



Original article

Nutritional and physical fitness parameters in adolescence impact cardiovascular health in adulthood



Jules Morcel ^{a,*}, Laurent Béghin ^a, Nathalie Michels ^b, Thaïs De Ruyter ^b, Elodie Drumez ^c, Emeline Cailliau ^c, Angela Polito ^d, Cinzia Le Donne ^d, Lorenzo Barnaba ^d, Elena Azzini ^d, Stefaan De Henauw ^b, Maria Luisa Miguel Berges ^{e,f}, Leandro Teixeira Cacau ^g, Luis A. Moreno ^{e,f}, Frédéric Gottrand ^a

^a Univ. Lille, Inserm, CHU Lille, U1286 - INFINITE - Institute for Translational Research in Inflammation, and CIC 1403 – Clinical Investigation Center, F-59000 Lille, France

^b Department of Public Health and Primary Care, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium

^c CHU Lille, Département de Biostatistiques, F-59000 Lille, France

^d Agricultural Research Council – Research Center on Food and Nutrition – (formerly INRAN), Rome, Italy

^e GENUD (Growth, Exercise, Nutrition and Development) Research Group, Escuela Universitaria de Ciencias de la Salud, Universidad de Zaragoza, Spain

^f Consorcio CIBER, M.P. Fisiopatología de la Obesidad y Nutrición (CIBEROBN), Instituto de Salud Carlos III (ISCIII), Madrid, Spain

^g Department of Nutrition, School of Public Health, University of São Paulo, São Paulo, 01246-904, Brazil

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SUMMARY

Background & aims: Cardiovascular diseases are the leading cause of mortality worldwide, originating in the first decades of life. A better understanding of their early determinants would allow for better prevention. This study aimed to evaluate the impact of nutritional and activity-related characteristics during adolescence on young adult cardiovascular risk factors.

Methods: The Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) study included adolescents (aged 12.5–17.5 years) in 10 European centres. Four centres designed a nested cohort including 236 participants who were reassessed as young adults (21–32 years). Food consumption was evaluated by dietary recalls, physical activity by accelerometers, physical fitness using physical tests and nutritional knowledge by questionnaires. Cardiovascular health was assessed by Pathobiological Determinants of Atherosclerosis in Youth (PDAY) Study risk scores and its components. Factors associated with cardiovascular risk were identified using a multivariable regression model.

Results: Higher Diet Quality Index (DQI, $P = 0.012$) and nutritional knowledge ($P = 0.015$) were significantly associated with lower modified PDAY risk scores. Ultra-processed foods were associated with a lower non-high-density lipoprotein (non-HDL) cholesterol ($P = 0.003$), whereas DQI ($P = 0.014$) and Planetary Health Diet Index ($P = 0.016$) were associated with a higher HDL cholesterol. Higher DQI was also related to a lower body mass index (BMI, $P = 0.006$). In addition, cardiorespiratory fitness was related to a lower BMI ($P = 0.004$).

Conclusions: Nutritional knowledge, diet quality and adherence to a sustainable diet in adolescence decrease cardiovascular risk in adulthood, whereas ultra-processed food consumption increases risk. These factors appear as targeted prevention tools for promoting a healthier adolescent lifestyle to decrease long-term cardiovascular risk.

Clinical trial registry number: Clinicaltrials.gov NCT02899416.

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1. Introduction

Coronary heart disease and stroke are the most common cardiovascular diseases, and are the primary cause of mortality worldwide, accounting for 14.2 millions deaths in 2019 [1]. Beyond

* Corresponding author.

E-mail address: jules1.morcel@chu-lille.fr (J. Morcel).

Abbreviations

AA	abdominal aorta
BELINDA	better life by nutrition during adulthood
BMI	body mass index
CA	coronary arteries
CRF	cardiorespiratory fitness
DQI	diet quality index
HbA1c	glycated hemoglobin
HDL	high density lipoprotein
HELENA	healthy lifestyle in Europe by nutrition in adolescence
HPDI	healthful plant-based diet index
LBES	lower body explosive strength
MBP	mean blood pressure
MVPA	moderate-to-vigorous physical activity
NKT	nutritional knowledge test
PDAY	pathobiological determinants for atherosclerosis in youth
UBMS	upper body muscular strength
UPF	ultraprocessed food

mortality, these conditions profoundly affect the quality of life of surviving individuals through chronic pain, physical limitations or psychological stress. Cardiovascular diseases are caused by the obstruction of arteries through the formation of atherosclerotic plaques. Longitudinal studies using recent non-invasive imaging technologies [2,3] have shown that atherosclerosis and cardiovascular risk accumulation begin at a young age and are promoted by easily measurable risk factors, including dyslipidaemia, high blood pressure, smoking, elevated blood glucose levels or an increased body mass index (BMI) [4–7]. Risk factors identified between six and 18 years of age may increase vascular aging and predict cardiovascular risk after 30 years of follow-up [8]. Similarly, risk factors identified in childhood and adolescence are associated with higher risks of cardiovascular events and death before the age of 60 years [9]. The aim of primary prevention is to limit the development of diseases or health disorders in a healthy population. It could play a crucial role in early detection and implementation of interventions to alter the trajectories of cardiovascular health and to reduce the incidence of severe complications later in life. As adolescence is a key life period marked by the transition from a parent-controlled lifestyle to independence [10], nutritional choices, physical activity, physical fitness and sleep rhythm are highly heterogeneous [11]. Although there is a lack of information on this issue in the literature, it seems essential to identify which parameters during adolescence can influence future cardiovascular risk. Using a nested longitudinal cohort of adolescents reassessed in early adulthood, we tested 13 nutritional and activity-related parameters during adolescence as potential predictors of cardiovascular risk in adulthood.

