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The association of adolescent fitness with cardiometabolic diseases in late adulthood: A 45-year longitudinal study

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Abstract

Objectives: The aim of this study was to examine the associations of adolescent cardiorespiratory fitness (CRF), muscular fitness (MF), and speed-agility fitness (SA) with middle-aged cardiometabolic disease risk and explore sex differences.

Methods: This 45-year prospective cohort study examined the associations between objectively measured fitness at adolescence (12–19 years) and physician-ascertained diabetes mellitus, elevated blood pressure (BP), and coronary heart disease reported either in early (37–44 years) or late (57–64 years) middle age, and self-measurement of waist circumference (WC) in late middle age. Fitness measurements for healthy adolescents in baseline included CRF (1.5 km [girls] and 2 km [boys] run), MF (standing broad jump, sit-ups, pull-ups [boys], and flexed-arm hang [girls]), and SA (50 m dash and 4 × 10 m shuttle run). Logistic regression and general linear models were adjusted for baseline age, sex, and body mass index (BMI), involving data from baseline and at least one follow-up measurement (N up to 1358, 47% males).

Results: Adolescent CRF was inversely, and regardless of adiposity, associated with middle age accumulated burden of cardiometabolic conditions in the whole sample ($N = 562$, $\beta = -0.10$, 95% confidence intervals [CI] [−0.18, −0.03], $p = 0.006$), and elevated BP in females ($N = 256$, OR = 0.71, 95% CI [0.51, 0.91]). Overall, we observed stronger associations in females than in males. An inverse association of adolescent MF and SA with middle-aged WC was observed, but it did not show as consistent associations as with CRF.

Conclusions: In this study, adolescent fitness, particularly CRF, was inversely associated with the burden of cardiometabolic conditions up to 45 years. Promotion of fitness in youth may be beneficial in preventing adulthood cardiometabolic diseases.

KEYWORDS

adolescence, cardiometabolic disease, cohort study, longitudinal, physical fitness

1 | INTRODUCTION

Health-related physical fitness is an important component in the prevention of cardiometabolic diseases (CMD).[1–6] It can be divided into components of cardiorespiratory fitness (CRF), musculoskeletal fitness (MF), flexibility, and body composition[7] but does not include components such as speed and agility (SA), probably because only a few previous studies have investigated the associations of SA with health outcomes in the past. Evidence indicates that both CRF and MF in adulthood are inversely associated with cardiovascular disease (CVD),[2,4–6,8,9] metabolic syndrome (MetS),[4,10] and diabetes mellitus (DM),[11,12] and that this association generates already in youth.[13,14] Results concerning these associations in the youth–adulthood transition are more uncertain.

CMD refers to conditions sharing the same risk factors: overweight, obesity, dyslipidemia, and elevated blood pressure (EBP). CMDs vary in terms of severity, beginning with insulin resistance progressing to CVD and type 2 DM (T2DM).[15,16] Body composition measures – body mass index (BMI; kg/m^2), waist circumference (WC), and waist-to-hip circumference ratio – are strong risk factors for CMD.

In addition to the well-known link between CRF and CMD in adults,[1–6,11,17] evidence suggests that CRF in adolescence may have prognostic value for cardiometabolic health in adulthood.[18–22] However, there are also conflicting findings.[23,24] Several studies indicate that higher childhood/adolescent CRF is associated with lower risk for CVD mortality[21] and morbidity,[19,22,25,26] T2DM,[18] MetS[27] and the risk factors such as high BP,[22,28] central obesity,[22] adverse glucose metabolism[20,22,28] and blood lipid profile[22,28] in young adulthood (21–27 years) and middle age (35–64 years). Whether these associations are stronger in males than in females, vice versa, or equal is not clear. Two studies reported similar associations in males and females,[20,22] whereas one study, although conducted using an indirect CRF assessment, indicated a stronger association for females.[28] The largest and longest duration cohorts[18,19,21,25] included only male participants, underlining the need for long-duration follow-ups involving males and females. The results have remained concordant regardless of the study design, CRF measurement method (indirect VO^2_{max} or field test), the baseline age (7–18 years), and the length of follow-up (6–46 years) although the association tended to wane as the follow-up time is extended.[23,27]

The evidence concerning youth MF's association with adulthood cardiometabolic health is more uncertain, even though MF has been shown to be associated with lower CMD morbidity and mortality[9,29] in adulthood. Longitudinal inverse associations have been reported between adolescent MF and adult chronic disability due to CVD,[26] risk for premature death due to CVD,[30] incidence of T2DM,[18] strokes,[19] and risk factors for CMD.[20,31–33] However, two of the studies[32,33] reported conflicting findings and three[18,19,26] found adolescent MF to be less influential on future CVD and T2DM than CRF is. No association for adulthood ischemic heart disease was detected in Crump et al.[25] MF in these studies has been ascertained with relative[31,32] and absolute strength tests.[18–20]

Despite evidence of the association between adolescent fitness and adulthood metabolic health, studies with an objective baseline fitness measurement involving males and females in their late middle age are scarce. Moreover, as previous literature has focused on CRF and MF as the main fitness components, studies concerning SA's role in subsequent health are lacking. To our knowledge, this study is the first to follow its participants in both sexes from adolescence up to age 57–64 years in terms of CRF, MF, and SA and their association with health. This is important since the length of follow-up might be a moderator of the association.[23,27] Additionally, extended longitudinal investigation is justifiable as the prevalence of cardiometabolic conditions increases along with age.[30,31]

