G-P, Giardini A, Dimopoulos K, Gargiulo G, Müller J, Derrick G, et al. Predictors of morbidity and mortality in contemporary Fontan patients: results from a multicenter study including cardiopulmonary exercise testing in 321 patients. European heart journal. 2010;31(24):3073-83.

[56] Müller J, Hager A, Diller G-P, Derrick G, Buys R, Dubowy K-O, et al. Peak oxygen uptake, ventilatory efficiency and QRS-duration predict event free survival in patients late after surgical repair of tetralogy of Fallot. International journal of cardiology. 2015;196:158-64.

[57] Brudy L, Meyer M, Oberhoffer R, Ewert P, Müller J. Move more–be happier? physical activity and health-related quality of life in children with congenital heart disease. American Heart Journal. 2021;241:68-73.

[58] Banks L, Rosenthal S, Manlhiot C, Fan C-PS, McKillop A, Longmuir PE, et al. Exercise capacity and self-efficacy are associated with moderate-to-vigorous intensity physical activity in children with congenital heart disease. Pediatric cardiology. 2017;38(6):1206-14.
[59] Stefan MA, Hopman WM, Smythe JF. Effect of activity restriction owing to heart disease on obesity. Archives of pediatrics & adolescent medicine. 2005;159(5):477-81.
[60] Longmuir PE, McCrindle BW. Physical activity restrictions for children after the Fontan operation: disagreement between parent, cardiologist, and medical record reports. American heart journal. 2009;157(5):853-9.
[61] Ong L, Nolan RP, Irvine J, Kovacs AH. Parental overprotection and heart-focused anxiety in adults with congenital heart disease. International journal of behavioral medicine. 2011;18(3):260-7.
[62] Reybrouck T, Mertens L. Physical performance and physical activity in grown-up congenital heart disease. European Journal of Preventive Cardiology. 2005;12(5):498-502.
[63] Moola F, Faulkner GE, Kirsh JA, Kilburn J. Physical activity and sport participation in youth with congenital heart disease: perceptions of children and parents. Adapted Physical Activity Quarterly. 2008;25(1): 49-70.
[64] Pratt M, Varela AR, Salvo D, Kohl III HW, Ding D. Attacking the pandemic of physical inactivity: what is holding us back? British journal of sports medicine. 2020;54(13):760-2.
[65] Kuan MT, Hemphill NM, Harris KC. Reduced physical activity during COVID-19 in children with congenital heart disease: A longitudinal analysis. CJC Pediatric and Congenital Heart Disease. 2022;1(5):219-25.
[66] Williams CA, Wadey C, Pieles G, Stuart G, Taylor RS, Long L. Physical activity interventions for people with congenital heart disease. Cochrane Database of Systematic Reviews. 2020(10).
[67] Ding D, Lawson KD, Kolbe-Alexander TL, Finkelstein EA, Katzmarzyk PT, Van Mechelen W, et al. The economic burden of physical inactivity: a global analysis of major non-communicable diseases. The Lancet. 2016;388(10051):1311-24.
[68] Kohl 3rd HW, Craig CL, Lambert EV, Inoue S, Alkandari JR, Leetongin G, et al. The pandemic of physical inactivity: global action for public health. The lancet. 2012;380(9838):294-305.
[69] Guthold R, Stevens GA, Riley LM, Bull FC. Global trends in insufficient physical activity among adolescents: a pooled analysis of 298 population-based surveys with 1· 6 million participants. The Lancet Child & Adolescent Health. 2020;4(1):23-35.
[70] Brudy L, Meyer M, Garcia-Cuenllas L, Oberhoffer R, Hager A, Ewert P, et al. Objective Physical Activity Assessment in Clinical Congenital Heart Disease Research: A Systematic Review on Study Quality, Methodology, and Outcomes. Cardiology. 2021;146(2):240-52.
[71] Siaplaouras J, Niessner C, Helm PC, Jahn A, Flemming M, Urschitz MS, et al. Physical activity among children with congenital heart defects in Germany: a nationwide survey. Frontiers in Pediatrics. 2020;8:170.
[72] Brudy L, Hock J, Häcker A-L, Meyer M, Oberhoffer R, Hager A, et al. Children with congenital heart disease are active but need to keep moving: A cross-sectional study using wrist-worn physical activity trackers. The Journal of pediatrics. 2020;217:13-9.

