Longitudinal association between dysmenorrhoea in adolescence and chronic pain in adulthood: a UK population-based study

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Summary

Background Dysmenorrhoea affects many adolescents and often goes untreated for various sociocultural reasons. Dysmenorrhoea frequently co-occurs with other chronic pain conditions, and adult women with dysmenorrhoea have greater sensory sensitivity compared with controls. We aimed to test the hypothesis that adolescent dysmenorrhoea leads to the development of general chronic pain, including pain outside the pelvis, by estimating the risk of chronic pain in adulthood following the experience of dysmenorrhoea at age 15 years.

Methods We used data from the Avon Longitudinal Study of Parents and Children (ALSPAC) a longitudinal birth cohort of mothers with an expected delivery date between April 1, 1991, and Dec 31, 1992, and their children in Avon, UK. Each year from ages 8 to 17 years, children were asked about dysmenorrhoea. At age 15, participants were also asked to describe their experience of dysmenorrhea as mild, moderate, or severe. At age 26 years, participants reported any pain in response to the questions: "Have you had any aches or pains that have lasted for a day or longer in the past month?" (yes or no); and "When did the pain start?" (<3 months ago or ≥3 months ago). Any chronic pain (≥3 months in duration) was the primary outcome. For the analysis, we excluded participants with a pain condition before menarche and participants with acute pain lasting less than 3 months at age 26 years. Missing data were addressed by multiple imputation. To estimate the risk of chronic pain at age 26 years when experiencing dysmenorrhoea in adolescence (none, mild, moderate, or severe), we used multivariable logistic regression models, adjusted for confounders previously associated with dysmenorrhoea and chronic pain (ethnicity, mother's education level, adverse childhood experiences from ages 0–10 years, depressive symptoms preceding menarche, frequency of vigorous physical activity at menarche, smoking at menarche, polyunsaturated fatty acid intake as per food diaries completed at age 10 years, and BMI at menarche), to generate relative risks [RRs] for chronic pain. Dose response was investigated in an adjusted regression model with dysmenorrhoea severity as a numeric variable. We examined anxiety and depressive symptoms in the 2 years after dysmenorrhoea was reported as potential mediators using bootstrapping with 1000 simulations.

Findings The study sample included 1157 participants, 691 (59·7%) of whom reported moderate or severe dysmenorrhoea at age 15 years. Of the 307 (26·5%) participants who reported chronic pain at age 26 years, 32 (17·3%) had no dysmenorrhoea at age 15 whereas 62 (22·1%) had mild, 157 (30·0%) had moderate, and 56 (33·5%) had severe dysmenorrhoea. Adjusted RRs for any chronic pain at age 26 years were 1·23 (95% CI 0·85–1·74, p=0·27) for mild, 1·65 (1·22–2·18, p=0·0021) for moderate, and 1·76 (1·23–2·39, p=0·0030) for severe dysmenorrhoea at age 15 years compared with no dysmenorrhoea. These findings correspond to an absolute adjusted risk difference of 4·8 percentage points (95% CI –2·5 to 12·1) for mild dysmenorrhoea, 12·7 percentage points (5·9 to 19·4) for moderate dysmenorrhoea, and 16·2 percentage points (7·2 to 25·2) for severe dysmenorrhoea compared with no dysmenorrhea. Anxiety and depressive symptoms mediated a small proportion of the association between severe dysmenorrhoea and chronic pain. The mediating role of anxiety and depressive symptoms was greatest among participants with severe dysmenorrhoea.

Interpretation Dysmenorrhoea in adolescence adversely affects immediate wellbeing and contributes to an increased risk of chronic pain in adulthood, thus lending supporting evidence to calls to consider adolescent dysmenorrhoea a crucial public health issue. Future work should focus on early identification and effective management, including non-pharmacological strategies and self-management, which relies on continuing work to improve young people's menstrual literacy.

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Research in context

Evidence before this study

We searched PubMed for articles published from database inception to Feb 07, 2024, using search terms including "adolescen*", "teenage*" "dysmenorrh*", "menstrual pain", "chronic pain", "longitudinal", "prospective", and "association". Evidence shows that dysmenorrhoea is highly prevalent among adolescents. In adults, dysmenorrhoea frequently co-occurs with chronic pelvic pain and non-pelvic pain conditions such as migraine and fibromyalgia. One retrospective study found that dysmenorrhoea preceded chronic pain in adults, and two small clinical cohort studies reported conflicting results for the development of pelvic pain in adolescents with dysmenorrhoea. Current evidence is limited by a lack of focus on adolescent populations (or small samples with poor generalisability in the two studies identified in adolescents), lack of longitudinal studies, and few high-quality observational studies (as evaluated by Newcastle–Ottawa Scale). The relationship between adolescent dysmenorrhoea and chronic pain in adulthood is underexplored, especially in the context of chronic pain outside the pelvis from adolescence onwards. We found no examples of published or ongoing research testing the hypothesis that dysmenorrhoea during adolescence is an independent risk factor for chronic pain in adulthood or of research exploring anxiety and depressive symptoms as potential mediators.

Added value of this study

Moderate or severe dysmenorrhoea was common in a large sample of adolescents in a nationally representative UK birth cohort. We noted clear evidence of a dose–response relationship between dysmenorrhoea severity in adolescence and chronic pain in adulthood, whereby mild, moderate, and severe dysmenorrhoea in adolescence was associated with a 23%, 65%, and 76% increased risk of future chronic pain, respectively. Dysmenorrhoea was associated with most chronic pain sites, particularly abdominal and lower back pain. Although we found that dysmenorrhoea was associated with incident higher anxiety and depression scores, these factors explained only a small proportion of the association between dysmenorrhoea and chronic pain, suggesting that other unknown mechanisms predominate.