2 | METHODS

2.1 | Study population

This study is based on the LISE follow-up project launched in April–May 1976, and it includes three measurements: the baseline in 1976 including objectively measured fitness tests and a physical activity (PA) questionnaire; the first follow-up in 2001 including a postal questionnaire; the second follow-up in 2021 including a postal questionnaire and WC self-measurement. At baseline, we used a stratified random sampling, recruiting 56 schools from eastern, western, central and northern Finland, including urban and rural districts. Classes at school were selected randomly and the pupils were drawn either in alphabetical order or by selecting every second or third. The original baseline sample consisted of 9–21-year-old children and adolescents, of which 12–19-year-old adolescents (mean age 14.9) with eligible PF test data were qualified for the final sample (N max = 1794). The first follow-up in 2001 consisted of 1196 (67% of the baseline) participants, then aged 37–44 years, providing eligible baseline PF test data and the first follow-up CMD assessment data. The second follow-up in 2021 consisted of 768 participants (43% of the baseline), then aged 57–64 years, with eligible data from the baseline PF tests and the

second follow-up CMD assessment. LISE-project study population and data acquisition in detail are presented in Laakso et al.[36]

Participants with eligible baseline PF test data and at least one of the follow-ups qualified for the longitudinal analyses and the exact number of participants in each analysis varied from 341 to 1358 depending on the association studied, that is, available data for each pair of variables examined. The variation was due to the uneven number of test results at baseline, responses per question in the follow-up questionnaires, and the overall number of participants between the two follow-ups. A flow chart of the data structure is presented in Figure 1, and the exact *N* of each analysis is in Tables 3–5 and Tables S3–S5.

2.2 | Assessment of physical fitness

The fitness tests, based on International Fitness Test guidelines,[37] in 56 schools in April–May 1976 were conducted by a trained research team using a consistent measurement protocol. All participants performed an identical warm-up routine and their height (cm) and weight (kg) were measured objectively by a school health care professional. CRF was measured with a 2000-/1500-m run; MF with standing broad jump, sit-ups, and pull-ups/flexed arm hang; and SA with a 50-m dash and a 4×10-m shuttle run. Cronbach's alpha for MF was 0.709 and for SA 0.689. For detailed descriptions of the tests, see Table S1. The test scores were subsequently adjusted for age and sex by calculating z-scores for each age group in both sexes separately.

