Age at puberty and accelerometer-measured physical activity: findings from two independent UK cohorts

ABSTRACT

Background: It is unclear if puberty timing influences future physical activity (PA).

Aim: Investigate association of puberty timing with PA across adolescence and adulthood.

Subjects and methods: Data were from two British cohorts. Participants from an adolescent birth cohort (females=2,349, males=1,720) prospectively reported age at menarche and voice break and had PA recorded by Actigraph accelerometers at ages 14y and 16y. A cohort of middle-aged and older adults (40-70y; females=48,282; males=36,112) recalled their age at puberty and had PA (mean acceleration; *mg*) measured by AxivityAX3 accelerometers.

Results: After adjustment for age, education, smoking and BMI, per 1-year older age at menarche was associated with higher mean counts/minute at age 14y (0.07SD counts/minute; 95% CI: 0.04, 0.11) with associations attenuated at age 16y (0.02SD; -0.03, 0.07). Difference in mean acceleration per older year at menarche were close to the null in women aged 40-49y (0.02SDmg; 0.01, 0.03), 50-59y (0.01; 0.00, 0.02) and 60-70y (0.01; 0.00, 0.01). Age at voice break and PA associations were close to the null in both cohorts.

Conclusion: We found a positive association between puberty timing and PA in females which weakened at older ages and limited evidence of an association at any age in males.

KEY WORDS

ALSPAC; Life-course; Physical activity; Puberty**;** UK Biobank

INTRODUCTION

Healthy levels of physical activity in adolescence are related to healthier cardio-metabolic health and with physical activity levels in adulthood (Nechuta et al. 2015; Rangul et al. 2012; Telama 2009) and thus understanding factors that influence physical activity at this age could identify targets for preventing cardiovascular diseases. Evidence from mostly cross-sectional studies suggest that early maturing girls may be less physically active than their peers (Sherar et al. 2010; Bacil et al. 2015). Most of these studies included only females and only a single measure of physical activity, meaning it is unclear how associations vary through puberty or if findings extend to males. Further, as most studies of adolescents have been cross-sectional, reverse causality may possibly explain these findings (Moisan, Meyer, and Gingras 1991).

Whilst Mendelian randomisation studies suggest a causal effect of age at menarche on body mass index (BMI) (Gill et al. 2018), blood glucose (Au Yeung et al. 2017), lung impairment (Gill et al. 2017) and asthma (Minelli et al. 2018) in adults, few studies have examined if age at puberty is associated with physical activity beyond adolescence. Two recent studies found little evidence of association between puberty timing and self-reported leisure-time physical activity in adults (Elhakeem et al. 2017; Pinto Pereira, Li, and Power 2014), but these studies may have been biased by use of self-reported physical activity due to associated measurement and recall errors, particularly in older adults (Schrack et al. 2016; Troiano et al. 2014). Thus, it remains unclear whether any associations of pubertal timing with physical activity in adolescence persist into adulthood.

Therefore, the aim of this study was to determine associations between age at puberty in males and females and accelerometer-measured physical activity across adolescence in a prospective birth cohort and in a large adult cohort with relevant data on almost 100,000 participants thus allowing analyses stratified by sex and age group.

SUBJECTS AND METHODS

Study populations

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a prospective birth cohort study, which recruited pregnant women residing in and around the city of Bristol in southwest England with an expected date of delivery between April 1991 and December 1992. In total, 15,247 eligible pregnancies were enrolled in ALSPAC (75% response) resulting in 14,973 live births of whom 14,899 were alive at one year of age (Fraser et al. 2013; Boyd et al. 2013). The mothers, their partners and the index children have been followed-up with record linkage, questionnaires and dedicated research clinics since recruitment. The present study is concerned with offspring who attended one or more of clinic assessments at mean ages 13.8 and 15.5 years (henceforth referred to as 14 and 16 years respectively) at which they were invited to wear an accelerometer. Ethical approval was obtained from the ALSPAC Ethics and Law committee and the Local Research Ethics Committees. Parental informed consent and child's agreement were obtained for all participants. Details of all available data can be found in the ALSPAC study website which includes a fully searchable data dictionary and variable search tool (http://www.bristol.ac.uk/alspac/researchers/our-data/).

