Body mass index, fitness and physical activity from childhood through adolescence

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ABSTRACT

Background OBesity, sedentary lifestyle and poor cardiorespiratory fitness in childhood may increase the risk of health problems later in life. Purpose The authors studied the association of early childhood weight status with cardiorespiratory fitness and leisure-time physical activity (LTPA) in adolescence. The stability and associations of LTPA and fitness from childhood through adolescence were also studied. Methods Body mass index (BMI) was assessed annually since birth in a prospective, longitudinal study. The mean BMI between ages 2 and 7 years indicated weight status at preschool age. Fitness was studied with a shuttle run test at age 9 and with a maximal cycle ergometer test at age 17. The same questionnaire was used to assess LTPA at age 9, 13 and 17. Complete data on preschool BMI, LTPA at ages 13 and 17 and fitness at age 17 years was provided by 351 children, while fitness and LTPA data were available for 74 children at ages 9 and 17.

Results Preschool BMI was inversely associated with fitness in adolescence independently of adolescent LTPA (p<0.0001). Children who had a high preschool BMI but whose weight status was reduced in adolescence had similar fitness in adolescence as the children with a persistently low BMI. Regardless of the fitness level in childhood, the children whose LTPA increased between age 9 and 17 had a similar adolescent fitness level as persistently active subjects.

Conclusions It is important to maintain a healthy body weight and a physically active lifestyle from very childhood through adolescence to improve fitness during adolescence.

INTRODUCTION

The soaring prevalence of childhood overweight and obesity that has occurred during the past decades gives cause for great concern. Among the detrimental consequences of childhood overweight on current and future health, children and adolescents with overweight are less fit than their leaner peers.1–3 Also, overweight may lead to inactivity and not be the result of it.4 Whether weight in early childhood is associated with cardiorespiratory fitness (referred later as fitness) or engagement in physical activity in adolescence is, however, not known.

Lack of physical activity is globally the fourth most important risk factor associated with mortality.5 From very early childhood, a sedentary lifestyle and poor fitness carry many unfavourable health effects. Fitness tracks moderately well from childhood to adolescence, while physical activity shows somewhat weaker stability.6–9 Fitness is strongly determined by heredity; approximately half of the interindividual variance of fitness may be explained by genetic factors.10–12 Fitness can be improved by increasing physical activity, but the magnitude of improvement varies markedly.13–14 In children and adolescents, the association between physical activity and fitness is rather weak or lacking.15–17 There are only a few longitudinal studies on fitness and physical activity among children and adolescents, and there is very little data on the effect of changes in physical activity during childhood and adolescence on subsequent fitness.

The main aim of this study was to examine how early childhood weight status is related to fitness and physical activity later in life. We studied the association of preschool body mass index (BMI) and the change in weight status from early childhood to adolescence with fitness and leisure-time physical activity (LTPA) in adolescence. We also studied the stability of LTPA and fitness and their associations through childhood to adolescence. We specifically asked, whether LTPA predicts fitness at age 17 independently of childhood fitness.

METHODS

Study design and subjects

This study is a part of an on-going prospective, randomised study, the Special Turku Coronary Risk Factor Intervention Project for Children (STRIP).18 Briefly, between February 1990 and June 1992, families with 6-month-old infants were recruited at well-baby clinics in Turku, Finland. At the age of 7 months, 1062 infants (56.5% of the eligible age-cohort; n=1880) were randomly allocated to a dietary intervention (n=540) or control group (n=522). The intervention group has received individualised dietary and antismoking counselling at least biannually. The study was approved by the Joint Commission on Ethics of the Turku University and the Turku University Hospital. Written informed consent was obtained from the parents in the beginning of study and from the adolescents at age 15.

In this study, the associations of preschool BMI and the change in weight status from early childhood to adolescence with fitness and LTPA in adolescence were studied in the children who provided complete data on LTPA at age 13, and LTPA and fitness at age 17 (figure 1; cohort A). In these children, the associations between LTPA and fitness in adolescence were also studied. The stability of LTPA and fitness, and their associations through...
childhood to adolescence were studied in a subcohort of the STRIP study children (figure 1; cohort B). At the age of 13 years, 558 adolescents provided LTPA data (99% of those who visited the STRIP study; n=565) and 498 (89%) of them responded to the same questionnaire at age 17 (figure 1). Of these respondents, fitness data were available for 351 (70%; 174 girls, 177 boys: cohort A). Lack of time was reported as the main reason for not taking part in the fitness test at age 17.

