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Effects of eHealth physical activity encouragement in adolescents with complex congenital heart disease: The PReVaiL randomized clinical trial

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ABSTRACT

Objective: To assess benefit and harms of adding an eHealth intervention to health education and individual counseling in adolescents with congenital heart disease.
Design: Randomized clinical trial.
Setting: Denmark.
Patients: A total of 158 adolescents aged 13–16 years with no physical activity restrictions after repaired complex congenital heart disease.
Interventions: PReVaiL consisted of individually tailored eHealth encouragement physical activity for 52 weeks. All patients received 45 min of group-based health education and 15 min of individual counseling involving patients' parents.
Outcomes: The primary outcome was maximal oxygen uptake (VO_2 peak) at 52 weeks after randomization. The secondary outcome was physical activity. Exploratory outcomes were generic and disease-specific questionnaires.
Results: In the intervention group, 58 patients (72%) completed the final test, but of those, only 46 (57%) fulfilled the compliance criteria of using the eHealth application for at least 2 consecutive weeks. In the control group, 61 patients (79%) completed both exercise tests. Adjusted for baseline values, the difference between the intervention group and the control group in mean VO_2 peak at 1 year was −0.65 $ml \cdot kg^{-1} \cdot min^{-1}$ (95% CI −2.66 to 1.36). Between-group differences at 1 year in physical activity, generic health-related quality of life, and disease-specific quality of life were not statistically significant.
Conclusions: Adding a tailored eHealth intervention to health education and individual counseling did not affect outcomes among adolescents with congenital heart disease. Our results do not support the use of this eHealth intervention in adolescents with complex congenital heart disease.
Trial registration: Clinical trials.gov identifier: NCT01189981

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1. Introduction

Cardiorespiratory fitness, measured as maximal oxygen uptake VO_2, is an important predictor of morbidity and mortality [1]. Adolescents and adults with congenital heart disease (CHD) have lower VO_2 than healthy individuals [2–4]. Although structural heart abnormalities partly explain this discrepancy, low levels of physical activity among patients with CHD may contribute to the overarching problem [5]. Physical activity counseling in adolescent heart patients seems to be underused, presumably due to logistic problems, expense, and parental anxiety about adverse events [6].

Home- or facility-based exercise training programs may improve VO_2 in patients with CHD [7–9]. However, methodological limitations of high risks of systematic error (such as selection bias, no stratification for sex, no random sequence generation, allocation concealment, nor blinding of outcome assessors and statistician), random error (such as no predefined outcomes), and design errors (such as no dealing with missing data) hamper the internal validity of previous studies [8,10–14]. Thus, no evidence-based guidelines exist regarding the most

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effective way to encourage adolescents with CHD to be more physically active.

The prevalence of CHD is increasing worldwide [15], and there is a resulting need to assess the effects of rehabilitation programs that can safely and inexpensively connect with adolescents, including those geographically distant from specialist centers [16]. The potential of eHealth—health services and information delivered or supported through the Internet and related technologies [17]—is largely unexplored in this group of patients. Our objective was to assess the effect of adding a home-based eHealth intervention to health education and individual counseling among adolescents with CHD.

2. Methods

2.1. Design

The Paediatric Rehabilitation for Vanguard in Lifeskills (PReVaiL) trial was a nationwide, parallel group, randomized clinical trial conducted in Denmark between 2010 and 2014. The trial protocol was published before randomizing patients [18]. Deviations from the original protocol were approved by the Regional Ethics Committee trial protocol H-1-2010-025 and applied to the ClinicalTrials.gov identifier. Protocol changes addressed an insufficient inclusion rate and minimally broadened inclusion criteria, adding patients with other congenital heart diagnoses and those with forced expiratory volume (FeV1) ≤ of expected 80% after indications of asthma were excluded. The trial conformed to the CONSORT criteria for research on eHealth intervention and adhered to the framework for complex interventions described by the Medical Research Council [19,20].

2.2. Eligibility and inclusion

Patients were identified from the Danish National Register of Patients. Inclusion criteria were as follows: age between 13 and 16 years, previous repair for a complex CHD, and assignment to lifelong medical follow-up [18]. Complex CHD was defined as "vulnerable to additional acquired co-morbidities that impact both their cardiac and medical care, including hypertension, pulmonary, renal, and myocardial disease, and coronary artery disease" [21]. Exclusion criteria were residual defects significant for physical activity restrictions, assessed by the participants' regular cardiologist [18,22]. Patient health records were manually checked for clinically important co-morbidities that could lead to exclusion [22].

