Early life mental health, biomarkers in mid-life, and premature all – cause mortality: the 1958 British birth cohort

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Abstract

Background

Early life mental health is known to be associated with later socio-economic adversity and mental health in adulthood, but less is known on potential associations with ohysical health and mortality. We investigated the association between trajectories of conduct problems and affective symptoms with biomarkers in mid-life and premature all-cause mortality.

Methods

We used the 1958 British birth cohort study (National Child Development Study) which includes prospective data on early life mental health (age 7 to 16), a biomedical survey at age 44/45 (n = 9210) and information on all – cause mortality up to age 58 (n = 17657). Latent profile analysis was used to derive a longitudinal typology of early life mental health. Linear and log binomial regressions and the Cox proportional hazards model were employed to investigate the association of mental health with biomarkers in mid-life and all-cause mortality by age 58.

Results

We identified a four group longitudinal typology of early life mental health: “Stable low” (n = 5456), ii) “Adolescent onset” (n = 2093), iii) “Moderate” (n = 3293), iv) “Stable high” (n = 934). Compared to the ‘stable low’ group, the “stable high” (beta coefficient; 95% confidence interval: 2.426; 0.288 to 4.564) and ‘adolescent onset’ groups (2.045; 0.647 to 3.443) had less favourable levels of fibrinogen in middle-age and b = We observed some effect modification by sex such that relative to the ‘stable low’ group differences in high-density lipoproteins (3.279; -5.602 to -0.956), and abdominal obesity (risk ratios; 95% CI: = 1.534; 1.288 to 1.826) were only observed in females. All groups had elevated risk for mortality compared to the “stable low” group.

Conclusion

Experiencing early mental health problems is associated with less favourable levels of biomarkers 29 years later and elevated risk of premature mortality. The associations with biomarkers in mid-life were more commonly seen in females.

Introduction

Mental health problems in childhood and adolescence are known to be associated with psychological distress in adulthood [1], low educational attainment, unemployment, unstable family formation, and criminal offending [2, 3], as well as premature all – cause mortality [4, 5]. There is, however, a paucity of evidence concerning the prospective association between early life mental health with health in adulthood and, in the few studies that have investigated this link [6, 7], the developmental perspective in the emergence of mental health symptomatology in childhood and adolescence [8] has been neglected.

There are various plausible mechanisms of action through which early life mental health may be linked with mid-life health and mortality. For example, early life mental health has been shown to be associated with lower levels of physical activity, and a greater prevalence of smoking, alcohol use [9, 10] [11] and socio-economic adversity in adulthood [3, 11, 12], while specific pathways to mortality include drug overdose, accidents or homicide [13]. In this study we capitalise on the availability of three assessments of mental health spanning childhood and adolescence in a population based prospective birth cohort to investigate their association with biomarkers in mid-life and all-cause mortality in early old age. We hypothesised that early life mental health is associated with biomarkers in mid-life and premature all - cause mortality. Considering that females live longer than males and that they are on average less healthy, we investigated modification of all hypothesised associations by sex.

Methods

Data

Participants in the British National Child Development Study (NCDS) [14] have been resurveyed on 10 occasions since birth. The initial sample of 17,415 individuals – consisting of all babies born in Great Britain in a single week in 1958 – are now 61 years of age with most recent follow-up at age 55, providing prospective data on social, biological, physical, and psychological phenotypes at every sweep. In 2002, when respondents were 44-45 years old, a biomedical survey was conducted in more than 9,000 respondents.

Measures

Early life mental health problems

Conduct problems and affective symptoms in childhood and adolescence were assessed using the modified version of the Rutter 'A' scale [15]. This version of the scale was completed by the mothers of the participants at ages 7 and 11 years, and by both mother and teachers at age 16. Mother and teacher reports were employed to capture symptoms both at home and school, as is well known that maternal and teacher reports are weakly correlated and that triangulating information from multiple informants may bring unique insights into children's behaviour [16]. Affective symptoms included being worried, solitary or miserable, while conduct problems refer to behaviour such as being disobedient, destructive and being involved in fights. Descriptive statistics of all mental health items are presented in the Supplementary files.

