

Relationship between pubertal timing and chronic non-specific pain in adolescent girls:

The Young-HUNT3 study (2006-2008)

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Abstract

The aim of this study was to examine a possible relationship between early puberty and chronic non-specific pain in 13-18 years old girls. All adolescents in Nord-Trøndelag County, Norway, were invited to participate in the Young-HUNT3 study (2006-2008). Of the invited girls 81% answered the questionnaire and of these 3982 were 13-18 years. Menarche and perceived physical maturation were used as exposure measures. Early menarche was defined as <12 years, normal menarche as ≥ 12 and <14 years, and late menarche as ≥ 14 years. Perceived physical maturation was divided into maturing earlier, the same or later than others of their own age. Main outcome measure was chronic non-specific pain, defined as pain in at least one location not related to any known disease or injury, for at least once a week during the last three months. Median age at menarche was 13.2 years. Chronic non-specific pain was more prevalent among girls with early menarche (68%, 95% CI 64-72%) compared to girls with either normal (55%, 95% CI 53-57%), late (50%, 95% CI 46-54%) or no menarche (35%, 95% CI 29-40%). The association persisted after adjusting for age, body mass index, socioeconomic factors and anxiety and depression. A similar association was found between girls that perceived themselves as earlier physically matured than their peers and chronic non-specific pain.

Headache/migraine was the most common type of chronic non-specific pain regardless of menarcheal age. In all reported locations, pain was more prevalent in the group with early menarche compared to normal or late menarche.

1. Introduction

Chronic non-specific pain is a lasting sensation of pain in the absence of past injury or body damage. The International Classification of Diseases (ICD) defines chronic pain as persistent or recurrent pain lasting longer than 3 months [51]. Even though there is no consensus definition of chronic pain in children or adolescents, many studies explore and show that chronic non-specific pain in adolescents is common [13; 21]. In girls the prevalence of reported pain is higher and increases more with age than in boys [15; 21]. Children with chronic pain report limitations in social functioning and have an increased risk of pain persisting into adulthood [6; 13; 22]. Musculoskeletal pain is a major health problem and expensive to society [28]. Suggested causes of chronic non-specific pain include genetic, physical, mechanical and psychological factors [9; 13; 38; 47], fitting well with the biopsychosocial understanding of pain [11].

Within human populations there is a 4-5 years' variation in onset of puberty [29]. Age at menarche has a strong genetic component, and about half of the phenotypical variation is due to genetic factors [50]. During the last century improvements in nutrition, general health and other living conditions have been associated with a secular decline in mean menarcheal age [39]. This trend seems to level off in Northern Europe [39]. Adverse physical, social conditions or psychosocial stress like starvation and exposure to war are associated with later menarche, while childhood obesity and rapid prepubertal weight gain are associated with earlier menarche [33]. Socioeconomic factors like living in urban areas, having parents with higher education levels are associated with earlier menarche [33]. Emotional stress within a family like increased conflict levels, divorce, adoption or sexual abuse also correlates with earlier menarche [33]. This may indicate that early menarche can develop as a function of two diametrically different life situations, on one hand as a response to better life conditions, and on the other hand as a function of adverse situations within a family.

Hormonal factors may contribute to the development of chronic pain. Pain has been shown to increase with pubertal development [19; 24], and pain symptoms show variation across the menstrual cycle [27]. Early menarche may be a stressful event connected to more behavioral problems, depression, eating disorders, self-harming and substance abuse than found in later maturing girls [41]. A possible explanation may be that early maturing girls must cope with both physical and lifestyle changes and altered expectations from the environment before they are emotionally ready [31]. Anxiety and depression are previously shown to be related to early menarche [20; 41], and also to chronic non-specific pain [13; 47].

The primary aim of the project was to study whether early menarche and early pubertal development were associated with chronic non-specific pain in adolescent girls in a large population-based study in a representative county in Norway. The second aim was exploring if this potential association could be explained by psychosocial or psychological factors.

2. Method

2.1. Study population and procedure

The Young-HUNT3 is a cross-sectional population-based study conducted in Nord-Trøndelag County between 2006 and 2008. The county is regarded to be representative for the Norwegian population [35]. All adolescents in the county (10 464) were invited to participate and of these 5087 were girls. Of these girls, 4129 (81%) chose to join the study, filled in a questionnaire within one school lesson and participated in a brief clinical examination, including length and weight measures. Adolescents not attending school (apprentices and school dropouts), or not being present at school on the day of the study, could complete the

questionnaire on the day of the clinical examination. Of the girls that participated in the study 3982 were 13-18 years, and these constituted the final study population.