[73] Voss C, Harris KC. Physical activity evaluation in children with congenital heart disease. Heart. 2017;103(18):1408-12.
[74] Dollman J, Okely AD, Hardy L, Timperio A, Salmon J, Hills AP. A hitchhiker's guide to assessing young people's physical activity: Deciding what method to use. Journal of science and medicine in sport. 2009;12(5):518-25.
[75] Drehlich M, Naraine M, Rowe K, Lai SK, Salmon J, Brown H, et al. Using the technology acceptance model to explore adolescents' perspectives on combining technologies for physical activity promotion within an intervention: usability study. Journal of Medical Internet Research. 2020;22(3):e15552.
[76] Müller J, Hoch A-M, Zoller V, Oberhoffer R. Feasibility of physical activity assessment with wearable devices in children aged 4–10 years—A pilot study. Frontiers in pediatrics. 2018;6:5.
[77] Peyer KL, Hamilton KC. Validity of the Garmin Vivofit Jr. to Measure Physical Activity During a Youth After-School Program. Journal for the Measurement of Physical Behaviour. 2022;5(2):61-8.
[78] Willinger L, Brudy L, Meyer M, Oberhoffer-Fritz R, Ewert P, Müller J. Overweight and obesity in patients with congenital heart disease: a systematic review. International Journal of Environmental Research and Public Health. 2021;18(18):9931.
[79] Andonian C, Langer F, Beckmann J, Bischoff G, Ewert P, Freilinger S, et al. Overweight and obesity: an emerging problem in patients with congenital heart disease. Cardiovascular Diagnosis and Therapy. 2019;9(Suppl 2):S360.
[80] Diao J, Chen L, Wei J, Shu J, Li Y, Li J, et al. Prevalence of malnutrition in children with congenital heart disease: a systematic review and meta-analysis. The Journal of Pediatrics. 2022;242:39-47.
[81] Pinto NM, Marino BS, Wernovsky G, De Ferranti SD, Walsh AZ, Laronde M, et al. Obesity is a common comorbidity in children with congenital and acquired heart disease. Pediatrics. 2007;120(5):e1157-e64.
[82] Moola F, Fusco C, Kirsh JA. The perceptions of caregivers toward physical activity and health in youth with congenital heart disease. Qualitative health research. 2011;21(2):278-91.
[83] Willinger L, Brudy L, Oberhoffer-Fritz R, Ewert P, Müller J. Association between Objectively Measured Physical Activity and Arterial Stiffness in Children with Congenital Heart Disease. Journal of Clinical Medicine. 2021;10(15):3266.
[84] Moola F, McCrindle BW, Longmuir PE. Physical activity participation in youth with surgically corrected congenital heart disease: devising guidelines so Johnny can participate. Paediatrics & Child Health. 2009;14(3):167-70.
[85] Neidenbach R, Achenbach S, Andonian C, Beckmann J, Biber S, Dittrich S, et al. Medical care of adults with congenital heart diseases: Present and future. Herz. 2019;44:553-72.
[86] McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: new concepts are needed to study research participation effects. Journal of clinical epidemiology. 2014;67(3):267-77.
[87] Boyes NG, Stickland MK, Fusnik S, Hogeweide E, Fries JT, Haykowsky MJ, et al. Physical activity modulates arterial stiffness in children with congenital heart disease: a CHAMPS cohort study. Congenital heart disease. 2018;13(4):578-83.
[88] Lopez JR, Voss C, Kuan MT, Hemphill NM, Sandor GG, Harris KC. Physical activity is associated with better vascular function in children and adolescents

with congenital heart disease. Canadian Journal of Cardiology. 2020;36(9):1474-81.
[89] Aroor AR, Jia G, Sowers JR. Cellular mechanisms underlying obesity-induced arterial stiffness. American Journal of Physiology-Regulatory, Integrative and Comparative Physiology. 2018;314(3):R387-R98.
[90] Lona G, Hauser C, Köchli S, Infanger D, Endes K, Schmidt-Trucksäss A, et al. Association of blood pressure, obesity and physical activity with arterial stiffness in children: a systematic review and meta-analysis. Pediatric Research. 2022;91(3):502-12.
[91] Sawyer SM, Afifi RA, Bearinger LH, Blakemore S-J, Dick B, Ezeh AC, et al. Adolescence: a foundation for future health. The lancet. 2012;379(9826):1630-40.
[92] Ahmed SP, Bittencourt-Hewitt A, Sebastian CL. Neurocognitive bases of emotion regulation development in adolescence. Developmental cognitive neuroscience. 2015;15:11-25.
[93] Moons P, Bratt E-L, De Backer J, Goossens E, Hornung T, Tutarel O, et al. Transition to adulthood and transfer to adult care of adolescents with congenital heart disease: a global consensus statement of the ESC Association of Cardiovascular Nursing and Allied Professions (ACNAP), the ESC Working Group on Adult Congenital Heart Disease (WG ACHD), the Association for European Paediatric and Congenital Cardiology (AEPC), the Pan-African Society of Cardiology (PASCAR), the Asia-Pacific Pediatric Cardiac Society (APPCS), the Inter-American Society of Cardiology (IASC), the Cardiac Society of Australia and New Zealand (CSANZ), the International Society for Adult Congenital Heart Disease (ISACHD), the World Heart Federation (WHF), the European Congenital Heart Disease Organisation (ECHDO), and the Global Alliance for Rheumatic and Congenital Hearts (Global ARCH). European heart journal. 2021;42(41):4213-23.
[94] Mackie AS, Ionescu-Ittu R, Therrien J, Pilote L, Abrahamowicz M, Marelli AJ. Children and adults with congenital heart disease lost to follow-up: who and when? Circulation. 2009;120(4):302-9.
[95] Kovacs AH, Brouillette J, Ibeziako P, Jackson JL, Kasparian NA, Kim YY, et al. Psychological outcomes and interventions for individuals with congenital heart disease: a scientific statement from the American Heart Association. Circulation: Cardiovascular Quality and Outcomes. 2022;15(8):e000110.
[96] Kaemmerer H, Andonian C, Ewert P, Freilinger S, Nagdyman N, Neidenbach R, et al. Transition–Nachsorge für Erwachsene mit angeborenen Herzfehlern. DMW-Deutsche Medizinische Wochenschrift. 2021;146(18):1192-9.
[97] Remmele J, Schiele S, Oberhoffer-Fritz R, Ewert P, Bauer UM, Helm PC. Endangered patients with congenital heart defect during transition—Germany-wide evaluation of medical data from National Register for Congenital Heart Defects (NRCHD). Cardiovascular Diagnosis and Therapy. 2021;11(6):1284.
[98] Telama R, Yang X, Viikari J, Välimäki I, Wanne O, Raitakari O. Physical activity from childhood to adulthood: a 21-year tracking study. American journal of preventive medicine. 2005;28(3):267-73.
[99] Gordon-Larsen P, Nelson MC, Popkin BM. Longitudinal physical activity and sedentary behavior trends: adolescence to adulthood. American journal of preventive medicine. 2004;27(4):277-83.
[100] Hansen PG, Skov LR, Skov KL. Making healthy choices easier: regulation versus nudging. Annual review of public health. 2016;37:237-51.

