

# Congenital Heart Disease: Growth Evaluation and Sport Activity in a Paediatric Population

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## Research Article

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# Abstract

**Objective:** To understand the anthropometric changes in paediatric patients with CHD, to evaluate their status and to assess their sport activity frequency.

**Methods:** Of 535 children on follow up, we selected 368 Caucasian children (aged 2-18 years) with CHD, had at least one visit with measured weight and height, with no comorbidities that could influence growth. A total of 1690 complete anthropometric measurements were analyzed. Anthropometric z-scores were computed using formulae based on the LMS method according to Cacciari growth standards.

Underweight, overweight and obesity were defined using BMI percentile cut-offs. Sport activity was collected through a phone interview.

The CHD severity was classified as mild, moderate, severe, univentricular or unclassified.

**Results:** Significant increase with age was observed for weight z-score [ $\beta$  (95%CI): 0.03 (0.02,0.05) for one-unit of age] and BMI z-score [0.06 (0.03,0.08)] but not for height z-score. The percentage of underweight increased with disease severity, and the percentages of overweight and obese patients consequently decreased. The percentage of obesity in patients with mild CHD (5.9% [95%CI: 3.4,8.4]) was not significantly different from that in patients with moderate CHD (3.3% [1.5,5.0]), whereas it was lower in patients with severe CHD (0.4% [0.0,0.9]). No obese patients with univentricular heart defect was observed. Days spent in sport activities was equal to 1.9 [95%CI: 1.6,2.2] days/week, 1.9 [1.5,2.2], 1.4 [1.1,1.7] and 0.7 [0.1,1.3] in patients with mild, moderate, severe and univentricular CHD, respectively.

**Conclusions:** Children with mild and moderate CHD present a risk of becoming overweight or obese that could not be underestimated and on the other hand could be prevented or reduced promoting a healthy lifestyle.

## Summary

This study evaluates growth and physical activity practised by children affected by congenital heart disease in follow up at "Mother and Son Hospital" Verona, Italy.

### What is known ?

- Children affected by congenital heart disease are known to present a higher prevalence of underweight especially in early ages, on the other hand prevalence of overweight and obesity in these population is still matter of debate.

### What is new?

- A decline in the proportion of underweight children and an increase in the proportion of overweight children were observed with increased age.

Low levels of sport practice per week have been highlighted.

## Introduction

Congenital heart diseases (CHDs) are the most common congenital disorder [1] and may present with a wide and heterogeneous spectrum of signs and symptoms depending on the cardiac defect [2]. Because of significant progress in paediatric cardiology and cardiac surgery, an increasing number of children affected by CHD reach adult age [3]. Growth delay remains one of the most common medical issues faced by these children [4]. However, since an increasing number of individuals affected by CHD reach adult age, acquired cardiovascular risk factors like hypertension, smoking, type 2 diabetes, dyslipidaemia and obesity are becoming increasingly important. These conditions are well known and can also be found in adults with CHDs [5]. In adult CHD population, the main cause of death continues to be CHD related to heart failure [6], although comorbidities and additional cardiovascular risk factors still play a key role as determinants in mortality, especially in people who reach elderly ages [7]. The prevalence of obesity has been gradually increasing in children and adolescents worldwide [8]. Recent studies have confirmed a similar trend also in the CHD population [9, 10]. The recommendation to restrict physical activity together with the consumption of high calorie foods to make up for slow growth are factors that may increase the risk of overweight and obesity in children with CHD [9, 10]. Considering that physical inactivity and obesity in adults with CHD may exacerbate cardiovascular risks, measures to control excessive weight gain are a fundamental part of the care of patients with CHD [11].

The present study aimed to understand the anthropometric changes that occurred in Caucasian children with CHD in Italy, to estimate the proportion of overweight and obese patients and to assess the frequency of their sport activity.

## Materials And Methods

Recorded data referring to children diagnosed with CHD was collected from the electronic register of the outpatient clinic of Paediatric Cardiology at the Women & Children's University Hospital of Verona, Italy. Data from all the visits between December 2005 and October 2018 were available. For every patient, the following data was recorded at every visit to the clinic: sex, date of birth, ethnicity, height, weight, body mass index (BMI), severity of the disease, surgical procedures and comorbidities. Information on sport activity was collected through a phone interview with their parents or guardians at the end of the study. Informed consent was obtained from all parent/legal guardian.

The study was approved by our Ethics Committee and University of Verona, informed consent was obtained from all participants. The study has been designed without Patients involvement, none of the data presented in the study is linkable to a single patient.

All methods were carried out in accordance with relevant guidelines and regulations.

Of the 535 children who came to the clinic between 2005 and 2018, 402 Caucasian children (aged 2-18 years) were diagnosed with CHD and had at least one measurement with complete data for weight and height, thus being eligible for inclusion in our study cohort. Patients with comorbidities that could possibly influence their growth and development were excluded (**Table S1 in Supplementary materials**); also, we did not consider duplicated medical records (based on identification code, birthdate and measurement date) and measures showing a loss of height over time. In the end, a total of 368 children and 1690 complete anthropometric measurements (median [range]: 7 [1-21] per patient) were included in our analysis (**Figure 1**). Of these, 266 patients were reachable by phone.