Biomarkers in mid-life and all – cause mortality

We used biomarkers as collected at age 44 - 45 *Fibrinogen*: a marker of inflammation and cardiovascular disease (g/L); *C-reactive protein*: an indicator of inflammation and cardiovascular disease (g/L); *Glycated haemoglobin (HbA1c)*, an index of glucose metabolism over the previous 30−90 days, which is used as a marker of diabetes. High Density Lipoproitein (HDL) and Low Density Lipoportein (LDL) cholesterol (mmol/L) as markers of cardiovascular risk; *High blood pressure*: three measures of systolic and diastolic blood pressure were taken. The mean of valid readings was used, and an individual was recorded as having high blood pressure if the average value was above 140/90. Participants that reported use of blood pressure related medication were classified as having high blood pressure. *W*aist and hip circumferences were measured and the ratio of waist over hip calculated and was employed as a measure of abdominal obesity. To assess respiratory function we used *Forced Expiratory Volume in one second (FEV1)*, with the highest measurement used. FEV is a measure of how much air a person can exhale during forced breath during the first second. Details on the measurement procedures and equipment are available on the biomedical sweep technical report [17] and elsewhere [23, 24]. All-cause mortality up to age 58 was recorded by NHS Digital notifications combined with information of the address database held at the Centre for Longitudinal Studies.

All continuous biomarkers were logged with the natural logarithm and multiplied by 100, so regression coefficients can be interpreted as percentage difference in means [18] . Despite the relatively low prevalence of participants on any form of medication, we corrected for bias with methods used previously in this cohort study [19, 20] and estimated our models with these versions of the outcomes. Corrections were made for participants on lipid lowering drugs (n = 163, +25% for total cholesterol; +54% for LDL cholesterol and -25% for HDL cholesterol), those treated for high blood pressure (n = 615, classified as having high blood pressure) and participants on diabetes related medication (n = 176, +1% in absolute terms for HbA1c). Results without corrections were similar to those presented here (available from corresponding author).

Potential confounders

We included potential confounders from birth to age 7. Birth characteristics included birthweight; maternal smoking during pregnancy; maternal age and whether the participants were ever breastfed. Parental characteristics included maternal employment up to age 5. At age 7 we included parents reading to child, parental interest in school, divorce by age 7 and separation from child from more than one month. Indicators of early life socio-economic position included paternal social class at birth; financial difficulties at age 7; age mother stayed at school; housing tenure at age 7; access to household amenities and housing difficulties at age 7. Characteristics of the cohort member at age 7 were cognitive ability, enuresis, a summary of health conditions assessed in the medical visit at age 7 and the Body Mass Index. Descriptive statistics and detailed information on all potential confounders included in our models are presented in the Supplement.

Statistical Modelling

Analytic Strategy

We derived latent summaries for each dimension of early life mental health at 7, 11 and 16 years of age by modelling the probability of response to the Rutter items with a 2 parameter probit latent variable measurement model [21, 22] and calculated latent trait scores for conduct problems and affective symptoms as separate early life mental health dimensions. The variables summarising conduct problems and affective symptoms were entered in a latent profile analysis [23] that has been used in a wide

range of applications [24] in order to derive a longitudinal typology of mental health from ages 7 to 16. The development of mental health symptoms through childhood is complex and single time point or population average estimates of symptom development over time can obscure subgroups with different patterns of behaviour.

The longitudinal typology of mental health trajectories (ages 7 to 16) was used as a predictor of biomarkers in midlife and all-cause mortality in models that included confounders up to age 7. For continuous outcomes we estimated Ordinal Least Squares (OLS) regression and for binary outcomes (abdominal obesity and high blood pressure) a log binomial model with robust standard errors that returns risk ratios as both outcomes were not rare (>20%) to avoid bias due to non-collapsibility of the odds ratio [25]. The relation between early mental health trajectories and mortality was analysed with the standard Cox regression model, after ascertaining with Schoenfeld residuals and graphs that the proportional odds assumption held. In Table 3 we present fully adjusted linear regression coefficients, risk ratios, the hazard ratio and associated 95% confidence intervals. In all models the 'stable low' are the reference group. We report 95% confidence intervals and use the 5% level of statistical significance. We also present results from the Bonferroni correction [26], that controls for family wise error rate due to multiple testing. Considering that defining what constitutes a "family" of tests is not straightforward we present results from various scenarios. Finally, we also discuss our findings going beyond the null hypothesis significance testing dichotomy interpreting the pattern and magnitude of point estimates and coverage of confidence intervals.

