

Data supplement to Sequeira et al. Association of timing of menarche with depressive symptoms and depression in adolescence: Mendelian randomisation study. Br J Psychiatry doi: 10.1192/bjp.bp.115.168617

*Table DS1 Means and Standard Deviations of Continuous Variables*

<b>Variable</b>	<b>Number</b>	<b>Mean</b>	<b>Std. Dev.</b>	<b>Min.</b>	<b>Max.</b>
<b>Age at menarche (months)</b>	4282	151.52	14.11	91	203
<b>Genetic risk score</b>	4075	121.39	6.74	99.87	143.09
<b>Genetic risk score without adult BMI SNPs<sup>1</sup></b>	4075	116.45	6.60	95.01	138.09
<b>Genetic risk score without childhood BMI SNPs<sup>1</sup></b>	4075	120.59	6.69	98.88	142.09
<b>Genetic risk score without adult or childhood BMI SNPs<sup>1</sup></b>	4075	115.66	6.55	94.01	137.82
<b>SMFQ<sup>2</sup> result at 14</b>	3076	5.71	4.93	0	26
<b>SMFQ<sup>2</sup> result at 16</b>	2969	7.00	6.02	0	26
<b>SMFQ<sup>2</sup> result at 18</b>	2152	7.63	6.21	0	26
<b>BMI at 9</b>	4236	17.93	3.10	11.47	45.89
<b>BMI at 15</b>	2846	21.82	3.70	14.09	42.00

<sup>1</sup>Genetic risk score created for sensitivity analyses; <sup>2</sup>Short Moods and Feelings Questionnaire

*Table DS2 The Mean Age at Menarche of Girls with Short Moods and Feelings Questionnaire (SMFQ) and Clinical Interview Schedule – Revised (CIS-R) Measures in Middle to Late Adolescence.*

<b>Population</b>	<b>No. Observations</b>	<b>Mean age at menarche (months)</b>	<b>Standard deviation</b>	<b>Minimum</b>	<b>Maximum</b>
All girls with age at menarche data	3982	151.86	14.02	91.00	203.00
SMFQ at 14 years	2804	152.87	13.80	91.00	200.00
SMFQ at 17 years	2659	152.52	14.19	91.00	203.00
SMFQ at 19 years	1902	152.58	13.92	91.00	200.00
CIS-R at 18 years	2208	152.54	13.80	91.00	200.00

*Table DS3: Number and Proportion of Girls with Depressive Symptoms (Short Moods and Feelings Questionnaire (SMFQ) $\geq$ 11) and Depression (Clinical Interview Schedule – Revised (CIS-R)) by Age at Menarche (Early/Normative/Late)*

<b>Age at menarche</b>		<b>SMFQ<math>\geq</math>11 at 14</b>	<b>SMFQ<math>\geq</math>11 at 17</b>	<b>SMFQ<math>\geq</math>11 at 19</b>	<b>CIS-R indicates depression at 18</b>
<b>Early</b>	<b>Number</b>	439	439	301	354
	<b>% with depressive symptoms (SMFQ) or depression (CIS-R)</b>	19.82	23.92	22.92	12.43
<b>Normative</b>	<b>Number</b>	1611	1523	1099	1274
	<b>% with depressive symptoms (SMFQ) or depression (CIS-R)</b>	16.08	23.44	22.66	10.68
<b>Late</b>	<b>Number</b>	754	697	502	580
	<b>% with depressive symptoms (SMFQ) or depression (CIS-R)</b>	11.94	20.23	20.92	7.93
<b>Total</b>	<b>Number</b>	2804	2659	1902	2208
	<b>% with depressive symptoms (SMFQ) or depression (CIS-R)</b>	15.55	22.68	22.24	10.24