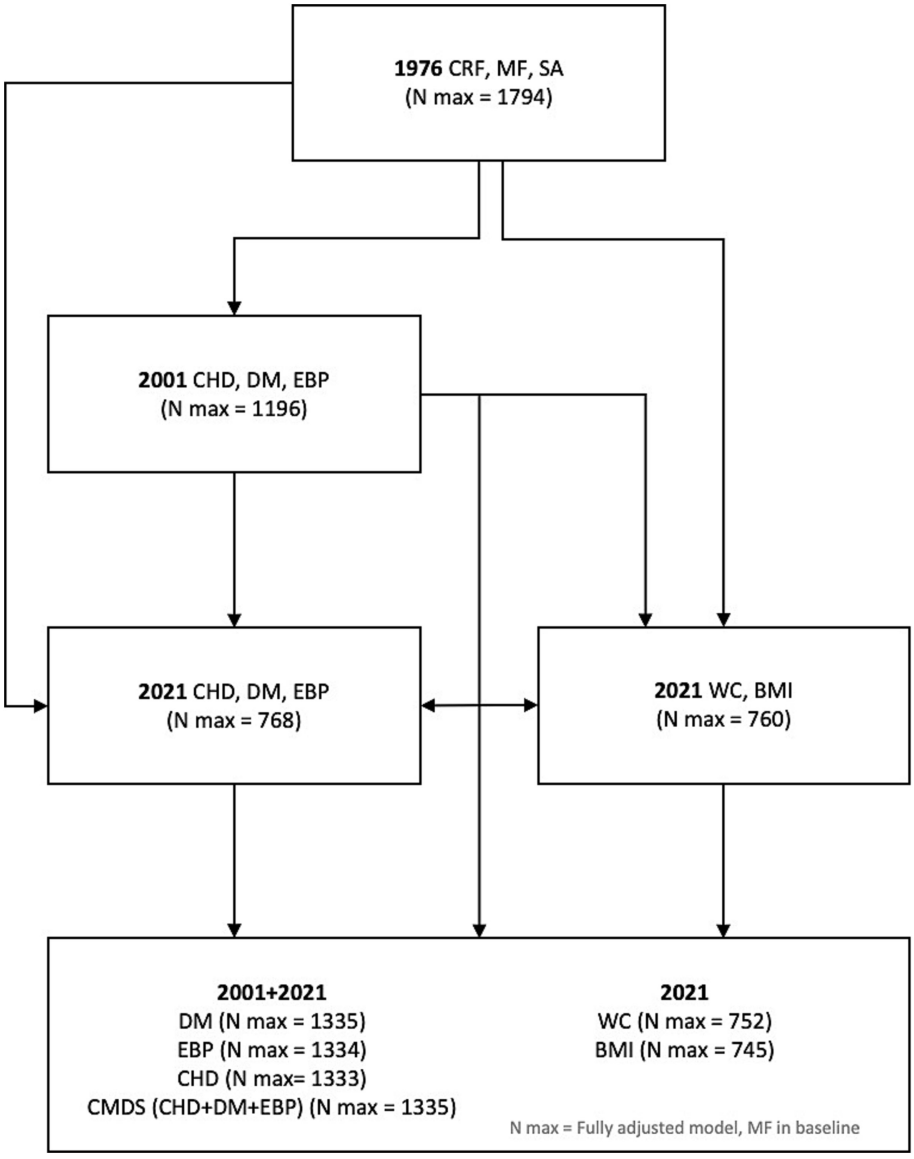

FIGURE 1 The data structure of the longitudinal analyses. BMI, body mass index; CHD, coronary heart disease; CMDS, cardiometabolic disease score; CRF, cardiorespiratory fitness; DM, diabetes mellitus; EBP, elevated blood pressure; MF, muscular fitness; SA, speed-agility; WC, waist circumference.

2.3 | Assessment of physical activity

PA was self-reported by the participants at the second follow-up in March 2021. To eliminate the impact of COVID-19 and follow social contact restrictions, the participants were asked to assess their PA behavior concerning time before the pandemic. MET-hours/day value was calculated from the reported frequency, duration, and intensity of PA. Detailed information on the PA questionnaire used is presented elsewhere.[36]

2.4 | Ascertainment of cardiometabolic health

CMD and related risk factors were investigated by the following indicators: (1) EBP, ≥140/90 mmHg, ascertained by health care professional; (2) coronary heart disease (CHD) ascertained by a physician; (3) DM ascertained by a physician, diagnosed at the age of 25 years or later; (4) BMI (kg/m^2); (5) WC (cm). Indicators 1–3 were determined by a self-reported (physician-diagnosed) structured postal follow-up questionnaire in 2001 and 2021, including identical questions. The questions were designed for the LISE project but derived mainly from a FinHealth survey.[38] The health conditions (1–3) were asked in the following way: "Have you ever been diagnosed with a [condition] which has been ascertained by a physician?" (yes/no). For EBP, participants reporting "ascertained to be >140/90 mmHg" qualified and those reporting "not measured"," not sure if measured" and "ascertained to be <140/90 mmHg" were removed. BMI was computed from self-reported height (cm) and weight (kg). To investigate the incidence of cardiometabolic conditions in middle age, data from the first and the second follow-up was amalgamated regarding the identically measured indicators 1–3 (Figure 1). Finally, a cardiometabolic disease score variable (CMDS) with a scale of 0–3 was calculated as a sum of EBP, CHD, and DM diagnoses to investigate the accumulated burden of the conditions. WC measurement was conducted by a self-measurement in 2021 alongside the postal questionnaire. A measurement tape, with pictorial and verbal instructions (Table S2), was sent to the participants to conduct the measurement.

2.5 | Statistical analyses

Analyses were conducted with IBM SPSS (version 28.0.0.0). Continuous composite variables for SA were computed from the 50-m dash and the shuttle run z-scores, and for MF from the broad jump, sit-ups and pull-ups/flexed arm hang z-scores. Z-scores from the 1500-/2000-m run were used as such as a continuous CRF variable. Categorized variables were formed by dividing the continuous variable into tertiles: low, average, and high.

To investigate the associations of continuous and categorized CRF, MF, and SA with continuous CMDS, WC, and BMI, a general linear model (GLM) with adjustment for baseline age and BMI was conducted. GLM parameter estimates were bootstrapped to increase confidence in data representativeness. To investigate the associations of continuous and categorized CRF, MF, and SA with dichotomic CMDS, DM, EBP, and CHD, logistic regression analysis with adjustment for baseline age and BMI was used. Odds ratios with 95% confidence intervals (CI) were calculated to indicate risk differences for CMD indicators in middle age according to adolescent fitness. In addition, relative risks were calculated for analyses using categorized exposures and dichotomic outcomes. Interaction effect with sex was tested in all analyses. In the exploratory analyses, we tested the effect of additional adjustment for PA at the end point (2021).

3 | RESULTS

The descriptive statistics of the participants involved in the between-measurement analyses are presented in Table 1. Sex-stratified prevalence of CMD in participants involved in between-measurement analyses reported at either the follow-up 1 or 2, is presented in Table 1.

Baseline CRF, MF, and SA z-scores between dropouts and non-dropouts were evaluated using Little's MCAR test. The test indicated that the follow-up 1 non-dropouts had healthier characteristics than dropouts. Such a difference in baseline z-scores was not seen between the follow-up 2 non-dropouts and dropouts (Table 2).

3.1 | Longitudinal associations between adolescent physical fitness and middle-aged cardiometabolic health

3.1.1 | Cardiorespiratory fitness

The result of GLM, based on continuous CRF variable (Table 3), showed a significant ($p = 0.006$) inverse BMI-independent association between adolescent CRF and middle-aged CMDS, indicating that a 1 SD increase in the CRF test z-score in adolescence was associated with 0.1 (scale 0–3) lower CMDS in middle age. When GLM was repeated with the categorized CRF variable, the lowest CRF tertile differentiated significantly ($p = 0.021$) from the highest in terms of CMDS (Table S3). In analysis using

TABLE 1 Characteristics of the participants at the different time points.

