Original Article

The role of fitness in the association between fatness and cardiometabolic risk from childhood to adolescence


Background: Fatness and fitness both influence cardiometabolic risk. Objective: The purpose of this study was to investigate whether childhood fatness and increasing fatness from childhood to adolescence are associated with cardiometabolic risk during adolescence and how fitness affects this association.

Subjects and methods: Of 565 adolescents (283 boys and 282 girls) from the TRacking Adolescents Individual Life Survey (TRAILS) data on anthropometric parameters (age 11 and 16), metabolic parameters, and fitness (age 16) were available. Body mass index and skinfolds were used as measures for fatness. Increasing fatness was calculated by subtracting Z-scores for fatness at age 11 from Z-score fatness at age 16. Cardiometabolic risk was calculated as the average of the standardized means of mean arterial pressure, fasting serum triglycerides, high-density lipoprotein-cholesterol, glucose, and waist circumference. Insulin resistance was calculated by homeostasis model assessment-insulin resistance (HOMA-IR). Fitness was estimated as maximal oxygen consumption (VO2max) during a shuttle run test.

Results: Boys showed a higher clustered cardiometabolic risk when compared to girls (p < 0.01). Childhood fatness (age 11) and increasing fatness were independently associated with cardiometabolic risk during adolescence. In boys, high fitness was related to a reduced effect of increasing fatness on clustered cardiometabolic risk. Childhood fatness, increasing fatness, and fitness were independently associated with HOMA-IR. Moreover, in boys this association was dependent of fatness.

Conclusions: Childhood fatness and increasing fatness are associated with increased cardiometabolic risk and HOMA-IR during adolescence, but a good fitness attenuates this association especially in fat boys.

According to the World Health Organization, 4.9–22.5% of European boys are overweight and 2.4–0.3% are obese. In girls, overweight ranges from 6.9 to 19.9% and obesity from 2.0 to 12.3% (1). In children, overweight is of clinical interest because of its association with metabolic risk factors for cardiovascular disease, such as hyperlipidemia, hypertension (2, 3), hyperglycemia, and insulin resistance (4). Studies on tracking overweight report an increased risk of overweight and obese youth becoming overweight adults (5) and therefore childhood overweight has significant long-term consequences (6).

Several studies have shown that, in adults, higher cardio respiratory fitness attenuates cardiometabolic risk.
risk (7, 8). Especially among those with obesity, fitness attenuates cardiometabolic risk. This finding generated the ‘fat but fit’ paradigm which states that fat but fit people have healthier cardiometabolic outcomes than fat but unfit people, and are sometimes even as healthy as unfit but not fat people. Cross-sectional studies on children and adolescents have also reported that among children and adolescents with high fatness, high fitness is related to decreased cardiometabolic risk (9).

The influence of childhood fatness, and in particular the changes in fatness on cardiometabolic risk and how fitness effects this association has not been studied in depth. Therefore, the aim of this study was to investigate whether childhood fatness and increasing fatness from childhood to adolescence are associated with cardiometabolic risk during adolescence and how fitness affects this association.

Methods

Subjects

Data was collected as part of the ‘TRacking Adolescents’ Individual Lives Survey’ (TRAILS) (10). TRAILS is a prospective cohort study in healthy Dutch children who have been followed from age 11 into adolescence. TRAILS participants were selected from five municipalities in the North of The Netherlands. This study involves data from the first (mean age 11.4 yr, SD = 0.56) and third (mean age 16.1 yr, SD = 0.5) examination which ran from March 2001 to July 2002 and from September 2005 to December 2007, respectively. The initial TRAILS population consisted a total of 2230 children. Biochemical data and fitness were only measured in the third examination. For financial and practical reasons, schools were selected at random to participate in the collection of biochemical measures and/or fitness test. For this study 1665 children were excluded because no data were available on biochemical measures or fitness measures or children suffered from physical complaints which interfered with measurement of fitness (knee injuries). The final sample size included 565 children (283 boys and 282 girls). The study protocol was approved by the National Dutch Medical Ethics Committee on research involving human subjects. Written informed consent was obtained from the children and the children’s parents or custodians.