Missing Data

We employed Multiple Imputation with chained equations [27] and generated 50 imputed datasets. Multiple imputation operates under the Missing at Random (MAR) assumption [28], which implies that our estimates are valid if missingness is due to variables included in the imputation phase. We estimated separate imputations for mortality and the biomarkers, where the imputation phase was also stratified by sex More information on our missing data analysis strategy is available in the Supplement.

Sensitivity analysis

To probe the no unmeasured confounders assumption we employed the E Value approach [29, 30] which with minimal assumptions allows researchers to calculate the strength of confounding that is needed to fully explain away their results (results available in the Supplement)

INSERT TABLE 1 ABOUT HERE

Results

Early life mental health trajectories

A four group solution was selected based on various criteria and quality of allocation/misclassification indices (results presented in the Supplementary file). The solution was very similar in men and women, we therefore classified participants based on a pooled sample model. Descriptive statistics of all summary variables are presented in Table 1. The four longitudinal groups were: i) Stable low (n = 5456 – 46.3%). This group was characterised by absence of conduct problems and affective symptoms at all ages. ii) Adolescent onset (n = 2093 – 17.7%). Absence of affective symptoms and conduct problems at ages 7 and 11, followed by sharp increase in levels of both dimensions, but predominantly conduct problems, at age 16 as reported by teachers. Considering that mothers of this group did not report an increase at age 16 and that teacher reports were not available at ages 7 and 11, it could be argued that participants experienced persistent mental health problems at ages 7 and 11 too, but these were mostly manifested at school and thus were not captured by our typology. Sensitivity analysis with information on psychiatric treatment obtained from the medical examination at age 11 and teacher reports at ages 7 and 11 using the Bristol Adjustment Guide showed that the adolescent onset group experienced low to moderate mental health symptoms at ages 7 and 11 and that as captured by our longitudinal typology they experienced the onset of severe mental health symptoms after age 11 (results available in the Supplement). iii) Moderate (n = 3293, 28%). This group experienced moderate levels of conduct problems and affective symptoms in childhood (ages 7 and 11), followed by a decline - that signifies improvement - in both dimensions at age 16 as reported by teachers, but a mild increase in both dimensions reported by mothers. iv) Stable high (n = 934, 17%). Persistent experience of both

conduct problems and affective symptoms from age 7 to 16 reported consistently by both mothers and teachers.

INSERT TABLE 2 ABOUT HERE

Biomarkers

In Table 2 we present descriptive statistics of all outcomes in the whole sample as well as stratified by group. A systematic pattern emerged with respect to all outcomes, with the four groups being consistency ordered with respect to biomarker level and mortality rate. The 'Stable high' group had the least favourable levels on all biomarkers and the highest mortality rate. The 'adolescent onset' group had the second worst biomarker levels and morality rate, followed by the 'moderate' group. The 'stable low' group had the most favourable biomarker levels and the lowest mortality rate. In Table 3 we present OLS regression coefficients, risk ratios and the hazard ratio for the association between early mental health trajectories and the outcomes after multivariable adjustment. With a conventional 5% alpha level, early life mental health was associated with less favourable levels of fibrinogen, C-reactive protein, HDL cholesterol and abdominal obesity. The associations with fibrinogen, HDL and abdominal obesity were partly due to the "stable high" group having different levels in these biomarkers compared to the "stable low" group. Compared to "stable low", the "adolescent onset" group had higher levels of fibrinogen b = 2.045, 95%CI (0.647 to 3.443), p = 0.004, as well as CRP b = 11.636, 95%CI (3.999 to 19.273), p = 0.003 and were more likely to be abdominal obese, RR = 1.124, 95%CI = (1.026 to 1.231), p = 0.012.