Implications of all the available evidence

Dysmenorrhoea in adolescents is an important public health issue that might have serious long-term health implications, warranting attention through further research and wider social policy. Although the effect of early intervention for dysmenorrhoea on the risk of future chronic pain remains unknown, these findings should be considered in the context of few young people with dysmenorrhoea seeking health care and therefore missed opportunities for support. Improving menstrual literacy and increasing the confidence to self-manage symptoms are priorities.

Introduction

Chronic pain is more common in individuals assigned female at birth than in individuals assigned male.[1] This trend emerges after puberty,[2] suggesting that sexually dimorphic changes during this life stage could be aetiological factors in the development of chronic pain. Menarche is an important change during female puberty. Menstruation is often a painful, difficult experience, with up to 91% of reproductive-aged women reporting dysmenorrhoea, while more severe dysmenorrhoea is reported in younger people (<30 years).[3] In adolescence, dysmenorrhoea is associated with school absences, reduced participation and concentration in class, and avoidance of sports and social activities.[4,5] Thus, dysmenorrhoea can impair academic performance and compromise mental health. Despite these serious impacts, dysmenorrhoea is commonly normalised within society by both young people and their caregivers. This normalisation might explain why some young people with dysmenorrhoea do not seek care and why some of those who do seek care report feeling dismissed by caregivers, including health-care professionals and those within the school setting.[6] The long-term consequences of dysmenorrhoea in adolescence that is inadequately treated are unknown.

People with chronic pain show differences in a variety of physiological systems compared with healthy, pain-free individuals. These differences include alterations in sensory processing,[7] brain structure and function,[8] and the activity of the hypothalamic–pituitary–adrenal axis and autonomic nervous system.[9] However, whether these differences are a cause or consequence (or both) of chronic pain is unknown. Experimental evidence suggests that adult women with dysmenorrhoea also show a variety of changes, such as increased sensitivity to varying noxious stimuli at both pelvic (somatic and visceral) and non-pelvic sites,[10–12] altered brain activity during noxious stimulation,[11] altered brain structure,[13] and reduced activity of the hypothalamic–pituitary–adrenal axis.[11] It is therefore plausible that the presence of dysmenorrhoea during adolescence, when the nervous system is particularly plastic, could lead to alterations in the function of these systems, thus increasing vulnerability to the development of other forms of chronic pain.

Few longitudinal studies have examined the epidemiological relationship between dysmenorrhoea and chronic pain. A 2020 meta-analysis reported an odds ratio (OR) for dysmenorrhoea of 2·50 (95% CI 2·03–3·10) in women aged 14–60 years with chronic pain compared with those with no reported chronic pain.[14] Similar effect sizes were seen for chronic pelvic pain and chronic non-pelvic pain. However, only one of the 32 included studies was longitudinal, and this study focused specifically on

temporomandibular disorder.[14] In a longitudinal study published in 2021, women in the USA aged 25–62 years who reported dysmenorrhoea at baseline had an adjusted 41% (95% CI 6–88) increased risk of for developing chronic pain after 10 years.[15]

Although small prospective studies have explored the relationship between adolescent dysmenorrhoea and chronic pelvic pain in adulthood,[16,17] to our knowledge, none has looked at this in the context of chronic pain outside the pelvis. This absence of research examining wider chronic pain outcomes from adolescence onwards is notable. Intervention might be of particular importance at younger ages due to the heightened neuroplasticity, higher rates of dysmenorrhoea, and susceptibility to related adverse psychosocial and educational impacts in this population. We aimed to address this research gap, and we hypothesised that dysmenorrhoea during adolescence is an independent risk factor for chronic pain in adulthood (definitions of adolescence vary; in this study, we used the WHO definition of ages 10–19 years). We also aimed to explore anxiety and depressive symptoms as potential mediators. It is possible that such mental health symptoms might follow dysmenorrhoea because of its substantial burden on quality of life in adolescents. Additionally, anxiety and depression often precede or co-occur with chronic pain in adults.[18,19]

Methods

Study design and participants

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a prospective birth cohort study that recruited pregnant women living in Avon, UK, with expected delivery dates between April 1, 1991, and Dec 31, 1992.[20,21] The original ALSPAC cohort included 14 541 pregnancies, resulting in 13 988 children who were alive at age 1 year. Following later attempts to bolster the original sample, the total sample included 15 447 pregnancies, resulting in 14 901 children who were alive at age 1 year and who were then followed up to early adulthood.

Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Informed consent for the use of ALSPAC data was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time. This study and analysis were developed in collaboration with a patient and public involvement group of eight menstruating adolescents aged 16–18 years living in south England. The group represented diversity in ethnicity and in lived experience, including of menstruation. Their advice for the development of the study aims and materials and their thoughts on the importance, interpretation, and presentation of findings are summarised in the appendix (p 2). The analysis plan was pre-registered on Open Science Framework on Feb 7, 2024, and the findings are reported in line with STROBE guidelines.

See Online for appendix

For more on the **analysis plan** see https://osf.io/nhvye/

For more on the **STROBE guidelines** see https://www.strobe-statement.org/checklists/

Exposures

From ages 8 to 17 years, ALSPAC participants were asked about dysmenorrhoea in a series of nine "puberty questionnaires". These were completed at home; it was stated that the mother or daughter could complete the first five questionnaires (ages 8–12 years), while the young person was asked to self-complete questionnaires six to nine (ages 13–17 years). Participants with dysmenorrhoea were identified from responses to the following questions, which were asked of participants at age 15 years: "Have you ever had any of the following symptoms associated with your period?"; "Pain with your period?"; and "If yes, were they mild, moderate (painful enough that you could not easily forget about them, whatever was going on), or severe (so that you were unable to continue with normal activities)?" The questionnaire completed at age 15 had the largest response rate and was the only questionnaire to capture data on dysmenorrhoea severity. All other years featured a binary dysmenorrhoea question.