2. Methods

2.1. Study population

The Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) study was performed between 2006 and 2007 as a European multicentre cross-sectional study including 3528 healthy adolescents aged from 12.5 to 17.5 years in 10 investigation centres within nine countries. The HELENA study assessed the cardiovascular status and health-related parameters such as nutrition,

physical activity, physical fitness, lifestyle habits, clinical and anthropometric measures, and biological samples (blood, stool and hair), constituting a large database and biobank [12]. A decade later, the Better Life by Nutrition During Adulthood (BELINDA) study was designed as a nested follow-up cohort. This study reassessed adolescents who became young adults ten to 14 years after their participation between 2016 and 2020. Four investigation centers accepted to participate to this follow-up study: Ghent (Belgium), Lille (France), Rome (Italy), and Zaragoza (Spain). Of the 1327 eligible subjects in the four centers, 1095 were unreachable, untraceable, refused, or were unable to participate because of the COVID-19 pandemic. Then, 232 young adults were included, 215 of whom had available cardiovascular risk factors data recorded [13]. The mean age at inclusion was 14.8 ± 1.2 years in adolescence and 25.8 ± 1.4 years at follow-up. There were no exclusion criteria, only that participants must have participated in the HELENA study, signed an informed consent form, and had health insurance at the time of enrolment. The flow diagram of the inclusions have also been previously published [13] and is presented in [Supplemental Fig. 1](#).

2.2. Study design

This multicentre nested follow-up study reassessed the subjects at the age of 21–32 years, ten to 14 years after their first participation. All participants were invited to come fasting to the investigation centre to make an entire day visit to collect and measure anthropometrics, nutritional, physical fitness, physical activity and biological parameters. Three 24-h dietary recalls were also applied, including two weekdays and one weekend day. In addition, participants wore a three-dimensional accelerometer for a week after their visit to measure physical activity. The same tools and materials were used between adolescence and adulthood to make measures reliable and reproducible. The details of the study population, methodology used and chosen parameters justification have been described elsewhere [12].

2.3. Outcome evaluation primary outcome

The Pathobiological Determinants for Atherosclerosis in Youth (PDAY) risk scores are based on the PDAY study [14] involving autopsies of 1117 subjects aged from 15 to 34 years between 1987 and 1994, who died from external causes, such as accident, homicide or suicide. Strong et al. [14] aimed to identify subjects with grade IV and V coronary artery (PDAY CA) and abdominal aorta (PDAY AA) atherosclerotic lesions, according to the American Heart Association [15]. These scores are recognized as a strong predictor of sub-clinical atherosclerosis over a long-term period [16] and have proven their reliability in the Coronary Artery Risk Development in Young Adults (CARDIA) study [17] and in the Cardiovascular Risk in Youth Finns Study [18]. Variables used for the calculation of the scores are divided into two categories, non-modifiable risk factors (age and sex) and modifiable risk factors (high-density lipoprotein [HDL] and non-HDL cholesterol, smoking habits, mean blood pressure (MBP), BMI and glyco-haemoglobin (HbA1c) level [16]. As in the CARDIA study [19], a modified PDAY risk score was used, excluding non-modifiable parameters to decrease the potential bias due to the age heterogeneity in our population ([Table 1](#)).

2.4. Measurement methods

We collected data on tobacco consumption using a self-administered questionnaire. The concentration of total cholesterol and HDL cholesterol was measured on fresh blood samples by an enzymatic method and the non-HDL cholesterol concentration was

Table 1

Modified PDAY risk scores, predicting target lesions in the coronary arteries and the abdominal aorta.

	Risk factors	Modified PDAY risk scores	
	Non-modifiable parameters	Coronary arteries	Abdominal aorta
Age (years)	15–19 ^a	–	–
	20–24	–	–
	25–29	–	–
	30–34	–	–
Sex	Male ^a	–	–
	Female	–	–
Non-HDL cholesterol (mg/dL)	Modifiable parameters		
	<130 ^a	0	0
	130–159	2	1
	160–189	4	2
	190–219	6	3
HDL cholesterol (mg/dL)	≥220	8	4
	<40	1	0
	40–59 ^a	0	0
	≥60	–1	0
Tobacco consumption	Non-smoker ^a	0	0
	Smoker	1	4
Blood pressure (mmHg)	Normotensive ^a	0	0
	Hypertensive	4	3
Obesity (BMI ≥30 kg/m ²)	Men		
	No ^a	0	0
	Yes	6	0
	Female		
	No ^a	0	0
Hyperglycaemia (% HbA1c)	Yes	0	0
	<8 ^a	0	0
	≥8	5	3

Abbreviations: BMI, body mass index; HbA1c, glycated haemoglobin; HDL, high-density lipoprotein; PDAY, Pathobiological Determinants for Atherosclerosis in Youth.^aReference category.^a Reference category.

calculated by subtraction. Concentrations of HDL and non-HDL cholesterol were stratified in categories as reported in Table 1. HbA1c concentration was measured by capillary electrophoresis using a frozen red blood cell sample with a cut-off established at 8%, according to the material used [20]. BMI was calculated from weight and height measured in underwear and without shoes. Adults were classified as obese when they had a BMI ≥30 kg/m², while the International Obesity Task Force guidelines were used for adolescents [21]. Blood pressure was measured three times by tensiometer and hypertension was defined by MBP ≥110 mmHg (sum of higher systolic plus twice diastolic divided by 3) [22]. Each single risk factor included in modified PDAY risk scores was explored as secondary cardiovascular risk outcomes.