We observed evidence of modification by sex in the association between early life mental health, HDL and abdominal obesity. With respect to HDL there was strong evidence of modification by sex on the 'adolescence onset' group, b = -6.288, 95%CI (-9.351 to -3.224), p<0.001 and considering that interaction terms require more power, some evidence for the 'stable high' group, b = -4.427, 95%CI (-9.214 to 0.361), p = 0.070. For abdominal obesity there was strong evidence of modification by sex on the 'stable high' group, RR = 1.376, 95%CI (1.090 to 1.738), p = 0.007. In Graphs 1 & 2 we present results (point estimates and 95% confidence intervals) from models stratified by sex, where early life mental health is associated with both outcomes only in females. With respect to HDL, the 'adolescent onset' and 'stable high' groups had

less favourable levels compared to the 'stable low' group, b = -3.279, 95%CI (-5.602 to -0.956), p = 0.006 and b = -4.180, 95%CI (-7.669 to -0.691), p = 0.019 respectively. Similarly, with respect to abdominal obesity, the adolescent onset' and 'stable high' groups were more likely to be abdominally obese, compared to the 'stable low' group, with RR = 1.201, 95% CI (1.030 to 1.400), p = 0.019 & RR = 1.534, 95% CI (1.288 to 1.826), p < 0.001.

Considering that we carried out multiple tests and that from a conventional null hypothesis significance testing perspective this increases the probability of Type I error we further evaluate our findings with the Bonferroni correction. Considering each biomarker as a 'family' of tests, with three tests carried out the alpha level is 0.05/3 = 0.166. Using this level we are able to detect associations with fibrinogen, CRP, HDL (women only) and abdominal obesity (women only). In a more conservative scenario, where all biomarkers are considered a 'family' of tests, the Bonferroni adjusted alpha level would be 0.05/(3*8) = 0.002. Within this very conservative correction we are able to detect an association with abdominal obesity (women only). Going beyond the conventional NSHT dichotomy and considering the magnitude and patterns of point estimates as well as coverage of confidence intervals as presented in Table 3, we observed a systematic pattern of associations with fibrinogen, CRP, HDL, HbA1c, and abdominal obesity.

INSERT TABLE 3 ABOUT HERE

All – cause mortality by age 58

For those that participated in the age 16 sweep, we observed 1068 deaths and analysed a total of 765,209 person years, with age 58 being the last year of observation. The early life mental health trajectories were associated with premature all – cause mortality, with all groups having elevated risk of mortality compared to the "stable low" group, HR = 1.838 95%CI = (1.466 to 2.304), p<0.001 for the 'stable high' group, HR = 1.187 95%CI = (1.002 to 1.405), p = 0.047 for the 'moderate' group and HR = 1.423, 95%CI = (1.183 to 1.712), p<0.001 for 'adolescent onset'. With no evidence of effect modification by sex in the mental health–mortality relation, we present results from the pooled sample. We are able to detect an association with all – cause mortality under any family wise error rate correction.

INSERT GRAPHS 1 & 2 ABOUT HERE

Discussion

Our main finding was that we observed associations between early life mental health, biomarkers in mid-life and premature all-cause mortality up to age 58. The associations with biomarkers in mid-life were more commonly seen in females, whereas as expected from an earlier follow-up of the present birth cohort and one other study [4, 5, 31] associations with all – cause mortality were observed in both males and females. Persistent experience of high levels of conduct problems and affective symptoms from age 7 to 16 was associated with fibrinogen, C – reactive protein, HDL and abdominal obesity 29 years later, as well as elevated risk for premature all-cause mortality. We observed effect modification by sex in the associations between persistent early life mental health problems with HDL and abdominal obesity, as they were only observed in females.

We found that experiencing the onset of severe conduct problems and affective symptoms in the transition from childhood to adolescence is detrimental with respect to mortality risk, fibrinogen and C-reactive protein. We also observed associations with HDL and abdominal obesity in females only. As the prior to age 16 assessment was carried out at age 11, it appears that that the transition from childhood to adolescence is a sensitive period that warrants further research to elucidate the mechanisms that links the onset of mental health symptoms during this period to adult health and mortality. Considering that this period is marked by various physical, neurodevelopmental as well as psychosocial changes, it is difficult to speculate whether it's the interaction of these with the experience of mental health symptoms that lead to worse outcomes in adulthood, or whether in this particular group it's the severity and/or timing of these changes along with other environmental and social influences that cause the emergence of mental health symptoms.