In the puberty questionnaires young people reported whether they used oral contraceptives or birth control pills, which we consider indicative of the use of combined or progestin-only oral contraceptive pills (OCPs).

Depressive symptoms (scored on a 0–26 scale) were assessed via the Short Mood and Feelings Questionnaire (SMFQ) at age 16 years, and an anxiety score (0–4) was derived from the Clinical Interview Schedule—Revised conducted at age 17 years. Participants with probable depression (SMFQ score ≥10 preceding menarche), or an anxiety disorder meeting ICD-10 or Diagnostic and Statistical Manual of Mental Disorders IV criteria at age 13 years, were excluded.

Outcomes

In a questionnaire received at age 26 years, participants reported whether they experienced any pain in response to the questions: "Have you had any aches or pains that have lasted for a day or longer in the past month?" (yes or no); and "When did the pain start?" (less than 3 months ago or more than 3 months ago). In the same questionnaire, participants indicated where in the body chronic pain was experienced (head, jaw, neck, shoulder, upper arm, elbow, lower arm, wrist or hand, upper back, chest, lower back, abdomen, hip, thigh, knee, lower leg, and ankle or foot). Any chronic pain was the primary outcome; site-specific pain and the number of pain sites (0–17) were secondary outcomes.

Statistical analysis

This analysis included all participants with complete data through to age 26 years, except those who reported experiencing chronic pain before menarche (using the question "Has anyone ever thought there might be a problem with aches and pains, including headache?"; reported by parents when the child was aged 8 or 11·7 years) and those who reported experiencing acute pain lasting

less than 3 months at age 26 years. In the case of twins, one girl was randomly selected for inclusion.

Variables were explored using descriptive statistics. Baseline characteristics are presented for the total sample and by dysmenorrhoea status (aggregating no dysmenorrhoea with mild dysmenorrhoea, and moderate dysmenorrhoea with severe dysmenorrhoea, to overcome issues relating to disclosure risk from small cell counts when using four groups).

Univariate and multivariable logistic regression models were conducted for binary outcomes, and zero-inflated negative binomial regression was used for the number of pain sites (identified as the optimal model following comparison of Akaike Information Criterion values with those from Poisson, quasi-Poisson, and negative binomial models). To address the expected overinflation of effect measures due to a high chronic pain prevalence, ORs were converted to risk ratios (RRs) using a standard equation (appendix p 3). Dose–response was investigated by rerunning the covariate-adjusted regression model with dysmenorrhoea severity as a numeric variable and with an additional polynomial term to assess linearity of the trend.

Multivariable models were adjusted for confounders previously associated with dysmenorrhoea and chronic pain: ethnicity, mother's education level, adverse childhood experiences (ACEs) from ages 0–10 years (physical, sexual, and emotional abuse; emotional neglect; parental separation; household substance abuse; domestic violence; bullying; parental mental health issues or suicide; and convicted offence within the family), depressive symptoms preceding menarche (at ages 9 or 12 years; SMFQ score), frequency of vigorous physical activity at menarche, smoking at menarche, polyunsaturated fatty acid intake as per food diaries completed at age 10 years, and BMI at menarche (appendix pp 3–4, 10). We adjusted for confounders as