Identification of nutrition and physical activity parameters We identified *a priori*, 13 adolescent nutritional and physical activity parameters for their potential impact on cardiovascular and atherogenic risk in a healthy adult European population (Table 2).

Justification for part of the selected parameters is reported elsewhere [13]. In this paper, for nutritional parameters we have also used the Planetary Health Diet Index (PHDI) [23], a 16-component diet score based on the EAT-Lancet Commission dietary guidelines [24] and validated among adolescents and middle-aged adults [25], but never used in the context of a longitudinal study. The nutritional knowledge score, calculated by using the Nutritional Knowledge Test (NKT) was also added to the analysis [26].

2.5. Statistical analysis

At the outset, 280 analysable subjects were planned to allow the inclusion of 14 independent variables into multivariate analyses according to the rule of thumb of 10–20 subjects per independent variable analysed [27,28]. With a study sample of 215 subjects and

13 independent variables analysed, the number of subjects per variable was 16.5 subjects. Statistical testing was done at the two-tailed level of 0.05. No correction for multiple testing was applied. Data were analysed using the SAS software package (release 9.4; SAS Institute, Cary, NC, USA). Categorical variables are expressed as numbers (percentage) and quantitative variables are expressed as mean (standard deviation, SD) or median (25th–75th percentile) according to normality. The normality of distribution was assessed graphically and using the Shapiro–Wilk test. For variables where the normality of distribution was not satisfied, even after a log transformation, variables were analysed as two- or three-level categorical variables, according to the distribution. We firstly assessed the evolution between adolescence and adulthood in cardiovascular, nutritional, physical activity, and physical fitness parameters by performing intra-subject comparisons with paired Student *t*-tests or Wilcoxon's signed rank test according to the normality of intra-subject differences. We secondly identified predictors of cardiovascular risk scores and their main components (i.e. PDAY AA > 0, PDAY CA > 0, BMI, MBP, HDL, non-HDL) at adulthood among nutritional and physical activity parameters in adolescence. For each outcome, independent predictors were identified using a multivariable logistic or linear regression model with the bootstrapping selection procedure proposed by Sauerbrei [29] to account for potential collinearity and to limit the instability of the final multivariable models. Missing data in candidate variables and each outcome were handled by combining the bootstrap method with multiple imputations [30]. The first stage of this procedure consisted of creating imputed datasets ($m = 35$, calculated regarding the rule of thumb to have a maximal fraction of missing information $FMI/m < 1\%$) [31] for the full primary multivariable regression model) from the original dataset using a regression switching approach (chained equation) under missing at random hypothesis with a predictive mean matching method for

Table 2

List of adolescent parameters included in the multivariate analysis.

Variables		Analysed parameters
Nutrition	1	Salt intake
	2	Eicosapentaenoic acid + docosahexaenoic acid intakes
	3	Fructose from processed food intake
	4	DQI
	5	HPDI
	6	Ultra-processed food consumption (NOVA classification)
	7	PHDI
	8	NKT
Physical activity and fitness	9	Moderate-to-vigorous physical activity
	10	Sedentary time
	11	CRF
	12	UBMS by hand-grip test
	13	LBES by standing broad jump

Abbreviations: CRF, cardiorespiratory fitness; DQI, Diet Quality Index; HPDI, Healthful Plant-based Diet Index; LBES, lower body explosive strength; NKT, Nutritional Knowledge Test; PHDI, Planetary Health Diet Index; UBMS, upper body muscular strength.

quantitative variables and logistic regression models (binary, ordinal or polynomial) for categorical variables. The second stage consisted of creating bootstrap resamples ($n = 200$) from each imputed dataset, yielding 7000 replicates. In the third stage, a multivariable regression model with a backward selection at the 0.05 level was performed on each of these replicates. In the fourth stage, for each candidate variable and each possible pair of candidate variables (to acknowledge the collinearity issue), the proportion of replicates, in which that variable (or pair of variables) was retained in the selected model, were determined. Variables selected in at least 70% of replicates and variables with the highest selection frequency from the pairs selected in at least 90% of replicates were retained as independent variables to build the final multivariable model. Finally, the final predictive model was obtained by performing a multivariable regression model in the 35 imputed datasets, including the variables retained in stage 4 and by applying Rubin's rules to combine the regression coefficients estimates.

2.6. Patient involvement

Patients were actively involved in recruitment of the HELENA and BELINDA study. The results of this study will be disseminated to the BELINDA participants through oral and written communications.

3. Results

Cardiovascular risk scores in adulthood and evolution of the cardiovascular risk factors included in the modified PDAY scores are presented in Table 3. Both non-HDL ($P < 0.001$) and HDL ($P < 0.001$) increased significantly between these two time periods, as well as BMI ($P < 0.001$).

A Sankey diagram is presented in Fig. 1 to highlight individual variations of BMI group classification.

Tobacco habits and MBP did not change significantly. HbA1c measurements were not performed at adolescence. Changes in nutritional and physical activity parameters are presented in Table 4.

Upper body muscular strength (UBMS) and sedentary time increased whereas lower body explosive strength (LBES) and moderate-to-vigorous physical activity (MVPA) decreased significantly. Regarding nutritional parameters, salt and ultra-processed food (UPF) intake decreased whereas PHDI and NKT increased significantly. No changes were observed in HPDI and DQI scores.