The mechanisms of action that underlie the observed modification by sex in the association with biomarkers in mid-life may include societal pressures and/or gender related inequalities that may exacerbate the association of conduct problems and affective symptoms with mid-life health in females, pointing to sex specific pathways, in a similar manner as to those suggested for adult depression [32]. Considering that depression appears to have a stronger genetic component in females [33] [34] [35], a

gene environment interaction may also underlie the observed differences. A common genetic cause of both early life mental health and mid-life health which operates only in females is also possible, but considering the well documented gender inequalities [36] and that common genetic variation is a time invariant exposure with its effect at least partially blocked by the use of lags (results not shown, available from corresponding author), we believe this explanation is less likely. An implication of the stronger – compared to males - association between early life mental health and biomarkers in females, is that at least in this cohort it appears that early life mental health may be one of the factors that underlie the so called 'sex survival paradox', a term that describes the observation that females are on average less healthy but live longer than males [37, 38]. As expected, in the 1958 birth cohort there were fewer premature deaths observed in females, but at the same time they appear to be less healthy in various observer measured and self - reported health indicators (results not shown, available from corresponding author).

Strengths of this study include the availability of a large population based and representative prospective study, the three assessments of early life mental health, the inclusion of both conduct problems and affective symptoms in our models and the wealth of information on potential confounders. However, our findings can only be generalised to those born in Britain in 1958 or close to this year. Furthermore, our data are derived from an observational longitudinal study and bias due to unmeasured confounding cannot be ruled out. However, sensitivity analysis suggests that for the association between early life mental health and abdominal obesity, an independent of all confounders included in our models association with early life mental health trajectories and abdominal obesity of a risk ratio with a magnitude of 2.44 and lower limit of the 95%CI of 1.9 would be needed in order to completely explain away our findings. With respect to all-cause mortality a hazard ratio of 3.19 with lower limit of 2.39 for the 95% CI would be needed to explain away our findings. Similar results were obtained with all other outcomes (results presented in the Supplement) indicating that strong confounding, in most cases stronger than that observed in our data, would be needed to completely explain away our findings. As in any longitudinal survey, missing data due to attrition are unavoidable. We employed multiple imputation, augmenting our models with auxiliary variables in the imputation phase to maximise the plausibility of the missing at random assumption, but bias due to a non-ignorable missing data generating mechanism cannot be ruled out.

Our modelling strategy corrects for measurement error in early life mental health and sensitivity analysis taking into account measurement error in the mental health trajectories returned similar results (results presented in the Supplement). However, the extent to which undetected systematic error may have biased our results is unknown. Furthermore, we had reports available from both mothers and teachers only at age 16. While they agreed in their assessment of those who experienced persistent mental health symptoms and those that didn't, there was stark disagreement in the 'adolescent onset' group. However disagreement does not necessarily reflect lack of valid judgements by one informant, but can be due to the report of uniquely different information [39]. Results from sensitivity analysis further reinforced our interpretation that this group experienced the onset of severe symptoms in the transition from childhood to adolescence. We did not observe groups that experienced conduct problems but not affective symptoms or vice versa, as it has been shown in a more recently born cohort [8]. This may be due to the measures we have available for this study or due to generational differences, but more work is needed to fully disentangle the relative contribution of the two mental health dimensions in the association with adult outcomes.

Our findings, if causal, have potential implications for public health policy, especially if mental health is worse in more recently born cohorts as it has recently been shown [40]. Interventions on early life mental health, especially in the transition from childhood to adolescence, have the potential to shift the distribution of risk [41] and improve population health overall.