Measures of fatness and associated metabolic factors

Height, weight, waist circumference, and skinfolds were measured at school after removing shoes and heavy clothing. Weight was measured in kilograms using a calibrated analogue Seca balance scale (Model 770; SECA Corp., Hamburg, Germany). Height was measured in centimeters using a Seca stadiometer (model 214; SECA Corp.). Waist circumference was measured in centimeters taken midway between the lowest rib and the iliac crest. Four skinfolds (triceps, biceps, subscapular, and suprailiac) were measured by trained study personnel using standardized protocols and calibrated equipment, i.e., a Harpenden skinfold caliper (CMS instruments, London, UK). Glucose, insulin, triglycerides, total cholesterol, high- and low-density lipoprotein-cholesterol (HDL-C) were determined from a fasting blood sample according to standard laboratory procedures. Low-density lipoprotein-cholesterol was calculated according to Friedwald’s equation (11). Insulin resistance was calculated as homeostasis model assessment-insulin resistance (HOMA-IR) using the following equation: (\( \text{insulin} \times \text{glucose} \))/22.5 (12).

Resting diastolic blood pressure (DBP) and systolic blood pressure (SBP) were measured using Dinamap Critikon® 1846SX (Critikon® inc., Tampa, FL, USA) on the right arm in a horizontal resting position. Mean arterial pressure (MAP) was calculated as: DBP + [1/3 \times (SBP − DBP)].

Clustered cardiometabolic risk score

A continuous variable was calculated for the clustered cardiometabolic risk. Waist circumference, fasting glucose, triglycerides, MAP, and HDL-C were transformed into Z-score and added. The metabolic risk score was calculated as the sum for the five Z-scores divided by 5. Thereby triglycerides were Ln-transformed to obtain a normal distribution and HDL-C was inverted. In the same manner a clustered metabolic Z-score was obtained with the exclusion of waist circumference.

Cardio respiratory fitness

A 20-m shuttle run test was used as an objective and validated measurement to assess fitness (13). Participants had to run back and forth on a 20-m course and pivot on the 20-m line, while keeping pace with audio signals emitted from a pre-recorded compact disc. The initial speed was 8 km/h and the speed increased by 0.5 km/h every minute. In a subsample of 272 (48.1%) participants, heart rate (HR) monitoring was performed using Polar Team System series 1 (Polar, Kempele, Finland). In this group, an extra criterion for maximum exertion was applied as a HR above 185 beats/min. Performance on the test, measured by VO\(_2\)max, did not differ between participants wearing a HR monitor and participants who did.
not \((46.3 \pm 7.4 \text{ mL/min/kg; } 46.3 \pm 6.8 \text{ mL/min/kg;}\ p = 0.212, \text{ respectively})\). The estimated VO\(_2\)max was calculated using the following equation: \(\text{VO}_2\text{max} = 31.025 + (3.238 \times \text{speed}) - (3.248 \times \text{age}) + 0.1536 \times (\text{speed} \times \text{age})\). (14).

Pubertal stage

The stage of pubertal development at age 11 yr was assessed by parent ratings using schematic drawings of secondary sex characteristics associated with the five Tanner stages (15, 16). At age 16 yr, the Pubertal Development Scale (PDS) questionnaire (17) was used to assess pubertal development filled in by the adolescents themselves. The PDS questionnaire was recorded into five stages comparable to the Tanner stages (18).