Eligibility to participate was confirmed by each patient's cardiologist. Eligible patients were contacted between May 2010 and May 2013 by a letter providing information about the trial and soliciting participation. Two weeks later, eligible patients' parents were contacted by telephone; with their approval, study staff also spoke by phone with adolescents to know if they would participate. All trial information was repeated at the test site before study inclusion. Parents and adolescents were then asked to provide signed consent (Fig. 1).

2.3. Randomization

The randomization was performed by the Copenhagen Trial Unit ten days after the baseline test [12,23]. A trial investigator centrally randomized eligible patients 1:1. The computer-generated allocation sequence used permuted blocks with varying sizes of 6, 8, or 10. The allocation sequence and block size were unknown to the trial investigators. Patients were stratified according to gender and high or low VO_2 peak, using age-matched Scandinavian adolescents with similar cardiac diagnoses [24]. High VO_2 peak in girls was defined as greater than 35.9 $ml \cdot kg^{-1} \cdot min^{-1}$. High VO_2 peak in boys was defined as greater than 45.9 $ml \cdot kg^{-1} \cdot min^{-1}$.

2.4. Trial settings

All tests were performed at the Institute of Sports Medicine in Copenhagen by a team consisting of three nurses, a health coach specializing in adolescence, and two exercise physiologists. The team was blinded to the group allocation of patients.

2.5. Interventions

All patients received 45 min of group health education and 15 min of individual counseling with their parents. Health education and individual counseling was provided in compliance with the Helsinki Declaration and the UNICEF Convention on the Rights of the Child, which decree that patients participating in research should gain personal benefits [25,26].

The goal of the health education was to stimulate sources of self-efficacy before baseline tests. Inspired by Bandura's Social Cognitive Theory, health education was provided to small groups of same-gender adolescents [27]; the curriculum covered physical activity, smoking, alcohol, diet, and sleep. In the group setting, patients shared experiences with physical activity and other incidental experiences. The individual coaching was intended to reinforce patients' perceived competence after baseline tests and action planning based on health education and personal preferences. Behavior change techniques applied in the intervention included the following: (1) information on benefits of physical activity, (2) goal setting, (3) action planning, (4) barrier identification and problem solving, (5) setting of graded tasks, (6) environmental structuring, (7) facilitation of social comparison, (8) time management, and (9) stimulation of future rewards [28].

2.6. The experimental intervention

The experimental intervention consisted of a 52-week Internet, mobile application, and SMS-based program delivering individually tailored text messages to encourage physical activity. The intervention was feasibility tested and concurrently adapted by the software developer [18]. The program encompassed three main approaches: health education, tailored interactive text encouragements, and a personal exercise planning tool.

Text messages encouraged short-term activities with at least 10 min of high intensity as often as possible throughout the day. High intensity was defined for the patients as physical exertion leading to increased heart rate and respiration. The program adhered to guidelines for healthy adolescents that recommend being physically active for at least 60 min per day. The activity should be of moderate to high intensity and should extend beyond the usual short-term daily activities. If the 60 min were divided, each activity should last 10 min or more [29]. The patients allocated to the eHealth intervention were sent health information and a new encouragement every week. Examples of such encouragements could, e.g., be "the challenge this week is that you must run the longest trip you've ever run" or "try to see how long you can keep yourself going".

Patients recorded exercise duration and type in a mobile application that translated intensity into virtual points, a system designed to provide motivation. The mobile application could also be used to plan and register all other activities during the day. The patients could monitor their results on a personal website, with a goal of achieving a bronze, silver, or gold level of points on a weekly basis. The intervention did not allow for interaction between patients due to concerns regarding safeguarding minors on the Internet. We used an existing and widely used eHealth platform, Mobile Fitness A/S Copenhagen, Denmark [30].

Behavior change techniques applied to the eHealth intervention were as follows: (1) action planning tools, (2) rewards for successful behavior, (3) self-monitoring of behavior, (4) feedback on performance, and (5) demonstration of selected behaviors delivered as short videos via the mobile phone [28].

2.7. Adherence to the intervention

Adherence to the eHealth program was assessed by patient registration of physical activities via the eHealth application for at least two consecutive weeks during the trial. The risk of adverse events from participating in the purposed trial was minimal. Patients were instructed to contact their usual health care providers if medical problems occurred.