	Males			Females			Total
Follow-up (years)	**Baseline ($N=861$)**	**25 ($N=552$)**	**45 ($N=370$)**	**Baseline ($N=933$)**	**25 ($N=644$)**	**45 ($N=398$)**	
Age range (years)	12–19 years	37–44 years	57-64 years	12–19 years	37–44 years	57-64 years	
Age (years)	14.9 (1.7)	39.9 (1.7)	59.9 (1.7)	14.8 (1.7)	39.8 (1.7)	59.8 (1.7)	
Height (cm)	168.2 (11.2)	179.6 (6.3)	176.5 (8.6)	162.0 (6.5)	165.8 (5.4)	167.7 (7.2)	
Weight (kg)	56.2 (12.4)	83.2 (11.8)	83.9 (14.7)	52.5 (8.2)	66.6 (11.7)	75.7 (16.1)	
BMI (kg/m^2)	19.6 (2.7)	25.8 (3.3)	26.9 (4.1)	20.0 (2.5)	24.2 (4.0)	26.9 (5.3)	
Waist circumference (cm)			97.7 (12.1)			92.9 (13.9)	
Sit-ups in 30 s	20.4 (4.2)			16.6 (3.8)			
Standing broad jump (cm)	213.2 (30.1)			174.1 (21.4)			
Flexed arm hang (s)				13.9 (9.9)			
Pull-ups	5.7 (4.0)						
4 × 10 m shuttle run (s)	11.8 (0.9)			12.7 (0.9)			
50 m dash (s)	8.3 (0.9)			9.0 (0.8)			
1500 m (s)				495.6 (87.0)			
2000 m (s)	582.5 (121.1)						
Diabetes mellitus (cases)		7	27		9	35	78
Elevated blood pressure		83	138		73	139	433
Coronary heart disease		3	17		0	10	30

Note: Values = means (standard deviations) except disease prevalence. At least baseline and one follow-up required for a participant to be included.

categorized CRF and dichotomic CMDS, the baseline age and BMI-adjusted relative risk for one or more cardiometabolic conditions was significantly lower on average (RR = 0.85, 95% CI [0.71, 0.99]) and high (RR = 0.76, 95% CI [0.62, 0.90]) CRF tertile compared to low (Table S3). GLM with continuous CRF (Table 3) showed a significant interaction ($p = 0.031$) with sex, indicating that the association between adolescence CRF and middle-aged CMDS was stronger among females. This was confirmed in further sex-specific analyses, based on continuous (Table 3) and dichotomic (Table 3) CMDS variables. For example, logistic regression analysis based on the dichotomic CMDS variable showed that in females a 1 SD increase in the CRF test score in adolescence significantly lowered the odds (OR = 0.71, 95% CI [0.56, 0.91]) for one or more cardiometabolic condition in middle-aged (Figure 2).

When the health conditions were studied separately with logistic regression, a significant reduction (OR = 0.72, 95% CI [0.56, 0.91]) in odds for middle-aged EBP by a 1 SD increase in the adolescent CRF test score independent of BMI was detected (Figure 2) among females. Also, a significant association among females was found between adolescent CRF and middle-aged CHD, but due to a low number of cases ($n = 2$ in Model 2) this result was negligible. The associations between adolescent CRF and middle-aged DM and late middle-aged WC or BMI were not statistically significant in any of the analyses.

3.1.2 | Muscular fitness

The results showed an inverse association between adolescent muscular fitness (MF) and late middle-aged WC and BMI. However, the association was strongly attenuated after controlling for baseline BMI. In GLM with a continuous MF variable (Table 4), a significant inverse association with late middle-aged WC ($p = 0.049$) and BMI ($p < 0.001$) in the age and sex-adjusted model was found. In the BMI-adjusted model, the trend for inverse association remained for both outcomes, but did not reach statistical significance. No interactions between MF and sex were detected in associations for WC or BMI. MF in adolescence was not associated with CMDS, separately tested health conditions, or dichotomic CMDS in middle age regarding the two models, nor with males or females combined or separated (Table S4).

3.1.3 | Speed-agility

The association of adolescent SA with cardiometabolic health in middle age was equivocal. GLM for association between SA and WC, based on categorized SA variable, indicated interaction by sex leading to further sex-specific analyses with a categorized SA variable (Table S5). This analysis revealed a significant difference ($p = 0.013$) between low and high adolescence SA group males' WC in late middle age, persisting throughout the adjustment for

age and BMI (Table S5). No other GLM (Table 5; Table S5) or logistic regression analyses (Table 5; Table S5) in either model could establish a significant association between adolescent SA and middle-aged cardiometabolic health.

TABLE 2 Missing value analysis of follow-up and non-follow-up participants.

	CRF 1976	*N*	MF 1976	*N*	SA 1976	*N*
CMD 2001						
Follow-ups	0.06	835	0.14	1196	−0.28	554
Non-follow-ups	−0.12	423	−0.27	598	−0.43	249
p	0.004*		0.001*		0.047*	
CMD 2021						
Follow-ups	0.01	475	0.08	769	−0.31	382
Non-follow-ups	−0.01	783	−0.05	1025	−0.42	421
p	0.768		0.273		0.404	

Note: Values = age & sex standardized z-score means. Little's MCAR test $[\chi^2(643) = 766.003, p < 0.001]$ indicated that missing values were not completely missing at random (MCAR).

