Childhood muscular fitness phenotypes and adult metabolic syndrome

Short Running Title: Child muscular fitness and adult MetS

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Abstract

Introduction: To determine whether childhood muscular fitness phenotypes (strength, endurance, power) are independently associated with adult metabolic syndrome (MetS).

Methods: Longitudinal study including 737 participants who had muscular fitness measures in 1985 when aged 9, 12, or 15 years and attended follow-up in young adulthood 20 years later when measures of MetS were collected. Childhood measures of muscular fitness included strength (right and left grip, leg, shoulder extension and flexion), endurance (number of push-ups in thirty seconds), and power (distance of a standing long jump). A muscular fitness score was created using all individual muscular fitness phenotypes. In adulthood, waist circumference, blood pressure, high-density lipoprotein cholesterol, triglycerides, and glucose were measured. Adult outcomes were MetS defined using the Harmonized definition and a continuous metabolic syndrome (cMetS) risk score.

Results: Participants with childhood muscular strength, muscular power and combined muscular fitness score in the highest third had significantly lower relative risk (RR) for MetS and a lower cMetS score in adulthood independent of cardiorespiratory fitness (CRF), than those in the lowest third (strength: RR=0.39 (0.19,0.78); β=-0.39 (-0.52, -0.25), power: RR=0.32 (0.15,0.68); β=-0.39 (-0.53, -0.26), fitness score: RR=0.30 (0.14,0.63); β=-0.45 (-0.58, -0.31)). However, adjustment for childhood waist circumference reduced the effect sizes for both adult outcomes by 44-51%.

Conclusion: Phenotypes of childhood muscular fitness predict adult MetS independent of CRF. Although approximately half of the effect of childhood muscular fitness on adult MetS is potentially being mediated by child waist circumference, these data suggest promotion of muscular fitness among children might provide additional protection against developing adult MetS.

Keywords: cohort, epidemiology, adiposity, cardiorespiratory fitness, pediatric

Introduction

Metabolic syndrome (MetS), the clustering of abdominal obesity, elevated blood pressure, elevated triglycerides, decreased high-density lipoprotein cholesterol (HDL-C), and elevated fasting plasma glucose, remains a major public health burden with the prevalence of the syndrome increasing in concert with obesity and sedentary lifestyles(2). MetS affects both children and adults and has been linked with clinical manifestations in cardiovascular disease (CVD) and type 2 diabetes (T2D)(2, 21, 27). Consequently, means of prevention and treatment for MetS, particularly those commencing in childhood, are of interest(14, 22, 28).

Cross-sectional and longitudinal studies among children and adults have shown higher levels of cardiorespiratory fitness (CRF) to associate with healthier cardiometabolic profiles, reduced clustering of metabolic risk factors, and decreased MetS(3, 9, 17-19, 34). Longitudinal data suggests that CRF in childhood and adulthood predict adult MetS independent of adiposity levels(19, 30). Muscular fitness, a unique fitness phenotype, is becoming increasingly recognized in health promotion and disease prevention guidelines(26, 37, 39, 40) owing to its association with important chronic disease outcomes, independent of CRF.

Muscular fitness incorporates the phenotypes of muscular strength, muscular power and muscular endurance. Recent data has shown low grip strength in adults to be associated with all-cause death, cardiovascular death, and CVD, exhibiting greater effects with mortality than hypertension(20). Past findings suggest that phenotypes of muscular fitness are associated with insulin sensitivity, beta cell function and decreased CVD risk factors, independent of CRF(11, 12). Muscular fitness has been shown to be inversely associated with MetS prevalence in adult cross sectional(16) and longitudinal data(15). In childhood, muscular fitness has been crosssectionally linked with cardiometabolic risk factors including waist circumference(24). Childhood waist circumference presented as one of the strongest predictors of subsequent MetS in adulthood in past longitudinal data(31). Previous data have investigated the relationship between muscular strength in adolescents and cardiovascular risk in young adulthood, independent of CRF(12). However, what is lacking is longitudinal evidence of the association between muscular fitness in childhood and MetS in adulthood, independent of CRF. Therefore, using 20-year follow-up data from the Childhood Determinants of Adult Health (CDAH) Study we aimed to determine the association of childhood muscular fitness, incorporating all three phenotypes of muscular strength, muscular power, and muscular endurance, with adult MetS.

Materials and methods

Participants

The CDAH study collected baseline data on a nationally representative sample of 8,498 Australian schoolchildren in 1985 aged between 7 and 15 years. During this time, children aged 9, 12 and 15 (N=2,726) received additional measurements of blood pressure, blood sampling, and more detailed fitness tests that included measures of muscular strength. Of those eligible from this subset at baseline, 741 participants (27.2%) attended one of 34 follow-up clinics held across Australia from 2004-2006 and had measures for MetS collected. Of these, four pregnant participants were excluded leaving an analysis subset of 737 participants. A flow chart of participation is given in figure 1. In 1985, consent was obtained from both parent and child prior to inclusion in the study. At follow-up, written informed consent was obtained from the participant. The State Directors General of Education approved the baseline study and the Southern Tasmania Health and Medical Human Research Ethics Committee approved the follow-up study.