[101] Li M, Chapman GB. Nudge to health: Harnessing decision research to promote health behavior. Social and Personality Psychology Compass. 2013;7(3):187-98.
[102] Chapman GB. A decision-science approach to health-behavior change. Current Directions in Psychological Science. 2019;28(5):469-74.
[103] Schmidt AT, Engelen B. The ethics of nudging: An overview. Philosophy Compass. 2020;15(4):e12658.
[104] Thaler RH, Sunstein CR. Nudge: Improving Decisions About Health, Wealth and Happiness. Yale University Press; 2021.
[105] World Health Organization (WHO). Global strategy on digital health 2020-2025. Geneva: World Health Organization. 2021. Licence: CC BY-NC-SA 30 IGO.
[106] Chow CK, Ariyarathna N, Islam SMS, Thiagalingam A, Redfern J. mHealth in cardiovascular health care. Heart, Lung and Circulation. 2016;25(8):802-7.
[107] Bhavnani SP, Parakh K, Atreja A, Druz R, Graham GN, Hayek SS, et al. Roadmap for innovation—ACC health policy statement on healthcare transformation in the era of digital health, big data, and precision health: a report of the American College of Cardiology Task Force on Health Policy Statements and Systems of Care. Journal of the American College of Cardiology. 2017;70(21):2696-718.
[108] Dorsey ER, Topol EJ. State of telehealth. New England journal of medicine. 2016;375(2):154-61.
[109] Michie S, Yardley L, West R, Patrick K, Greaves F. Developing and evaluating digital interventions to promote behavior change in health and health care: recommendations resulting from an international workshop. Journal of medical Internet research. 2017;19(6):e232.
[110] Kharrazi H, Faiola A, Defazio J, editors. Healthcare game design: behavioral modeling of serious gaming design for children with chronic diseases. International Conference on Human-Computer Interaction; 2009: Springer.
[111] Oyibo K, Adaji I, Vassileva J. Social cognitive determinants of exercise behavior in the context of behavior modeling: a mixed method approach. Digital health. 2018;4:1-19.
[112] Bandura A. The self system in reciprocal determinism. American psychologist. 1978;33(4):344.
[113] Müller AM, Maher CA, Vandelanotte C, Hingle M, Middelweerd A, Lopez ML, et al. Physical activity, sedentary behavior, and diet-related eHealth and mHealth research: bibliometric analysis. Journal of medical Internet research. 2018;20(4):e8954.
[114] Armanasco AA, Miller YD, Fjeldsoe BS, Marshall AL. Preventive health behavior change text message interventions: a meta-analysis. American journal of preventive medicine. 2017;52(3):391-402.
[115] Schwerdtfeger AR, Schmitz C, Warken M. Using text messages to bridge the intention-behavior gap? A pilot study on the use of text message reminders to increase objectively assessed physical activity in daily life. Frontiers in psychology. 2012;3:270.
[116] Stephens J, Allen J. Mobile phone interventions to increase physical activity and reduce weight: a systematic review. The Journal of cardiovascular nursing. 2013;28(4):320.
[117] Siopis G, Chey T, Allman-Farinelli M. A systematic review and meta-analysis of interventions for weight management using text messaging. J Hum Nutr Diet.28(Suppl. 2):1-15.

[118] Lee AM, Chavez S, Bian J, Thompson LA, Gurka MJ, Williamson VG, et al. Efficacy and effectiveness of mobile health technologies for facilitating physical activity in adolescents: scoping review. JMIR mHealth and uHealth. 2019;7(2):e11847.

