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ORIGINAL CONTRIBUTION

Clinical and physical characteristics of thinness in adolescents: the HELENA study

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Abstract

Purpose Thinness in adolescence has not been studied as extensively as overweight or obesity. The aim of this study was to assess the prevalence, characteristics, and health impacts of thinness in a European adolescent population.

Methods This study included 2711 adolescents (1479 girls, 1232 boys). Blood pressure, physical fitness, sedentary behaviors, physical activity (PA), and dietary intake were assessed. A medical questionnaire was used to report any associated diseases. A blood sample was collected in a subgroup of the population. Thinness and normal weight were identified using the IOTF scale. Thin adolescents were compared with adolescents of normal weight.

Results Two hundred and fourteen adolescents (7.9%) were classified as being thin; the prevalence rates were 8.6% in girls and 7.1% in boys. Systolic blood pressure was significantly lower in adolescents with thinness. The age at the first menstrual cycle was significantly later in thin female adolescents than in those with normal weight. Upper-body muscular strength measured in performance tests and time spent in light PA were significantly lower in thin adolescents. The Diet Quality Index was not significantly lower in thin adolescents, but the percentage of adolescents who skipped breakfast was higher in adolescents with a normal weight (27.7% vs 17.1%). Serum creatinine level and HOMA-insulin resistance were lower and vitamin B12 level was higher in thin adolescents.

Conclusions Thinness affects a notable proportion of European adolescents with no physical adverse health consequences.

Keywords Thinness · Youth · Prevalence · Europe · Characteristics · Lifestyle

Introduction

Thinness in children and adolescents is clinically defined as a low body mass index (BMI) using international age- and sex-specific cutoff points [1]. A recent systematic review and meta-analysis showed that the prevalence of thinness in children and adolescents increased in several European countries between 2000 and 2017 [2]. Based on the International Obesity Task Force (IOTF) definitions, it has been estimated that about 10% of European children and adolescents are thin [2]. The Childhood Obesity Surveillance Initiative has also reported an increase in the prevalence of thinness, particularly in Eastern Europe [3], which raises concerns about possible adverse health consequences. Thinness is associated with a poor quality of life, lower physical fitness level, amenorrhea, decreased bone mineral content, scoliosis, negative body image, and fatigue in childhood and adolescence, and with increased mortality in later life [4–8]. However, most epidemiological studies have not separated the pathological (e.g., anorexia nervosa) from nonpathological thinness characterized by resistance to weight gain.

Thinness in adolescence has not been studied as extensively as overweight or obesity, and there is a lack of information about the characteristics and associated factors, including lifestyle factors such as physical activity (PA), sedentary behaviors, dietary habits, and physical fitness. We hypothesized that thinness is constitutional in European adolescents and has no adverse health consequences for lifestyle habits.

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Materials and methods

Study design

The present ancillary study is based on the Healthy Lifestyle in Europe by Nutrition in Adolescence (HELENA) study. The aim of the HELENA study was to obtain a broad range of standardized, reliable, and comparable nutrition and health-related data from a random sample of European adolescents aged 12.5–17.5 years. The HELENA study was performed from 2006 to 2007 in 10 European cities: Vienna (Austria), Ghent (Belgium), Lille (France), Athens (Greece), Heraklion (Greece), Pecs (Hungary), Rome (Italy), Dortmund (Germany), Zaragoza (Spain), and Stockholm (Sweden). Details of the recruitment, sampling, standardization, and harmonization processes were published elsewhere [9, 10].

The aims and objectives were explained carefully to each adolescent and their parents. Written, informed consent was obtained from the adolescent and their parents. The HELENA study was approved by the local ethics committee for each country, and all procedures were performed in accordance with the ethical standards of the Helsinki Declaration of 1975 as revised in 2008 [11].

A summary of the recruitment process is shown in Fig. 1. All participants were recruited at school and met the general HELENA inclusion criteria. From the total population of 3528 adolescents, a subsample of 2711 (76.8%) was included in the present analysis after exclusion of adolescents with overweight ($n = 619$) or obesity ($n = 198$). Based on the International Obesity Task Force (IOTF) definitions and among the 2711 adolescents, 214 with thinness and 2497 with a normal-weight status, and the latter were classified as the control group. From a total of 3528 adolescents included in the HELENA study, one-third of the school classes were randomly selected in each center for blood collection, and a total of 846 adolescents (62 with thinness and 784 as controls) were included in a subsample analysis.