2.2. Measures

2.2.1. Outcome measure – Chronic non-specific pain

To assess chronic non-specific pain the adolescents were asked if they had experienced pain in one of ten locations during the last three months, not related to any known disease or injury. Participants were asked to specify frequency of pain in the following locations; head (headache/migraine), neck/shoulder, upper back, lower back/buttocks, chest, stomach, left arm, right arm, left leg and right leg. Locations were shown on a figure. Five response alternatives were given to describe the frequency in each localization; never or seldom, about once a month, about once a week, more than once a week, almost every day. Chronic non-specific pain was defined as pain in at least one location not related to any known disease or injury, for at least once a week during the last three months [13-15; 32].

2.2.2. Exposure measures - Menarche and Physical maturation

To establish age at menarche the girls were asked whether they had started their periods and if so, their age in years and months at their first period. Because of the interpopulation variation in onset of menarche in different populations [39], there are no established age cutoffs that defines early, normal and late menarche. Early, normal and late menarche must be interpreted in the context of the norms of the population studied. The cutoffs used for early, normal and late menarche in our study are chosen from the 25th and the 75th percentile that is rounded to nearest whole year. Thus, early menarche was defined as less than 12 years of age, normal menarche as equal to or more than 12 years and less than 14 years, and late menarche as equal

to or more than 14 years. In a subanalysis, menarcheal age was included as a continuous variable to evaluate the association between menarche and chronic non-specific pain. In another subanalysis, the population studied was restricted to girls aged 14 or older, and girls reporting not having had menarche were included in the late group.

The girls were also asked if they perceived themselves as maturing earlier or later than others of their own age, using a previously applied scale measure [8]. They were given seven response alternatives, and these were collapsed into three levels where “much earlier” and “earlier” were defined as early physical maturation, “a little bit earlier”, “the same as others” and “a little bit later” represented normal physical maturation, and “later” and “much later” represented late physical maturation.

2.2.3. Covariates

Weight and height were obtained by trained nurses at the clinical examination. Body mass index (BMI) was calculated from weight in kilograms divided by the square of height in meters. BMI was further classified in three groups; normal, overweight and obese using cut-off values for different ages from the International Obesity Task Force [7].

Anxiety and depressive symptoms were measured with the Symptoms Check List 5 (SCL-5) shown to be reliable [49]. SCL-5 consists of five questions with four response alternatives each. Mean score was calculated by dividing total score with the number of items. A cut-off point of >2 was used to determine if the adolescents had symptoms of anxiety and depression [49].

Socioeconomic status was measured by both parents' highest education and the sum of both parent's income in 2007. Mother's and father's highest level of education was classified in five levels; primary school (7-10 years of education), secondary school (11-12 years), high school (13-14 years), less than 5 years of higher education and 5 years or more of higher

education. Parents' combined income was divided into quintiles. Measures of socioeconomic status were obtained from Statistics Norway.

2.3. Statistical analyses

Statistical analyses were conducted in Stata (StataIC 13.1, StataCorp LP, College Station, Texas, USA). Age at the time of the study was treated as a continuous variable. Median age at menarche with 25th percentile and 75th percentile was estimated by using Kaplan-Meier survival analysis. Included in the survival analysis were the girls that had specified age at menarche, and girls that answered that they had not started their periods. For girls providing only year of menarche ($n=760$), the month was set to six. Kendall's tau-b correlation was used to measure the association between age at menarche and physical maturation. Binary logistic regression was used to estimate the crude odds ratios (ORs) and 95% confidence intervals (CI) for the association between the dependent variable; chronic non-specific pain, and the independent variables; age at menarche or perceived physical maturation. Multivariable binary logistic regression was used to estimate the adjusted ORs and 95% CI. Model 1 included the following covariates; age at time of study, BMI, parents' combined income, mothers' level of education and fathers' level of education. Model 2 included the same variables as Model 1, and in addition SCL-5 that measures anxiety and depression. To get a measure for trend for each categorical variable, the categorical variables were treated as continuous variables in a binary regression analysis. Binary logistic regression was used to estimate odds ratios and the corresponding 95% confidence interval for the association between chronic non-specific pain and menarcheal age as a continuous variable. Proportions were estimated with 95% confidence intervals. Two-sided significance level in the statistical analyses was set at $p < 0.05$.