2.8. Outcomes

2.8.1. Primary outcomes

Peak oxygen uptake, VO_2 peak = $ml\ O_2 \cdot kg^{-1} \cdot min^{-1}$, was assessed by an incremental cardiorespiratory exercise test performed on a bicycle ergometer, Monark Ergomedic 839E, Monark Exercise AB, Sweden [18,31,32]. After a 10-min warm-up period, patients followed the incremental protocol starting at 20 W + 20 W/min for girls and 25 W + 25 W/min for boys until volitional exhaustion. Patients were encouraged to maintain a cadence above 80 rounds per minute and to continue for as long as possible during the tests; equivalent levels of encouragement were provided during all exercise tests. To avoid any adverse events, patients did not have to meet specific criteria for achieving VO_2 peak during the tests. Instead, they were encouraged to stop when they felt exhausted or experienced adverse symptoms. The mean respiratory exchange ratio (RER) achieved during the tests was 1.3 (SD 0.1; range 1.0–1.61), and the mean maximum heart rate (HRmax) achieved was 189 (SD 11.7; range 157–217), following exclusion of an outlier only reaching 102. These results indicate that efforts at or near the maximum were generally achieved, as criteria for achievement of peak oxygen uptake are usually considered a combination of volitional exhaustion, heart rate HR near maximum, and RER above a certain level, e.g., 1.1 [33]. The protocol was designed to achieve exhaustion within 6–12 min, which was the case for 61% of patients, with a mean time to exhaustion of 8.3 min (SD 1.9; range 4.1 to 13.3 min). All exercise tests were performed without adverse events. Peak oxygen uptake was defined as the highest value obtained over a 5-s averaging interval, using breath-by-breath measures. The term "peak," rather than "maximal oxygen consumption," acknowledges that it was the peak value achieved under the specific conditions, which is not necessarily the true maximum but was verified by the described criteria.

2.8.2. Secondary outcomes

Physical activity was assessed using a commercially available accelerometer: ActiGraph model 77,146, Pensacola, FL. Patients were asked to wear the monitors, which were set to record at five-second epochs, on the left hip from 6 AM to 10 PM for two weekend days and four weekdays [18]. Total minutes per day spent in moderate to vigorous physical activity (MVPA) were assessed using 2000 accelerometer cut-point counts per minute as the lower threshold of moderate-intensity activity [34]. Recordings of at least one weekend day and one weekday of at least 10 h were defined as valid. Days with more than 10 h of recordings that included periods where the accelerometer was not worn were adjusted to a full-day of 14 h estimated awake time for this population [35].

Physical activity was also assessed by an electronic questionnaire validated by the Health Behavior of School-aged Children survey [36]. Acceptable reliability and validity have been reported [37].

