ORIGINAL RESEARCH

Pediatric OBESITY   WILEY

Prospective physical fitness status and development of cardiometabolic risk in children according to body fat and lifestyle behaviours: The IDEFICS study

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Summary

Background: Elevated cardiometabolic risk (CMR) is an important factor for cardio-vascular diseases later in life while physical fitness seems to decrease CMR.

Objective: Thus, the aim of the present study is to assess the association between muscular fitness (MF) and cardiorespiratory fitness (CRF) on CMR in European children, both cross-sectional and longitudinally.

Methods: A total of 289 children (49.5% males) from eight European countries, aged 6 to 9, with longitudinal information on blood pressure, triglycerides, total cholesterol, HDL-cholesterol, homoeostasis model assessment, body mass index, data on fitness level, objectively measured physical activity (PA), diet quality, and total screen time

were included. A CMR score was calculated and dichotomized. MF and CRF were also dichotomized. Cross-sectional and longitudinal multilevel logistic regressions adjusting for lifestyle behaviours were performed.

Results: Reaching a high level of MF during childhood as well as remaining in that level over-time were associated with an 82% and 62% lower probability of high CMR at follow-up, respectively. Also, children who became top CRF over time, showed a 77% lower probability ($P < 0.05$) of being in the highest CMR quartile at follow-up, independently of sociodemographic and lifestyle indicators.

Conclusions: A high MF at early childhood and during childhood reduces the odds of having CMR. Same occurs with the improvement of CRF during childhood. These findings highlight the importance of enhancing fitness to avoid CMR already in children.

KEYWORDS

cardiometabolic, childhood, European, fitness, longitudinal

1 | INTRODUCTION

Cardiovascular disease (CVD) is currently the leading cause of death and health loss in adults[1] and has its origin in early life.[2] In addition, it has been suggested that childhood cardiovascular risk tracks into adulthood[3] and has been associated with several diseases even among individuals with normal-weight.[4] It has been suggested that clustering of CVD risk factors seem to be a better measure of cardiovascular health in children than single risk factors.[5] Some of these scores include relevant cardiometabolic risk (CMR) markers in the composite risk and have shown associations between physical activity and clustered cardiovascular risk.[6] However, fitness, instead of physical activity, has been considered a powerful marker of health and seems to play an important role in cardiometabolic health, even in children and adolescents.[7] In this regard, muscular fitness (MF) and cardiorespiratory fitness (CRF) have been considered key fitness components associated with cardiovascular risk factors.[7] In youth, MF has been associated with CMR[8] even after controlling for weight and height, body mass index (BMI), and body fat.[9] In adolescents, CRF and MF have been independently associated with metabolic risk in European adolescents.[10]

It has been suggested that physical fitness in childhood and adolescence is a useful early predictor of CVD risk factors.[7] In childhood, a systematic review assessing the association between CRF and future cardiovascular risk factors found that CRF reported inverse associations with BMI, body fatness and metabolic syndrome.[11] In European children, it has also been observed an inverse association between fitness and CMR.[12] However, many of the previous studies did not account for body composition or lifestyle behaviours when investigating associations between physical fitness and CMR, such as dietary intake,[13] objectively measured physical activity,[14] or sedentary behaviours.[15] Nowadays, there is a lack of longitudinal studies using standardized and objective measures that help to understand the association between physical fitness and cardio metabolic health during childhood.

Taking all this into consideration, the main aims of the present study are (1) to assess cross-sectional associations between MF and CRS levels and individual and grouped markers of CMR and (2) to analyse longitudinally the effect of a transition fitness change over a two-year period on the individual and grouped markers of CMR in a sample of European children, taking into consideration body composition and lifestyle behaviours.

2 | MATERIAL AND METHODS

2.1 | Study design

The Identification and prevention of Dietary- and lifestyle- induced health EFects In Children and Infants (IDEFICS) study is a multi-centre population-based study performed in children from eight European countries: Belgium, Cyprus, Estonia, Germany, Hungary, Italy, Spain and Sweden, which included an intervention component. A community intervention was developed, including a control and intervention region per country, geographically apart; it included diet, physical activity and stress modules. Design and main procedures have been described in detail elsewhere.[16] Baseline (T0) measurements were performed between September 2007 and May 2008, and the follow-up (T1) measurements between September 2009 and May 2010, after 2 years.

Ethics committees in each centre provided an authorization, and parents also provided written informed consent and children their oral assent. The study was performed according to the ethical guidelines of the Edinburgh revision of the 1964 Declaration of Helsinki (2000).

2.2 | Study sample

At baseline (T0), the study included 16 229 children from 2 to 9 years and, at follow-up (T1), 11 038 children aged 4 to 11 years. The

minimum age to perform the physical fitness tests was 6 years old so only those aged 6 and above were included in the analysis. A cross-sectional sample of 6086 children meeting the age criteria, were measured either at T0 or T1. Children with a complete data set consisting of socio-demographic, cardiometabolic risk markers, body composition indicators, physical fitness and dietary and sedentary behaviours information in both time points were included in the current analysis (n = 289, 49.7% males). Figure 1 summarizes the flow chart of the study population.

2.3 | Measurements

Standardized procedures were used for the anthropometric measurements.[17] Height was measured with a stadiometer (SECA 225, Birmingham, UK), while weight and percentage of body fat were measured with a child-adapted Tanita BC 420 SMA. Sex- and age-standardized body mass index z-scores (zBMI) according to Cole et al.[18] were calculated. Skinfolds thicknesses were measured twice with a Holtain caliper (Holtain Ltd., Croswell, UK) at the triceps, biceps, subscapular and suprailiac sites, and the mean was used for the analysis. Then, sum of the four skinfold thicknesses was calculated. Blood pressure was measured with an

electronic sphygmomanometer (Welch Allyn 4200B-E2, Welch Allyn Inc., Skaneateles Falls, New York) in the right arm, with the child in sitting position. Two measurements were taken at 2 minutes intervals. Differences higher than 5% of magnitude lead to a third measurement. Means of replicate measurements were used in all analyses. The systolic blood pressure (SBP) will be included in the CMR score.