At the age of 9 years, physical activity and fitness were assessed in a randomly selected subgroup of the STRIP cohort between May 1999 and May 2000 (figure 1). Of the 118 children with data on LTPA and fitness at 9 years of age, 96 (81%) responded to a similar LTPA questionnaire at age 17 and, of them, 74 (77%; 30 girls, 44 boys) completed a fitness test (cohort B).

Both cohorts were comparable (LTPA, BMI, and total and high-density lipoprotein cholesterol) regarding participants who provided data at age 17 and at baseline (age 13 or 9 years) to those who were lost to follow-up.

**Physical activity and fitness**

The participants completed a self-administered questionnaire at ages 9, 13 and 17 years for assessment of LTPA. At age 9, the children responded together with their parents. In the questionnaire, the frequency, duration and intensity of habitual LTPA were reported. Habitual physical activity rather than physical activity during a strictly defined time period was assessed to avoid bias caused by temporary intermissions in physical activity, for example, illness during past week or month. LTPA was calculated by multiplying frequency, mean duration and mean intensity (multiple of the resting metabolic rate; MET) of weekly LTPA and expressed as MET h/week. LTPA comprised recreational and organised physical activity/sports outside school hours. The questions on LTPA thus excluded physical education lessons given at school and active commuting to school. The questionnaire correlates moderately well with physical activity data derived from accelerometers (r=0.26–0.40) and pedometers (r=0.30–0.39) in young adults, and also with the maximal exercise capacity (r=0.49–0.53).

Fitness at 9 years of age was estimated using the 20-meter shuttle run test. The test consists of running back and forth between two lines 20 meters apart at a given pace. The speed is paced by a sound signal and each stretch of 20 meters is called a shuttle. The protocol starts at 8.0 km/h, and the speed increases by 0.5 km/h by 1 min intervals. Performance is maximal when the child fails to reach the line on two consecutive shuttles. The score of the test is the number of shuttles completed.

At the age of 17 years, fitness was measured with a maximal exercise test on a cycle ergometer (Ergoselect 100 K, Ergoline, Germany). The test began at a workload of 50 W, which was increased by 30 W (boys) or 25 W (girls) every 2 min until exhaustion. The mean workload during the last 4 min of work was calculated and the VO2max was estimated according to the American College of Sports Medicine. Participants who failed to reach a heart rate of 177 beats per minute (bpm) ((205 bpm – 0.5×age)×0.9) were excluded.

**Physical examination**

Height was measured by a Harpenden stadiometer (Holtain, Crymych, UK) and weight in light clothing with an electronic scale (Soehnle S10, Soehnle, Murrhardt, Germany) at every study visit beginning at the age of 2 years. The measurements were done close to the child’s birthday. BMI was calculated as weight divided by height squared (kg/m²). International, gender and age-specific BMI cut-off points for overweight were used to describe the cohorts (table 1). Pubertal status was recorded according to Tanner.

**Statistical analyses**

The analyses were done separately for the two cohorts (figure 1). Pubertal status at age 9, 13 or 17 years was not associated with LTPA or fitness and was not included in the analyses. There was no interaction between gender and LTPA when fitness at age 17 was used as the dependent variable. Therefore, boys and girls were analysed together with gender as a covariate. The STRIP intervention and control groups were also combined. Since LTPA values were non-normally distributed and clustered, physical activity groups based on LTPA tertile cut-off points were formed (table 1). The change in LTPA was described by a variable with four values set for both cohorts: (1) LTPA increase: from sedentary (group I) to moderately active (group II) or active (group III), (2) LTPA decrease: from active/moderately active to sedentary, (3) Persistently sedentary: sedentary at both ages, and (4) Persistently active: moderately active/active at both ages.