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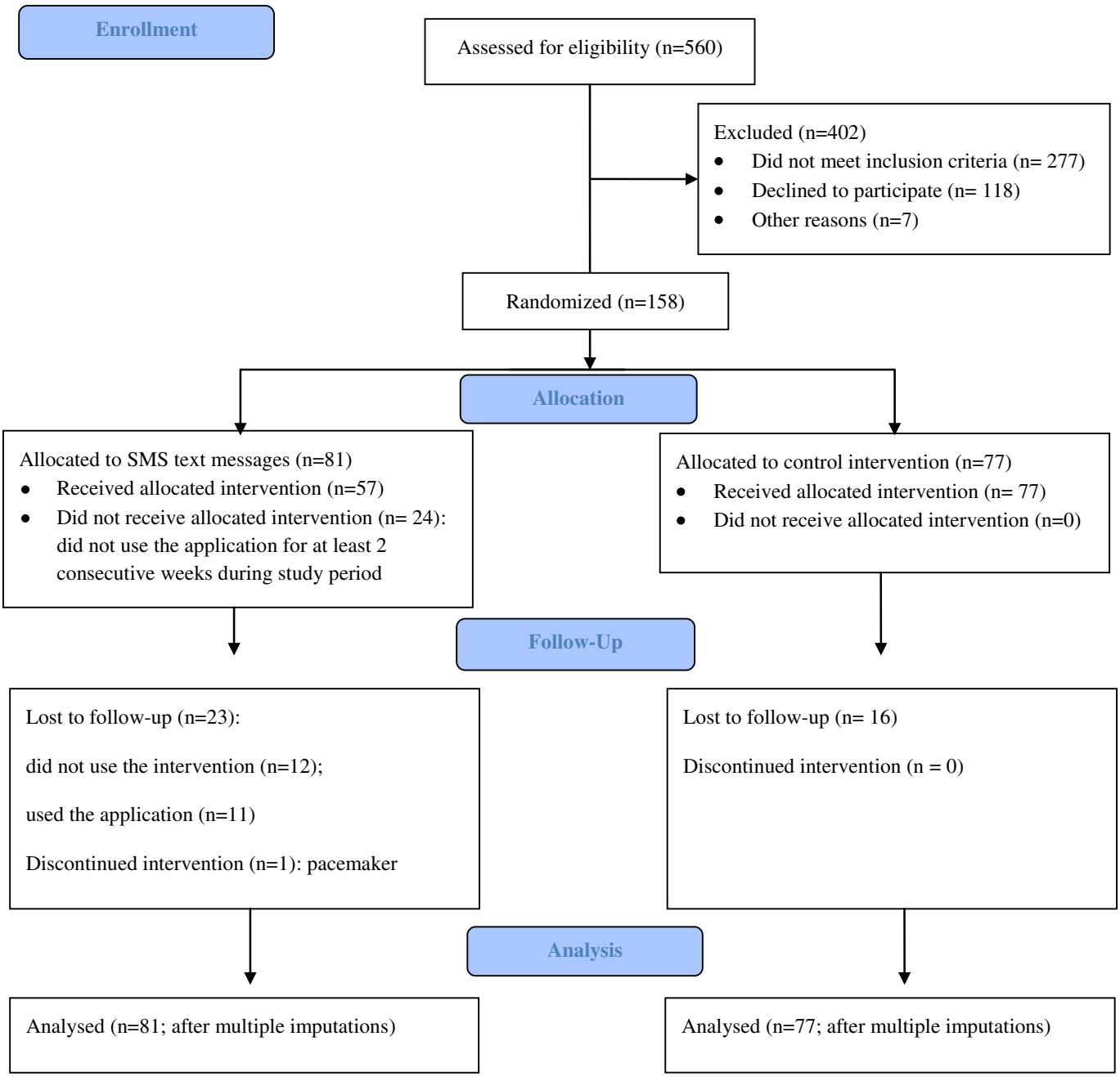

Fig. 1. CONSORT diagram.

The investigator read the items to patients and recorded their responses. This took place in a separate room; patients' parents were not present.

2.8.3. Exploratory outcomes

Health-related quality of life was assessed by the Danish version of the Paediatric Quality of Life Inventory questionnaire for teens ages 13–18 years, using the generic and the disease-specific version [38]. Good reliability and validity have been reported [39,40]. The generic module assessed four domains: physical functioning, emotional functioning, social functioning, and school functioning. The disease-specific module assessed six domains: heart problems and treatment, treatment II, perceived physical appearance, treatment anxiety, cognitive problems, and communication. The disease-specific questionnaire was translated into Danish and linguistically validated by six age-matched patients and 12 healthy adolescents.

2.9. Sample size estimation

Sample size was estimated based on existing research with adolescents with CHD [11]. Assuming a mean difference of 13 W in the cardiorespiratory exercise test between the intervention group and the control group, a standard deviation of 34 W, and a risk of Type I error of 5% and a risk of Type II error of 20%, we estimated that a total of 216 patients needed to be randomized.

2.10. Statistical analysis

Data were analyzed using SPSS, version 20.0 and STATA version 13. The statistical analysis plan was published before access to data. The primary analyses for all continuous outcomes were analysis of covariance (ANCOVA), adjusted for VO_2 peak at baseline and for the stratification variables of gender and high/low exercise capacity. The primary analysis for all binary outcomes was a logistic regression adjusted for the stratification variables. The secondary analysis for all continuous outcomes was an ANCOVA adjusted for VO_2 peak at baseline, the stratification variables of gender and high/low exercise capacity, age at test years, lung function, muscle strength, and body composition. The secondary analysis for all binary outcomes was an unadjusted logistic regression. The tertiary analysis for all continuous outcomes was an ANCOVA adjusted for baseline values, stratification variables, and cluster association. The tertiary analysis for all binary outcomes was a logistic regression adjusted for the stratification variables and the cluster association.

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Three populations were analyzed. In the intention-to-treat population, multiple imputations were used to handle missing data [41,42]. The per-protocol population included all patients randomized to the intervention who recorded physical activities to the eHealth application in at least two consecutive weeks. The cluster population derived from a published cluster analysis on baseline health-related fitness variables associated with cardiorespiratory fitness, body composition, and muscle strength [43]. A statistician blinded to the intervention allocation performed all statistical analyses. The authors interpreted the results and formulated the main conclusions before the group allocation was revealed.