[119] Ludwig K, Arthur R, Sculthorpe N, Fountain H, Buchan DS. Text messaging interventions for improvement in physical activity and sedentary behavior in youth: systematic review. JMIR mHealth and uHealth. 2018;6(9):e10799.

[120] Roberts AL, Fisher A, Smith L, Heinrich M, Potts HW. Digital health behaviour change interventions targeting physical activity and diet in cancer survivors: a systematic review and meta-analysis. Journal of Cancer Survivorship. 2017;11:704-19.

[121] Newton KH, Wiltshire EJ, Elley CR. Pedometers and text messaging to increase physical activity: randomized controlled trial of adolescents with type 1 diabetes. Diabetes care. 2009;32(5):813-5.

[122] Garnett C, Crane D, West R, Brown J, Michie S. Identification of behavior change techniques and engagement strategies to design a smartphone app to reduce alcohol consumption using a formal consensus method. JMIR mHealth and uHealth. 2015;3(2):e3895.

[123] Monshouwer K, Smit F, Ruiter M, Ormel H, Verhulst F, Vollebergh W, et al. Identifying target groups for the prevention of depression in early adolescence: The TRAILS study. Journal of affective disorders. 2012;138(3):287-94.

[124] Chapman GB CH, Convery K, Coups EJ. Goals and Social Comparisons Promote Walking Behavior. Medical Decision Making 2016;36(5):472-8.

[125] Zhang J BD, Yang S, Becker J, Herbert N, Centola D. . Support or competition? How online social networks increase physical activity: A randomized controlled trial. Prev Med Rep. 2016;8(4):453-8.

[126] Brannon EE, Cushing CC, Walters RW, Crick C, Noser AE, Mullins LL. Goal feedback from whom? A physical activity intervention using an N-of-1 RCT. Psychology & health. 2018;33(6):701-12.

[127] Schoeppe S, Alley S, Rebar AL, Hayman M, Bray NA, Van Lippevelde W, et al. Apps to improve diet, physical activity and sedentary behaviour in children and adolescents: a review of quality, features and behaviour change techniques. International Journal of Behavioral Nutrition and Physical Activity. 2017;14:1-10.

[128] Jone P-N, Gearhart A, Lei H, Xing F, Nahar J, Lopez-Jimenez F, et al. Artificial Intelligence in Congenital Heart Disease: Current State and Prospects. JACC: Advances. 2022;1(5):1-18.

[129] Orwat S, Arvanitaki A, Diller G-P. A new approach to modelling in adult congenital heart disease: artificial intelligence. Revista Espanola de Cardiologia (English ed). 2021;74(7):573-5.

[130] Bauman AE, Reis RS, Sallis JF, Wells JC, Loos RJ, Martin BW. Correlates of physical activity: why are some people physically active and others not? The lancet. 2012;380(9838):258-71.

Appendix I: Digital Health Nudges (German)

Verhaltens Determinante: Fertigkeiten & Praxis	
1.	Hi {Name Studienteilnehmer*in}, ab heute geht es los mit den täglichen Nachrichten. 😊 Die Weltgesundheitsorganisation empfiehlt für Jugendliche mindesten 60 Minuten am Tag körperlich aktiv zu sein. Versuch heute die 60 Minuten zu erreichen, um ein Gefühl dafür zu bekommen wie viel 60 Minuten sind. 💪🙆
2.	Nimm doch heute mal die Treppen, anstatt mit Aufzug oder Rolltreppe zu fahren. ⛰😉🏃 Kein großer Aufwand und du tust etwas Gutes für dich!🙆
3.	Geh doch heute mal eine Strecke zu Fuß 👣 oder fahr mit dem Fahrrad 🚴♂🚴▩ anstatt mit dem Auto oder den öffentlichen Verkehrsmitteln zu fahren. So kannst du auch im Alltag deiner Gesundheit etwas Gutes tun! ▯💪✨
4.	Fühlt sich fast so an, als wäre der Sommer vorbei 😬🌪Macht aber nichts, Bewegung an der frischen Luft macht bei jedem Wetter Spaß 💪🏃♀🏃♂ Also zieh dir die kommenden Tage warme Klamotten an und ab nach draußen 🙆
5.	Laut einer aktuellen Statistik der Weltgesundheitsorganisation bewegen sich 80% der Kinder und Jugendliche nicht ausreichend. 📈📊 Ufff das sollten wir dringend ändern!! 😬😳 Mach heute noch eine Runde Sport und bewege dich an der frischen Luft. 🏃♀🏃🌿☀
6.	Das Wetter ist gut ☀ Nutz den Start ins Wochenende, um dir selbst und deiner Gesundheit was Gutes zu tun! Es gibt schließlich nichts Wichtigeres im Leben. ✨✨
7.	Die Weltgesundheitsorganisation empfiehlt, dass Jugendliche an 3 Tagen der Woche so richtig ins Schwitzen kommen sollten. Wie schaut`s aus, hast du diese Woche schon ausreichend geschwitzt? ▯😉🏃🏊♀🏊
8.	Wusstest du, dass laut der Weltgesundheitsorganisation Zeit, die im Sitzen verbracht wird, eines der größten gesundheitlichen Risiken darstellt?! 😱▩💻▯Die Zeit im Sitzen solltest du also so weit wie möglich reduzieren und durch ausreichend Aktivität ausgleichen. 🏊♀🚴▩🤸♀🤸▩♀▯▩
9.	Jeder Schritt zählt! 🏃🏃♀ An Tagen an den du noch weit entfernt bist von deinem Ziel, mach noch ein paar Schritte, bevor du ins Bett gehst. Rückschläge an manchen Tagen gehören dazu, lass dich nicht davon aufhalten. ✋✨