## Definitions

The percentiles and z-scores for all three anthropometric indicators (weight, height and BMI) were computed using formulae based on the LMS method. Weight, height and BMI were converted into age and sex-based z-scores using the formula:  $Z = ((X/M)^L - 1) / (L * S)$ . LMS values were retrieved from the Cacciari standards for the central-north Italian population [12].

The cut-off points for overweight and obesity were set at the 75<sup>th</sup> and 95<sup>th</sup> percentiles of BMI-for-age and sex, respectively. Patients with a BMI lower than the 5<sup>th</sup> percentile were classified as underweight.

The severity of CHD was classified as mild (biventricular without any history of surgical intervention), moderate (biventricular with simple defects and a history of surgical interventions), severe (biventricular with complex defects and a history of surgical interventions), univentricular (history of single ventricle diagnoses or palliative surgery including Norwood, Glenn and Fontan) and unclassified. Simple and complex defects were defined according to the diagnosis hierarchy proposed by Erikssen et al. [13].

Frequency of sport activity was based on the question “How many days a week does the child exercise/participate in sport activities in the last year?” and it was collected through the phone interview.

## Statistical analysis

Two-level linear regression models [14] with measurement occasions (level 1 units) nested in patients (level 2 units) were used to estimate the anthropometric changes in children with CHD. Each model had a random intercept term at level 2, a random slope for age at level 2, an unstructured variance-covariance matrix of the random effects at level 2, a 1<sup>st</sup> order autoregressive error at level 1, and sex and age at clinical visit as fixed effects. The proportions of underweight, overweight and obese patients were estimated by using a two-level multinomial logistic regression model with random intercept term at level 2, an unstructured variance-covariance matrix of the random effects at level 2, and sex and age at clinical visit as fixed effects. The models were also estimated according to CHD severity, adding the severity variable and the indicator of post-first surgery/intervention to the fixed part of the models.

For patients who were reachable by phone at the end of the study, a Poisson regression model was used to estimate the expected number of days spent per week on sport activities, according to their CHD

severity. The model had CHD severity as the covariate, and the age at the time of the phone interview and sex as potential confounders.

In all models, age was included as a linear covariate since non-linear terms did not improve goodness-of-fit. Furthermore, the interaction terms between severity and age could not be evaluated due to sparseness of data.

The statistical analyses were carried out using STATA 15 (StataCorp, College Station, TX, USA) and R 3.6.3 (<http://www.R-project.org/>).

## Results

### Patient characteristics

Of the 368 patients (40.8% female) included in our analysis, the median age at first recording was 5 years (range: 2 to 14 years). Median follow-up was 5.2 years (range: 0.0-12.7 years), and 24.7% of our patients had only one recording of height and weight in the medical register. The distribution of CHD severity was: 143 (39.9%) mild, 97 (26.3%) moderate, 68 (18.5%) severe, 12 (3.3%) univentricular and 48 (13.0%) unclassified. At first recording, most of the children had normal BMI (58.2%), 24.7% were underweight and 17.1% were overweight or obese. On average, the 266 children (aged 7-18 years) who were reachable by phone spent less than two days a week doing sport activities in the last year. (**Table 1**)

### Anthropometric trends

In the regression model adjusted only for sex (*Model 1* in **Table 2, Figure 2**), an increase with age was observed for weight z-score [beta regression coefficient (95%CI): 0.03 (0.02, 0.05) for one-unit of age] and BMI z-score [0.06 (0.03, 0.08)] but not for height z-score. The strength of these associations did not change when the severity variable was added to the models (*Model 2* in **Table 2**). Levels of weight and BMI z-scores decreased with increasing severity of disease, whereas height z-score decreased statistically significantly only in children with a univentricular heart defect as compared to patients with mild CHD.

### Percentage of underweight, overweight and obesity

The expected percentages of underweight, overweight and obesity were 19.3% [95%CI: 16.9, 21.8], 14.7% [12.6, 16.9] and 3.0% [2.0, 3.9] of the total sample, respectively. The risk of underweight decreased with increasing age [relative risk ratio (RRR) (95%CI): 0.89 (0.84, 0.93) for 1 year], whereas the risk of obesity increased [1.27 (1.09, 1.49)] and that of overweight remained stable [1.03 (0.98, 1.08)] (**Figure 3**). Furthermore, the percentage of underweight patients increased with disease severity, and the percentages of overweight and obese patients consequently decreased (**Figure 4**). In fact, the percentage of underweight was statistically significantly higher in patients with univentricular heart defect (37.3% [95%CI: 19.7, 54.9]) and severe CHD (25.2% [95%CI: 19.3, 31.0]), as compared to patients with mild CHD (12.3% [95%CI: 8.7, 15.8]). Instead, it was statistically indistinguishable between patients with moderate (18.5% [95%CI: 14.0, 22.9]) and those with mild CHD. In addition, we found no difference in overweight

percentages between patients with mild (19.9% [95%CI: 15.3, 24.5]), moderate (16.3% [95%CI: 12.1, 20.5]) and severe (11.0% [95%CI: 7.4, 14.5]) CHD, but it was lower in patients with univentricular heart defect (1.1% [95%CI: 0.0, 3.4]). Finally, the percentage of obesity in patients with mild CHD (5.9% [95%CI: 3.4, 8.4]) was not statistically indistinguishable from that in patients with moderate CHD (3.3% [95%CI: 1.5, 5.0]). It was lower in patients with severe CHD (0.4% [95%CI: 0.0, 0.9]) compared to patients with mild CHD. No obese patients were observed among those affected by univentricular heart defect.

