DATA NOTE



REVISED Menstrual cycle features in mothers and daughters in

the Avon Longitudinal Study of Parents and Children (ALSPAC)

[version 2; peer review: 1 approved, 1 approved with

reservations]

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Abstract

Problematic menstrual cycle features, including irregular periods, severe pain, heavy bleeding, absence of periods, frequent or infrequent cycles, and premenstrual symptoms, are experienced by high proportions of females and can have substantial impacts on their health and well-being. However, research aimed at identifying causes and risk factors associated with such menstrual cycle features is sparse and limited. This data note describes prospective, longitudinal data collected in a UK birth cohort, the Avon Longitudinal Study of Parents and Children (ALSPAC), on menstrual cycle features, which can be utilised to address the research gaps in this area. Data were collected in both mothers (G0) and index daughters (G1) across 21 and 20 timepoints respectively between 1991 and 2020. This data note details all available variables, proposes methods to derive comparable variables across data collection timepoints, and discusses important limitations specific to each menstrual cycle feature. Also, the data note identifies broader issues for researchers to consider when utilising the menstrual cycle feature data, such as hormonal contraception, pregnancy, breastfeeding, and menopause, as well as missing data and misclassification.

Keywords

ALSPAC, menstruation, menstrual cycle, cohort, longitudinal

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view

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Any reports and responses or comments on the article can be found at the end of the article.



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REVISED Amendments from Version 1

The second version of this manuscript considers the useful and constructive comments from the reviewer. We have made minor changes, including correcting citations and abbreviations, adding information about the location and time of data collection in the Abstract, and adding a clarification to Figure 2 in a footnote. We have also added some text in the Introduction, highlighting the differences in previous research between high-income and low-and-middle-income countries, and the Further Considerations, discussing the possibility of participants interpreting questions differently.

Any further responses from the reviewers can be found at the end of the article

Introduction

Problematic menstrual cycle features have been reported to affect high proportions of adolescent girls, women, and people who menstruate. Previous research had indicated that 11-46% of females experience irregular periods1-6, 42-95% dysmenorrhea (menstrual pain)^{1-4,7}, 3-13% amenorrhea (absence of periods)^{5,8,9}, 37-78% premenstrual syndrome (PMS)^{1,4}, 1-19% frequent or infrequent cycles (less than 24 or more than 38 days)^{1,8,10}, and 4-58% heavy menstrual bleeding (HMB)^{4,8,11}. Whilst most of these estimates come from research conducted in high income countries (HICs), the research conducted in low and middle income countries (LMICs) indicates similar prevalence ranges. However, the estimates do vary considerably, possible due to factors such as age, the setting and population under study, measurement and definition of the feature, and contextual attitudes towards menstruation. Such features may be related to other conditions, such as endometriosis, polycystic ovary syndrome (PCOS), or fibroids; however, many are idiopathic^{10,12,13}. These relatively common problematic menstrual cycle features have been associated with several adverse physical and mental health outcomes, including infertility, anaemia, pain sensitivity, sleep disturbances, anxiety, and depression^{7,8,14}. Research has also demonstrated a substantial impact on social wellbeing; negatively impacting school, work, relationships, exercise, and health-related quality of life^{8,15}.

Despite this, there has been relatively limited research to understand the causes and risk factors associated with problematic menstrual cycle features. Previous research has highlighted ethnicity¹⁶, family history^{1,2,7,12}, smoking^{6,12}, high or low BMI^{2,6,7}, earlier age at menarche^{2,6,7,12}, presence of other menstrual problems^{1,7,12}, and low socioeconomic position^{1,2,6,14,16,17} (SEP) as possible risk factors. However, much of the evidence comes from cross-sectional studies and research in clinical populations or university students. This means that many findings may be unrepresentative of broader populations, reports of menstrual cycle features may be hindered by recall bias, and there is a limited understanding of whether associations reflect causal effects or otherwise (e.g., confounding) and the direction of any causal effect. Further research is therefore necessary to understand the burden, life course risk factors, causes, and consequences of problematic menstrual cycle features, and provide insights into the causes

and consequences of within and between woman variation in menstrual features. This would require greater use of prospective, longitudinal data on the menstrual cycle as well as factors that may be confounders, mediators, or moderators to enhance the accuracy of reporting and enable exploration of causal relationships.

Whilst there are limited resources that provide such rich menstrual cycle data, the Avon Longitudinal Study of Parents and Children (ALSPAC) is a longitudinal birth cohort with repeated measures data on features of the menstrual cycle across two generations of females, as well as data on a wide range of physical, psychological, social, and genetic factors. This data note aims to promote the use of the detailed menstrual cycle data available in ALSPAC to address these research needs. We describe the menstrual cycle data collected in the mothers (G0) and index daughters (G1) enrolled in ALSPAC, including repeated measures on menstrual cycle features throughout puberty and into early adulthood from questionnaire and clinic assessments.

Methods

ALSPAC

ALSPAC is a longitudinal birth cohort where pregnant women resident in Avon, UK with expected dates of delivery between 1st April 1991 and 31st December 1992 were invited to take part in the study. The initial number of pregnancies enrolled was 14,541, resulting in 13,988 children who were alive at 1 year of age.

When the oldest children were approximately 7 years of age, an attempt was made to bolster the initial sample with eligible cases who had failed to join the study originally. The total sample size for analyses using any data collected after the age of 7 is therefore 15,447 pregnancies and, of these, 14,901 children were alive at 1 year of age. There were 14,203 unique mothers initially enrolled in study but as a result of the additional phases of recruitment, 14,833 unique mothers enrolled in ALSPAC as of September 2021.

Study data gathered from participants at 22 years and onwards were collected and managed using Research Electronic Data Capture (REDCap) tools hosted at the University of Bristol¹⁸. REDCap is a secure, web-based software platform designed to support data capture for research studies.

Further details on ALSPAC have been published elsewhere^{19–21}. Please note that the study website contains details of all the data that is available through a fully searchable data dictionary and variable search tool (http://www.bristol.ac.uk/alspac/researchers/our-data/). Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees (ALEC; IRB00003312). Detailed information can be found on the study website http://www.bristol.ac.uk/alspac/researchers/research-ethics/. Implicit consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time.

This data note focuses on two samples: G0 (mothers) and G1 (daughters) who have been asked about several menstrual cycle features at multiple timepoints. The G0 sample comprises mothers who were asked to report on their menstrual cycle features from the index pregnancy to menopause. Figure 1 shows the number of G0 participants responding to questions about periods at each relevant timepoint, and whether they had experienced a recent period. The female offspring (G1) sample comprises female participants who provided information, either reported by their mother or themselves, about menstrual cycle features from age 8 to age 24. Figure 2 shows the number of respondents who had started their period up until age 21.

Mothers (G0) Data

Participants answered questions relating to menstrual cycle length, absence of periods, regularity, heaviness, pain, and PMS-related symptoms across 17 questionnaires from the index pregnancy (reporting on menstruation prior to pregnancy) up to 28 years following birth of the index child (mean age 28.6 to 57.7 years). Participants also provided data on menstrual cycle features at four clinic assessments from mean age 47.4 to 52.6 years (Table 1). Table 1 provides an overview of the ALSPAC questionnaires and clinics, participants mean age, and the relevant menstrual cycle feature variables at each timepoint, as well as contraception variables at each available timepoint.

Cycle length

In the first three questionnaires asking about cycle length (mean age 28.6, 37.8, and 40.3 years), participants were asked how many days there were from the start of one period to the start of the next one if their periods were regular. At the mean age 49.7 years questionnaire, participants were asked if their periods were regular and could select yes, alongside multiple options for the length of their cycle, or no. Similarly, at the aged 51.3 years questionnaire, participants were asked how many days there usually were between the start of one period and the start of the next and were provided with multiple categorical options, as well as an option to report that their periods were too irregular to estimate. These questions and variables are summarised in Table 2.

Amenorrhea

At the mean age 37.8- and 40.3-year questionnaires, participants who reported not having periods were asked whether this was because of pregnancy, hysterectomy, menopause, or another reason. At the aged 47.4 questionnaire, participants were asked whether they had a period in the last 12 months. Participants were also asked whether they had a period in the last 12 months at the mean aged 51.3 and 57.7 year questionnaires and all of the clinics, as well as additionally being asked whether they had a period in the last 3 months. Those who reported not having a period were subsequently asked to report the reason for this. Responses included surgery,



Figure 1. Number of G0 participants (mothers) with recent periods. 'No recent period' includes participants who reported no period in the last 12 months, no 'recent' periods, or no 'periods nowadays'.



Figure 2. Number of G1 participants (daughters) who have started periods. 'Started period' includes participants who responded yes when asked whether they had started their period yet or not at each timepoint.

Table 1. Source of G0 menstrual cycle and contraception data.

ALSPAC Source File Mean (SD) Age				G0 variable	names		
	Cycle length	Amenorrhea	Cycle regularity	Heavy/ prolonged bleeding	Pain	PMS	Contraception
d Quest 28.6 (4.86) years*	d012	d012	d011	-	-	-	
f Quest 29.2 (4.78) years	-	-	-	-	-	f036 f036a	f068 f068a
g Quest 30.0 (4.74) years	-	-	-	-	-	g036 g036a	g054 g054a g133- g141
h Quest 32.0 (4.74) years	-	-	h112	h110 h113 h115a	h111 h115b	h028 h028a	h044 h044a h098a- h098h h098j
j Quest 33.1 (4.69) years	-	-	j143	j141 j144	j142	j027 j027a	j049 j049a j113- j121
k Quest 34.0 (4.67) years	-	-	k1292	k1290 k1293 k1301	k1291 k1302	k1031 k1035	k1051 k1203-k1213

ALSPAC Source File Mean (SD) Age				G0 variable	names		
	Cycle length	Amenorrhea	Cycle regularity	Heavy/ prolonged bleeding	Pain	PMS	Contraception
l Quest 35.1 (4.62) years	-	-	13352	13350 13353	l3351	3031 3360 3370 3380 3390 3400	3051 3300- 3310
m Quest 36.1 (4.61) years	-	-	-	m4201	m4202	-	-
n Quest 37.8 (5.48) years	n1122	n1122 n1123	n1121	-	-	-	n1130 n1133
p Quest 38.3 (4.60) years	-	-	p1262	p1260 p1263	p1261	p1031 p1270- p1274 p1280- p1284	p1061 p1243- p1253
q Quest 39.3 (4.61) years	-	-	-	-	q4020	-	q4280
r Quest 40.3 (4.63) years	r2082	r2082 r2083	r2081	-	-	-	r2090 r2093 r2173- r2183
s Quest 41.4 (4.55) years	-	-	s1262	s1260 s1263	s1261 s4020	s1031 s1270- s1274 s1280- s1284	s1243-s1253 s4280
FOM1 Clinic 47.4 (4.52) years		fm1ob120 fm1ob121 fm1ob126	fm1ob130	-	-	-	fm1ob100 fm1ob101
t Quest 48.6 (4.49) years	-	t4800 t4801 t4802 t4803 t4804 t4805	t4837	t4835 t4838 t4901	t4836 t4902	t4850-t4859	t4520-t4531 t5414
u Quest 49.7 (4.52) years	u1050	-	u1050	-	-	-	u1030-u1034
FOM2 Clinic 50.3 (4.42) years		fm2ob120 fm2ob121 fm2ob126	fm2ob130	-	-	-	fm2ob100 fm2ob101
v Quest 51.3 (4.49) years	V4831	V4800 V4801 V4802 V4803 V4804 V4805 V4810	V4831 V4837	V4835 V4838 V4901	V4836 V4902	V4840 V4850- V4859	V4550-V4565
FOM3 Clinic 51.6 (4.47) years		fm3ob120 fm3ob121 fm3ob126	fm3ob130	-	-	-	fm3ob100 fm3ob101
FOM4 Clinic 52.6 (4.42) years		fm4ob120 fm4ob121 fm4ob126	fm4ob130	-	-	-	fm4ob100 fm4ob101
Y Quest 57.7 (4.48) years	_	Y5070 Y5080 Y5081 Y5082 Y5083 Y5084 Y5085 Y5100	-	-	-	_	Y5000-Y5014

*12 weeks' gestation

Question	28.6 years	37.8 years	40.3 years	49.7 years	51.3 years
		Original variable	s		
If regular, how many days were	e there from the s	start of one perio	od to the start of	the next one?	
Mean (SD)	27.54 (3.85)	25.90 (6.36)	25.73 (6.57)	-	-
< 15 days*	107 (1.16)	419 (7.24)	388 (7.46)	-	-
15–20 days*	50 (0.54)	47 (0.81)	45 (0.87)	-	-
21–25 days*	1218 (13.15)	873 (15.08)	831 (15.98)	-	-
26–30 days*	7072 (76.35)	4103 (70.89)	3689 (70.96)	-	-
31–35 days*	747 (8.07)	322 (5.56)	226 (4.35)	-	-
36–40 days*	42 (0.45)	16 (0.28)	9 (0.17)	-	-
> 40 days*	26 (0.28)	8 (0.14)	11 (0.21)	-	-
Are your periods regular?					
Yes, every 23 days or less	-	-	-	283 (10.98)	-
Yes, between 24 and 35 days	-	-	-	1420 (55.10)	-
Yes, more than every 35 days	-	-	-	86 (3.34)	-
No	-	-	-	788 (30.58)	-
In the years before your last pe the start of the next period?	eriod, how many	days do you usua	ally have betwee	n the start of on	e period and
Less than 21 days	-	-	-	-	329 (11.14)
21–25 days	-	-	-	-	594 (20.12)
26–31 days	-	-	-	-	1066 (36.11)
32–39 days	-	-	-	-	161 (5.45)
40–50 days	-	-	-	-	78 (2.64)
More than 50 days	-	-	-	-	96 (3.25)
Too irregular to estimate	-	-	-	-	628 (21.27)
		Derived variable	S		
Normal (24–38 days)	8246 (89.03)	4846 (83.72)	4331 (83.30)	-	-
Frequent (<24 days)	978 (10.56)	926 (16.00)	852 (16.39)	-	_
Infrequent (>38 days)	38 (0.41)	16 (0.28)	16 (0.31)	-	-

Table 2. Original and derived G0 cycle length variables (N (%)).

*Continuous responses recoded.

ablation or resection, chemotherapy or radiation therapy, pregnancy or breastfeeding, menopause, various methods of contraception, and other reasons. Table 3 provides a summary of these questions and responses. Moreover, as mentioned above, participants were asked to report the number of days from the start of one period to the start of the next in three questionnaires (mean age 28.6, 37.8, and 40.3 years). These variables may also be informative regarding amenorrhea if participants have reported long cycle lengths (e.g., 84 days or 3 months between two periods).