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Table 1. Mean and standard deviation of latent trait scores of conduct problems and affective symptoms

		Age 7		Age 11		Age 16 – Mother		Age 16 - Teacher	
		Conduct problems	**Affective symptoms**	**Conduct problems**	**Affective symptoms**	**Conduct problems**	**Affective symptoms**	**Conduct problems**	**Affective symptoms**
Stable low (n= 5456)	**Mean**	-0.422	-0.099	-0.578	-0.094	-0.813	-0.229	-1.473	-0.402
	SD	0.840	0.240	0.916	0.171	0.768	0.273	0.559	0.885
Adolescence onset (n = 2093)	**Mean**	-0.080	-0.083	-0.074	-0.062	-0.163	-0.125	3.250	0.490
	SD	0.914	0.241	0.992	0.173	1.106	0.311	1.441	0.994
Moderate (n = 3293)	**Mean**	0.474	0.176	0.648	0.149	0.866	0.320	-1.213	-0.089
	SD	0.893	0.264	0.994	0.189	1.092	0.350	0.776	1.051
Stable high (n = 934)	**Mean**	0.932	0.154	1.309	0.162	2.221	0.522	4.401	1.247
	SD	1.014	0.290	1.151	0.213	1.192	0.387	1.808	1.185
Pooled sample	**Mean**	-0.002	0.002	0.002	0.000	0.004	0.001	-0.050	-0.019
	SD	0.998	0.282	1.163	0.213	1.352	0.417	2.421	1.096

Table 2. Descriptive statistics of all outcomes

		Fibrinogen	CRP	HDL	LDL	HbA1c	FEV1	Abdominal obesity	High blood pressure	Mortality
Stable low	**Mean *(f)***	2.911	1.534	1.582	3.397	5.237	3.291	999	593	278
	SD *(%)*	0.582	1.741	0.403	0.892	0.640	0.866	26.70	15.98	5.09
Adolescent onset	**Mean *(f)***	3.017	1.855	1.531	3.465	5.281	3.226	411	204	170
	SD *(%)*	0.601	1.992	0.391	0.968	0.760	0.840	33.61	16.76	8.24
Moderate	**Mean *(f)***	2.960	1.704	1.563	3.440	5.231	3.201	641	325	217
	SD *(%)*	0.613	1.907	0.387	0.924	0.673	0.874	30.24	15.38	6.65
Stable high	**Mean *(f)***	3.074	1.912	1.486	3.438	5.377	3.129	189	89	96
	SD *(%)*	0.656	2.013	0.373	0.879	0.945	0.889	41.18	19.52	10.74
Pooled sample	**Mean *(f)***	2.952*	1.656	1.563	3.423	5.251	3.245	2,240	1,211**	761**
	SD *(%)*	0.600	1.852	0.396	0.913	0.692	0.867	29.70	16.15	6.51

*Descriptive statistics are presented for the raw data without corrections for medicines use

****** Prevalence for those with valid information on early life mental health trajectories, for full sample the prevalence is 16.05% (1,483)