Also, the highest parental education level according to the International Standard Classification of Education (ISCED)[19] was categorized.

2.4 | Physical fitness

Physical fitness was measured following the ALPHA Health-Related Fitness Test Battery for Children and Adolescents.[20] The upper-body MF was assessed using the handgrip strength test through a dynamometer with an adjustable grip (TKK 5401 Grip D, Takey, Tokyo, Japan). Participants were instructed to squeeze continuously for ≥2 seconds with the elbow in full extension. The best score of the two attempts for each hand was chosen and averaged. Relative upper-body MF was expressed per kg of body mass (handgrip strength [kg/kg]).[21] The lower-body MF was assessed by the standing long jump test. Participants had to jump as far as forward possible. The distance reached
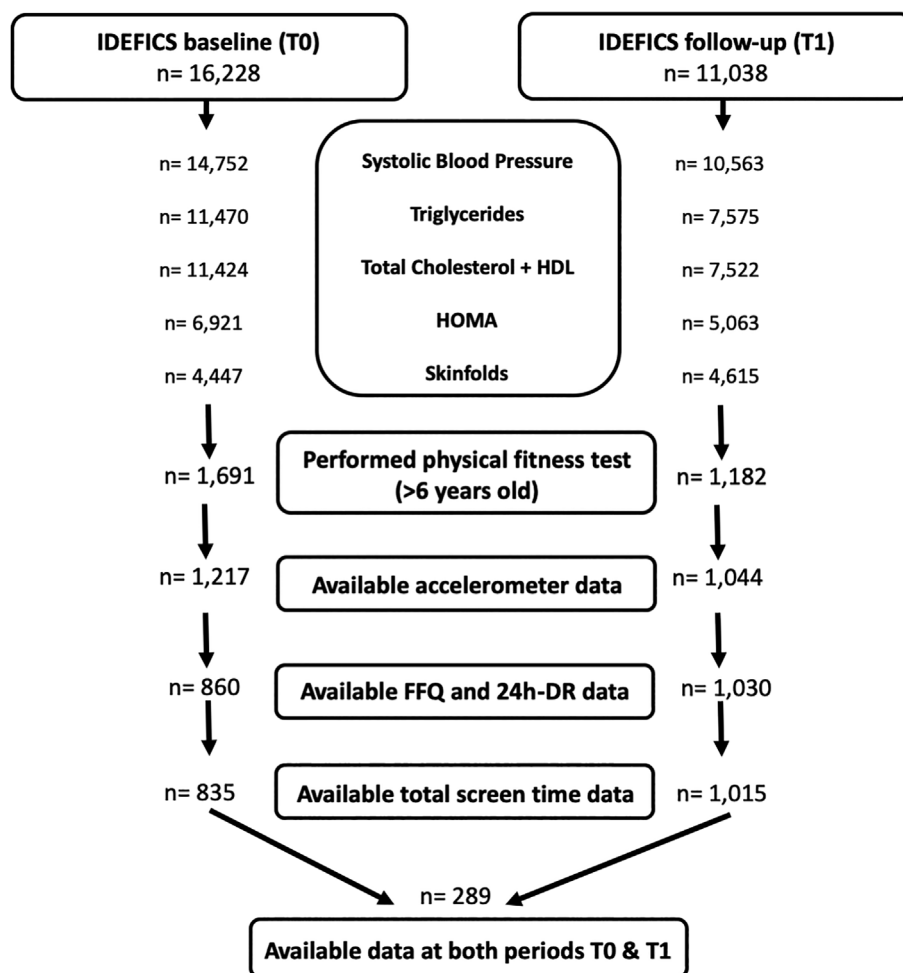
FIGURE 1 Flow chart of the population involved in the current study from the IDEFICS study. Abbreviations: T0, at baseline; T1, at follow-up; HDL, high-density lipoprotein; HOMA, Homeostasis Model Assessment Index; FFQ, food frequency questionnaire; 24H-DR, 24-hour dietary-recall

was taken from the take-off line and the heel of the nearest foot at landing. The longest attempt out of two was chosen.

Based on these two fitness tests, a MF score (MF z-score) was computed by combining upper-body and lower-body results. Each of these variables was standardized as follows: z-score = (ith value − mean)/SD. The MF z-score was based on previous studies[21] and calculated as the mean of the two standardized scores (handgrip strength and standing long jump).

The CRF level was assessed using the 20 m' shuttle run test, which estimates the aerobic capacity. The results of all the centres were unified according to the Leger test protocol.[22,23] The number of shuttles was used as an indicator of the cardiorespiratory level with a greater number of shuttles indicating better performance.

Both indicators, MF and CRF, were dichotomized. Thus, the first group included those children in the first, second or third quartile (Q1-Q3); and the group II included those children at the top quartile (Q4). Additionally, combinations of grouping between surveys were created and the cumulative fitness score (MF + CRF), including the MF and CRF as continuous variables, was calculated at T0, T1, and the delta values of this score, that is, differences between T1 and T0.

2.5 | Biological samples

Children were asked to participate in fasting blood collection, on a voluntary basis in the study.[24] Blood sampling was performed after an overnight-fast. Blood glucose, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c) and triglycerides (TG) were assessed at each study centre by point-of-care analysis (Cholestech LDX analyzer, Cholestech Corp., Hayward, California). Serum insulin concentrations were determined by luminescence immunoassay Immulite 2000 (Siemens, Eschborn, Germany) in a central laboratory. Insulin resistance was defined by the homoeostasis model assessment (HOMA)[25] and calculated from fasting glucose and plasma insulin via a standard equation: HOMA = (insulin (μIU/mL) × glucose (mg/dL))/405. The TC/HDL-c ratio was computed.