Measurements

Anthropometric measures

Anthropometric measurements were obtained using standard techniques [12]. Weight was measured with the participant in underwear and without shoes to the nearest 0.1 kg using an electronic scale (Seca 871; Seca, Hamburg, Germany). Height was measured with the participant barefoot without shoes in the Frankfurt plane to the nearest 0.1 cm using a telescopic height-measuring instrument (Seca 225). BMI was calculated from weight (kg) divided by squared height (m^2). Thinness and normal weight were identified using the IOTF scale [1]. The IOTF cutoffs link BMI values at 18 years to

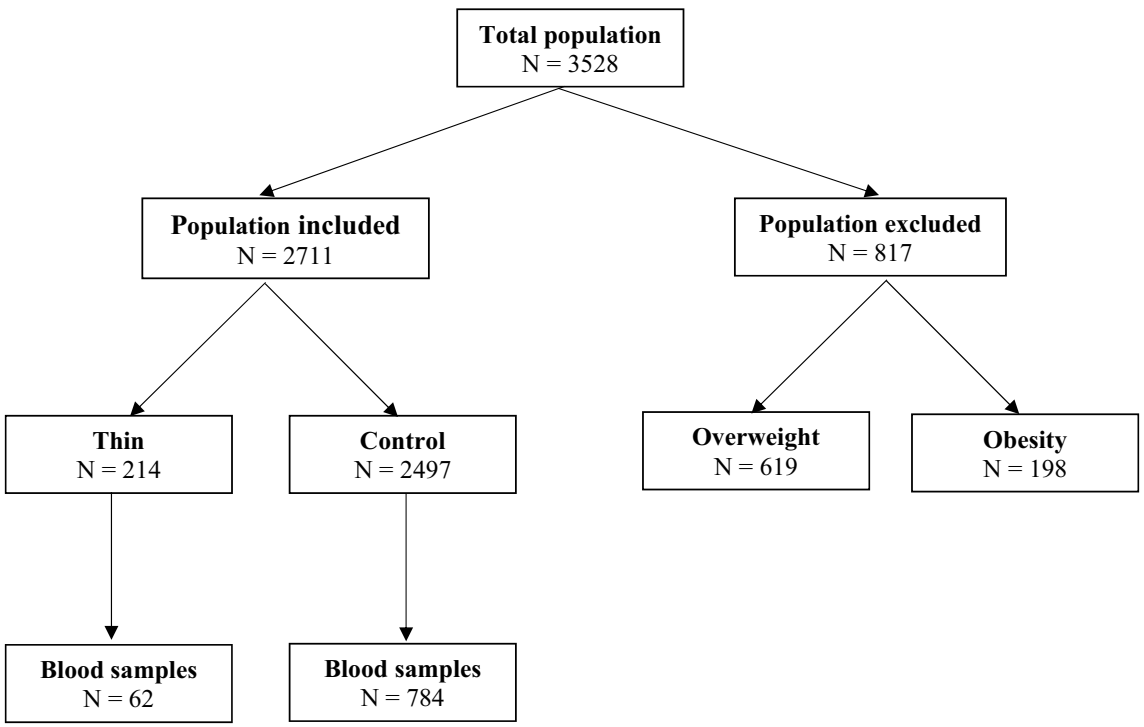

Fig. 1 Flowchart of the study

centiles in childhood, giving: thinness < 18.5 kg/m^2 and normal weight between ≥ 18.5 kg/m^2 and < 25 kg/m^2 [1].

Prenatal and birth factors

A parental questionnaire was developed to collect information about exclusive breastfeeding duration, gestational duration, and birth weight and height [13]. Parents were asked to recall this information based on their child's health record booklets. Exclusive breastfeeding duration was reported in four categories: no breastfeeding, < 3 months, ≥ 3 to < 6 months, and ≥ 6 months [14]. The gestational duration was reported in three categories: < 35 weeks, 35–40 weeks, and > 40 weeks. The questionnaire was sent to parents before study inclusion and was collected at their adolescent's examination.

Body composition

Indices of fat and fat-free mass were assessed by two methods. Fat mass was evaluated using the bicipital, tricipital, subscapular, suprailiac, thigh, and medial calf skinfold thicknesses measured on the left side of the body to the nearest 0.2 mm with a Holtain caliper (Holtain, Ltd., Wales, UK). Measurements were performed three consecutive times, and the mean was used for the analysis. Fat mass was calculated using skinfold thickness and Slaughter's equation, validated in children and adolescents, and is expressed as a percentage of body weight [15]. Total fat-free mass was estimated after a 10-h overnight fast using bioelectrical impedance analysis (BIA) (Akern®, BIA101 Akern, Pontassieve Italy). Shoes, socks, watches, and jewelry were removed. Participants were fasted and were requested to void the bladder before testing. Electrode tape, conductivity gel, and current electrodes were placed on the dorsal surfaces of the right hand and foot at the distal metacarpals and metatarsals, respectively. Detector electrodes were applied at the right pisiform prominence of the wrist and between the medial and lateral malleoli at the ankle [16]. The BIA value was expressed in resistance and was used to calculate fat-free mass using the equation of Houtkooper et al., validated in youth aged 10–19 years [17].

Social factors

Parental educational level was classified using a specific questionnaire completed by the mothers. This questionnaire was adapted from the International Standard Classification of Education (ISCED) (https://ec.europa.eu/eurostat/statisticsexplained/index.php/International_Standard_Classification_of_Education_ISCED). Educational level was scored as 1 = primary and lower education (levels 0, 1, and 2 in the ISCED classification); 2 = higher secondary (levels 3 and 4 in the ISCED classification); and 3 = tertiary (levels 5 and 6 in the ISCED classification) [18].

The family affluence scale was included in a questionnaire completed by the adolescents. This scale is an indicator of material affluence and considers parameters such as car ownership, having one's own bedroom, Internet availability, and computer ownership. The score ranges from 0 (lowest) to 8 (highest), and these scores were recategorized as low (0–2), medium (3–5), and high (6–8) [19].