2.4. Ethics

The study was approved by The Regional Committee for Medical and Health Research Ethics. The Norwegian Data Protection Authority and the Norwegian Tax Administration have approved the coupling of data on socioeconomic status from Statistics Norway with the Young-HUNT3 data, by using data from The Family Register.

3. Results

Of the 3982 girls, 13-18 years, 3748 completed the pain questions and of these 286 did not answer the questions on menarche and 335 did not answer the question on physical maturation. Of the 3462 girls answering questions about their periods, 3149 stated that they had started their periods, 3008 specified year at menarche and 2248 also specified the month. At the time of the survey 313 reported that they had not started their periods, and 62 had started their period during the last 3 months. Median age at the time of the survey was 15.7 years (CI 15.6-15.8).

3.1. Age at menarche and physical maturation

Median age at menarche in the population measured by Kaplan-Meier survival analysis was 13.2 years (25th percentile 12.4, 75th percentile 14.0). Included in the estimation were girls that specified year at menarche (n=3008) and girls that answered that they had not started their periods (n=313). The distribution of age at menarche in the Young-HUNT3 population is given in Figure 1. Of the 3008 girls that specified menarcheal age, 17% reported

menarche before the age of 12 (early menarche), and 19% reported menarche when they were 14 years or older (late menarche). Among the 3413 girls that answered the physical maturation questions, 23% regarded themselves as maturing earlier than their peers. Only 7% reported that they matured late. Age at menarche and perceived physical maturity correlated (Kendall's tau-b=0.39 (n=2938), p<0.0001). The clinical and demographic characteristics of the adolescents are given in Table 1.

3.2. Pubertal characteristics and chronic non-specific pain

Of the 3748 girls that completed the pain questions, 54% reported that they experienced chronic non-specific pain (Table 1). Chronic non-specific pain was more prevalent among girls with early menarche (68%, 95% CI 64-72%) compared to girls with either normal (55%, 95% CI 53-57%), late (50%, 95% CI 46-54%) or no menarche (35%, 95% CI 29-40%). Excluding the 62 girls with menarche <3 months before filling in the questionnaire, the prevalence of chronic pain in girls with early menarche was 68% (95% CI 64-72%), versus 55% (95% CI 53-57%) in girls with normal and 51% (95% CI 46-55%) in girls with late onset menarche. Those reporting chronic non-specific pain had a slightly higher median age (15.9, 95% CI 15.8-16.0) compared to the group that did not report pain (15.4, 95% CI 15.3-15.6). Also, girls that perceived themselves as maturing earlier physically than their peers reported more chronic pain (65%, 95% CI 62-68%) than girls that regarded themselves as normal (51%, 95% CI 49-53%) or late maturing (52%, 95% CI 46-59%). The prevalence of chronic pain in overweight (62%, 95% CI 58-66%) and obese girls (73%, 95% CI 65-79%) was higher than in normal weight girls (51%, 95% CI 49-53%). Girls with high symptom score of anxiety and depression have an 81% (95% CI 78-84%) prevalence of chronic non-specific pain compared to girls with low symptom score (48%, 95% CI 46-49%).

3.3. Prevalence of region-specific pain in relation to menarche

Headache/migraine was the most common type of chronic non-specific pain reported in the study regardless of menarcheal age (Figure 2). After headache/migraine the contributions to chronic non-specific pain ranked by decreasing importance were neck/shoulder, back, stomach and extremities. In all reported locations, pain was more prevalent in the group with early menarche compared to normal or late menarche.

3.4. Early puberty and association with chronic non-specific pain

Early menarche was associated with chronic non-specific pain in adolescence both in crude and adjusted analyses (Table 2). Girls with early menarche had an odds ratio of 1.8 (95% CI 1.4-2.2) of reporting chronic non-specific pain compared to girls with normal menarche in the crude analysis. Girls with late menarche had slightly lower odds of reporting chronic pain than girls with normal menarche, OR 0.9 (95% CI 0.7-1.0). When adjusting for participants' age, BMI and socioeconomic factors in Model 1, the results were almost the same as in the crude analysis. When including anxiety and depression in addition to the other covariates in Model 2 the associations were slightly attenuated with an OR for reporting chronic non-specific pain of 1.5 (95% CI 1.2-1.9) in girls with early menarche. If menarcheal age was treated as a continuous variable in the logistic regression, chronic non-specific pain was inversely related to menarcheal age (OR 0.84, 95% CI 0.79-0.90).