UK Biobank is a large population-based cohort study of 502 682 adults (5% response) aged 40–69 years at baseline assessments in 2006-2010 (Sudlow et al. 2015; Collins 2012). Study participants were registered with the UK National Health Service and residing within 25 miles from one of twenty-two assessment centres. Baseline assessments included touchscreen questionnaires, physical assessments and blood sample collection. The present study uses data from a subsample of UK Biobank participants who were invited to wear an accelerometer in 2013-2015. Ethical approval was granted by the NHS National Research

Ethics Service Committee North West – Haydock (Ref 11/NW/0382). All participants provided informed written consent.

Age at puberty

Age at puberty in ALSPAC was derived from responses to 9 postal questionnaires (sent at approx. ages 8, 9, 10, 11, 13, 14, 15, 16 and 17 years). Each questionnaire was completed by either the main caregiver (>70% up to age 11), a combination of the main caregiver and child or by the child. At each questionnaire, mothers reported whether their daughter had started her menstrual periods and how old she was (in years and months) when she had her first period. Each questionnaire also asked if the son's voice has changed and whether it was occasionally a lot lower or if it had changed totally. For these analyses, the first-reported age at menarche, and the age corresponding to the questionnaire where the first report that voice was either occasionally a lot lower or had changed totally were used as measures of age at puberty (Joinson et al. 2012). Participants with inconsistent voice break status (i.e. reporting a less developed voice status than in any previous year) were excluded (n=129).

In UK Biobank, age at puberty was recalled at the touch-screen questionnaire assessments in 2006-2010, when participants were aged 40-69 years (Day et al. 2015). Women recalled age at menarche in whole years. Men recalled age at voice break relative to their peers as younger than average age, about average age, or older than average age. We used the 'younger than average age at voice break' group as the reference category in our analyses. This was done to make these results as comparable as possible to those in ALSPAC males, in whom we examined a linear trend of age at voice break across the distribution (from younger to older) with physical activity.

Physical activity

All ALSPAC children who attended the 14-year and 16-year clinic assessments were asked to wear an Actigraph AM7164 2.2 waist-worn accelerometer (Actigraph LLC, Fort Walton Beach, FL, USA) for seven days during waking hours, removing only for showering, bathing and water sports. These devices have been validated for use in children (Ekelund et al. 2001; Mattocks et al. 2007) and capture movements in terms of accelerations as a combined function of frequency and intensity. Data were processed according to a predefined protocol described elsewhere (Mattocks et al. 2008; Riddoch et al. 2009). At both ages, we derived mean activity counts per minute (average acceleration counts over the full period of valid recording, that is, at least 10 hours a day for at least three days), and time spent (minutes per day) in moderate-to-vigorous activity (>3600 counts/minute).

In 2013-2015, eligible UK Biobank participants were invited to wear an Axivity AX3 wrist-worn accelerometer (Open Lab, Newcastle University) on the dominant hand for seven consecutive days (Doherty et al. 2017). Data Processing and evaluation has been described in detail elsewhere (Doherty et al. 2017). Briefly, physical activity information was extracted from 100Hz raw triaxial acceleration data after calibration, removal of gravity and sensor noise, and identification of wear and non-wear episodes. Mean acceleration vector magnitude measured in milli-gravity units (*mg*) was used as a proxy summary measure of total physical activity, similar to previous studies in UK Biobank (Cassidy et al. 2018; Doherty et al. 2017; Firth et al. 2017; Hamer, Sharma, and Batty 2018). The Axivity AX3 accelerometers were shown to have equivalent acceleration profiles to Actigraph devices when worn at the same locations (Rowlands et al. 2018).

Confounding factors

Early life socioeconomic position, smoking status and BMI were considered to be confounders because of the known relationship to age at puberty and physical activity

(Bauman et al. 2012; Elhakeem et al. 2015; Mishra et al. 2009; Richmond et al. 2014). In ALSPAC, socioeconomic position was based on mothers' highest educational attainment reported in pregnancy. At the age 14-year clinic assessment, participants reported whether they had ever smoked cigarettes, and trained nurses measured heights using a Harpenden Stadiometer and weights using a Tanita Body Fat Analyser. In UK Biobank, early life socioeconomic position was based on participants highest educational qualification (Galobardes et al. 2006) which they reported at the touchscreen questionnaire, along with their smoking status. During physical assessments, trained nurses recorded each participants' height using a Seca 202 device and weight using a Tanita body fat analyser. BMI in both cohorts was calculated as weight (in kilograms) divided by height squared (in metres).