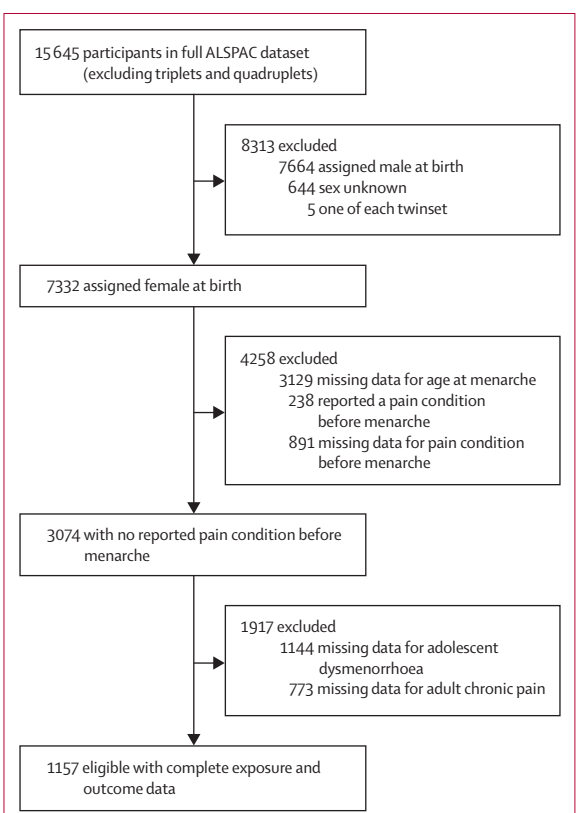


Figure 1: **Identification of the eligible study sample**

	No or mild dysmenorrhoea (n=466)	Moderate or severe dysmenorrhoea (n=691)
Mean age at menarche, years	12·59 (1·11)	12·15 (1·06)
Ethnicity		
White	445 (95%)	669 (97%)
Non-White	21 (5%)	22 (3%)
Mother's education level		
None	41 (9%)	56 (8%)
Vocational	34 (7%)	46 (7%)
GCSE or O-level	172 (37%)	229 (33%)
GCE or A-level	122 (26%)	203 (29%)
University degree	97 (21%)	157 (23%)
Adverse childhood experience score at age 0–10 years		
0	142 (30%)	175 (25%)
1	144 (31%)	211 (31%)
2	79 (17%)	138 (20%)
3	56 (12%)	85 (12%)
≥4	45 (10%)	82 (12%)
Short Mood and Feelings Questionnaire score at or before menarche		
0	188 (40%)	216 (31%)
1–2	143 (31%)	225 (33%)
3–4	71 (15%)	112 (16%)
5–6	26 (6%)	69 (10%)
7–8	19 (4%)	30 (4%)
>8	19 (4%)	39 (6%)
Had smoked at or before menarche		
Yes	43 (9%)	96 (14%)
No	423 (91%)	595 (86%)
Vigorous physical activity at menarche, times per week		
<1	27 (6%)	36 (5%)
1–3	240 (52%)	375 (54%)
4–6	151 (32%)	222 (32%)
Daily	48 (10%)	58 (8%)
Median BMI at menarche, kg/m²	18·63 (17·18–20·61)	19·08 (17·34–21·45)
Median polyunsaturated fatty acid intake at age 10 years, g/day	11·17 (8·94–14·14)	11·78 (8·86–14·69)
Oral contraceptive pill use at age 15 years		
Yes	32 (7%)	98 (14%)
No	434 (93%)	593 (86%)

Data are mean (SD), n (%), or median (IQR).

Table: **Baseline characteristics of the study sample by dysmenorrhoea status**

close to menarche as possible to ensure that we did not introduce reverse causation, considering that many girls who reported dysmenorrhoea at age 15 years had also experienced it in previous years. We also adjusted for age at menarche to reduce potential biases introduced by differential follow-up durations between participants—this was additionally included as a quadratic term to account for a non-linear relationship to the exposure.

Multiple imputation was conducted for covariates using 30 imputations (chosen based on the expected fraction of missing data)[22] and 33 iterations. Multicollinearity was assessed by pairwise Spearman's rank correlations between all variables (appendix p 5). In cases of high correlation ($\rho \geq 0{\cdot}7$), the variable deemed less relevant to the research question or with lower theoretical significance was to be excluded from the analysis; however, this was not necessary.

Two sensitivity analyses were conducted for the primary outcome to address bias introduced by missing data, to compare results across methods, and to assess robustness of findings: a complete-case analysis, and an analysis that included binary indicators for covariates for which missingness was associated with the outcome ($p<0{\cdot}1$; ie, depressive symptoms, ACE score, and physical activity).

We included the use of OCPs from ages 15 to 17 years as a potential effect modifier, because combined or progestin-only OCPs are recommended as a first-line treatment for dysmenorrhoea in adolescents and the potential pain relief from such treatment, in addition to the neuroendocrine influence of exogenous hormone preparations, could modify any relationship between dysmenorrhoea and chronic pain. Stratified regression models were run using ever use of OCPs (yes or no) and years of OCP use (0, 1, 2, or 3 years) as strata. A likelihood ratio test was conducted to assess whether inclusion of OCP use as an interaction term improved model fit for the primary outcome.

We examined the potential mediating role of anxiety and depressive symptoms in the 2 years after dysmenorrhoea was reported. Kruskal–Wallis and Bonferroni-corrected Dunn tests examined pairwise differences between groups. The RStudio mediation package with bootstrapping (1000 simulations) was used to generate statistics for the average causal mediation effect, average direct effect, total effect, percentage mediated, and p values. Models were adjusted with the same covariates as in the primary analysis.