The association of preschool BMI and the change in weight status from early childhood to adolescence with fitness and LTPA in adolescence was studied in cohort A. A mean BMI between ages 2 and 7 years was used to indicate preschool BMI. Age 7 years was used as the upper cut-off point since in Finland children begin school at that age. Data on BMI through ages 2 and 7 was available for all children. A z-score of the preschool BMI was calculated and the mean was used in the analyses. Similarly, a z-score of BMI at age 17 was calculated. Four BMI change groups were formed by BMI z-score quintiles:
(1) Persistently low BMI: BMI z-score in the four lowermost quintiles at preschool age and at age 17.

(2) BMI decrease: BMI z-score in the highest quintile at preschool age and in the four lowermost quintiles at age 17.

(3) BMI increase: BMI z-score in the four lowermost quintiles at preschool age and in the highest quintile at age 17.

(4) Persistently high BMI: BMI z-score in the highest quintile at preschool age and at age 17.

The association between preschool BMI and fitness at age 17 was studied with linear regression analysis. Multivariable Analyses of Covariance (ANCOVA) was used to study the association of BMI, gender, STRIP study group, LTPA at age 9 or 13, and change in LTPA with fitness at age 17. For cohort B, fitness at age 9 was also included. The association of BMI change group with adolescent fitness and LTPA was studied with an analysis of variance (ANOVA) model. Pearson’s partial correlation coefficient was calculated to study the stability of fitness from age 9 to 17. Tracking of LTPA from age 9 or 13 to 17 years was studied with Spearman’s partial correlation coefficient. The stability of fitness and tracking of LTPA were further estimated with Cochran-Mantel-Haenszel’s method (non-zero correlation test).

A p-value of less than 0.05 was considered statistically significant. Post-hoc pairwise comparisons within the ANOVA or ANCOVA models were adjusted with the Tukey-Kramer method. Model fit ($R^2$) was calculated to indicate the proportion of variation explained by the variables included in the analysis. Analyses were performed using the SAS 9.2 software (SAS Institute, Cary, North Carolina, USA).

RESULTS

Association of preschool BMI with adolescent fitness and LTPA (cohort A)

Children with a high BMI before they started school were less fit in adolescence than children who had a low BMI at that time ($p=0.0078$). This association was independent of gender and of LTPA in adolescence (table 2; model 1, $R^2=0.46$). Preschool BMI was associated with BMI at age 17 ($r=0.54$, $p<0.0001$). Children with a persistently low BMI were more fit in adolescence than children whose BMI increased or who had a persistently high BMI (table 3). Also, children whose BMI decreased from preschool age to adolescence were more fit than children whose BMI decreased or was persistently high. Importantly, the fitness level of children with persistently low BMI and whose BMI decreased was similar in adolescence.

The preschool BMI did not predict LTPA at age 13 or 17 years ($p=0.98$ and $p=0.46$, respectively; adjusted for gender)

Table 1: Mean (SD) body mass index (BMI), fitness and LTPA in cohorts A and B. Range for fitness and LTPA in the tertile groups (I-III) are also presented

