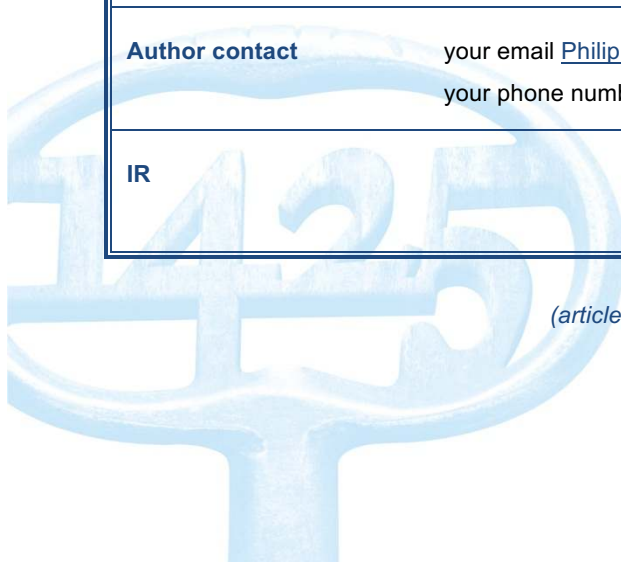




<b>Citation</b>	<p>Ko JM, White KS, Kovacs AH, Tecson KM, Apers S, Luyckx K, Thomet C, Budts W, Enomoto J, Sluman MA, Wang JK, Jackson JL, Khairy P, Cook SC, Subramanyan R, Alday L, Eriksen K, Dellborg M, Berghammer M, Johansson B, Mackie AS, Menahem S, Caruana M, Veldtman G, Soufi A, Fernandes SM, Callus E, Kutty S, Gandhi A, Moons P, Cedars AM; APPROACH-IS consortium and International Society for Adult Congenital Heart Disease (ISACHD).</p> <p><b>Physical Activity-related Drivers of Perceived Health Status in Adults with Congenital Heart Disease</b></p> <p>Am J Cardiol. 2018 Oct 15;122(8):1437-1442</p>
<b>Archived version</b>	<p>Author manuscript: the content is identical to the content of the published paper, but without the final typesetting by the publisher</p>
<b>Published version</b>	<p><a href="https://doi.org/10.1016/j.amjcard.2018.06.056">https://doi.org/10.1016/j.amjcard.2018.06.056</a></p>
<b>Journal homepage</b>	<p><a href="https://www.ajconline.org/">https://www.ajconline.org/</a></p>
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## **Physical Activity-related Drivers of Perceived Health Status in Adults with Congenital Heart Disease**

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**There are no conflicts of interest for any author.**

**Disclosures:** The authors have nothing to disclose.

**Running Title:** Physical Activity and Perceived Health Status

### **Abstract**

Data on the differential impact of physical activity on perceived health status (PHS) in a large adult congenital heart disease (ACHD) patient population is lacking. We conducted a cross-sectional assessment of 4,028 ACHD patients recruited from 24 ACHD-specialized centers in 15 countries across 5 continents to examine the association between physical activity and PHS in a large international cohort of ACHD patients. A linear analog scale of the EuroQol-5D 3 level version and the 12-item Short Form Health Survey - version 2 were used to assess self-reported health status and the Health-Behavior Scale-Congenital Heart Disease was used as a subjective measure of physical activity type, participation, and level. Correlation analyses and Wilcoxon Rank Sum tests examined bivariate relations between sample characteristics and PHS scores. Then, multivariable models were constructed to understand the impact of physical activity on PHS. Only 30% of our sample achieved recommended physical activity levels. Physically active individuals reported better PHS than sedentary patients; however, the amount of physical activity was not associated with PHS. Further statistical analyses demonstrated that specifically sport participation regardless of physical activity level was a predictor of PHS. In conclusion, the majority of ACHD patients across the world are physically inactive. Sport participation appears to be the primary physical activity-related driver of PHS. By promoting sport-related exercise ACHD specialists thus may improve perceived health status in ACHD patients.

**Key Words:** Physical activity; Perceived health status; Self-efficacy; Psychological benefits

## Introduction

Alarming only a small portion of adult congenital heart disease (ACHD) patients reach the World Health Organization recommended levels of physical activity (i.e., 5 x 30 minutes of moderate-intensity or 3 x 20 minutes of vigorous-intensity activities per week).<sup>1-4</sup> Considering the negative clinical and psychosocial effects of a sedentary lifestyle on ACHD patients, one often overlooked but important component of care is the development of exercise promotion strategies in ACHD-specialized centers.<sup>5</sup> Aside from direct physiologic benefit, numerous studies have demonstrated a positive correlation between physical activity participation and perceived health status (PHS).<sup>6,7</sup> As PHS measures are excellent predictors of adverse clinical outcomes and directly reflect patient's experiences, understanding the relationship between physical activity and PHS is fundamental to improving patients' overall care quality.<sup>8</sup> Data on the differential impact of PA on PHS in a large ACHD patient population specifically are, however, lacking. In the present study, we investigated the relationship between physical activity and PHS in a large international cohort of ACHD patients.