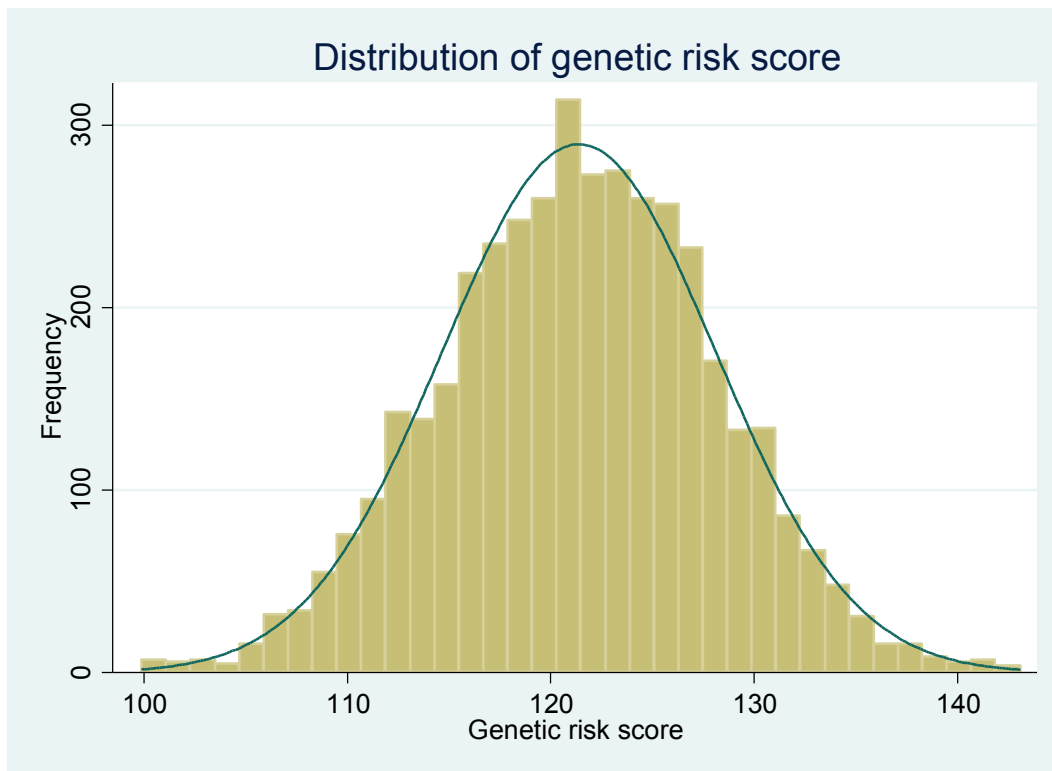


Fig. DS1 Distribution of the Continuous Genetic Risk Score

Table DS4: The Mean Genetic Risk Score of Girls with Short Moods and Feelings Questionnaire (SMFQ) and Clinical Interview Schedule – Revised (CIS-R) Measures in Middle to Late Adolescence.

Population	No. Observations	Mean genetic risk score	Standard deviation	Minimum	Maximum
All girls with genetic data	4075	121.39	6.74	99.87	143.09
SMFQ at 14 years	2404	121.28	6.87	99.87	143.09
SMFQ at 17 years	2145	121.35	6.84	99.87	143.09
SMFQ at 19 years	1570	121.31	6.83	99.87	143.09
CIS-R at 18 years	1910	121.40	6.88	99.87	143.09

*Table DS5: Observational Analyses: Adjusted Odds Ratios (and 95% Confidence Intervals) for Depressive Symptoms at Ages 14, 17 and 19 Years (SMFQ $\geq$ 11), and for Depression Diagnosis Consistent with ICD-10 Criteria at Age 18. Results Shown for Models with Continuous and Categorical Age at Menarche Variables*

	<b>Depressive symptoms (SMFQ<math>\geq</math>11) at 14 (n=2,113)</b>	<b>Depressive symptoms (SMFQ<math>\geq</math>11) at 17 (n=1,913)</b>	<b>Depressive symptoms (SMFQ<math>\geq</math>11) at 19 (n=1,408)</b>	<b>Depression (CIS-R) at 18 (n=1,648)</b>
<b>Continuous age at menarche</b>				
<b>Per 1-month later menarche</b>	0.99 (0.98, 0.995) p=0.003	0.99 (0.99, 1.003) p=0.20	0.999 (0.99, 1.01) p=0.85	0.99 (0.98, 1.004) p=0.16
<b>Categorical age at menarche</b>				
<b>Normative</b>	1.00	1.00	1.00	1.00
<b>Early</b>	1.17 (0.84, 1.62) p=0.36	0.83 (0.61, 1.15) p=0.27	0.88 (0.61, 1.28) p=0.51	1.02 (0.65, 1.60) p=0.93
<b>Late</b>	0.68 (0.50, 0.92) p=0.01	0.72 (0.54, 0.95) p=0.02	0.89 (0.64, 1.23) p=0.49	0.71 (0.46, 1.07) p=0.10
<b>p-value for linear trend</b>	0.02	0.06	0.69	0.24
All analyses adjusted for: BMI at 9 years; BMI at 15 years; No. older siblings; Maternal education; Maternal age; Maternal AN depression; Maternal PN depression; Father absence; Social class; Financial problems; Home ownership.				