Statistics

Data were analyzed using spss 18.0. Boys and girls were analyzed separately due to complex interactions between pubertal stage, fatness, CRF, and cardiometabolic risk that were related to gender differences. Triglycerides, insulin, and HOMA-IR were Ln-transformed because of lack of normality. A two-tailed Student’s t-test was used to test for gender differences or Fisher’s exact test in case of categorical data. Increasing fatness was calculated by subtracting Z-scores for fatness [body mass index (BMI) and skinfolds] at age 11 from Z-score fatness at age 16. The associations between childhood fatness, increasing fatness and fitness, and cardiometabolic outcomes during adolescence were studied by Pearson correlations. Regression analysis was performed to identify the independent contribution of fatness, increasing fatness and fitness to the clustered cardiometabolic risk score, and HOMA-IR. Children were categorized into four groups based on the increasing fatness. Two groups were created for children with negative scores (\(\Delta\text{BMI} 1 < -1\) and \(\Delta\text{BMI} 2\) between \(-1\) and \(0\)), which means that those children gained the least weight; two groups were created for children with positive scores (\(\Delta\text{BMI} 4 > 1\) and \(\Delta\text{BMI} 3\) between \(0\) and \(1\)), which means that those children gained the most weight. In model 1, we evaluated the association between childhood fatness (age 11) and the clustered cardiometabolic risk score in adolescence, adjusted for age and study location, Tanner stage (age 11), and pubertal development stage (age 16). In model 2, increasing fatness was added to test its relation with the clustered cardiometabolic risk score. In model 3, fitness was added to evaluate its contribution independent of fatness and increasing fatness. In the final model, model 4, an interaction between fitness and increasing fatness was added.
Table 1. Descriptive characteristics of Dutch adolescents in the TRAILS cohort

<table>
<thead>
<tr>
<th>Boys (N = 283)</th>
<th>Girls (N = 282)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age 11</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>11.1 ± 0.5</td>
<td>11.0 ± 0.6</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>17.6 ± 2.4</td>
<td>17.6 ± 2.4</td>
</tr>
<tr>
<td>Sum of skinfolds (cm)</td>
<td>38.8 ± 16.8</td>
<td>43.8 ± 16.3</td>
</tr>
<tr>
<td>Pubertal stage (%)</td>
<td>31.1, 65.0, 3.9, 0, 0</td>
<td>35.8, 41.5, 17.4, 5.0, 0.4</td>
</tr>
<tr>
<td><strong>Age 16</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>16.1 ± 0.5</td>
<td>16.0 ± 0.5</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>20.7 ± 2.7</td>
<td>21.1 ± 2.5</td>
</tr>
<tr>
<td>Sum of skinfolds (cm)</td>
<td>38.3 ± 19.6</td>
<td>57.1 ± 17.0</td>
</tr>
<tr>
<td>Pubertal stage (%)</td>
<td>0.7, 1.4, 33.2, 64.7, 0</td>
<td>0.3, 3.5, 75.9, 20.6</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>74.4 ± 7.3</td>
<td>74.0 ± 6.5</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>59.7 ± 6.4</td>
<td>61.5 ± 6.9</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>121.4 ± 12.0</td>
<td>113.4 ± 10.2</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>80.2 ± 6.9</td>
<td>78.8 ± 7.1</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>2.16 ± 0.61</td>
<td>2.33 ± 0.61</td>
</tr>
<tr>
<td>HDL-C (mmol/L)</td>
<td>1.40 ± 0.29</td>
<td>1.54 ± 0.31</td>
</tr>
<tr>
<td>Total-C (mmol/L)</td>
<td>3.62 ± 0.67</td>
<td>3.93 ± 0.68</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>0.70 (0.53, 0.87)</td>
<td>0.61 (0.48, 0.88)</td>
</tr>
<tr>
<td>Glucose (mmol/L)</td>
<td>4.60 ± 0.42</td>
<td>4.48 ± 0.46</td>
</tr>
<tr>
<td>Insulin (mU/L)</td>
<td>11.8 (8.6, 15.0)</td>
<td>12.25 (9.6, 16.0)</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.35 (1.06, 3.07)</td>
<td>2.48 (1.90, 3.15)</td>
</tr>
<tr>
<td>Clumped cardiometabolic risk</td>
<td>0.08 ± 0.57</td>
<td>−0.08 ± 0.50</td>
</tr>
<tr>
<td>Clumped cardiometabolic risk without waist</td>
<td>0.09 ± 0.59</td>
<td>−0.09 ± 0.54</td>
</tr>
<tr>
<td>VO₂max (mL/min/kg)</td>
<td>50.3 ± 6.4</td>
<td>42.3 ± 5.2</td>
</tr>
</tbody>
</table>

BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein-cholesterol; HOMA-IR, homeostasis model assessment-insulin resistance; LDL-C, low-density lipoprotein-cholesterol; MAP, mean arterial pressure; SBP, systolic blood pressure; TRAILS, TRacking Adolescents Individual Life Survey.