Medical history and clinical and biological assessments

Each participant underwent a detailed medical examination. Medical history and medications were recorded in a specific case report form for each participant. Pubertal status was assessed by direct observation according to Tanner and Whitehouse, performed by a well-trained pediatrician [20]. Signs of puberty were scored according to pubic hair status using the standard pictures of pubic hair development from the Tanner scale. For girls, the age at the first menstrual cycle was obtained in a questionnaire. Blood pressure was measured twice (Omron M6, HEM 70,001; Omron, Kyoto, Japan). For blood pressure measurement, the participant was seated with the back supported and feet on the ground in a separate quiet room for 10 min. Two readings of systolic blood pressure were taken after 10-min intervals of quiet rest, and the lower of the two was recorded for analysis. Blood samples were collected by venipuncture after an overnight fast. Heparinized tubes were used for blood collection and centrifuged within 30 min (3500 rpm for 15 min) to avoid hemolysis. Samples were stored and transported at 4–7 °C to the central laboratory of the study (Bonn, Germany) and stored there at – 80 °C until assayed.

Lifestyle factors

The lifestyle factors assessed in our study included daily PA, sedentary behaviors, sleep habits, and the dietary profile including dietary quality, total energy intake, and breakfast consumption (skipping or consuming).

PA was assessed using accelerometry, an objective measure for use with youth [21]. The accelerometer used was the ActiGraph® monitor (ActiGraph®, GT1M®, Pensacola, FL, USA). The epoch interval for the ActiGraph monitor was set at 15 s. Adolescents wore the accelerometer on their lower back beneath their clothing using an elastic belt with adjustable buckle for 7 consecutive days. Participants who did not record at least 3 days with a minimum of 8 h of activity per day were excluded from the analyses. Zero-activity periods of 20 min or longer were interpreted as "not worn time", and these periods were removed from the summation of activity. The PA patterns were assessed using the thresholds used in previous studies of adolescents. The assessment of time

spent in each PA level was based on cutoff points of 0–500, 501–1999, 2000–2999, and > 2999 counts/min [22].

Sedentary behaviors were assessed using a structured questionnaire that included questions about the amount of time spent habitually in front of the television or a computer, or playing video games during school days and school-free days. The questionnaire used questions such as: "On weekdays, how many hours do you usually spend watching television?", "On weekdays, how many hours do you usually spend on computers?", and "On weekdays, how many hours do you usually spend playing video games?" The answers were classified into two categories: 0–2 h/day and > 2 h/day [23, 24]. This measure has been shown to provide a reliable (intraclass correlation = 0.82; 95% CI 0.75–0.87) and valid (criterion validity = 0.3) tool for assessing sedentary time [24].

Sleep habits were estimated using a questionnaire that included two questions on sleep duration: "During weekdays, how many hours (and minutes) do you usually sleep?" and "During weekend days, how many hours (and minutes) do you usually sleep?"

Dietary intake was assessed using two nonconsecutive 24-h recalls performed on any two convenient days of the week [25]. The 24-h recalls were recorded using a self-administered, computer-based HELENA Dietary Intake Assessment Tool (HELENA-DIAT) that has been validated in European adolescents [26]. Detailed descriptions of the data collection and analysis have been published elsewhere [18, 27–29]. The Diet Quality Index for Adolescents (DQI-AM) was used to assess the overall quality of the diet. The DQI-AM comprises four components: quality, diversity, equilibrium, and meal frequency [18, 27–29]. A score was calculated for each day, and the mean daily score was taken as the participant's overall index. The intakes of foods and nutrients were calculated for each adolescent. A breakfast assessment was also performed. Adolescents reported their breakfast habits by responding to the following statement, "I often skip breakfast", which had seven possible answers ranging from strongly disagree (1) to strongly agree (7). The participants were categorized into three groups: consumers (answer 1 or 2); occasional consumers (answer 3, 4, or 5); and skippers (answer 6 or 7).

Smoking status was recorded using a questionnaire. There were four possible answers and the participants were categorized into three groups: regular consumer (answer 1); occasional consumer (answer 2 or 3); and nonsmoker (answer 4).

Physical fitness

Health-related physical fitness components were assessed by incorporating the Eurofit and FitnessGram tests. The protocols and procedures to assess health-related physical fitness in the HELENA study have been published elsewhere [30]. Briefly, cardiorespiratory fitness was assessed using the 20-m shuttle run test, upper- and lower-body muscular strength were assessed by measuring handgrip strength and the standing long jump test, respectively, and speed–agility was assessed using the 4 × 10-m shuttle run test. All tests were performed twice, and the best score was recorded except for the cardiorespiratory fitness test, which was performed only once. Good reliability has been reported in young people for all tests used in this study using the Bland–Altman plots [31]. It has been shown that the systematic error when fitness assessment was performed twice was nearly 0 for all the tests [31].