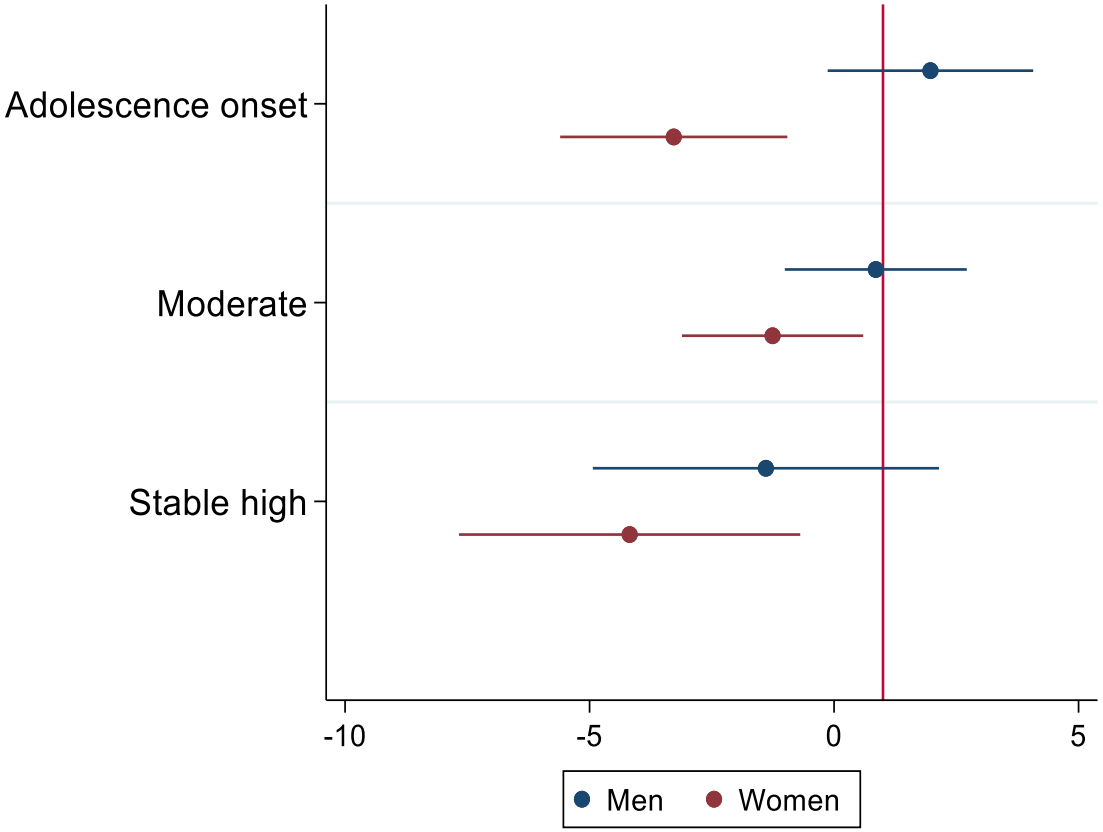
*******Number of deaths for those with valid information on the early life mental health trajectories. Total observed deaths are 1964, 1064 after age 16

Table 3 Linear regression coefficients/risk ratios/hazard ratio and 95% confidence intervals of the association between early life mental health trajectories, biomarkers in midlife and premature all – cause mortality

	Fibrinogen			**CRP**			**HDL**			**LDL**					
Stable low	0 (ref)			0			0			0					
Adolescent onset	2.044	0.647	3.442	11.636	3.999	19.273	-0.306	-1.880	1.266	0.401	-1.536	2.337			
Moderate	0.343	-0.784	1.471	3.065	-3.391	9.521	-0.305	-1.610	0.999	1.120	-0.501	2.741			
Stable high	2.426	0.289	4.563	10.145	-1.536	21.828	-3.016	-5.540	-0.492	1.878	-1.245	5.001			
	HbA1c			**FEV**			**Abdominal obesity**			**High blood pressure**			**All – cause mortality**		
Stable low	0			0			1			1			1		
Adolescent onset	0.006	-0.048	0.061	-1.560	-3.396	0.275	1.124	1.026	1.231	1.032	0.896	1.191	1.427	1.186	1.716
Moderate	-0.019	-0.064	0.025	-1.029	-2.567	0.509	1.081	0.997	1.171	0.933	0.823	1.058	1.187	1.002	1.405
Stable high	0.081	-0.006	0.169	-1.510	-4.326	1.306	1.302	1.153	1.470	1.115	0.916	1.357	1.890	1.512	2.364

*****Parameters are adjusted for birthweight; maternal smoking during pregnancy; maternal age and ever being breastfed, maternal employment up to age 5; parents reading to child at age 7; parental interest in school at 7; divorce by age 7, separation from child from more than one month at 7, paternal social class at birth; financial difficulties at age 7; age mother stayed at school; housing tenure at age 7; access to household amenities at 7, housing difficulties at age 7, cognitive ability at age 7, enuresis at 7, a summary of health conditions assessed during the medical visit at age 7 and the Body Mass Index at 7

