

Brief reflection of my 6-week research project

I completed my six-week research project at the Institute of Sports Exercise and Health, under the supervision of Dr Jo Blodgett. My time at the ISEH involved various activities, traditional research components as well as less conventional experiences, which provided me with a wide range of opportunities to learn, explore and grow.

My research project was focused on exploring the association between the emotional wellbeing of 16-year-old girls and the menstrual symptoms that they experience across their life. To do so, I extracted data from a large ongoing cohort study – the 1970 British Cohort Study – and utilised R to clean, filter and analyse the data. The end-product, which is still in the works, is the publication of my first research paper.

The completion of the research project involved a variety of activities. Specific to the write-up of my paper, I learned how to use R to carry out data analysis with the support of my supervisor and two PhD students. My growing confidence in coding, an area I was very inexperienced with at the start of the research project, is one of the many valuable skills I have had the opportunity to develop. Other skills include the ability to extract relevant information from literature and to identify gaps and limitations to guide my research and shape its value, to organise my resources and time so that I meet my deadlines and work effectively, to explore different strategies to ensure clear communication with my supervisor and be able to translate my findings to an expert and non-expert audience. In my last week at the ISEH, I gave a short presentation about the topic of my research project, sharing the process I had undergone and the findings I had already come across. This was a good opportunity for me to go out of my comfort zone and practice communicating my research to a non-expert audience.

Alongside my research, I also had the opportunity to attend seminars and departmental lunches, to listen and learn about the research of PhD students in similar and completely different fields, and to observe and participate as a test subject in research studies being carried out at the ISEH.

All in all, my six-week research project was an enriching and enjoyable experience. Not only did I take considerable value from the insights of my own research (discussed in detail in the research paper below), but also from the overall immersion in an unfamiliar and professional environment. I am thankful for this opportunity and all the connections and friendships I have cultivated. From learning about the different projects being carried out at the ISEH to getting involved in an environment that welcomed me with open arms, taught me various transferrable skills, provided me a sense of purpose, and inspired me to explore a career path I hadn't seriously considered before.

Associations between emotional wellbeing in adolescence and menstrual symptoms across life: longitudinal evidence from a British birth cohort study

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Abstract

Purpose

This study aimed to investigate the association between psychological distress (PD) in adolescence and the menstrual symptoms experienced across women's life.

Methods

Up to 2584 females from the 1970 British Cohort Study, a birth cohort study of individuals born within 1 week in 1970, were included. PD at age 16 was measured with the 12-item General Health Questionnaire; three categories were considered: no/mild PD (<11), moderate PD (11-15), and severe PD (>15). Five menstrual health symptoms were self-reported at ages 16, 30 and 42 years. Binomial logistic regressions, with multiple imputation by chained events, examined associations between PD at age 16 and each individual symptom.

Results

Prevalence of individual menstrual symptoms ranged from 3% to 61%; pain (61%), painful period (10%) and heavy period (33%) were most prevalent at age 16, 30 and 42 respectively. At age 16, those with severe PD were more likely to experience depression (2.92(95% CI:2.31,3.70)), irritability (1.67(1.33,2.11)), menstrual pain (1.34(1.01,1.80)), and headaches (1.29(1.02,1.63)). A weak association was found between severe PD and pre-menstrual tension at age 30 (1.72(1.01,2.83)). At age 42, those with severe PD were more likely to experience pre-menstrual tension (1.89(1.46,2.44)), painful periods (1.64(1.27,2.11)), and heavy periods (1.28(1.00,1.62)).

Discussion

Menstruating females with poorer emotional wellbeing at adolescence have an increased risk of menstrual symptoms at age 16 and in midlife. Our findings suggest the potential for early-life psychological interventions to improve women's menstrual experiences across their reproductive years, and the myriad of ways it affects women's and society's quality of life.

1.Introduction

Poor menstrual experiences are more than coincidental inconveniences; they reoccur in traceable patterns and are one of the primary factors challenging the quality of life of girls and women every day [1-3]. Over 14% of girls are absent from education for a day or two each month, which can amount to a total of 140 million hours of absence a year [4]. Not only does menstrual discomfort disrupt female students' ability to learn [1, 5, 6], but it can also be detrimental to women's performance in the workplace. For example, evidence from the United States suggests that 13% to 51% of women are absent from work at least once throughout their career and, more concerning, 5-14% are absent regularly as a result of their menstrual symptoms [7, 8]. On top of the destabilizing emotional effects, menstrual discomfort may be an indicator of underlying health conditions, such as pelvic disease [9], and certain menstrual abnormalities could be causing or exacerbating other physical issues, including iron-deficiency anemia [1, 3]. The increased demand for medical care to address the adverse menstrual conditions, and the numerous side effects that come with it, have led to rising medical costs [10, 11], and may aggravate supply chain challenges in the healthcare industry [10, 11].

Positive menstrual health experiences are an integral determinant of women's quality of life. When compromised, they significantly reduce their physical and mental wellbeing. Studies have shown that psychological factors can further exacerbate the discomfort caused by menstruation [12, 13]. Yet, existing evidence has primarily examined the contribution of medically diagnosed cases of depression and anxiety on menstrual pain [12-16]. Despite the diverse experiences of menstrual symptoms, with up to 200 symptoms reported [17], previous evidence has focused nearly entirely on dysmenorrhea – defined as painful menstrual-related abdominal cramps [1]. To better understand and reduce the consequences of negative menstrual experiences, it is necessary to investigate the prevalence and factors associated with a range of commonly reported menstrual symptoms – including but not limited to dysmenorrhea.