Data are presented as means ± SD. Ln-transformed data are presented as median (25th–75th percentile). Tanner stage and pubertal stage are presented as % in phase 1–5 (prepubertal, early pubertal, mid-pubertal, late pubertal, and postpubertal, respectively). Clustered cardiometabolic risk is presented as a Z-score with average = 0 and SD = 1. A two-tailed Student’s t-test for independent samples was used to test for gender differences. Differences in categorical data were tested with the Fisher’s exact test.

Children, childhood fatness predicted clustered cardiometabolic risk during adolescence (model 1). Model 2 showed that independently from childhood fatness, increasing fatness between age 11 and 16 was associated with clustered cardiometabolic risk. Weight gain in ΔBMI 1, ΔBMI 2, ΔBMI 3, and ΔBMI 4 was 13.6 ± 7.5, 19.6 ± 5.3, 26.0 ± 5.5, and 31.4 ± 7.2 kg, respectively. Model 3 shows that in boys, fitness was associated with clustered cardiometabolic risk independent of fatness and increasing fatness in girls. In girls, there was only a trend for this association. The interaction between increasing fatness and fitness (model 4) was only significant in boys. When adjusting the interaction to the model, the independent effect of fitness disappeared (β = 0.023; 95% CI: −0.006, 0.053), whereas the influence of increasing fatness increased. This interaction in boys was only significant when using BMI as a measure for fatness and not when skinfolds were used as a measure for fatness (β = −0.008; 95% CI: −0.08, 0.003). After excluding waist from the clustered cardiometabolic risk the interaction was no longer significant (β = 0.000; 95% CI: −0.014, 0.012). This interaction between fatness and fitness is graphically depicted in Fig. 1A, B.

Children, increasing fatness, VO₂max, and HOMA-IR

In boys, childhood fatness was related to insulin and HOMA-IR at age 16, whereas in girls increasing fatness was positively related to HOMA-IR (Table 2). VO₂max also correlated inversely with insulin and HOMA-IR. These correlations were moderate for boys (r = −0.314, −0.310, respectively) and small to moderate for girls (r = −0.180, −0.186, respectively). When adjusting for age, study location, and pubertal development, childhood fatness predicted HOMA-IR in boys (model 1) but not in girls. Increasing fatness (model 2) was associated with HOMA-IR independent of fatness (age 11) in girls but not in boys. Fitness (model 3) was associated with HOMA-IR independent of fatness and increasing fatness in both boys and girls. Only in boys was there a significant interaction between increasing fatness and fitness (model 4). As in the clustered cardiometabolic risk, when adding the interaction to the model, the independent effect of fitness disappeared (β = 0.008; 95% CI: −0.22, 0.038). Furthermore, the effect of increasing fatness increased and became significant (β = 0.592; 95% CI: 0.056, 1.129). Thus for
boys the contribution of fitness to HOMA-IR depends on the growth in BMI between age 11 and 16. The larger this growth the higher the contribution of fitness. This interaction between fatness and fitness is graphically depicted in Fig. 2A, B.

**Discussion**

This study shows that childhood fatness and increasing fatness are independently associated with increased cardiometabolic risk and HOMA-IR during adolescence, and that good fitness attenuates this association especially in fat boys. In addition, in boys the effect of fitness on cardiometabolic risk and HOMA-IR depends on the increasing fatness. In girls, fitness only influenced HOMA-IR but not the cardiometabolic risk independent of childhood fatness and increasing fatness.

In boys, measures of childhood fatness correlated to the clustered cardiometabolic risk either with or without waist circumference during adolescence. In girls, measures of childhood fatness were also correlated with the clustered cardiometabolic risk; however, this was fully explained by a correlation with waist circumference. Associations between childhood fatness and individual cardiometabolic risk factors in later life were found before in a study of 31 obese children who were followed from the age of 13 till age 22 (20). Another study showed that the degree of fatness in childhood is tightly linked to adverse cardiometabolic outcomes in adulthood (21). An interesting question that rises is whether there is an association between the initial degree of childhood fatness and later cardiometabolic risk or that childhood fatness is only relevant if it has tracked into later life. This study shows that, independent of the effects of childhood fatness, increasing fatness from childhood into adolescence is associated with clustered cardiometabolic risk and HOMA-IR during adolescence. A study with 186 obese adolescents who were followed for 19 months found that fatness was linked to individual cardiometabolic risk factors and changes in insulin sensitivity (22). Cardiometabolic risk factors and changes in insulin sensitivity were assessed at baseline and after 19±7 months. The cohort was stratified into three categories based on the 25th and 75th percentile of BMI Z-score change. Subjects who reduced their BMI Z-score significantly decreased their fasting and 2-h glucose levels and triglyceride levels and increased their high density lipoprotein cholesterol