An additional subanalysis was performed that included only the girls that were over the age of 14, and girls reporting not having menarche were included in the late group. In this subanalysis girls with early menarche had an odds ratio of 2.0 (95% CI 1.5-2.5) of reporting

chronic non-specific pain compared to girls with normal menarche in the crude analysis. Girls with late menarche had lower odds of reporting chronic pain than girls with normal menarche, OR 0.8 (95% CI 0.6-0.9).

The results for self-reported physical maturation showed similar results. Girls who regarded themselves as earlier physically matured more often reported chronic non-specific pain than those who regarded themselves as normal (crude OR 1.9, 95% CI 1.6-2.2), and also for this association the results were only slightly attenuated in the fully adjusted Model 2 (OR 1.6, 95% CI 1.3-1.9).

4. Discussion

Median age at menarche in the Young-HUNT3 population was 13.2 years. Girls with early menarche experienced more pain than girls with normal or late menarche, and this was similar within all pain locations. The most prevalent chronic non-specific pain reported was headache/migraine. The association between early menarche and chronic non-specific pain persisted after controlling for age, BMI, socioeconomic factors. Although slightly attenuated, the association remained after controlling for anxiety and depression, indicating that early menarche is an independent factor associated with chronic pain. The perception of being earlier matured than peers was also associated with chronic non-specific pain. The menarcheal groups and the physical maturation groups were clearly correlated, but not identical.

A strength of the study is the large and unselected population with a high participation rate. The composition of the study population makes it possible to assume that the results are representative for the Norwegian population [35]. Measures of height and weight were performed by trained nurses, thus reducing information bias. Most of the girls reported month in addition to year of menarche which give more precise information of menarcheal age.

Possible socioeconomic confounders were reduced by using parent's income and education as objective measures. A major strength of the study is the ability to adjust for anxiety and depression with a validated measurement (SCL-5), as these factors have been shown to have a strong association to chronic pain [13; 38; 47].

Limitations of the study include the cross-sectional design that makes it impossible to determine cause and effect relationship between variables. Some selection bias is possible although the participation rate was high. The high prevalence of chronic non-specific pain in the cohort might imply that the measurement is not specific enough, but the results are within the range found in previous studies [21; 37]. The percentage of chronic non-specific pain might be higher among students not attending school on the day of the study, or among school dropouts, because pain could be a reason for not attending/dropping out of school. Girls with early menarche have been shown to have higher school truancy and this could also lead to selection bias [20]. A limitation of the study is that we did not have access to data on health status among girls in the cohort and could therefore not adjust for poor health in the analyses. In the whole Young-Hunt3 population of both boys and girls, 89% reported good or very good health, and only 0.8% reported poor health [18]. Overall, 93% reported no impairment due to somatic illness [17], and 92% reported no impairment due to mental health problems [16]. We also lacked access to information of use of oral contraceptives. It is improbable that pain related to the girl's period would have had substantial impact on pain prevalence, as the chronic pain definition includes only those with pain at least once a week, and not once a month. It is a limitation that girls in the younger age-groups in the study is less likely to have had menarche and will not be included in the statistical analysis. However, the results were strengthened by including a subanalysis using only girls above 14 years.

Except for the measures of BMI and socio-economy the data were self-reported with the possibility of information bias. The ability to remember age at menarche is an uncertainty

in this kind of studies, but the reliability of self-reported menarche is well established [34]. Furthermore, menarcheal age was reported relatively shortly after the onset of menarche and this would reduce potential recall bias. The recollection period of the pain questions was three months, and studies have shown that adolescents accurately report their pain experience during such a period of time [30]. There is no internationally validated definition of chronic non-specific pain in children, but the definition used in the study has previously been used in this population [13-15] and in similar studies among children [32]. The SCL-5 is a brief assessment of mental status, but is found to correspond well with larger versions such as SCL-25 [49].