Statistical analyses

We used multivariable linear regression models to examine associations of age at puberty with accelerometer-measured physical activity in ALSPAC and UK Biobank. All analyses were performed separately for males and females due to differences in measures of age at puberty and expected differences in association with physical activity (Elhakeem et al. 2017; Sherar, Baxter-Jones, and Mirwald 2004). In ALSPAC, separate models were used to regress mean activity counts per minute and time spent in moderate-to-vigorous activity at age 14 and 16 years on age at menarche and voice break. To correct standard errors and minimise bias due to missing data, we used multivariable imputation by chained equations (White, Royston, and Wood 2011) to impute missing data for those with complete age at puberty data in addition to data on physical activity from age 14 and/or 16 (total imputed: n=1031 males, n=1363 females). Imputation models were fitted separately in males and females and run using 20 multiply imputed data sets that were combined using Rubin's combination rules (White, Royston, and Wood 2011).

In UK Biobank, associations of retrospectively reported age at menarche and relative age at voice break with mean acceleration were examined separately in 40-49-, 50-59- and 60-70-year-old participants. Two models were fitted for each set of analyses in both cohorts; an initial age-adjusted model followed by a second model that was further adjusted for early life socioeconomic position, smoking and BMI. To investigate if any associations found could be due to reverse causality, analyses in ALSPAC were repeated after removing participants with an age at puberty that was older than their age at accelerometer assessment. We explored evidence of deviation from linearity in the association of menarche with physical activity in UK Biobank by testing models with a quadratic term for age at menarche. In a sensitivity analysis in UK Biobank we refitted models after excluding those with any self-reported doctor-diagnosed disease that might influence activity levels, either directly or through associated conditions to see what effect this had on our estimates (diabetes: n=1615 males, n=1056 females; heart problems: n=10,476 males, n=9634 females, blood clot, deep vein thrombosis, bronchitis, emphysema, asthma, rhinitis, eczema or allergy: n= 11,556, n=17,222 females, cancer: n=2017 males; n=4021 females, other serious medical condition/disability: n=7152 males, n=9117 females, overall: n=22,943 males, n=29,494 females. Lastly, we used quantile regression (adjusted for all confounders) to examine whether any of the associations found in UK Biobank varied across the physical activity distribution (Koenker 2005; Bann et al. 2018; Bann, Fitzsimons, and Johnson 2019). All analyses were performed in R version 3.5.1 (R Foundation for Statistical Computing, Vienna).

RESULTS

Participant characteristics

A total of 2349 female and 1720 male adolescents from ALSPAC with data on age at puberty and physical activity data at age 14 and/or 16 years were included (Figure 1). Of these, 2154

females and 1586 males had activity data at age 14 only; and 1263 females and 866 males at age 16 only, and 1086 females and 732 males at both ages. Mean age at menarche was 12.8 years and mean age at voice breaking was 14 years (Table 1). Females had lower mean activity counts per minute and spent less time in moderate-to-vigorous activity than males at both ages 14 and 16 years (Table 1).

Complete data on age at puberty, physical activity and confounders were available for 48,282 female and 36,112 male adults with mean age of 55.6 years from UK Biobank (Figure 2). Of these, 21,276 were aged 40-49 years, 31,438 aged 50-59 years and 31,889 were 60-70-years old (Table 2). Mean age at menarche was 12.9 years in all women combined, 4.3% of all men reported their voice breaking at a younger age than their peers, whilst 7.3% recalled they were older than their peers when their voice broke (Supplementary file 1). Overall women had higher mean acceleration count than men (Supplementary file 1). Mean acceleration counts were lower in older age groups in both men and women (Table 2).

Age at puberty and physical activity in ALSPAC adolescents

Figure 2 shows associations of age at puberty with physical activity in ALSPAC. In females, there was evidence from both age- and fully adjusted models to suggest that older age at menarche was associated with higher mean activity counts per minute at age 14 (Figure 2). However, there was no evidence from either age- or fully adjusted models of an association between age at menarche and activity counts per minute at age 16 (Figure 2). At both ages, there was no evidence from both age- and fully adjusted models of difference in time spent at moderate-to-vigorous activity per older year at menarche (Figure 2). All estimates were unchanged after excluding 86 females in whom menarche occurred after age at accelerometer assessment (data not shown). In males, and at both ages, there was no strong evidence of association between older age at voice break and mean activity counts per minute or time

spent at moderate-to-vigorous activity, though with some suggestion of positive associations with both activity outcomes at age 16 years (Figure 2).