10.	Das Wochenende steht vor der Tür und du hast hoffentlich Ferien. 🌞👌 Ich hoffe du hast viel Zeit dich auszuruhen und schöne Dinge zu tun. ✨ Nutz die freie Zeit auch für Sport und Bewegung. 🏃♀🏄♀🚴♂🧗□♀
11.	Für einen aktiven Lebensstil ist es am einfachsten Sport in den Alltag zu integrieren. Fahr mit dem Fahrrad in die Schule, geh zu Fuß zu Verabredungen und triff dich mit Freunden zum Spazieren gehen. 🚲🚶♀🌞 Überlege dir drei Möglichkeiten die zu dir und deinem Alltag gut passen und setzte sie um! ✅😊
12.	Wie wäre es diese Woche mal mit einer Challenge? Versuche diese Woche jeden Tag die 60 Aktivitätsminuten zu erreichen. 🤸♀💪
13.	Wie wäre es diese Woche mal mit einer Challenge? Die kommende Woche erreichst du täglich mindestens 10 000 Schritte. Auf geht's, zusammen schaffen wir das! 💪
14.	Integrierst du Dehn-Übungen regelmäßig in deinen Alltag? □♀🏅□♂✨ Dehnen ist super wichtig und sollte ein Teil deiner Workout-Routine werden. □
15.	Frisbee, Ballspiele, Yoga, Krafttraining, Schwimmen, Radeln, Wandern, Laufen. 🤸🏏🏓🏊♀🚴🧘♀□♀🏃♀🚲 Es gibt so viele Möglichkeiten sich zu bewegen und dabei Spaß zu haben! Bestimmt ist auch was für dich dabei. Probier's aus und werde aktiv! 😊
16.	Wenn Bewegung ein Medikament wäre, dann wäre es bestimmt ein absoluter Verkaufsschlager.💊💰 Eigentlich doch sehr gut zu wissen, dass wir so etwas Wirksames für unsere Gesundheit haben und so einfach selbst anwenden können. 🧘🌳🏃♀
17.	Die erste Woche ist schon vorbei. Schau doch mal in deiner APP nach wie aktiv du warst und wie es dir dabei gegangen ist. Bleib dran und erreiche deine Ziele! 🎯
18.	Beweg dich am besten direkt nach dem Lesen dieser Nachricht. So schiebst du es nicht unnötig auf und es fällt dir leichter deine Ziele in die Tat umzusetzen. 😊
19.	Probiere doch diesen Monat mal was Neues aus. Bring frischen Wind in deinen Alltag und vielleicht findest du dabei ja sogar ein neues Hobby. 👍 Wie wäre es mit einer Runde Tischtennis im Park, Yoga oder Jonglieren? 🏓□🤹♂ Viel Spaß beim Ausprobieren!
20.	Wenn es dir mal schwer fallen sollte dich zum Sport zu motivieren, denk an das Gefühl nach dem Sport. ✨💪 Hilft immer!
21.	Leg dir deine Sportsachen direkt für morgen bereit, dann fällt es leichter dies auch direkt in die Tat umzusetzen. 😊💪

22.	Endlich Wochenende und die Sonne scheint. ☀😊 Wie wär's mit einem Ausflug in die Berge oder einer Runde Sport an der frischen Luft ⛰🌈🚵‍♀️☀ Schönes Wochenende! 
23.	Leg deinen Schulweg öfter mal zu Fuß oder mit dem Radl zurück. So integrierst du Aktivität in den Alltag und tust du etwas Gutes für dich selbst. 😊💪
24.	Bei uns in München ist graues Wetter. 🌧☂ Da fällt es manchmal schwer sich für Sport zu motivieren. Umso besser fühlt man sich aber, wenn man es trotzdem macht! 💪 Entweder du trotzt dem Regen und gehst trotzdem raus 🌩⛈ oder du machst einfach ein Home-Workout im Trockenen. Du wirst sehen, deine Stimmung nach dem Sport ist bestimmt besser! ✨
25.	Du fühlst dich energielos und hast das Gefühl du hast keine Kraft für Sport? Ich denke das Gefühl kennt jeder! Oft geht es einem nach Bewegung aber deutlich besser und die Energie kommt zurück. 💪 Probiere es aus! ✨😊 
26.	Du hast einen richtig faulen Sonntag? Das darf auch mal sei✨ Ruh dich aus und sammle vielleicht bei einem Spaziergang noch ein paar Schritte. Falls du einen aktiven Sonntag hast, natürlich umso besser. 😊
27.	Oft fällt es leichter, wenn man Sport in Gruppe macht. Verabrede dich mit Freunden oder einem Trainingspartner. Dann macht es direkt mehr Spaß! 💪✨ 