2.6 | Cardio metabolic risk

2.6.1 | CMR scores

A continuous score of clustered CMR factors was computed according to Andersen et al.[6]: SBP, TG, ratio TC/HDL-c, HOMA and sum of four skinfolds. Age- and sex-specific z-scores were calculated for each risk factor. All individual z-scores were added up to create the clustered CMR score. The lower the score the lower the overall cardiovascular risk. Also, two additional CMR scores were developed including two body composition indices, WC or FMI, instead of sum of four skinfolds, resulting in three CMR scores: (1) CMR score with sum of skinfolds, (2) CMR score with WC, and (3) CMR score with FMI. The WC and FMI were standardized with and age- and sex-specific z-scores for subsequent inclusion in the corresponding clustered CMR score.

2.6.2 | CMR categories

For the individual risk factors, the population for each crude indicator was allocated into two groups. The first group included those children in the first, second or third quartile (Q1-Q3) of each individual crude indicator; and the group II included those children at the top quartile (Q4). For the CMR scores that included the sum of the individual risk z-scores, participants were allocated in two groups, taking into consideration the cut-off proposed by Andersen of 1 SD.[6]

2.6.3 | Physical activity

Physical activity (PA) was objectively measured using a uniaxial accelerometer (ActiTrainer or GT1M Actigraph; ActiGraph, LLC, Pensacola, Florida). Children wore the accelerometer for up to seven consecutive days.[26] Only those with at least 3 days' worth of valid accelerometer data, with at least 8 hours of valid data were included. The average time spent in moderate-to-vigorous PA (MVPA) was calculated using the Evenson cut-offs[27] and used as marker of PA.

2.7 | Dietary intake

The food frequency questionnaire (FFQ),[28] which was part of the Children's Eating Habits Questionnaire in the IDEFICS study was used to derive the diet quality index (DQI). A computer-assisted 24-HDR, called SACINA ('Self-Administered Children and Infant Nutrition Assessment') was used in T0 and T1.[29] As we used a qualitative FFQ, sex-, age-, and country-specific medians of the portion sizes of the corresponding food groups were derived based on the 24-hours dietary recall (24-HDR) and the obtained information was used to derive the DQI from the FFQ.

The DQI, adapted for children,[30] was used as a proxy indicator for the overall children's diet.

2.8 | Total screen time

Total screen time was derived from the parent-reported questionnaire. The questions included the time spent watching TV, videos and DVDs, and the time using a computer and/ or playing videogames on a weekday and a weekend day separately.[31] The average total screen time in hours per week was calculated.

2.9 | Statistical analysis

Descriptive study characteristics are shown as mean and SD for continuous variables and number of cases and percentages for categorical variables.

For the cross-sectional analysis, a multilevel logistic regression analysis (levels: country and intervention vs control area) was

performed using the individual risk factors and CMR score at both time points as dependent variable. This analysis was performed to assess the odds for having a higher individual and CMR status when participants were in the top level of fitness (Group II, top fit, Q4), compared with those who were in the low-medium level of fitness (Group I, low-medium fit, Q1-Q3), of fitness which were considered as the reference group. The cross-sectional analysis between fitness and individual risks and CMR score was performed using three models adjusting for potential covariates and levels (country and intervention vs control region). Model 0 was not adjusted. Model 1 included sex, age, zBMI and parental education level as covariates. Model 2 included covariates of Model 1 and also MVPA, DQI, total screen time as covariates. The models for the individual body composition indicators (sum of skinfolds, WC or FMI) and also the CMR did not include the zBMI as a covariate in order to avoid over-adjustment.

To analyse the longitudinal effect association between fitness and individual risk and CMR scores, several analyses were performed. A multilevel logistic regression analysis (levels: country and intervention vs control area) was performed using the individual risk and CMR scores at T1 as dependent variable to assess the odds for having a higher cardiometabolic risk status when participants presented a specific fitness level (MF or CRF) at T0 and T1. Four transition groups of fitness were created (Figure 2): Group I, unchanged fitness at low-medium level over time (remain low-medium fit), which included children being in the low-medium fitness level (Q1-Q3) of MF or CRF at T0 and T1; Group II, decreased fitness over time (became low-medium fit), which included those children being in the highest quartile of the MF or CRF (Q4) at T0, and being in the low-medium fitness level (Q1-Q3) at T1; Group III, improved fitness over time (became top fit), which included those children being in the low-medium fitness level (Q1-Q3) of MF or CRF at T0 and being in the highest quartile at T1 (Q4); and Group IV, unchanged fitness at top level over time (remained top fit), which included children being in the highest fitness MF or cardiorespiratory fitness (Q4) at both time points (T0&T1).

The longitudinal multilevel logistic regression analysis was applied using three models, adjusting for potential covariates and levels

(country and intervention vs control region). Model 0 was the non-adjusted model, which included the corresponding baseline individual or CMR score category. Model 1 included also sex, age, zBMI at T1 and education level. Model 2 included, MVPA, DQI, total screen, also at follow-up (T1). The models for the sum of skinfolds and also the CMR did not include the zBMI as a covariate in order to avoid an over-adjustment.

Sensitivity analysis was applied between included and excluded participants in order to check differences in some of the common measurements. Included participants were older and having high SES than the excluded ones ($P < 0.05$). However, no differences were observed in terms of BMI categories according to Cole et al.[18]

The analysis was performed using the Statistical Package for the Social Sciences (version 21.0, SPSS) and Stata (version 13.0) for the multilevel logistic regression.

3 | RESULTS

Table 1 shows the main characteristic of the study participants at baseline (T0) and follow-up (T1) by sex.