Cycle regularity

Participants were asked whether their periods were regular or not in three of the questionnaires (mean age 28.6, 37.8, and 40.3 years) and were also asked whether their periods were very, moderately, mildly, or not at all irregular in eight of the questionnaires (mean age 32.0, 33.1, 34.0, 35.1, 38.3, 41.4, 48.6, and 51.3 years). In the four clinics (mean age 47.4, 50.3, 51.6, and 52.6 years) and mean age 49.7 years questionnaire, participants were asked about the regularity or length of their menstrual cycle and were able to report that

Table 3. Original and derived G0 amenorrhea variables (N (%)).

Question	28.6 years	37.8 years	40.3 years	47.4 years clinic	48.6 years	50.3 years clinic	51.3 years	51.6 years clinic	52.6 years clinic	57.7 years
			(Original v	ariables					
If regular, how ma	ny days wer	re there fr	om the st	art of one	e period to	the start	of the ne	xt one?		
Mean (SD)	27.54 (3.85)	25.90 (6.36)	25.73 (6.57)	-	-	-	-	-	-	-
< 15 days*	107 (1.16)	419 (7.24)	388 (7.46)	-	-	-	-	-	-	-
15–20 days*	50 (0.54)	47 (0.81)	45 (0.87)	-	-	-	-	-	-	-
21–25 days*	1218 (13.15)	873 (15.08)	831 (15.98)	-	-	-	-	-	-	-
26–30 days*	7072 (76.35)	4103 (70.89)	3689 (70.96)	-	-	-	-	-	-	-
31–35 days*	747 (8.07)	322 (5.56)	226 (4.35)	-	-	-	-	-	-	-
36-40 days*	42 (0.45)	16 (0.28)	9 (0.17)	-	-	-	-	-	-	-
> 40 days*	26 (0.28)	8 (0.14)	11 (0.21)	-	-	-	-	-	-	-
If you have no peri	ods now, is	this beca	use of:							
Pregnant	-	92 (12.37)	49 (4.79)	-	-	-	-	-	-	-
Hysterectomy	-	183 (24.60)	282 (27.54)	-	-	-	-	-	-	-
Menopausal	-	79 (10.62)	213 (20.80)	-	-	-	-	-	-	-
Other reason	-	363 (48.79)	467 (45.61)	-	-	-	-	-	-	-
Don't know	-	27 (3.63)	13 (1.27)	-	-	-	-	-	-	-
In the last 12 mon	ths, have yo	u had a p	eriod or m	nenstrual	bleeding?					
Yes	-	-	-	3470 (69.15)	2669 (64.13)	1671 (56.26)	2206 (46.69)	1454 (46.57)	1175 (38.73)	571 (11.87)
No	-	-	-	1548 (30.85)	1493 (35.87)	1299 (43.74)	2519 (53.31)	1668 (53.43)	1859 (61.27)	4239 (88.13)
In the last 3 month	ns, have you	ı had a pe	riod or me	enstrual b	leeding?					
Yes	-	-	-	3149 (90.93)	-	1398 (64.48)	1855 (83.75)	1209 (49.57)	971 (82.64)	406 (71.86)
No	-	-	-	314 (9.07)	-	770 (35.52)	360 (16.25)	1230 (50.43)	204 (17.36)	159 (28.14)

Question	28.6 years	37.8 years	40.3 years	47.4 years clinic	48.6 years	50.3 years clinic	51.3 years	51.6 years clinic	52.6 years clinic	57.7 years
			(Original v	ariables					
Reason why period	ls stopped									
Hysterectomy	-	-	-	339 (21.68)	-	199 (15.81)	-	219 (12.81)	233 (12.53)	-
Ablation or resection	-	-	-	24 (1.53)	-	-	-	-	-	-
Chemotherapy or radiation therapy	-	-	-	38 (2.43)	-	32 (2.54)	-	43 (2.51)	36 (1.94)	-
Menopause	-	-	-	763 (48.79)	-	751 (59.65)	-	1081 (63.22)	1237 (66.54)	-
Contraceptive: hormonal coil	-	-	-	256 (16.37)	-	-	-	243 (14.21)	203 (10.92)	-
Contraceptive: injection	-	-	-	62 (3.96)	-	-	-	-	-	-
Contraceptive: implant	-	-	-	5 (0.32)	-	-	-	-	-	-
Contraceptive: pill	-	-	-	59 (3.77)	-	-	-	-	-	-
Contraceptive: other	-	-	-	6 (0.38)		-		-	-	
Other medical reason	-	-	-	12 (0.77)	-	277 (22.00)	-	124 (7.25)	150 (8.07)	-
Were your periods	stopped by	:								
Surgery	-	-	-	-	273 (20.15)	-	-	-	-	-
Chemotherapy or radiation therapy	-	-	-	-	48 (3.54)	-	-	-	-	-
Pregnancy or breastfeeding	-	-	-	-	6 (0.44)	-	-	-	-	-
No obvious reason / menopause	-	-	-	-	791 (58.38)	-	-	-	-	-
Other reason	-	-	-	-	237 (17.49)	-	-	-	-	-
Were your periods	stopped by									
Surgery	-	-	-	-	-	-	325 (14.39)	-	-	-
Chemotherapy or radiation therapy	-	-	-	-	-	-	63 (2.79)	-	-	-
Pregnancy or breastfeeding	-	-	-	-	-	-	-	-	-	-
No obvious reason / menopause	-	-	-	-	-	-	1494 (66.16)	-	-	-
Contraception	-	-	-	-	-	-	372 (16.47)	-	-	-

Question	28.6 years	37.8 years	40.3 years	47.4 years clinic	48.6 years	50.3 years clinic	51.3 years	51.6 years clinic	52.6 years clinic	57.7 years
			(Original v	ariables					
Were your periods	stopped by:	:								
Surgery	-	-	-	-	-	-	-	-	-	410 (10.30)
Chemotherapy or radiation therapy	-	-	-	-	-	-	-	-	-	66 (1.66)
Pregnancy or breastfeeding	-	-	-	-	-	-	-	-	-	<5
Menopause	-	-	-	-	-	-	-	-	-	3134 (78.76)
Contraception	-	-	-	-	-	-	-	-	-	257 (6.46)
Other reason	-	-	-	-	-	-	-	-	-	109 (2.74)
			I	Derived v	ariables					
Period in last 3 months	9262 (NA)	5788 (NA)	5198 (NA)	3149 (62.84)	2669 (64.13)	1398 (47.93)	1855 (39.18)	1209 (39.01)	971 (32.00)	406 (8.45)
No period in last 3 months	<5	<5	<5	1862 (37.16)	1493 (35.87)	1519 (52.07)	2879 (60.82)	1890 (60.99)	2063 (68.00)	4398 (91.55)

Cell counts below 5 have been replaced with <5, and this may include 0.

their cycle was not regular or too irregular to estimate their cycle length. Table 4 gives an overview of these variables.

Heavy or prolonged bleeding

G0 participants were asked about heavy bleeding and prolonged bleeding separately. Participants were asked whether their periods were very, moderately, mildly, or not at all heavy in eight questionnaires (mean age 32.0, 33.1, 34.0, 35.1, 38.3, 41.4, 48.6, and 51.3 years). In addition, participants were asked whether they had had a dilation and curettage (D&C)/scrape due to heavy bleeding in five questionnaires (mean age 32.0, 34.0, 36.1, 48.6, and 51.3 years). In terms of prolonged bleeding, participants were asked to report the number of days that bleeding usually lasts for in eight questionnaires (mean age 32.0, 33.1, 34.0, 35.1, 38.3, 41.4, 48.6, and 51.3 years). These questions are summarised in Table 5.

Menstrual pain

Participants were asked whether their periods were very, moderately, mildly, or not at all painful in eight questionnaires (mean age 32.0, 33.1, 34.0, 35.1, 38.3, 41.4, 48.6, and 51.3 years) (Table 6). Also, respondents were asked whether they had had a D&C/scrape due to painful periods in five questionnaires (mean age 32.0, 34.0, 36.1, 48.6, and 51.3 years) and whether they had used any medicines due to painful periods in two questionnaires (mean age 39.3 and 41.4 years).

Premenstrual symptoms

In eight questionnaires, participants were asked if they had any recent 'problems with their period' (mean age 29.2, 30.0, 32.0, 33.1, 34.0, 35.1, 38.3, and 41.1 years). Additionally, at the mean age 34.0 years questionnaire, participants were asked whether they had 'pre-menstrual tension' in the past year, and at the mean age 51.3 years questionnaire, participants were asked whether they had 'particular problems' in the days before or during their periods. Furthermore, in the latter five questionnaires (mean age 35.1, 38.3, 41.4, 48.6, and 51.3 years), those who reported having experienced problems with their periods were also asked which symptoms they experienced (very fatigued, irritable, depressed, anxious, or other) and whether each of these symptoms was experienced before their periods, during, or both. Table 7 summarises these questions and variables.

Daughters (G1) Data

Participants who had started their periods reported on menstrual regularity, heaviness, pain, cycle length, absence of periods, and PMS-related symptoms at multiple timepoints ranging from average 8 to 24 years. This included nine 'puberty' questionnaires, where mothers reported on their daughter's menstrual cycle at age 8.1, 9.6, 10.6, 11.6, and 13.1 years before participants reported on their own menstrual cycle at age 14.6, 15.5, 16, and 17 years. Mothers also responded on behalf of their daughters at three 'child-based' questionnaires at age 13.1, 13.8, and 16.5 years. Participants

Table 4. Original and derived G0 cycle regularity variables (N (%)).

Question	28.6 years	32.0 years	33.1 years	34.0 years	35.1 years	37.8 years	38.3 years	40.3 years	41.4 years	47.4 years clinic	48.6 years	49.7 years	50.3 years clinic	51.3 years	51.6 years clinic	52.6 years clinic
							Original	variable	S							
In the year befo	ire this preg	nancy, w	ould you	say youı	periods	were regi	ular?									
Yes	9880 (80.36)	I	I		ı	ı.	I	I	I	ı		,	I	ı	I	
No	2415 (19.64)	I	I	I	I	I	I	I	I	I	I	I	I	I	I	I
How would you	describe you	ur recent	: periods:	Irregula	1.2											
Very	I	737 (8.63)	732 (8.49)	I	665 (8.79)	I	I	I	I	I	I	I	I	I	I	ı
Moderately		670 (7.85)	708 (8.21)	I.	721 (9.53)	I	I	I	I	ı	1	I	I	I	I	
Mildly	ı	1315 (15.40)	1404 (16.28)	1	1319 (17.43)	ı	I	I	I	ı			I	I	ı	
Not at all	1	5815 (68.12)	5782 (67.03)	I	4862 (64.25)	I.	I	I	I	ı	ı	I.	I	I	I	ı
Are your period:	s irregular?															
Very	1	1	1	931 (11.40)	ı	ı	872 (12.09)	1	770 (12.87)	1	671 (22.28)	,	1	1115 (26.20)	1	
Moderately	ı	ı	I	778 (9.52)	I	ı	790 (10.95)	I	706 (11.80)	ı	454 (15.07)	ı	I	857 (20.14)	ı	
Mildly	1	1	1	1376 (16.84)	1	,	1254 (17.39)	ı	1153 (19.27)	1	570 (18.92)		I	823 (19.34)	ı	
Not at all	I	I	I	5084 (62.24)	I	I	4297 (59.57)	I	3355 (56.07)	I	1317 (43.73)	I	I	1461 (34.33)	I	I
Would you say y	/our periods	are regu	ilar nowa	Idays?												
Yes	ı	1	I	I	I	6019 (83.31)	I	5393 (81.65)	I	ı	ı	ı	I	I	I	
No	1	1	1	1	ı	1206 (16.69)	I	1212 (18.35)	I	1		,	1	I	1	
Periods are regu	ular															
Yes, every 28–30 days		ı	ı	ı	ı	ī	ı	ı	ı	1793 (51.78)	1	ı	626 (29.81)	ı	489 (23.68)	352 (29.98)
Yes, < every 28 days	ı	ı	ı	ı	ı	ı	I	I	I	343 (9.90)	1	ı	198 (9.43)	I	140 (6.78)	102 (8.69)
Yes, > every 30 days	ı	ı	ı	ı	I	I	I	I	I	111 (3.21)	ı	ı	68 (3.24)	I	70 (3.39)	32 (2.73)

52.6 years clinic		688 (58.60)		I	I	ı	I		ı	I	ı	I	I	I	I		486 (41.40)	688 (58.60)
51.6 years clinic		1366 (66.15)		I	ı	ı	I		ı	I	,	I	ı.	ı	ı		699 (33.85)	1366 (66.15)
51.3 years		I		I	ı	I	ı		329 (11.14)	594 (20.12)	1066 (36.11)	161 (5.45)	78 (2.64)	96 (3.25)	628 (21.27)		2284 (53.67)	1972 (46.33)
50.3 years clinic		1208 (57.52)		ı	ı.	I	I.	t period?	ı	I	,	I	ı.	I	ı		892 (42.48)	1208 (57.52)
49.7 years		ı		283 (10.98)	1420 (55.10)	86 (3.34)	788 (30.58)	of the nex	ı	I	ı.	ı	T	ı	ı		1789 (69.42)	788 (30.58)
48.6 years		I		ı	I	I	I	he start o	ı	I	I	I	I	I	ı		1887 (62.65)	1125 (37.35)
47.4 years clinic		1216 (35.11)		ı		ı	ı	period and t	ı	ı		ı		ı	ı		2247 (64.89)	1216 (35.11)
41.4 years	S	I		I	I	I	I	rt of one	ı	I	T	I	I	I	I	10	4508 (75.33)	1476 (24.67)
40.3 years	variable	I		I	I	I	I	n the stai	ı	I	T	I	I	I	I	variable	5393 (81.65)	1212 (18.35)
38.3 years	Original	I		I	I	I	I	e betweei	I	I	I	I	I	I	I	Derived	5551 (76.96)	1662 (23.04
37.8 years		I		I	ı	I	I	ually have	I.	I	ı	I	I	I	ı		6019 (83.31)	1206 (16.69)
35.1 years		I		I	ı	I	I	an not op	I	I	1	I	I	I	ı		6181 (81.68)	1386 (18.32)
34.0 years		I		I	ı.	I	ı.	ny days d	ı	I	,	I	ı.	I	ı		6460 (79.08)	1709 (20.92)
33.1 years		I		I	T	I	I	how mai	I	I	ı	I	I	I	I		7186 (83.31)	1440 (16.69)
32.0 years		ı		I	ı	ı	I	st period,	ı	I	ı.	ı	I.	ı	ı		7130 (83.52)	1407 (16.48)
28.6 years		I	s regular?	I	I	I	I	ore your las	ı	I	T	I	I	I	I		9880 (80.36)	2415 (19.64)
Question		No	Are your period:	Yes, every 23 days or less	Yes, between 24 and 35 days	Yes, more than every 35 days	No	In the years bef	Less than 21 days	21–25 days	26–31 days	32–39 days	40–50 days	More than 50 days	Too irregular to estimate		Regular	Irregular