Due to small sample sizes and a scarcity of longitudinal data, present evidence regarding the relationship between emotional and menstrual wellbeing remains inconclusive [1, 3, 12, 15]. The majority of research is cross-sectional in nature and involves sample sizes below 500 participants [5, 13, 15, 16, 18, 19], limiting the generalizability of findings. Without repeated prospective measurement of menstrual symptoms across the reproductive years, it is difficult to comprehend the intricate nature of the association between emotional and menstrual health and identify reasonable timings and targets for intervention.

Therefore, there is a critical need to examine longitudinal associations between emotional wellbeing and a myriad of menstrual symptoms across the reproductive life course. We aimed to investigate the association between psychological distress (PD) in adolescence (age 16) and menstrual symptoms experienced across women's life (ages 16, 30 and 42).

2.Methods

2.1 Study sample

The 1970 British Cohort Study (BCS70) follows the lives of a large cohort, initially comprising of 17,198 individuals, born in England, Scotland or Wales between the 5th and 11th of April in 1970. To date, the cohort has been surveyed at birth and in ten subsequent waves at ages 5, 10, 16, 26, 30, 34, 38, 42, 46 and 51 [20]. The present analysis involves data collected from self-reported questionnaires or interviews at ages 16, 30, and 42 [20].

2.2 Exposure – psychological distress (age 16 years)

The 12-item General Health Questionnaire (GHQ-12) is a validated screening tool used to measure the PD of participants. Participants were asked to report how frequently they experienced twelve unique emotional patterns in a 4-point scale (see **Supplemental Table 1** for list). negatively worded items were scored such that "less than usual"= 0 and "much more than usual"= 3, and reverse scoring was used for positively worded items. All items were summed to provide a total score (range:

0-36), where a higher score is indicative of severe levels of PD. The established cut-off point of 11 was used to categorize participants with no/mild PD (<11). Due to a high prevalence of those experiencing significant PD (≥ 11) [21], a further cut-point was applied based on the median compromised score to indicate the severity of PD. Therefore, the three categories were: no/mild PD (GHQ<11), moderate PD (GHQ 11-15) and severe PD (GHQ>15).

2.3 Outcome – menstrual symptoms (ages 16, 30, 42 years)

Age 16: Participants self-reported whether they had started their menstrual period and if they experience unpleasant symptoms before or during their menstrual period. If the response was ‘yes’ to both questions, participants were asked to specify which unpleasant symptoms they experience from a list of five binary items: pain, depression, irritability, headaches, and cramps.

Age 30: Participants were asked in a 60-minute interview if they have ‘ever had or been told that [they] had a problem with [their] periods’ since they were 16 years old and, if so, to specify as many as five menstrual problems (binary yes/no): heavy periods, painful periods, bleeding at irregular intervals, bleeding between periods and pre-menstrual tension.

Age 42: Participants were asked in a 60-minute interview if they had experienced one or more of a list of fourteen menstrual and gynecological problems, from which five were relevant to menstrual symptoms: heavy periods, painful periods, bleeding at irregular intervals, bleeding between periods, and premenstrual tension. All symptoms were coded as binary variables (yes/no).

2.4 Covariates

Covariates were measured at age 16 and chosen a priori based on associations with PD and menstrual health symptoms [3, 22-26]. The *age of menarche* and *regularity of menstrual cycle* were reported in a maternal health questionnaire where mother of participant was asked “at what age did your teenage girl have her first menstrual period?” and “have her periods been regular in the past year?”. With regards to *difficulty sleeping* and *appetite problems*, the parents of participant were asked if their teenager struggles with each condition in separate questions; answer was provided in a Y/N format. To quantify the subject’s level of physical activity, a count-based physical activity score

was derived from binary parent-reported participation in (1) running/jogging, (2) keep fit exercises, (3) walks, (4) other forms of exercise (0-4, where 4 indicates participation in all 4 activities). Lastly, the socioeconomic position of the participant was categorized using the Registrar General's Social Classification of the father's occupational class: I unskilled, II partly skilled, III skilled manual IV managerial/technical V professional [27].

2.5 Statistical analyses

Chi-square tests and one-way ANOVAS were used to assess differences in covariates across no/mild, moderate, and severe PD groups. Binomial logistic regression models were used to measure associations between PD at age 16 (ref: no/mild PD) and each menstrual symptom at ages 16, 30 and 42. At age 16, outcomes included: (1) pain (2) depression (3) irritability (4) headaches and (5) cramps. At age 30 and 42, outcomes included: (1) heavy period (2) painful period (3) irregular bleeding (4) bleeding between periods and (5) pre-menstrual tension. For each outcome, two models were constructed: (1) unadjusted and (2) adjusted for all covariates, described above. In the latter, we used multiple imputations chained events to impute missing covariate data under a missing-at-random assumption. The estimates across 35 imputed datasets were combined using Rubin's rule [28]. The missing data ranged from 19.6% (appetite problems) to 33.5% (level of physical activity).