Odds ratio (OR) and 95% confidence interval (CI) for the cross-sectional associations between fitness MF and individual and CMR score categories are shown in Table 2. In T0, children at top MF levels had 85% and 50% lower probabilities of being allocated in the upper category of sum of skinfolds and CMR, respectively, compared with children at low-medium MF levels, after controlling for education and lifestyle behaviours (MVPA, DQI and total screen time). In T1, children at top MF levels had 47%, 82% and 75% lower probability of being allocated in the upper category of the ratio total cholesterol/HDL, sum of skinfolds and CMR, respectively, compared with the children with low-medium MF levels, after controlling for education and lifestyle behaviours.

Table 3 shows OR and 95% CI for the cross-sectional associations between CRF fitness level groups, and individual and CMR score categories. In both T0 and T1, top fit children had 60% or 64% lower

FIGURE 2 Muscular fitness and Cardiovascular fitness grouping design between baseline and follow-up. MF or CRF transition groups over time: Group I, unchanged fitness at low-medium level over time (remain low-medium fit) (N = 188 for MF and N = 184 for CRF); Group II, decreased fitness over time (became low-medium fit) (N = 30 for MF, and N = 38 for CRF); Group III, improved fitness over time (became top fit) (N = 30 for MF, and N = 37 for CRF); Group IV, unchanged fitness at top level over time (remain top fit) (N = 41 for MF, and N = 30 for CRF)
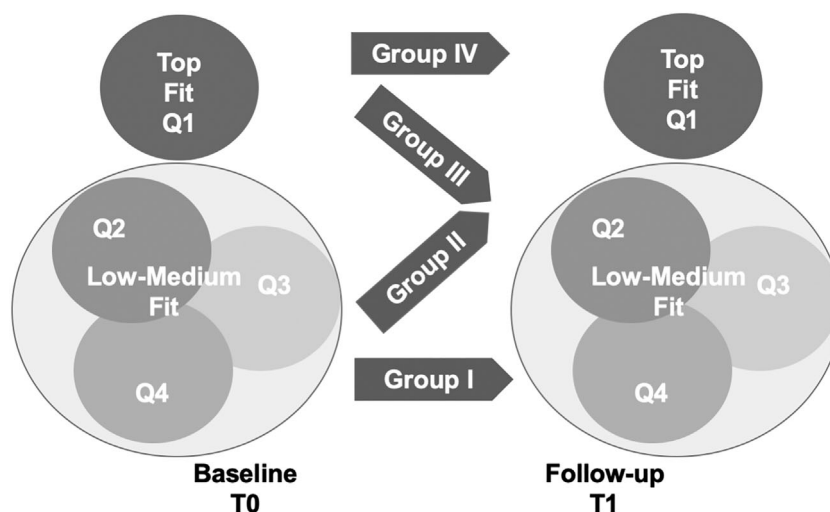
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TABLE 1 Description of included study population and the continuous cardiometabolic factors by gender at baseline (T0) and follow-up (T1)

		T0			T1			
		Male n = 143	Female n = 146	p¹	Male n = 143	Female n = 146	p¹	p²
Age (x̄±SD)		7.6 (0.7)	7.5 (0.6)	0.263	9.6 (0.7)	9.5 (0.6)	0.176	**<0.001**
Parental education n(%)	Low	3 (2.1)	5 (3.4)	0.778	4 (2.8)	2 (1.4)	0.696	**<0.001**
	Medium	65 (45.8)	65 (44.5)		66 (46.2)	68 (46.6)		
	High	74 (52.1)	76 (52.1)		73 (51.0)	76 (52.1)		
Region n(%)	Intervention	73 (51.0)	71 (48.6)	0.681	73 (51.0)	71 (48.6)	0.681	**<0.001**
	Control	70 (49.0)	75 (51.4)		70 (49.0)	75 (51.4)		
Systolic Blood Pressure, mm Hg (x̄±SD)		105.3 (8.8)	104.4 (8.6)	0.366	108.6 (9.9)	107.7 (9.7)	0.460	**<0.001**
Triglycerides, mg/dL (x̄±SD)		50.4 (13.3)	53.9 (23.7)	0.130	54.4 (21.7)	57.6 (24.9)	0.234	**<0.001**
Ratio total cholesterol/HDL, (x̄±SD)		2.88 (1.0)	3.23 (1.0)	**0.003**	3.0 (1.2)	3.3 (1.3)	0.051	0.159
Homeostatic Model Assessment index, (x̄±SD)		0.93 (0.6)	1.01 (0.7)	0.233	1.49 (0.8)	1.61 (1.2)	0.287	**<0.001**
Sum of skinfolds, mm (x̄±SD)		31.1 (16.1)	36.0 (15.2)	**0.009**	36.9 (20.5)	42.2 (18.6)	0.023	**<0.001**
ZBMI (x̄±SD)		0.353 (1.05)	0.500 (1.01)	0.224	0.402 (1.10)	0.468 (0.99)	0.595	**<0.001**
Cardiometabolic risk score (x̄±SD)		0.03 (2.9)	0.00 (3.4)	0.941	0.02 (3.3)	0.00 (3.5)	0.953	0.990
Cardiometabolic risk score categories[a] (n,%)	Category I	100 (69.9)	104 (71.2)	0.808	101 (70.6)	105 (71.9)	0.809	**<0.001**
	Category II	43 (30.1)	42 (28.8)		42 (29.4)	41 (28.1)		
MF z-score (x̄±SD)		−0.01 (1.69)	0.00 (1.61)	0.957	−0.007 (0.99)	0.00 (0.99)	0.955	0.978
CRF, number of shuttles (x̄±SD)		21.0 (10.9)	16.6 (8.7)	**<0.001**	29.2 (14.0)	22.9 (11.3)	**<0.001**	**<0.001**
MVPA, minutes (x̄±SD)		51.2 (22.9)	40.3 (20.2)	**<0.001**	49.8 (22.9)	37.8 (19.0)	**<0.001**	0.149
DQI (x̄±SD)		90.2 (18.3)	90.4 (13.7)	0.924	89.5 (15.2)	90.6 (12.9)	0.501	0.793
Total screen time, hours per week(x̄±SD)		13.8 (6.8)	11.6 (6.0)	**0.004**	15.0 (7.3)	12.8 (7.1)	**0.008**	**0.001**

Abbreviations: SD, SD; zBMI, body mass index z score by Cole et al.; MF, muscular fitness score; CRF, Cardiorespiratory fitness; MVPA, Moderate to vigorous physical activity; DQI, diet quality index.