28.	Du kannst jederzeit anfangen! 😊 Warte nicht auf das neue Jahr oder einen neuen Monat, sondern starte direkt heute, du wirst es nicht bereuen! ⏰✨👋
29.	Wusstest du, dass du jetzt im Jugendalter deine Anlagen für dein Erwachsenen Alter legst? 👵👴 Studien haben gezeigt, dass das Aktivitätsverhalten in der Kindheit und Jugend häufig im Erwachsenenalter beibehalten wird. 🚴 🤸‍♀️Wenn das mal kein Anreiz für einen aktiven Lebensstil ist. 😊
30.	Laut Studien dauert es ungefähr 10 Wochen um eine Routine/Gewohnheit zu etablieren. ✨ Mit der Zeit wird es einfacher und irgendwann wirst du feststellen, dass du körperliche Aktivität in deinen Alltag integrierst ohne darüber nachdenken zu müssen. Also bleib dran und mach es zur Gewohnheit! ⏰💪♀🏃‍♀🤸🧗🏄‍♀
31.	Die Nachricht heute richtet sich vor allem an die Mädels. Es ist bekannt, dass sich Mädchen und junge Frauen weniger bewegen als gleichaltrige Jungs und Männer. Sport gilt immer noch mehr als Jungen-Sache soll als Erklärung dafür herhalten. 🤦 Das sollten wir ändern! Also Mädels, werdet aktiv und lasst uns zeigen, dass Sport und Bewegung nichts mit Geschlecht zu tun hat! 😊🤸🏃‍♀
32.	Dreh die Musik lauf auf und tanz eine Runde durch dein Zimmer 💃🎶 oder wenn Tanzen nicht so deins ist mach ein kurzes Workout. 🏋️‍♀ 💪😊!
33.	Leg dein Smartphone zur Seite und beweg dich noch eine Runde. 😊 Am besten du machst es jetzt direkt, dann musst du dich später nicht mehr motivieren! 😉👟😊
34.	Überleg welche Sportarten dir Spaß machen und gut tun! ✨ Dir fallen welche ein? Super, dann machen damit weiter. 😊 Falls dir nichts einfällt, kein Problem! Du hast wahrscheinlich einfach noch nicht das Richtige für dich gefunden! Probier doch in den nächsten Tagen und Wochen ein paar neue Dinge aus, bestimmt ist auch etwas für dich dabei! 🏃‍♀🏋️‍♂🤸‍♂🚶‍♂🚴‍♂🤾🏄‍♀🤹
35.	Hast du dein Aktivitätsziel heute schon erreicht? Schau doch mal auf deine Aktivitätsuhr und beweg dich noch eine Runde. 🎾🏸🏒🥊🏋️‍♀🧗‍♂🏊‍♀🚴‍♀🎳
36.	Es dauert eine Weile, um einen aktiven Lebensstil zur Gewohnheit zu machen. Warum beginnst du nicht einfach mit einer ganz einfachen Herausforderung? Nimm dir vor in der kommenden Woche jeden Tag 10.000 Schritte zu machen. 🎯 Das ist gar nicht so einfach, aber ich bin sicher du kannst es schaffen! 😊✨
37.	Jeder Mensch ist anders, finde heraus welche Form von Bewegung dir gut tut und Spaß macht. Falls du es noch nicht rausgefunden hast, probiere einfach noch ein paar Dinge aus. 🏈🚴‍♂🏃‍♀🏐🎾🏸🏒🥊🏋️‍♀🧗‍♂🏊‍♀🚴‍♀🎳