Figure 2 shows the multivariable analysis identifying nutritional and physical activity parameters in adolescence impacting cardiovascular risk scores and factors in adulthood.

Non-significant parameters are reported in Supplemental Tables 1 and 2. Modified PDAY CA and PDAY AA scores were classified into two groups for analyses according to score categories: No cardiovascular risk (≤ 0) and minimal-to-moderate cardiovascular risk (≥ 1). Higher DQI was associated with a lower probability of minimal-to-moderate cardiovascular risk according to modified PDAY CA (odds ratio [OR] for 10-unit increase = 0.71; 95% confidence interval [CI] = 0.54–0.93; $P = 0.012$). For modified PDAY AA, only NKT was associated with a lower risk of minimal-to-moderate cardiovascular risk (OR = 0.97; 95% CI = 0.94–1.00; $P = 0.015$). No physical activity nor physical fitness parameters were found as associated with PDAY risk scores. Next, each cardiovascular risk factor included in the PDAY risk score were tested. Regarding physical activity parameters, UBMS was significantly related to higher BMI and MBP. Cardiorespiratory fitness (CRF) was significantly related to a lower BMI. Regarding diet quality parameters, subjects with high DQI had a significantly lower BMI ($P = 0.006$) and higher HDL ($P = 0.014$). Higher consumption of UPF was related to higher non-HDL ($P = 0.003$). Higher adherence to PHDI was related to a higher HDL ($P = 0.016$).

4. Discussion

To the best of our knowledge, this study is the first to assess the impact of combined physical activity, fitness and nutritional parameters of healthy adolescents on cardiovascular risk in adulthood. While a few studies based on a similar design have been published, none has addressed all the dimensions of nutrition and physical activity [32,33]. The majority of previous studies addressing nutritional factors associated with cardiovascular risk are cross-sectional or with a short follow-up and therefore the risk factors and cardiovascular risk have been evaluated at the same age [34–36]. Since pathophysiological studies demonstrate that atherosclerosis starts early in life and needs decades before influencing cardiovascular health [37], it is our opinion that pertinent parameters influencing cardiovascular risk should be identified decades before adulthood in the context of a preventive approach. However, we acknowledge that our cohort characteristics changed over time in terms of cardiovascular risk factors, nutritional habits and physical activity and that could have influenced our results.

The main finding of our study is that cardiovascular risk in young adulthood, i.e., PDAY risk scores, lipid profile, and BMI, is mostly influenced by diet quality and nutritional knowledge, while fitness has controversial influence on a few of these factors.

Table 3

Evolution of cardiovascular risk factors from adolescence to adulthood and cardiovascular risk scores at adulthood.

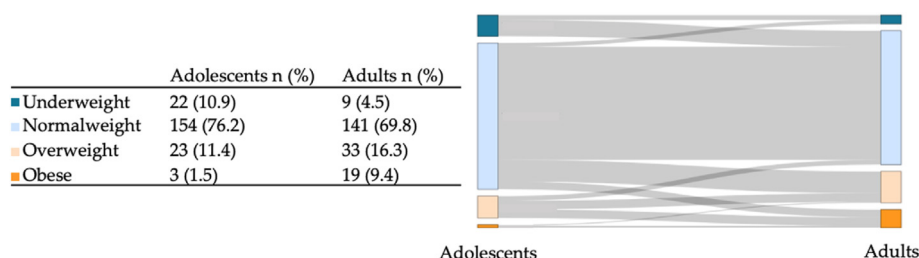
	N	Adolescents	Adults	Differences	P
BMI (kg/m ²)	202	20.0 (18.3–22.1)	22.6 (21.0–25.1)	2.7 (1.4–4.8)	<0.001 ^a
MBP (mmHg)	202	83.3 (78.0–89.0)	83.7 (79.0–89.0)	0.8 (–5.0–6.3)	0.52 ^a
Non-HDL (mg/dL)	74*	98.6 (86.0–110.9)	107.0 (88.0–132.0)	14.0 (–10.1–29.2)	<0.001 ^a
HDL-CH (mg/dL)	74*	55.1 ± 10.3	61.2 ± 16.9	6.2 (2.8–9.5)	<0.001 ^b
Smoker n (%)	201	54 (26.9)	51 (25.4)	–	0.69 ^c
Modified PDAY CA (–1–25 points)	215	–	0 (–1–1)	–	–
>0 n (%)			81 (37.7)		
Modified PDAY AA (0–14 points)	215	–	0 (0–4)	–	–
>0 n (%)			92 (42.8)		

*reference category.

For adolescents and adults, values are frequency (percentage), mean ± standard deviation or median (25th–75th percentile). For a change from adolescence to young adulthood, values are presented as mean (95% confidence interval, CI) or median (25th–75th percentile).

Abbreviations: BMI, body mass index; MBP, mean blood pressure; Non-HDL-CH, non-high-density lipoprotein cholesterol; HDL-CH, HDL cholesterol.

*Blood sampling was realized on one-third of the entire adolescent population.

^a Calculated using Wilcoxon signed rank test.^b Calculated using paired Student t test.^c Calculated using McNemar test.**Fig. 1.** Sankey diagram, tracking weight status between adolescence and adulthood.**Table 4**

Changes of physical activity, physical fitness and nutritional parameters between adolescence and adulthood.