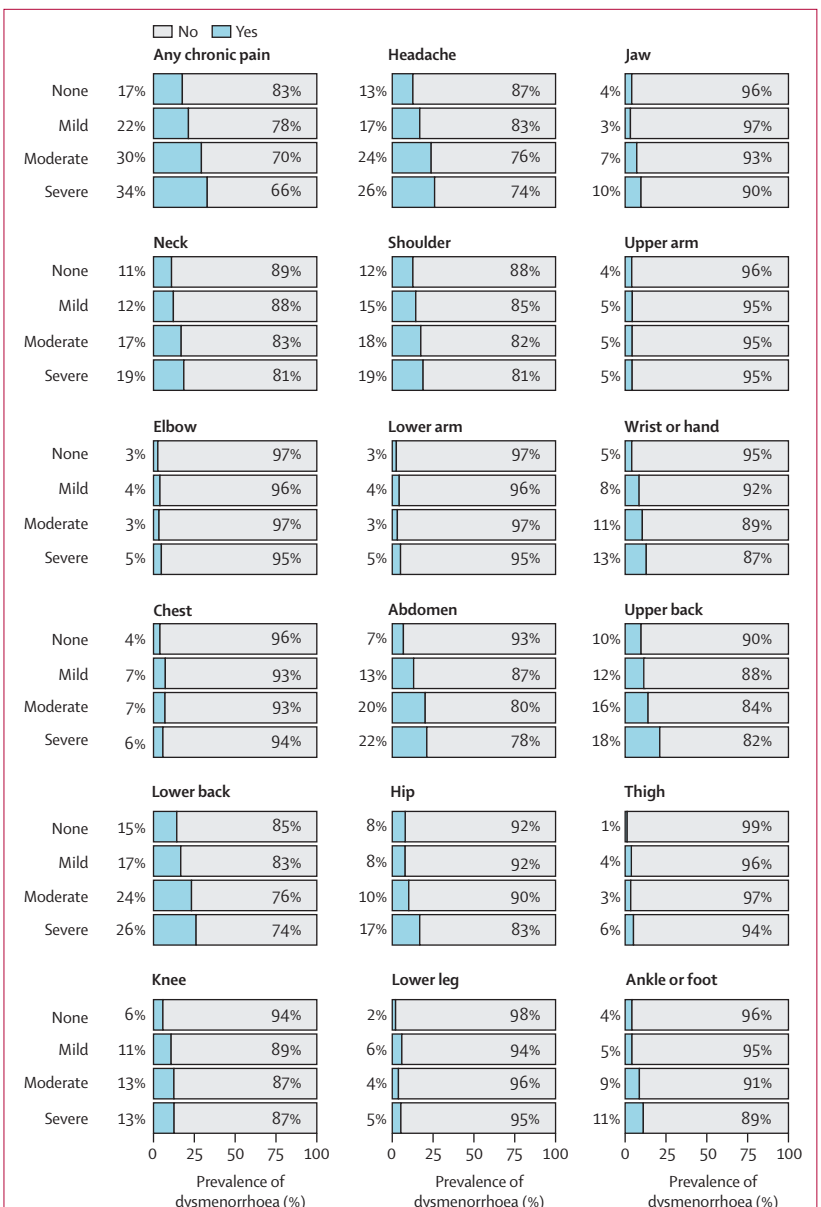


Figure 2: **Prevalence of any and site-specific pain at age 26 years stratified by adolescent dysmenorrhoea status (N=1157)**
Dysmenorrhoea status is stratified by none, mild, moderate, or severe.

Role of the funding source

The funders of this study had no role in study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit for publication.

Results

The eligible study sample included 1157 participants (figure 1). The study sample was predominantly White, and the proportion of university-educated mothers in the study sample was slightly higher than the contemporary population average (table). 972 (84%) of 1157 participants reported any dysmenorrhoea at age 15 years: 281 (24%) reported mild pain; 524 (45%) moderate pain; and 167 (14%) severe pain. At baseline, participants with moderate or severe dysmenorrhoea were proportionally more likely than those with no or mild dysmenorrhoea to have smoked, score 5 or higher on the SMFQ, or experienced at least one adverse childhood experience (table). The proportion of missing data was low (<10%) for all covariates aside from ACE score (31·6%) and OCP use (39·4%; appendix p 11).

At age 26 years, the overall prevalence of chronic pain in the study sample was 307 (26·5%; appendix p 11). A dose-dependent trend was evident for dysmenorrhoea severity (figure 2). Chronic pain at 26 years was reported in 32 (17·3%) individuals with no dysmenorrhoea, 62 (22·1%) with mild dysmenorrhoea, 157 (30·0%) with moderate dysmenorrhoea, and 56 (33·5%) with severe dysmenorrhoea (appendix p 11). This dose-dependent trend was also observed for 12 (71%) of 17 specific pain sites (figure 2). The highest prevalence and greatest disparity between the no dysmenorrhoea and severe dysmenorrhoea groups were seen in lower back pain (14·6% *vs* 26·3%), headache (13·0% *vs* 26·3%), and abdominal pain (7·0% *vs* 21·6%).

Unadjusted and adjusted RRs and 95% CIs from logistic regression models for the association between dysmenorrhoea severity and any chronic pain at age 26 years are shown in figure 3. ORs are given in the appendix (p 12). In adjusted models, dysmenorrhoea was associated with an increased risk of chronic pain, with notably higher point estimates for moderate dysmenorrhoea (RR 1·65 [95% CI 1·22–2·18], p=0·0021) and severe dysmenorrhoea (1·76 [1·23–2·39], p=0·0030) compared with mild dysmenorrhoea (1·23 [0·85–1·74], p=0·27). A linear dose–response trend was observed (p=0·0003). These findings correspond to a higher absolute risk of 4·8% (95% CI –2·5 to 12·1) in the mild, 12·7% (5·9 to 19·4) in the moderate, and 16·2% (7·2 to 25·2) in the severe dysmenorrhoea group when compared with the no dysmenorrhoea group. The results of the complete-case and sensitivity analyses support these findings (appendix p 12).

Ever-use of an OCP from ages 15 to 17 years was common (529 [45·7%] of 1157 participants). Two-hundred and eighty-four (54%) had used an OCP for 1 year, 169 (32%) for 2 years, and 76 (14%) for 3 years. Ever use, and longer duration of use, were more frequent in those who reported severe dysmenorrhoea (appendix p 6).

Stratified regression analyses indicated that the association between dysmenorrhoea and chronic pain was stronger in ever-users than in never-users of OCPs (appendix p 13). Further stratification by number of years of OCP use revealed that the association between dysmenorrhoea and chronic pain was strongest for the 284 participants who reported using an OCP for only 1 year between ages 15 and 17 years, 230 (81%) of whom reported using an OCP at age 17 years only while fewer participants used OCPs only at age 15 years (20 [7%]) or 16 years (34 [12%]; appendix p 13).

A likelihood ratio test comparing models with and without OCP ever-use versus never-use from ages 15 to 17 years as an interaction term yielded a deviance of 6·23 with 3df (p=0·10), suggesting no improvement in model fit. Similar results were obtained when using years of OCP use (never, 1 year, 2 years, or 3 years) as the interaction term (deviance 4·94, p=0·18).