### **Sport activity**

Among the 266 patients who were reachable by phone (72.3% of total), patients with moderate or severe CHD reported a number of days spent in sport activities (mean [95%CI]: 1.9 [1.5, 2.2] days/week and 1.4 [1.1, 1.7], respectively) that was not statistically different from those with mild CHD (1.9 [1.6, 2.2]). On the other hand, patients with univentricular heart defect reported spending fewer days in sport activities (0.7 [0.1, 1.3]) than patients with mild or moderate CHD (**Figure 5**).

## **Discussion**

In the present study, we evaluated the changes in anthropometric measurements with age and disease severity in Caucasian children with a diagnosis of CHD, using data retrospectively collected from the hospital register in Verona, Italy. Furthermore, we evaluated the weight status (underweight, overweight and obesity) of children and the frequency of their sport activity. To the best of our knowledge, there are no previous longitudinal studies on this in a pediatric population with CHD in Italy.

### **Anthropometric trends**

In order to obtain weight and BMI z-scores, we used the Italian growth curve [12], which are similar to those of the WHO and are more representative of the country where patients live. We found that weight and BMI z-scores increased with increasing age in our pediatric patients with CHD, whereas height z-score did not change. These results are in line with a previous study that suggest a trend toward increasing adiposity over time[15]. In addition, we found an inverse relationship between anthropometric indicators and CHD severity. In fact, our patients with mild CHD had statistically significantly lower BMI and weight z-scores compared to patients with moderate CHD or univentricular heart defect. This supports a previous study that pointed out that cardiac surgery, when performed during early childhood, could have a remarkable impact on physical growth [16].

### **Proportion of underweight, overweight and obesity over time**

The prevalence of obesity has been steadily increasing over the past decades [8] and the trend is similar in patients with CHD (9, 10, 15). Recent studies using the American dataset [9] and the Canadian CHD registry [17] found no difference in overweight and obesity rates between CHD and non-CHD paediatric populations. In a recent cohort study, the rates of metabolic syndrome were similar between adults with CHD and healthy control subjects [18].

As reported in previous studies, at early age, a high proportion of patients are characterized by underweight that decreases substantially with age [10, 16] and they become overweight/obese at around the age of 10. This BMI shift from underweight to overweight and obesity was firstly reported in Asian children and adolescent patients [20]. The high proportion of underweight in our patients with the most severe disease status is presumably due to chronic long-term issues like heart failure and failure to thrive that often affect patients with univentricular heart defect [21]. Seventeen-point one percent of our sample were overweight or obese, whereas in Italy the overall prevalence of obesity is 17.0% and the overall prevalence of overweight, including obesity, is 39.4% [22]. Although the population of our study presented overall better rates of overweight and obesity compared to national and international rates, our purpose and advice is to strictly monitoring the emergence of these risk factors [19, 22]. Indeed, in patients with heart disease, overweight and obesity in pediatric age increase the risk of morbidity/mortality and comorbidities, particularly in the cases of cardiac surgery or other interventions [15, 23].

### Sport activities

A recent review by Caterini et al. reports as up to 38% of patients experience some level of restriction by their cardiologists, and 70% of caregivers report that their child's activity is restricted [19]. However, most patients with CHD are relatively sedentary even when they are not limited by their physiology or when no exercise restrictions have been imposed by their cardiologists [21].

The repercussions of leading a sedentary life are an increased risk of overweight and obesity and related comorbidities, even after cardiac repair [21]. In adult with CHD, low exercise capacity is associated with an increased risk of hospitalization and death [19].

In our study, we chose to investigate children' sport activity and exercise rather than their normal everyday physical activity because of the difficulty involved in assessing how much a child moves physically during the week. Even though physical activity and practicing a sport are not the same thing, they have been proved to be closely related [23]. Indeed, patients who exercise more are normally more active in general and less prone to lead a sedentary life.

In line with previous studies [24], our patients reported low levels of daily sport activity, which decreased in patients with more severe cardiac defects. In fact, patients with a biventricular complex defect and a history of surgical interventions spent less than 1.5 days per week in sport activities, even though tetralogy of Fallot and transposition of the great arteries defects do not involve any limitations to moderate activity [25, 26]. Patients with univentricular heart defect (for instance, those who had been palliated with a Glenn and/or Fontan procedure) were physically active less than one day a week. The attitude towards sport activity of children with moderate CHD did not differ from that of children with mild severity - around 2 days of activity per week. These results are daunting considering the physical and psychosocial health benefits of an active lifestyle. Active children with CHD develop better motor capacity [27], have a higher quality of life [28], greater self-esteem [29], and have a lower risk of becoming overweight or obese [30].