Age at puberty and physical activity in UK Biobank adults

Figure 3 shows associations of age at puberty with physical activity in UK Biobank. In females, there was evidence from age-adjusted models to suggest that older age at menarche was modestly associated with higher mean acceleration (Figure 3). After adjustment for BMI, smoking and educational status, associations were attenuated to the null in the oldest women; a weak association persisted after notable attenuation in the youngest (40-49-year-old) women (Figure 3). This was largely consistent with results of analyses performed after excluding women with self-reported doctor-diagnosed disease (Supplementary file 1). Quantile regression results showed that the associations found between older age at menarche and higher mean acceleration in 40-49-year old women were progressively stronger at the upper ends of the physical activity distribution, being strongest at the 90th quantile of mean acceleration (supplementary file 3).

In males, when compared with a younger than average age at voice break, there was evidence from age-adjusted models to suggest that an older age at voice break was associated with higher mean accelerations (Figure 3). However, these associations were largely attenuated after adjustment for confounders (Figure 3). These estimates were attenuated further after sensitivity analyses excluding men with diagnosed disease (Supplementary file 2).

DISCUSSION

This study used data from two large independent UK cohorts to investigate associations of age at puberty in both females and males with accelerometer-measured physical activity across adolescence and in middle-aged and older adults. Our findings from the adolescent ALSPAC cohort indicate evidence of an association between an older age at menarche and

higher activity counts at age 14 but not by age 16, with no evidence of an association with moderate-to-vigorous activity at either age. In 40-70-year old women from UK Biobank, we found a positive modest association between age at menarche and physical activity in younger (40-49-year-old) but not older women, which was strongest at the upper end of the activity distribution. For males from both cohorts, there was not much evidence of association between age at voice break and physical activity.

The positive association between age at menarche and physical activity at age 14, which agrees with previous studies in young adolescents (Bacil et al. 2015; Sherar et al. 2010), might be due to negative self-perceptions and subsequent avoidance of activity in early maturing girls (Mrug et al. 2014). This has some support from a Mendelian randomisation study in ALSPAC of a causal association between earlier age at menarche and depressive symptoms at age 14 (Sequeira et al. 2017). In addition, because of their older appearance, early maturing girls may also mix with older friends and, given that physical activity declines with chronological age across adolescence, they may adopt the lower activity of their new older peer group (Mrug et al. 2014). They may also be pressured into unhealthy behaviours like smoking, which can cluster with other unhealthy habits such as low physical activity (Mrug et al. 2014). That associations were attenuated in females later in adolescence may suggest that menarche- or puberty-related differences in total physical activity are no longer seen once girls transition beyond puberty (Cumming et al. 2012). It is also possible that reverse causality explains the association at age 14 whereby physical activity influences puberty timing (Moisan, Meyer, and Gingras 1991).

The weaker associations in the adult UK Biobank women reported here agree with previous findings from two British birth cohorts which showed little evidence of associations between age at menarche and self-reported leisure-time physical activity in 33- to 68-year-old women (Elhakeem et al. 2017; Pinto Pereira, Li, and Power 2014). However, it is worth noting that

the modest positive association in 40-49-year-old women from UK Biobank is similar in direction to those previous studies (including our findings of an association with physical activity at age 14 in ALSPAC presented here). We also found that this association in the 40-49-year-old women was strongest at the upper end of the activity distribution. This finding may reflect heterogenous causal effects of age at menarche on physical activity, differential confounding and/or effect modification, or an artefact of the scaling of the physical activity measure (Bann, Fitzsimons, and Johnson 2019).

Our finding of no clear associations in males is consistent with some previous studies in adolescents (Bacil et al. 2015; Sherar et al. 2010), including earlier findings from ALSPAC of no association between biological maturation (based on the % of predicted adult stature attained) at age 11 and physical activity two years later (Cumming et al. 2014). Our findings also agrees with studies using self-reported activity in adults (Elhakeem et al. 2017; Pinto Pereira, Li, and Power 2014) and with the only previous study using accelerometer data in adults which found no correlation between age at peak height velocity (a marker of puberty timing) and total activity counts in 166 Belgian men aged 40-years old (Beunen et al. 2004). Interestingly however, the association estimates were stronger in males at age 16 including for both mean counts per minute and MVPA which agrees with males reaching puberty later and having higher levels of MVPA than females.

That we did not find any strong associations in males may be due to our markers of age at puberty not being directly comparable between males and females. For instance, age at menarche is a precise milestone whereas in males, less precise measures of voice break were used (Dorn et al. 2006). Another possible explanation for finding an association in females and not males could be due to menarche being a more noticeable event than the gradual changes in male's voice and thus more likely to influence contemporaneous activity levels. Adjustment for confounders, in particular BMI, resulted in greater attenuation to the null in

UK Biobank compared with ALSPAC and in females more so than males. This may reflect effects of ageing in the older UK Biobank cohort and sex differences in body composition.