3. Results

3.1. Flow of patients

We aimed to include 216 patients but were only able to include 158 patients because of lack of interest or active sports participation (Fig. 1). Out of 560 adolescents assessed for eligibility, 66 girls and 92 boys were randomized to either the intervention group ($n = 81$) or control group ($n = 77$). The scheduled enrolment period was extended by six months due to slow recruitment. Of 158 enrolled patients, 119 (75%) completed both exercise tests; 58 (72%) of the test group and 61 (79%) from the control group.

3.2. Adherence to the intervention

Of 81 patients in the intervention group, just 46 (57%) patients used the eHealth application for at least two consecutive weeks and completed both exercise tests. Only 8 (10%) patients were active users during the last week of the intervention. Just 57 (70%) of the patients in the intervention group adhered to the intervention using the eHealth application for at least two consecutive weeks. The 24 patients (30%) in the intervention group that did not actively use the eHealth application for at least 2 consecutive weeks during the 1-year trial period were defined as not adhering to the protocol.

3.3. Baseline characteristics

Baseline characteristics were largely similar between the intervention and control groups (Table 1). Patients' mean age was 14.6 years (SD 1.3) at the time of baseline testing, and BMI was 21.2 (SD 3.6) among girls and 19.5 (SD 3.0) among boys. Average VO_2 among girls was 37.5 $ml \cdot kg^{-1} \cdot min^{-1}$ (SD 8.1) and among boys 47.9 $ml \cdot kg^{-1} \cdot min^{-1}$ (SD 7.9). One third of all patients had had surgery for coarctation of aorta, 22% had had surgery for transposition of the great arteries, and 13% had had surgery for tetralogy of Steno–Fallot (Table 2).

3.4. Outcomes

3.4.1. Primary outcome

At 1 year, the mean VO_2 peak was 43.2 (SD 9.7) in the intervention group and 46.3 (SD 10.1) $ml \cdot kg^{-1} \cdot min^{-1}$ in the control group (Table 3). In the primary analysis adjusted for baseline VO_2 peak and stratification variables of gender and exercise capacity, the 95% CI of the difference in mean VO_2 peak between the intervention and control groups included zero and excluded a minimal relevant difference of 3 ml/kg/min. In the fully adjusted analysis, the difference in mean VO_2 peak between the intervention and control group of −0.41 (95% CI −2.45 to 1.63) included zero and excluded relevant difference. Sensitivity analyses after excluding participants with Fontan circulation found a difference between intervention groups of −0.74 (−2.76 to 1.28). Subgroup analyses by gender and per-protocol recipients of the intervention did not reveal statistically significant differences. Subgroup analyses by

Table 1
Baseline characteristics of patients.