Accordingly, the American Heart Association has encouraged daily participation in appropriate physical activity for all patients with CHD, with the exception of patients with rhythm disorders and the avoidance of contact sport in patients with anticoagulation therapy [31]. At least 60 minutes of physical activity per day are recommended for children; vigorous activities are recommended at least 3 days a week [31]. Furthermore, the 36<sup>th</sup> Bethesda Conference and the Association of European Pediatric Cardiology asserted that children with univentricular heart defect, after a complete diagnostic evaluation, can participate in low-intensity competitive sports like bowling and golf and, if the ventricular function lies within normal range, sports like table tennis and volleyball [25, 26]. In Italy, the Cardiological Organizing Committee for Sport Suitability allows moderate to vigorous physical activities after an extensive cardiological evaluation (including cardiac ultrasound, ECG, ergometric test and even cardiac MRI) [32]. In spite of all these recommendations, practitioners are often reluctant to encourage an active lifestyle for children with CHD because they may not have extensive knowledge about cardiac effects and risks related to sport activity [32]. Furthermore, physical activity restrictions may sometimes be self-imposed or initiated by anxious parents [24] due to conflicting or incomplete information they get from practitioners [33]. In addition, sociocultural factors can affect physical activity levels. In fact, bullying by peers and a lack of understanding by teachers are not uncommon for children with CHD [33].

According to the literature [19,34], given the low levels of sport practice observed in our population, this study support the need for the implementation of physical activity and exercise in common clinical practice approaching exercise prescription the same way medical therapy is approached.

### **Study limitations**

This is a retrospective medical record study. Therefore, the data collection has not been standardized and nor were measurements filed at regular intervals of time. In addition, the use of medications and the socioeconomic status, which may influence body composition, were not available. Finally, when interpreting our results, it should be noted that the patients studied were from a single centre. Despite these limitations, to our knowledge, this is the largest pediatric population with CHD that has undergone a longitudinal evaluation in Italy.

### **Conclusion**

Underweight remains one of the major problems in pediatric patients diagnosed with CHD, especially at young ages; but the risk of becoming overweight and obese should not be underrated. In fact, patients tend toward increasing adiposity with increased age, most likely because their physical activity levels are lower than those of national and international recommendations. Our patients with mild and moderate defects were the majority with overweight and obesity, although their participation in appropriate physical activity is recommended. Therefore, our study stresses that promoting a healthy lifestyle is necessary to prevent the onset of obesity and overweight, especially in children with mild or moderate heart defects. These results should be taken into account when planning and setting up counselling programmes to promote better nutrition and physical activities for CHD paediatric patients and their families.

# Abbreviations

95%CI

95% credibility interval

BMI

Body mass index

CHD

Congenital heart disease

RRR

Relative risk ratio

# Declarations

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**Conflicts of Interest:** The authors have no conflicts of interest relevant to this article to disclose.

**Availability of data and material:** All data are available upon request

**Code availability:** N/A

## Authors' contributions:

Study conception and design: Maria Antonia Prioli, Angelo Pietrobelli, Thomas Zoller, Maria Clemente, Lucia Calciano.

Acquisition of data: Maria Antonia Prioli, Thomas Zoller, Maria Clemente, Maria Pilati, Camilla Sandrini.

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Interpretation of data: Angelo Pietrobelli, Thomas Zoller, Maria Clemente, Maria Antonia Prioli, Marco Deganello Saccomani.

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**Ethics approval:** The study was approved by our Ethics Committee and University of Verona, informed consent was obtained from all participants.

**Consent to participate and publication:** The study has been designed without Patients involvement, none of the data presented in the study is linkable to a single patient. Informed consent was obtained from all parent/legal guardian.

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## Tables

**Table 1.** Main characteristics of patients included in the analysis

	N = 368
Sex (female), %	40.8
Age at first recording (years), median (range)	5 (2-14)
Age at last measurement (years), median (range)	10 (2-18)
Duration of follow-up (years), median (range)	5.2 (0.0-12.7)
Number of measurements per patient, median (range)	7 (1-21)
Patients with only one recording of height and weight, %	24.7
CHD severity, %	
mild	38.9
moderate	26.3
severe	18.5
univentricular	3.3
not classified	13.0
Number of surgical interventions, median (range)	0 (0-4)
Height at first recording (centimeters), mean $\pm$ sd	110.5 $\pm$ 18.8
Height z-score at first recording, mean $\pm$ sd	0.1 $\pm$ 1.2
Weight at first recording (kilograms), mean $\pm$ sd	20.2 $\pm$ 9.6
Weight z-score at first recording, mean $\pm$ sd	-0.5 $\pm$ 1.2
Body-mass index at first recording, mean $\pm$ sd	15.7 $\pm$ 2.5
Body-mass index z-score at first recording, mean $\pm$ sd	-0.8 $\pm$ 1.9
BMI category at first recording, %	
Underweight	24.7
Normal	58.2
Overweight	15.2
Obese	1.9
Age at end of the study (years) *, median (range)	12 (7-18)
CHD severity*, %	
mild	34.6
moderate	28.2

severe	20.3
univentricular	2.6
not classified	14.3
Number of days spent per week in sports activities*, mean $\pm$ sd	1.7 $\pm$ 1.3

sd: standard deviation; \*of 266 patients who were reachable by phone at the end of the study.