Notes: p¹ gender differences; p² time-point differences. Bold letters indicate p < 0.05 between gender.

[a]Cardiometabolic Risk Score categories: Category I, < 1SD; Category II, ≥ 1 SD. Based on Andersen et al.[5]

TABLE 2 Cross-sectional multilevel logistic regression between grouping of muscular fitness (MF) and individual indicators and cardiometabolic risk score at baseline (T0) and follow up (T1)

Predictor and outcomes		MF groups[a]			
		At baseline (T0)		At follow-up (T1)	
		OR	95% CI	OR	95% CI
Systolic blood pressure [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.77	0.44;1.35	**0.58**	**0.33;0.99**
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	1.19	0.64;2.22	0.99	0.54;1.79
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	1.18	0.63;2.24	0.96	0.52;1.76
Triglycerides [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.78	0.43;1.42	1.13	0.66;1.94
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.99	0.53;1.86	1.40	0.80;2.49
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	1.06	0.55;2.06	1.38	0.77;2.50
Ratio total cholesterol/ high density lipoprotein [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.52**	**0.30;0.90**	**0.41**	**0.23;0.72**
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.61	0.34;1.09	**0.49**	**0.27;0.89**
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.71	0.39;1.28	**0.53**	**0.29;0.96**
Homeostatic model assessment [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.67	0.38;1.20	0.73	0.43;1.25
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	1.17	0.61;2.23	1.07	0.60;1.89
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	1.36	0.70;2.67	1.06	0.59;1.90
Sum of skinfolds [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.14**	**0.07;0.30**	**0.18**	**0.10;0.33**
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.14**	**0.06;0.29**	**0.17**	**0.09;0.31**
Model 2	Group I, low-medium fit (Ref)	1		1	

(Continues)

TABLE 2 (Continued)

Predictor and outcomes		MF groups[a]			
		At baseline (T0)		At follow-up (T1)	
		OR	95% CI	OR	95% CI
	Group II, top fit	**0.15**	**0.07;0.32**	**0.18**	**0.10;0.33**
Cardiometabolic risk score [c]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.45**	**0.23;0.87**	**0.22**	**0.11;0.52**
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.44**	**0.23;0.86**	**0.24**	**0.11;0.52**
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.50**	**0.25;0.98**	**0.25**	**0.11;0.56**

Abbreviations: MF, muscular fitness; OR, odds ratio; CI, confident interval.
Notes: All models of the multilevel logistic regression included random effects (country, study region [intervention or control]). Multilevel logistic regression analysis between each MF groups and systolic blood pressure (SBP), triglycerides (TRG), ratio total cholesterol/high-density lipoprotein (TC/HDL), homeostatic model assessment (HOMA), sum of skinfolds (Skinfolds) or cardiometabolic risk score (CMR score). Model 0, non-adjusted; Model 1, adjusted by sex, age, parental education and zBMI (except for the Sum of skinfolds and CRM Score) at baseline (T0) or follow-up (T1); Model 2, Model 1 adjusted + Moderate to vigorous physical activity, diet quality index and total screen time at baseline (T0) or follow-up (T1), respectively. *Odds of being allocated to the highest SBP, TGR, TC/HDL, HOMA, Skinfolds, CMR score category. Bold letters indicates $P < 0.05$.
[a]MF groups: Group I, low-medium MF quartiles (Q1-Q3) at T0 or T1; Group II, top MR quartile (Q4) at T0 or T1.
[b]SBP, TGR, TC/HDL, HOMA, Skinfolds categories: Category I, first and second tertile; Category II, third tertile.
[c]CMR score categories: Category I, <1SD; Category II, ≥ 1SD.

probability of being allocated in the upper category of the sum of skinfolds, respectively, compared with low CRF, after controlling for all the potential confounders. Also, in T0, the top fit children had 69% lower probability of being allocated in the upper category of CMR score after controlling for all the confounders, and in T1, the significant effect disappeared after included the lifestyle behaviours as covariates in the model.

Taking into consideration the transition fitness groups over time, the highest proportion of children was those who remained in the low-medium MF or CRF level (Group I), being respectively the 65% and 63.7% of total sample. A low proportion of children become top fit (10.4% for MF and 12.8% for CRS) or become low fit over a two-year period (10.4% for MF, and 13.1% for CRF). Finally, a 14.2% of the sample for MF, and 10.4% for CRF remained in the top fit level. Table 4 shows separately the OR and 95%CI for the longitudinal associations between the individual and CMR categories, and the transition MF and CRF group over time. The strongest associations were observed for those become top MF over time (group III), they showed a 71% and 82% lower probability of being in the highest sum of skinfolds and CMR score categories, respectively, than those who remained low-medium fit. Also, those children who remained in

TABLE 3 Cross-sectional multilevel logistic regression between grouping of cardiorespiratory fitness (CRF) and individual indicators and cardiometabolic risk score at baseline (T0) and follow up (T1)