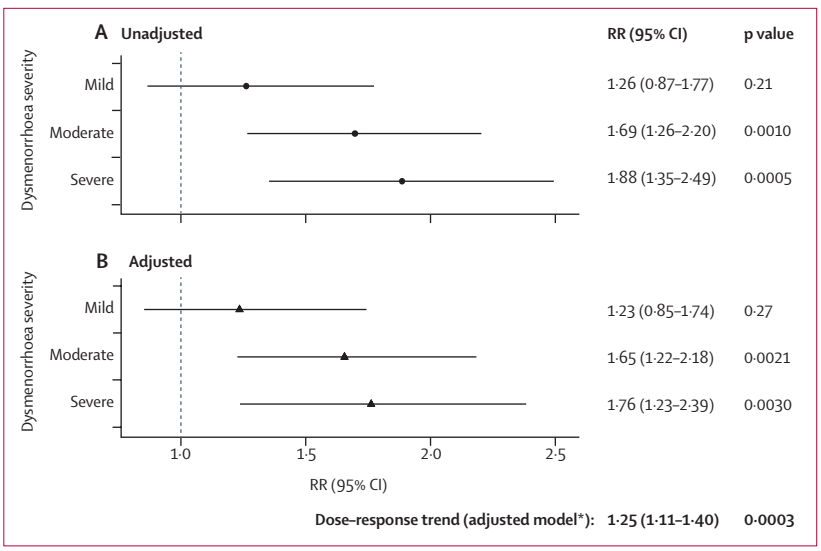
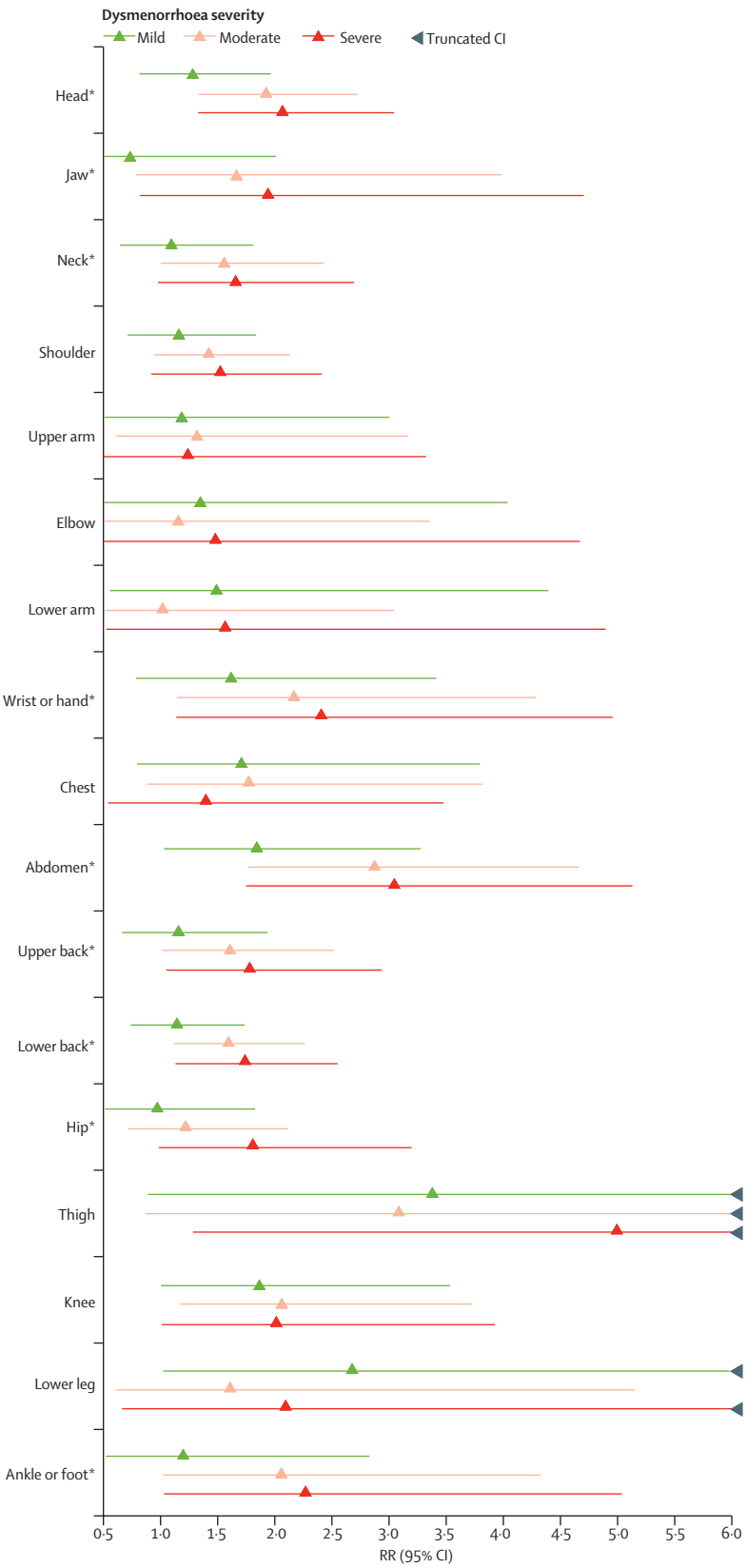


Figure 3: **Unadjusted and adjusted logistic regression models for the relationship between adolescent dysmenorrhoea status and any chronic pain at age 26 years (N=1157)**
Dysmenorrhoea status is stratified by mild, moderate, or severe in reference to no dysmenorrhoea. RR=relative risk. *p=0·44 for the polynomial term in the dose–response model.

Kruskal–Wallis and Dunn post-hoc tests revealed that the moderate and severe dysmenorrhoea groups had higher SMFQ scores at age 16 years than the no dysmenorrhoea group, and higher anxiety scores at age 17 years than the no and mild dysmenorrhoea groups (appendix p 7). Linear regression models showed that moderate and severe dysmenorrhoea were positively associated with depressive symptoms at age 16 years (moderate β=1·82 [95% CI 0·80–2·84], p=0·0005; severe β=1·85 [0·56–3·13], p=0·0049; appendix p 13), and with anxiety score at age 17 years (moderate β=0·23 [0·09–0·37], p=0·0013; severe β=0·34 [0·17–0·51], p=0·0001; appendix p 14), after confounder adjustment. Adjusted linear models did not find an association between mild dysmenorrhoea and either outcome (appendix pp 13–14). Depressive and anxiety scores were weakly correlated (Spearman's ρ=0·25).