Table DS6: Sensitivity Analyses: Odds ratios and 95% Confidence Intervals for Depressive Symptoms at Ages 14, 17 and 19 Years (SMFQ $\geq$ 11), and for Depression Diagnosis Consistent with ICD-10 Criteria at Age 18, by Continuous and Categorical Risk Scores.

	(1) Risk score with adult BMI variants removed (score includes 115 variants)		(2) Risk score with childhood BMI variants removed (score includes 119 variants)		(3) Risk score with adult and childhood BMI SNPs removed (score includes 114 variants)	
<b>Continuous risk score</b>						
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
MFQ at 14 <sup>1</sup>	1.02 (1.01, 1.04)	0.005	1.02 (1.00, 1.04)	0.01	1.02 (1.01, 1.04)	0.006
MFQ at 17 <sup>2</sup>	1.00 (0.99, 1.02)	0.61	1.00 (0.99, 1.01)	0.84	1.00 (0.99, 1.02)	0.84
MFQ at 19 <sup>3</sup>	1.00 (0.99, 1.02)	0.63	1.00 (0.98, 1.02)	0.96	1.00 (0.99, 1.02)	0.96
CISR at 18 <sup>4</sup>	1.01 (0.99, 1.03)	0.45	1.00 (0.98, 1.02)	0.84	1.01 (0.99, 1.03)	0.84
<b>Categorical risk score</b>						
<b>Depressive symptoms (SMFQ) at 14 (n=2,404)</b>						
2nd Quartile	1.47 (1.06, 2.05)	0.02	1.59 (1.15, 2.19)	0.005	1.36 (0.98, 1.88)	0.005
3rd Quartile	1.46 (1.06, 2.02)	0.02	1.47 (1.06, 2.04)	0.02	1.43 (1.04, 1.98)	0.029
4th Quartile	1.67 (1.21, 2.30)	0.002	1.58 (1.13, 2.19)	0.006	1.59 (1.15, 2.18)	0.005
Trend	1.16 (1.05, 1.28)	0.004	1.13 (1.02, 1.25)	0.02	1.15 (1.04, 1.27)	0.006
<b>Depressive symptoms (SMFQ) at 17 (n=2,145)</b>						
2nd Quartile	1.00 (0.75, 1.34)	1.00	0.96 (0.72, 1.28)	0.8	0.98 (0.74, 1.31)	0.90
3rd Quartile	1.02 (0.77, 1.35)	0.91	0.93 (0.70, 1.25)	0.65	0.90 (0.68, 1.20)	0.49
4th Quartile	1.09 (0.82, 1.45)	0.54	1.03 (0.78, 1.37)	0.82	1.07 (0.81, 1.42)	0.64
Trend	1.03 (0.94, 1.13)	0.54	1.01 (0.92, 1.10)	0.88	1.01 (0.93, 1.11)	0.79
<b>Depressive symptoms (SMFQ) at 19 (n=1,570)</b>						
2nd Quartile	0.93 (0.66, 1.31)	0.67	0.73 (0.52, 1.03)	0.07	0.79 (0.56, 1.11)	0.17
3rd Quartile	0.96 (0.69, 1.34)	0.81	0.83 (0.60, 1.15)	0.26	0.93 (0.67, 1.29)	0.66
4th Quartile	1.06 (0.76, 1.49)	0.73	0.96 (0.69, 1.33)	0.80	1.00 (0.72, 1.40)	0.99
Trend	1.02 (0.92, 1.14)	0.72	1.00 (0.89, 1.11)	0.93	1.02 (0.91, 1.13)	0.79
<b>Depression (CIS-R) at 18 (n=1,910)</b>						
2nd Quartile	0.73 (0.47, 1.13)	0.16	1.10 (0.72, 1.66)	0.67	0.88 (0.57, 1.34)	0.54
3rd Quartile	0.88 (0.58, 1.34)	0.55	0.95 (0.62, 1.44)	0.79	0.83 (0.55, 1.27)	0.39
4th Quartile	1.20 (0.81, 1.79)	0.36	1.09 (0.72, 1.66)	0.69	1.19 (0.80, 1.77)	0.40
Trend	1.08 (0.95, 1.23)	0.26	1.01 (0.89, 1.14)	0.88	1.05 (0.92, 1.20)	0.47
<sup>1</sup> n=2,404; <sup>2</sup> n=2,145; <sup>3</sup> n=1,570; <sup>4</sup> n=1,910						