The inclusion of two independent cohorts with large sample sizes and assessment of physical activity with accelerometers at different ages across adolescence and in heterogeneously aged adults are key strengths of this study. The use of two different cohorts also has its limitations due to the different characteristics of the cohorts including in their measurement of physical activity. For instance, whilst our estimate of physical activity in UK Biobank was derived using a well-defined protocol and has been validated in relation to different health prospects (Cassidy et al. 2018; Firth et al. 2017; Hamer, Sharma, and Batty 2018), we did not have a measure of higher intensity activity like in ALSPAC. However, higher intensity activity is likely to be less important in older adults since, with increasing age, lighter intensity activity makes up a growing proportion of total time spent in physical activity (Schrack et al. 2014). Future studies could make use of recent advances in accelerometer output analyses to derive more detailed activity outcomes (Millard et al. 2017; Willetts et al. 2018). They could also examine how associations might vary across the physical activity distribution.

Age at puberty was prospectively collected in ALSPAC meaning it is less susceptible to recall errors and misclassification (Cooper et al. 2006), unlike in UK Biobank which relied upon participants' long-term recall. ALSPAC had good response rates and is representative of its source populations in terms of key sociodemographic characteristics (Boyd et al. 2013), In contrast, and despite its large size, UK Biobank suffers from a poor response rate meaning it is not representative of the general population. Whilst it has previously been argued that valid assessments of exposure-outcome relationships do not require participants to be representative of the source population (Rothman, Gallacher, and Hatch 2013), recent evidence indicates that this selection bias might influence estimates of association (Munafo et al. 2018), particularly where effect sizes are small like in our study. We a priori considered

BMI to be a confounder, given evidence that BMI influences puberty (Mumby et al. 2011, Bell et al. 2018) and physical activity (Richmond et al. 2014), thus fulfilling the criteria of a confounder.

In conclusion, we examined data from two independent British cohorts of adolescents and adults and found some evidence of lower accelerometer-measured physical activity in younger-aged early maturing adolescent girls but little evidence of associations after puberty completion in older females or at any age in males. Overall, these findings are reassuring as they suggest that the timing of puberty is unlikely to be an important determinant of physical activity in later life. Future studies may benefit from harmonising accelerometer outputs across different cohorts prior to analysis.

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Table 1 Characteristics of adolescents from the Avon Longitudinal Study of Parents and Children with data on age at puberty and physical activity at age 14 and/or 16 years.

	Females (n=2349)	Males (n=1720)
Age at accelerometer assessment, years [Mean (SD)]		
14-year follow-up	13.8 (0.2)	13.8 (0.2)
16-year follow-up	15.4 (0.3)	15.4 (0.3)
Physical activity parameters [Mean (SD)]		
14-year follow-up		
mean activity counts/min	486.8 (161.4)	598.9 (197.2)
moderate-to-vigorous activity, min/day	19.5 (14.3)	28.8 (18.6)
16-year follow-up		
mean activity counts/min	433.5 (144.5)	540.4 (202.5)
moderate-to-vigorous activity, min/day	18.3 (15.4)	30.0 (20.5)
Age at menarche, years [Mean (SD)]	12.8 (1.2)	-
Age at voice breaking, years [Mean (SD)]	-	14.0 (1.6)
Body mass index at age 14, kg/m^2 [Mean (SD)]	20.8 (3.6)	19.9 (3.2)
Smoking status at age 14 [N (%)]		
no	1853 (78.9)	1432 (83.3)
yes	403 (17.2)	229 (13.3)
Maternal education [N (%)]		
certificate of Secondary Education	242 (10.3)	160 (9.3)
vocational	155 (6.6)	137 (8.0)
O-level	772 (32.9)	550 (32.0)
A-level	614 (26.1)	478 (27.8)
degree or higher	401 (17.1)	287 (16.7)

Table 2 Characteristics of adults from UK Biobank with data on age at puberty, physical activity and confounders, stratified by age group.