## Methods

We assessed the association between physical activity and PHS in 4,028 ACHD patients who were enrolled from 15 countries across 5 continents in a cross-sectional, multicenter international study from April 2013 till March 2015. The detailed study protocol and a full list of demographic, clinical, and psychological variables have been previously summarized by Apers et al.<sup>9</sup> Two PHS instruments (i.e., the 12-item Short Form Health Survey - version 2 [SF-12] and a linear analog scale [LAS] of the EuroQol-5D 3 level version [EQ-5D]) were used to comprehensively capture patient's self-assessed health condition in various domains: the SF-12 yields physical and mental health scores while the EQ-5D LAS assesses patient's overall self-

reported health status.<sup>10,11</sup> The Health-Behavior Scale-Congenital Heart Disease was used for subjective measurements (participation and the time spent) of physical activity, which consists of 2 domains – active commute (i.e., walking or cycling to work or school) and sport participation (i.e., all physical activities other than active commute performed at minimal [e.g., golf and darts], moderate [e.g., jogging and dancing], or vigorous [e.g., basketball and rowing] intensity).<sup>12</sup> To limit inferences to participants healthy enough to be employed or attend school, our analysis included only those who were employed or were students. We calculated the physical component score (PCS) and the mental component score (MCS) of the SF-12 according to the validated scoring algorithm and used the raw score from the EQ-5D LAS.<sup>13</sup> We calculated the physical activity levels as the amount of energy expenditure (MJ/h) in both physical activity domains.<sup>14</sup>

To identify differences in PHS between sedentary (i.e., neither active commuters nor sport participants) and physically active participants, we performed Wilcoxon Rank Sum tests. To assess associations of physical activity levels in both domains with the 3 PHS scores stratified by country, we utilized Spearman correlations. Similarly, to assess bivariate relations between sample characteristics and the 3 PHS domains, we used correlation analyses and Wilcoxon Rank Sum or Kruskal-Wallis tests, as appropriate. Then, to understand the unique impact of physical activity on PHS, we constructed multivariable linear mixed models, using country as a random effect to account for differences between countries. We built separate models for all 3 PHS domains and both PA domains. Our model included the list of significant covariates identified by Apers et al. (i.e., age, gender, employment, marital status, and New York Heart Association [NYHA] class).<sup>15</sup> Finally, we built fully-adjusted models for the effect of sport participation on PHS via stepwise selection, which considered all variables having significant relations with PHS in bivariate analyses and missing at a rate of < 5%. We used the methods of Xu (2003) to

calculate the percent of explained variability,  $R^2$ .<sup>16</sup> Continuous variables are presented as medians [quartile 1, quartile 3]. Categorical variables are presented as frequencies and percentages. Analyses were performed in SAS 9.4 (Cary, NC).

## Results

The total cohort used in this analysis has been previously described.<sup>15</sup> Table 1 shows that physically active individuals reported more favorable physical and mental health than physically inactive ones. Of 3,087 people who were either employed or students, 1,084 (35%) were active commuters and 1,074 provided further information on the daily round-trip travel time spent: 421 (39%) commuted <15 minutes; 408 (38%), 15-30 minutes; 148 (14%), 30-45 minutes; and 97 (9%), >45 minutes. The rates of active commute differed significantly by country ( $p < 0.001$ ), ranging from 18% (the United States) to 55% (France) (Figure 1).

Of 3,955 patients who provided information on sport participation, 1,703 (43%) practiced sport(s). The rates of sport participation differed significantly by country ( $p < 0.001$ ), ranging from 10% (India) to 66% (Norway). When patients did participate in sport, the majority in all countries, except in France and Japan, did  $\geq 150$  minutes of moderate-intensity or  $\geq 60$  minutes of vigorous-intensity exercise per week (Figure 2). About 30% of 3,955 patients achieved recommended physical activity levels. The median hours spent per week doing vigorous-, moderate-, and minimal-intensity exercise were 1 [0, 3], 2 [0, 3], and 0 [0, 2], respectively, among those who did participate in sport.