Childhood muscular fitness

Muscular strength was measured as maximum voluntary contractile force in kilograms of right grip, left grip, shoulder flexion, shoulder extension, and leg, using isometric dynamometers (Smedley's Dynamometer, TTM, Tokyo, Japan). Each strength measure was repeated twice, with the maximum of the two attempts used in the analysis. Right and left grip strength was measured as participants held the dynamometer with one hand, supported it on the opposite shoulder, and gripped with maximum force. Shoulder strength in the form of shoulder flexion and extension was measured as participants held the dynamometers in front of their chest with both hands parallel to the ground and then either pulled or pushed with maximum effort trying to get their hands as far apart or as close together as possible. For leg strength, participants were asked to stand on the dynamometer with flat feet, a straight back, with their body flat against a wall. Whilst holding a hand bar with an overhand grip, knees were flexed until an angle of 115° was measured, at which point the bar was attached to the dynamometer by a chain; participants then pulled the bar as far as possible by moving their body upwards. In order to obtain a single measure of muscular strength, we performed principal component analysis to estimate the first principal component of the five measures of childhood muscular strength (factor loadings presented in Table S1, SDC 1)(29). Childhood muscular power was measured as the best resulting distance in centimeters from two standing long jump tests that required a two-footed takeoff. Each child was encouraged to swing their arms and bend their knees to provide drive. Muscular endurance was measured as the number of correctly completed inclined push-ups in 30 seconds. Starting, with two hands placed on the front edge of a chair shoulder width apart, with legs straight at a 90° angle to the body and arms fully extended, a *correct* push up was defined as when their body was lowered until their chest touched the chair and then raised until the arms were back to a fully extended position. All muscular fitness phenotypes were adjusted for body weight (by regressing body weight on each phenotype and using the residuals) to create indices uncorrelated with body weight(29) and standardized for age and sex. Finally, a combined childhood muscular fitness score was created using the first principal component of all childhood muscular fitness phenotypes (factor loadings presented in Table S2, SDC 2).

Childhood clinical measurements

CRF in childhood was measured indirectly using a Monark 818E bicycle ergometer (Monark Exercise AB, Vansbro, Sweden) as Physical Work Capacity at a heart rate of 170 beats per minute (PWC_{170})(8). PWC_{170} has previously shown to be highly correlated with maximal oxygen consumption (VO_2 max) (r=0.83) and is a more appropriate test for field-based settings(10). This sub-maximal test incorporates three successive 3-minute workloads that step-wise increased resistance. Heart rate and watts, recorded in the final minute of each workload, were plotted and extrapolated to provide PWC_{170}. Absolute CRF was adjusted for lean body mass in this study to provide a measure uncorrelated with lean body mass(29), as the absolute work load achieved is a function of muscle mass(5). Body mass was measured to the nearest 0.5kg using regularly calibrated scales. Waist circumference was measured to the nearest 0.1cm at the level of the umbilicus using a constant-tension tape. Height was measured to the nearest 0.1cm using a Kawe height tape. Childhood lean body mass was calculated using weight (kg) and estimates of percentage body fat derived from the sum of skin folds. Triceps, bicep, subscapular and suprailiac skinfolds were measured to the nearest 0.1mm using Holtain Calipers (Holtain, Crymych, UK). Body density was calculated from the log of the sum of four skinfolds using age-specific regression equations(7) and fat percentage was determined. Lean body mass was then calculated by subtracting fat mass from total body mass.

Adult clinic measurements

In adulthood, blood samples were collected from participants who observed a 12-hour fast prior to the clinic. Fasting status was enquired from participants on arrival. Serum triglyceride, HDL-C, and glucose concentrations were measured enzymatically(23). Resting systolic and diastolic blood pressure readings were recorded after 5 minutes of quiet sitting using an OMRON HEM907 Digital Automatic Blood Pressure Monitor (Omron Healthcare Co., Ltd, Kyoto, Japan) with the mean of three recordings used for analysis. Adult waist circumference was measured at the narrow most point between the lower costal border and iliac crest to the nearest 0.1cm using a constant tension tape. A Leicester height measure (Invicta, Leiscester, UK) was used to measure height and Heine scales (Heine, Dover, NH, USA) were used to measure weight in adult clinics. Adult BMI was calculated as weight in kilograms divided by height in meters squared. Participants self-reported medication use and previous physician-diagnosed conditions.

Adult metabolic syndrome and continuous metabolic syndrome score

MetS was determined using the Harmonized definition(2), where MetS is diagnosed when at least three of the following five components are present: waist circumference (male ≥102 cm; female ≥88 cm), fasting plasma glucose (≥5.6 mmol/L [≥100 mg/dL] or drug treatment for elevated blood glucose), serum triglycerides (≥1.7 mmol/L [≥150 mg/dL] or treatment for elevated triglycerides), HDL-C (male <1.03 mmol/L [<40 mg/dL]; female <1.3 mmol/L [<50 mg/dL] or drug treatment for this lipid abnormality) and blood pressure (≥130/85 mmHg or treatment of previously diagnosed hypertension)(2). A continuous metabolic syndrome (cMetS) score was created by aggregating age and sex specific standardized residuals of the five components in MetS (blood pressure, triglyceride, HDL-C, glucose, and waist circumference), as we have previously described(31). The cMetS score was computed from weighted principal components, as described by Wijndaele et al(38), with a higher cMetS score representing a less favorable MetS profile(38).

Statistical analyses

All statistical analyses were performed using Stata (Version 12.1, StataCorp, College Station, Texas).

Demographics

Participant baseline and follow-up characteristics for continuous variables are presented as mean and standard deviation for normally distributed data and as median and interquartile range (25th, 75th percentile) for skewed data. N values and proportions are reported for categorical values.

Loss to follow-up

Comparison of baseline characteristics between participants and non-participants in adulthood was analyzed using t-tests for continuous variables and Chi-squared tests for categorical variables. Where continuous variables were not normally distributed, values were log-transformed prior to analysis with geometric means reported. Non-participants were classified as those who had complete muscular fitness measures in childhood and either did not participate at follow-up or lacked a full set of MetS measures in adulthood.