Abbreviations: CMD, cardiometabolic disease (diabetes mellitus, elevated blood pressure, coronary heart disease); CRF, cardiorespiratory fitness; MF, muscular fitness; SA, speed-agility.

*$p < 0.050$.

3.1.4 | Exploratory analyses

We tested whether the significant associations outlined above persisted after additional adjustment for PA at the end point (Table S6). Overall, the findings were consistent and CRF was significantly associated with CMD, even after adjustment for PA at end point.

4 | DISCUSSION

In this long follow-up study, CRF in adolescence was inversely associated with the accumulated burden of CMD in late adulthood. MF and SA in adolescence, in turn, were only weakly associated with WC and BMI after 45 years, and not consistently by sex and after adjustment for baseline BMI. The inverse association between CRF and burden of CMD was independent of body mass and PA and was stronger in females than in males.

The finding that CRF in adolescence was associated with CMD in middle age independent of BMI is in line with previous studies[18–20,25] and highlights several explanatory factors behind the phenomenon. First, CMD is regulated by multiple factors in adulthood, of which CRF has been acknowledged as a substantial and independent one.[39,40] Nevertheless, as adiposity remains a strong early

TABLE 3 CRF in adolescence and cardiometabolic disease in middle age (unstandardized coefficients; all continuous variables are expressed as standard deviation increments).

		Model 1					Model 2				
Analysis		*N*/cases	*ß* (LR)	OR	95% CI	*p*	*N*/cases	*ß* (LR)	OR	95% CI	*p*
CRF											
DM (dichotomic)	LogR	932/48		0.90	0.62, 1.32	0.600	562/32		1.24	0.70, 2.18	0.466
EBP (dichotomic)[a]	LogR	933/286		0.90	0.75, 1.09	0.289	562/193		0.97	0.78, 1.20	0.747
CHD (dichotomic)[b]	LogR	931/15		0.88	0.52, 1.51	0.650	561/9		0.89	0.46, 1.72	0.719
CMDS (dichotomic)[c]	LogR	933/313		0.91	0.76, 1.10	0.323	562/209		0.99	0.80, 1.23	0.938
WC (continuous)	GLM	468	−0.26		−1.89, 1.34	0.723	341	−0.19		−1.98, 1.52	0.815
BMI (continuous)	GLM	464	−0.35		−1.08, 0.23	0.297	337	−0.28		−0.91, 0.35	0.325
CMDS (continuous)[d]	GLM	933/313	−0.07		−0.13, −0.01	0.013*	562/209	−0.10		−0.18, −0.03	0.006*

Note: Model 1: adjusted for baseline age and sex; Model 2: Model 1 + adjusted for baseline BMI.

Abbreviations: CHD, coronary heart disease; CMDS (continuous), cardiometabolic disease score, scale 0–3 (DM, EBP, CHD), CMDS (dichotomic) (0, no conditions; 1, 1–3 conditions); CRF, cardiorespiratory fitness; DM, diabetes mellitus; EBP, elevated blood pressure; GLM, general linear model; LogR, logistic regression.

*$p < 0.050$.

[a]Interaction EBP*sex: Model 1: OR = 0.86; 95% CI = 0.65, 1.14; $p = 0.288$; Model 2: OR = 0.74; 95% CI = 0.54, 1.03; $p = 0.073$ (Figure 2).

[b]Interaction CHD*sex: Model 1: OR = 0.41; 95% CI = 0.17, 0.96; $p = 0.040$; Model 2: OR = 0.28; 95% CI = 0.08, 0.97; $p = 0.045$ (Figure 2).

[c]Interaction CMDS_di*sex: Model 1: OR = 0.85; 95% CI = 0.65, 1.12; $p = 0.252$; Model 2: OR = 0.72; 95% CI = 0.52, 0.99; $p = 0.046$ (Figure 2).

[d]Interaction CMDS*sex: Model 1 ($F = 1.07$; $p = 0.302$): $ß = -0.07$; 95% CI = 0.04, 0.11; $p = 0.302$; CMDS females: $ß = -0.07$; 95% CI = −0.13, −0.01; $p = 0.024$, CMDS males: $ß = -0.03$; 95% CI = −0.08, 0.02; $p = 0.182$. Model 2 ($F = 4.65$; $p = 0.031$): $ß = 0.10$; 95% CI = 0.01, 0.18; $p = 0.036$; CMDS females: $ß = -0.10$; 95% CI = −0.17, −0.03; $p = 0.005$, CMDS males: $ß = 0.00$; 95% CI = −0.06, 0.05; $p = 0.999$.