Supplemental Tables 1 and 2 display differences in demographic, clinical, and psychological characteristics between 2 groups (active commuters and those not; sport participants and those not, respectively). Active commuters and sport participants were more likely to be younger, unmarried/never married, without child(ren), highly educated, not



religious/spiritual, less depressed, less likely to have a history of arrhythmia or to have medical comorbidities, and more likely to have NYHA class < II.

Active commute was associated with all 3 PHS domains in only 3 countries while sport participation was linked to all PHS domains in 8 countries (Supplemental Table 3). The amount of energy expended during active commute or sport participation did not correlate with PHS outcomes in most countries; in the few countries where significance was found, correlations were very weak as shown in Supplemental Table 4.

Bivariate (unadjusted) relations between physical activity and PHS revealed consistently stronger associations between sport participation and PHS than active commute and PHS (Table 2). Active commute explained 0.40%, 0.14%, and 0.35% of the variability in PCS, MCS, and LAS, respectively, while sport explained 8%, 4% and 5%, respectively. While practicing a sport had a significant relation to all 3 PHS domains even after adjusting for age, sex, employment, marital status, and NYHA class, we found that active commute remained significant only for PCS. In the fully-adjusted models, the effect of sport participation remained significant for all measures of PHS ( $p$ 's < 0.001). Fully adjusted models were not constructed for active commute given the borderline statistical significance of the partially adjusted model for only one PHS metric. The full list of model covariates is found in Table 2.

## **Discussion**

In the present study, we explored the relationship between physical activity and PHS in 4,028 ACHD patients followed at 24 ACHD-specialized hospitals in 15 countries in 5 continents. This is the first large-scale international study not only to examine the relationship between physical activity and PHS, but also to provide information on the differential impact of active commute versus sport on PHS. We found that, physically active ACHD patients reported better

PHS than sedentary ones. Surprisingly, however, the amount of energy expended during physical activity overall was not associated with the PHS measures. We also observed consistently stronger associations between sport participation and PHS than active commute and PHS. These results indicate that the primary physical activity-related driver of variability in PHS is participation specifically in sport regardless of the degree of exertion. This may be interpreted to suggest that physical activity self-efficacy coupled with the psychological benefit from sport participation is responsible for the association rather than a direct biological effect of physical activity.

Physical activity self-efficacy is person's belief in one's ability to perform physically demanding activities.<sup>17</sup> It is an important motivational factor in deciding to participate in exercise and is positively correlated with physical activity participation in both children and adults with CHD.<sup>3,17</sup> It may be further enhanced by benefits associated with sport participation, e.g., a sense of enjoyment, mastery, and/or confidence in physical ability as well as increased exercise capacity and muscle strength, which may in turn contribute to a positive association of sport-related exercise participation with PHS.

Unlike sport participation, active commute may not be largely influenced by self-efficacy or entail perceived health benefits which this may explain the lack of association between active commute and PHS in this study. The present data on the relationship between total physical activity energy expenditure and PHS differs from previous findings. Humphreys et al. observed a positive correlation between time spent in active commute and the PCS of the Medical Outcomes Study Short Form-8, in a sample of working people aged  $\geq 16$  years.<sup>18</sup> Other studies, some including ACHD patients, have shown a correlation between total physical activity level and PHS.<sup>19,20</sup> Possible explanations for this discrepancy are the different methodological approaches

between studies and the unique nature of ACHD patients many of whom maintain a sedentary lifestyle. In support of the latter possibility, Moons et al. found an increase in perceived physical function among children with CHD who attended a sport camp which far exceeded that experienced by their healthy peers.<sup>21</sup> Patients in the present study might have experienced the maximum degree of perceived health benefit at the lowest level of physical activity whereas other more active populations require greater degrees to experience a similar benefit.

Consistent with previous data, only 30% of our study cohort achieved the recommended physical activity levels.<sup>3,4</sup> Compared to 69% of the world's adult population meeting the recommended levels, this is strikingly a low rate.<sup>1</sup> Interestingly though, among those who engaged in physically demanding activities, the majority (71%) achieved at least a moderate-intensity level. In spite of patient and provider reservations regarding sports participation, CHD patients are willing to exercise if properly instructed.<sup>3,22</sup> Furthermore, directed exercise has been demonstrated to be safe regardless of CHD lesion complexity and to improve objective physiologic exercise response with lasting beneficial effects.<sup>2</sup> Nevertheless, patient education and specific exercise guidance in ACHD-specialized clinics is lacking.<sup>23</sup>