Childhood muscular fitness and adult metabolic syndrome

Each variable of muscular fitness was categorized into thirds. The relative risk and 95% confidence intervals of dichotomous MetS in adulthood was estimated for each childhood muscular fitness phenotype using Poisson regression with robust errors. Multivariable linear regression was used to determine the relationship between thirds of childhood muscular fitness phenotypes and adult cMetS score. In all analyses the lowest third of each muscular fitness phenotype was used as the reference group. Three multivariable models with successive adjustment were considered. The first model adjusted for childhood age, sex and length to follow-up; the second model adjusted for model one covariates and additionally for childhood CRF; model three adjusted for model two covariates and additionally for childhood waist circumference. Using model three, we additionally considered interactions between muscular fitness phenotypes with age, sex, and CRF by fitting separate multiplicative interaction terms. We found no evidence of significant interaction. The above analyses were repeated for each component of MetS and cMetS. These associations were adjusted for age at baseline, sex, length to follow-up and childhood CRF. For the cMetS component outcome of continuous triglycerides, values were log transformed and geometric means reported, owing to a skewed distribution.

Results

Demographics

Baseline and follow-up characteristics of the 737 participants are presented in Table 1. Mean (SD) length to follow-up was 19.9 (0.6) years, ranging from 18.7-21.0 years. Males tended to have higher fitness phenotypes in childhood. In adulthood, males had a greater prevalence of MetS compared with females, as well as a higher cMetS score.

Loss to follow-up

Participants had on average a longer standing long jump (151.9cm vs 149.1cm, p=0.03) and higher combined muscular fitness score (0.10 vs -0.04, p=0.01) at baseline compared with non-participants (see Table S3, SDC 3). Non-participants had higher measures of BMI (18.8kg/m^2 vs 18.5kg/m^2, p=0.02) and waist circumference (65.6cm vs 64.8cm, p=0.04) and greater proportions of low socioeconomic position (9.5% vs 7.9%, p<0.001) and smokers (15.5% vs 11.9%, p=0.06) compared with participants. No other differences were found between participants and non-participants at baseline.

Childhood muscular fitness and adult metabolic syndrome

Table 2 shows the longitudinal association between childhood muscular fitness phenotypes and dichotomous MetS in adulthood. Participants with higher levels of the combined muscular fitness score, muscular strength, and muscular power in childhood had lower risk of adult MetS independent of CRF (Model 2, highest versus lowest third: fitness score: RR=0.30 (0.14, 0.63), strength: RR=0.39 (0.19, 0.78), power: RR=0.32 (0.15, 0.68)). Although the effect estimates for the combined muscular fitness score, muscular strength, and muscular power remained suggestive of a protective effect, when child waist circumference was included in the model the main effects reduced substantially (range 44-48%) and confidence intervals crossed one.

Similar results were observed for the cMetS score (Table 3). Higher levels of the combined muscular fitness, muscular strength, and muscular power in childhood were associated with a lower adult cMetS score, independent of CRF (Model 2, highest versus lowest third: fitness score: β=-0.45 (-0.58, -0.31), strength: β=-0.39 (-0.52, -0.25), power: β=-0.39 (-0.53, -0.26)), all p-trend<0.001). Although associations remained statistically significant after additional adjustment for child waist circumference (Model 3), the effect estimates were reduced by 49% to 51%.

Supplemental Tables S4 and S5 show associations between the combined child muscular fitness score and components of MetS. When the components were considered as continuous outcomes (see Table S4, SDC 4), the combined childhood muscular fitness score (high versus low) was associated with significantly lower waist circumference (β=-9.44cm, p=<0.001), diastolic blood pressure (β=-2.40mmHg, p=0.004), triglycerides (β=-0.18mmol/L, p=0.002), and higher HDL-C (β=0.07mmol/L, p=0.002) in adulthood. For the association between the combined muscular fitness score in childhood with dichotomous MetS components in adulthood (see Table S5, SDC 5), all associations suggested a protective effect of higher muscular fitness levels in childhood on abnormal adult risk factor levels. However, the only statistical significant effect seen was for waist circumference (high versus low fitness: RR=0.15, (0.08, 0.29).

Sensitivity analyses

To determine whether the association between childhood muscular fitness and adult MetS is independent of adult muscular fitness; adult muscular strength and muscular power (methods presented in SDC 6) were additionally adjusted for. The independent effect remained after adjustment of these adult factors (strength β=-0.19, SE=0.08, p-value=0.02; power β=-0.19, SE=0.08, p-value=0.01). Furthermore, to determine if other childhood measures of MetS beyond waist circumference, systolic and diastolic blood pressure, triglycerides and HDL-C (methodology shown in SDC 6), mitigated the association between the child combined muscular fitness score and adult MetS, we performed a sensitivity analysis that adjusted for these factors in addition to those in Model 3. In this model, the effect for the combined child muscular fitness score changed by less than 10% and remained statistically significant. Moreover, child smoking status and socioeconomic position (methods presented in SDC 6) were adjusted for in addition to Model 3 covariates. Though potential confounders, these additional covariates were not included in model one as these variables were missing for a proportion of our sample. It was found that additional adjustment for child smoking status and socioeconomic position did not further reduce the effect estimate for both the dichotomous and continuous MetS outcomes. To account for differential loss to follow-up in the combined muscular fitness score, waist circumference, and SES that was observed in Table S3, we performed inverse propensity weighting as a sensitivity analysis to determine the likely effect on our reported findings. The weighted analysis returned a regression coefficient about 10% lower (β=-0.20, SE=0.07), however the results remained statistically significant (p-value=0.006).