3. Results

Of 17 196 individuals who participated in the BCS70 initial data collection at birth, 11 622 (68%) participated in the age 16 wave, of which 5 800 were female. After the exclusion of incomplete GHQ-12 data, due largely to a teacher strike, the study sample narrowed to 2 831 (49%) [29]. To be eligible for inclusion in the study sample, individuals had to have complete data on the GHQ-12 at age 16 and data on 1+ menstrual symptom at ages 16, 30 or 42. Therefore, the final sample size ranged from 2584 to 2134; see **Figure 1** for derivation of each individual sample size across all three ages.

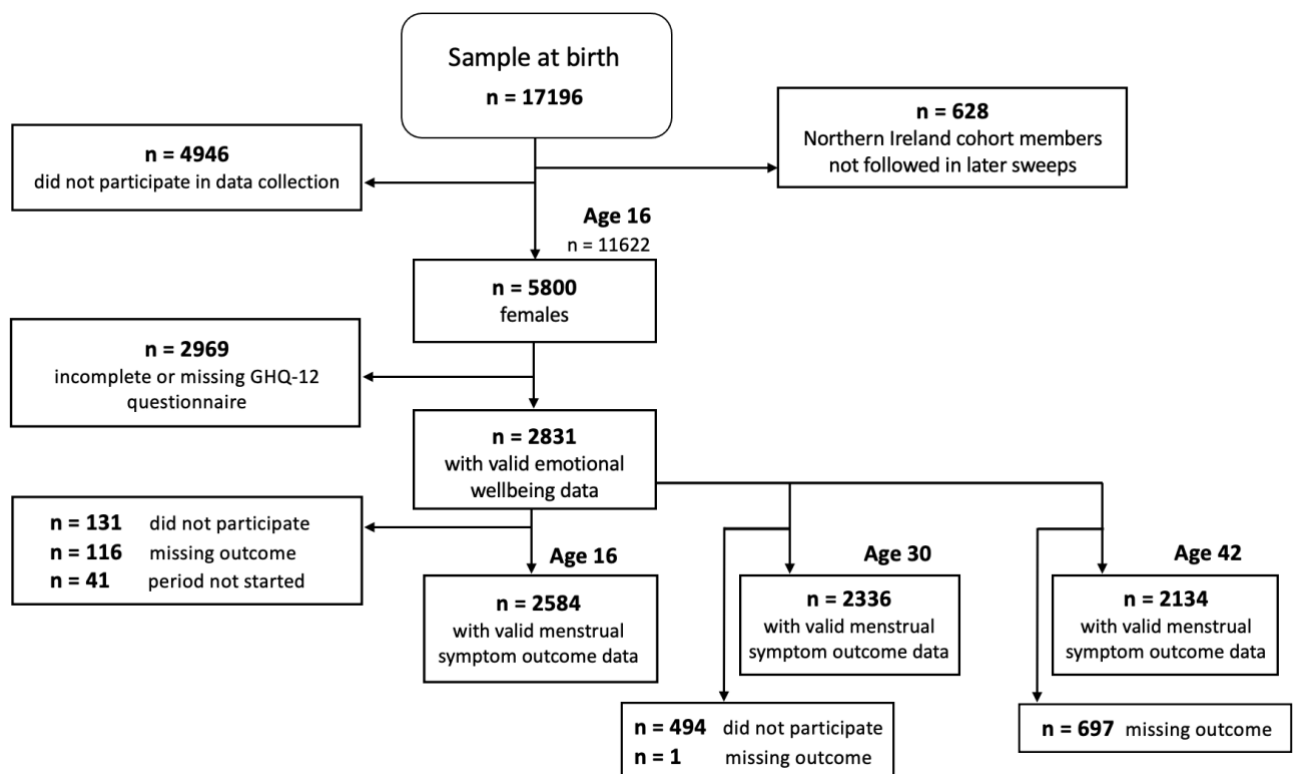


Figure 1 – Sample flowchart

Table 1 provides the prevalence of symptoms at each age. At age 16, 78% of participants reported experiencing unpleasant menstrual symptoms. Individual prevalence of symptoms ranged from 28 to 61%, where *pain* was the most reported source of discomfort (n=1579, 61%), followed by *irritability* (n=991, 38%). At age 30, the prevalence of menstrual symptoms was substantially lower (range: 3-10%) where *painful period* was most common (n=226, 10%). At age 42, the prevalence ranged from 10 to 33%, where *heavy period* was the most prevalent (n=707, 33%), followed by *painful period* (n=559, 26%) and *pre-menstrual tension* (n=548, 26%).

Table 1 - Descriptive characteristics of prevalence of menstrual symptoms at ages 16, 30 and 42

age of survey	menstrual symptom	prevalence
age 16 (n=2584)*	pain	1579 (61%)
	cramps	1062 (41%)
	irritability	991 (38%)
	headaches	722 (28%)
	depression	726 (28%)
age 30 (n=2336)	painful period	226 (10%)
	heavy period	185 (8%)
	irregular bleeding	164 (7%)
	pre-menstrual tension	90 (4%)
	bleeding between periods	70 (3%)
age 42 (n=2134)	heavy period	707 (33%)
	painful period	559 (26%)
	pre-menstrual tension	548 (26%)
	irregular bleeding	285 (13%)
	bleeding between periods	215 (10%)

*78% of participants at age 16 reported to experience unpleasant symptoms and were thus asked to specify which of the five symptoms they experienced. The former was not explored as an outcome due to its high prevalence.