Question	32.0 years	33.1 years	34.0 years	35.1 years	36.1 years	38.3 years	41.4 years	48.6 years	51.3 years
			Ori	ginal varia	bles				
How heavy are you	r periods?								
Very	1321 (15.47)	1412 (16.35)	1408 (17.05)	1448 (18.48)	-	1305 (17.95)	1127 (18.65)	765 (24.56)	1293 (29.81)
Moderately	4430 (51.89)	4522 (52.35)	4342 (52.59)	4049 (51.68)	-	3712 (51.06)	2961 (48.99)	1293 (41.51)	1537 (35.44)
Mildly	2001 (23.44)	1884 (21.81)	1810 (21.92)	1775 (22.66)	-	1583 (21.77)	1361 (22.52)	710 (22.79)	925 (21.33)
Not at all	785 (9.20)	820 (9.49)	696 (8.43)	562 (7.17)	-	670 (9.22)	595 (9.84)	347 (11.14)	582 (13.42)
How many days do	es bleedin	g usually la	ast?						
Mean (SD)	5.26 (2.01)	5.26 (1.89)	5.23 (1.86)	5.22 (1.85)	-	5.17 (1.85)	5.19 (2.14)	5.31 (2.35)	5.77 (3.14)
< 3 days*	129 (1.52)	157 (1.85)	165 (20.04)	143 (1.85)	-	188 (2.72)	191 (3.33)	132 (4.36)	139 (3.34)
3 days	654 (7.72)	673 (7.95)	655 (8.12)	705 (9.13)	-	65 (9.43)	564 (9.83)	318 (10.50)	370 (8.89)
4 days	1793 (21.16)	1732 (20.46)	1708 (21.16)	1601 (20.74)	-	1455 (21.08)	1176 (20.50)	563 (18.59)	645 (15.50)
5 days	3188 (37.62)	3073 (36.30)	2900 (35.93)	2737 (35.46)	-	2376 (34.42)	1979 (34.50)	962 (31.76)	1338 (32.16)
6 days	1276 (15.06)	1331 (15.72)	1227 (15.20)	1174 (15.21)	-	976 (14.14)	796 (13.88)	402 (13.27)	560 (13.46)
7 days	997 (11.77)	1055 (12.46)	972 (12.04)	942 (12.20)	-	909 (13.17)	698 (12.17)	433 (14.30)	661 (15.89)
8 days	179 (2.11)	182 (2.15)	181 (2.24)	181 (2.34)	-	139 (2.01)	124 (2.16)	65 (2.15)	106 (2.55)
9 days	55 (0.65)	63 (0.74)	63 (0.78)	58 (0.75)	-	51 (0.74)	41 (0.71)	28 (0.92)	48 (1.15)
< 9 days*	203 (2.40)	199 (2.35)	200 (2.48)	178 (2.31)	-	158 (2.29)	167 (2.91)	126 (4.16)	294 (7.07)
Have you ever had	a dilatatio	n and cure	ttage (D&C	C / scrape)?	If yes, wa	s this beca	use of: hea	vy periods	?
Yes	172 (1.84)	-	62 (28.84)	-	73 (52.52)	-	-	116 (77.33)	146 (74.11)
No	9179 (98.16)	-	153 (71.16)	-	66 (47.48)	-	-	34 (22.67)	51 (25.89)
			De	rived varia	bles				
Binary Heavy Bleeding**									
Heavy	5751 (67.37)	5934 (68.70)	5750 (69.65)	5497 (70.17)	-	5017 (69.01)	4088 (67.64)	2058 (66.07)	2830 (65.25)
Not heavy	2786 (32.63)	2704 (31.30)	2506 (30.35)	2337 (29.83)	-	2253 (30.99)	1956 (32.36)	1057 (33.93)	1507 (34.75)

Table 5. Original and derived G0 heavy and/or prolonged bleeding variables (N (%)).

Question	32.0 years	33.1 years	34.0 years	35.1 years	36.1 years	38.3 years	41.4 years	48.6 years	51.3 years
			De	rived varia	bles				
Binary Prolonged B	leeding								
More than 8 days	258 (3.04)	262 (3.10)	263 (3.26)	236 (3.06)	-	209 (3.03)	208 (3.63)	154 (5.08)	342 (8.22)
8 days or less	8216 (96.96)	8203 (96.90)	7808 (96.74)	7483 (96.94)	-	6694 (96.97)	5528 (96.37)	2875 (94.92)	3819 (91.78)
Binary Heavy or Pr	olonged Bl	eeding							
Heavy or prolonged bleeding	5780 (68.15)	5961 (69.67)	5781 (70.65)	5527 (71.03)	-	5037 (70.42)	4117 (69.54)	2083 (67.65)	2868 (67.74)
Neither heavy nor prolonged bleeding	2701 (31.85)	2595 (30.33)	2402 (29.35)	2254 (28.97)	-	2116 (29.58)	1803 (30.46)	996 (32.35)	1366 (32.26)

*Continuous responses recoded.

**Heavy bleeding is defined as reporting 'very' or 'moderately' heavy periods, whereas not heavy is defined as reporting periods that are 'mildly' or 'not at all' heavy.

Table 6. Original and derived G0 menstrua	l pain variables (N (%)).
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Question	32.0 years	33.1 years	34.0 years	35.1 years	36.1 years	38.3 years	39.3 years	41.4 years	48.6 years	51.3 years
				Origina	al variable	es				
How painful a	re your pe	riods?								
Very	526 (6.16)	592 (6.85)	581 (7.07)	610 (7.85)	-	559 (7.73)	-	459 (7.64)	263 (8.56)	466 (10.86)
Moderately	2063 (24.17)	2302 (26.65)	2217 (26.97)	2231 (28.73)	-	2005 (27.72)	-	1662 (27.66)	798 (25.97)	1084 (25.27)
Mildly	3388 (39.69)	3205 (37.11)	3256 (39.61)	3017 (38.85)	-	2820 (38.99)	-	2242 (37.32)	1127 (36.67)	1441 (33.59)
Not at all	2560 (29.99)	2538 (29.39)	2166 (26.35)	1908 (24.57)	-	1848 (25.55)	-	1645 (27.38)	885 (28.80)	1299 (30.28)
Have you ever	had a dila	tation and	d curettag	e (D&C / s	crape)? If	yes, was t	nis becaus	e of: painf	ful periods	?
Yes	134 (1.43)	-	48 (23.76)	-	48 (40.00)	-	-	-	52 (52.00)	60 (43.17)
No	9217 (98.57)	-	154 (76.24)	-	72 (60.00)	-	-	-	48 (48.00)	79 (56.83)
Please indicat	e if you ha	ve used a	ny medicir	nes in the	last 12 mo	nths: pair	ful period	s		
Yes	-	-	-	-	-	-	2310 (28.37)	1909 (26.85)	-	-
No	-	-	-	-	-	-	5833 (71.63)	5200 (73.15)	-	-
				Derive	d variable	s				
Painful*	2589 (30.33)	2894 (33.51)	2798 (34.04)	2841 (36.58)	-	2564 (35.45)	-	2121 (35.30)	1061 (34.53)	1550 (36.13)
Not painful*	5948 (69.67)	5743 (66.49)	5422 (65.96)	4925 (63.42)	-	4668 (64.55)	-	3887 (64.70)	2012 (65.47)	2740 (63.87)

*Painful periods are defined as reporting 'very' or 'moderately' painful periods, whereas not painful is defined as reporting periods that are 'mildly' or 'not at all' painful.

				an offinition						
Question	29.2 vears	30.0 vears	32.0 vears	33.1 vears	34.0 vears	35.1 vears	38.3 vears	41.4 vears	48.6 vears	51.3 vears
	years	years	years	Origin	al variable	es	years	years	years	years
Have you had was 18 month	any probl s old / chi	lems with ld's 5th bir	your perio thday / ch	od since yo nild's 6th b	our baby w irthday / c	vas born / :hild's 10th	toddler w birthday	as 8 mont ?	hs old / st	udy child
Yes, and saw a doctor	1135 (10.08)	1092 (10.65)	1148 (11.80)	-	-	1146 (13.39)	1357 (17.09)	984 (14.09)	-	-
Yes, and did not see a doctor	980 (8.70)	670 (6.54)	601 (6.18)	-	-	867 (10.13)	684 (8.62)	603 (8.63)	-	-
No	9150 (81.23)	8488 (82.81)	7976 (82.02)	-	-	6544 (76.48)	5898 (74.29)	5397 (77.28)	-	-
Have you had	any probl	ems with y	your perio	d in the la	st year?					
Yes, and saw a doctor	-	-	-	1284 (13.39)	-	-	-	-	-	-
Yes, and did not see a doctor	-	-	-	752 (7.84)	-	-	-	-	-	-
No	-	-	-	7550 (78.76)	-	-	-	-	-	-
In the past ye	ar, have y	ou had pro	blems wit	th your pe	riod?					
Yes, and saw a doctor	-	-	-	-	1128 (12.61)	-	-	-	-	-
Yes, and did not see a doctor	-	-	-	-	697 (7.79)	-	-	-	-	-
No	-	-	-	-	7119 (79.60)	-	-	-	-	-
In the past ye	ar, have y	ou had pre	e-menstru	al tension	?					
Yes, and saw a doctor	-	-	-	-	428 (4.79)	-	-	-	-	-
Yes, and did not see a doctor	-	-	-	-	2970 (33.22)	-	-	-	-	-
No	-	-	-	-	5542 (61.99)	-	-	-	-	-
Do you genera	ally find in	the days	before or o	during yoເ	ur periods	you have	particular	problems	?	
Yes	-	-	-	-	-	-	-	-	-	2241 (52.89)
No	-	-	-	-	-	-	-	-	-	1996 (47.11)
Do you genera	ally find in	the days	before or o	during you	ur periods	you have	particular	problems	?	
Very fatigued before	-	-	-	-	-	3252 (37.78)	3016 (37.67)	2523 (35.73)	1264 (37.51)	1121 (26.18)
Very fatigued during	-	-	-	-	-	2534 (29.47)	2266 (28.36)	1857 (26.35)	1049 (31.13)	768 (17.96)
Irritable before	-	-	-	-	-	6350 (73.71)	5826 (72.56)	4683 (66.03)	2107 (62.52)	1744 (40.66)
Irritable during	-	-	-	-	-	1954 (22.74)	1479 (18.51)	1142 (16.24)	601 (17.83)	419 (9.80)
Depressed before	-	-	-	-	-	2682 (31.19)	2221 (27.79)	1598 (22.67)	864 (25.64)	759 (17.74)

Table 7. Original and derived G0 premenstrual symptoms variables (N (%)).

Question	29.2 years	30.0 years	32.0 years	33.1 years	34.0 years	35.1 years	38.3 years	41.4 years	48.6 years	51.3 years
				Origin	al variable	es				
Depressed during	-	-	-	-	-	807 (9.40)	642 (8.05)	458 (6.52)	270 (8.01)	234 (5.47)
Anxious before	-	-	-	-	-	2038 (23.71)	1662 (20.82)	1380 (19.59)	635 (18.84)	590 (13.79)
Anxious during	-	-	-	-	-	564 (6.57)	461 (5.78)	356 (5.07)	193 (5.73)	200 (4.68)
Other before	-	-	-	-	-	1149 (13.37)	970 (12.16)	954 (13.57)	371 (11.01)	369 (8.64)
Other during	-	-	-	-	-	476 (5.54)	414 (5.19)	388 (5.53)	134 (3.98)	156 (3.65)
				Derive	ed variable	es				
Binary variab	le: very fat	tigued*								
Very fatigued	-	-	-	-	-	4413 (51.26)	4114 (51.35)	3396 (48.03)	1662 (49.32)	1466 (34.18)
Not very fatigued	-	-	-	-	-	4196 (48.74)	3898 (48.65)	3675 (51.97)	1708 (50.68)	2823 (65.82)
Binary variab	le: irritabl	e*								
Irritable	-	-	-	-	-	6679 (77.53)	6098 (75.92)	4903 (69.12)	2183 (64.78)	1860 (43.34)
Not irritable	-	-	-	-	-	1936 (22.47)	1934 (24.08)	2190 (30.88)	1187 (35.22)	2432 (56.66)
Binary variab	le: depress	ed*								
Depressed	-	-	-	-	-	2955 (34.37)	2454 (30.69)	1787 (25.34)	932 (27.66)	866 (20.22)
Not depressed	-	-	-	-	-	5643 (65.63)	5541 (69.31)	5264 (74.66)	2438 (72.34)	3416 (79.78)
Binary variab	le: anxious	5 *								
Anxious	-	-	-	-	-	2252 (26.20)	1859 (23.27)	1522 (21.60)	681 (20.21)	695 (16.24)
Not anxious	-	-	-	-	-	6345 (73.80)	6129 (76.73)	5524 (78.40)	2689 (79.79)	3585 (83.76)
Binary variab	le: other s	ymptoms*								
Other symptoms	-	-	-	-	-	1302 (15.15)	1120 (14.04)	1074 (15.28)	415 (12.31)	444 (10.39)
No other symptoms	-	-	-	-	-	7292 (84.85)	6857 (85.96)	5957 (84.72)	2955 (87.69)	3830 (89.61)
Number of PM	/IS-related	symptom	s							
0	-	-	-	-	-	1502 (17.49)	1467 (18.40)	1689 (24.07)	806 (23.92)	2117 (49.59)
1	-	-	-	-	-	1794 (20.88)	1727 (21.67)	1504 (21.43)	767 (22.76)	548 (12.84)
2	-	-	-	-	-	2167 (25.23)	2134 (26.77)	1743 (24.84)	831 (24.66)	676 (15.84)
3	-	-	-	-	-	1448 (16.86)	1324 (16.61)	1055 (15.03)	507 (15.04)	444 (10.40)
4	-	-	-	-	-	1329 (15.47)	1066 (13.37)	810 (11.54)	372 (11.04)	393 (9.21)
5	-	-	-	-	-	350 (4.07)	253 (3.17)	217 (3.09)	87 (2.58)	91 (2.13)

*Participants are classified as experiencing the PMS-related symptom (very fatigued, irritable, depressed, anxious, or other) if they reported the symptom either before or during their period, whereas they are classified as not experiencing the symptom if they did not report the symptom before and during their period.

answered further questions regarding their menstrual cycle features at two later 'child-completed' questionnaires (age 19.6 and 21 years) and six clinic assessments (age 11.7, 12.8, 13.8, 15.5, 17.8, and 24 years). Table 8 provides an overview of the relevant ALSPAC variables at each timepoint according to menstrual cycle features, as well as contraception variables at each available timepoint.