Statistical analysis

Categorical variables are reported as frequency (percentage) and continuous variables as mean ± standard deviation (SD) for data with a normal distribution or as median (interquartile range) otherwise. Normality was assessed graphically and using the Shapiro–Wilk test. To evaluate the magnitude of the differences in characteristics according to thinness status, the absolute standardized differences were calculated, and an absolute standardized difference > 20% was interpreted as a meaningful imbalance. Each outcome was compared between adolescents with thinness and controls using linear regression models for continuous outcomes (after applying a log or rank transformation if needed) and logistic regression models for categorical outcomes (binary or multinomial logistic according to the number of modalities). For these analyses, pubertal status (I + II vs III vs IV vs V) and center were included as confounding factors. From these models, effects sizes and 95% confidence intervals (CIs) were estimated as the odds ratios for categorical outcomes and as standardized differences (Cohen's d) for continuous outcomes. According to Cohen, a standardized difference < 0.2 is considered as null, 0.2–0.5 as small, 0.5–0.8 as medium, and > 0.8 as large [32]. All effect sizes were calculated using adolescents with normal weight as the reference group. *P* values were corrected for multiplicity by controlling the false discovery rate using the Benjamini–Hochberg procedure applied to a set of outcomes in the same domain. All comparisons were performed separately for boys and girls as a sex-stratified analysis using the same methodology. All statistical analyses were performed using SAS software (release 9.4; SAS Institute, Cary, NC, USA).

Results

A total of 2711 adolescents were included. The prevalence of thinness was 7.9% in the overall population (95% CI = 6.9 to 8.9; *n* = 214): 7.1% in boys (95% CI = 5.6 to 8.5; *n* = 87/1145) and 8.6% in girls (95% CI = 7.2 to 10.0;

Table 1 Characteristics of participants

	Overall $n=2711$	Thin $n=214$	Controls $n=2497$	ASD (%)*
Sex				10.5
Boys	1232/2711 (45.4)	87/214 (40.7)	1145/2497 (45.9)	
Girls	1479/2711 (54.6)	127/214 (59.3)	1352/2497 (54.1)	
Age (yrs)[1]	14.8 ± 1.2	14.8 ± 1.2	14.9 ± 1.2	4.0
Weight (kg)	54.7 ± 8.7	44.2 ± 6.0	55.6 ± 8.3	157.1
Height (cm)	165.8 ± 9.1	164.2 ± 8.8	165.9 ± 9.1	19.4
Body mass index (kg/m^2)	19.8 ± 2.0	16.3 ± 1.0	20.1 ± 1.8	261
Smoking consumption				7.0
Regular smoker	245/2637 (9.3)	17/211 (8.1)	228/2426 (9.4)	
Occasional consumer	220/2637 (8.3)	17/211 (8.1)	203/2426 (8.4)	
No smoker	2172/2637 (82.4)	177/211 (83.9)	1995/2426 (82.2)	
Body composition				
Fat-free mass (%)[2]	45.0 ± 7.6	39.7 ± 5.2	45.4 ± 7.6	87.7
Fat mass (%)[3]	20.4 ± 6.7	15.3 ± 4.5	20.8 ± 6.7	98.0
Mother education level**				8.3
I	828/2556 (32.4)	62/202 (30.7)	766/2354 (32.5)	
II	788/2556 (30.8)	59/202 (29.2)	729/2354 (31.0)	
III	940/2556 (36.8)	81/202 (40.1)	859/2354 (36.5)	
Socioeconomic status				10.2
Low	471/1851 (25.4)	38/152 (25.0)	433/1699 (25.5)	
Medium	1005/1851 (54.3)	77/152 (50.7)	928/1699 (54.6)	
High	375/1851 (20.3)	37/152 (24.3)	338/1699 (19.9)	
Neonatal characteristics				
Weight (kg)[4]	3.3 ± 0.6	3.4 ± 0.6	3.3 ± 0.6	12.4
Height (cm)[5]	50.4 ± 3.2	50.6 ± 3.1	50.4 ± 3.2	5.7
Exclusive breastfeeding				10.1
Never	465/2054 (22.6)	33/157 (21.0)	432/1897 (22.8)	
< 3 months	718/2054 (35.0)	61/157 (38.9)	657/1897 (34.6)	
3 to 5 months	646/2054 (31.5)	49/157 (31.2)	597/1897 (31.5)	
> 6 months	225/2054 (11.0)	14/157 (8.9)	211/1897 (11.1)	
Underlying disease				4.9
Yes	1358/2711 (50.1)	112/214 (52.3)	1246/2497 (49.9)	
No	1353/2711 (49.9)	102/214 (47.7)	1251/2497 (50.1)	
Pubertal status				43.0
I	9/2456 (0.4)	2/204 (1.0)	7/2252 (0.3)	
II	144/2456 (5.9)	23/204 (11.3)	121/2252 (5.4)	
III	585/2456 (23.8)	68/204 (33.3)	517/2252 (23.0)	
IV	1031/2456 (42.0)	78/204 (38.2)	953/2252 (42.3)	
V	687/2456 (28.0)	33/204 (16.2)	654/2252 (29.0)	

Values are expressed as n/N (percentage) or mean ± standard deviation

[1]29 missing values. [2]54 missing values. [3]138 missing values. [4]568 missing values. [5]621 missing values

ASD absolute standardized difference; *BMI* body mass index

*ASD an absolute standardized difference > 20% was interpreted as a meaningful imbalance