Predictor and outcomes		CRF groups[a]			
		At baseline (T0)		At follow-up (T1)	
		OR	95% CI	OR	95% CI
Systolic blood pressure [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	1.61	0.93;2.79	**0.55**	**0.32;0.96**
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**2.05**	**1.11;3.80**	0.80	0.44;1.46
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**2.14**	**1.12;4.08**	0.71	0.38;1.33
Triglycerides [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.53	0.28;1.02	0.90	0.52;1.57
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.55	0.28;1.10	1.06	0.59;1.90
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.66	0.32;1.34	1.25	0.68;2.30
Ratio total cholesterol/ high-density lipoprotein [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.66	0.39;1.14	0.82	0.48;1.39
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.81	0.46;1.43	1.08	0.62;1.92
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.86	0.47;1.56	1.05	0.58;1.90
Homeostatic model assessment [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.55	0.30;1.02	0.64	0.37;1.09
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.60	0.30;1.20	0.93	0.52;1.66
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	0.65	0.32;1.34	0.98	0.53;1.81
Sum of skinfolds [b]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.44**	**0.24;0.79**	**0.35**	**0.20;0.61**
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.34**	**0.18;0.64**	**0.33**	**0.19;0.57**
Model 2	Group I, low-medium fit (Ref)	1		1	

TABLE 3 (Continued)

Predictor and outcomes		CRF groups[a]			
		At baseline (T0)		At follow-up (T1)	
		OR	95% CI	OR	95% CI
	Group II, top fit	**0.40**	**0.21;0.76**	**0.36**	**0.20;0.64**
Cardiometabolic risk score [c]					
Model 0	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.30**	**0.14;0.64**	**0.44**	**0.22;0.88**
Model 1	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.26**	**0.12;0.57**	**0.44**	**0.22;0.88**
Model 2	Group I, low-medium fit (Ref)	1		1	
	Group II, top fit	**0.31**	**0.14;0.68**	0.55	0.27;1.12

Abbreviations: CRF, cardiorespiratory fitness; OR, odds ratio; CI, confident interval.
Notes: All models of the multilevel logistic regression included random effects (country, study region [intervention or control]). Multilevel logistic regression analysis between each MF groups and systolic blood pressure (SBP), triglycerides (TRG), ratio total cholesterol/high-density lipoprotein (TC/HDL), homeostatic model assessment (HOMA), sum of skinfolds (Skinfolds) or cardiometabolic risk score (CMR Score). Model 0, non-adjusted; Model 1, adjusted by sex, age, parental education and zBMI (except for the Sum of skinfolds and CRM Score) at baseline (T0) or follow-up (T1); Model 2, Model 1 adjusted + Moderate to vigorous physical activity, diet quality index and total screen time at baseline (T0) or follow-up (T1), respectively. *Odds of being allocated to the highest SBP, TGR, TC/HDL, HOMA, Skinfolds, CMR score category. Bold letters indicate p < 0.05.
[a]CRF groups: Group I, low-medium CRF quartiles (Q1-Q3) at T0 or T1; Group II, top CRF quartile (Q4) at T0 or T1.
[b]SBP, TGR, TC/HDL, HOMA, Skinfolds categories: Category I, first and second tertile; Category II, third tertile.
[c]CMR score categories: Category I, <1SD; Category II, ≥ 1SD.

the top MF group over time (group IV) had 69% lower probabilities of being in the highest sum of skinfolds category after controlling for the potential confounders. In the same vein, those in the top fit group over-time (group IV) showed also lower probabilities of a high CMR score after controlling for all covariates (OR = 0.38; CI: 0.13-1.08).

Those in the remain top CRF group (group IV) had lower odds of being in the high group of sum of skinfolds in comparison with those who remain in the low-medium fit CRF group over-time in the fully adjusted model (OR = 0.33; CI:0.12;0.91). Those children who became top fit (group III) had a 74% less odds of being in the highest sum of skinfolds quartile. Finally, those became low-medium CRF over-time (group II), had a 77% less odds of being in the highest CMR quartile in comparison to those who maintained a low-medium fit CRF group over-time in the fully adjusted level.

4 | DISCUSSION

In the present study, the impact of physical fitness as predictor of CMR was investigated, both cross-sectional and longitudinally, finding

TABLE 4 Longitudinal multilevel logistic regression between grouping of muscular fitness (MF) or cardiorespiratory fitness (CRF) and individual indicators and cardiometabolic risk (CMR) score at follow up (T1)