38.	Schau doch mal in deiner Garmin APP nach, ob es Tage gibt, an denen es dir besonders schwer fällt körperlich aktiv zu sein? 📊📈 Vielleicht ist es der Sonntag oder ein Tag unter der Woche an dem du viel zu tun hast. Überleg dir, wie und wann du an diesen Tagen Aktivität einbauen kannst, um auch an diesen Tagen deine Aktivität zu steigern. 🚴💪🙌
39.	Ich denke jeder von uns kennt die Tage, an denen es uns schwer fällt uns für Bewegung zu motivieren. Aber denke daran: Jede Bewegung ist besser als keine Bewegung! ✨
40.	Deine eigene Gesundheit sollte eine hohe Priorität für dich haben. Nimm dir die Zeit auf dich zu achten und dir was Gutes zu tun. ☀✨
41.	Im Alltag ist die Zeit oft knapp und wir nehmen uns häufig nicht die Zeit für das, was uns Wichtig ist. Sport und Bewegung ist jedoch gerade in stressigen Zeiten sehr wichtig und tut uns gut. Nimm dir die Zeit! ✨
42.	Eat like you love yourself. Move like you love yourself. Speak like you love yourself. Act like you love yourself ✨✨ Motivation für ein aktiven Lebensstil sollte dein eigenes Wohlbefinden sein, wenn das nicht Grund genug ist. 🙌
43.	Das Geheimnis des Erfolgs ist anzufangen – Mark Twain. ✨✨
44.	In einem Jahr wirst du dir wünschen du hättest heute angefangen. 🙌 Aller Anfang ist schwer, aber sobald du dir eine Routine erarbeitet hast, wird es leichter. ✨💪 Fang am besten direkt heute an! ▯✨
45.	Die American Heart Association unterstreicht die Wichtigkeit von täglicher körperlicher Aktivität und die Verringerung von sitzendem Verhalten für die Gesundheit und das Wohlbefinden von Jugendlichen mit angeborenem Herzfehler. ✨
46.	Es ist wichtig, Bewegung in den Alltag zu integrieren. Fahr mit dem Fahrrad in die Schule, geh zu Fuß zu Verabredungen und triff dich mit Freunden zum Spaziergehen. Schreib drei Möglichkeiten auf, die zu dir und deinem Alltag passen und setzte sie um! 🙌
47.	Das Wochenende steht vor der Tür. ☀ Ich hoffe du hast Zeit dich auszuruhen und schöne Dinge zu tun. Nutze die freie Zeit auch für Sport und Bewegung. ▯♀🏃♀⛷🧗🏄♀

Persönliche Determinante	
Ergebnis Erwartung	
48.	Wusstest du, dass körperliche Aktivität bei Jugendlichen nachweislich mit verbesserter körperlicher, geistiger und kognitiver Gesundheit verbunden ist? □ Ziemlich gut zu wissen, dass wir selbst so einen großen Einfluss auf unsere Gesundheit haben oder? Auf geht's, beweg dich noch eine Runde und tu etwas Gutes für deine Gesundheit🏃‍♀️🏊‍♀️🚴‍♂️
49.	Körperlich aktiv zu sein ist entscheidend für Gesundheit und Wohlbefinden – es kann dem Leben mehr Jahre und den Jahren mehr Leben bringen", sagte WHO-Generaldirektor Tedros Adhanom Ghebreyesus. ✨✨
50.	Körperliche Bewegung hat Einfluss auf viele Faktoren in unserem Leben. Es ist nachgewiesen, dass körperliche Aktivität einen positiven Einfluss auf mentale Gesundheit hat. ✨□ Mentale Gesundheit ist so wahnsinnig wichtig und dennoch wird sie häufig noch nicht ausreichend thematisiert. Achte auf deine mentale Gesundheit und wirke durch einen aktiven Lebensstil positiv auf deine mentale Gesundheit. 🧘
51.	Ist momentan viel los bei dir und du hast das Gefühl keine Zeit für Sport und Bewegung zu haben? 🎯⏰⏱ Körperliche Bewegung baut Stress ab und sorgt für größere Ausgeglichenheit. ✨ Es lohnt sich also auf jeden Fall wenn du dir auch in stressigen Phasen die Zeit für ausreichend körperliche Aktivität nimmst. 🧘
52.	Du verbringst momentan viel Zeit in der Schule und am Schreibtisch? □Häufig verbringen wir so viel zu viel Zeit im Sitzen. □ Wusstest du, dass körperliche Aktivität einen positiven Einfluss auf dein Gehirn hat? □ Also gestalte deine Pausen aktiv und an der frischen Luft. 🏃🌞🌼🌼
53.	Es gibt Studien, die herausgefunden haben, dass körperliche Bewegung einen positiven Einfluss auf Schulnoten haben. □🏫📝 Wahnsinn was durch Bewegung alles erreicht werden kann, oder? Mach doch heute noch eine Runde Sport und tue damit nicht nur deiner Gesundheit, sondern auch deiner Karriere was Gutes. 📖👦🏻💻👩🏻💻
54.	Sport und Bewegung führt zu besserem Schlaf. Das ist super, weil Schlaf einen großen Einfluss auf unsere Gesundheit und unser Wohlbefinden im Allgemeinen hat. 😴💤