	N ^a	Adolescents	Adults	Differences	P
UBMS (kg)	202	27.5 (23.2–35.2)	35.4 (30.0–49.1)	7.2 (4.0–13.0)	<0.001 ^b
LBES (cm)	196	162.5 (143.0–186.0)	152.5 (127.5–184.5)	–11.0 (–27.5–5.0)	<0.001 ^b
CRF (stage)	97	6.0 (4.0–7.5)	6.0 (3.0–7.0)	–0.5 (–1.0–1.0)	0.093 ^b
MVPA (min/day)	125	51.6 (40.9–69.6)	41.9 (31.3–60.3)	–10.0 (–25.9–9.1)	<0.001 ^b
Sedentary time (min/day)	125	559.7 ± 63.2	588.9 ± 98.8	29.2 (10.5–47.9)	0.003 ^c
Salt intake (g/day)	159	4.96 (3.31–7.78)	4.65 (3.33–6.24)	–0.54 (–2.50–1.64)	0.034 ^b
EPA + DHA intakes (mg/day)	126	169.8 (123.3–313.8)	93.0 (33.6–366.3)	–63.8 (–168.9–209.0)	0.32 ^b
Fructose from processed food (g/day)	124	13.3 (9.5–24.0)	16.3 (9.3–29.5)	0.9 (–5.8–11.0)	0.16 ^b
DQI (score, –33–100%)	142	64.8 ± 11.9	63.5 ± 12.7	–1.3 (–3.6–1.0)	0.26 ^c
HPDI (score, 0–90 points)	136	53.6 ± 5.3	54.6 ± 6.1	1.0 (–0.2–2.1)	0.10 ^c
UPF consumption (g/day)	148	543.1 (324.0–740.6)	417.0 (245.0–628.4)	–81.5 (–323.9–121.2)	0.010 ^b
PHDI (score, 0–150 points)	131	45.7 ± 12.3	48.6 ± 10.4	2.9 (0.4–5.5)	0.025 ^c
NKT (score, 0–100%)	143	62.5 ± 12.8	77.3 ± 11.3	14.8 (12.6–17.1)	<0.001 ^c

For adolescents and adults, values are presented as mean ± standard deviation or median (25th–75th percentile). For change from adolescence to adulthood, values are presented as mean (95% CI) or median (25th–75th percentile).

Abbreviations: CRF, cardiorespiratory fitness; DHA, docosahexaenoic acid; DQI, Diet Quality Index; EPA, eicosapentaenoic acid; HPDI, Healthful Plant-based Diet Index; LBES, lower body explosive strength; MVPA, moderate-to-vigorous physical activity; NKT, Nutritional Knowledge Test; PHDI, Planetary Health Diet Index; UPF, ultra-processed food.^a The difference in the number of subjects corresponds to missing or unusable data.^b Calculated using Wilcoxon signed rank test.^c Calculated using paired Student t test.

Previous cross-sectional studies showed that diet quality is associated with lower obesity [33,37–39], cardiovascular risk [39,40] and food behaviours such as meal skipping [34] in adolescent or adult populations but we could not find any data using these parameters from longitudinal studies. Nutritional knowledge showed no associations with BMI [35] in adolescent cross-sectional populations. To the best of our knowledge this is the first time that the impact of these parameters at adolescence have been studied on follow-up.

Surprisingly, even though UBMS and LBES showed a positive association with cardiovascular health in adolescence in the context of the LabMed study [41], contradictory results were observed concerning the effect of physical fitness tests in adolescence on cardiovascular risk in adulthood in our study. Some tests had no influence, higher score of UBMS was associated with higher BMI and higher MBP and higher CRF was associated with lower BMI. This suggests physical fitness in adolescents is not a major determinant of cardiovascular health.