<table>
<thead>
<tr>
<th></th>
<th>Cohort A – 13 and 17 year (n=351)</th>
<th>Cohort B – 9 and 17 year (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preschool BMI (2–7 y), kg/m²</td>
<td>15.9 (1.2) 351</td>
<td>17.0 (2.2) 74</td>
</tr>
<tr>
<td>BMI at age 9, kg/m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight*, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI at age 13, kg/m²</td>
<td>19.3 (3.0) 351</td>
<td>12.2 9</td>
</tr>
<tr>
<td>Overweight†, %</td>
<td>15.1 53</td>
<td></td>
</tr>
<tr>
<td>BMI at age 17, kg/m²</td>
<td>21.4 (3.1) 351</td>
<td>21.8 (3.3) 74</td>
</tr>
<tr>
<td>Overweight‡, %</td>
<td>15.7 55</td>
<td>16.2 12</td>
</tr>
<tr>
<td>Fitness at age 9, number of shuttles run</td>
<td>34.3 (12.5)</td>
<td>38.6 (15.7) 23</td>
</tr>
<tr>
<td>Least fit</td>
<td>I 11–28</td>
<td>II 29–37</td>
</tr>
<tr>
<td>Most fit</td>
<td>III 38–69</td>
<td></td>
</tr>
<tr>
<td>Fitness at age 17, (V̇O₂max), ml/kg/min</td>
<td>40.4 (7.2) 117</td>
<td>40.1 (7.6) 25</td>
</tr>
<tr>
<td>Least fit</td>
<td>I 23.4–37.2 117</td>
<td>24.0–37.0 25</td>
</tr>
<tr>
<td>Most fit</td>
<td>III 43.4–58.0 117</td>
<td>42.7–55.5 25</td>
</tr>
<tr>
<td>LTPA at age 9, MET h/week</td>
<td>Sedentary I 0–5.0 25</td>
<td>19.0 (17.9) 25</td>
</tr>
<tr>
<td>Active</td>
<td>III 21.1–93.4 24</td>
<td></td>
</tr>
<tr>
<td>LTPA at age 13, MET h/week</td>
<td>27.9 (21.7) 114</td>
<td>25.7 (23.5) 24</td>
</tr>
<tr>
<td>Sedentary</td>
<td>I 0–13.3 114</td>
<td>0–8.0 24</td>
</tr>
<tr>
<td>Active</td>
<td>III 32.6–93.4 104</td>
<td>11.8–31.3 25</td>
</tr>
<tr>
<td>LTPA at age 17, MET h/week</td>
<td>28.1 (22.9) 129</td>
<td>32.6–93.4 25</td>
</tr>
<tr>
<td>Sedentary</td>
<td>I 0–11.8 119</td>
<td>0–8.0 24</td>
</tr>
<tr>
<td>Active</td>
<td>III 35.0–93.4 103</td>
<td>11.8–31.3 25</td>
</tr>
<tr>
<td>Change in mean LTPA, MET h/week</td>
<td>0.2 (22.2) 24</td>
<td>6.7 (23.1) 25</td>
</tr>
</tbody>
</table>

*BMI>19.1 kg/m² in girls and 19.1 kg/m² in boys.
†BMI>22.6 kg/m² in girls and 21.9 kg/m² in boys.
‡BMI>24.7 kg/m² in girls and 24.5 kg/m² in boys.
LTPA, leisure-time physical activity; MET, metabolic equivalent.
and it was similar in children who were persistently sedentary or persistently active between age 13 and 17 (p=0.57; adjusted for gender).

**LTPA and fitness in adolescence (cohort A)**

LTPA at age 13 was associated with LTPA at age 17 (r=0.52, p<0.001) and tracked significantly (p<0.001). Of the active 13 year olds, 58% were active 4 years later and of the sedentary ones, 55% were sedentary at age 17. The mean LTPA remained similar throughout adolescence (table 1).

The adolescents who were sedentary at age 13 were less fit 4 years later than their physically more active peers (table 4). Persistently active adolescents were more fit than adolescents whose LTPA increased or decreased, or who were persistently sedentary.

The LTPA change group, gender and BMI at age 17 were independently associated with fitness at age 17 (table 2; model 2, R²=0.59). The active adolescents whose LTPA decreased had a similar fitness level to those who were persistently sedentary.

**Fitness and LTPA from childhood to adolescence (cohort B)**

Fitness at age 9 was associated with fitness at age 17 (r=0.58, p<0.001). Similarly, the stability of fitness was significant (p<0.001) (table S1, online publication).

**DISCUSSION**

Poor and decreased fitness during childhood predict overweight and weight gain in youth, and adulthood, but there is no data on whether high weight already between ages 2 and 7 years is associated with fitness in adolescence. This study shows that a high BMI already at preschool age is associated with a lower fitness level more than 10 years later. The detrimental effect of a high preschool BMI on later fitness was independent of LTPA during adolescence. As fitness is an important determinant of health at all ages, these results further highlight the importance of maintaining a healthy body weight from the very first years of life.