Table 2 describes sample characteristics across the three PD groups. Briefly, participants with severe or moderate PD were more likely to have difficulties sleeping (12.7% vs 8.9% vs 4.8%; $p < 0.001$) and appetite problems (10.0% vs 6.4% vs 5.6%; $p = 0.01$) compared to those with no/mild PD. those with severe PD had a younger mean age of menarche than those with moderate PD and no/mild PD (12.56 ± 1.36 vs 12.69 ± 1.36 vs 12.72 ± 1.35 ; $p = 0.05$). There were also noticeable differences within the father's occupation amongst the three PD groups ($p = 0.03$). Participants with moderate or severe PD were more likely to have a father in a managerial/technical or professional occupational class (44.7%, 39.5% and 35.6% for moderate PD, severe PD, and no/mild PD respectively). The prevalence of experiencing irregular menstrual cycles and the level of participants' physical activeness did not differ by PD group.

Table 2 - Descriptive characteristics of cohort study (n=2584) at age 16

	psychological distress (PD)			p-value
	no/mild PD n = 1700	moderate PD n = 628	severe PD n = 503	
<i>age of menarche (mean, SD)</i>	12.72, 1.35	12.69, 1.36	12.56, 1.36	0.05
<i>irregular cycle (Y, %)</i>	255, 19.1%	113, 23.1%	82, 21.1%	0.45
<i>difficulty sleeping (Y, %)</i>	67, 4.8%	44, 8.9%	51, 12.7%	<0.001
<i>appetite problems (Y, %)</i>	77, 5.6%	32, 6.4%	40, 10.0%	0.01
<i>physically active (0-4, %)</i>				0.70
0 (very inactive)	57, 4.9%	14, 3.5%	18, 5.5%	
1	578, 50.1%	190, 47.0%	156, 48.0%	
2	368, 31.9%	140, 34.7%	105, 32.3%	
3	119, 10.3%	48, 11.9%	33, 10.2%	
4 (very active)	31, 2.7%	12, 3.0%	13, 4.0%	
<i>father's occupation (type, %)</i>				0.03
unskilled	31, 2.5%	11, 2.4%	13, 3.6%	
partly skilled	121, 9.7%	35, 7.6%	26, 7.1%	
skilled manual	485, 38.9%	147, 32.1%	126, 34.6%	
skilled non-manual	140, 11.2%	52, 11.4%	42, 11.5%	
managerial/technical	355, 28.5%	155, 33.8%	118, 32.4%	
professional	88, 7.1%	50, 10.9%	26, 7.1%	

*p-values indicate differences between groups using chi-square or one-way ANOVAs.

Menstrual symptoms at age 16:

High levels of PD at age 16 was associated with greater risk of having unpleasant menstrual symptoms (see **Figure 2**), with strongest associations for depression and irritability. For example, in unadjusted models, those with moderate or severe PD had 1.77 (95% CI: 1.41, 2.22) and 2.92 (2.31, 3.70) times higher odds of depression during menstruation than those with no/mild PD. Similarly, those with moderate or severe PD had higher odds of irritability than those with no/mild PD (1.50 (1.20, 1.86) and 1.67 (1.33, 2.11) respectively). Those with severe PD had 1.29 (1.02, 1.63) greater odds of having period-related headaches, although there was no increased risk for those with moderate PD (p>0.10). Associations did not change after adjustment for relevant covariates. Finally, there was no evidence of an association between PD and cramps (all p>0.10), with some evidence to suggest that those with severe PD were more likely to have period-related pain (1.35 (1.00,1.83) in adjusted).