Also consistent with existing data, our study showed that sport participants were more likely to be males and people who were younger and clinically healthier than their sedentary counterparts.<sup>4-6,24</sup> Given that an individual's age, sex, and general health are determinants of self-efficacy, this strengthens our postulation of a close relationship between self-efficacy, physical activity, and PHS.<sup>25,26</sup> In ACHD patients in particular Bay et al demonstrated low physical activity self-efficacy among those who were older, had worsening NYHA functional class, and were physically less active.<sup>27</sup> Nevertheless, even among patients who are very deconditioned or frail, carefully guided low-level exercise is associated with health benefits.<sup>28,29</sup> Moreover, among

patients with acquired heart disease guided exercise prescriptions leads to improvements in exercise capacity, autonomic tone and ventilatory response during exercise.<sup>30</sup>

In conclusion, the majority of ACHD patients across the world are physically inactive. Sport participation, however, correlates with PHS in this population. Our data suggest sport-related exercise promotion in ACHD clinics is a high yield area for future investigation.

There are limitations to the present study. A recall bias is a potential problem as all patient-reported outcomes depend on self-reporting. Some incomplete or incorrect clinical data may be present as all clinical data were collected by chart review. The results may not be generalizable to all ACHD patients as the study cohort was recruited only from ACHD-specialized centers. A geographic- and age-matched control population is lacking this study and the specific activities recommended might vary depending on CHD type in this patient population; these should be taken into consideration when interpreting the data on the relatively low rates of physical activity. Patients who participated in a sport had approximately 3.5 points higher PCS scores on average. While this finding is statistically significant, it is unclear if it is clinically relevant. Confounding variables, such as geographic and cultural differences might have affected the results; however, the analysis techniques employed controlled for factors attributed to differences in country. Lastly, associations identified in the study cannot be used to make conclusions about causation as the data were from a cross-sectional study, but are intended to be hypothesis-generating.

**Acknowledgements:** We are grateful to the study participants who made this study possible as well as all individuals at the participating centers who made substantial contributions to this international study. This work was supported by the Research Fund – KU Leuven (Leuven,

Belgium) through grant OT/11/033 to K.L. and P.M.; by the Swedish Heart-Lung Foundation (Sweden) through grant number 20130607 to M.D.; by the University of Gothenburg Centre for Person-centred Care (Gothenburg, Sweden) to M.D. and P.M.; and by the Cardiac Children's Foundation (Taiwan) through grant CCF2013\_02 to J.K.W. Furthermore, this work was endorsed by and conducted in collaboration with the International Society for Adult Congenital Heart Disease. This work was also funded, in part, by the Baylor Health Care System Foundation.

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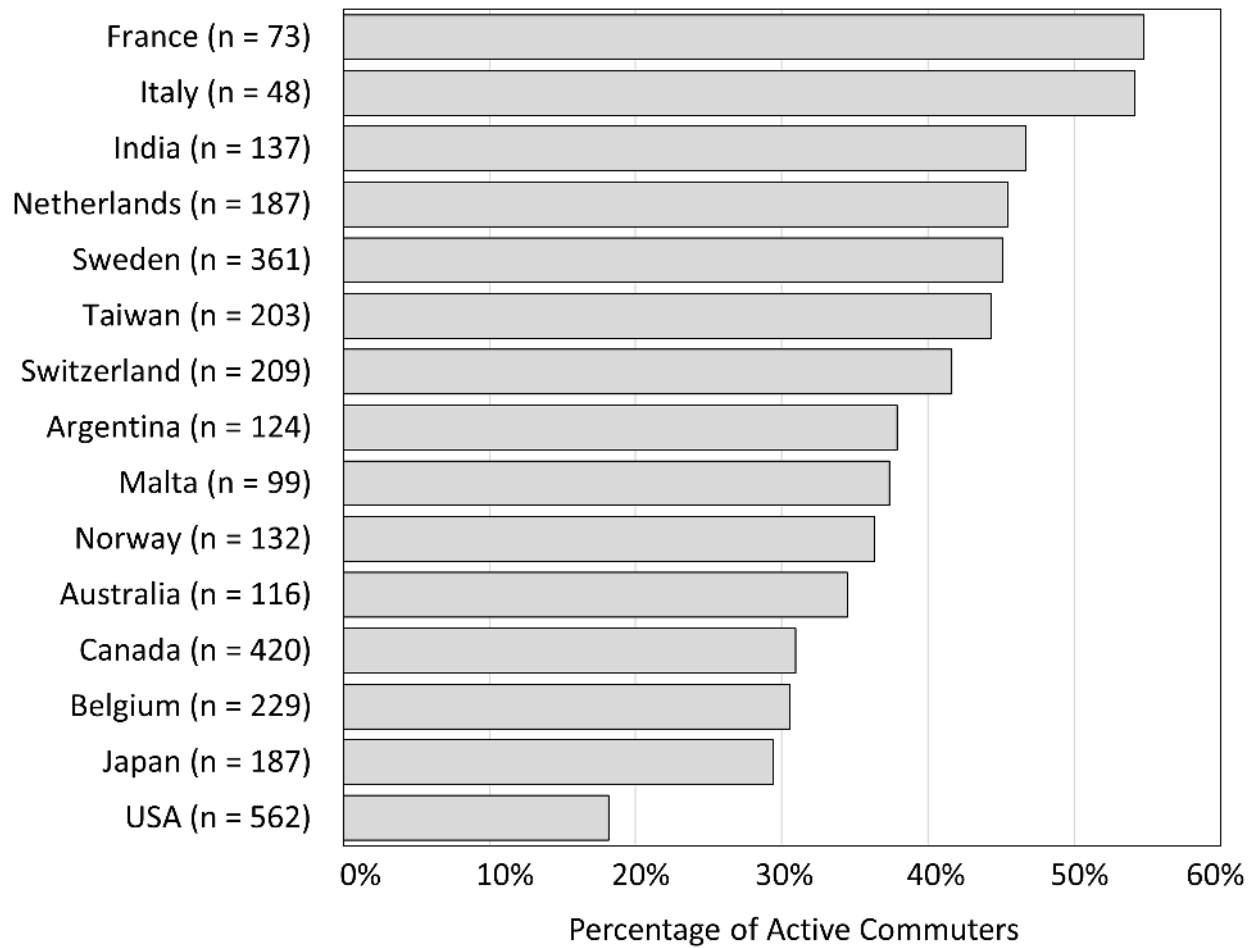
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**Figure 1. Proportion of Active Commuters by Country**