**Lower education I; higher secondary education II; higher education or university degree (III)

$n=127/1352$). The adolescents' characteristics are presented in Table 1. The mean ages of the 214 adolescents with thinness and 2497 normal-weight adolescents were 14.8 ± 1.2 and 14.9 ± 1.2 years, respectively. No between-group differences were observed with respect to sex, age, height, socioeconomic status, or mother's educational level, except for anthropometric data such as weight and body composition. Thin adolescents had lower fat and fat-free masses, and

weight compared with controls. Pubertal status was delayed in the thin group (16% with pubertal status *V* compared with 29% in controls). Medical history (antecedents and actual diseases) did not differ between the thin and normal-weight groups. The data for neonatal characteristics are also presented in Table 1. No meaningful differences were found between the two groups for weight and height at birth, gestational duration, or breastfeeding duration.

The comparisons of clinical characteristics between adolescents with thinness and controls are presented in Table 2. Relevant differences were observed between the two groups for systolic blood pressure and the age at the first menstrual cycle. Systolic blood pressure was lower in thin adolescents ($d = -0.43$; 95% CI = – 0.57 to – 0.29). Similar results were found in the sex-stratified analyses (in boys, $d = -0.56$; 95% CI = – 0.78 to – 0.35; in girls, $d = -0.31$; 95% CI = –0.50 to – 0.12) (Supplemental Fig. 1). At the age at the first menstrual cycle, female adolescents with thinness were older (13.1 years) than those with a normal weight (12.5 years) ($d = 0.47$; 95% CI = 0.25 to 0.70).

The comparisons of lifestyle behaviors and physical fitness between the thin and control adolescents are shown

Table 2 Comparisons of clinical characteristics according to weight status

	Thin $n = 214$	Controls $n = 2497$	Effect size (95%CI)[1]	P^1
Blood pressure ($n = 2656$)[2]				
Systolic (mmHg)	109.3 ± 11.3	115.0 ± 12.5	– 0.43 (– 0.57 to –0.29)	< 0.001
Diastolic (mmHg)	63.6 ± 8.9	64.3 ± 8.3	– 0.02 (– 0.16 to 0.13)	0.81
First menstrual cycle *(yrs) ($n = 1281$)	13.1 ± 1.1	12.5 ± 1.2	0.47 (0.25 to 0.70)	< 0.001

Values are expressed as frequency (percentage) or mean ± standard deviation

*Only for girls

Effect sizes are standardized differences using normal weight as reference

P values are corrected using false discovery rate adjustment

[1]Adjusted for center and pubertal status

[2]3 missing values for thin group and 52 missing values for control group

Table 3 Comparisons of lifestyle behaviors and physical fitness between thin and controls

	Thin $n = 214$	Controls $n = 2497$	Effect size (95%CI)[1]	P^1
Physical activity ($n = 1735$)[2]				
Sedentary (min.day^{-1})	549.0 ± 73.3	543.2 ± 80.3	0.07 (– 0.10 to 0.24)	0.76
Light (min.day^{-1})	160.5 ± 37.7	166.7 ± 40.7	– 0.23 (– 0.39 to – 0.06)	0.043
Moderate (min.day^{-1})	38.0 ± 14.5	39.4 ± 14.3	– 0.13 (– 0.30 to 0.04)	0.57
Vigorous (min.day^{-1})	19.7 ± 12.4	19.7 ± 14.0	0.01 (– 0.16 to 0.18)	0.90
MVPA (min.day^{-1})	57.7 ± 23.3	59.1 ± 23.9	– 0.07 (– 0.24 to 0.10)	0.76
Sedentary behaviors ($n = 2613$)[3]				
≥ 2 h.day^{-1} in school days	116 (55.5)	1322 (55.0)	1.09 (0.81 to 1.47)	0.76
≥ 2 h.day^{-1} in weekend days	160 (76.9)	1868 (77.8)	0.96 (0.68 to 1.37)	0.90
Physical fitness ($n = 2544$)[4]				
Cardiorespiratory fitness (mL.kg.min^{-1})	41.9 ± 6.9	41.8 ± 7.5	– 0.05 (– 0.21 to 0.10)	0.76
Lower muscular strength (cm)	165.8 ± 31.5	167.7 ± 34.9	– 0.04 (– 0.19 to 0.10)	0.76
Upper muscular strength (kg)	25.9 ± 6.9	30.4 ± 8.6	– 0.43 (– 0.57 to -0.29)	< 0.001
Speed/agility (s)	12.1 ± 1.1	12.1 ± 1.3	– 0.03 (– 0.17 to 0.12)	0.86
Sleep duration (h) ($n = 2558$)[5]	8.2 ± 1.1	8.0 ± 1.2	0.05 (– 0.09 to 0.20)	0.76

Values are expressed as frequency (percentage) or mean ± standard deviation

Effect sizes are standardized differences for quantitative variables and odds ratio for categorical variables using normal weight as reference