	Models for the MF[a] Groups						Models for the CRF[a] Groups					
	Model 0		Model 1		Model 2		Model 0		Model 1		Model 2	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Systolic blood pressure												
Group I, remain low-medium fit (Ref)	1		1		1		1		1		1	
Group II, became low-medium fit	0.74	0.32;1.71	1.23	0.49;3.22	1.35	0.53;3.43	0.91	0.43;1.94	1.26	0.55;2.86	1.28	0.56;2.92
Group III, became top fit	0.33	0.13;0.84	0.52	0.20;1.40	0.52	0.19;1.38	0.40	0.18;0.91	0.56	0.24;1.34	0.51	0.21;1.24
Group IV, remain top fit	0.71	0.34;1.47	1.14	0.52;2.47	1.21	0.55;2.66	0.63	0.27;1.45	0.96	0.39;2.37	0.86	0.34;2.18
Triglycerides												
Group I, remain low-medium fit (Ref)	1		1		1		1		1		1	
Group II, became low-medium fit	0.54	0.23;1.28	0.67	0.27;1.65	0.65	0.26;1.61	1.08	0.51;2.27	1.11	0.50;2.42	1.08	0.49;2.42
Group III, became top fit	1.36	0.61;2.99	1.64	0.72;3.73	1.65	0.72;3.82	1.04	051;2.15	1.21	0.57;2.57	1.42	0.65;3.12
Group IV, remain top fit	1.11	0.55;2.21	1.26	0.61;2.62	1.22	0.58;2.58	0.90	0.40;2.02	1.00	0.43;2.33	1.18	0.50;2.79
Ratio total cholesterol/ high-density lipoprotein												
Group I, remain low-medium fit (Ref)	1		1		1		1		1		1	
Group II, became low-medium fit	1.02	0.44;2.43	1.27	0.53;3.06	1.42	0.58;3.43	0.60	0.26;1.36	0.87	0.37;2.09	0.88	0.37;2.13
Group III, became top fit	0.53	0.22;1.25	0.64	0.26;1.58	0.66	0.27;1.63	0.94	0.42;2.10	1.23	0.53;2.83	1.19	0.50;2.82
Group IV, remain top fit	0.37	0.16;0.85	0.38	0.16;0.94	0.42	0.17;1.05	1.74	0.78;3.87	2.44	1.05;5.70	1.17	0.90;5.27
Homeostatic model assessment												
Group I, remain low-medium fit (Ref)	1		1		1		1		1		1	
Group II, became low-medium fit	0.32	0.14;0.70	0.44	0.19;1.01	0.46	0.20;1.08	0.80	0.39;1.68	1.20	0.54;2.66	1.17	0.52;2.61
Group III, became top fit	0.60	0.27;1.32	0.80	0.35;1.83	0.78	0.33;1.80	0.71	0.35;1.44	0.99	0.47;2.09	0.98	0.45;2.13
Group IV, remain top fit	0.81	0.40;1.62	1.09	0.53;2.26	1.09	0.52;2.30	0.73	0.33;1.60	1.11	0.48;2.59	1.24	0.51;3.00
Sum of Skinfolds[b]												
Group I, remain low-medium fit (Ref)	1		1		1		1		1		1	
Group II, became low-medium fit	0.47	0.18;1.21	0.48	0.18;1.25	0.48	0.18;1.27	0.25	0.09;0.70	0.29	0.10;0.84	0.27	0.09;0.80
Group III, became top fit	0.34	0.13;0.89	0.31	0.11;0.85	0.29	0.10;0.81	0.31	0.12;0.80	0.31	0.12;0.83	0.26	0.09;0.71
Group IV, remain top fit	0.32	0.13;0.80	0.32	0.12;0.83	0.31	0.12;0.82	0.41	0.16;1.08	0.38	0.14;1.03	0.33	0.12;0.91

(Continues)

TABLE 4 (Continued)

	Models for the MF[a] Groups						Models for the CRF[a] Groups					
	Model 0		Model 1		Model 2		Model 0		Model 1		Model 2	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Cardiometabolic risk score[c]												
Group I, remain low-medium fit (Ref)	1		1		1		1		1		1	
Group II, became low-medium fit	0.47	0.15;1.46	0.46	0.25;1.43	0.49	0.16;1.53	0.21	0.06;0.79	0.21	0.06;0.82	0.23	0.06;0.88
Group III, became top fit	0.19	0.04;0.90	0.18	0.04;0.87	0.18	0.04;0.89	0.32	0.11;0.96	0.32	0.11;0.97	0.39	0.13;1.22
Group IV, remain top fit	0.34	0.12;0.96	0.35	0.13;0.98	0.38	0.13;1.08	0.95	0.35;2.62	0.98	0.35;2.75	1.19	0.41;3.42

Abbreviations: MF, muscular fitness; CRF, cardiorespiratory fitness; Ref, reference group; OR, odds ratio; CI, confident interval.
Note: All models of the multilevel logistic regression included random effects (country, study region (intervention or control). Multilevel logistic regression analysis between each MF or CRF groups and systolic blood pressure (SBP), triglycerides (TRG), ratio total cholesterol/high-density lipoprotein (TC/HDL), homeostatic model assessment (HOMA), sum of skinfolds (Skinfolds) or cardiometabolic risk score (CMR Score). Model 0, non-adjusted, with the dependent baseline (T0) categories; Model 1, adjusted by sex, age, parental education and zBMI (except for the Sum of skinfolds and CRM Score) at follow-up (T1); Model 2, Model 1 adjusted + Moderate to vigorous physical activity, diet quality index and total screen time at baseline (T0) or follow-up (T1), respectively. * Odds of being allocated to the highest zSBP, zTGR, zTC_HDL, zHOMA, zskinfolds, CVD score category. Bold letters indicates p < 0.05.
[a]Muscular fitness (MF) or cardiorespiratory fitness (CRF) transition groups over time: Group I, unchanged fitness at low level over time (remain low fit); Group II, improved fitness over time (became top fit); Group III, decreased fitness over (became low fit); Group IV, unchanged fitness at top level over time (remain top fit).
[b]SBP, TGR, TC/HDL, HOMA, skinfolds categories: Category I, first and second tertile; Category II, third tertile.
[c]CMR score categories: Category I, <1SD; Category II, ≥ 1SD.

associations even after controlling for sociodemographic and lifestyle behaviours in a sample of European children. In addition, both MF and CRF were associated with the sum of skinfolds (individual CMR marker). Furthermore, we found that those children who reached the top MF level or remained in this level of MF during childhood had lower CMR than the rest of the children. Finally, those children who became top CRF over-time had lower probability of elevated CMR. These results were found after controlling by body mass index and lifestyle behaviours: objectively measured PA, DQI and total screen-time.

Despite the strong effort supporting the promotion of high levels of physical activity and fitness, a decline in fitness levels in children and adolescents has been reported worldwide.[32-35] In a recent review[36] of large-scale epidemiological studies it has been observed that the majority of studies reported a decline of fitness over time; specifically, performance in endurance, strength, and flexibility decreased over time. In a previous publication from the IDEFICS study, it has been observed that there are factors determining physical fitness in European children.[37] Thus, it is important to take into account these factors when assessing fitness in children.