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Table 2. Correlations between BMI age 11, skinfolds age 11, increasing fatness, VO₂ max, and the metabolic risk factors at age 16

<table>
<thead>
<tr>
<th>Outcome measures (age 16)</th>
<th>BMI (age 11)</th>
<th>Skinfolds (age 11)</th>
<th>ΔBMI (increasing fatness at age 11 to 16)*</th>
<th>ΔSkinfolds (increasing fatness at age 11 to 16)*</th>
<th>VO₂ max (age 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Boys</td>
<td>Girls</td>
<td>Boys</td>
<td>Girls</td>
<td>Boys</td>
</tr>
<tr>
<td>Clustered cardiometabolic risk</td>
<td>0.476**</td>
<td>0.163**</td>
<td>0.466**</td>
<td>0.177**</td>
<td>0.193**</td>
</tr>
<tr>
<td>Clustered cardiometabolic risk (without waist)</td>
<td>0.308**</td>
<td>−0.017</td>
<td>0.297**</td>
<td>0.025</td>
<td>0.094</td>
</tr>
<tr>
<td>Waist circumference (cm)†</td>
<td>0.590**</td>
<td>0.471**</td>
<td>0.536**</td>
<td>0.414**</td>
<td>0.308**</td>
</tr>
<tr>
<td>MAP (mmHg)†</td>
<td>0.171**</td>
<td>0.021</td>
<td>0.188**</td>
<td>−0.034</td>
<td>0.117**</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>0.026</td>
<td>−0.024</td>
<td>0.079</td>
<td>−0.050</td>
<td>0.067</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>0.292**</td>
<td>0.053</td>
<td>0.269**</td>
<td>−0.080</td>
<td>0.157**</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)†</td>
<td>0.259**</td>
<td>−0.073</td>
<td>0.247**</td>
<td>−0.042</td>
<td>0.113</td>
</tr>
<tr>
<td>HDL-C (mmol/L)†</td>
<td>−0.219**</td>
<td>−0.015</td>
<td>−0.103</td>
<td>−0.057</td>
<td>0.068</td>
</tr>
<tr>
<td>LDL-C (mmol/L)</td>
<td>0.171</td>
<td>0.015</td>
<td>0.218**</td>
<td>−0.041</td>
<td>0.149*</td>
</tr>
<tr>
<td>Total-C (mmol/L)</td>
<td>0.150*</td>
<td>0.020</td>
<td>0.217**</td>
<td>−0.047</td>
<td>0.154*</td>
</tr>
<tr>
<td>Glucose (mmol/L)†</td>
<td>0.073</td>
<td>−0.006</td>
<td>0.155**</td>
<td>0.067</td>
<td>0.048</td>
</tr>
<tr>
<td>Insulin (mU/L)</td>
<td>0.207**</td>
<td>0.042</td>
<td>0.300**</td>
<td>0.026</td>
<td>0.052</td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>0.204**</td>
<td>0.037</td>
<td>0.304**</td>
<td>0.039</td>
<td>0.056</td>
</tr>
</tbody>
</table>

BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein-cholesterol; HOMA-IR, homeostasis model assessment-insulin resistance; LDL-C, low-density lipoprotein-cholesterol; MAP, mean arterial pressure; SBP, systolic blood pressure.

Data are Pearson correlation coefficients; *p < 0.05; **p < 0.01; ΔBMI: Z-score BMI age 16 to Z-score BMI age 11.

*Increasing fatness was calculated by subtracting Z-scores for fatness (BMI and skinfolds) at age 11 from Z-score fatness at age 16.