**Figure 2. Proportion of Sport Participants by Country.** Meeting recommended PA level = proportion of individuals who did  $\geq 150$  minutes/week of moderate-intensity sport [e.g., jogging and dancing] or  $\geq 60$  minutes/week of vigorous-intensity sport [e.g., basketball and rowing]).

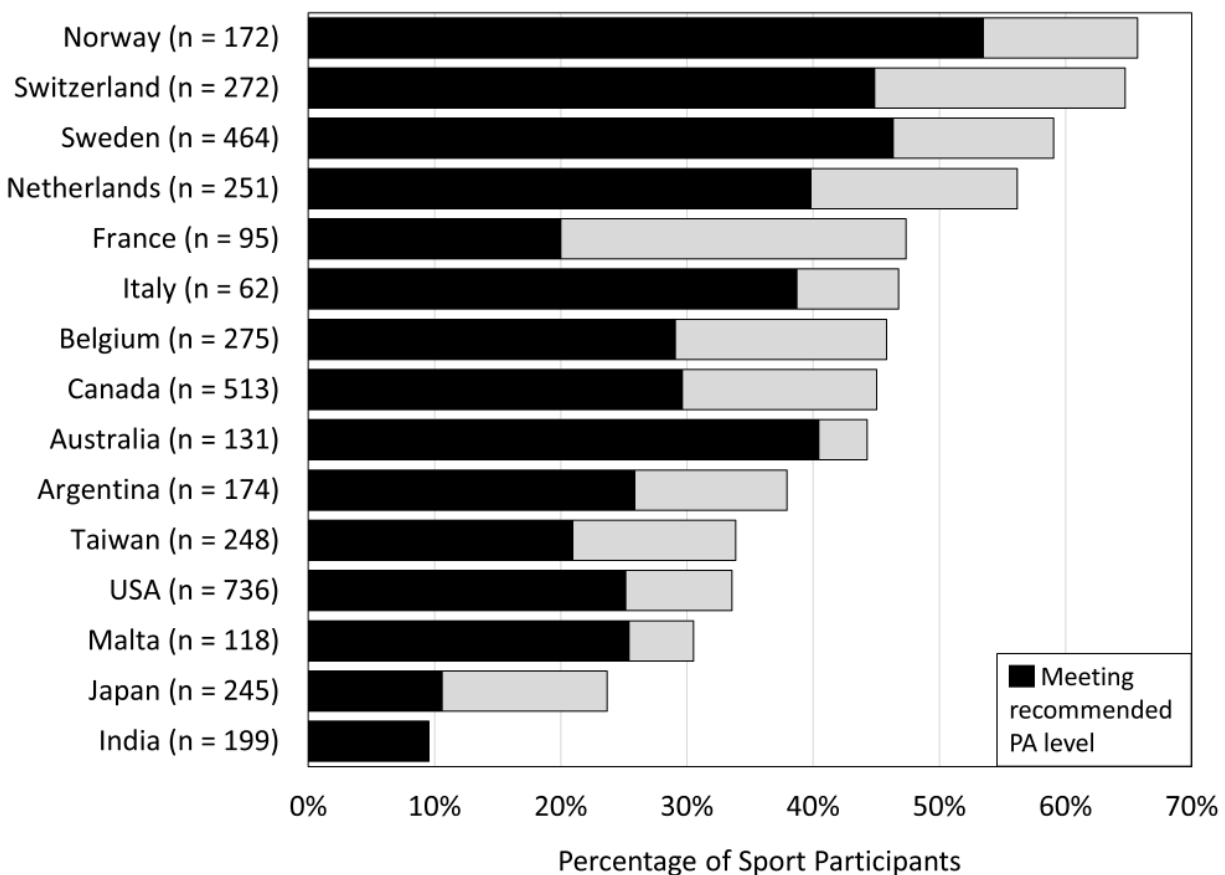


Table 1. Perceived health status in patients with a sedentary lifestyle versus patients who are physically active\* (Medians [quartile 1, quartile 3])

Perceived Health Status Measure	Sedentary (n=1,578) <sup>†</sup>	Physically Active (n=2,372) <sup>†</sup>	p-value
SF-12: PCS	77.5 [58.8, 90]	86.9 [71.3, 96.3]	<0.001
SF-12: MCS	71.9 [53.1, 84.4]	78.1 [65.6, 87.5]	<0.001
EQ-5D: LAS	80 [65, 90]	80 [75, 90]	<0.001

EQ-5D= EuroQol-5D 3 level version; LAS= linear analog scale; MCS= mental composite score; PCS= physical component score; SF-12= 12-item Short Form Health Survey – version 2

\*Physically active individuals were either active commuters or sport participants.

<sup>†</sup>The number of patients who completed both the physical activity and perceived health status questionnaires.

Table 2. The effect of physical activity on perceived health status

Model	SF-12		EQ-5D
	Physical Composite Score	Mental Composite Score	Linear Analog Scale
Active Commute (y/n)			
Percent of variability explained by the model	0.40%	0.14%	0.35%
Estimate (P-value) for active commute	2.3 (<0.001)	1.3 (0.04)	1.8 (0.001)
Active Commute (y/n) + country			
Percent of variability explained by the model	9%	5%	3%
Estimate (P-value) for active commute	2.6 (<0.001)	1.3 (0.04)	1.5 (0.006)
Active Commute (y/n) + country + partial adjustment*			
Percent of variability explained by the model	46%	21%	23%
Estimate (P-value) for active commute	1.3 (0.01)	0.95 (0.12)	0.96 (0.06)