Cycle length

In the nine puberty questionnaires, as well as in the 12.8 year clinic, participants (or their mothers up to 13.1 years) were asked to report the length of their menstrual cycle. In two later questionnaires (19.6 and 21 years), participants were asked about their cycle length but were given multiple categorical options instead of reporting the exact number of days. At the age 24 clinic, participants were asked to provide the exact number of days of their usual menstrual cycle or, if they were unsure, they could select an approximate length from multiple categorical options. Table 9 provides an overview of these questions and variables.

Amenorrhea

In the 13.1, 13.8, and 16.5 year child-based questionnaires, mothers were asked whether there had been months when their daughter's periods had not happened at all (if they had started regular periods) and subsequently, if yes, whether she had a period in the last three months. Similarly, at age 21, participants were asked if they had a period in the last three months and, if not, why their periods had stopped. Options included surgery, chemotherapy or radiation therapy, pregnancy or breastfeeding, no obvious reason or menopause, contraception, or that their periods had not started yet. Table 10 summarises these questions. Also, as discussed above, participants reported the length of their menstrual cycle in the nine puberty questionnaires and the 12.8 and 24 year clinic. These variables could provide further insight into amenorrhea where participants have reported long menstrual cycles (e.g., 84 days or 3 months between two periods).

Cycle regularity

At the first three research clinics (11.7, 12.8, and 13.8 years), participants reported whether their periods were regular or not (or they didn't know). At two later clinics (17.8 and 24 years) and two child-completed questionnaires (19.6 and 21 years), respondents were asked about the regularity or length of their cycle and, alongside a series of different cycle length options, were able to report that their cycle was not regular or too irregular for them to estimate their cycle length. In addition, in the mean age 21 questionnaire, participants were asked whether their periods were very, moderately, mildly, or not at all irregular. Table 11 provides an overview of these variables and summarises the responses of those who had started their periods.

Heavy or prolonged bleeding

In the nine puberty questionnaires, participants (or their mothers up to 13.1 years) were asked whether they had experienced heavy or prolonged bleeding with their period. Following this, participants who reported heavy or prolonged bleeding were asked whether they had contacted a doctor for this. Participants were also asked to report the number of days bleeding they normally experienced. If participants were unsure about the exact number of days, they could instead select one of three options: 3 days or less, 4–6 days, or 7 days or more. In the age 21 questionnaire, participants were asked whether their periods were very, moderately, mildly, or not at all heavy. Table 12 provides a summary of these variables and the responses amongst G1 participants who had started their periods.

Menstrual pain

In the puberty questionnaires, except for 15.5 years, participants (or their mothers up to 13.1 years) were asked whether or not they had experienced severe cramps with their periods. At age 15.5, they were instead asked whether they had experienced pain with their periods, and then, for those who answered yes, whether the pain was severe, moderate, or mild. All puberty questionnaires also asked participants who reported severe cramps or pain with their periods whether they had contacted a doctor for this. In the age 21 questionnaire, participants were asked whether their periods were very, moderately, mildly, or not at all painful. Table 13 provides a summary of these variables.

Premenstrual symptoms

At 21 years only (Table 14), participants were asked whether they experienced 'particular problems' in the days before or during their periods. Those who responded yes were subsequently asked which problems they experienced and were provided with multiple symptoms: very fatigued, irritable, depressed, anxious, or other. Respondents indicated whether they experienced each of these symptoms before their periods, during their periods, or not at all (participants were able to select more than one option).

Using the menstrual cycle feature data

Whilst few of the menstrual cycle feature variables are consistent across all available timepoints, it is possible to derive comparable variables for most features and timepoints. However, there are some important limitations that need to be considered when deriving such variables and planning analyses.

Cycle length

For both G0 and G1, participants reported the exact number of days of their menstrual cycle at multiple timepoints and this data could be used continuously or could be used to create categorical variables. For the continuous data, it is important to be aware of outliers in the data, with a small number of G0 participants reporting cycle lengths as long as 90 days and G1 participants reporting cycle lengths up to 150 days. It is challenging to know whether these responses reflect genuine long cycle lengths, for example reflecting an episode of amenorrhea, or if they are due to data entry errors or participants misunderstanding these questions. Approaches to managing these potential erroneous outliers will depend on the research questions being addressed and could include keeping all participants in the analyses and then repeating analyses with those whose cycle lengths are notably different to most participants (e.g. 4 standard deviations away from

Table 8. Source of G1 menstrual cycle feature and contraception data.

				G1 variable nar	nes		
ALSPAC Source File Timepoint	Cycle length	Amenorrhea	Cycle regularity	Heavy/ prolonged bleeding	Dysmenorrhea/ pain	PMS	Contraception
pub1 Puberty Quest 8.1 years	pub117	pub117	-	pub115 pub116 pub120	pub122 pub123	-	pub127
pub2 Puberty Quest 9.6 years	pub217	pub217	-	pub215 pub216 pub220	pub222 pub223	-	pub227
pub3 Puberty Quest 10.6 years	pub317	pub317	-	pub315 pub316 pub320 pub321	pub322 pub323	-	pub327
pub4 Puberty Quest 11.6 years	pub417	pub417	-	pub415 pub416 pub420 pub421	pub422 pub423	-	pub427
F11 Clinic 11.7 years	-	-	femn013	-	-	-	-
tf1 Clinic 12.8 years	ff2094	ff2094	ff2093	-	-	-	-
pub5 Puberty Quest 13.1 years	pub517	pub517	-	pub515 pub516 pub520 pub521	pub522 pub523	-	pub527
ta Child-Based Quest 13.1 years	-	ta6190 ta6191	-	-	-	-	-
tb Child-Based Quest 13.8 years	-	tb8390 tb8391	-	-	-	-	-
tf2 Clinic 13.8 years	-	-	fg6193	-	-	-	-
pub6 Puberty Quest 14.6 years	pub617	pub617	-	pub615 pub616 pub620 pub621	pub622 pub623	-	pub627
pub7 Puberty Quest 15.5 years	pub717	pub717	-	pub715 pub716 pub720 pub721	pub722 pub723 pub724	-	pub727
pub8 Puberty Quest 16 years	pub817	pub817	-	pub815 pub816 pub820 pub821	pub822 pub823	-	pub827
tc Child-Based Quest 16.5 years	-	tc5200 tc5201	-	-	-	-	-
pub9 Puberty Quest 17 years	pub917	pub917	-	pub915 pub916 pub920 pub921	pub922 pub923	-	pub927
tf4 Clinic 17.8 years	-	-	FJMS040	-	-	-	FJMS010- FJMS014
ccxf Quest 19.6 years	ccxf3000	-	ccxf3000	-	-	-	ccxf2000- ccxf2004
YPA Quest 21 years	YPA7042	YPA7010 YPA7020- YPA7025	YPA7042 YPA7052	YPA7050	YPA7051	YPA7060- YPA7075	YPA3270- YPA3291
F24 Clinic 24 years	FKFH1020 FKFH1021	FKFH1020	FKFH1021	-	-	-	FKFH1040

Question	8.1 years	9.6 years	10.6 years	11.6 years	12.8 years clinic	13.1 years	14.6 years	15.5 years	16 years	17 years	19.6 years	21 years	24 years clinic
					0	riginal v	ariables	;					
In the past y	ear, wh	at was t	he usual	length	of your c	laughte	r's mens	trual cycl	e?				
Mean (SD)	NA	18 (18.84)	27.13 (14.86)	26.56 (11.29)	-	26.20 (10.09)	-	-	-	-	-	-	-
< 15 days*	<5	<5	6 (15.00)	38 (12.54)	-	140 (12.96)	-	-	-	-	-	-	-
15–20 days*	<5	<5	<5	8 (2.64)	-	14 (1.30)	-	-	-	-	-	-	-
21–25 days*	<5	<5	6 (15.00)	40 (13.20)	-	125 (11.57)	-	-	-	-	-	-	-
26–30 days*	<5	<5	17 (42.50)	175 (57.76)	-	651 (60.28)	-	-	-	-	-	-	-
31–35 days*	<5	<5	7 (17.50)	22 (7.26)	-	94 (8.70)	-	-	-	-	-	-	-
36-40 days*	<5	<5	<5	6 (1.98)	-	15 (1.39)	-	-	-	-	-	-	-
> 40 days*	<5	<5	<5	14 (4.62)	-	41 (3.80)	-	-	-	-	-	-	-
If your perio e.g. 30, 28)	ds are ı	regular, l	how long	g on avei	age wou	uld you s	say your	cycle is?	(i.e. nun	nber of c	lays bet	ween eac	h period
Mean (SD)	-	-	-	-	28.30 (2.40)	-	-	-	-	-	-	-	-
< 15 days*	-	-	-	-	<5	-	-	-	-	-	-	-	-
15–20 days*	-	-	-	-	<5	-	-	-	-	-	-	-	-
21–25 days*	-	-	-	-	44 (5.44)	-	-	-	-	-	-	-	-
26–30 days*	-	-	-	-	726 (89.74)	-	-	-	-	-	-	-	-
31–35 days*	-	-	-	-	29 (3.58)	-	-	-	-	-	-	-	-
36–40 days*	-	-	-	-	<5	-	-	-	-	-	-	-	-
> 40 days*	-	-	-	-	<5	-	-	-	-	-	-	-	-
In the past y	ear, ho	w many	days we	re there	usually	betweer	n your p	eriods?					
Mean (SD)	-	-	-	-	-	-	28.35 (7.12)	27.81 (4.97)	27.62 (5.62)	27.32 (5.28)	-	-	-
< 15 days*	-	-	-	-	-	-	13 (1.39)	12 (1.31)	11 (0.91)	11 (0.89)	-	-	-
15–20 days*	-	-	-	-	-	-	18 (1.93)	12 (1.31)	37 (3.08)	14 (1.13)	-	-	-
21-25 days*	-	-	-	-	-	-	138 (14.79)	168 (18.36)	229 (19.04)	311 (25.20)	-	-	-
26–30 days*	-	-	-	-	-	-	636 (68.17)	610 (66.67)	791 (65.75)	773 (62.64)	-	-	-
31–35 days*	-	-	-	-	-	-	92 (9,86)	89 (9.73)	109 (9.06)	98 (7.94)	-	-	-

Table 9. Original and derived G1 cycle length variables (N (%)).

Question	8.1 years	9.6 years	10.6 years	11.6 years	12.8 years clinic	13.1 years	14.6 years	15.5 years	16 years	17 years	19.6 years	21 years	24 years clinic
					0	riginal v	variables	5					
36–40 days*	-	-	-	-	-	-	12 (1.29)	12 (1.31)	14 (1.16)	16 (1.30)	-	-	-
> 40 days*	-	-	-	-	-	-	24 (2.57)	12 (1.31)	12 (1.00)	11 (0.89)	-	-	-
Are your per	iods re	gular?											
Yes, every 23 days or less	-	-	-	-	-	-	-	-	-	-	423 (22.23)	-	-
Yes, between 24 and 35 days	-	-	-	-	-	-	-	-	-	-	973 (51.13)	-	-
Yes, > every 35 days	-	-	-	-	-	-	-	-	-	-	47 (2.47)	-	-
No	-	-	-	-	-	-	-	-	-	-	460 (24.17)	-	-
How many d	ays do	you usua	ally have	betwee	n the sta	art of on	e perioc	and the	start of	the nex	t period?	?	
Less than 21 days	-	-	-	-	-	-	-	-	-	-	-	103 (5.03)	-
21–25 days	-	-	-	-	-	-	-	-	-	-	-	697 (34.07)	-
26–31 days	-	-	-	-	-	-	-	-	-	-	-	752 (36.75)	-
32–39 days	-	-	-	-	-	-	-	-	-	-	-	115 (5.62)	-
40–50 days	-	-	-	-	-	-	-	-	-	-	-	38 (1.86)	-
More than 50 days	-	-	-	-	-	-	-	-	-	-	-	40 (1.96)	-
Too irregular to estimate	-	-	-	-	-	-	-	-	-	-	-	301 (14.71)	-
What is the you are NOT	length o using o	of your u oral cont	isual me raceptio	nstrual c n, inject	ycle (the	e interva implant	al from f ?	first day o	f period	to first	day of n	ext perio	d), when
Mean (SD)	-	-	-	-	-	-	-	-	-	-	-	-	25.74 (9.47)
< 15 days*	-	-	-	-	-	-	-	-	-	-	-	-	122 (11.87)
15–20 days*	-	-	-	-	-	-	-	-	-	-	-	-	13 (1.26)
21–25 days*	-	-	-	-	-	-	-	-	-	-	-	-	154 (14.98)
26–30 days*	-	-	-	-	-	-	-	-	-	-	-	-	645 (62.74)

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31–35 days*

36–40 days*

> 40 days*

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69 (6.71)

11 (1.07)

14 (1.36)

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Question	8.1 years	9.6 years	10.6 years	11.6 years	12.8 years clinic	13.1 years	14.6 years	15.5 years	16 years	17 years	19.6 years	21 years	24 years clinic
					0	riginal v	variables	;					
If you don't l	know ex	kactly, w	ould you	u say it w	as:								
Less than 25 days	-	-	-	-	-	-	-	-	-	-	-	-	154 (12.10)
25–34 days	-	-	-	-	-	-	-	-	-	-	-	-	833 (65.44)
35–60 days	-	-	-	-	-	-	-	-	-	-	-	-	72 (5.66)
More than 60 days	-	-	-	-	-	-	-	-	-	-	-	-	15 (1.18)
Too irregular to estimate	-	-	-	-	-	-	-	-	-	-	-	-	199 (15.63)
					D	erived v	ariables						
Normal (24–38 days)	<5	<5	26 (74.29)	221 (82.46)	776 (95.92)	806 (85.38)	788 (85.47)	762 (83.83)	981 (82.02)	975 (79.40)	-	-	782 (85.56)
Frequent (<24 days)	<5	<5	6 (17.14)	31 (11.57)	28 (3.46)	87 (9.22)	104 (11.28)	128 (14.08)	197 (16.47)	232 (18.89)	-	-	112 (12.25)
Infrequent (>38 days)	<5	<5	<5	16 (5.97)	5 (0.62)	51 (5.40)	30 (3.25)	19 (2.09)	18 (1.51)	21 (1.71)	-	-	20 (2.19)

Cell counts below 5 have been replaced with <5, and this may include 0.

*Continuous values recoded.