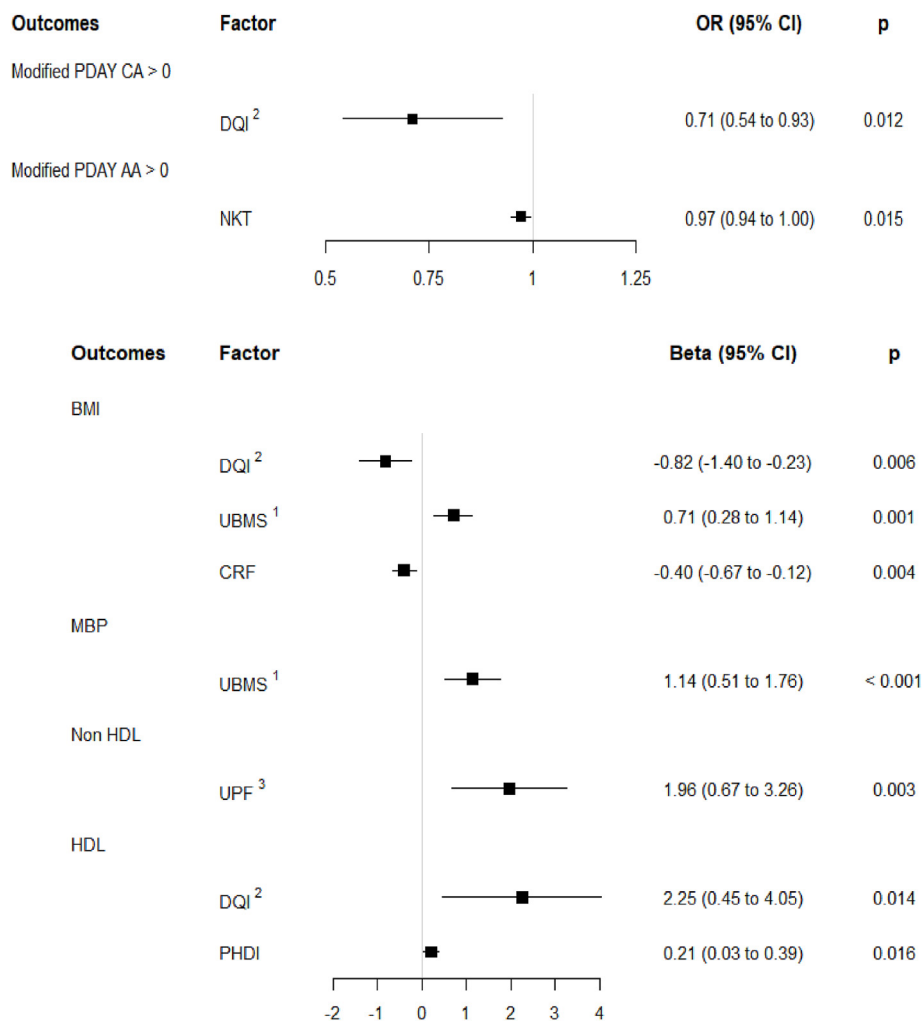


Fig. 2. Forest plot identifying adolescent parameters impacting cardiovascular risk scores factors in adulthood. Effect sizes (OR or beta), 95%CI and p-value were calculated using a multivariable logistic or linear regression model with the bootstrapping selection procedure proposed by Sauerbrei to account for potential collinearity and to limit the instability of the final multivariable models. Missing values were handled by multiple imputation ($m = 35$). ¹ Effect size (beta and OR) calculated for 5-kg increase; ² Beta calculated for 10-unit increase; ³ Beta calculated for 100 g per day increase; ⁴ OR calculated for 15-min increase. **Abbreviations:** BMI, body mass index; CRF, cardiorespiratory fitness; DQI, Diet Quality Index; HDL, high-density lipoprotein; MBP, mean blood pressure; NKT, Nutritional Knowledge Test; PDAY AA, PDAY risk score for abdominal aorta; PDAY CA, PDAY risk score for coronary arteries; PHDI, Planetary Health Diet Index; UBMS, upper body muscular strength; UPF, ultra-processed food.

Previous analysis at adolescence (the HELENA study) showed that our population was rather active and from a favourable socioeconomic background [13]. In adulthood, our subjects remained healthy with a low prevalence of obesity (9.4%), and metabolic syndrome (1.4%), and finally a low cardiovascular risk. As a comparison, in the American Add Health study, 11% of the child–adolescent subjects (seven–12 years) were obese and at follow-up in adulthood (24–32 years) 37% were obese. In that study, obesity was associated with higher cholesterol, diabetes, and hypertension, but no nutritional nor physical activity data were collected [42]. In the context of our study, almost 70% of young adults had a normal weight. Even if the prevalence of overweight and obesity increased twofold between adolescence and young adulthood in our population, it remains lower than that of other longitudinal cohort studies. This probably explains the low cardiovascular risk in our population, and our results should be more applicable on healthy and active populations.

The strengths of our study are the multiple risk factors approach which allow the establishment of a global cardiovascular risk overview. The long-term follow-up (ten–14 years) including

biological samples in the two time periods and the statistical method are also methodological strengths. The limitation of this study is the relatively small number of reassessed subjects at adulthood. We found that subjects included in the BELINDA study had a significantly lower BMI and a significantly higher socioeconomic status than those who did not participate in this follow-up study [13]. This constitutes a follow-up bias within the study population. Neither family history nor genetic information were included in the statistical models.

The challenge of this study was to identify the physical activity, physical fitness and nutritional parameters during adolescence that influence cardiovascular risk in adulthood to target adolescents' clusters on which health promotion campaigns should focus. Our findings highlight that while physical activity and fitness should not be ignored in adolescence, we found that the strongest long-term determinants of cardiovascular health in adolescence were related to diet quality and dietary knowledge. The DQI, NKT, UPF classification and EAT-Lancet Commission guidelines are easy-to-use health assessment tools in primary and secondary schools that could be used for screening adolescents for health promotion campaigns.

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Author contributions

Jules Morcel: Conceptualization, Methodology, Formal analysis, Methodology, Visualization, Writing – original draft. Laurent Béghin: Conceptualization, Methodology, Validation, Investigation, Writing – review & editing, Supervision, Project administration, Funding acquisition. Nathalie Michels: Conceptualization, Methodology, Validation, Investigation, Writing – Review & Editing, Supervision, Project administration. Thaïs de Ruyter: Formal analysis, Resources, Writing – Review & Editing. Elodie Drumez: Formal analysis, Writing – Review & Editing. Emeline Cailliau: Formal analysis, Writing – Review & Editing. Angela Polito: Conceptualization, Methodology, Validation, Investigation, Writing – Review & Editing, Supervision, Project administration. Cinzia Le Donne: Validation, Writing – Review & Editing. Lorenzo Barnaba: Validation, Writing – Review & Editing. Elena Azzini: Validation, Writing – Review & Editing. Stefaan De Henauw: Conceptualization, Methodology, Validation, Investigation, Writing – review & editing, Supervision, Project administration, Funding acquisition. Maria Luisa Miguel Berges: Formal analysis, Resources, Writing – Review & Editing. Leandro Teixeira Cacao: Formal analysis, Resources, Writing – Review & Editing. Luis Moreno: Conceptualization, Methodology, Validation, Investigation, Writing – review & editing, Supervision, Project administration, Funding acquisition. Frédéric Gottrand: Conceptualization, Methodology, Validation, Investigation, Writing – review & editing, Supervision, Project administration, Funding acquisition.