Sport Participation(y/n)			
Percent of variability explained by the model	8%	4%	5%
Estimate (P-value) for sport participation	11.7 (<0.001)	7.6 (<0.001)	7.2 (<0.001)
Sport Participation (y/n) + country			
Percent of variability explained by the model	11%	6%	6%
Estimate (P-value) for sport participation	11.1 (<0.001)	7.3 (<0.001)	7.3 (<0.001)
Sport Participation (y/n) + country + partial adjustment*			
Percent of variability explained by the model	56%	26%	32%
Estimate (P-value) for sport participation	4.3 (<0.001)	3.4 (<0.001)	3.5 (<0.001)
Sport Participation (y/n) + country + full adjustment <sup>†</sup>			
Percent of variability explained by the model	60%	31%	35%
Estimate (P-value) for sport participation	3.5 (<0.001)	3.0 (<0.001)	3.2 (<0.001)

EQ-5D= EuroQol-5D 3 level version; SF-12= 12-item Short Form Health Survey – version 2

\*Covariates for partial adjustment were age, sex, employment, marital status, and NYHA class.

<sup>†</sup>Covariates for full adjustment for physical composite score model were age, sex, education level, employment status, spirituality, congestive heart failure, arrhythmia, other medical conditions, mood, anxiety, other psychiatric disorders, follow-up frequency, and NYHA class.

<sup>†</sup>Covariates for full adjustment for mental composite score model were age, sex, marital status, education level, spirituality, congenital heart defect complexity, mood, anxiety, other psychiatric disorders, number of surgeries, follow-up frequency, and NYHA class.

<sup>†</sup>Covariates for full adjustment for linear analog scale model were age, employment and marital status, education level, mood, anxiety, other psychiatric disorders, number of surgeries, other medical conditions, and NYHA class.