**Variables derived in line with clinical guidelines. 24–38 days is considered a normal cycle length, whereas less than 24 days is a frequent menstrual cycle and more than 38 days is an infrequent menstrual cycle.

the mean), or some other threshold to see if the outlying values influence results, and reclassifying some participants at each reporting timepoint as having amenorrhea if they report a cycle length of 84 days or more (cessation of menstruation for three months). A further issue, however, is that of small peaks in the distribution around 5 days at some of the timepoints (Figure 3), suggesting that some individuals are reporting the number of days bleeding rather than cycle length. This needs to be managed when deriving variables for analyses. One possible method is to use multiple imputation to impute responses less than a certain threshold (e.g., 10), with responses to the same question at other timepoints contributing to the imputation model. Similar to managing outliers, there will be multiple methods that could be adopted to handle these possible misinterpretations, and a sensitivity analysis to compare results with different approaches is advised. Moreover, the wording of the questions varied at different timepoints for the G1 sample, which may have impacted how participants responded. For example, some questions specified that the length of a usual menstrual cycle referred to the interval from the first day of period to the first day of next period whereas others did not provide this clarification. It is possible therefore that some participants may have reported the number of days between the end of the first period and the start of the next period at some timepoints, possibly impacting the accuracy of reporting and how appropriate it is to compare responses between timepoints. Researchers should

consider how to manage this limitation when designing their analyses.

Researchers may want to derive categorical variables to describe infrequent, frequent, and normal cycles (Table 2 and Table 9). Normal cycles are considered to range from 24-38 days, whereas cycles shorter than 24 days are considered frequent and those longer than 38 days are considered infrequent¹⁰. Such variables could be derived from the continuous variables (noting the issues above). Unfortunately, although ALSPAC also collected categorical data at some timepoints, the original variable categories do not always align with the clinical definitions of infrequent/frequent/normal. Moreover, the boundaries vary between the data collection timepoints. At some G0 and G1 timepoints, the categories are 23 days or less, 24-35 days, and more than every 35 days, whereas at others, the categories are less than 21 days, 21-25 days, 26-31 days, 32-39 days, 40-50 days, and more than 50 days. Finally, at the age 24 timepoint for G1, the categories are less than 25 days, 25-34 days, 35-60 days, and more than 60 days. Therefore, it may not be plausible to include all the available timepoints in the desired analyses, depending on its nature and the timepoints of interest.

Amenorrhea

Binary variables can be derived for amenorrhea for both G0 and G1 (no period in at least the last 3 months vs. had a period

	24.0 years clinic			ī	ı	ı.	ı	ī	I	ı.	I		ı	ı		ī	I	ī	I	ı		ī	ı	ī
	21.0 years			ı	I	ı	I	I	ı	,	I		I			ı	I	I	I	ı		ı	I	,
	17.0 years			ı	ı	ī	ı	ı	ı	ı	I		ı	ı		ı	ı	ı	I	I		,	ı	ı
	16.5 years CBQ			I	I	ı	I	I	I	I	I	, 28)	I	ı	ı	I	I	I	I	I		429 (14.92)	2185 (75.97)	262 (9.11)
	16.0 years			ı			·	ı	ı	ı	ı	eriod e.g. 30	ı	ı			ı	,	I	ı	en at all?		,	ı
	15.5 years			ı	ı		ı		ı	,	I	tween each p	ı				ı	ı	ı	ı	didn't happe		,	ı
	14.6 years	les		ı	1		ı	ı	ı	ı	ı	r of days bet	ı	ı	ı	ı	ı	ı	I	I	n the period		,	ı
	13.8 years CBQ	ıl variab		I	,	ı.		ī	ı	T	I	numbe	·	ı	ı.	ı.	I	ı	ī	ī	ths whe	605 (20.88)	2107 (72.71)	186 (6.42)
	13.1 years CBQ	Origina	cycle?	,				,	ı		ı	e is? (i.e.	ı				ı	,		ı	ny mon	487 (21.66)	1596 (71.00)	165 (7.34)
	13.1 years		enstrual	26.20 (10.09)	140 (12.96)	14 (1.30)	125 (11.57)	651 (60.28)	94 (8.70)	15 (1.39)	41 (3.80)	our cycle				,	ı	,	,	ı	e been a	i.		ı
N (%)).	12.8 years clinic		hter's m	ı.	ı	ı.	ı	ı.	I	ı.	I	rou say y	28.30 (2.40)	ر ک	ر ح	44 (5.44)	726 (89.74)	29 (3.58)	<5 <5	ج ک	ave there	ī	ı	ı.
ea variables (11.6 years		ח of your dau	26.56 (11.29)	38 (12.54)	8 (2.64)	40 (13.20)	175 (57.76)	22 (7.26)	6 (1.98)	14 (4.62)	erage would y	ı			ı	ı	1	ı	ı	llar periods, h	ı	ı	ı
amenorrh	10.6 years		sual lengtl	27.13 (14.86)	6 (15.00)	ر ۲	6 (15.00)	17 (42.50)	7 (17.50)	۲ ۲	S N	ong on av	ı	ı	ı	ı	ı	1	I	I	d her regu			ı
derived G1	9.6 years		was the us	18 (18.84)	٨ 5	۲ ک	<5 S	<5 ~	۲ ک	Ś	~2 2	gular, how l		ı	ı	,			1	I	has starte			ı
al and o	8.1 years		ar, what	NA	۲ د	ŝ	S ~	S ~	Ч С	ŝ	د ۲	s are rec	I	ı	I	ı	ı	ı	ı	I	ughter)	ı.		I
Table 10. Origir	Question		In the past ye	Mean (SD)	< 15 days*	15-20 days*	21–25 days*	26–30 days*	31–35 days*	36-40 days*	> 40 days*	If your period:	Mean (SD)	< 15 days*	15-20 days*	21–25 days*	26–30 days*	31–35 days*	36-40 days*	> 40 days*	If she (your da	Yes	Νο	Don't know

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24.0 years clinic			I	I		I	I	I	I	I	I	I	I		I	I		I	I	I	I	I	I
21.0 years				ı			ı	ı	I	ı	ı	ı			1784 (82.75)	372 (17.25)		<5	<5	41 (12.85)	10 (3.13)	260 (81.50)	6 (1.88)
17.0 years			ı	I		27.32 (5.28)	11 (0.89)	14 (1.13)	311 (25.20)	773 (62.64)	98 (7.94)	16 (1.30)	11 (0.89)		I	ı		ı	ı	I		I	ı
16.5 years CBQ			1569 (95.32)	77 (4.68)		ı	ï	ī	,	I	ī	,	ī		ī	ŀ		ı.			,	1	,
16.0 years			ı	I		27.62 (5.62)	11 (0.91)	37 (3.08)	229 (19.04)	791 (65.75)	109 (9.06)	14 (1.16)	12 (1.00)		I	I		I	I	I	ı	I	I
15.5 years			ı	I		27.81 (4.97)	12 (1.31)	12 (1.31)	168 (18.36)	610 (66.67)	89 (9.73)	12 (1.31)	12 (1.31)		ı	I		ı	I	ı	ı	I	ı
14.6 years	les			I		28.35 (7.12)	13 (1.39)	18 (1.93)	138 (14.79)	636 (68.17)	92 (9.86)	12 (1.29)	24 (2.57)		ı	I		ı	ı	ı	ı	I	
13.8 years CBQ	al variat		580 (93.40)	41 (6.60)		ı.	ı	I	,	ı	ı	ı	ı.		ı	ı		ī				ı	
13.1 years CBQ	Origina		503 (94.02)	32 (5.98)	s?	I	ı	I	ı	I	ı	I	ı		ī	I		I	,	I	ı.	I	ı
13.1 years			,	ı	ır period	ı.	ı	I		ī	ı	ı	,	<u>i</u> g;	ı	ı		T				ı	
12.8 years clinic			,	I	ween you	I	ı	I	,	I	ı	ı	,	al bleedin	ı	I		ı	ı.	ı		I	ı.
11.6 years		3 months?	,	,	re usually bet			ı	ı					d or menstru	ı	·			ı	ı	ŗ	ı	ı
10.6 years		n the last	ı	ı	were the	ı	ı	ı	ı	ı	ı	ı	ı	ad a peric	ı	ı	by:	ı	ı	ı	,	I	ı
9.6 years		y periods ir	1	I	many days	ı	ı	ı	ı	I	ı	ı		have you h	ı	ı	ds stopped	ı	ı	ı	1	ı	ı
8.1 years		had any	,	I	ar, how	I	ī	ı	ı	I	,	ı		onths, l		I	ur perio	ı	ı	1	1	ı	1
Question		If yes, has she	Yes	Νο	In the past ye	Mean (SD)	< 15 days*	15–20 days*	21–25 days*	26–30 days*	31–35 days*	36–40 days*	> 40 days*	In the last 3 m	Yes	No	If no, were you	Surgery	Chemotherapy or radiation therapy	Pregnancy or breastfeeding	No obvious reason / menopause	Contraception	Periods not started yet

Question	8.1 years	9.6 years	10.6 years	11.6 years	12.8 years clinic	13.1 years	13.1 years CBQ	13.8 years CBQ	14.6 years	15.5 years	16.0 years	16.5 years CBQ	17.0 years	21.0 years	24.0 years clinic
							Originā	al variat	oles						
What is the lei injections, or i	ngth of mplant	your usual	menstrua	nl cycle (the in	iterval fro	m first (day of p	eriod to	first day of I	next period),	when you ar	e NOT us	ing oral co	ontraception,	
Mean (SD)		I	I		I	I.	I.	I.			ı	1	ı	ı	25.74 (9.47)
< 15 days*	I	I	I	1	I	I	I	I	1	ı	'	ı	I	I	122 (11.87)
15–20 days*	,	I	I		I	I	ı.	I				ı	I	ı	13 (1.26)
21–25 days*	I	I	I		ı	I	I	I		ı		ı	I	I	154 (14.98)
26–30 days*		ı	ı	1	1	I	I	I		ı		ı	1	ı	645 (62.74)
31–35 days*	I	I	I	1	I	I	I	I	1	ı	'	ı	I	I	69 (6.71)
36–40 days*	1	ı	ı	ı	,	I	I	I				ı	ı	ı	11 (1.07)
> 40 days*	I	I	I		ı	I	I	I		ı		ı	I	I	14 (1.36)
							Derive	d variab	les						
Period in last 3 months	Š	6 (NA)	39 (NA)	300 (NA)	809 (NA)	1077 (NA)	503 (94.02)	580 (93.40)	930 (NA)	915 (NA)	1201 (NA)	1569 (95.32)	1233 (NA)	1784 (82.75)	1024 (NA)
No period in last 3 months	~ 2	<5	~5	<5	<5	Ś	32 (5.98)	41 (6.60)	<5	~5	<5	77 (4.68)	S S	372 (17.25)	С V

CBQ: child-based questionnaire completed by mothers.

Cell counts below 5 have been replaced with <5, and this may include 0.

*Continuous responses recoded.

Question	11.7 years clinic	12.8 years clinic	13.8 years clinic	17.8 years clinic	19.6 years	21 years	24 years clinic
			Original vari	ables			
(Teenagers') periods are	e regular						
Yes	274 (51.99)	817 (49.13)	1309 (61.03)	-	-	-	-
No	155 (29.41)	504 (30.31)	560 (26.11)	-	-	-	-
Don't know	98 (18.60)	342 (20.57)	276 (12.87)	-	-	-	-
Periods are regular							
Yes, occur every 28–30 days	-	-	-	1843 (66.80)	-	-	-
Yes, occur less than every 28 days	-	-	-	220 (7.97)	-	-	-
Yes, occur more than every 30 days	-	-	-	132 (4.78)	-	-	-
No	-	-	-	564 (20.44)	-	-	-
Are your periods regula	ar?						
Yes, every 23 days or less	-	-	-	-	423 (22.23)	-	-
Yes, between 24 and 35 days	-	-	-	-	973 (51.13)	-	-
Yes, > every 35 days	-	-	-	-	47 (2.47)	-	-
No	-	-	-	-	460 (24.17)	-	-
Are/were your periods	irregular?						
Very	-	-	-	-	-	326 (15.62)	-
Moderately	-	-	-	-	-	300 (14.37)	-
Mildly	-	-	-	-	-	443 (21.23)	-
Not at all	-	-	-	-	-	1018 (48.78)	-
How many days do you	usually have	between the	start of one p	eriod and the	start of the ne	ext period?	
Less than 21 days	-	-	-	-	-	103 (5.03)	-
21–25 days	-	-	-	-	-	697 (34.07)	-
26–31 days	-	-	-	-	-	752 (36.75)	-
32–39 days	-	-	-	-	-	115 (5.62)	-
40–50 days	-	-	-	-	-	38 (1.86)	-
More than 50 days	-	-	-	-	-	40 (1.96)	-
Too irregular to estimate	-	-	-	-	-	301 (14.71)	-
Approximate length of	usual mensti	rual cycle					
Less than 25 days	-	-	-	-	-	-	154 (12.10)
25–34 days	-	-	-	-	-	-	833 (65.44)
35–60 days	-	-	-	-	-	-	72 (5.66)
More than 60 days	-	-	-	-	-	-	15 (1.18)
Too irregular to estimate	-	-	-	-	-	-	199 (15.63)
			Derived varia	ables			
Regular	274 (63.87)	817 (61.85)	1309 (70.04)	2195 (79.56)	1443 (75.83)	1448 (68.37)	1074 (84.37)
Irregular	155 (36.13)	504 (38.15)	560 (29.96)	564 (20.44)	460 (24.17)	670 (31.63)	199 (15.63)

Table 11. Original and derived G1 cycle regularity variables (N (%)).