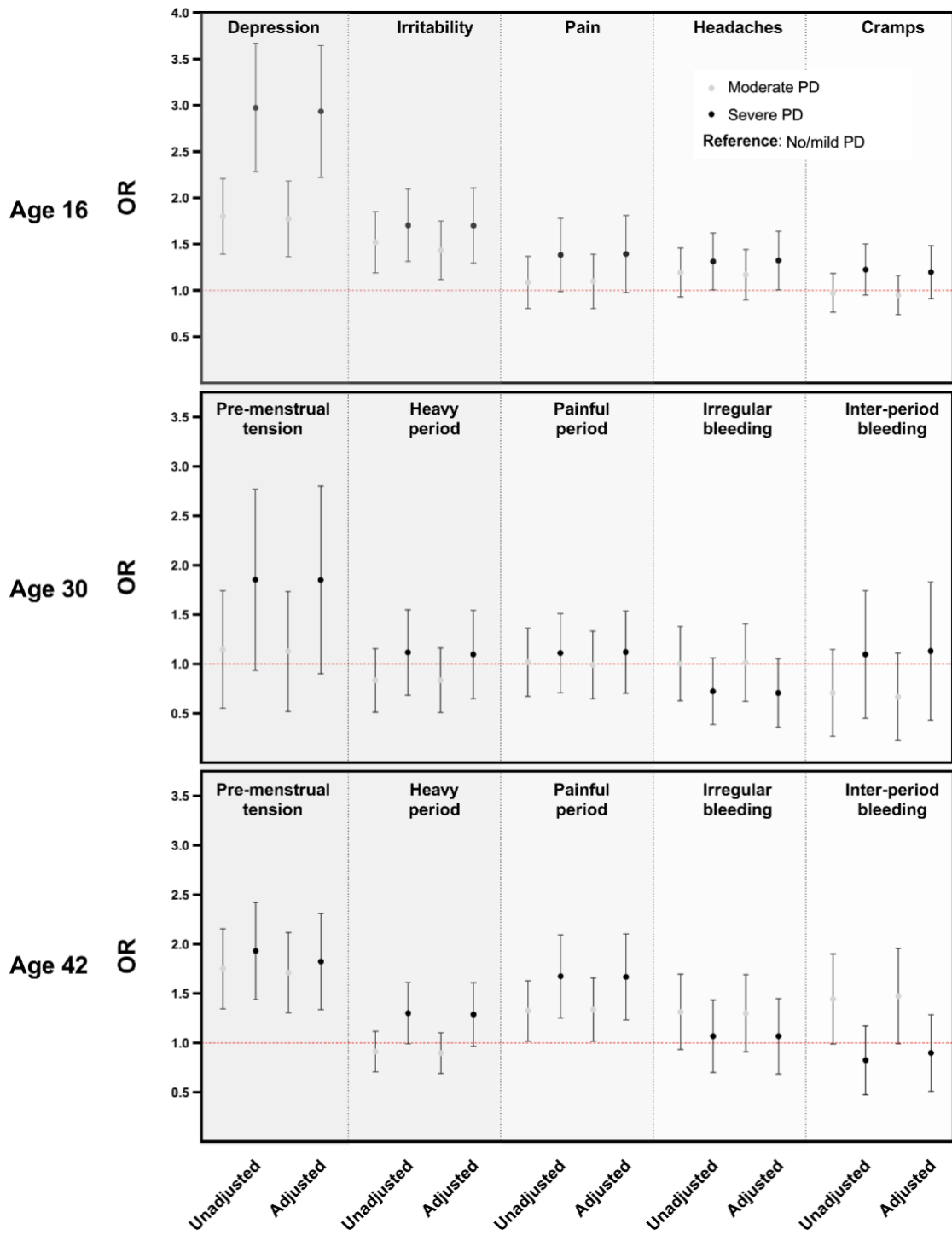


Figure 2 – Forest plot portraying menstrual symptoms present at ages 16, 30 and 42 with respect to PD group [OR= odds ratio]

Menstrual symptoms at age 30:

No associations were observed between PD at age 16 and heavy period, painful period, irregular bleeding, and bleeding between periods at age 30 (all $p > 0.05$). Those with severe PD had 1.72 (1.01, 2.83; unadjusted model) higher odds of experiencing pre-menstrual tension than those with no/mild PD, with very little change after adjustment for relevant covariates (1.69 (0.99, 2.87)). No increased risk was observed in those with moderate PD ($p > 0.10$).

Menstrual symptoms at age 42:

Significant PD at age 16 was associated with greater risk of having unpleasant menstrual symptoms at age 42, with strongest associations for pre-menstrual tension and painful period. In unadjusted models (ref: no/mild PD), those with moderate and severe PD had 1.72 (1.36, 2.17) and 1.89 (1.46, 2.44) times higher odds of having pre-menstrual tension and 1.30 (1.03, 1.64) and 1.64 (1.27, 2.11) greater odds of having painful periods, respectively. Associations did not change after adjustment for covariates. Those with moderate PD had 1.40 (1.01, 1.92) higher odds of bleeding between periods, when sex-adjusted, but no association was observed in those with severe PD (0.78 (0.50, 1.19)). Those with severe PD in adolescence were more likely to experienced heavy periods at age 42 (sex adjusted: 1.28 (1.00, 1.62), covariate-adjusted: (1.26 (0.98, 1.62))). Finally, there was no evidence of an association between PD and irregular bleeding.

4. Discussion

In a large birth cohort study of girls followed across the life course, we found that significant levels of psychological distress at age 16 was associated with a higher risk of experiencing a range of adverse menstrual symptoms at adolescence and during middle adulthood. Associations were strongest for mood-related symptoms, including depression and irritability at age 16 and pre-menstrual tension at age 30 and 42. These findings highlight the need for serious consideration of mental health as both an acute and long-term indicator, contributor, and potential determinant, of women's menstrual

experiences and consequently the quality of life they may enjoy – or be compromised by – in the near and far future.

The positive association between significant PD and increased risks of experiencing mood-related symptoms is consistent with previous cross-sectional research. Past studies have found that psychological disorders can exacerbate the number and severity of menstrual symptoms girls and women experience [4, 13, 22, 30]. In a cross-sectional study of 154 girls of mean age of 15.4 years, it was found that subjects with more depressive and anxious psychological symptoms experienced a greater number of unspecified menstrual symptoms [13]. A similar study that integrated a short follow-up component of three annual surveying visits found comparable results [30]. Interview-based evidence from a larger sample (n=1831 women, age range: 18-50 years) reported an association between increased severity of psychological distress and six domains directly related to pre-menstrual syndrome. This association was strongest with anxiety/mood menstrual-related symptoms (odds ratio: 2.75(1.92,3.94)) [22]. In this study, younger women of age 18-30 years were shown to report symptoms more frequently than women aged above 30-50 years; they were 1.35(0.93,1.97) times more likely to report anxiety/mood changes [22]. This is consistent with the results found in the present study where associations were seen to be strongest for mood symptoms reported by the age 16 group. Distinctive to these cross-sectional studies, our findings provide novel insights into the potential long-term consequences of poor emotional wellbeing, by demonstrating sustained associations into midlife.