Overweight in childhood is associated with sustained negative health effects later in life even if the person reaches a normal body weight. This study shows that this is not universally true: if a child has a high BMI before starting school but it decreases thereafter, the child’s fitness as an adolescent is similar to the one of adolescents with a low BMI since childhood. Thus, improved fitness and the health benefits associated with fitness can be gained by weight loss in later childhood and adolescence.
adolescence. This is an obvious positive message for health educators who tackle childhood overweight.

Overweight children tend to be physically less active than children with normal body weight.34–36 Rather than the cause, physical inactivity may be the result of obesity.3 Maybe overweight makes physical activities – playing, running, etc – less fun for overweight children who thus prefer to withdraw from such activities. Physical activity is essential, for example, for the development of various motor skills in early childhood. Lack of physical activity may lead to impaired skills which, in turn, discourage the child from engaging in physical activity and eventually fitness decreases. A positive message from this study is that being heavier at preschool age is not associated with LTPA in adolescence, that is, bigger body size in early childhood does not impair physical activity habits during adolescence.

Although physical activity and fitness are closely interrelated, fitness is strongly determined by heredity,12 37 and similar physical activity levels result in different fitness levels.13 Particularly in prepubertal children, fitness is strongly determined by genetic factors, since the response to aerobic exercise training at this age is limited. We show that although childhood fitness is closely associated with adolescent fitness, increasing LTPA from childhood to adolescence improves fitness independently of the fitness level at the outset (in childhood).

The sedentary children who increased their LTPA between 9 and 17 years of age reached a similar fitness level as the persistently active children did, while fitness in adolescence was similar among the children whose LTPA decreased or who were persistently sedentary. During adolescence, increased LTPA was no longer associated with a fitness level similar to the level of persistently active adolescents. One of the reasons for this finding may be that the types of sports and physical activities preferred at this age do not improve cardiorespiratory fitness. Taken together, this study shows that the benefits of physical activity on fitness are not preserved but determined by current physical activity.

Physical activity declines from childhood to adolescence38–40 and this may take place already between ages 7 and 9 years.41 In this study, however, LTPA of the children on average slightly increased between ages 9 and 17 years and was similar from age 13 to 17 years (table 1). This suggests that, although physical activity during the entire day may decrease from childhood to adolescence, engagement in physical activity in leisure-time remains fairly stable in youth. The spasmodic nature of children’s physical activity makes accurate assessment of physical activity difficult and may have led to an underestimation of LTPA at age 9. Furthermore, there was a marked variation in LTPA indicating that in many of the children LTPA level changed. Taken together, physical activity during leisure-time needs to be promoted continuously, and, in addition, special efforts should be made to support a physically active lifestyle for children and adolescents.

Table 4  Fitness at age 17 years by LTPA groups and LTPA change groups, and the association of LTPA and LTPA change with fitness at age 17 years. Data are mean (SD) and range

<table>
<thead>
<tr>
<th>LTPA group</th>
<th>Fitness at age 17 y (ml/kg/min)</th>
<th>n</th>
<th>p*</th>
<th>LTPA change</th>
<th>Fitness at age 17 y (ml/kg/min)</th>
<th>n</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cohort A</strong></td>
<td></td>
<td></td>
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<tr>
<td>Age 13 years</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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</tr>
<tr>
<td>I (sedentary)</td>
<td>36.5 (6.2), 23.4–50.3†</td>
<td>114</td>
<td>&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>41.5 (6.9), 27.5–58.0</td>
<td>133</td>
<td>0.19 (0.09 to 0.29)</td>
<td>0.0003</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>III (active)</td>
<td>43.3 (6.9), 26.5–58.0</td>
<td>104</td>
<td>p=0.30</td>
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<td></td>
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<tr>
<td><strong>Cohort B</strong></td>
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<td></td>
<td></td>
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<tr>
<td>Age 13–17 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) LTPA increase</td>
<td>36.6 (5.5), 27.1–49.7</td>
<td>51</td>
<td>p&lt;0.0001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2) LTPA decrease</td>
<td>38.4 (6.3), 27.5–52.9</td>
<td>56</td>
<td>0.97</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3) Persistently sedentary</td>
<td>36.5 (6.8), 23.4–50.3</td>
<td>63</td>
<td>p=0.0003</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4) Persistently active</td>
<td>43.5 (6.7), 26.5–58.0</td>
<td>181</td>
<td></td>
<td></td>
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<td></td>
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</tr>
</tbody>
</table>