The median age at menarche found in this study corresponds with previous results from Norwegian contemporary populations. In the first Young-HUNT study from 1995-1997, with a follow-up in 1999-2000, mean menarcheal age was 13.2 years [5]. In a large study among Norwegian pregnant women mean age at menarche was 13.0 years [3]. Age at menarche in our population has not changed much since 1980-1985, when a mean menarcheal age of 13.3 years was reported [26]. However, among all 10th-graders of Norwegian/Western origin in Oslo in 1999-2001 median age was 12 years 7 months [25]. As the capital of Norway, Oslo is known to represent a more heterogeneous population than ours.

Increased prevalence of adolescent pain conditions with age or pubertal status has been found in several studies. A population-based study from northwest England showed that the prevalence of low back pain increased with age in both girls and boys 11 to 14 years [53]. Musculoskeletal pain tended to persist more in pubertal than in prepubertal groups [48]. Adolescents with rapid growth showed a higher risk of low back pain [42]. The probability of experiencing pain from multiple locations increased with pubertal development in girls [24]. Pubertal status was associated with back pain, overtiredness and dizziness, but not with stomach pain and headache, in a follow-up study among American and Dutch adolescents

[19]. The prevalence of temporomandibular disorders increased with pubertal growth in girls, but decreased in boys [12]. Also pain in other locations increased with advancing puberty [12].

Even if many studies have looked at age, gender and pubertal development in relation to pain [10; 15; 24], few have studied associations between early menarche and pain. In a previous study from Nord-Trøndelag from 1995-1997 it was found that widespread musculoskeletal pain was more prevalent in adult women reporting menarche ≤ 12 compared to ≥ 12 years [23]. Headache was more prevalent among adolescents with early menarche in a previous study from the same area [1]. It has been shown that adult women with early menarche experienced more pelvic girdle syndrome in pregnancy than those who matured later [3]. These studies show that girls with early menarche have a higher prevalence of pain in specific locations compared to normal or late menarche. The prevalence of musculoskeletal pain in different location found in our study is comparable for most body sites with a study among adolescents in Trondheim, Norway [37]. Our study confirms the association between early menarche and pain, but also indicates that pain in general might be more important for this association than the specific pain location.

Many studies have shown that early menarche is associated with different types of adverse health outcomes. Women with early menarche had a fivefold higher risk of obesity than those with later menarche [36]. Girls with early menarche also had increased risk of adult onset diabetes, breast cancer, cardiovascular disease and all-cause mortality [2; 43]. Our study confirms that chronic non-specific pain is another negative health outcome that can be included on the list of adverse associations in girls with early menarche.

Possible explanations for the differences seen in chronic non-specific pain between girls with early menarche and those maturing later include hormonal changes in puberty. Higher levels of estradiol were found in girls with early menarche compared to those with

later menarche [52]. Other studies show association between hormones and pain [40]. Increase in estradiol and progesterone were associated with increase in pain perception in one study [44]. Another study showed that falling estrogen levels lead to more migraine attacks, and that increase in estrogen levels offered protection against migraine [27], demonstrating that associations may go in both directions. Sex hormones are thought to explain some of the gender differences found in chronic non-specific pain reports [40]. Overweight and obesity are clearly associated with early menarche [4]. Leptin, a hormone produced by adipocytes, plays an essential role in the regulation of pubertal onset [45]. Higher levels of serum leptin have been associated with increased prevalence of low back pain in women [46].

The feeling of being earlier matured regardless of menarche is associated with reporting more chronic non-specific pain. This indicates that other factors in addition to physiological changes might be linked to chronic non-specific pain, such as the psychological feeling of being different. Coexisting psychiatric symptoms were associated with chronic multisite pain in adolescent girls [47]. Previous research found that girls maturing “on time” with respect to pubertal development had the most positive feelings about puberty [8].

The results presented here should increase awareness of the strong association between early puberty and chronic non-specific pain in adolescent girls. Increased knowledge of associated factors for adolescent pain may lead to new hypotheses for preventive strategies in the future. More knowledge is needed about why early maturing girls appear to be at higher risk for experiencing chronic pain, and whether this risk extends to early maturing boys. Further longitudinal studies are needed to establish possible causal relationship between early puberty and chronic non-specific pain.

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Figure captions

Figure 1. Distribution of self-reported age at menarche in adolescent girls aged 13-18 years in the Young-HUNT3 study (2006-2008).

Figure 2. Prevalence (%) and 95% confidence intervals of chronic non-specific pain in different anatomical regions in relation to menarcheal age reported by adolescent girls in the Young-HUNT3 study (2006-2008). N=3008.