Question	8.1 years	9.6 years	10.6 years	11.6 years	13.1 years	14.6 years	15.5 years	16 years	17 years	21 years
				Or	riginal varia	bles				
Has your dau	ighter ev	er had any	of the follo	owing symp	otoms assoc	iated with	their period	: heavy or p	orolonged b	leeding?
Yes	<5	<5	9 (12.33)	99 (18.97)	421 (21.92)	-	-	-	-	-
No	<5	13 (NA)	64 (87.67)	423 (81.03)	1500 (78.08)	-	-	-	-	-
Have you had	d any of t	he followi:	ng sympton	ns associat	ed with you	r period: he	eavy or prol	onged blee	ding?	
Yes	-	-	-	-	-	908 (34.15)	850 (34.34)	1007 (36.53)	920 (35.91)	-
No	-	-	-	-	-	1751 (65.85)	1625 (65.66)	1750 (63.47)	1642 (64.09)	-
If yes, did yo	u contac	t a doctor f	or this?							
Yes	<5	<5	<5	22 (22.45)	56 (13.37)	128 (14.17)	145 (17.26)	268 (26.61)	289 (31.58)	-
No	<5	<5	6 (NA)	76 (77.55)	363 (86.63)	775 (85.83)	695 (82.74)	739 (73.39)	626 (68.42)	-
In the past y	ear, how	many days	of bleedin	g has your	daughter u	sually had o	during each	period?		
Mean (SD)	2 (NA)	2.50 (1.78)	4.48 (1.93)	5.22 (1.66)	5.41 (1.44)	-	-	-	-	-
< 3 days*	<5	9 (75.00)	12 (19.05)	17 (3.97)	21 (1.37)	-	-	-	-	-
3 days	<5	<5	6 (9.52)	42 (9.81)	80 (5.24)	-	-	-	-	-
4 days	<5	<5	11 (17.46)	60 (14.02)	252 (16.49)	-	-	-	-	-
5 days	<5	<5	16 (25.40)	139 (32.48)	510 (33.38)	-	-	-	-	-
6 days	<5	<5	9 (14.29)	71 (16.59)	332 (21.73)	-	-	-	-	-
7 days	<5	<5	7 (11.11)	87 (20.33)	273 (17.87)	-	-	-	-	-
8 days	<5	<5	<5	6 (1.40)	39 (2.55)	-	-	-	-	-
9 days	<5	<5	<5	<5	8 (0.52)	-	-	-	-	-
> 9 days*	<5	<5	<5	5 (1.17)	13 (0.85)	-	-	-	-	-
In the past y	ear, how	many days	of bleedin	g have you	usually had	l during ea	ch period?			
Mean (SD)	-	-	-	-	-	5.54 (2.15)	5.38 (1.33)	5.39 (1.32)	5.31 (1.94)	-
< 3 days*	-	-	-	-	-	6 (0.36)	11 (0.69)	15 (0.78)	21 (1.11)	-
3 days	-	-	-	-	-	72 (4.29)	74 (4.62)	90 (4.66)	107 (5.68)	-
4 days	-	-	-	-	-	264 (15.74)	277 (17.29)	318 (16.48)	359 (19.05)	-
5 days	-	-	-	-	-	602 (35.90)	579 (36.14)	715 (37.05)	700 (37.14)	-
6 days	-	-	-	-	-	365 (21.77)	344 (21.47)	384 (19.90)	339 (17.98)	-

Table 12. Original and derived G1 heavy and/or prolonged bleeding variables (N (%)).

Question	8.1 years	9.6 years	10.6 years	11.6 years	13.1 years	14.6 years	15.5 years	16 years	17 years	21 years
				Oı	riginal varia	bles				
7 days	-	-	-	-	-	300 (17.89)	262 (16.35)	347 (17.98)	296 (15.70)	-
8 days	-	-	-	-	-	44 (2.62)	39 (2.43)	37 (1.92)	39 (2.07)	-
9 days	-	-	-	-	-	7 (0.42)	7 (0.44)	11 (0.57)	8 (0.42)	-
> 9 days*	-	-	-	-	-	17 (1.01)	9 (0.56)	13 (0.67)	16 (0.85)	-
If you don't	know, is i	t probably:								
7 days or more	<5	<5	<5	15 (11.72)	46 (9.89)	141 (11.52)	122 (11.52)	118 (11.71)	104 (12.46)	-
4–6 days	<5	<5	6 (50.00)	86 (67.19)	352 (75.70)	1016 (83.01)	884 (83.47)	826 (81.94)	656 (78.56)	-
3 days or less	<5	<5	6 (50.00)	27 (21.09)	67 (14.41)	67 (5.47)	53 (5.00)	64 (6.35)	75 (8.98)	-
How heavy w	vere/are	your period	ls?							
Very	-	-	-	-	-	-	-	-	-	312 (14.89)
Moderately	-	-	-	-	-	-	-	-	-	1060 (50.57)
Mildly	-	-	-	-	-	-	-	-	-	581 (27.72)
Not at all	-	-	-	-	-	-	-	-	-	143 (6.82)
				De	erived varia	bles				
Heavy or prolonged bleeding**	<5	<5	10 (13.51)	100 (18.87)	429 (22.14)	919 (34.04)	852 (34.18)	1012 (36.44)	923 (35.90)	1372 (65.46)
Neither heavy nor prolonged bleeding**	<5	13 (NA)	64 (86.49)	430 (81.13)	1509 (77.86)	1781 (65.96)	1641 (65.82)	1765 (63.56)	1648 (64.10)	724 (34.54)

Cell counts below 5 have been replaced with <5, and this may include 0.

*Continuous responses recoded.

**Heavy bleeding is defined as reporting 'heavy or prolonged bleeding', more than 8 days bleeding, or 'very'/'moderately' heavy periods, whereas not heavy is defined as reporting 'no heavy or prolonged bleeding', bleeding for 8 days or less, or periods that are 'mildly'/'not at all' heavy.

in the last 3 months) at each timepoint (Table 3 and Table 10). However, most respondents who reported not having a period in the last 3 months provided a reason (e.g., surgery, chemotherapy, pregnancy, menopause, contraception, or not started their periods yet). It is also possible that this may be the case at timepoints where participants were not asked to provide a reason. Information on contraception use and other possible explanations is available from other data collection waves but not necessarily from same wave in which information on amenorrhea was collected (see further considerations below). This could be utilised to attempt to infer whether a participant who has reported not having a period in the last 3 months was also on contraception that could have explained this. The cycle length variables whereby participants reported the exact number of days of their cycles could also be utilised. To be consistent with the above variables, the cycle length variables could be used to derive binary variables reflecting cycles of 84 days or more (i.e., no period in the last 3 months) compared with cycles of less than 84 days. This would be consistent with clinical guidelines which characterise amenorrhea, specifically secondary amenorrhea, as the cessation of menstruation for three months^{13,22}. However, as discussed above, it is possible that the high values reported by participants in response to questions about their cycle length could be the result of data entry errors and therefore researchers should be cautious including these variables.

Question	8.1 years	9.6 years	10.6 years	11.6 years	13.1 years	14.6 years	15.5 years	16 years	17 years	21 years					
				Orig	inal variab	les									
Has your daug	ghter ev	er had any	of the fol	lowing syr	nptoms as	sociated v	vith her pe	riod: seve	re cramps?	•					
Yes	<5	5 (33.33)	10 (15.87)	126 (26.30)	563 (32.13)	-	-	-	-	-					
No	<5	10 (66.67)	53 (84.13)	353 (73.70)	1189 (67.87)	-	-	-	-	-					
Have you ever	had any	y of the fo	llowing sy	mptoms a	ssociated v	with your	period: sev	vere cramp	s?						
Yes	-	-	-	-	-	1271 (48.85)	-	1515 (56.32)	1451 (57.92)	-					
No	-	-	-	-	-	1331 (51.15)	-	1175 (43.68)	1054 (42.08)	-					
Have you ever	lave you ever had any of the following symptoms associated with your period: pain with your period?														
Yes	-	-	-	-	-	-	2108 (85.10)	-	-	-					
No	-	-	-	-	-	-	369 (14.90)	-	-	-					
If so, were the	If so, were they mild, moderate, or severe?														
Severe	-	-	-	-	-	-	405 (19.33)	-	-	-					
Moderate	-	-	-	-	-	-	1114 (53.17)	-	-	-					
Mild	-	-	-	-	-	-	576 (27.49)	-	-	-					
If yes, did you	contact	a doctor f	or this?												
Yes	<5	<5	<5	14 (11.20)	49 (8.81)	148 (11.75)	194 (9.29)	327 (21.61)	371 (25.76)	-					
No	<5	<5	6 (NA)	111 (88.80)	507 (91.19)	1112 (88.25)	1894 (90.71)	1186 (78.39)	1069 (74.24)	-					
How painful a	re/were	your perio	ods?												
Very	-	-	-	-	-	-	-	-	-	327 (15.60)					
Moderately	-	-	-	-	-	-	-	-	-	686 (32.73)					
Mildly	-	-	-	-	-	-	-	-	-	785 (37.45)					
Not at all	-	-	-	-	-	-	-	-	-	298 (14.22)					
				Deri	ved variab	les									
Painful*	<5	<5	10 (15.87)	126 (26.30)	563 (32.13)	1271 (48.85)	1519 (61.65)	1515 (56.32)	1451 (57.92)	1013 (48.33)					
Not painful *	<5	10 (NA)	53 (84.13)	353 (73.70)	1189 (67.87)	1331 (51.15)	945 (38.35)	1175 (43.68)	1054 (42.08)	1083 (51.67)					

Table 13. Original and derived G1 menstrual pain variables (N (%)).

Cell counts below 5 have been replaced with <5, and this may include 0.

*Painful periods are defined as reporting 'severe cramps', 'severe/moderate pain with your period', or 'very/moderately' painful periods, whereas not painful is defined as reporting 'no severe cramps', 'mild/no pain with your period', or periods that are 'mildly/not at all' painful.

Table 14. Original and derived G1 premenstrual symptoms variables(N (%)).

Question	21 years
Original variables	
Do/did you generally find that in the days before or du periods you have particular problems?	ring your
Yes	1101 (52.23)
No	1007 (47.77)
If yes, which problems do you experience: very fatigued	d?
Yes, before	438 (20.48)
Yes, during	460 (21.50)
No, I don't experience this	425 (19.87)
If yes, which problems do you experience: irritable?	
Yes, before	790 (36.90)
Yes, during	523 (24.44)
No, I don't experience this	124 (5.80)
If yes, which problems do you experience: depressed?	
Yes, before	466 (21.80)
Yes, during	324 (15.15)
No, I don't experience this	482 (22.53)
If yes, which problems do you experience: anxious?	
Yes, before	274 (12.82)
Yes, during	188 (8.79)
No, I don't experience this	723 (33.80)
If yes, which problems do you experience: other?	
Yes, before	288 (13.47)
Yes, during	154 (7.20)
No, I don't experience this	374 (17.48)
Derived variables	
Binary variable: very fatigued*	
Very fatigued	668 (32.19)
Not very fatigued	1407 (67.81)
Binary variable: irritable*	
Irritable	986 (47.04)
Not irritable	1110 (52.96)
Binary variable: depressed*	
Depressed	613 (29.56)
Not depressed	1461 (70.44)
Binary variable: anxious*	
Anxious	365 (17.66)
Not anxious	1702 (82.34)

Question	21 years										
Derived variables											
Binary variable: other symptoms*											
Other symptoms	288 (17.45)										
No other symptoms	1362 (82.55)										
Number of PMS-related symptoms											
0	998 (61.38)										
1	138 (8.49)										
2	189 (11.62)										
3	161 (9.90)										
4	92 (5.66)										
5	48 (2.95)										

*Participants are classified as experiencing the PMS-related symptom (very fatigued, irritable, depressed, anxious, or other) if they reported the symptom either before or during their period, whereas they are classified as not experiencing the symptom if they did not report the symptom before and during their period.

Cycle regularity

For both G0 and G1, the cycle regularity data could be used to derive a binary variable at each timepoint (regular vs. irregular) whereby a participant is classified as having irregular periods if they reported that their period was not regular, too irregular to estimate their cycle length, or very/moderately irregular (Table 4 and Table 11). Alternatively, the more granular 4-level variables for G0 (very, moderately, mildly, or not at all irregular) could be maintained as they are available at half of the timepoints (mean age 32.0 33.1, 34.0, 35.1, 38.3, 41.4, 48.6, and 51.3 years) if these are the only timepoints being considered in the analysis.

Heavy or prolonged bleeding

For the G0 sample, granular 4-level heavy bleeding variables (very, moderately, mildly, or not at all) could be utilised as these are available at each timepoint or binary variables could be derived (very or moderately heavy vs. mildly or not at all heavy). Also, at each of these timepoints, participants reported the duration of bleeding. Binary variables for prolonged bleeding, which is defined as more than 8 days bleeding¹⁰, could therefore also be derived (>8 days bleeding vs. 8 days bleeding or less) (Table 5).

For G1 however, it is not possible to separate heavy and prolonged bleeding in line with clinical guidelines due to the questions that were asked¹⁰. Instead, binary variables for heavy or prolonged bleeding could be derived (heavy or prolonged bleeding vs. neither heavy nor prolonged bleeding), whereby those who reported heavy or prolonged bleeding, very or moderately heavy bleeding, or bleeding for more than 8 days are classified as having heavy or prolonged bleeding (Table 12). Unfortunately, the G1 categorical response variables for days bleeding (3 days or less, 4–6 days, or 7 days or more) do not reflect the clinical guidelines regarding prolonged bleeding so are more challenging to incorporate into this binary definition. It would also be possible to derive the same binary variables for the G0 sample if it was more appropriate for the specific research question to have comparable variables across the two generations (Table 5).

A key consideration with regards to the number of days bleeding variables is that there are some outliers. For example, at the G0 mean age 41.4 year questionnaire and the aged 14.6 and 17 G1 puberty questionnaire, participants reported up to 60 days bleeding. These outliers could be due to data entry errors, participants misunderstanding the question as relating to intervals between periods, or they could be genuine responses reflecting very long periods of bleeding. It is not possible with the available data to distinguish the reasons for such high values and therefore there is no clear way to handle such outliers. Approaches could include recoding such values (e.g., 4 SDs from the mean or the 99th percentile) as missing, imputing them based on available data at other timepoints, or replacing them with the highest non-outlier value ('top-coding'). The most appropriate method will depend on the nature of the analyses being conducted; however, it may be beneficial to conduct a sensitivity analysis to compare the results with different approaches to handling the outliers.

Menstrual pain

It is possible to derive binary pain variables for both G0 and G1 (Table 6 and Table 13). Most of the G1 pain-related variables are already in a binary format except for the age 15 and 21 ones. These variables could be dichotomised whereby those reporting severe or moderate pain are categorised as having pain associated with their periods. The G0 variables could be dichotomised whereby those reporting very/moderately painful periods could be categorised as having pain associated with their periods as having pain associated with their periods. The G0 variables could be categorised as having pain associated with their periods as having pain associated with their periods as having pain associated with their periods, or these could be utilised as 4-level variables if appropriate for the analysis to maintain granularity.



Figure 3. Histograms showing G0 and G1 cycle length variables. 3A is from the G0 37.8 year questionnaire and 3B is from the G0 40.3 year questionnaire. 3C is from the G1 13.1 year puberty questionnaire and 3D is from the G1 age 24 clinic assessment.

However, some caution is needed regarding the G1 variables as the differences in the wording of the questions may mean that participants responded differently to the binary puberty questions. The majority of the puberty questions ask about 'severe cramps' whereas the 15.5 puberty question asks about 'pain with your period' and, subsequently, whether these are severe, moderate, or mild. These are slightly different concepts, and this does appear to be reflected in the responses as the preceding and following timepoint have 48.9% and 56.3% of people reporting severe cramps respectively, but only 16.4% of all respondents at 15.5 report severe pain and 61.7% report severe or moderate pain.