Note: *p Values for the main effect of the covariate versus fitness at age 17 years, adjusted for gender.
†Tukey-Kramer adjusted p (sedentary vs active)<0.0001, p (sedentary vs moderately active) <0.0001.
‡Tukey-Kramer adjusted p (persistently active vs persistently sedentary)<0.0001, p (persistently active vs LTPA decrease)<0.0001, p (persistently active vs LTPA increase)<0.0001.
§Tukey-Kramer adjusted p (persistently active vs persistently sedentary)=0.0074, p (persistently active vs LTPA decrease)=0.0011.
LTPA, leisure-time physical activity.

Table 5  Determinants of fitness at age 17 years in cohort B (data at 9 and 17 years, n=74)

<table>
<thead>
<tr>
<th>Determinant</th>
<th>β* (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fitness at age 9, number of shuttles run</td>
<td>0.19 (0.09 to 0.29)</td>
<td>0.0003</td>
</tr>
<tr>
<td>LTPA change</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LTPA increase vs LTPA decrease</td>
<td>4.27 (0.08 to 8.46)†</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LTPA increase vs persistently sedentary</td>
<td>5.11 (−0.03 to 10.26)†</td>
<td>0.052†</td>
</tr>
<tr>
<td>LTPA decrease vs persistently active</td>
<td>−2.20 (−5.88 to 1.48)†</td>
<td>0.40†</td>
</tr>
<tr>
<td>LTPA decrease vs persistently sedentary</td>
<td>0.85 (−4.35 to 6.04)†</td>
<td>0.97†</td>
</tr>
<tr>
<td>Gender (girls compared with boys)</td>
<td>−3.87 (−6.25 to −1.52)</td>
<td>0.0017</td>
</tr>
<tr>
<td>BMI at age 17, kg/m²</td>
<td>−0.82 (−1.17 to −0.47)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*Regression coefficient for a change in fitness when the explanatory variable increases one unit.
†Mean (95% CI) differences of least square means, that is estimated mean difference between groups.
Tukey-Kramer adjusted p values.
LTPA, leisure-time physical activity.
The strengths of our study are that the children have been closely followed up with well-established methods since birth through childhood to adolescence. An objective method was used to assess fitness at age 17. A limitation is that physical activity was self-reported and LTPA rather than total physical activity was assessed. Self-reported questionnaires may be confounded by recall bias, especially by children. It is often claimed that people overestimate their self-reported physical activity, but – interestingly – children may underestimate physical activity compared with objective measurements. Questionnaires may sometimes describe preferentially participation in organised physical activity while unorganised, recreational activity may go under-reported. The assessment of physical activity only during leisure-time, excluding for example, physical education at school, may have caused bias in our study if adolescents reporting low physical activity during leisure-time are physically active at other times of the day. LTPA is, however, the important discriminating factor regarding physical activity, since physical education given at school is compulsory. A limitation also is that data on all of the children in the initial STRIP cohort were not available for this study, and fitness was assessed with different methods at ages 9 and 17. Longitudinal fitness data were, however, used only for correlational analyses, not to study change in fitness per se. The feasibility of BMI to define weight status can be debated since it does not take into account body composition.

In summary, a persistently high BMI from a very young age is associated with poorer fitness during adolescence regardless of the level of physical activity. Fortunately, if children with a high preschool BMI reduce their BMI by adolescence, their fitness level during adolescence is similar to the children with a persistently low BMI. Increasing the LTPA from childhood to adolescence is associated with improved fitness independently of childhood fitness level. Since fitness is an important health determinant, these data emphasise the importance of maintaining a healthy body weight and a physically active lifestyle throughout childhood and adolescence.

Contributors Authors included in the manuscript meet all of the following conditions: (1) substantial contributions to the conception and design, acquisition of data, or analysis and interpretation of data; (2) drafting the article or revising it critically for important intellectual content; and (3) final approval of the version to be published. All authors are responsible for reported research.

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Competing interests None.

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