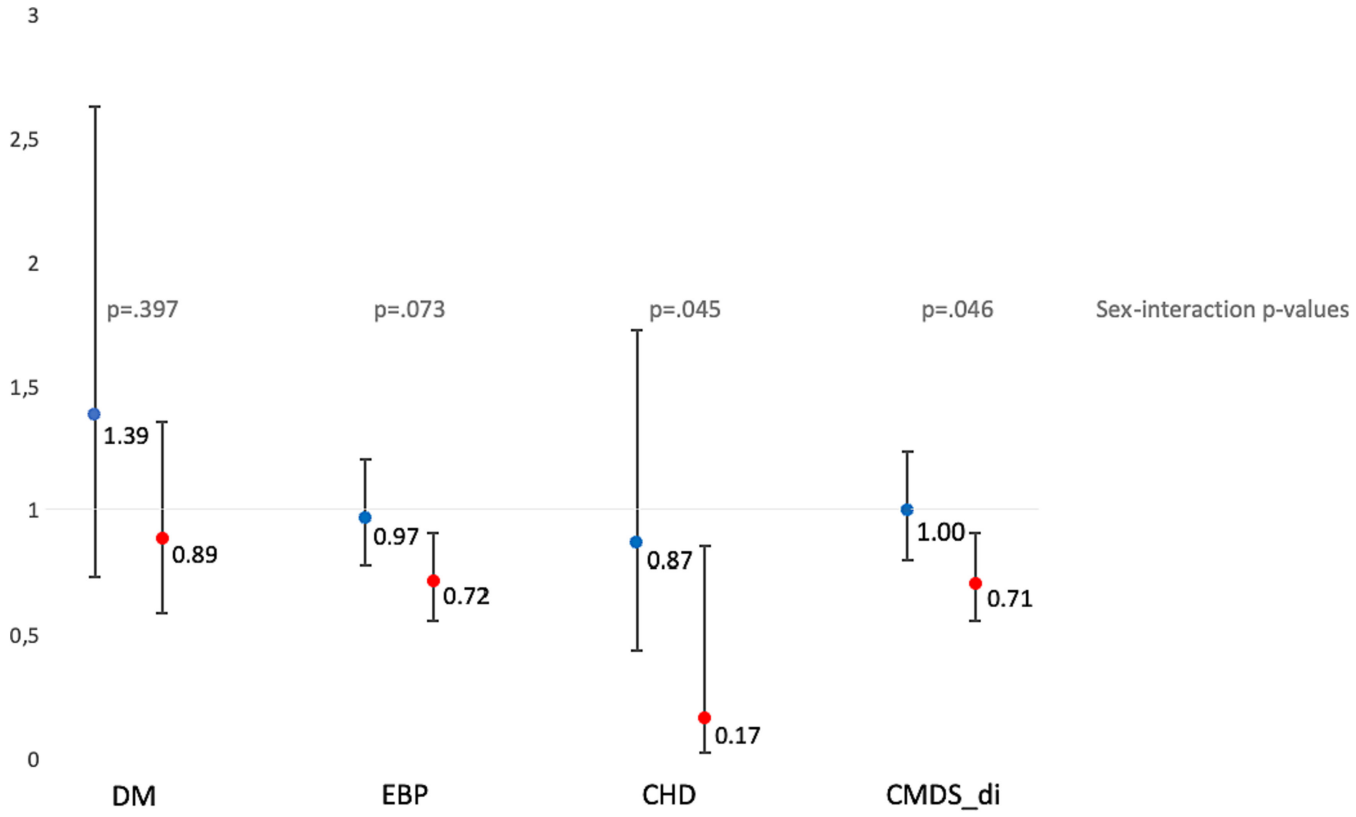

FIGURE 2 Odds ratios for CMD indicators in middle age by 1 SD increase in adolescent mean CRF-score (sex-separated analyses adjusted for baseline age and BMI). Males = blue; females = red; y-axis = odds ratio; error bars = 95% confidence intervals. CHD, coronary heart disease; CMDS_di, dichotomized cardiometabolic disease score (DM, EBP, CHD); DM, diabetes mellitus; EBP, elevated blood pressure.

TABLE 4 MF in adolescence and cardiometabolic disease in middle age (unstandardized coefficients; all continuous variables are expressed as standard deviation increments).

		Model 1					Model 2				
Analysis		***N*/cases**	***ß* (LR)**	**OR**	**95% CI**	***p***	***N*/cases**	***ß* (LR)**	**OR**	**95% CI**	***p***
MF											
DM (dichotomic)	LogR	1358/78		1.06	0.92, 1.23	0.422	1335/78		1.07	0.93, 1.24	0.348
EBP (dichotomic)	LogR	1357/433		1.00	0.93, 1.07	0.965	1334/424		1.00	0.93, 1.07	0.952
CHD (dichotomic)	LogR	1356/30		1.03	0.86, 1.25	0.735	1333/29		1.02	0.84, 1.24	0.831
CMDS (dichotomic)	LogR	1358/475		1.00	0.93, 1.07	0.991	1335/465		1.00	0.93, 1.07	0.933
WC (continuous)	GLM	760	−0.61		−1.17, −0.01	0.049*	752	−0.36		−0.93, 0.23	0.221
BMI[a] (continuous)	GLM	753	−0.31		−0.52, −0.11	<0.001**	745	−0.19		−0.38, 0.01	0.055
CMDS (continuous)	GLM	1358/475	−0.01		−0.03, 0.01	0.254	1335/465	−0.01		−0.03, 0.01	0.308

Note: Model 1: adjusted for baseline age and sex; Model 2: Model 1 + adjusted for baseline BMI.

Abbreviations: CHD, coronary heart disease; CMDS (continuous), cardiometabolic disease score, scale 0–3 (DM, EBP, CHD), CMDS (dichotomic) (0 = no conditions; 1 = 1–3 conditions); DM, diabetes mellitus; EBP, elevated blood pressure; GLM, general linear model; LogR, logistic regression; MF, muscular fitness.

*$p < 0.050$; **$p < 0.001$.