It remains unclear whether the association between PD and menstrual health is purely correlational or if there is an element of causality involved. There is some evidence in literature to support the plausibility of the latter. Prostaglandins are important compounds with hormone-like effects that help regulate pain perception and bodily inflammation [31]. Release and circulation of prostaglandins must be maintained in equilibrium to ensure that physiological processes such as uterine

contractions during menstruation are carried out effectively. Experience of intense emotions can lead to the release of stress hormones (i.e., cortisol and adrenaline), which stimulate the production of prostaglandins [32]. Reoccurring incidences of psychological distress can lead to destabilizing levels of prostaglandins circulating the body, which could interfere with the body's mediation of abdominal/uterine inflammation and sensitivity to pain [4, 31]. Consequently, those with severe levels of PD may therefore explore a greater intensity of unpleasant menstrual symptoms. Further research is required to formally test if prostaglandins and/or stress hormones mediate this association.

Significant levels of PD was more strongly associated with mood-related symptoms (i.e., depression, irritability, and pre-menstrual tension) when compared to somatic menstrual outcomes (i.e., heavy period and irregular bleeding). This was observed at ages 16, 30 and 42, yet particularly evident at 16 and 42. It is plausible that more severe PD can increase one's sensitivity to discomfort such that one is more likely to recognize and report unpleasant menstrual symptoms [33]. Since the experience of mood-related symptoms can be argued to be of more subjective nature than their somatic counterparts [4], it is plausible that the effect is heightened for the former. It was notable that strong associations were observed for menstrual symptom outcomes at both age 16 and age 42. It is possible that severe PD at adolescence is sustained into midlife or could predispose the participants to greater emotional sensitivity, such that emotional imbalances are more easily triggered during sensitive time points. As women begin to approach perimenopause and experience hormonal fluctuations - particularly in the production of luteinizing hormone and follicle stimulating hormone-, this can often result in increased irregularity of menstrual cycles and variability in symptoms [34]. This transition brings uncertainty which can intensify negative emotional responses and shift one's perception and sensitivity in the reporting of unpleasant menstrual symptoms.

At age 30, severe PD was weakly associated with a single outcome, pre-menstrual tension. Around this age, women are typically in their childbearing years; therefore, it is possible that disrupted

menstrual cycles due to pregnancy or hormonal contraceptives could contribute to a scarcity of negative menstrual symptoms. This is consistent with the decrease in the prevalence of unpleasant menstrual symptoms reported (see **Table 1**) and could be because the unpleasant symptoms ceased to be experienced temporarily, they are less prevalent as menstrual experiences have stabilized, or they are unnoticed and thus under-reported.

Key strengths of this study include the large age-homogenous sample size, ascertainment of multiple symptoms and the longitudinal study design. The majority of previous studies is limited to samples below five hundred participants and informed by a single time point, which makes it difficult to contextualize their timeframe of relevance and to understand long term consequences of these associations. The present findings help to fill this gap as they are informed by a cohort of over 2000 individuals with menstrual symptom data from over a 25-year period (from age 16 to 42).

There were few limitations in the present study that are equally important to recognize. The binary nature of menstrual health questions is unable to capture the severity of symptoms, as well as the extent to which they affect the participant's ability to carry out daily life activities. This information would be of value since it could help to understand which symptoms require most attention to improve women's menstrual experiences and their quality of life. Another limitation is that ascertainment of menstrual symptoms was not consistent across the three time points. Although reflective of secular understandings of menstrual symptoms at data collection timepoints, these differences limit the ability to infer age-dependent patterns about specific symptoms. Finally, the sample size was reduced due to missing or incomplete GHQ and menstrual health data as well as overall attrition in the study (see **Figure 1**). However, compared to prior research, a relatively large sample was still assembled such that the loss of data did not come as a significant shortcoming but rather as an area that could be further strengthened.

This paper provides novel insights into short and long-term associations between emotional health and the odds of experiencing negative menstrual symptoms, that can guide future research and ultimately support the improvement of menstrual health experiences for girls and women worldwide. To our knowledge, it is the first study to examine long-term associations between menstrual and emotional health; the age-homogeneity of the sample removes any age-related differences that are typically observed in menstrual symptom prevalence. Results from this study encourage the consideration of early-life psychological interventions as a vehicle to reduce unpleasant menstrual outcomes in later stages of female lives. Poor emotional health at age 16 was found to be strongly associated with unpleasant menstrual outcomes at adolescence as well as midlife years. Early-life psychological interventions have the potential to not only improve girls' wellbeing but may also produce a positive long-term effect on the quality of their menstrual experiences throughout their lives. This may better their quality of life in numerous ways, and in turn, society as a whole.