Supplemental Table 1. Relation of demographic, clinical, and psychological factors with active commute (for those who are students or employed)

Variable	Active Commute	No Active Commute	P-value
Age	29 [23, 38]	31 [25, 40]	<0.001
Sex (male)	550 (51%)	989 (50%)	0.51
Marital status			<0.001*
Unmarried / Never married	575 (53%)	850 (43%)	
Married or Living with partner	471 (43.7%)	1045 (52%)	
Divorced or Widowed	30 (4%)	100 (5%)	
Other	2 (<1%)	3 (<1%)	
Child(ren) present	319 (30%)	777 (39%)	<0.001
Education level			0.04
Less than high school	31 (3%)	67 (3%)	
High school	424 (39%)	805 (41%)	
College degree	224 (21%)	473 (24%)	
University degree	400 (37%)	643 (32%)	
Considered religious/spiritual	473 (45%)	969 (49%)	0.02
Complexity of CHD defect*			0.08
Simple	310 (29%)	501 (25%)	
Moderate	502 (46%)	994 (50%)	
Complex	272 (25%)	508 (25%)	
New York Heart Association Class			0.04
I	656 (61%)	1143 (58%)	
II	351 (33%)	694 (35%)	
III	40 (4%)	110 (6%)	
IV	21 (2%)	29 (2%)	
History of other medical conditions	365 (34%)	835 (42%)	<0.001
History of arrhythmia	231 (22%)	524 (26%)	0.003
Device implantation			0.95
None	829 (90%)	1615 (90%)	
ICD	33 (4%)	65 (4%)	
Pacemaker	59 (6%)	121 (7%)	
Number of cardiac surgeries	1 [1, 2]	1 [1, 2]	0.04
Frequency of follow-up	2 [2, 3]	2 [1, 3]	<0.001
Total adult cardiac admissions	0 [0, 1]	0 [0, 1]	0.15
Cognitive impairment	8 (1%)	21 (1%)	0.4
Chart-documented mood disorder	36 (3%)	112 (6%)	0.005
Chart-documented anxiety disorder	33 (3%)	91 (6%)	0.04
Chart-documented other psychiatric disorder	20 (2%)	29 (2%)	0.4

CHD=congenital heart disease; ICD=implantable cardioverter defibrillator

Supplemental Table 2. Relation of demographic, clinical, and psychological factors with sport participation

Variable	Sport	No Sport	P-value
Age	31 [24, 40]	32 [25, 43]	0.001
Sex (male)	868 (51%)	998 (44%)	<0.001
Marital status			<0.001
Unmarried / Never married	728 (43%)	1007 (45%)	
Married or Living with partner	894 (53%)	1107 (49%)	
Divorced or Widowed	71 (4%)	124 (6%)	
Other	3 (<1%)	3 (<1%)	
Child(ren) present	624 (37%)	918 (41%)	0.008
Education level			<0.001
Less than high school	50 (3%)	156 (7%)	
High school	664 (39%)	1020 (46%)	
College degree	334 (20%)	498 (20%)	
University degree	643 (38%)	551 (25%)	
Employment status			<0.001
Part time or full-time work	1189 (30%)	1339 (34%)	
Homemaker or Retired	85 (5%)	221 (10%)	
Unemployed or Disability	140 (8%)	356 (16%)	
Full-time student	151 (9%)	174 (8%)	
Other	128 (8%)	149 (7%)	
Considered religious/spiritual	744 (45%)	1156 (53%)	<0.001
Complexity of CHD defect*			<0.001
Simple	480 (28%)	542 (24%)	
Moderate	848 (50%)	1071 (48%)	
Complex	375 (22%)	639 (28%)	
New York Heart Association Class			<0.001
I	1086 (65%)	999 (46%)	
II	496 (30%)	854 (39%)	
III	68 (4%)	214 (10%)	
IV	22 (1%)	128 (6%)	
History of other medical conditions	639 (38%)	1054 (47%)	<0.001
History of arrhythmia	434 (26%)	641 (29%)	0.033
Device implantation			0.646
None	1276 (89%)	1804 (88%)	
ICD	59 (4%)	91 (4%)	
Pacemaker	101 (7%)	159 (8%)	
Number of surgeries	1 [1, 2]	1 [1, 2]	0.261
Frequency of follow-up	2 [2, 3]	2 [1, 2]	<0.001
Total adult cardiac admissions	0 [0, 1]	0 [0, 1]	<0.001
Cognitive impairment	15 (1%)	32 (1%)	0.117
Chart-documented mood disorder	70 (4%)	179 (8%)	<0.001
Chart-documented anxiety disorder	73 (4%)	114 (5%)	0.256
Chart-documented other psychiatric Disorder	23 (1%)	50 (2%)	0.045

CHD=congenital heart disease; ICD=implantable cardioverter defibrillator

\*A few examples of each lesion complexity type are as follows. Simple = atrial or ventricular septal defect, bicuspid aortic valve; Moderate = tetralogy of Fallot, Epstein anomaly; Complex = transposition of great vessels, single ventricle.