[a]Interaction BMI*sex: Model 1 (F = 3.87; $p = 0.050$): $ß = 0.29$; 95% CI = 0.01, 0.55; $p = 0.035$: CMDS females: $ß = -0.31$; 95% CI = −0.50, −0.12; $p = 0.003$, CMDS males: $ß = -0.03$; 95% CI = −0.19, 0.13; $p = 0.758$. Model 2 (F = 2.37; $p = 0.124$): $ß = 0.22$; 95% CI = −0.05, 0.50; $p = 0.107$: CMDS females: $ß = -0.15$; 95% CI = −0.34, 0.06; $p = 0.124$; CMDS males: $ß = 0.02$; 95% CI = −0.14, 0.17; $p = 0.825$.

predictor for CMD,[41,42] combining sufficient levels of CRF and low adiposity in youth seems to form a robust base for cardiometabolic health across the life course according to our findings and previous research.[21,25] Second, the BMI-independent association possibly illustrates the earlier suggested[43] genetic regulation of maximal oxygen uptake in adolescence which becomes visible among fat-but-fit youth who tend to maintain normal aerobic capacity

TABLE 5 Speed-agility in adolescence and cardiometabolic disease in middle age (unstandardized coefficients; all continuous variables are expressed as standard deviation increments).

		Model 1					Model 2				
Analysis		***N*/cases**	***β* (LR)**	**OR**	**95% CI**	***p***	***N*/cases**	***β* (LR)**	**OR**	**95% CI**	***p***
Speed & aglity											
DM (dichotomic)	LogR	632/35		0.99	0.73, 1.34	0.947	625/35		0.99	0.73, 1.40	0.951
EBP (dichotomic)	LogR	632/203		0.95	0.84, 1.09	0.468	625/201		0.95	0.84, 1.09	0.471
CHD (dichotomic)	LogR	631/11		1.10	0.71, 1.71	0.669	624/11		1.12	0.71, 1.76	0.630
CMDS (dichotomic)	LogR	632/223		0.95	0.83, 1.08	0.421	625/221		0.95	0.83, 1.08	0.422
WC (continuous)	GLM	378	−0.04		−1.27, 1.26	0.941	376	0.23		−0.84, 1.50	0.611
BMI (continuous)	GLM	373	−0.11		−0.48, 0.28	0.573	371	0.03		−0.37, 0.43	0.832
CMDS (continuous)	GLM	632/223	−0.01		−0.05, 0.03	0.652	625/221	−0.01		−0.04, 0.03	0.530

Note: Model 1: adjusted for baseline age and sex; Model 2: Model 1 + adjusted for baseline BMI.

Abbreviations: CHD, coronary heart disease; CMDS (continuous), cardiometabolic disease score, scale 0–3 (DM, EBP, CHD), CMDS (dichotomic) (0 = no conditions; 1 = 1–3 conditions); DM, diabetes mellitus; EBP, elevated blood pressure; GLM, general linear model; LogR, logistic regression.

and gain no additional risk for subsequent CMD[44] despite the risk of excess adiposity causes.[45] Despite evidence establishing the inverse association, the mechanism through which sufficient CRF in youth elicits the lowered risk for CMD in adulthood is not clear. Gutin[46] proposed that this may be related to stem-cell differentiation in youth because of vigorous aerobic training. Another hypothesis favors CRF-associated metabolism, which is associated with lower CMD risk.[47] Finally, we traced the inverse association between adolescent CRF and middle-aged CMD to originate mainly from the low CRF in females. The finding is important for PA promotion in youth while it also supplements the previous results concerning males,[19,25,26] demonstrating that the adolescents with the lowest CRF are at the highest risk for adulthood CMD.

The analyses showed persistent longitudinal CRF-CMD association even after controlling for PA, which is suggesting that regardless of the activity levels performed in late adulthood (i.e., PA assessed at the end point, when participants were aged ~ 60 years), CRF in pediatric ages has a prognostic value for CMD. Heritability of CRF has been reported to be roughly 50%[43] leaving room for environmental factors, including PA and exercise, to produce individual variation on CRF levels. Regardless of its genetic component, CRF is a modifiable factor and PA, and particularly that of high intensity is known to have an impact on CRF.[48] In fact, previous evidence from twin studies supports that long-term leisure-time PA also during adulthood is beneficial for health even after controlling for other genetic factors.[49] Therefore, this evidence together with the findings of this study suggests that enhancing CRF at pediatric ages could have long-lasting effects on future CMD.

Although we found associations between adolescent CRF and CMD, they were not strong. Presumably, this refers to the low overall prevalence of CMD in the study population, and on the other hand, the relatively low number of participants with data on adolescent CRF and middle-aged CMD. According to the literature, the low prevalence of CVD at the age of our study population is not uncommon, as the prevalence of CVD and DM in the population under 65 years remains relatively low compared to those over 65 years.[34,35] Second, presumably the self-reports of CMD likely underestimated the prevalence because of undiagnosed cases, which in the case of DM can be substantial.[50] Hence, implementing more sensitive methods, such as blood samples as in the reference studies,[20,32] to analyze dyslipidemia and adverse glucose profile would have revealed pre-existing conditions and affected the longitudinal associations. The finding that CRF was inversely associated with the risk for hypertension, and accordingly a higher accumulated burden of CMD particularly in females supports the finding of Hamer et al.[28] who reported a stronger link among females between childhood CRF and middle-aged cardiometabolic health. However, another long follow-up with males and females[22] could not identify sex differences. Given that CVD in middle age tends to develop earlier in males,[46] finding an explanation for the sex difference in literature,[24] and our data calls for further investigation. Finally, the large follow-up time explains the parsimonious associations and is endorsed by previous research.[23,27] Long duration presumably highlights the multifactorial and slowly progressive nature of CMD. Nevertheless, we detected an association between CRF and CMD across a substantial period, which is an important result. For future research, we suggest following participants over the age of 65 years whereupon the prevalence of CMD is shown to increase.[34,35]