Table 1

Prevalence of chronic non-specific pain in relation to menarche, physical maturation, age, BMI, anxiety and depressive symptoms and socio-economy in adolescent girls aged 13-18 years in the Young-HUNT3 study (2006-2008).

	Total n	Chronic Non-Specific Pain ^a n (%)
Total	3748	2029 (54)
Menarche^b		
Early	517	352 (68)
Normal	1908	1047 (55)
Late	583	294 (50)
Yes to menarche, no age	141	69 (49)
No menarche	313	108 (35)
Missing	286	159 (56)
Physical Maturation^c		
Early	779	507 (65)
Normal	2392	1213 (51)
Late	242	127 (52)
Missing	335	182 (54)
BMI		
Normal	2707	1377 (51)
Overweight	595	369 (62)
Obese	154	112 (73)
Missing	292	171 (59)
Anxiety and depressive symptoms^d		
Low	2986	1420 (48)
High	700	570 (81)
Missing	62	39 (63)
Parents combined income		
First Quintile (Lowest Income)	718	402 (56)
Second Quintile	717	402 (56)
Third Quintile	721	382 (53)
Fourth Quintile	713	383 (54)
Fifth Quintile (Highest Income)	720	366 (51)
Missing	159	94 (59)
Mothers educational level		
Primary school (7-10 years)	576	340 (59)
Secondary school (11-12 years)	490	279 (57)
High school (13-14 years)	1287	702 (55)
Higher education <5 years	1245	628 (50)
Higher education ≥5 years	112	57 (51)
Missing	38	23 (61)
Fathers educational level		
Primary school (7-10 years)	654	387 (59)
Secondary school (11-12 years)	506	260 (51)
High school (13-14 years)	1625	898 (55)
Higher education <5 years	634	318 (50)
Higher education ≥5 years	241	114 (47)
Missing	88	52 (59)

^a Pain at least once a week during the last three months, not related to any known disease or injury.

^b Early menarche: <12 years, normal menarche: 12 - <14, and late menarche: ≥14 years. Yes to menarche, no age: Girls that reported having menarche, but did not report age.

^c The girls' own perception of being earlier or later physically matured compared to their peers. Response alternatives "much earlier" and "earlier" were defined as early physical maturation, "a little bit earlier", "the same as others" and "a little bit later" represented normal physical maturation, and "later" and "much later" represented late physical maturation.

^d Anxiety and depressive symptoms measured with the Symptoms Check List (SCL-5). A cut-off point of >2 determined if the girls had symptoms of anxiety and depression.

Table 2
Odds ratios (95% CI) for chronic non-specific pain in relation to menarche and physical maturation in adolescent girls aged 13-18 years in the Young-HUNT3 study (2006-2008).

	Chronic Non-Specific Pain ^a versus No Chronic Non-Specific Pain			
	OR (95% CI)			P Value for Trend ^d
	Crude	Model 1 ^b	Model 2 ^c	
Menarche^e	n = 2590			
Early	1.8 (1.4-2.2)	1.7 (1.4-2.1)	1.5 (1.2-1.9)	<.001
Normal	1.0 (ref)	1.0 (ref)	1.0 (ref)	
Late	0.9 (0.7-1.0)	0.8 (0.7-1.0)	0.8 (0.7-1.0)	
Physical Maturation^f	n = 2985			
Early	1.9 (1.6-2.2)	1.7 (1.4-2.1)	1.6 (1.3-1.9)	.001
Normal	1.0 (ref)	1.0 (ref)	1.0 (ref)	
Late	1.2 (0.9-1.6)	1.3 (0.9-1.7)	1.2 (0.9-1.6)	

^a Pain at least once a week during the last three months, not related to any known disease or injury.

^b Model 1 adjusts for age of the participants, BMI, parents' combined income and both parents' highest education.

^c Model 2 adjusts for the same variables as Model 1 and in addition anxiety and depression symptoms (SCL-5).

^d The p value for trend was analyzed in the adjusted Model 2.

^e Early menarche: <12 years, normal menarche: 12 - <14, and late menarche: ≥14years.

^f The girls' own perception of being earlier or later physically matured compared to their peers. Response alternatives "much earlier" and "earlier" were defined as early physical maturation, "a little bit earlier", "the same as others" and "a little bit later" represented normal physical maturation, and "later" and "much later" represented late physical maturation.