Supplemental Table 3. P-values of the association of physical activity type with perceived health measures

Country	Active Commute (Yes/No)			Sport Participation (Yes/No)		
	SF-12		EQ-5D	SF-12		EQ-5D
	PCS	MCS	LAS	PCS	MCS	LAS
Argentina	0.27	0.16	0.24	<0.01*	<0.01*	0.08
Australia	0.23	0.61	0.38	<0.01*	0.05	0.01*
Belgium	0.83	0.98	0.37	<0.01*	<0.01*	<0.01*
Canada	0.01*	0.01*	<0.01*	<0.01*	<0.01*	<0.01*
France	0.35	0.8	0.93	<0.01*	<0.01*	0.03*
India	0.37	0.09	0.84	0.01*	0.23	0.22
Italy	0.49	0.8	0.52	0.01*	0.65	0.25
Japan	0.05	0.15	0.29	<0.01*	0.24	0.03*
Malta	0.56	0.95	0.44	<0.01*	0.72	0.08
Norway	<0.01*	0.05	0.01*	<0.01*	0.01*	<0.01*
Sweden	0.03*	0.69	0.2	<0.01*	<0.01*	<0.01*
Switzerland	0.04*	0.03*	0.06	<0.01*	<0.01*	<0.01*
Taiwan	0.03*	0.03*	0.02*	0.02*	0.07	0.19
the Netherlands	<0.01*	0.03*	<0.01*	<0.01*	<0.01*	<0.01*
USA	0.18	0.23	0.95	<0.01*	<0.01*	<0.01*

EQ-5D= EuroQol-5D 3 level version; LAS= linear analog scale; MCS= mental composite score; PCS= physical component score; SF-12= 12-item Short Form Health Survey – version 2

\*P-value < 0.05 (P-values < 0.05 in all 3 perceived health status measures are highlighted.)

Supplemental Table 4. Correlation between energy expended during physical activity and perceived health measures  
(Correlation; P-value)

Country	Active Commute			Sport		
	SF-12		EQ-5D	SF-12		EQ-5D
	PCS	MCS	LAS	PCS	MCS	LAS
Argentina	0.179; 0.151	0.015; 0.906	0.086; 0.494	0.104; 0.411	-0.014; 0.915	0.068; 0.593
Australia	0.029; 0.848	0.204; 0.175	0.062; 0.685	0.02; 0.879	0.045; 0.739	0.132; 0.323
Belgium	0.157; 0.153	0.083; 0.455	0.099; 0.374	0.132; 0.141	0.078; 0.39	0.118; 0.189
Canada	0.013; 0.871	-0.04; 0.619	0.041; 0.621	0.211; 0.001*	0.193; 0.003*	0.205; 0.002*
France	0.059; 0.685	0.142; 0.325	0.084; 0.566	0.546; <0.001*	0.462; 0.001*	0.292; 0.054
India	-0.105; 0.368	-0.069; 0.558	-0.038; 0.75	0.164; 0.503	0.109; 0.656	0.43; 0.066
Italy	0.058; 0.758	0.171; 0.359	-0.057; 0.77	-0.024; 0.905	0.137; 0.487	0.138; 0.483
Japan	0.329; 0.011*	0.193; 0.139	-0.00; 1	0.042; 0.774	0.029; 0.843	-0.026; 0.858
Malta	-0.074; 0.629	0.118; 0.439	0.073; 0.644	-0.049; 0.775	0.121; 0.482	0.254; 0.147
Norway	-0.052; 0.696	-0.153; 0.252	-0.083; 0.534	0.188; 0.046*	0.015; 0.877	0.126; 0.185
Sweden	0.073; 0.307	0.141; 0.049	0.076; 0.291	0.134; 0.027	0.021; 0.737	0.086; 0.159
Switzerland	-0.092; 0.348	-0.082; 0.4	-0.097; 0.32	0.2; 0.008*	0.057; 0.451	0.176; 0.02*
Taiwan	-0.003; 0.972	0.007; 0.943	0.184; 0.058	0.043; 0.701	0.117; 0.289	0.045; 0.686
the Netherlands	0.182; 0.057	0.113; 0.241	0.17; 0.08	0.143; 0.087	0.176; 0.034*	0.095; 0.261
USA	-0.112; 0.214	-0.038; 0.678	-0.002; 0.982	0.266; <0.001*	0.207; 0.001*	0.215; <0.001*

EQ-5D= EuroQol-5D 3 level version; LAS= linear analog scale; MCS= mental composite score; PCS= physical component score; SF-12= 12-item Short Form Health Survey – version 2

\*P-value < 0.05