**Table 2:** Estimated change in height, weight and BMI z-scores

		Height z-score	Weight z-score	BMI z-score
Variables of interest		beta (95%CI)	beta (95%CI)	beta (95%CI)
<b>Model 1*</b>	Age (years)	0.00 (-0.01, 0.01)	<b>0.03 (0.02, 0.05)</b>	<b>0.06 (0.03, 0.08)</b>
<b>Model 2*</b>	Age (years)	0.00 (-0.01, 0.02)	<b>0.03 (0.01, 0.04)</b>	<b>0.05 (0.02, 0.08)</b>
Severity (vs mild)				
	moderate	-0.13 (-0.49, 0.23)	<b>-0.52 (-0.86, -0.17)</b>	<b>-0.88 (-1.41, -0.36)</b>
	severe	-0.19 (-0.58, 0.20)	<b>-0.70 (-1.08, -0.32)</b>	<b>-1.12 (-1.67, -0.57)</b>
	univentricular	<b>-1.13 (-1.81, -0.45)</b>	<b>-1.85 (-2.5, -1.16)</b>	<b>-1.73 (-2.60, -0.86)</b>
	not classified	-0.07 (-0.41, 0.27)	-0.04 (-0.39, 0.32)	-0.12 (-0.51, 0.28)

CI: confidence interval.

\*Model 1: adjusted for sex. Model 2: adjusted for sex and the indicator of post-first surgery/intervention

The estimates in bold are statistically significant (p-value <0.05).

## Figures

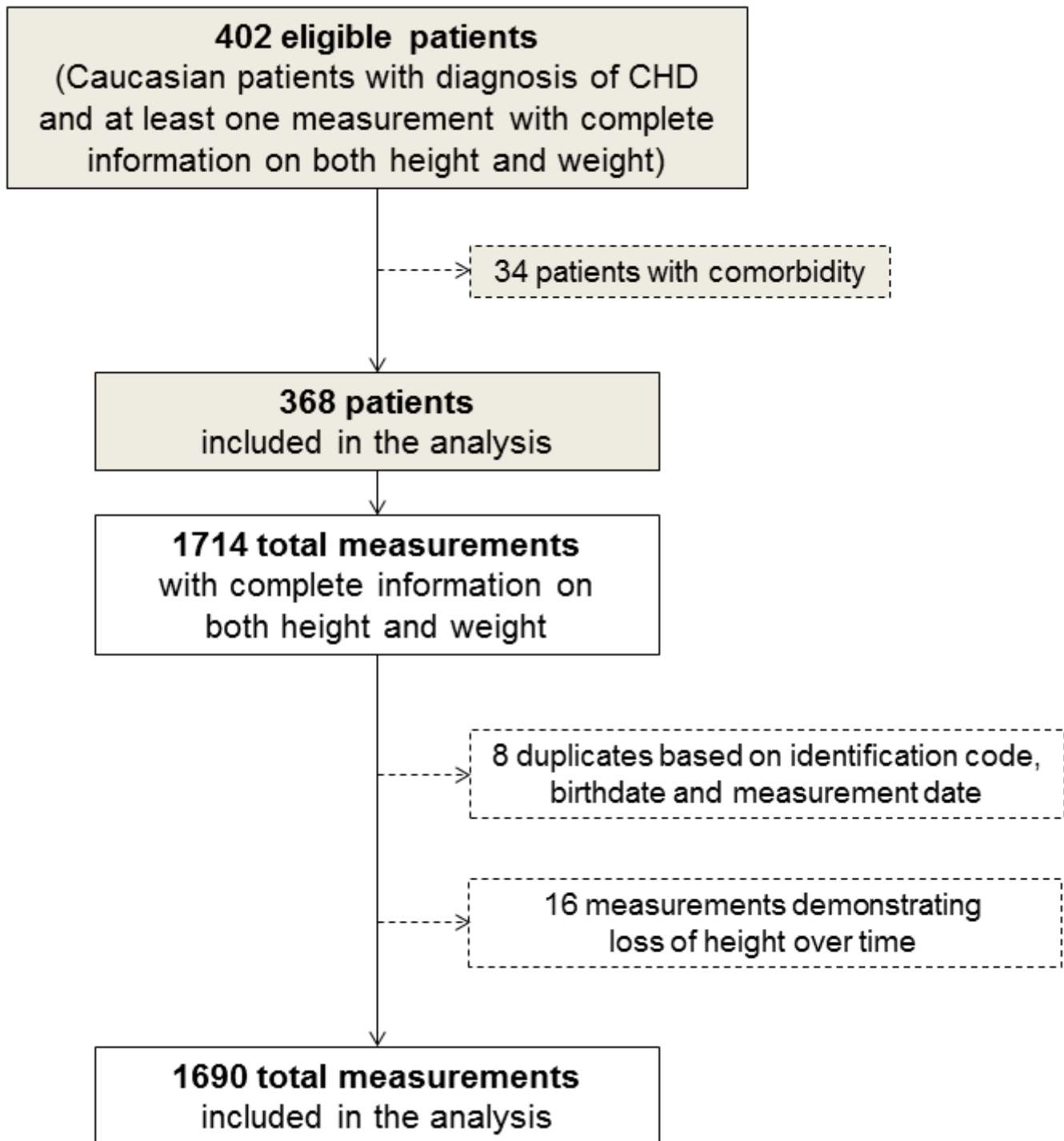
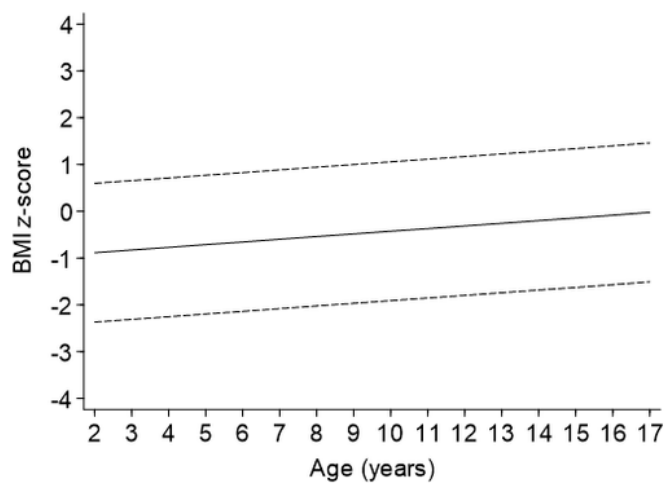
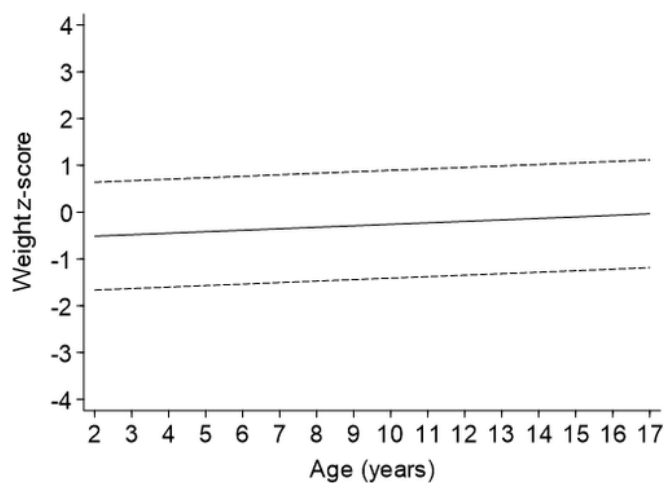
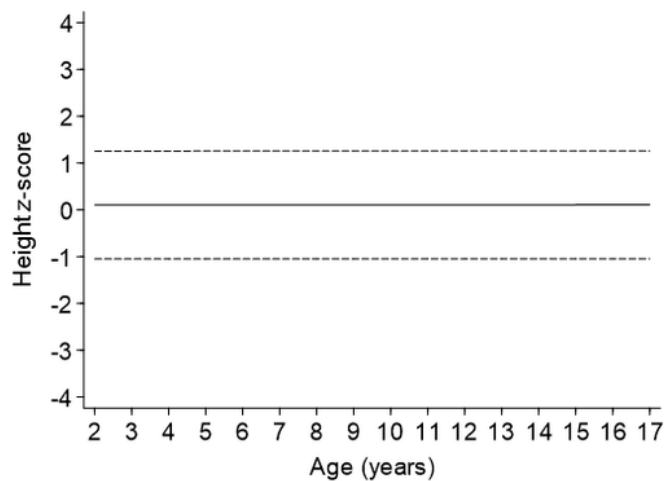