Overall, anxiety and depressive symptoms mediated a small proportion of the association between dysmenorrhoea and chronic pain (appendix pp 15–16). These psychological factors mediated the greatest proportion of the association between dysmenorrhoea and chronic pain in the severe dysmenorrhoea group (23% [95% CI 1 to 92], p=0·040, for anxiety symptoms; 12% [–1 to 68], p=0·14, for depressive symptoms). For moderate dysmenorrhoea, the proportion mediated by anxiety symptoms was 8% (1–23, p=0·014) and depressive symptoms 9% (1–26, p=0·020) of the relationship.

Moderate to severe dysmenorrhoea was associated with chronic headache, upper and lower back pain, joint pain (wrist or hand, or knee; figure 4, appendix p 8). Any dysmenorrhoea was associated with chronic abdominal pain, but especially moderate (RR 2·87 [95% CI 1·75–4·66]) and severe (3·05 [1·75–5·14])



	RR (95% CI)	p value
Mild	1·28 (0·81–1·97)	0·30
Moderate	1·92 (1·32–2·74)	0·0012
Severe	2·06 (1·32–3·04)	0·0022
Mild	0·73 (0·26–2·02)	0·53
Moderate	1·66 (0·78–3·83)	0·22
Severe	1·94 (0·81–4·71)	0·15
Mild	1·09 (0·64–1·82)	0·76
Moderate	1·56 (1·00–2·41)	0·057
Severe	1·66 (0·97–2·71)	0·065
Mild	1·15 (0·71–1·83)	0·57
Moderate	1·42 (0·94–2·14)	0·11
Severe	1·51 (0·91–2·41)	0·11
Mild	1·18 (0·48–3·00)	0·72
Moderate	1·32 (0·60–3·17)	0·51
Severe	1·23 (0·44–3·33)	0·69
Mild	1·35 (0·49–4·04)	0·57
Moderate	1·16 (0·45–3·36)	0·78
Severe	1·48 (0·48–4·68)	0·50
Mild	1·49 (0·55–4·41)	0·45
Moderate	1·02 (0·39–3·05)	0·97
Severe	1·57 (0·52–4·90)	0·43
Mild	1·62 (0·78–3·42)	0·21
Moderate	2·17 (1·14–4·28)	0·027
Severe	2·40 (1·14–4·96)	0·027
Mild	1·71 (0·80–3·80)	0·18
Moderate	1·78 (0·87–3·81)	0·13
Severe	1·39 (0·54–3·46)	0·48
Mild	1·84 (1·03–3·29)	0·047
Moderate	2·87 (1·75–4·66)	0·0001
Severe	3·05 (1·75–5·14)	0·0003
Mild	1·15 (0·66–1·94)	0·62
Moderate	1·61 (1·02–2·52)	0·049
Severe	1·78 (1·04–2·93)	0·040
Mild	1·14 (0·73–1·73)	0·57
Moderate	1·60 (1·11–2·27)	0·016
Severe	1·73 (1·12–2·55)	0·016
Mild	0·97 (0·51–1·83)	0·93
Moderate	1·22 (0·71–2·13)	0·49
Severe	1·81 (0·98–3·20)	0·060
Mild	3·37 (0·88–18·55)	0·12
Moderate	3·09 (0·86–16·86)	0·13
Severe	4·99 (1·28–25·76)	0·040
Mild	1·86 (0·99–3·54)	0·064
Moderate	2·05 (1·16–3·74)	0·021
Severe	2·01 (1·01–3·93)	0·053
Mild	2·68 (1·00–8·25)	0·072
Moderate	1·60 (0·60–5·16)	0·39
Severe	2·10 (0·66–7·12)	0·22
Mild	1·20 (0·52–2·83)	0·67
Moderate	2·05 (1·03–4·31)	0·055
Severe	2·27 (1·03–5·02)	0·051

Figure 4: **Adjusted logistic regression models for the relationship between adolescent dysmenorrhoea status and chronic pain sites at age 26 years (N=1157)**
Dysmenorrhoea status is stratified by mild, moderate, or severe in reference to no dysmenorrhoea. RR=relative risk. *Dose–response trend p<0·05.

dysmenorrhoea. Severe dysmenorrhoea increased the risk of thigh pain (4·99 [1·28–25·76]) and probably also hip pain (1·81 [0·98–3·20]; figure 4). A dose–response trend was evident for nine (53%) of 17 sites (headache, jaw, neck, wrist or hand, upper and lower back, abdomen, hip, and ankle or foot; figure 4; appendix p 17). Dysmenorrhoea was not associated with the number of chronic pain sites at age 26 years (1·00 [0·92–1·08]; appendix p 9).

Discussion

Moderate or severe dysmenorrhoea was common in our sample (691 [59·7%] of 1157 participants). A dose–response relationship between dysmenorrhoea severity in adolescence and chronic pain in adulthood was found for overall pain and pain at most body sites. However, there was no relationship between dysmenorrhoea severity and the number of pain sites.

The high prevalence of dysmenorrhoea in our cohort supports previous research[3] and is an important finding, highlighting that most young menstruators had period pain severe enough that it could not be ignored or interrupted their daily life. Recent evidence suggests that young people do not receive adequate support to manage their pain.[23] Menstrual stigma remains pervasive in society, resulting in little menstrual education,[24] a reluctance to discuss menstrual issues with caregivers, and concealment and endurance of pain.[23]

This high prevalence of moderate and severe dysmenorrhoea is concerning, considering that we also found a 65% increased risk of future chronic pain in people with moderate dysmenorrhoea in adolescence and 76% with severe dysmenorrhoea in adolescence. Our findings support those from a previous meta-analysis, which estimated 2·5 times the odds of co-occurring chronic pain in women with dysmenorrhoea compared with those without.[14] Our slightly lower odds of chronic pain (1·98 for moderate and 2·18 for severe dysmenorrhoea) might be explained by younger age or exclusion of children with pre-menarche pain conditions. The dose–response trend we observed (with a 25% greater chronic pain risk per unit increase in dysmenorrhoea severity) is similar to that found by Li and colleagues[15] (a 22% increase per unit in a prospective study of adult women in the USA).