References

1. Bajalan, Z., et al., *Mental health and primary dysmenorrhea: a systematic review*. Journal of Psychosomatic Obstetrics & Gynecology, 2019. **40**(3): p. 185-194.
2. Guimarães, I. and A.M. Póvoa, *Primary Dysmenorrhea: Assessment and Treatment*. Rev Bras Ginecol Obstet, 2020. **42**(8): p. 501-507.
3. Ju, H., M. Jones, and G. Mishra, *The prevalence and risk factors of dysmenorrhea*. Epidemiol Rev, 2014. **36**: p. 104-13.
4. Pakpour, A.H., et al., *Depression, anxiety, stress, and dysmenorrhea: a protocol for a systematic review*. Syst Rev, 2020. **9**(1): p. 65.
5. Hailemeskel, S., A. Demissie, and N. Assefa, *Primary dysmenorrhea magnitude, associated risk factors, and its effect on academic performance: evidence from female university students in Ethiopia*. International Journal of Women's Health, 2016. **8**: p. 489-496.
6. Jeon, G.E., N.H. Cha, and S.R. Sok, *Factors Influencing the Dysmenorrhea among Korean Adolescents in Middle School*. J Phys Ther Sci, 2014. **26**(9): p. 1337-43.
7. Proctor, M. and C. Farquhar, *Diagnosis and management of dysmenorrhoea*. BMJ, 2006. **332**(7550): p. 1134-1138.
8. Weissman, A.M., et al., *The natural history of primary dysmenorrhoea: a longitudinal study*. Bjog, 2004. **111**(4): p. 345-52.
9. Critchley, H.O.D., et al., *Menstruation: science and society*. Am J Obstet Gynecol, 2020. **223**(5): p. 624-664.
10. Schoep, M.E., et al., *The impact of menstrual symptoms on everyday life: a survey among 42,879 women*. Am J Obstet Gynecol, 2019. **220**(6): p. 569.e1-569.e7.
11. Poon, Y.R., et al., *A global overview of healthcare workers' turnover intention amid COVID-19 pandemic: a systematic review with future directions*. Hum Resour Health, 2022. **20**(1): p. 70.
12. Wang, L., et al., *Stress and dysmenorrhoea: a population based prospective study*. Occup Environ Med, 2004. **61**(12): p. 1021-6.
13. Dorn, L.D., et al., *Menstrual symptoms in adolescent girls: association with smoking, depressive symptoms, and anxiety*. J Adolesc Health, 2009. **44**(3): p. 237-43.
14. Rodrigues, A.C., et al., *[Dysmenorrhea in adolescents and young adults: prevalence, related factors and limitations in daily living]*. Acta Med Port, 2011. **24 Suppl 2**: p. 383-88; quiz 389-92.
15. Ziba Raisi, D., *53: EVALUATE THE EFFECT OF PERCEIVED STRESS ON DYSMENORRHEA*. BMJ Open, 2017. **7**(Suppl 1): p. bmjopen-2016-015415.53.
16. Gagua, T., et al., *Assessment of anxiety and depression in adolescents with primary dysmenorrhea: a case-control study*. J Pediatr Adolesc Gynecol, 2013. **26**(6): p. 350-4.
17. Campagne, D.M. and G. Campagne, *The premenstrual syndrome revisited*. European Journal of Obstetrics & Gynecology and Reproductive Biology, 2007. **130**(1): p. 4-17.
18. Verma, K. and G.C. Baniya, *Prevalence of Depression, Anxiety and Quality of Life in Adolescent Girls with Dysmenorrhoea in a Remote Area of Western Rajasthan*. J Obstet Gynaecol India, 2022. **72**(Suppl 1): p. 281-289.
19. Pitanguí, A.C., et al., *Menstruation disturbances: prevalence, characteristics, and effects on the activities of daily living among adolescent girls from Brazil*. J Pediatr Adolesc Gynecol, 2013. **26**(3): p. 148-52.
20. Sullivan, A., et al., *Cohort Profile Update: The 1970 British Cohort Study (BCS70)*. International Journal of Epidemiology, 2022. **52**(3): p. e179-e186.
21. Baksheev, G.N., et al., *Validity of the 12-item General Health Questionnaire (GHQ-12) in detecting depressive and anxiety disorders among high school students*. Psychiatry Research, 2011. **187**(1): p. 291-296.
22. AlQuaiz, A., et al., *Dietary, Psychological and Lifestyle Factors Associated with Premenstrual Symptoms*. Int J Womens Health, 2022. **14**: p. 1709-1722.

23. Armour, M., et al., *Exercise for dysmenorrhoea*. Cochrane Database Syst Rev, 2019. **9**(9): p. Cd004142.
24. Cholbeigi, E., et al., *Are health promoting lifestyles associated with pain intensity and menstrual distress among Iranian adolescent girls?* BMC Pediatr, 2022. **22**(1): p. 574.
25. De Sanctis, V., et al., *Primary Dysmenorrhea in Adolescents: Prevalence, Impact and Recent Knowledge*. *Pediatr Endocrinol Rev*, 2015. **13**(2): p. 512-20.
26. Sharma, P., et al., *A cross-sectional study on prevalence of menstrual problems, lifestyle, mental health, and PCOS awareness among rural and urban population of Punjab, India*. *J Psychosom Obstet Gynaecol*, 2022. **43**(3): p. 349-358.
27. Galobardes, B., J. Lynch, and G.D. Smith, *Measuring socioeconomic position in health research*. *Br Med Bull*, 2007. **81-82**: p. 21-37.
28. Rubin, D.B., *Flexible Imputation of Missing Data, Second Edition*. 2nd ed. 2018: Chapman and Hall/CRC. 34.
29. Sullivan, A., et al., *Cohort Profile Update: The 1970 British Cohort Study (BCS70)*. *International Journal of Epidemiology*, 2023. **52**(3): p. e179-e186.
30. Beal, S.J., et al., *Characterizing the longitudinal relations between depressive and menstrual symptoms in adolescent girls*. *Psychosom Med*, 2014. **76**(7): p. 547-54.
31. Smith, R., *The Role of Prostaglandins in Dysmenorrhea and Menorrhagia*. 2018. p. 75-88.
32. García-Bueno, B., et al., *Stress Mediators Regulate Brain Prostaglandin Synthesis and Peroxisome Proliferator-Activated Receptor- γ Activation after Stress in Rats*. *Endocrinology*, 2008. **149**(4): p. 1969-1978.
33. Evans, S., et al., *Pain catastrophizing, but not mental health or social support, is associated with menstrual pain severity in women with dysmenorrhea: A cross-sectional survey*. *Psychol Health Med*, 2022. **27**(6): p. 1410-1420.
34. Hoyt, L.T. and A.M. Falconi, *Puberty and perimenopause: reproductive transitions and their implications for women's health*. *Soc Sci Med*, 2015. **132**: p. 103-12.