	Intervention $n = 81$	Control $n = 77$	Girls $n = 66$	Boys $n = 92$
Age, years, mean (SD)	14.6 (1.3)	14.6 (1.2)	14.5 (1.3)	14.6 (1.3)
Baseline anthropometrics, mean (SD)				
Height, cm	166 (10.4)	165 (9.5)	162 (6.6)	167 (11.2)
Weight, kg	57.0 (11.0)	58.0 (13.4)	57.9 (11.9)	56.8 (12.5)
BMI	20.0 (2.9)	20.5 (3.9)	21.2 (3.6)	19.5 (3.0)
Body surface area, m^2	1.6 (0.2)	1.6 (0.2)	1.6 (0.2)	1.6 (0.2)
Waist, cm	72.0 (7.9)	73.0 (9.1)	71.3 (8.2)	73.4 (8.6)
Hip, cm	87.7 (8.6)	88.4 (10.6)	91.7 (9.8)	85.4 (8.6)
Waist/hip ratio	0.82 (0.1)	0.83 (0.1)	0.78 (0.1)	0.86 (0.1)
Sum of skinfolds, mm	13.3 (8.5)	12.5 (8.2)	17.8 (10.9)	9.4 (2.1)
Systolic BP, mm hg	119 (12.7)	118 (10.8)	116 (11.9)	120 (11.4)
Diastolic BP, mm hg	67.1 (6.6)	67 (6.7)	67.2 (5.5)	66.8 (7.4)
Resting pulse	69.2 (11.4)	71 (9.9)	70.8 (10.0)	69.6 (11.2)
Muscle strength, kg	29.1 (8.5)	27.9 (7.5)	26.1 (4.7)	30.2 (9.4)
Baseline lung function, mean (SD)				
Fev1/s	3.0 (0.7)	3.0 (0.7)	2.7 (0.5)	3.2 (0.8)
Fev1/s:% of predicted	94% (0.1)	94% (0.1)	96% (0.1)	92% (0.1)
Cardiorespiratory fitness, mean (SD)				
Maximal oxygen uptake	43.7 (9.8)	43.3 (9.3)	37.5 (8.1)	47.9 (7.9)
VO_2 ml/min/kg				
HRR beats/min	122.8 (15.1)	122.0 (15.9)	121 (13.9)	120.7 (14.1)
Oxygen pulse	13.1 (3.3)	12.9 (3.6)	11.3 (1.9)	14.2 (3.8)
Max work load (W)	185 (48.1)	182 (46.6)	158 (26.6)	201 (50.6)
Anaerobic threshold	0.7 (0.2)	0.7 (0.1)	0.67 (0.2)	0.72 (0.1)
RER	1.3(0.1)	1.3 (0.1)	1.3 (0.1)	1.3 (0.1)
Physical activity, mean (SD)				
Time physical activity, minutes	438 (159)	475 (176)	430 (178)	476 (159)
Minutes ≥2000 counts	45.8 (24.1)	49.8 (26.6)	43.0 (27.0)	51.3 (23.7)
Leisure time, days per week, hours	3.1 (0.7)	2.9 (0.2)	4.3 (1.5)	4.4 (1.5)
Sedentary time, week day, hours	3.2 (1.6)	3.2 (1.7)	3.1 (1.3)	3.9 (1.7)
Sedentary time, weekend day, hours	4.4 (1.9)	4.9 (1.9)	4.2 (1.5)	5.3 (1.9)
MVPA ≥60 min a day, percent of patients	32%	26%	18%	34%
Health-related quality of life, mean (SD)				
Generic	80.0 (9.4)	80.4 (9.5)	78.9 (10.5)	81.3 (8.4%)
Disease-specific	85.2 (10.7)	84.6 (9.7)	82.6 (12.3)	86.6 (7.8)

Abbreviations: BMI, body mass index; Fev1, forced expiratory volume; HRR, heart rate reserve; RER, respiratory exchange ratio; MVPA, moderate vigorous physical activity.

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Table 2
Prevalence of congenital heart conditions, n (%).

	All patients $n = 158$	Intervention group $n = 81$	Control group $n = 77$	Girls $n = 66$	Boys $n = 92$
Coarctation of the aorta	52 (33%)	31 (38%)	21 (27%)	19 (29%)	33 (36%)
Transposition of the great arteries	35 (22%)	21 (26%)	14 (18%)	13 (20%)	22 (24%)
Steno–Fallot tetralogy	21 (13%)	8 (10%)	13 (17%)	9 (14%)	12 (13%)
Double outlet right ventricle	7 (4%)	4 (5%)	3 (4%)	4 (6%)	3 (3%)
Truncus arteriosus	4 (3%)	3 (4%)	1 (1%)	2 (3%)	2 (3%)
Atrioventricular septal defect	9 (6%)	1 (1%)	8 (11%)	6 (9%)	3 (3%)
Total cavopulmonary connection surgery	6 (4%)	2 (2%)	4 (5%)	2 (2%)	4 (4%)
Other	24 (15%)	11 (14%)	13 (17%)	11 (17%)	13 (14%)

high/low VO_2 peak showed a difference between intervention groups of −1.10 (−4.19 to 1.97) in the participants with low oxygen uptake at baseline, and −0.74 (−3.70 to 2.22) in the participants with high oxygen uptake at baseline. The subgroup analysis adjusted for cluster allocation yielded similar results (not shown).

3.4.2. Secondary and exploratory outcomes

Patients in the intervention group spent a mean of 40.3 (SD 21.8) minutes per day in moderate to vigorous physical activity compared to 41.3 (22.9) minutes per day in the control group. The between-group difference of −0.04 min day (95% CI −2.23 to 0.23) was not significantly different. Assessments of physical activity by questionnaires yielded similar results.

Differences in generic (0.32 points; 95% CI −2.39 to 3.14) and disease-specific health-related quality (−0.72 points; 95% CI −3.73 to 2.89) of life between the intervention and the control group were not significantly different.