Discussion

Our results address a current gap in the literature by showing that higher childhood levels of muscular strength, muscular power and a combined muscular fitness score are associated with a reduced risk of dichotomous MetS and lower cMetS score in adulthood, independent of CRF. However, upon additional adjustment for waist circumference, the strength of the observed associations were reduced by half. These results suggest that childhood waist circumference is a potential mediator of the association between childhood muscular fitness and both adult MetS outcomes, although the possibility that it is a confounder may also be true.

However, there is biological plausibility to suggest childhood waist circumference is mediating part of the effect of child muscular fitness on adult MetS outcomes via an indirect pathway of increased child muscular fitness leading to decreased child adiposity that is subsequently reducing adult MetS. This plausible mechanism is substantiated by our previous cross-sectional results in the childhood sample where muscular fitness phenotypes were inversely and independently related with waist circumference and BMI(24) as well as findings from intervention studies showing improvements to body composition among overweight and obese youth who underwent resistance training(32). The link between child adiposity and adult MetS is well substantiated(25, 33), including previous data from CDAH that showed childhood waist circumference to be the strongest predictor of adulthood dichotomous MetS, with these associations remaining independent of changes in waist circumference that had occurred between childhood and adulthood(31). Our sensitivity analyses suggested that the remaining effect is not being mediated through adult muscular fitness levels or other childhood MetS risk factors in blood pressure and blood lipids. That child blood pressure and blood lipids are not mediating the association is no surprise given previous research found limited associations between muscular fitness phenotypes and these measures independent of BMI(24) and findings from the Bogalusa and Cardiovascular Risk in Young Finns studies(21) that showed child BMI to be as good a predictor of adult dichotomous MetS as child MetS status, plus other child MetS risk factors including blood pressure and lipids(21). Therefore, the remaining effect we observed may be mediated by other, unmeasured factors or represents a direct independent effect of child muscular fitness.

The mechanism responsible for the remaining effect is unknown, however pathways can be hypothesized with potential links via insulin-stimulated glucose uptake and whole-body energy expenditure, through skeletal muscle glucose and triglyceride metabolism(36). Increased muscular fitness via resistance training has been shown to result in skeletal muscle growth and hypertrophy(1) and increased insulin sensitivity(13). However, this enhanced skeletal muscle insulin sensitivity resultant from resistance training is likely to be independent of muscle mass increases(13). The biological mechanism behind the positive effect of resistance training may be attributable to proteins in the insulin-signaling cascade(13), providing a rationale as to how muscular fitness, insulin sensitivity and decreased MetS risk may be linked.

Previous results from cross-sectional childhood data in this and other cohorts have shown childhood muscular fitness to associate with lower CVD and metabolic risk, independent of childhood BMI and CRF(24, 35). The study by Magnussen et al also showed an interaction whereby the greatest effect of muscular power on clustered CVD risk was observed among those with the lowest CRF(24). This observation was not observed in our longitudinal analyses whereby muscular fitness and CRF appear to act independently on both MetS outcomes. Similar results were observed in cross-sectional analyses of adults in the Aerobics Centre Longitudinal Study (ACLS) cohort, where a muscular strength score had independent and joint inverse associations with CRF for dichotomous MetS(16). Furthermore, longitudinal findings from the ACLS cohort showed that the association between adult muscular strength and dichotomous MetS remained, yet was strongly reduced, when accounting for CRF(15). In the only other longitudinal study spanning childhood to adulthood, data from the European Youth Heart Study suggest childhood muscular strength (baseline age of 15 years) is associated with a modifiable CVD risk score in young adulthood (follow-up age=21-27 years) independent of both waist circumference and CRF(12). Although these results gave insight into the independent effect childhood muscular strength had on cardiometabolic outcomes, its effect on MetS was unable to be examined owing to low case numbers. Our current study expands on this existing literature by involving a longitudinal cohort with a long follow-up period, a greater sample size, and younger age at baseline. Furthermore, an expanded range of muscular fitness phenotypes was considered, whilst importantly looking at MetS risk via two MetS outcomes exclusively. Nevertheless, the key theme amongst these previous findings as well as our own, is that an association between muscular fitness phenotypes and cMetS score, dichotomous MetS or other cardiometabolic outcomes remains but is reduced upon further adjustment for a measure of adiposity or CRF.

Muscular conditioning activities in childhood have been advocated in the most recent physical activity guidelines(40). For children, these guidelines state that in addition to aerobic exercise, activities that aim to strengthen muscle and bone should be performed ≥3 days per week. In adults, muscle-strengthening activities that involve major muscle groups should be performed on ≥2 days each week(40). Consistent with these recommendations our results show some benefit of higher muscular fitness independent of CRF, thus reinforcing the importance of activities that promote muscular fitness in addition to increased CRF to reduce MetS risk in adulthood and improve one's cardiometabolic health profile.

The strengths of this study include the long follow-up period of a large national sample. Moreover, this study included a complete and diverse set of muscular fitness phenotypes. The validity of field-based measures of muscular fitness phenotypes has been the subject of previous systematic reviews(4, 6). Comparisons of field- and clinic-based measures in youth have found the field-based measures of handgrip strength(6) and standing long jump are valid tests of muscular strength and power(4). As these measures were collected in the CDAH study, they appear appropriate to test muscular fitness in childhood. Furthermore, the ability to assess the longitudinal association between childhood muscular fitness on two adult MetS outcomes, in the dichotomous and continuous definition, is a key strength in this study helping expand the application of these findings. Whereby, the dichotomous definition is clinically relevant and accepted, yet the cMetS score provides a more statistically powerful quantitative score, representing a continuum of metabolic risk(38).