Figure 1

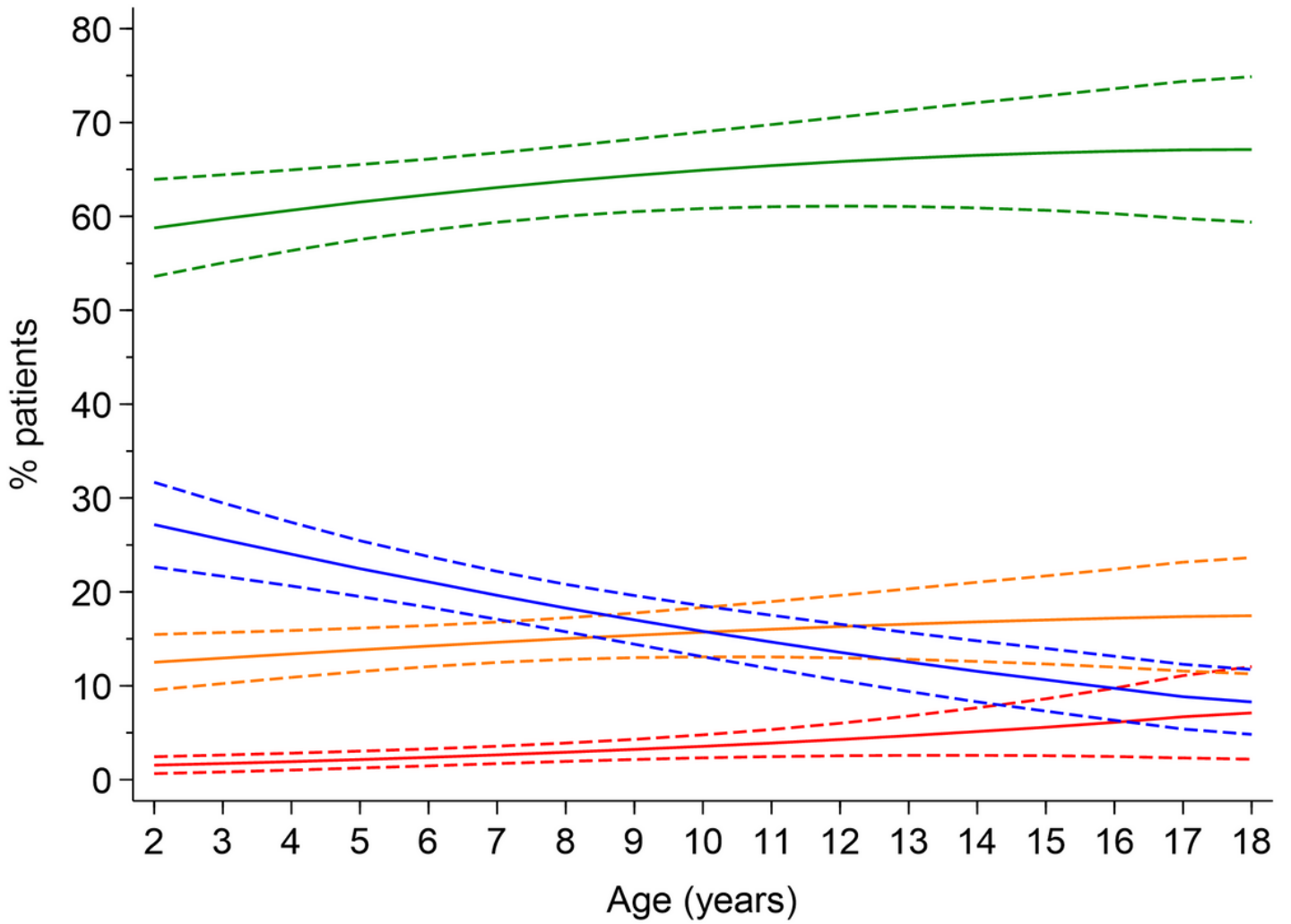
Flow chart of patient selection.