P values are corrected using false discovery rate adjustment

[1]Adjusted for center and pubertal status

[2]71 missing values for thin group and 905 missing values for control group

[3]5 missing values for thin group and 93 missing values for control group

[4]14 missing values for thin group and 153 missing values for control group

[5]12 missing values for thin group and 141 missing values for control group

in Table 3. No relevant differences were found between thin and normal-weight adolescents for sleep duration and time spent in sedentary behaviors. No meaningful differences were found for time spent at different daily PA levels, except for light PA (LPA). Thin adolescents spent less time in LPA compared with controls ($d = -0.23$; 95% CI = –0.39 to –0.06); despite the similar effect sizes in boys and girls, this difference was no longer significant in the sex-stratified analyses (Supplemental Fig. 2). Upper-body muscular strength was lower in thin adolescents than in controls ($d = -0.43$; 95% CI = – 0.57 to – 0.29). Similar results were found in the sex-stratified analyses (in boys, $d = -0.51$; 95% CI = – 0.70 to – 0.32; in girls, $d = -0.47$; 95% CI = – 0.66 to – 0.28; Supplemental Fig. 2).

The comparisons of dietary profiles between thin- and normal-weight participants are presented in Table 4. No relevant differences were found. Sex-stratified analyses shows that thin girls had higher energy intake ($d = 0.29$; 95% CI = 0.07 to 0.50), fat intake ($d = 0.30$; 95% CI = 0.10 to 0.50), and carbohydrate intake ($d = 0.31$; 95% CI = 0.11 to 0.51) and skipped breakfast less often (OR = 0.51; 95% CI = 0.30 to 0.89) compared with normal-weight girls (Supplemental Fig. 3).

The comparison of biological characteristics between thin and control adolescents are shown in Table 5. Compared with controls, thin adolescents had lower serum levels of creatinine ($d = -0.46$; 95% CI = – 0.71 to – 0.21) and insulin ($d = -0.41$; 95% CI = – 0.67 to – 0.14), and HOMA-insulin resistance ($d = -0.39$; 95% CI = – 0.66 to – 0.13), but a higher vitamin B12 level ($d = 0.28$; 95% CI = 0.11 to 0.64). In the sex-stratified analyses, only creatinine level was lower in thin girls compared with normal weighted girls ($d = -0.57$; 95% CI = – 0.91 to – 0.22; Supplemental Fig. 4).

Discussion

Prevalence of thinness in European adolescents

In the present study, we found a high prevalence of thinness in European adolescents, which was slightly higher in girls than in boys; the prevalence rates are consistent with those reported in a recent systematic review and meta-analysis [2]. Sex differences in body composition, patterns of weight gain, hormone biology, and susceptibility to certain social, ethnic, genetic, and environmental factors may explain the differences in the prevalence of thinness between boys and girls [33]. The HELENA study excluded all youth with a chronic medical condition, and the medical history did not differ between the thin and normal-weight participants [10]. In addition, the PA patterns did not differ between thin and normal-weight adolescents in

Table 4 Comparisons of dietary profile between normal weight and underweight participants

	Thin $n = 206$	Controls $n = 2239$	Effect size (95%CI)[1]	P^1
DQI-AM	62.0 ± 13.5	62.2 ± 13.8	– 0.04 (– 0.20 to 0.11)	0.67
Energy intake (kcal.day^{-1})	2269 (1748; 2854)	2102 (1605; 2780)	0.19 (0.02 to 0.36)[2]	0.091
Protein intake (g.day^{-1})	77.9 (58.8; 105.4)	80.3 (57.6; 107.7)	0.07 (– 0.09 to 0.22)[2]	0.53
Fat intake (g.day^{-1})	82.8 (62.2; 116.9)	80.3 (55.5; 114.0)	0.20 (0.05 to 0.36)[2]	0.091
Carbohydrates intake (g.day^{-1})	274.3 (211.5; 351.7)	254.5 (186.1; 342.7)	0.17 (0.01 to 0.32)[2]	0.091
Meat (g.day^{-1})	120.5 (60.0; 217.2)	123.1 (60.0; 205.0)	0.05 (– 0.10 to 0.19)[3]	0.63
Egg consumption (Yes)	57 (27.7)	741 (33.1)	0.80 (0.56 to 1.14)	0.39
Fish consumption (Yes)	50 (24.3)	554 (24.7)	0.97 (0.68 to 1.38)	0.86
Vitamin B12 (µg.day^{-1})	4.3 (2.9; 6.7)	4.3 (2.7; 6.7)	0.11 (– 0.04 to 0.27)[2]	0.35
Vitamin B6 (µg.day^{-1})	1474 (1103; 2037)	1487 (1065; 2079)	0.08 (– 0.07 to 0.24)[2]	0.44
Alcohol consumption (Yes)	0	30 (1.3)	NA	NA
Breakfast consumption				0.091
Consumer	115 (61.5)	1014 (49.2)	1.00 (ref.)	
Occasional consumer	40 (21.4)	477 (23.1)	0.57 (0.37 to 0.87)	
Skipper	32 (17.1)	572 (27.7)	0.84 (0.56 to 1.27)	

Values are expressed as frequency (percentage), mean ± standard deviation or median (interquartile range)

Effect sizes are standardized differences for quantitative variables and odds ratio for categorical variables using normal weight as reference

P values are corrected using false discovery rate adjustment

[1]Adjusted for center and pubertal status

[2]Calculated on log-transformed variable

[3]Calculated on rank-transformed variable

NA non-applicable

Table 5 Biological characteristics between normal weight and underweight participants