Premenstrual symptoms

There are multiple ways in which the PMS-related variables could be used depending on the nature of analysis. Firstly, a binary variable could be derived which reflects experiencing 'particular problems', 'problems with their period', 'pre-menstrual tension', or any of the listed problems related to periods (irritable, anxious, depressed, very fatigued, other) vs no problems. Secondly, binary variables could be derived for each of these symptoms separately (e.g., irritable vs not irritable). These variables could be derived separately or together for before and during the period. This would be useful for examining the timing of specific symptoms and for distinguishing symptoms occurring during a period from those occurring before, in line with clinical definitions of PMS^{23,24}. Finally, it would also be possible to derive a variable reflecting the number of PMS-related symptoms an individual experiences, either before their periods only (in line with clinical definitions of PMS) or during a period (Table 7 and Table 14). Whilst PMS is not defined by a specific number of symptoms, this variable, which would range from 0 (no PMS symptoms) to 5 (all listed PMS symptoms), could be useful to examine the severity of PMS as more symptoms may reflect a greater negative impact on daily functioning^{23,24}.

A key consideration for the PMS-related data is that PMS encompasses a wide range of physical and psychological symptoms. There are additional common PMS-related symptoms, such as headaches, acne, and breast tenderness^{23,24}, which are not reported in the ALSPAC data. Whilst there is an option for participants to report other problems with their period, we cannot be sure how participants have interpreted this, nor that people have reported all other relevant symptoms. A further issue with the G0 data is that some of the earlier timepoints only ask about 'particular problems' but are not followed up with questions about which symptoms are experienced and their timing. A broad range of problems could be labelled by participants as 'particular problems', not all of

which would necessarily be considered PMS. Therefore, there may be some misclassification. Misclassification may also arise due to the retrospective nature of such assessments, which have been suggested to result in an overreporting of symptoms compared with prospective diary reporting²⁵. Finally, the G1 data is somewhat limited because it is only available at one timepoint.

Further considerations

Contraception is a primary factor that must be considered when utilising the menstrual cycle feature data outlined above. Hormonal contraception is particularly prevalent and, although participants on hormonal contraception will not experience natural menstrual cycles, some will experience withdrawal bleeds that they may classify as menstrual periods (and respond to questions about their menstrual cycle features accordingly). In addition, hormonal contraception is often prescribed in response to menstrual cycle issues such as heavy menstrual bleeding, irregular cycles, or pain. Therefore, as menstrual cycle features and contraception are bidirectionally associated, it may be inappropriate to adjust for or exclude those on hormonal contraception depending on the analyses being conducted. For example, research examining whether BMI influences heavy menstrual bleeding would not want to exclude individuals on hormonal contraception as BMI can impact the likelihood of using hormonal contraception. Excluding would therefore result in collider bias and potentially result in a spurious association between BMI and heavy menstrual bleeding. There are other methods that may account for hormonal contraception when conducting analyses such as this, possibly including multiple imputation, meta-regression, and probability weighting, and there is data available on contraception in ALSPAC to enable this. Table 15 and Table 16 provide a summary of the available contraceptive variables for G0 and G1 respectively.

ALSPAC has collected data on multiple other reproductive factors that can influence menstrual cycle features, and researchers should consider these when planning analyses. Pregnancies and breastfeeding will result in absences of menstruation and can result in more problematic periods upon their initial resumption. Also, menopause and surgeries such as hysterectomies and oophorectomies will stop menstruation and therefore researchers will need to consider how to account for this. Age at menarche is another important factor assessed in ALSPAC which some researchers may want to consider depending on their research question. Whilst ALSPAC participants have been asked about recent pregnancies, breastfeeding, menopause, surgeries and hormonal contraceptive use, the questions are not necessarily asked at the same timepoint as the menstrual cycle features and therefore including such variables may require making inferences backwards or forwards in time.

Moreover, many of the menstrual cycle questions ask participants about their most recent period. Whilst most participants are likely to be answering such questions regarding a period they had up to one month ago, others may be answering about periods much further back in time prior to going on hormonal contraception, becoming pregnant, having a hysterectomy or oophorectomy or going through menopause. This further highlights the importance of considering other reproductive factors where possible to ensure only participants who are experiencing a menstrual cycle at the time of reporting are included in analyses. This is also important to consider as recall bias may become an issue for those who are answering questions about menstrual cycles that were experienced many months or years ago.

There is some limited data available on health conditions that might cause the problematic menstrual cycle features summarised in this data note. For example, participants were asked whether they had ever been diagnosed with PCOS at age 22 for G1 and mean age 49.7 for G0. The same question was asked about endometriosis at age 22 for G1 only. These data provide an opportunity to identify individuals whose problematic menstrual cycle features at previous timepoints are a result of one of these underlying disorders. However, as these conditions tend to be both underdiagnosed and take a long time to be diagnosed, the data is unlikely to capture all participants whose menstrual cycle features are due to either PCOS or endometriosis. There are many other factors which ALSPAC has detailed data on and, depending on the research question, researchers may wish to consider alongside menstrual features.

Missing data needs to be considered when using menstrual symptom data in ALSPAC. Missing data, for example due to loss to follow up, or participants not responding to some questions, could lead to selection bias if missingness is related to the exposure and outcome being explored²⁶. Missing menstrual symptom data could be due to a variety of reasons, including withdrawing from ALSPAC, loss to follow-up, not wanting to answer some questions, pregnancy, breastfeeding, menopause, contraception, and surgeries. It is plausible that several of these (e.g., withdrawal, loss to follow-up, pregnancy, breastfeeding) are socially patterned and hence likely to relate to the exposures and outcomes that are being related to the menstrual cycle features and therefore selection bias is possible. How this is explored and dealt with will depend on the specific research question being addressed and the pattern and extent of missing data. There are several papers that can help with exploring this, including ones that have been used previously in ALSPAC studies^{27,28}.

One of the primary benefits of the ALSPAC dataset is the repeated measures of menstrual cycle features at multiple timepoints. This may allow researchers to increase their sample size by maintaining participants who have missing data at one timepoint by combining with data from other similar timepoints with multiple imputation. Beyond this, repeated measures can enable trajectory modelling to explore the causes and consequences of different patterns of menstrual cycle features over time if appropriate for the research question. The longitudinal nature of the data enables it to be utilised to assess

	57.7 years		ı	I	I.	ı		I	i.	I	I	I	ı	ı	I	ı		I	ı
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	51.6 years clinic	ie followi	ı	I	I.			1	,	I	1	1		ı	,			1	
	51.3 years	u used th	ı.		I.			1										,	
	50.3 years clinic	have yo	I	I	I	I		I	I	I	I	I	ı	I	I	I		I	ı
	49.7 years	iow often	ı	I	ı	ı		I	ı	I	I	I	ı	I	I	ı		I	ı.
	48.6 years	t 2 years, ł	262 (6.63)	32 (0.81)	36 (0.91)	3624 (91.65)		T		ı	I.	I	1	ı	I	ı		84 (2.57)	252 (7.70)
	47.4 years clinic	n the las	ı	I	I.	ı		I	ı	I	I	I	ı	ı	I	ı		ı	ı
	41.4 years	rthday / ii		I	,			I	,	ı	ı	ı	1	ı	ı			190 (2.90)	809 (12.36)
	40.3 years	ild's 5 th bii		I	,			ı		ı	ı.			ı	ı			177 (2.50)	932 (13.14)
	39.3 years	year / ch	ı	I	ı	1		I	ı	ı	I	1	ı	I	ı	1		1	1
	38.3 years	ו the past	1229 (15.47)	190 (2.39)	213 (2.68)	6313 (79.46)		ı	,	ı	ı	ı	1	ı	ı.			207 (2.78)	1247 (16.72)
	37.8 years	:hs old / ir	ı	ı	ı.			1		ı	1	ı.			ı.			,	
	35.1 years	s 18 mont	1765 (20.63)	271 (3.17)	276 (3.23)	6243 (72.97)		I	ı	ı	I	ı	ı	ı	I	1		231 (2.96)	1953 (25.01)
	34.0 years	/ child wa	2066 (2.98)	296 (3.29)	344 (3.83)	6286 (69.91)		T	i.	ı	I.			ı	I			225 (2.86)	2221 (26.49)
l (%)).	33.1 years	onths old	2447 (25.60)	416 (4.35)	478 (5.00)	6216 (65.04)	;wou	237 (2.80)	2635 (31.08)	831 (9.80)	1863 (21.97)	183 (2.16)	101 (1.19)	131 (1.55)	885 (10.44)	1612 (19.01)	;wou		
iables (N	32.0 years	was 8 mo	2655 (27.55)	727 (7.54)	795 (8.25)	5460 (56.66)	you using	248 (2.60)	2964 (31.13)	757 (7.95)	1767 (18.56)	137 (1.44)	108 (1.13)	156 (1.64)	2272 (23.86)	1113 (11.69)	you using	,	
tion var	30.0 years	/ toddler	3414 (33.03	611 (5.91)	726 (7.02)	5585 (54.03)	otion are	204 (2.35)	3409 (39.31)	750 (8.65)	1861 (21.47)	138 (1.59)	149 (1.72)	158 (1.82)	1272 (14.67)	728 (8.40)	otion are	ı	
ontracep	29.2 years	was born pill?	4625 (40.99)	450 (3.99)	677 (6.00)	5530 (49.02)	contracep	,		ı		ı.					contrace	1	
Table 15. G0 c	Question	Since the baby contraceptive	Every day	Often	Sometimes	Not at all	What forms of	Withdrawal	The pill	IUCD / coil	Condom / sheath	Calendar / rhythm method	Diaphragm / cap	Spermicide	None	Other	What forms of	Withdrawal	The pill

57.7 years	1		ı	ı	I	ı		ı	I		,				ı			I
52.6 years clinic	ı	1	ı	ı	I	1	ı	ı	ı		1			ı.	1		,	I
51.6 years clinic	I			I.	I	1		I	I		I				ı			ı
51.3 years	I.	ı		ı.	I	ı		I.	ı		ı.	1			T		,	I
50.3 years clinic	ı	ı	ı	ı	I	T	ı	I	I		ı	1		1	T		ı	I
49.7 years	ı.			I.	,			ı.	ı		,							ı.
48.6 years	551 (16.83)	330 (10.08)	40 (1.22)	8 (0.24)	15 (0.46)	421 (12.86)	1047 (31.99)	399 (12.19)	126 (3.85)		I				T		ı	I
47.4 years clinic	I	ı	I	I.	I	T	I	I	I		I	ı		1	T		I	I
41.4 years	824 (12.59)	821 (12.55)	78 (1.19)	36 (0.55)	37 (0.57)	1025 (15.67)	1949 (29.79)	575 (8.79)	199 (3.04)		,			ı.	ı		788 (11.08)	6321 (88.92)
40.3 years	873 (12.31)	968 (13.65)	91 (1.28)	32 (0.45)	34 (0.48)	985 (13.89)	2060 (29.05)	613 (8.64)	327 (4.61)		7169 (94.12)	448 (5.88)		999 (13.91)	6184 (86.09)		1	I
39.3 years			ı	ı	I		ı	1	I						I		1184 (14.54)	6969 (85.46)
38.3 years	848 (11.37)	1126 (15.10)	101 (1.35)	43 (0.58)	54 (0.72)	983 (13.18)	1942 (26.05)	660 (8.85)	245 (3.29)						1			ı
37.8 years				ı.	,			1	I		7410 (94.85)	402 (5.15)		1402 (18.59)	6138 (81.41)	ive?		ı
35.1 years	856 (10.96)	1480 (18.95)	242 (3.10)	41 (0.53)	137 (1.75)	737 (9.44)	1383 (17.71)	434 (5.56)	315 (4.03)		,				,	ntracept	,	ı
34.0 years	858 (10.23)	1640 (19.56)	178 (2.12)	85 (1.01)	100 (1.19)	676 (8.06)	1221 (14.57)	816 (9.73)	363 (4.33)		1				ı	or: oral co		ı
33.1 years			ı	ı.	ı.			ı.	ı							months f		ı
32.0 years				I.	ı.		ı.	I.	I	tive pill?						he last 12		ı
30.0 years	1			I.	I		,	ı.	I	contracep					,	cines in tl	,	ı
29.2 years	I		ı	I.	I		ı	I	I	used the	I		pill now?		I	any medi	I	ı
Question	IUCD / coil	Condom / sheath	Calendar / rhythm method	Diaphragm / cap	Spermicide	I have been sterilised / am no longer fertile	My partner has been sterilised	None	Other	Have you ever	Yes	No	Are you on the	Yes	Νο	Have you used	Yes	No

57.7 years		101 (3.33)	2933 (96.67)		25 (0.82)	3009 (99.18)		Ţ	I	1	I			38 (0.80)	56 (1.19)	41 (0.87)	310 (6.56)	89 (1.88)
52.6 years clinic		ı	I		I	ı		1	ı	I	ı			ı	ı		1	ı
51.6 years clinic		ı	I		I	ı			ı	I	I			ı	ı	ı.	ı	ı
51.3 years		120 (3.83)	3011 (96.17)		31 (0.99)	3100 (99.01)			ı	1	ı			78 (1.81)	201 (4.68)	111 (2.58)	527 (12.26)	250 (5.82)
50.3 years clinic		149 (4.98)	2841 (95.02)		39 (1.31)	2936 (98.69)			ı	ı.	ı.			1	,	i.	,	,
49.7 years		ı	I		I	1		268 (27.10)	36 (3.64)	27 (2.73)	653 (66.03)	5 (0.51)		ı	I		I	ı
48.6 years		ı	I		ı			ı	I	I	ı				1	,	I	ı
47.4 years clinic		336 (6.69)	4686 (93.31)		42 (0.84)	4980 (99.16)			ı	ı	ı		onths)	1	1		ı	,
41.4 years		ı	I		I	1		,	ı	ı	ı		: past 3 m	ı	ı		I	ı
40.3 years		ı	I		ı	ı.			ı	ı	ı		sed in the	1			I	1
39.3 years		,	I		I	1			ı	ı	ı		u have u	1	ı		I	1
38.3 years			ı								ı		all that yo				I	
37.8 years			ı										ase cross				Ţ	
35.1 years		ı	I		I	1			ı	I	ı		ow? (ple	1	ı		I	ı
34.0 years			ı						ı		ı		er using r				I	
33.1 years	s??		ı	tion?									our partn				Ţ	
32.0 years	raceptive		ı	tive injec									/ou and y				Ţ	
30.0 years	oral cont		1	contracep									otion are)				ı	1
29.2 years	tly taking		1	tly using	,		tly using:		ı		ı		contracep		I		1	
Question	Are you curren	Yes	Νο	Are you curren	Yes	Νο	Are you curren	Oral contraceptive pill	Contraceptive injection	Contraceptive implant	Contraceptive coil with hormone	Contraceptive patch	What forms of	Withdrawal	The pill	IUD (coil, no hormones)	IUD (coil, with hormones, such as a mirena coil)	Condom / sheath