4. Discussion

4.1. Adding 52 weeks of eHealth encouragements to health education and individual counseling does not seem to increase physical fitness, physical activity, or health-related quality of life in adolescents with complex CHD

Rehabilitation studies in adolescents with CHD tend to investigate patients with Fontan-type circulation [44]. However, patients with Fontan-type circulation are not representative of the total population of patients with CHD allocated to lifelong care. We included adolescents with no limitations to physical activity across multiple diagnoses, increasing the generalizability of our findings to adolescents with CHD in general. Although it is a relatively small trial, the PreVaiL trial is larger than comparable home-based trials [45–47]. The fraction of eligible patients who enrolled was higher (58%) than in similar trials (29–36%) [45–47]. Home-based training studies in adults with CHD found between-group differences in VO_2 after both 10 and 24 weeks of graded training [46,47]. Factors like the time frame of the intervention, the patient's baseline VO_2 status, and the trial design may have influenced the results. A central question is how to motivate adolescents with CHD to be physically active on a regular basis. Two trials that included educational and motivational strategies reported a short-term effect on physical activity in adolescents and children with CHD [45,48]. No valid trial results so far has shown any long-term effects of any type of activity encouragement on physical fitness, physical activity, or health-related quality of life in patients with CHD. [44].

Table 3
Between-group differences at 1 year.

	Intervention group $n = 81$	Control group $n = 77$	Between-group difference (95% CI)	P value
VO_2 peak, mean (SD)	43.2 (9.7)	46.2 (10.1)	−0.65 (−2.66 to1.36)	0.52
Girls	37.5 (7.4)	36.6 (7.9)	0.04 (−2.91 to 2.83)	0.98
Boys	47.8 (9.0)	50.9 (7.6)	−1.47 (−4.23 to 1.31)	0.30
Per protocol[a]	44.1 (10.3)	46.2 (10.1)	−0.01 (−2.13 to 2.11)	0.99

[a] = The per-protocol population included all patients randomized to the intervention who recorded physical activities to the eHealth application in at least two consecutive weeks ($n = 57$).

4.2. Future research and eHealth interventions

Interventions using eHealth are low cost, but adding this 52-week Internet, mobile application, and SMS-based program delivering individually tailored text messages to encourage physical activity to health education and individual counseling does not seem to affect fitness, physical activity, and health-related quality of life in adolescents with CHD. It is possible that more intensive interventions are needed in order to change behavior in adolescents, or eHealth interventions might not generally benefit physical fitness and health-related quality of life in adolescents with CHD. Based on the present trial, we suggest that future eHealth interventions should be thoroughly piloted, to avoid problems of recruitment and retention.

Considering the amount of available funding in the Horizon 2020 program directed toward eHealth in empowering citizens to manage their own health [49], researchers should carefully consider which eHealth trials may be worth conducting as not to waste time and money. More evidence is needed about behavioral change strategies to inform health education and counseling.

4.3. Recommendations and motivation

Although evidence for the benefits of physical activity for health has been available since the 1950s [50], no long-term studies have confirmed that this is also the case for in participants with congenital heart disease. However, physical activity is necessary for the optimal physical, emotional, and psychosocial development in children with congenital heart disease (Takken 2011). Physical activity promotion by theoretical frameworks has been suggested in a Scientific Statement From the American Heart Association (Longmuir). The eHealth intervention did not adhere to a specified theoretical framework, as did the control intervention. The lack of effect questions whether the eHealth intervention could have been qualified by motivation patients according to a behavior change theoretical framework such as Bandura's Social Cognitive Theory or Self-Determination Theory. The eHealth intervention may in contrast have included elements that did not motivate to physical activity, such as feedback [51]. Interventions based on Self-Determination Theory have shown to stimulate autonomous motivation, which has shown to be strongly related to sustain changes in physical activity in healthy adolescents [52]. Yet it is unknown if this is effective in an eHealth setting. A systematic review of eHealth interventions that promote physical activity behavior change in healthy adolescents found that no interventions reported of an effect [53]. Also, no behavioral change theoretical frameworks were described in the trials reviewed. It is unknown whether a face-to-face intervention would have been more efficient in this population, as the trial included only two arms.