We found a sex-independent inverse association between adolescent MF and late middle-aged WC and BMI which, however, was dependent on baseline BMI. This finding is in line with previous long-duration follow-ups

indicating MF in youth to be less influential for subsequent cardiometabolic health than in CRF.[25,28,29,32,33] Given that such a strong genetic regulation as in CRF[43] affecting likely also later life cardiometabolic health[44,45] has not been established for MF, the absence of the individual longitudinal association is conceivable. Nevertheless, the association found (although BMI-dependent) seems to support the recent finding[29] suggesting the intertwined association between MF and body composition over the life course.

The association of adolescent SA with middle-aged cardiometabolic health was inconsistent in the present study. Our results indicated no longitudinal association between SA and CMD. Nevertheless, we found an association between SA and late middle-aged WC in males. An explanation for this link is difficult to find as reference studies are completely missing. Diminutive cross-sectional evidence among children suggests a moderate association between SA and CMD risk. According to our results and the literature,[31,32] SA has similarities with MF as both seem to be dependent on body mass. Hence, in the SA–WC association found in this study, extracting the contribution of SA from BMI tracking is not straightforward.

4.1 | Strengths and limitations

This study has some limitations which should be acknowledged. First, cardiometabolic conditions were assessed with physician-diagnosed self-reports, which might introduce a source of error. Although evidence indicates satisfactory concurrent validity between self-reports and medical records in CVD and DM,[52] for EBP the lack of repeated measures comprised a possible threat to validity.[53] Second, due to questionnaire-based cardiometabolic ascertainment in follow-ups, we were not able to conduct a time-adjusted survival analysis for the longitudinal associations. Third, the tests used for the baseline fitness measurement might have impacted the validity as field tests involve a risk for measurement error due to motivational issues. However, the criterion validity of field running tests to measure CRF has been shown to be good,[54] and measuring fitness in a rather large adolescent population other than by field tests would be difficult. Fourth, objective assessment of the fitness status in the follow-up measurements was not available which is a limitation considering the recent study of Kokkinos et al.[8] suggesting that change in CRF level over time moderates the longitudinal association between CRF and mortality. Fifth, skewness of the data in follow-up 1 (Table 2) might have impaired data representativeness. However, we could confirm that this did not change the main result as exploratory analysis (Table S6), conducted with not skewed follow-up 2 data only, showed identical results compared with the main analysis. Finally, no indicators of blood lipid profile were measured in this study. This is a limitation because low HDL, high LDL cholesterol, and triglycerides are risk factors for CMD[16] and MetS.[55]

A major strength of this study is that it involved both males and females which allowed to investigate the role of sex as a moderator in the associations between fitness components and CMD. Moreover, the 45-year follow-up design, based on a baseline random sampling across the whole country, connecting mid-adolescence with late adulthood (up to ~ 60 years of age) makes this study unique in the field. Another strength refers to the objective assessment of physical fitness, and the investigation of the speed-agility component in relation to future CMD, which was not available in previous studies in this field. Finally, in this study, we were able to explore the role of PA in the associations between physical fitness components and CMD as opposed to recent long cohorts.[18,19,21]

4.2 | Conclusions

The findings from this prospective study support that low CRF, but not MF and SA fitness, in adolescence is associated with increased risk for CMD in middle age, and that this association is stronger in females than in males. Assessment of fitness, particularly CRF, in youth, is clinically informative about the risk of future CMD in mid-adulthood. Moreover, enhancing CRF in the first decades of life might be beneficial for future life.

4.2.1 | Perspective

In this study, adolescent objectively measured CRF inversely, and regardless of sex and BMI, associated with the accumulated burden of cardiometabolic conditions up to 45 years. In females, adolescent CRF was inversely associated with middle age elevated BP. Moreover, adolescent speed agility, a previously understudied component in prospective cohorts, was inversely linked with late middle age WC in males. The findings extend previous evidence[18,19,25] suggesting youth low objectively measured cardiorespiratory and MF inversely associates with adulthood cardiometabolic disease risk in males. Physical fitness, particularly CRF, in youth may be beneficial in preventing CMD across the adulthood. Assessment and promotion of physical fitness in youth is clinically informative.

AUTHOR CONTRIBUTIONS

Perttu T. T. Laakso designed the study and wrote the manuscript with support from Francisco B. Ortega, Pertti Huotari,

Urho M. Kujala, and Timo T. Jaakkola. Asko J. Tolvanen analyzed the data. Timo Jaakkola supervised the project.

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The authors declare that the results of this study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation. The authors wish to thank Matt Wuethrich for his contribution to language editing and Heimo Nupponen for launching the LISE project and allowing the research data for further investigation.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflicting interests.

DATA AVAILABILITY STATEMENT

The datasets generated and/or analyzed during the current study are not publicly available due to sensitive personal information but are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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