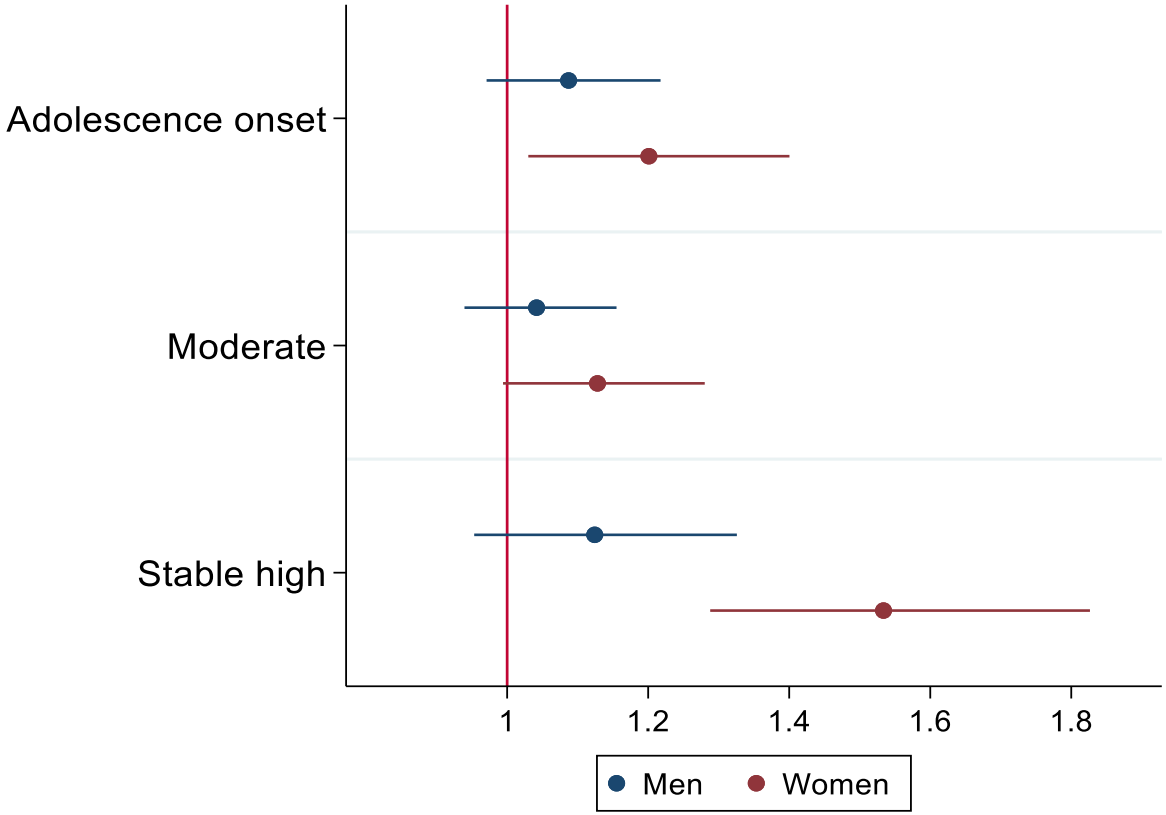
Figure 1. OLS regression coefficients and 95% confidence intervals of the association between early life mental health and HDL in females



*'Stable low are the reference group

**Parameters are adjusted for birthweight; maternal smoking during pregnancy; maternal age and ever being breastfed, maternal employment up to age 5; parents reading to child at age 7; parental interest in school at 7; divorce by age 7, separation from child from more than one month at 7, paternal social class at birth; financial difficulties at age 7; age mother stayed at school; housing tenure at age 7; access to household amenities at 7, housing difficulties at age 7, cognitive ability at age 7, enuresis at 7, a summary of health conditions assessed during the medical visit at age 7 and the Body Mass Index at 7

Figure 2. Risk ratios and 95% confidence intervals of the association between early life mental health and HDL in females



*'Stable low are the reference group

**Parameters are adjusted for birthweight; maternal smoking during pregnancy; maternal age and ever being breastfed, maternal employment up to age 5; parents reading to child at age 7; parental interest in school at 7; divorce by age 7, separation from child from more than one month at 7, paternal social class at birth; financial difficulties at age 7; age mother stayed at school; housing tenure at age 7; access to household amenities at 7, housing difficulties at age 7, cognitive ability at age 7, enuresis at 7, a summary of health conditions assessed during the medical visit at age 7 and the Body Mass Index at 7