Supplemental Table 1 – GHQ-12 items used to measure the PD of participants.

item number	statement
1	able to concentrate on what I am doing
2	capable of making decisions about things
3	able to face up to my problems
4	reasonably happy all things considered
5	able to enjoy normal daily activities
6	felt I am playing a useful part in things
7	lost much sleep over worry
8	felt constantly under strain
9	felt I couldn't overcome my difficulties
10	been feeling unhappy and depressed
11	been losing confidence in myself
12	thinking of myself as a worthless person

Supplemental Table 2 - Menstrual symptoms present at ages 16, 30 and 42 when considering the levels of PD of participants

Ref: no/mild PD

		depression (n=726)			irritability (n=991)			pain (n=1579)			headaches (n=722)			cramps (n=1062)		
— Age 16 —		OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Model 1 (unadjusted)	no/mild PD															
	moderate PD	1.77	1.41, 2.22	0.00	1.50	1.20, 1.86	0.00	1.06	0.82, 1.38	0.64	1.17	0.94, 1.47	0.16	0.96	0.77, 1.19	0.68
	severe PD	2.92	2.31, 3.69	0.00	1.67	1.33, 2.11	0.00	1.34	1.01, 1.80	0.05	1.29	1.02, 1.63	0.04	1.20	0.96, 1.51	0.11
Model 2 (adjusted)	no/mild PD															
	moderate PD	1.74	1.38, 2.20	0.00	1.41	1.13, 1.76	0.00	1.07	0.82, 1.40	0.61	1.15	0.91, 1.45	0.23	0.93	0.75, 1.17	0.54
	severe PD	2.88	2.25, 3.67	0.00	1.67	1.31, 2.12	0.00	1.35	1.00, 1.83	0.05	1.30	1.02, 1.65	0.04	1.18	0.92, 1.49	0.19
— Age 30 —		pre-menstrual tension (n=90)			heavy period (n=185)			painful period (n=226)			irregular bleeding (n=164)			bleeding between periods (n=70)		
		OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Model 1 (unadjusted)	no/mild PD															
	moderate PD	1.06	0.60, 1.78	0.84	0.80	0.53, 1.17	0.26	0.98	0.69, 1.38	0.93	0.96	0.65, 1.40	0.84	0.63	0.31, 1.18	0.17
	severe PD	1.72	1.01, 2.83	0.04	1.07	0.71, 1.57	0.74	1.07	0.73, 1.53	0.72	0.68	0.41, 1.08	0.12	0.99	0.51, 1.79	0.97
Model 2 (adjusted)	no/mild PD															
	moderate PD	1.02	0.58, 1.78	0.94	0.79	0.53, 1.18	0.26	0.95	0.67, 1.35	0.79	0.96	0.65, 1.43	0.84	0.57	0.28, 1.15	0.12
	severe PD	1.69	0.99, 2.87	0.05	1.04	0.68, 1.57	0.86	1.07	0.73, 1.56	0.73	0.65	0.39, 1.08	0.09	0.99	0.51, 1.89	0.97
— Age 42 —		pre-menstrual tension (n=548)			heavy period (n=707)			painful period (n=559)			irregular bleeding (n=285)			bleeding between periods (n=215)		
		OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value	OR	95% CI	p-value
Model 1 (unadjusted)	no/mild PD															
	moderate PD	1.72	1.36, 2.17	0.00	0.90	0.71, 1.12	0.34	1.30	1.03, 1.64	0.03	1.28	0.95, 1.71	0.10	1.40	1.01, 1.92	0.04
	severe PD	1.89	1.46, 2.44	0.00	1.28	1.00, 1.62	0.05	1.64	1.27, 2.11	0.00	1.03	0.72, 1.45	0.86	0.78	0.50, 1.19	0.27
Model 2 (adjusted)	no/mild PD															
	moderate PD	1.68	1.32, 2.13	0.00	0.88	0.70, 1.11	0.28	1.31	1.03, 1.67	0.03	1.26	0.93, 1.71	0.13	1.42	1.02, 1.98	0.04
	severe PD	1.78	1.36, 2.33	0.00	1.26	0.98, 1.62	0.07	1.63	1.25, 2.12	0.00	1.02	0.71, 1.47	0.89	0.84	0.54, 1.31	0.44