† Factors of the clustered cardio metabolic risk.
Table 3. (a) Association between BMI, ΔBMI, VO₂max, ΔBMI × VO₂max, and clustered cardiometabolic risk and (b) between BMI, ΔBMI, VO₂max, ΔBMI × VO₂max, and HOMA-IR

<table>
<thead>
<tr>
<th>Boys (N = 283)</th>
<th>Girls (N = 282)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Beta coefficient (95% CI)</strong></td>
<td><strong>aR²</strong></td>
</tr>
<tr>
<td>(a) Association between BMI, ΔBMI, VO₂max, ΔBMI × VO₂max, and clustered cardiometabolic risk</td>
<td></td>
</tr>
<tr>
<td>Model 1 BMI (age 11)</td>
<td>0.107** (0.082, 0.132)</td>
</tr>
<tr>
<td>Model 2 BMI (age 11)</td>
<td>0.130** (0.106, 0.155)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>0.263** (0.181, 0.345)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>0.121** (0.096, 0.145)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>0.255** (0.175, 0.336)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>−0.014* (−0.023, −0.005)</td>
</tr>
<tr>
<td>Model 3 BMI (age 11)</td>
<td>0.117** (0.092, 0.141)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>0.948** (0.418, 1.477)</td>
</tr>
<tr>
<td>ΔBMI × VO₂max</td>
<td>0.023 (−0.006, 0.053)</td>
</tr>
<tr>
<td>ΔBMI × VO₂max</td>
<td>−0.015* (−0.026, −0.004)</td>
</tr>
<tr>
<td>(b) Association between BMI, ΔBMI, VO₂max, ΔBMI × VO₂max, and HOMA-IR</td>
<td></td>
</tr>
<tr>
<td>Model 1 BMI (age 11)</td>
<td>0.041** (0.017, 0.065)</td>
</tr>
<tr>
<td>Model 2 BMI (age 11)</td>
<td>0.047** (0.022, 0.072)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>0.070 (−0.014, 0.154)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>0.033** (0.008, 0.058)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>0.059* (−0.022, 0.141)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>−0.021** (−0.030, −0.012)</td>
</tr>
<tr>
<td>VO₂max</td>
<td>0.030* (0.005, 0.055)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>0.592* (0.056, 1.129)</td>
</tr>
<tr>
<td>ΔBMI</td>
<td>0.008 (−0.22, 0.036)</td>
</tr>
<tr>
<td>ΔBMI × VO₂max</td>
<td>−0.011* (−0.023, 0.000)</td>
</tr>
</tbody>
</table>

aR², adjusted R-square; BMI, body mass index; CI, confidence interval.

Model 1: + BMI age 11; Model 2: + ΔBMI; Model 3: + VO₂max; Model 4: + ΔBMI × VO₂max. All models were adjusted for age, study location, Tanner (age 11), and Pubertal Development Scale (age 16). ΔBMI: categorized differences in Z-score BMI age 11 and Z-score BMI age 16; Two groups were created for children with negative scores (<−1 and between −1 and 0), two groups were created for children with positive scores (>1 and between 0 and 1); Beta coefficients are unstandardized: *p < 0.05; **p < 0.01.
in comparison to subjects who increased their BMI Z-score. BMI Z-score changes negatively correlated with changes in insulin sensitivity ($r = -0.36$, $p < 0.001$). Of 67 who had metabolic syndrome at baseline, 33 (50%), most of whom decreased their BMI Z-score, lost the diagnosis. However, these studies used clinical (obese) populations. TRAILS uses a general and not a clinical population. Therefore, the finding of this study can be best compared with the findings of an Australian cohort study in which 172 children were followed from the age of 8 to 15 yr (23). They reported that children who were overweight or obese at 8 yr of age were seven times as likely to have cardiometabolic risk clustering in adolescence than were their peers who were not overweight or obese. They also reported that those with an increased waist circumference at age 8 yr were four times more likely to have cardiometabolic risk clustering in adolescence than were children with a smaller waist circumference. It was concluded that association between measures of fatness in mid-childhood and later adverse cardiometabolic risk is a result of the tracking of fatness status.