Despite the strengths of this study, there were also limitations. These include some differential loss to follow-up whereby non-participants had lower combined muscular fitness, higher adiposity, and were of lower SES than participants. Upon further analysis that weighted on these factors, these differences resulted in a slight overestimation of the effect in our results, though statistical significance remained. Furthermore, due to the observational study design, one must consider the effects of unmeasured and residual confounding. This study implies that at baseline, children with increased muscular fitness engaged in more muscular conditioning activities, however we do not have data in support of this. Variations existed in our results with inconsistencies of statistical significance between MetS outcomes; these could be explained by the loss of statistical power associated with dichotomizing continuous variables(38). A weak or no effect for muscular endurance was observed in our analyses. These results may reflect a less important role of child muscular endurance for adult MetS outcomes but may have also been subject to increased measurement error compared with our other measures of muscular fitness, with questions raised in previous systematic reviews on the reliability of this measure(6).

In conclusion, these findings suggest that childhood muscular fitness predict adult MetS outcomes independently of childhood CRF, and approximately 50% of this effect is potentially mediated through childhood waist circumference. These results suggest that increased childhood muscular fitness protects against adult MetS and exercise that improves muscular fitness in combination with CRF might further reduce MetS risk in young adulthood.

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Conflict of interest

The authors declare no conflict of interest.

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Figure Legends

Figure 1. Participant flow chart for this study.

Supplementary Digital Content

Supplemental Digital Content 1.docx

Supplemental Digital Content 2.docx

Supplemental Digital Content 3.docx

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Tables

Table 1. Characteristics of participants at baseline and follow-up.

	Sex	
	Male	Female
Characteristic	Statistic	Statistic
n	361	376
Childhood		
Age, years	12.0 (2.4)	11.9 (2.5)
Right grip strength, kg	26.0 (10.7)	20.9 (6.6)
Left grip strength, kg	25.4 (10.7)	20.1 (6.3)
Shoulder flexion, kg	21.4 (14.2)	18.2 (8.9)
Shoulder extension, kg	17.8 (9.5)	13.8 (6.0)
Leg strength, kg	118.3 (60.0)	83.4 (34.5)
Standing long jump, cm	161.8 (31.6)	142.2 (23.4)
Push-ups, No.	13.9 (6.3)	7.3 (5.7)
Combined muscular fitness score	0.00 (1.24)	0.00 (0.94)
Cardiorespiratory fitness, PWC170, watts	109.5 (44.5)	77.3 (27.8)
Height, cm	153.3 (15.8)	149.6 (13.1)
Systolic blood pressure, mmHg	110.1 (13.1)	108.1 (12.3)
Diastolic blood pressure, mmHg	77.9 (11.9)	78.3 (12.0)

Triglycerides, mmol/L		0.64 (0.50-0.84)	0.64 (0.52-0.83)
HDL-C, mmol/L		1.44 (0.29)	1.50 (0.29)
Weight, kg		44.7 (14.5)	42.5 (12.1)
BMI, kg/m^2		18.5 (2.8)	18.6 (2.9)
Waist circumference, cm		66.3 (8.5)	63.3 (8.1)
Socioeconomic position, %			
	Low	31 (8.9)	25 (6.8)
	Middle	206 (59.4)	229 (62.6)
	High	110 (31.7)	112 (30.6)
Smoking status, %			
	Non-smoker	316 (89.5)	319 (86.7)
	Smoker	37 (10.5)	49 (13.3)
Adulthood			
Age, years		31.9 (2.5)	31.8 (2.6)
Metabolic syndrome, %		36 (10.0)	12 (3.2)
cMetS score		0.05 (0.69)	0.01 (0.75)
Right grip strength, kg		48.8 (7.5)	30.0 (5.1)
Left grip strength, kg		47.1 (7.8)	28.3 (5.1)
Shoulder flexion, kg		50.3 (13.2)	26.0 (7.5)
Shoulder extension, kg		40.9 (10.4)	21.3 (7.2)

Leg strength, kg	168.8 (37.5)	91.5 (29.0)
Muscular strength score	0.00 (1.25)	0.00 (0.89)
Standing long jump, cm	188.1 (25.1)	134.5 (27.2)
Systolic blood pressure, mmHg	125.7 (11.0)	111.3 (10.3)
Diastolic blood pressure, mmHg	75.6 (8.9)	70.5 (8.6)
HDL-C, mmol/L	1.29 (0.27)	1.54 (0.32)
Triglycerides, mmol/L	1.10 (0.70-1.60)	0.80 (0.60-1.10)
Glucose, mmol/L	5.20 (0.40)	4.80 (0.40)

Mean (SD) or median (interquartile range) for continuous variables or n (proportions) for categorical variables.
Abbreviations: PWC170, physical working capacity at 170 beats per minute; BMI, body mass index; cMetS, continuous metabolic syndrome score; HDL-C, high-density lipoprotein cholesterol.

Table 2. Multivariable associations between childhood muscular fitness phenotypes and adult metabolic syndrome.