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this work, none authors used any Generative AI and AI-assisted technologies in the writing process.

Conflicts of interest

Pr. Frédéric Gottrand has received consulting fees from Nestlé. The remaining authors do not have any conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.clnu.2024.06.022>.

References

- [1] WHO. Cardiovascular disease World organisation. 2021.
- [2] Gidding SS, Bookstein LC, Chomka EV. Usefulness of electron beam tomography in adolescents and young adults with heterozygous familial hypercholesterolemia. *Circulation* 1998;98(23):2580–3.
- [3] Fayad ZA, Fuster V, Nikolaou K, Becker C. Computed tomography and magnetic resonance imaging for noninvasive coronary angiography and plaque imaging: current and potential future concepts. *Circulation* 2002;106(15):2026–34.
- [4] Harttala O, Magnussen CG, Kajander S, Knuuti J, Ukkonen H, Saraste A, et al. Adolescence risk factors are predictive of coronary artery calcification at middle age: the cardiovascular risk in young Finns study. *J Am Coll Cardiol* 2012;60(15):1364–70.
- [5] Urbina EM, Khoury PR, Bazzano L, Burns TL, Daniels S, Dwyer T, et al. Relation of blood pressure in childhood to self-reported hypertension in adulthood. *Hypertension* 2019;73(6):1224–30.
- [6] Twig G, Yaniv G, Levine H, Leiba A, Goldberger N, Derazne E, et al. Body-mass index in 2.3 million adolescents and cardiovascular death in adulthood. *N Engl J Med* 2016;374(25):2430–40.
- [7] Pollock BD, Stuchlik P, Harville EW, Mills KT, Tang W, Chen W, et al. Life course trajectories of cardiovascular risk: impact on atherosclerotic and metabolic indicators. *Atherosclerosis* 2019;280:21–7.
- [8] Wang Y, Wang J, Zheng XW, Du MF, Zhang X, Chu C, et al. Early-life cardiovascular risk factor trajectories and vascular aging in midlife: a 30-year prospective cohort study. *Hypertension* 2023;80(5):1057–66.
- [9] Jacobs Jr DR, Woo JG, Sinaiko AR, Daniels SR, Ikonen J, Juonala M, et al. Childhood cardiovascular risk factors and adult cardiovascular events. *N Engl J Med* 2022;386(20):1877–88.
- [10] Kelder SH, Perry CL, Klepp KI, Lytle LL. Longitudinal tracking of adolescent smoking, physical activity, and food choice behaviors. *Am J Publ Health* 1994;84(7):1121–6.
- [11] Story M, Neumark-Sztainer D, French S. Individual and environmental influences on adolescent eating behaviors. *J Am Diet Assoc* 2002;102(3 Suppl):S40–51.
- [12] Moreno LA, De Henauw S, Gonzalez-Gross M, Kersting M, Molnar D, Gottrand F, et al. Design and implementation of the healthy lifestyle in Europe by nutrition in adolescence cross-sectional study. *Int J Obes* 2008;32(Suppl 5):S4–11.
- [13] Morcel J, Béghin L, Michels N, Vanhelst J, Labreuche J, Drumez E, et al. Identification of lifestyle risk factors in adolescence influencing cardiovascular health in young adults: the BELINDA study. *Nutrients* 2022;14(10).
- [14] Strong JP, Malcom GT, Oalmann MC, Wissler RW. The PDAY Study: natural history, risk factors, and pathobiology. *Pathobiological Determinants of Atherosclerosis in Youth*. *Ann N Y Acad Sci* 1997;811:226–35. ; discussion 235–227.
- [15] Stary HC, Chandler AB, Dinsmore RE, Fuster V, Glagov S, Insull Jr W, et al. A definition of advanced types of atherosclerotic lesions and a histological classification of atherosclerosis. A report from the Committee on Vascular Lesions of the Council on Arteriosclerosis, American Heart Association. *Arterioscler Thromb Vasc Biol* 1995;15(9):1512–31.
- [16] McMahan CA, Gidding SS, Fayad ZA, Zieske AW, Malcom GT, Tracy RE, et al. Risk scores predict atherosclerotic lesions in young people. *Arch Intern Med* 2005;165(8):883–90.
- [17] Gidding SS, Rana JS, Prendergast C, McGill H, Carr JJ, Liu K, et al. Pathobiological determinants of atherosclerosis in youth (PDAY) risk score in young adults predicts coronary artery and abdominal aorta calcium in middle age: the CARDIA study. *Circulation* 2016;133(2):139–46.
- [18] McMahan CA, Gidding SS, Viikari JS, Juonala M, Kahonen M, Hutri-Kahonen N, et al. Association of Pathobiologic Determinants of Atherosclerosis in Youth risk score and 15-year change in risk score with carotid artery intima-media thickness in young adults (from the Cardiovascular Risk in Young Finns Study). *Am J Cardiol* 2007;100(7):1124–9.
- [19] Gidding SS, Colangelo LA, Nwabuo CC, Lewis CE, Jacobs DR, Schreiner PJ, et al. PDAY risk score predicts cardiovascular events in young adults: the CARDIA study. *Eur Heart J* 2022;43(30):2892–900.
- [20] Sriwimol W, Choosongsang P, Choosongsang P, Treerut P, Muenniam B, Makkong P, et al. Strong correlation and high comparability of capillary electrophoresis and three different methods for HbA1c measurement in a population without hemoglobinopathy. *Scand J Clin Lab Invest* 2020;80(2):139–50.
- [21] Cole TJ, Lobstein T. Extended international (IOTF) body mass index cut-offs for thinness, overweight and obesity. *Pediatr Obes* 2012;7(4):284–94.
- [22] McGill Jr HC, Strong JP, Tracy RE, McMahan CA, Oalmann MC. Relation of a postmortem renal index of hypertension to atherosclerosis in youth. The pathobiological determinants of atherosclerosis in youth (PDAY) research group. *Arterioscler Thromb Vasc Biol* 1995;15(12):2222–8.
- [23] Cacao LT, De Carli E, de Carvalho AM, Lotufo PA, Moreno LA, Bensenor IM, et al. Development and validation of an index based on EAT-lancet recommendations: the planetary health diet index. *Nutrients* 2021;13(5).
- [24] Willett W, Rockstrom J, Loken B, Springmann M, Lang T, Vermeulen S, et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. *Lancet* 2019;393(10170):447–92.
- [25] Cacao LT, Hanley-Cook GT, Huybrechts I, De Henauw S, Kersting M, Gonzalez-Gross M, et al. Relative validity of the Planetary Health Diet Index by