In line with other studies fitness was inversely related to the clustered cardiometabolic risk with or without waist circumference (24, 25) and HOMA-IR (26). In boys, fitness was associated with clustered cardiometabolic risk and HOMA-IR independent of childhood fatness and increasing fatness. In girls, there was only an independent association with HOMA-IR but not with clustered cardiometabolic risk. This could be because of a lack of power or because of the absence of more overweight or obese girls in the study population. Nevertheless, these findings are in line with cross-sectional studies (27) which studied the mediation of fitness on the association between fatness and cardiometabolic risk by stratification. Children and adolescents with ‘high fatness and high fitness’ have better cardiometabolic risk profiles than those classified as ‘high fatness but low fitness’. However,
in these studies it is difficult to determine whether
fitness modifies the association between fatness and
cardiometabolic risk since fitness and fatness are
heavily intertwined. Stratification by fatness does not
always solve this problem because groups are not
always equally balanced, resulting in lower average
BMI in groups with ‘fat but fit’ children when
compared to ‘fat and unfit’ children.

This study further shows that in boys there
is a significant interaction between fitness and
fatness which states that high fitness attenuates
the association between fatness and clustered
cardiometabolic risk especially in those who had
higher increases in BMI between age 11 and age 16.
For HOMA-IR, comparable results were found. One
prospective study in which the association between
fatness, fitness, and cardiometabolic risk was found.
The Amsterdam Growth and Health Longitudinal
Study followed 364 individuals (189 women) from
adolescence (age 13) into adulthood (age 36) on
fatness, fitness, and cardiometabolic risk (28). This
study found independent influences of fatness and
fitness on cardiometabolic risk. The associations
between fitness and the metabolic syndrome decreased
considerably when adjusted for fatness, but the
associations remained statistically significant. The
authors suggest that poor fitness may be associated
with cardiometabolic risk partly because of its associations
with body fatness (29) and also because of other
mechanisms including insulin resistance (30), sub-
clinical inflammation (31), or a common genetic
background (32), (33) that predisposes to low fitness
and increased cardiometabolic risk.

Limitations and advantages

This study shows some limitations while overweight
girls were more often excluded due to missing data
on fitness which might result in selection bias. In this
study puberty was assessed by using two different
methods, one filled in by the parents (Tanner) at the
first examination and second filled in by the adolescents
(PDS) at the third examination. This might result into
a less accurate definition of the maturity status, but
does not influence the main outcomes. The advantage
of this study is that it shows in a longitudinal design
that childhood fatness, increasing fatness, and fitness
are independently associated with clustered metabolic
risk and HOMA-IR. However, only fatness measures
were tracked. In this study, BMI as well as skinfolds
were used as measures for fatness. Because BMI
showed more obvious associations with the clustered
cardiometabolic risk and HOMA-IR compared to
skinfold, most of the time results from BMI are
presented. This study used a valid measure of fitness
and a subsample of participants (48%) was checked
for maximal exhaustion rendering the measurements
accurate.

To improve cardiometabolic risk in adolescents,
interventions need to focus not solely on reducing
fitness but also on physical activities that improve
fitness.

Acknowledgements

This research is part of TRAILS. Participating centers of
TRAILS include various departments of the University Medical
Center and University of Groningen, the Erasmus University
Medical Center Rotterdam, the University of Utrecht, the
Radboud Medical Center Nijmegen, and the Parnassia Bavo
group, all in The Netherlands. TRAILS has been financially
supported by various grants from The Netherlands Organization
for Scientific Research NWO (Medical Research Council
program grant GB-MW 940-38-011; ZonMW Brainpower grant
100-001-004; ZonMw Risk Behavior and Dependence grants
60-60600-98-018 and 60-60600-97-118; ZonMw Culture and
Health grant 261-98-710; Social Sciences Council medium-
sized investment grants GB-MaGW 480-01-006 and GB-MaGW
480-07-001; Social Sciences Council project grants GB-MaGW
457-03-018, GB-MaGW 452-04-314, and GB-MaGW 452-06-
004; NWO large-sized investment grant 175.010.2003.005); the
Sophia Foundation for Medical Research (projects 301 and
393), the Dutch Ministry of Justice (WODC), the European
Science Foundation (EuroSTRESS project FP-006), and the
participating universities.

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