	Thin $n=62$	Controls $n=784$	Effect size (95%CI)[1]	P^1
White blood cell ($G.L^{-1}$)	5.9 (5.1; 7.2)	6.0 (5.2; 7.0)	0.00 (– 0.27 to 0.26) [2]	0.97
Neutrophil ($G.L^{-1}$)	3.0 (2.1; 4.0)	3.1 (2.5; 4.0)	– 0.11 (– 0.39 to 0.16) [2]	0.82
Lymphocyte ($G.L^{-1}$)	2.2 ± 0.5	2.2 ± 1.2	– 0.01 (– 0.28 to 0.25)	0.97
Red blood cell ($G.L^{-1}$)	4.8 ± 0.4	4.9 ± 0.5	– 0.13 (– 0.40 to 0.13)	0.77
Hemoglobin ($g.dl^{-1}$)	13.8 ± 1.1	14.0 ± 1.3	– 0.10 (– 0.36 to 0.16)	0.84
Hematocrit (%)	40.6 ± 2.9	41.2 ± 3.6	– 0.11 (– 0.38 to 0.14)	0.82
Platelet ($G.L^{-1}$)	259.5 ± 47.0	260.9 ± 59.7	– 0.05 (– 0.31 to 0.22)	0.97
Blood glucose (mg/dL)	91.0 ± 7.1	90.8 ± 7.3	– 0.05 (– 0.31 to 0.22)	0.97
Triglycerides (mg/dL)	58.0 (47.0; 80.0)	58.0 (44.5; 79.0)	– 0.03 (– 0.30 to 0.24) [2]	0.97
Total cholesterol (mg/dL)	159.7 ± 28.1	160.4 ± 27.3	– 0.05 (– 0.32 to 0.21)	0.97
HDL-C (mg/dL)	56.6 ± 9.4	56.5 ± 10.7	– 0.04 (– 0.30 to 0.23)	0.97
LDL-C (mg/dL)	92.9 ± 29.6	92.8 ± 24.1	– 0.01 (– 0.27 to 0.26)	0.97
TC/HDL-C	2.9 ± 0.8	2.9 ± 0.6	0.02 (– 0.25 to 0.29)	0.97
LDL/HDL-C	1.7 ± 0.8	1.7 ± 0.6	0.06 (– 0.21 to 0.32)	0.97
Creatinine (mg/dL)	0.67 ± 0.13	0.74 ± 0.14	– 0.46 (– 0.71 to – 0.21)	0.010
Uric acid (mg/dL)	4.1 ± 1.1	4.4 ± 1.1	– 0.28 (– 0.54 to – 0.01)	0.22
Albumin ($g.L^{-1}$)	48.0 ± 3.4	47.8 ± 3.9	– 0.01 (– 0.27 to 0.25)	0.97
GGT (UI/L)	15.0 (13.0; 18.0)	15.0 (13.0; 18.0)	– 0.10 (– 0.36 to 0.17) [2]	0.84
TGO (UI/L)	22.0 (17.0; 24.0)	21.0 (18.0; 25.0)	– 0.11 (– 0.38 to 0.15) [2]	0.82
TGP (UI/L)	18.0 (15.0; 21.0)	19.0 (16.0; 23.0)	– 0.25 (– 0.52 to 0.02) [2]	0.30
Vit D ($nmol.L^{-1}$)	61.4 ± 26.4	58.8 ± 23.1	0.07 (– 0.20 to 0.35)	0.87
Vit B12 (pmol/L)	388.5 (284.0; 529.0)	322.5 (241.0; 446.0)	0.28 (0.11 to 0.64) [2]	0.048
Vit C (mg/L)	11.0 ± 3.1	10.4 ± 3.4	0.18 (– 0.09 to 0.45)	0.57
C3 ($g.L^{-1}$)	1.06 ± 0.12	1.12 ± 0.17	– 0.32 (– 0.60 to – 0.04)	0.17
IgA ($mg.dl^{-1}$)	130.0 (98.0; 165.0)	123.0 (93.0; 164.0)	– 0.17 (– 0.11 to 0.45) [2]	0.62
IgG ($mg.dl^{-1}$)	1011 ± 261.2	1004 ± 214.9	– 0.03 (– 0.31 to 0.25)	0.97
IgM ($mg.dl^{-1}$)	114.0 (74.0; 153.0)	95.0 (72.0; 126.0)	0.20 (– 0.07 to 0.48) [2]	0.52
Basophil ($G.L^{-1}$)	0.03 (0.02; 0.05)	0.02 (0.01; 0.04)	0.19 (– 0.08 to 0.45) [3]	0.54
Insulin (µUI/mL)	6.8 (4.7; 9.4)	8.1 (6.0; 11.0)	– 0.41 (– 0.67 to – 0.14) [2]	0.040
Ferritin ((µg/L)	28.1 (12.1; 39.9)	26.0 (15.5; 42.5)	– 0.07 (– 0.35 to 0.20) [2]	0.97
HOMA-insulin resistance	1.6 (1.1; 2.2)	1.8 (1.3; 2.5)	– 0.39 (– 0.66 to – 0.13) [2]	0.040
C-reactive protein ($mg.L^{-1}$)	0.25 (0.10; 0.65)	0.32 (0.16; 0.80)	– 0.24 (– 0.52 to 0.04) [3]	0.35