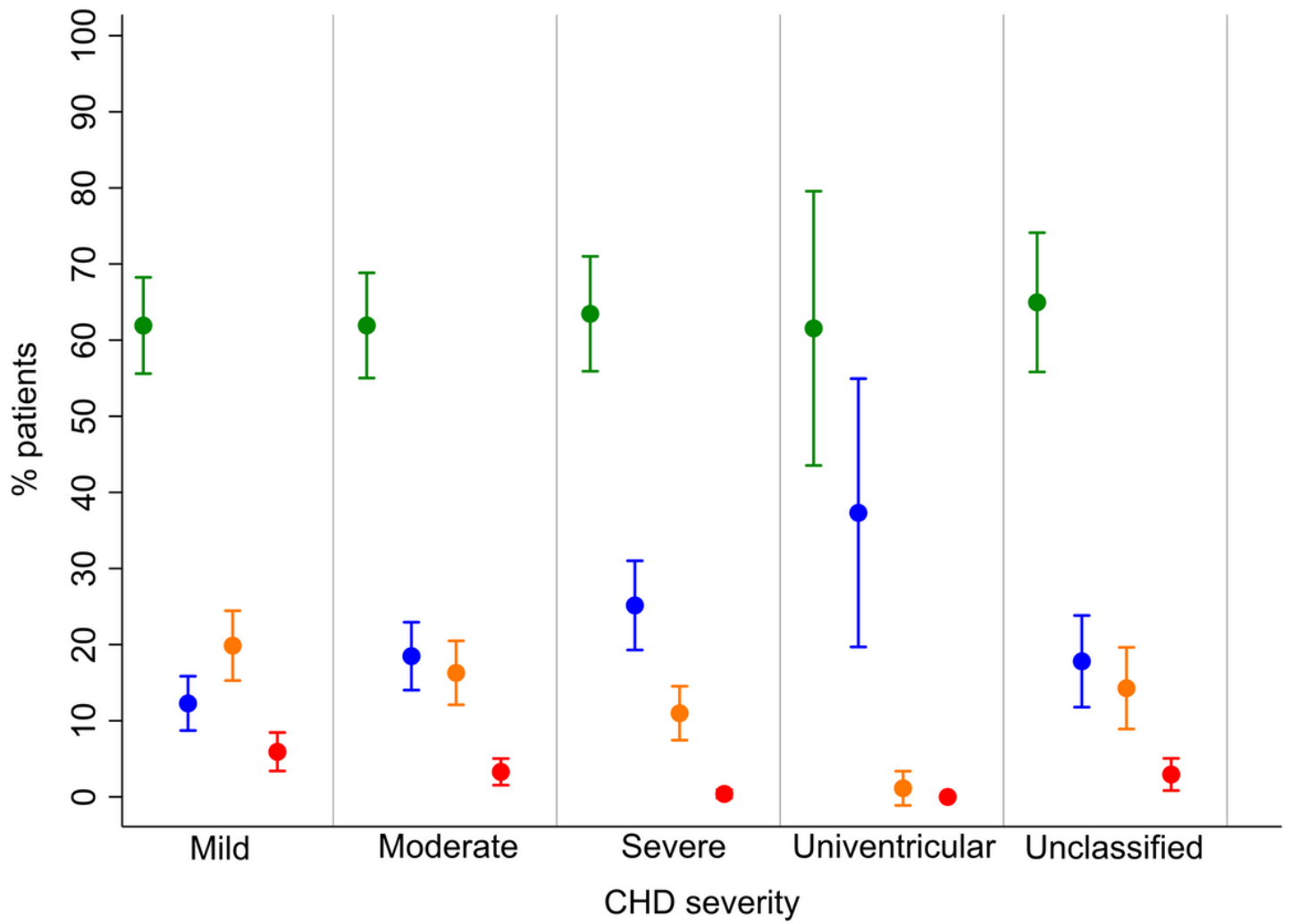
**Figure 2**

Change in height z-score, weight z-score and BMI z-score with age.



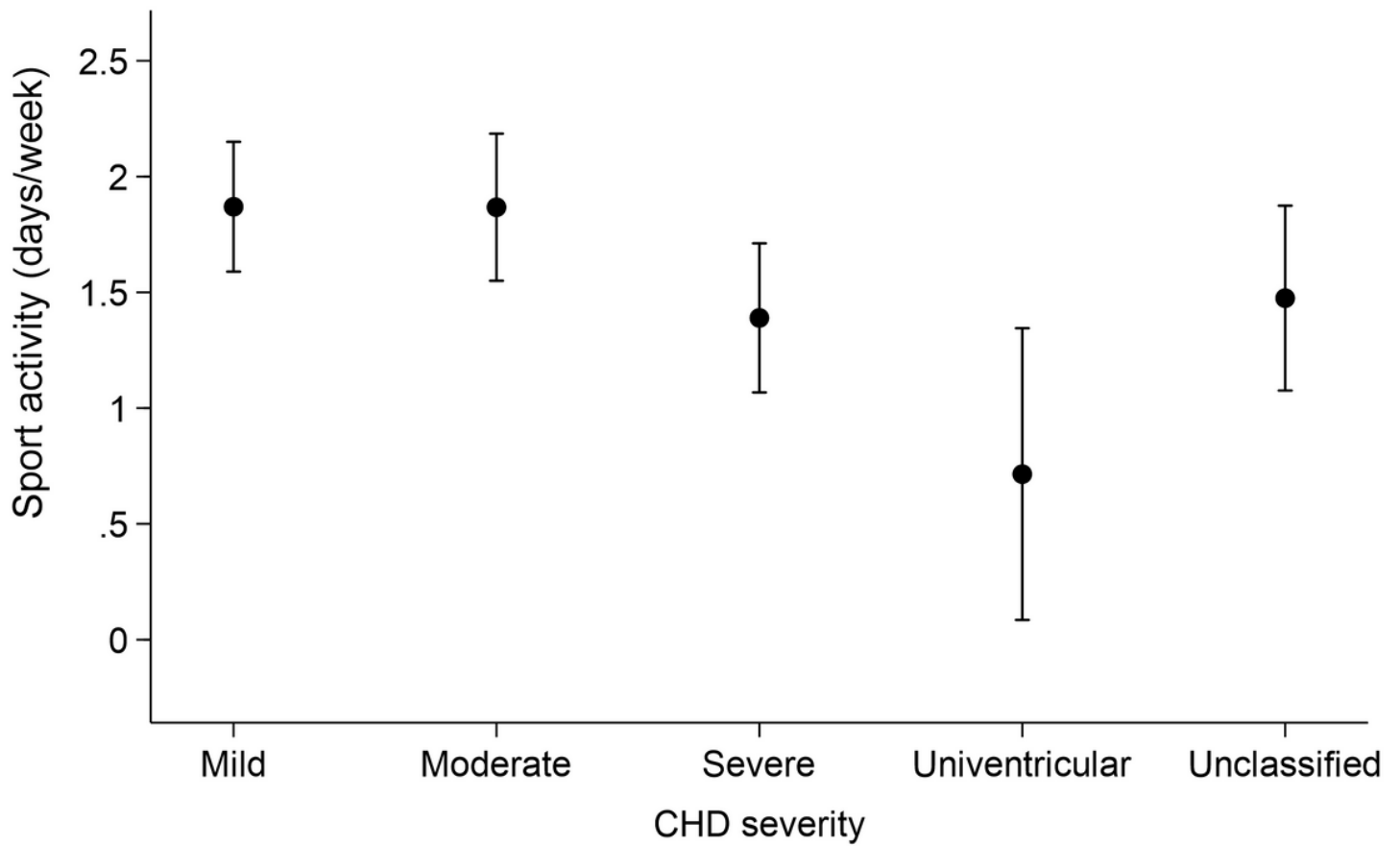
**Figure 3**

Change in expected proportion of underweight (blue), normal (green), overweight (orange) and obese (red) children with age.



**Figure 4**

Expected proportion of underweight (blue), normal (green), overweight (orange) and obese (red) according to CHD severity.



**Figure 5**

Expected number of days spent per week on sports activities in the last year according to severity in the 266 patients who were contactable by phone at the end of the study.

## Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [2.Supplementary.doc](#)