		Model 1		Model 2		Model 3	
Childhood muscular fitness measure	n/N	RR	95% CI	RR	95% CI	RR	95% CI
Muscular strength							
Lowest third	25/235	1	REF	1	REF	1	REF
Middle third	9/231	0.39	0.19-0.82	0.41	0.20-0.86	0.73	0.32-1.65
Highest third	11/233	0.36	0.18-0.73	0.39	0.19-0.78	0.71	0.32-1.56
p_{trend}		*0.004*		*0.007*		*0.39*	
Muscular endurance							
Lowest third	16/230	1	REF	1	REF	1	REF
Middle third	15/235	0.87	0.45-1.71	0.91	0.47-1.76	1.61	0.81-3.19
Highest third	14/234	0.70	0.35-1.41	0.72	0.36-1.44	1.27	0.64-2.54

p_{trend}			*0.32*		*0.35*		*0.49*
Muscular power							
Lowest third	24/230	1	REF	1	REF	1	REF
Middle third	11/233	0.40	0.20-0.81	0.42	0.21-0.83	0.65	0.31-1.35
Highest third	10/236	0.30	0.14-0.64	0.32	0.15-0.68	0.62	0.27-1.45
p_{trend}			*0.002*		*0.003*		*0.25*
Combined muscular fitness score							
Lowest third	27/234	1	REF	1	REF	1	REF
Middle third	8/229	0.31	0.14-0.67	0.33	0.15-0.71	0.52	0.22-1.20
Highest third	10/236	0.28	0.14-0.59	0.30	0.14-0.63	0.54	0.24-1.25
p_{trend}			*0.001*		*0.001*		*0.14*

Model 1 is adjusted for childhood age, sex and length to follow-up; Model 2 adjusted for model 1 covariates and additionally for childhood CRF; Model 3 adjusted for model 2 covariates and additionally for childhood waist circumference.
Abbreviations: CRF, cardiorespiratory fitness; RR, relative risk; CI, confidence intervals.

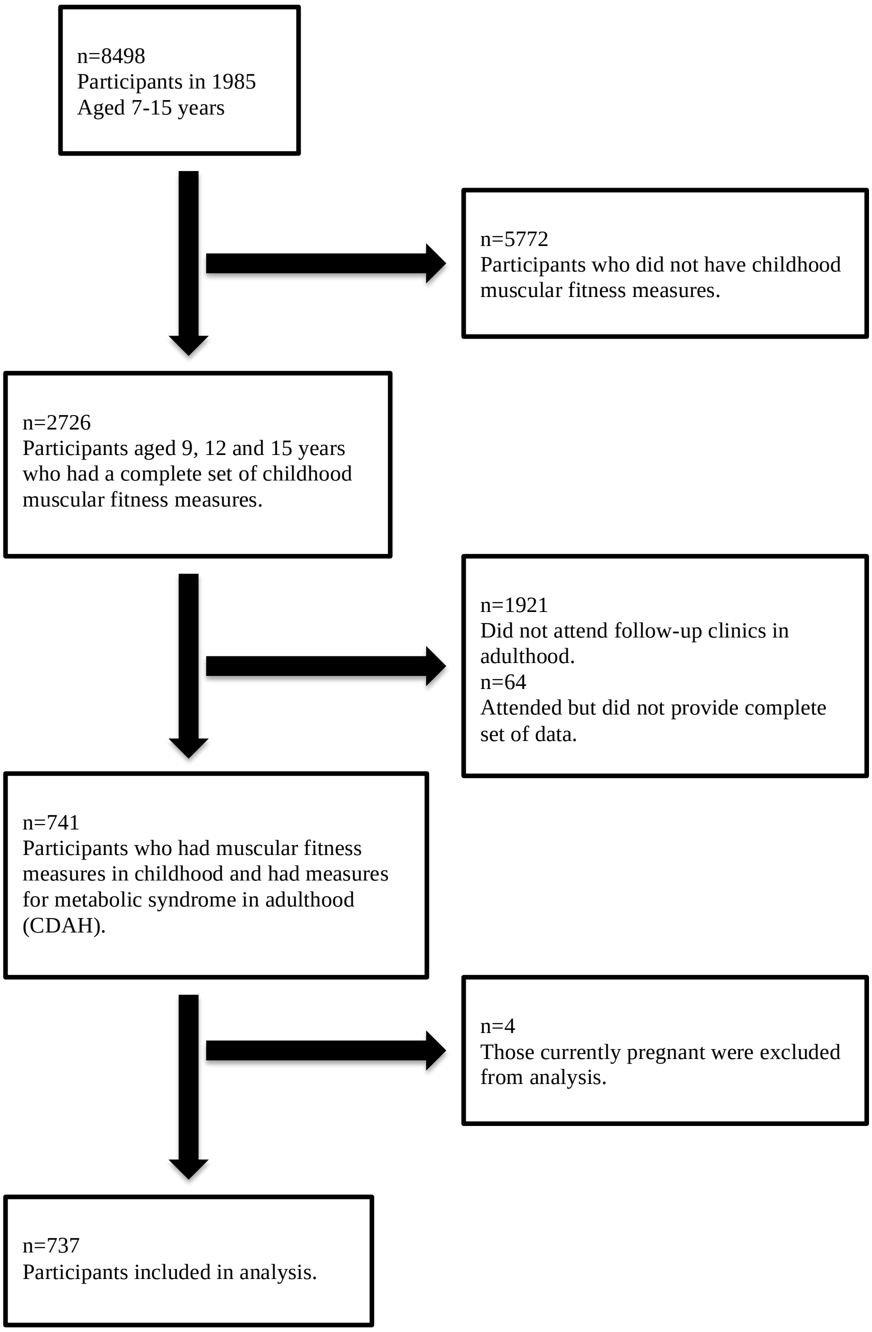
Table 3. Multivariable associations between childhood muscular fitness phenotypes and adult continuous metabolic syndrome score.