4.1 | Muscular fitness

It has been suggested that high MF is associated with a wide range of health benefits and lower metabolic risk factors in children and adolescents.[38] Indeed, several cross-sectional studies support a strong inverse relationship between low MF and CVD risk factors and metabolic risk in young people.[8,39] Also in the IDEFICS study, lower-limb muscular strength was a longitudinal predictor for metabolic syndrome.[12] Furthermore, in the present study for MF, some associations were found in baseline and follow-up with the individual markers of CMR, mainly in the unadjusted models. However, the main associations were found for MF with sum of skinfolds, among the metabolic biomarkers, and with the CMR score adjusting by education and lifestyle behaviours such as objectively measured PA, DQI and total screen-time. Those in the top MF level had lower risk of sum of skin folds and CMR score. These results suggest that associations between MF and CMR are already found in childhood. Thus, identification of young children at low levels of MF is important to avoid metabolic risk.

In addition, in previous studies, it has been observed that MF in youth is associated with adiposity and cardio-metabolic parameters later in life.[40] From our prospective results, we found that those who had a top MF level at baseline, even if the level decreased at follow up, or remained in the top MF level over time had lower probability for future sum of skinfolds and CMR. Additionally, in the present study, the probability of lower CMR remained significant for those in the top MF level even when adjusting by potential confounders. Also, these prospective results suggest that MF improvements should start early in life in order to prevent metabolic risk already in childhood, especially considering that youth with low levels of MF are at increased risk of maintaining a low level into adulthood.[41]

We also found that those individuals who remained at top MF level, had a 69% lower probability of having a high sum of skinfolds

even after adjusting by a set of confounders. This has been addressed in a previous review, where MF was associated to future lower risk of skinfold thickness later in life using also other cardiometabolic markers.[40] In this sense, the meta-analysis found a significant, moderate-large ($P < 0.05$) effect size between muscular fitness at baseline and skinfold thickness (r = − 0.32; 95% CI −0.40 to −0.23), and CVD risk score (r = − 0.29; 95% CI −0.39 to −0.18). Furthermore, another review that included both, cross-sectional and longitudinal data, reported a strong association between low MF and total and central adiposity among youth.[38] Also, those subjects with higher MF have also higher volume of muscle in detriment of fat and it is known that skeletal muscle is a tissue that highly contributes to basal metabolic rate.[42] Thus, this larger muscle mass and higher metabolic efficiency could result into a greater daily energy expenditure,[43] which could explain the inverse association with body fat in the present study.

4.2 | Cardiorespiratory fitness

A high CRF is found in children and adolescents with a healthier cardiovascular profile.[7] Previous studies have suggested that CRF may have a cardio protective role in youth[44] and that unfit subjects have higher CMR already in childhood.[45] Out of the cross-sectional results of the present study, we found that CRF was associated with CMR but only in the baseline examination, as the results became non-significant in older children when entering in the model the lifestyle behaviours.

In addition, CRF has been considered as a valid method of identifying children at risk of cardiometabolic abnormalities.[46] Previous prospective studies found inverse associations between CRF and future metabolic syndrome and its individual markers and BMI already in children and adolescents.[11,12] In our prospective analysis, we found that those who become fit over time, that is, who evolved from the low-medium fitness level at baseline and reached the highest level over time, had 77% lower probabilities of a high CMR score. Some previous articles showed prospective associations between higher CRF and lower CMR.[47] However, other articles showed no associations between CRF and metabolic risk but it should be noted that these studies were considering CRF from adolescence.[48,49] Also, previous studies assessing CRF and cardiovascular risk factors did not account for important confounding factors such as adiposity. This could be the reason for the lack of consistent findings in the literature.

Finally, most of our population were on the low-medium quartiles (Q1-Q3) of MF or CRF over time with more than 60% of subjects for each fitness component (65.1% and 63.7%, respectively). Previous findings, in line with those from the previous study, highlight the necessity of enhancing fitness in childhood to improve health, even in children and adolescents.[7] We know that children with low CRF in early life will most probably have low levels of fitness later in life.[50]

There are some limitations that need to- be accounted. Firstly, the use of covariates from lifestyle behaviours in the analysis reduced the sample size. Secondly, the use of a CMR score with the same weight for each metabolic marker could be considered as a limitation but they have been calculated by sex and age. On the other hand, the present study has some strengths. Firstly, the use of standardized data with validated methods from eight European countries should be considered a strength. Furthermore, the prospective design of the analysis gives a better insight of long-term associations. Also, the inclusion of several and objective measures used as confounders could be considered as a strength. Finally, this is the first study assessing the association between fitness and CMR in European children that takes into account body composition, objectively measured PA and relevant lifestyle behaviours such as diet quality and screen time. With the addition of a set of lifestyle behaviours as covariates, the association remained significant, highlighting the strong association between fitness and CMR, and the importance to take into consideration the energy balance-related behaviours.

5 | CONCLUSION

These results suggest that having a high MF level during childhood or improving that MF level over time reduces the odds of having elevated CMR in childhood. In the same vein, improving CRF during childhood showed the same effect. Additionally, these improvements were independent of PA level, diet quality and screen time. These results underline the importance of enhancing fitness, either MF or CRF, during childhood in order to reduce the CMR already in children.

CONFLICT OF INTEREST
The authors declare that they have no competing interests.

AUTHOR'S CONTRIBUTION
ASP, LGM, CB, WA, LMA and EMGG conceptualized and designed the study, collected data, carried out the initial analyses, drafted the initial manuscript and revised the manuscript. LL, DM, WA, TV, MT and SDH designed the data collection, coordinated and supervised data collection and reviewed the manuscript; FL, AH, LL and YK, designed critically reviewed the manuscript for important intellectual content. All authors have read and approved the final version of the manuscript, and agree with the order of presentation of the authors.

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SUPPORTING INFORMATION

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