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57.7 years	<5	~2 ~	<u>ک</u>	11 (0.23)	11 (0.23)	189 (4.00)	277 (5.86)	2156 (45.65)	1371 (29.03)	174 (3.68)
52.6 years clinic			ı		ı.		,	i.		
51.6 years clinic		1	ı	i.	I		1	ı	,	
51.3 years	21 (0.49)	~2	11 (0.26)	29 (0.67)	31 (0.72)	335 (7.79)	781 (18.17)	853 (19.84)	734 (17.07)	333 (7.75)
50.3 years clinic			ı	i.	I			ı	,	
49.7 years			ı		I		I	1	I	1
48.6 years										,
47.4 years clinic					ı.			1		
41.4 years										ı
40.3 years							,			
39.3 years					1		ı	i.		ı
38.3 years		,		1	I		I	I	ı	ı
37.8 years		ı.	ı	1	I	ı	I	I	ı	ı
35.1 years					ı.		ı			,
34.0 years										,
33.1 years					1		ı	1		ı
32.0 years		ı	I	ı	I	ı	I	I	I	ı
30.0 years			ı	i.	I		ı	ı	1	ı
29.2 years		1	ı	i.	I	1	ı	1		,
Question	Calendar / rhythm method	Diaphragm / cap	Spermicide	Contraceptive injection	Contraceptive implant	I have been sterilised	My partner has been sterilised	I am no longer fertile	None	Other

Question	8.1 years	9.6 years	10.6 years	11.6 years	13.1 years	14.6 years	15.5 years	16 years	17 years	17.8 years clinic	19.6 years	21 years	24 years clinic
Has your daughter	r taken	oral co	ntracep	tives or	birth cor	ntrol pills	s for any	reason d	uring the	e past 12	months	?	
Yes	<5	<5	<5	5 (0.96)	22 (1.13)	-	-	-	-	-	-	-	-
No	<5	15 (NA)	75 (NA)	518 (99.04)	1927 (98.87)	-	-	-	-	-	-	-	-
Have you taken or	al cont	raceptiv	ves or bi	irth con	trol pills	for any r	ອason dເ	uring the	past 12 ı	months?			
Yes	-	-	-	-	-	176 (6.55)	327 (13.16)	695 (25.20)	1110 (43.38)	-	-	-	-
No	-	-	-	-	-	2490 (92.70)	2139 (86.11)	2044 (74.11)	1435 (56.08)	-	-	-	-
Don't know	-	-	-	-	-	18 (0.72)	18 (0.72)	19 (0.69)	14 (0.55)	-	-	-	-
Currently taking c	ontrace	eption /	Are you	current	tly using								
Oral contraceptive pill	-	-	-	-	-	-	-	-	-	1069 (73.83)	1015 (52.97)	-	-
Contraceptive injection	-	-	-	-	-	-	-	-	-	115 (7.94)	74 (3.86)	-	-
Contraceptive implant	-	-	-	-	-	-	-	-	-	33 (2.28)	136 (7.10)	-	-
Contraceptive coil with hormone	-	-	-	-	-	-	-	-	-	7 (0.48)	25 (1.30)	-	-
Contraceptive patch	-	-	-	-	-	-	-	-	-	<5	5 (0.26)	-	-
None	-	-	-	-	-	-	-	-	-	221 (15.26)	661 (34.50	-	-
Which method of a	contrac	eption ((if any) a	are you o	or your s	exual pa	rtner cu	rrently u	sing? Cro	ss true o	r false fo	or each o	ption
I do not currently have a sexual partner	-	-	-	-	-	-	-	-	-	-	-	392 (11.88)	-
Not using any contraception	-	-	-	-	-	-	-	-	-	-	-	443 (13.42)	-
I / My partner has been sterilised	-	-	-	-	-	-	-	-	-	-	-	<5	-
Mini pill	-	-	-	-	-	-	-	-	-	-	-	150 (4.55)	-
Combined pill	-	-	-	-	-	-	-	-	-	-	-	519 (15.73)	-
Pill – not sure which	-	-	-	-	-	-	-	-	-	-	-	759 (23.00)	-
Mirena coil	-	-	-	-	-	-	-	-	-	-	-	72 (2.18)	-
Coil / other device	-	-	-	-	-	-	-	-	-	-	-	55 (1.67)	-
Condom	-	-	-	-	-	-	-	-	-	-	-	354 (10.73)	-

Table 16. G1 contraception variables (N (%)).

Question	8.1 years	9.6 years	10.6 years	11.6 years	13.1 years	14.6 years	15.5 years	16 years	17 years	17.8 years clinic	19.6 years	21 years	24 years clinic
Femidom	-	-	-	-	-	-	-	-	-	-	-	<5	-
Cap / diaphragm	-	-	-	-	-	-	-	-	-	-	-	<5	-
Foams / gels / sprays / pessaries	-	-	-	-	-	-	-	-	-	-	-	<5	-
Contraceptive sponge	-	-	-	-	-	-	-	-	-	-	-	<5	-
Persona	-	-	-	-	-	-	-	-	-	-	-	<5	-
Safe period / rhythm method	-	-	-	-	-	-	-	-	-	-	-	5 (0.15)	-
Withdrawal	-	-	-	-	-	-	-	-	-	-	-	80 (2.42)	-
Injection	-	-	-	-	-	-	-	-	-	-	-	91 (2.76)	-
Implant	-	-	-	-	-	-	-	-	-	-	-	273 (8.27)	-
Emergency contraception	-	-	-	-	-	-	-	-	-	-	-	49 (1.48)	-
Going without sex	-	-	-	-	-	-	-	-	-	-	-	42 (1.27)	-
Don't know / not sure	-	-	-	-	-	-	-	-	-	-	-	<5	-
Another method of contraception	-	-	-	-	-	-	-	-	-	-	-	5 (0.15)	-
Method of contrac	eption	used											
Combined pill	-	-	-	-	-	-	-	-	-	-	-	-	867 (36.72)
Progesterone only pill	-	-	-	-	-	-	-	-	-	-	-	-	200 (8.47)
Contraceptive injection	-	-	-	-	-	-	-	-	-	-	-	-	91 (3.85)
Contraceptive implant	-	-	-	-	-	-	-	-	-	-	-	-	282 (11.94)
Contraceptive patch	-	-	-	-	-	-	-	-	-	-	-	-	8 (0.34)
Coil	-	-	-	-	-	-	-	-	-	-	-	-	95 (4.02)
Hormonal coil / vaginal ring	-	-	-	-	-	-	-	-	-	-	-	-	111 (4.70)
Barrier methods	-	-	-	-	-	-	-	-	-	-	-	-	149 (6.31)
Natural family planning	-	-	-	-	-	-	-	-	-	-	-	-	27 (1.14)
None	-	-	-	-	-	-	-	-	-	-	-	-	531 (22.49)

causal relationships between menstrual cycle features and possible causes and consequences, reducing the likelihood of reverse causality.

However, researchers should also consider the possibility of misclassification. Whilst random measurement error is always a possibility, researchers should consider possible sources of systematic measurement error. For example, particular groups may feel more uncomfortable answering questions regarding their menstrual cycle and therefore provide answers that do not reflect their menstrual cycle features, or certain groups may be more or less likely to notice or report their menstrual cycle features. The subjective nature of many of the questions may also contribute to possible misclassification as participants may have different perspectives as to what constitutes certain symptoms, such as "heavy bleeding" or "severe cramps". However, subjective experience of these features is crucial and is considered in the clinical guidelines for diagnosis of HMB¹⁰. Moreover, menstrual cycle features may vary randomly over time, contributing to random error and the possibility of regression dilution when using repeated measures²⁹. Researchers therefore need to be aware of both random and systematic measurement error and address this as much as possible within their analysis.

Data availability

Underlying data

ALSPAC data access is through a system of managed open access. The steps below highlight how to apply for access to the data included in this data note and all other ALSPAC data. The datasets presented in this article are linked to ALSPAC project number B4175; please quote this project number during your application. The ALSPAC variable codes highlighted in the dataset descriptions can be used to specify required variables.

- 1. Please read the ALSPAC access policy which describes the process of accessing the data and samples in detail, and outlines the costs associated with doing so.
- 2. You may also find it useful to browse our fully searchable research proposal database which lists all research projects that have been approved since April 2011.
- 3. Please submit your research proposal for consideration by the ALSPAC Executive Committee. You will receive a response within 10 working days to advise you whether your proposal has been approved.

If you have any questions about accessing data, please email alspac-data@bristol.ac.uk. The study website also contains details of all the data that is available through a fully searchable data dictionary.

Acknowledgements

We are extremely grateful to all the families who took part in this study, the midwives for their help in recruiting them, and the whole ALSPAC team, which includes interviewers, computer and laboratory technicians, clerical workers, research scientists, volunteers, managers, receptionists and nurses.

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Version 2

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Thank you for the changes made. I have no further comments to make.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Menstrual health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 1

Reviewer Report 10 October 2023

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? 🛛 Jenny Doust 匝

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This paper outlines the data recorded on menstrual cycle features for mothers and index daughters in the Avon Longitudinal Study of Parents and Children. The multi-generational and longitudinal nature of the data makes it valuable to researchers.

The data note helpfully outlines what data has been collected over what period of time and by what methods. It is particularly helpful to researchers in outlining some of the difficulties and pitfalls when using this data. These aspects of the data appear to have been carefully thought through in this report. The authors also provide information on how to apply to use this data for research.

I have some minor comments for improving the paper. In the abstract, it would be helpful to understand the ages of the mothers and daughters. Currently it says that the data are collected at 21 and 20 timepoints but does not describe the ages of the participants. Secondly, in the description of the G1 cohort, for example in Figure 2, it is not clear if the ages described are the exact age of the participants or are the average ages.

Is the rationale for creating the dataset(s) clearly described?

Yes

Are the protocols appropriate and is the work technically sound? Yes

Are sufficient details of methods and materials provided to allow replication by others? $\ensuremath{\mathsf{Yes}}$

Are the datasets clearly presented in a useable and accessible format? $\ensuremath{\mathsf{Yes}}$

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Women's health Epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 19 September 2023

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? Mandikudza Tembo

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Abstract

Overall, the abstract and key messages read very well. However, it would be helpful if the abstract

noted where (geographical location) and when (time period including month and year) this research took place.

Introduction

Very well written. However, please note the following edits:

- Citation missing for the first line.
- Citation missing for line ending with "idiopathic".
- The introduction could be enriched by looking at the differences in research and reporting of problematic menstrual features between LMICs and HICs. I think this should be included to provide context. Also, there something to be said about perceptions – perhaps there is underreporting because there's a lack of understanding or education around what is considered "problematic"

Methods

- REDCap (Research Electronic Data Capture) should appear first before being abbreviated. Also is there a citation available for this?
- For figure 2 how was "started period" defined? Would one day of spotting suffice? Was three sequential months of bleeding? Girls often have irregular bleeding at menarche so it would be better to understand what "started period" actually meant to those reporting.
- The question around heavy bleeding is interesting as this is very subjective. Curious as to how this was interpreted by participants... Were they considering "heavy" in relation to their personal experiences or in comparison to their perception of what is "normal"?
- Similar comments for pain how is a participant interpreting this question? It may have been better to look at the effect of pain on the ability to conduct usual daily activities.
- I commend the use of repeated measures.
- Further considerations should also explore the effect of medications/vaccinations on the menstrual cycle. There is a growing body of literature that suggests these could inform the menstrual cycle.

Is the rationale for creating the dataset(s) clearly described?

Yes

Are the protocols appropriate and is the work technically sound?

Yes

Are sufficient details of methods and materials provided to allow replication by others? Partly

Are the datasets clearly presented in a useable and accessible format?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: menstrual health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 07 Oct 2023

Gemma Sawyer

We thank the reviewers for their constructive and helpful comments. We have detailed our response below (in italics) and hope these address the reviewer's critiques.

<u>Abstract</u> Overall, the abstract and key messages read very well. However, it would be helpful if the abstract noted where (geographical location) and when (time period including month and year) this research took place. *We have updated the abstract to include this information.*

The variables presented in this paper have been collected in a UK, Bristol-based cohort since 1991.

<u>Introduction</u> Very well written. However, please note the following edits: Citation missing for the first line. T

he citations to support the text in the first line are in the following sentence which outlines the specific proportion ranges for each feature.

Citation missing for line ending with "idiopathic".

Citations have been added.

The introduction could be enriched by looking at the differences in research and reporting of problematic menstrual features between LMICs and HICs. I think this should be included to provide context. Also, there something to be said about perceptions – perhaps there is underreporting because there's a lack of understanding or education around what is considered "problematic".

We have added a sentence to the first paragraph of the Introduction highlighting differences between LMICs and HICs.

<u>Methods</u> REDCap (Research Electronic Data Capture) should appear first before being abbreviated. Also is there a citation available for this?

We have addressed the order of the abbreviation. The citation is included (reference 18; Harris et al. 2009).

For figure 2 – how was "started period" defined? Would one day of spotting suffice? Was

three sequential months of bleeding? Girls often have irregular bleeding at menarche so it would be better to understand what "started period" actually meant to those reporting.

We have added a footnote to this figure to make it clear to the reader that 'started period' was based upon responses to the question "Have you started your period yet?" asked at each timepoint. No further information was provided in these questions to clarify how much bleeding would constitute having started their period.

The question around heavy bleeding is interesting as this is very subjective. Curious as to how this was interpreted by participants... Were they considering "heavy" in relation to their personal experiences or in comparison to their perception of what is "normal"?

We have added a few sentences to the final paragraph of the Further Considerations explaining the subjective nature of such questions and, whilst it may pose some limitations, it is also crucial to measure and understand people's experiences of such symptoms. Subjective reporting of heavy bleeding is also used for diagnosis of heavy menstrual bleeding.

Similar comments for pain – how is a participant interpreting this question? It may have been better to look at the effect of pain on the ability to conduct usual daily activities.

See comment above regarding heavy bleeding – we have added a few sentences to address this. Whilst a useful way of measuring and understanding menstrual pain, these measures are not available from the ALSPAC cohort.

I commend the use of repeated measures. Further considerations should also explore the effect of medications/vaccinations on the menstrual cycle. There is a growing body of literature that suggests these could inform the menstrual cycle.

We have added a sentence in the fourth paragraph of the Further Considerations highlighting that there are many factors we have not mentioned that are available in ALSPAC which researchers may want to consider, depending on their specific research question. We have not provided specific mention of medications/vaccinations as we do not aim to provide an exhaustive list of all such factors in this section.

Competing Interests: No competing interests were disclosed.