		Model 1			Model 2			Model 3		
Childhood muscular fitness measure	n	β	SE	p-value	β	SE	p-value	β	SE	p-value
Muscular strength										
Lowest third	235	0	REF	REF	0	REF	REF	0	REF	REF
Middle third	231	-0.22	0.06	0.001	-0.23	0.07	<0.001	-0.05	0.07	0.44
Highest third	233	-0.37	0.07	<0.001	-0.39	0.07	<0.001	-0.19	0.07	0.007
p_{trend}			*<0.001*			*<0.001*			*0.007*	
Muscular endurance										
Lowest third	230	0	REF	REF	0	REF	REF	0	REF	REF
Middle third	235	-0.05	0.07	0.43	-0.05	0.07	0.42	0.05	0.06	0.46
Highest third	234	-0.12	0.07	0.08	-0.12	0.07	0.08	0.02	0.06	0.80

p_{trend}			*0.08*			*0.08*			*0.81*	
Muscular power										
Lowest third	230	0	REF	REF	0	REF	REF	0	REF	REF
Middle third	233	-0.24	0.07	<0.001	-0.24	0.07	<0.001	-0.11	0.06	0.09
Highest third	236	-0.39	0.07	<0.001	-0.39	0.07	<0.001	-0.20	0.07	0.005
p_{trend}			*<0.001*			*<0.001*			*0.005*	
Combined muscular fitness score										
Lowest third	234	0	REF	REF	0	REF	REF	0	REF	REF
Middle third	229	-0.24	0.06	<0.001	-0.25	0.06	<0.001	-0.09	0.07	0.20
Highest third	236	-0.43	0.07	<0.001	-0.45	0.07	<0.001	-0.23	0.07	0.001
p_{trend}			*<0.001*			*<0.001*			*0.001*	

Model 1 is adjusted for childhood age, sex and length to follow-up; Model 2 adjusted for model 1 covariates and additionally for childhood CRF; Model 3 adjusted for model 2 covariates and additionally for childhood waist circumference.
Abbreviations: CRF, cardiorespiratory fitness; β, regression coefficient; SE, standard error.

Figures


n=8498
Participants in 1985
Aged 7-15 years
n=5772
Participants who did not have childhood muscular fitness measures.
n=2726
Participants aged 9, 12 and 15 years who had a complete set of childhood muscular fitness measures.
n=1921
Did not attend follow-up clinics in adulthood.
n=64
Attended but did not provide complete set of data.
n=741
Participants who had muscular fitness measures in childhood and had measures for metabolic syndrome in adulthood (CDAH).
n=4
Those currently pregnant were excluded from analysis.
n=737
Participants included in analysis.

Supplementary Digital Content 1

Table S1. Factor loadings from principal components factor analysis to derive the child muscular strength variable.

Childhood muscular strength component	Factor 1
Left grip strength	0.459
Right grip strength	0.459
Shoulder pull	0.446
Shoulder push	0.439
Leg strength	0.432
Total variance explained, %	87.6

Supplementary Digital Content 2

Table S2. Factor loadings from principal components factor analysis to derive the childhood combined muscular fitness variable.

Childhood combined muscular fitness component	Factor 1
Left grip strength	0.420
Right grip strength	0.420
Shoulder pull	0.407
Shoulder push	0.397
Leg strength	0.397
Push-ups	0.194
Standing long jump	0.360
Total variance explained, %	73.3

Supplementary Digital Content 3

Table S3. Comparison of baseline characteristics of participants and non-participants.

Characteristic	Non-Participants Statistic	Participants Statistic	p-value
n	1989	737	
Age, years	11.8 (2.4)	11.9 (2.5)	0.30
Male sex, %	1023 (51.4)	361 (49.0)	0.26
Right grip strength, kg	23.0 (8.8)	23.4 (9.2)	0.33
Left grip strength, kg	22.3 (8.5)	22.7 (9.1)	0.32
Shoulder flexion, kg	18.9 (11.5)	19.8 (11.9)	0.07
Shoulder extension, kg	15.6 (8.2)	15.7 (8.2)	0.76
Leg strength, kg	98.5 (47.3)	100.5 (51.7)	0.34
Standing long jump, cm	149.1 (28.9)	151.9 (29.4)	0.03
Push-ups	10.4 (7.0)	10.5 (6.9)	0.74
Combined muscular fitness score	-0.04 (1.22)	0.10 (1.12)	0.01
Cardiorespiratory fitness (PWC170, watts)	91.0 (37.3)	93.2 (40.4)	0.20
Height, cm	150.2 (14.2)	151.4 (14.6)	0.06
Weight, kg	43.5 (13.2)	43.6 (13.4)	0.92
BMI, kg/m^2	18.8 (3.0)	18.5 (2.8)	0.02

Waist circumference, cm	65.6 (8.9)	64.8 (8.4)	0.04
Socioeconomic position, %			
Low	183 (9.5)	56 (7.9)	<0.001
Middle	1326 (68.8)	43.5 (61.0)	
High	417 (21.7)	222 (31.1)	
Smoking status, %			
Non-smoker	1640 (84.5)	635 (88.1)	0.06
Smoker	300 (15.5)	86 (11.9)	

Mean (SD) for continuous variables or n (proportions) for categorical variables. P-value represented by a two-sample t test for continuous variables and Chi-squared test for categorical variables.
Abbreviations: PWC170, physical working capacity at 170 beats per minute; BMI, body mass index.

Supplementary Digital Content 4

Table S4. The association between metabolic syndrome components in adulthood and childhood muscular fitness levels.