	40-49-year-olds		50-59-year-olds		60-70-year-olds	
	Females (n=12,921)	Males (n=8,346)	Females (n=18,820)	Males (n=12,618)	Females (n=16,741)	Males (n=15,148)
Age at accelerometer assessment, years [Mean (SD)]	45.1 (2.7)	44.9 (2.8)	54.7 (2.8)	54.9 (2.9)	63.7 (2.7)	63.9 (2.8)
Mean acceleration, mg [Mean (SD)]	31.1 (8.6)	31.0 (9.5)	28.9 (7.8)	28.3 (8.5)	26.3 (7.0)	25.4 (7.6)
Age at menarche, years [Mean (SD)]	12.9 (1.6)	-	12.9 (1.5)	-	12.9 (1.5)	-
Relative age at voice breaking [N (%)]						
younger than average age	-	489 (5.9)	-	614 (4.9)	-	510 (3.4)
about average age	-	7108 (85.1)	-	10989 (87.1)	-	13769 (90.9)
older than average age	-	749 (9.0)	-	1015 (8.0)	-	869 (5.7)
Body mass index, kg/m^2 [Mean (SD)]	25.8 (5.0)	27.0 (4.1)	26.2 (4.9)	27.3 (4.1)	26.4 (4.6)	27.2 (3.8)
Smoking status [N (%)]						
Never	8429 (65.2)	5264 (63.1)	11608 (61.7)	7053 (55.9)	9868 (59.0)	7006 (46.3)
Former	3435 (26.6)	2148 (25.7)	6123 (32.5)	4562 (36.2)	6251 (37.3)	7224 (47.7)
Current	1057 (8.2)	934 (11.2)	1089 (5.8)	1003 (8.0)	622 (3.7)	918 (6.1)
Educational qualifications [N (%)]						
college or University degree	6432 (49.8)	4234 (50.7)	9114 (48.4)	6455 (51.2)	6782 (40.5)	7132 (47.1)
A levels/AS levels or equivalent	2149 (16.6)	1175 (14.1)	2946 (15.7)	1788 (14.2)	2353 (14.1)	1827 (12.1)
O levels/GCSEs or equivalent	2789 (21.6)	1686 (20.2)	4095 (21.8)	2211 (17.5)	4943 (29.5)	3165 (20.9)
GCEs or equivalent	803 (6.2)	613 (7.3)	906 (4.8)	661 (5.2)	424 (2.5)	267 (1.8)
NVQ or HND or HNC or equivalent	385 (3.0)	489 (5.9)	721 (3.8)	994 (7.9)	639 (3.8)	1739 (11.5)
other professional qualification	363 (2.8)	149 (1.8)	1038 (5.5)	509 (4.0)	1600 (9.6)	1018 (6.7)

Data for the combined age groups are presented in Supplementary file 1.

FIGURE LEGENDS

Figure 1 Study flowcharts for the Avon Longitudinal Study of Parents and Children (ALSPAC) and UK Biobank.

Figure 2 Difference in standard deviation (SD) units in total activity (mean counts per minute) and time spent in moderate-to-vigorous activity (minutes per day) at ages 14 and 16 years (A) per 1-year older age at menarche and (B) per 1-year older age at voice break in the Avon Longitudinal Study of Parents and Children. Model 1: adjusted for chronological age. Model 2: additional adjustment for BMI, smoking status and maternal education. Horizontal lines reflect 95% confidence interval. P-values from tests of association for the adjusted models were females-age 14: $P<0.001$ for counts/min and $P=0.7$ for MVPA, males-age 14: $P=0.4$ for counts/min and $P=0.1$ for MVPA, females-age 16: $P=0.3$ for counts/min and $P=0.5$ for MVPA, males-age 16: $P=0.2$ for counts/min at 14 and $P=0.2$ for MVPA.

Figure 3 Difference in standard deviation (SD) units in total activity (mean acceleration; *mg*) in 40-49-, 50-59- and 60-70-year-olds from UK Biobank (A) per 1-year older age at menarche and (B) by relative age at voice break (reference: younger than average age). Model 1 adjusted for chronological age. Model 2: additional adjustment for BMI, smoking status and education. Horizontal lines reflect 95% confidence interval. Different x-axis scales are used for females and males. P-values from tests of association for the adjusted models in females were: $P<0.001$ in 40-49-year-olds, $P=0.08$ in 50-59-year-olds and $P=0.1$ in 60-70-year-olds, and in males were $P=0.8$ in 40-49-year-olds, $P=0.07$ in 50-59-year-olds and $P=0.04$ in 60-70-year-olds. Tests of deviation from linearity using quadratic term for age menarche: $P=0.03$ for 40-49-year-olds, $P=0.4$ in 50-59-year-olds, $P=0.5$ in 60-70-year-olds, and $P=0.1$ in all the women combined.