- comparison with usual nutrient intakes, plasma food consumption biomarkers, and adherence to the Mediterranean diet among European adolescents: the HELENA study. *Eur J Nutr* 2023;62(6):2527–39.
- [26] Sichert-Hellert W, Béghin L, De Henauw S, Grammatikaki E, Hallstrom L, Manios Y, et al. Nutritional knowledge in European adolescents: results from the HELENA (healthy lifestyle in Europe by nutrition in adolescence) study. *Publ Health Nutr* 2011;14(12):2083–91.
- [27] Mitchell H. Multivariable analysis: a practical guide for clinicians and public health researchers. 3rd ed. Cambridge University Press; 2011.
- [28] Thomas P. Regression methods and correlations. John Wiley & Sons; 2013.
- [29] Sauerbrei W, Schumacher M. A bootstrap resampling procedure for model building: application to the Cox regression model. *Stat Med* 1992;11(16):2093–109.
- [30] Heymans MW, van Buuren S, Knol DL, van Mechelen W, de Vet HC. Variable selection under multiple imputation using the bootstrap in a prognostic study. *BMC Med Res Methodol* 2007;7:33.
- [31] White IR, Royston P, Wood AM. Multiple imputation using chained equations: issues and guidance for practice. *Stat Med* 2011;30(4):377–99.
- [32] Beslay M, Srouf B, Mejean C, Alles B, Fiolet T, Debras C, et al. Ultra-processed food intake in association with BMI change and risk of overweight and obesity: a prospective analysis of the French NutriNet-Sante cohort. *PLoS Med* 2020;17(8):e1003256.
- [33] Howie EK, McVeigh JA, Smith AJ, Zabatiero J, Bucks RS, Mori TA, et al. Physical activity trajectories from childhood to late adolescence and their implications for health in young adulthood. *Prev Med* 2020;139:106224.
- [34] Ojeda-Rodríguez A, Zazpe I, Morell-Azanza L, Chueca MJ, Azcona-Sanjulian MC, Martí A. Improved diet quality and nutrient adequacy in children and adolescents with abdominal obesity after a lifestyle intervention. *Nutrients* 2018;10(10).
- [35] Agustina R, Nadiya K, Andini EA, Setianingsih AA, Sadariskar AA, Prafiyanti E, et al. Associations of meal patterning, dietary quality and diversity with anemia and overweight-obesity among Indonesian school-going adolescent girls in West Java. *PLoS One* 2020;15(4):e0231519.
- [36] Reinehr T, Kersting DM, Chahda C, Wollenhaupt A, Andler W. Nutritional knowledge of obese and nonobese children. *J Pediatr Gastroenterol Nutr* 2001;33(3):351.
- [37] Cacau LT, Benseñor IM, Goulart AC, Cardoso LO, Lotufo PA, Moreno LA, et al. Adherence to the planetary health diet index and obesity indicators in the Brazilian longitudinal study of adult health (ELSA-Brasil). *Nutrients* 2021;13(11).
- [38] Genovesi S, Parati G. Cardiovascular risk in children: focus on pathophysiological aspects. *Int J Mol Sci* 2020;21(18).
- [39] Neri D, Steele EM, Khandpur N, Cediel G, Zapata ME, Rauber F, et al. Ultra-processed food consumption and dietary nutrient profiles associated with obesity: a multicountry study of children and adolescents. *Obes Rev* 2022;23(Suppl 1):e13387.
- [40] Srouf B, Fezeu LK, Kesse-Guyot E, Alles B, Mejean C, Andrianasolo RM, et al. Ultra-processed food intake and risk of cardiovascular disease: prospective cohort study (NutriNet-Sante). *BMJ* 2019;365:l1451.
- [41] Agostinis-Sobrinho C, Garcia-Hermoso A, Ramirez-Velez R, Moreira C, Lopes L, Oliveira-Santos J, et al. Longitudinal association between ideal cardiovascular health status and muscular fitness in adolescents: the LabMed Physical Activity Study. *Nutr Metabol Cardiovasc Dis* 2018;28(9):892–9.
- [42] Harris KM, Halpern CT, Whitel EA, Hussey JM, Killea-Jones LA, Tabor J, et al. Cohort profile: the national longitudinal study of adolescent to adult health (Add health). *Int J Epidemiol* 2019;48(5):1415.