	Child muscular fitness*									
	Low			Moderate			High			
Characteristic in adulthood	β	SE	p-value	β	SE	p-value	β	SE	p-value	p_{trend}
Waist circumference (cm)	0	REF	REF	-5.42	0.97	<0.001	-9.44	1.00	<0.001	*<0.001*
Systolic blood pressure (mmHg)	0	REF	REF	-1.87	1.00	0.06	-1.01	1.04	0.33	*0.32*
Diastolic blood pressure (mmHg)	0	REF	REF	-2.92	0.82	<0.001	-2.40	0.85	0.005	*0.004*
HDL-C (mmol/L)	0	REF	REF	0.05	0.03	0.11	0.07	0.03	0.01	*0.01*
Triglycerides (mmol/L)	0	REF	REF	-0.09	0.06	0.10	-0.18	0.06	0.002	*0.002*
Blood glucose (mmol/L)	0	REF	REF	0.01	0.04	0.74	-0.07	0.04	0.07	*0.07*

* Adjusted for age at baseline, sex, length to follow-up and childhood CRF.
Abbreviations: β, regression coefficient; SE, standard error; HDL-C, high-density lipoprotein cholesterol.

Supplementary Digital Content 5

Table S5. Relative risk of meeting abnormal levels of metabolic syndrome components in adulthood based on childhood muscular fitness levels.

	Child muscular fitness*									
	Low			Moderate			High			
Characteristic in adulthood	n/N	RR	95% CI	n/N	RR	95% CI	n/N	RR	95% CI	p_{trend}
Waist circumference (cm)	59/234	1	REF	34/229	0.54	0.37-0.78	11/236	0.15	0.08-0.29	*<0.001*
Blood pressure (mmHg)†	67/234	1	REF	44/229	0.73	0.53-1.01	54/236	0.76	0.56-1.04	*0.08*
HDL-C (mmol/L)	70/234	1	REF	61/229	0.88	0.66-1.18	52/236	0.73	0.52-1.02	*0.06*
Triglycerides (mmol/L)	43/234	1	REF	29/229	0.74	0.48-1.13	29/236	0.65	0.41-1.01	*0.05*
Blood glucose (mmol/L)	18/233	1	REF	21/229	1.21	0.67-2.18	26/236	1.16	0.67-2.00	*0.60*

*Adjusted for age at baseline, sex, length to follow-up and childhood CRF.
† Noted as having either elevated systolic and/or elevated diastolic blood pressure.
Abbreviations: RR, relative risk; CI, confidence intervals; WC, waist circumference; HDL-C, high density lipoprotein cholesterol.

Supplementary Digital Content 6

Supplementary Methods

Adult muscular fitness measures

Measurements of muscular strength and power in adulthood were performed using the same protocols as those performed in childhood. Muscular endurance was not measured in adulthood.

Muscular strength was measured from five sites in adulthood; right and left grip, shoulder flexion and extension, and leg strength using isometric dynamometers (Smedley's Dynamometer, TTM, Tokyo, Japan). The maximum of two attempts for each strength measure was used in the analysis. Right and left grip strength was measured as participants held the dynamometer with one hand, and gripped with maximum force whilst the dynamometer was supported on the opposite shoulder. Shoulder strength (flexion and extension) was measured as participants held the dynamometer in front of their chest with both hands parallel to the ground. For shoulder extension, participants pulled with maximum force, and for shoulder flexion, participants pushed with maximum force aiming to get their hands as far apart (extension) or close together (flexion) as possible. To measure leg strength, participants stood on the leg-back dynamometer base plate with their body flat against a wall behind them. A bar was held with an overhand grip, knees were flexed at an angle of 115°, at which point the bar was attached to the dynamometer by a chain. The bar was then pulled up as far as possible by moving their body upwards, maintain contact with the wall at all times during the effort. These strength measures were combined via principal component analysis. This combined adult strength measure was estimated via the first principal component of the five adult muscular strength measurements(4).

Muscular power was measured in adulthood as the distance in centimetres of a standing long jump. This test was repeated twice and required a two-footed take off. The attempt with the best resulting distance was used in the analysis.

Each adult muscular fitness phenotype (strength and power), was adjusted for total body weight (by regressing body weight on each phenotype and using the residuals) and standardised for age and sex. This was performed to create adult muscular fitness measures uncorrelated with body weight(4).

Childhood measures of metabolic syndrome

At baseline, a 15ml blood sample was collected from children aged 9, 12 and 15 years who had observed a 12-hour fast. From this blood sample, plasma triglycerides were determined according to the Lipids Research Clinic Program(1). HDL-C was analysed following precipitation of apolipoprotein-B containing lipoproteins with heparin-manganese(3).

Childhood resting blood pressure readings were recorded from the left brachial artery after participants had been seated quietly for 10 minutes using a mercury sphygmomanometer. Appropriately sized arm cuffs were selected. Korotkoff sounds I and IV were used to denote systolic and diastolic blood pressures respectively. This procedure was repeated twice, with the mean of the two measures taken.

Childhood smoking status

Childhood smoking status was ascertained from self-report in isolation from parents and teachers. Those who indicated “I don’t smoke” were classified as non-smokers and those who indicated any of the remaining responses (just started, 1-6 months, 7-12 months, 1-2 years, 2-4 years, >4 years) were defined as smokers.

Childhood socioeconomic position

Socioeconomic position at baseline was derived from residential postcode, using the Australian Bureau of Statistics Socio-economic Index for Areas (SEIFA) and 1981 census data; further details are described elsewhere(2). These postcodes were classified into four categories (low, medium-low, medium-high and high). In this study, the two medium categories have been combined and childhood SES is classified as either low, medium or high.

References:

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