55.	Durch Sport und Bewegung kannst du dein Selbstbewusstsein steigern. Integriere Bewegung in deinen Alltag und lerne in deine eigene Kraft und deine Fähigkeiten zu vertrauen.
56.	Bewegung führt nachweislich dazu, dass wir uns besser konzentrieren können. Integriere aktive Pausen am besten in deinen Schul- und Lernalltag. Wenn du zu Hause lernst oder Hausaufgaben machst, dann mach Pausen in denen du dich bewegst.
57.	Ausreichend körperliche Aktivität hat unter anderem positive Auswirkung auf dein Herz-Kreislaufsystem und Gefäßsystem. Also tu deinem Herzen was Gutes und beweg dich noch eine Runde.
58.	Aktivität und Bewegung stärkt deine Muskulatur und dein Immunsystem. Mach doch heute noch eine Runde Sport und tu etwas Gutes für deine Gesundheit.
59.	Körperliche Aktivität verbessert deine kardiovaskuläre Fitness. Körperliche Aktivität sollte in deinem Leben eine große Rolle spielen und du wirst dich fit und gesund fühlen.
Self-efficacy & Self-regulation	
60.	Wenn du klar weißt, was du erreichen willst, wirst du erfolgreich sein! Das heißt, du brauchst klare Ziele. Nimm dir heute 10 Minuten Zeit, um dir zu überlegen, was für die kommende Zeit dein Aktivitäts-Ziel ist. Am besten du gehst dabei nach der SMART Methode vor. Das geht so: **S:** spezifisch. Leg dein Ziel so genau wie möglich fest. **M:** messbar. Dein Ziel solltest du messen können, um deinen Weg immer wieder zu überprüfen. **A:** attraktiv. Das Ziel sollte für dich attraktiv und wichtig sein. **R:** realistisch. Das ist häufig schwierig, aber dein Ziel sollte in der Umsetzung realistisch sein. Man kann nicht von heute auf morgen einen Marathon laufen, also steck dir kleine, realistische Ziele. **T:** terminiert. Für das Erreichen deines Ziels solltest du einen konkreten Termin festlegen. Schreib dein Ziel auf und los geht's!

61.	Ziele werden häufiger eingehalten, wenn man sie aufschreibt. Nimm dir doch heute 10 Minuten Zeit und schreib dir dein Aktivitätsziel auf einen Zettel und hänge ihn auf, so dass du ihn häufig sehen kannst.
62.	Was steht dir im Weg deine gesundheitlichen Ziele zu erreichen? Finde heraus was dich davon abhält und überleg dir, was du tun kannst, um diese Barrieren zu überwinden. Nimm dir heute 10 Minuten Zeit und mach dir Gedanken, was dich davon abhält im Alltag aktiv zu sein. Schreib die Dinge auf, so bist du dir dessen bewusst und kannst sie leichter überwinden!!
63.	Der erste Monat ist schon rum. Nimm dir deine APP zur Hand und schau mal, wie es bisher so gelaufen ist?! Du weißt ja bereits, dass dein Ziel im Schnitt mindestens 60 Minuten Aktivität pro Tag sein sollte. Bleib dran und arbeite weiter an deinen Zielen!
64.	Gibt es eine Person, die dich sportlich und gesundheitlich motiviert? Vielleicht jemand in deiner Familie oder Bekanntenkreis oder natürlich ein Sportler oder eine bekannte Persönlichkeit? Super, lass dich davon inspirieren. Wenn dir spontan niemand einfällt, dann überleg ob du jemand findest oder such einfach mal im Internet. Vorbilder können einen stark motivieren
65.	Believe that you can and you're half way there! Glaub an dich selbst und dir wird vieles Gelingen im Leben. Du hast allen Grund dazu an dich selbst zu glauben.
66.	Obwohl wir wissen, wie gut uns Bewegung und ein aktiver Lebensstil tut, fällt es dennoch manchmal schwer dies im Alltag umzusetzen. Das ist zwar manchmal nervig, aber ich bin sicher du bist stärker als dein Schweinehund und schaffst es gegen ihn anzukämpfen und dich ausreichend zu bewegen.
67.	Plane deine Aktivität direkt für diese Woche. Wann hast du Zeit für Sport und Bewegung und was möchtest du machen? Lege deinen Plan so genau wie möglich fest, das wird dir dabei helfen ihn umzusetzen.
68.	Dein Schweinehund steht dir heute im Weg? Schieb ihn auf die Seite und besieg ihn! You can do it!
69.	Wie schaut's auf deiner Garmin Uhr aus? Hast du schon ausreichend Schritte gemacht heute? Ca. 10000 Schritte am Tag sind die Empfehlung, das ist gar nicht so einfach. Aber bleib dran!

70.	Wie schaut’s aus auf deiner Garmin Uhr aus? Hast du schon ausreichend Aktivitätsminuten gesammelt heute? 60 Minuten am Tag sind die Empfehlung, das ist gar nicht so einfach. Aber bleib dran, besonders wenn das Wetter so schön ist. ☀
71.	Wow wie schnell die Zeit vergeht, heute ist schon die letzte Nachricht, die wir dir senden. 😱 Aber viel wichtiger ist ja, dass du langfristig einen aktiven Lebensstil führst. In den letzten Wochen hast du viel über die Vorteile von Aktivität gelernt, und wir hoffen du hast vor Allem gelernt an dich selbst und deine Fähigkeiten zu glauben. Bleib dran und glaub an dich, wir tun es auf jeden Fall! Vielen Dank für die letzten Wochen, wir hoffen du hattest Spaß, wir hatten es auf jeden Fall! 💪

In addition to the 71 text messages, 13 video messages were sent as nudges.

Appendix II: Study Reprint Permissions

Scientific Publication I + II

Lorin Liu <lorin.liu@mdpi.com>
Mo 09.01, 03:01

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Best regards,
Lorin

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Scientific Publication III

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