Values are expressed as mean ± standard deviation or median (interquartile range)

Effect sizes are standardized differences using normal weight as reference

P values are corrected using false discovery rate adjustment

[1]Adjusted for center and pubertal status

[2]Calculated on log-transformed variable

[3]Calculated on rank-transformed variable

this study. We note that anorexia nervosa is characterized by high levels of PA, hyperactivity, and compulsive or excessive exercise [34]. In addition, the food records and dietary habits did not reveal any eating disorders or feeding restrictions in the thin adolescents in this study. We are therefore confident that our results support the idea that the thinness identified here reflects constitutional thinness.

Health-related fitness and lifestyle habits (PA and sedentary behaviors) in thin European adolescents

Physical fitness and PA are two important determinants of health. Our results suggest that thinness in European adolescents is not associated with changes in PA or in time spent in sedentary activities. In our study, the only difference was

that thin adolescents spent significantly less time in LPA compared with normal-weight adolescents, which may be advantageous for their future health [35–37] because medium and high levels of LPA are associated with a 2.89- and 3.07-years longer predicted life expectancy, respectively, and a decreased risk of death [37, 38]. However, the difference between groups in our study was small (on average 6 min) and may be considered as not clinically relevant. Taken together, our results suggest that thin European adolescents do not differ in their lifestyle habits compared with those of normal weight.

Although cardiorespiratory fitness, lower-body muscular strength, and speed–agility were similar in thin and normal-weight adolescents in this study, thin adolescents had a lower upper-body muscular strength than controls, a finding that is consistent with previous reports [39, 40]. One possible explanation for this difference is the lower fat-free mass in thin adolescents, which has also been reported [39, 40].

Dietary habits of thin European adolescents

Except for a higher fat intake, diet quality and total energy intake were similar in thin and normal-weight adolescents in this study. This finding suggests that the thin adolescents exhibited resistance to weight gain, which is a characteristic of a constitutionally thin population. A recent systematic review and meta-analysis confirmed that constitutionally thin adults also have a normal energy intake [41]. We also found no differences in micronutrient intake between the thin and normal-weight adolescents. Unexpectedly, a lower percentage of thin adolescents than controls skipped breakfast. Breakfast skipping in adults is associated with cardiometabolic risk, as shown by the metabolic risk profile, overweight, obesity, hypertension, diabetes mellitus, and presence of cardiovascular disease [42–44]. Similarly, in children and adolescents, regular breakfast consumption promotes good nutritional status, weight maintenance, cognitive performance, and well-being [45–47]. We have no clear explanation for this difference and note that this does not appear to be linked to differences in the mother's educational level or the family's socioeconomic status.

Metabolic profiles of thin European adolescents

Our study found, for the first time, that adolescents with thinness have a better metabolic profile, as shown by lower inflammatory markers, lower systolic blood pressure, and better insulin sensitivity, compared with normal-weight adolescents. Similar findings have been reported for adults with constitutional thinness; for example, adults with constitutional thinness have lower levels of insulin-like growth factor 1, estradiol, growth hormone, follicle-stimulating hormone, and luteinizing hormone [41]. Although having anorexia nervosa or a BMI < 20 kg/m^2 is associated with impaired glucose tolerance [48, 49], we found greater insulin sensitivity in the adolescents with constitutional thinness in our study (J curve relationship). The low serum creatinine concentration in adolescents with thinness in our study is not surprising because it reflects the muscle mass, which was probably lower in the thin adolescents, as reflected by the lower fat-free mass and upper-body muscular strength compared with the normal-weight participants.

Clinical characteristics in thin European adolescents

In our study, thinness was associated with pubertal delay, as previously reported [50, 51]. Underweight can delay the onset and progression of puberty and menarche [50]. Body composition is dependent on age, sex, and sexual maturation, and delayed sexual maturation may have contributed to thinness in these adolescents. The consequences for future health remain to be determined. Previous studies have shown that a delay in puberty can be protective for cardiometabolic health, although other studies have reported an increased risk of coronary heart and other vascular diseases [52–55].

Strengths and limitations

The major strengths of this study are the strict standardization of the fieldwork across the different centers of the HELENA study and the careful medical examination and assessment of any associated chronic diseases [10]. All assessments were valid, reliable, and harmonized between each center using standardized procedures. However, our study also has some limitations. First, the limited sample size of the thin group reduced the power of our analyses. The observations of the present study are also limited by the cross-sectional design nature, and causality cannot be determined. Lastly, even though the HELENA-DIAT has been validated against dietary recall with an interviewer, the main limitation is the subjectivity of the assessment of dietary intake that was evaluated only by the adolescent participants.

Conclusions

Thinness affects a notable proportion of European adolescents. However, thinness is not associated with reduced energy intake, increased PA level, or any adverse health consequences.

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analyzed data and performed statistical analysis; FG had primary responsibility for the final content. All authors read and approved the final manuscript.

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Data availability Data are available upon reasonable request.

Declarations

Conflict of interest The authors declare no conflict of interest.

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