Dysmenorrhoea was associated with most chronic pain sites, particularly abdominal and lower back pain. This is perhaps unsurprising considering that dysmenorrhoea is a common symptom of pathologies associated with pelvic pain, such as endometriosis and adenomyosis. The pelvis was not listed in our pain questionnaire; therefore, it is possible that pelvic pain cases were conflated with abdominal or lower back pain. Previous studies have revealed that dysmenorrhoea co-occurs with chronic pelvic pain in 81% of cases[25] and that 50% of individuals with severe dysmenorrhoea developed chronic pelvic pain over a 12-year period.[17]

Dysmenorrhoea was also associated with pain in the head, back, knee, wrist, hand, ankle, foot, thigh, and hip. These findings cannot be explained by predominantly regional phenomena such as viscero-visceral and viscero-somatic referral. Thus, it is likely that central mechanisms (including sensitisation) are involved—this is supported by evidence that has shown widespread sensory sensitivity and brain structural and functional differences in adults with dysmenorrhoea compared with healthy adults.[10,11,26] However, it is interesting that we did not observe a relationship with the number of pain sites, given that fibromyalgia—characterised by widespread myofascial pain—appears to be a condition predominant in individuals assigned female at birth.[27] It is possible that this pain phenotype takes longer to develop. The potential role of psychosocial factors in chronicity of pain must also be considered, for example, pain-related cognitions, cultural norms and experiences that determine health and health-care seeking behaviour.

Psychological variables are associated with central pain processing[28] and risk of chronic pain.[29] Research also shows that anxiety is more common in adolescents with dysmenorrhoea (44%) than without (10%),[30] which could be explained by the substantial time each month lived in anticipation or endurance of pain without effective management, coupled with concerns regarding a potential underlying pathology. As expected, we found that dysmenorrhoea was associated with incident higher anxiety and depression scores. However, these factors explained a small proportion of the association between dysmenorrhoea and chronic pain, suggesting that other unknown mechanisms predominate.

Although we did not find OCP use to be a significant interaction term, we found that chronic pain risk was higher in those with dysmenorrhoea who began OCPs later in adolescence. This could reflect that the successful treatment of dysmenorrhoea with OCPs reduces the risk of transition to chronic pain in the future. However, the sparse information available regarding OCP use in ALSPAC—including primary indication, contraceptive history, duration, and discontinuation—prohibits a confident interpretation of this finding.

This study benefited from a large sample size and nationally representative data spanning 26 years, which provided statistical power and a wide range of important variables, including numerous pain sites, confounders, potential mediators or interaction terms, and temporality. Biases from missing data were comprehensively addressed. Furthermore, missing outcome data did not correlate with dysmenorrhoea status, suggesting that there was minimal risk of attrition bias.

We also acknowledge some limitations of this study. Although we aimed to ensure that participants were free from chronic pain at baseline, childhood pain was reported by parents, which introduces a small risk of misclassification. There is also a misclassification risk for chronic pain as some respondents might have

experienced prolonged pain for anywhere between 2 and 3 months, hindered by the questionnaire wording. Additionally, it is possible that those describing chronic abdominal or back pain were describing symptoms of dysmenorrhoea. Also, we did not have data on medical treatment or self-management of dysmenorrhoea, visceral pain conditions, and chronic widespread pain in adulthood.

At present, most young people with dysmenorrhoea do not present to health care; therefore, improving menstrual literacy and increasing the confidence to self-manage symptoms are priorities. It is important for interactions with medical professionals to be validating and supportive, with further investigation offered where indicated (eg, pain unresponsive to pharmacological treatments).

A growing body of research reveals negative attitudes towards and reduced uptake of hormonal contraceptives among adolescents.[31] Non-pharmacological strategies might therefore be increasingly important. The role of psychological interventions for menstrual pain should be explored, considering that such strategies have shown benefit for other forms of paediatric chronic pain.[32] Of course, discussion of potential psychological interventions should be carefully approached to avoid perpetuation of the dismissive narrative that pain is imagined.

It is also important to improve the early identification and management of adolescent dysmenorrhoea, and to understand potential mechanisms that underlie the relationship with chronic pain. Pain neuroscience and genetic epidemiology approaches (such as Mendelian randomisation and biological pathway analysis of derived genes) could aid in this.

Contributors

All authors conceptualised the study and designed the methodology. RR-M curated, analysed, and visualised the data, drafted the manuscript, and was guarantor for the study. OBP-N, KS, SD, EC, LC, MF, MN, GCS, KZ, and KV reviewed and edited the manuscript. KV was responsible for funding acquisition and project administration. This research is the collaborative work of all listed authors. RR-M, OBP-N, KS, KV, and GCS had full access to the individual-level data in the study and all authors had access to group-level data. RR-M and OBP-N verified the data. All authors had final responsibility for the decision to submit for publication.

Declaration of interests

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Data sharing

ALSPAC data can only be accessed by those authorised by the University of Bristol (Bristol, UK) following an application process. Any derived variables created in this study have been provided to ALSPAC. The study protocol and code written for the analysis will remain available at https://osf.io/nhvye/ indefinitely.

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