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4.4. Strengths and limitations

This trial has a number of strengths. The trial was conducted according to the CONSORT criteria, valid statistical methods were used, and there were only minor deviations from the pre-specified methodology, which was published in a protocol before randomization. Furthermore, multiple imputations were used to handle missing data decreasing the likelihood that the effect was affected by missing data under the assumption that data was missing at random. All tests were performed on the same site using the same equipment operated by the same team of experienced assessors, and validated tools measured VO_2, physical activity, and health-related quality of life. The VO_2 was assessed by a bicycle ergometer test to exhaustion with breath-by-breath measurements of oxygen consumption and other respiratory variables, which increases internal validity. Finally, the intervention drew on an existing and widely used eHealth platform experienced in designing eHealth applications [30].

This trial also has a number of limitations. We were only able to randomize 158 patients out of the 216 originally planned, and only 119 (75%) patients completed the trial. Our sample size was estimated based on the standard deviation obtained from a watt max test in a small study with the highest methodological quality existing at the time the protocol was written [18]. Using the observed standard deviation of the current trial, based on the more precise outcome of VO_2, the necessary sample size to detect a clinically relevant difference of 3.00 $ml \cdot kg^{-1} \cdot min^{-1}$ would be 160 patients. The 95% confidence interval for effect on the primary outcome reported here was −2.66 to 1.36, excluding a clinically relevant effect. "It was possible to use the application despite no registration of points. The adherence criteria were applied in order to exclude participants who entered data irregularly, indicating that the application was not used for recording physical activities on a regular basis.

We are aware that the intervention may have acted counterproductively, as it may have demotivated to registering activities due to a sense of being kept under surveillance. As seen in the figure: Percentage of active patients throughout the 1-year intervention, now added in Fig. 2, no more than 57% of the participants used the application at any one point in time, and further, this number was only recorded over the first weeks. In this population, more restrict compliance criteria would have excluded more participants.

We still believe that all together did not lead to an improvement in exercise capacity after 52 weeks intervention. If a low number of participants used the intervention during the trial, then it is probable that a low number of real life patients would use the intervention outside a trial setting. Whether the participants adhered to the intervention or not is, therefore, not that important because the overall result, including patients regardless of adherence, probably reflects (or even overestimates) the real life effects (intention-to treat effects) of the eHealth intervention."

Finally, the blinding of outcome assessors cannot be fully ensured in behavioral interventions because patients may reveal their group assignment during testing. However, to minimize risk of bias we instructed all patients not to disclose their allocation prior to outcome testing.

5. Conclusion

Adding our tailored eHealth intervention to health education and individual counseling does not seem to have any effect in adolescents with congenital heart disease and the few experimental participants using this eHealth intervention possibly contributed to the lack of effect. Our results do not support the use of this 52-week Internet, mobile application, and SMS-based program, delivering individually tailored text messages to encourage physical activity in adolescents with complex congenital heart disease.

Conflict of interest

All authors declare they have no conflicts of interest.

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Author contributions

SHK, LLA, URM, LS, and JW designed the project and revised the manuscript. JCJ, SHK, LLA, LS, VZ, and JW analyzed and interpreted the data and revised the manuscript: JW is the guarantor. URM, KD, and AK collected data and revised the manuscript. All authors approved the final version of the paper.

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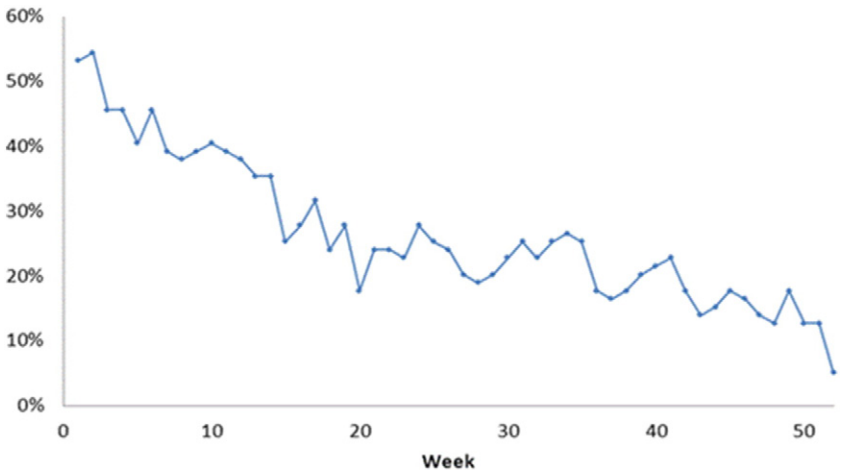

Fig. 2. Percentage of active patients throughout the 1-year intervention.

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