Adolescent affective symptoms and mortality

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Background
Little is known about the relationship between adolescent affective problems (anxiety and depression) and mortality.

Aims
To examine whether adolescent affective symptoms are associated with premature mortality, and to assess whether this relationship is independent of other developmental factors.

Method
Data (n = 3884) was from Britain’s oldest birth cohort study – the National Survey of Health and Development. Adolescent affective symptoms were rated by teachers at ages 13 and 15 years: scores were summed and classified into three categories: mild or no, moderate and severe symptoms (1st–50th, 51st–90th and 91st–100th percentiles, respectively). Mortality data were obtained from national registry data up to age 68 years. Potential confounders were parental social class, childhood cognition and illness, and adolescent externalising behaviour.

Results
Over the 53-year follow-up period, 12.2% (n = 472) of study members died. Severe adolescent affective symptoms were associated with an increased rate of mortality compared with those with mild or no symptoms (gender adjusted hazard ratio 1.76, 95% CI 1.33–2.33). This association was only partially attenuated after adjustment for potential confounders (fully adjusted hazard ratio 1.61, 95% CI 1.20–2.15). There was suggestive evidence of an association across multiple causes of death. Moderate symptoms were not associated with mortality.

Conclusions
Severe adolescent affective symptoms are associated with an increased rate of premature mortality over a 53-year follow-up period, independent of potential confounders. These findings underscore the importance of early mental health interventions.

Declaration of interest
None.

Keywords
Mortality; depression; adolescent; cohort studies; affective disorders.

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Adolescent affective symptoms

Affective symptoms were assessed by teachers, using a forerunner of the Rutter B questionnaire, which predates the introduction of diagnostic criteria. At ages 13 and 15 years, teachers were asked to rate the study member’s behaviour compared with other children in the class, using a three-category response scale: more than, the same or less than other children. The questionnaires were subjected to exploratory factor analysis, which identified three distinct factors relating to emotional problems, externalising behaviour (conduct problems) and self-organisation. Ten items were indicators of emotional problems: anxious, always tired and washed out, frightened of rough games, extremely fearful, avoids attention, usually gloomy and sad, timid child, unable to make friends, diffident about competing and unduly miserable or worried about criticism; model fit indices of measurement invariance indicated excellent fit, suggesting adequate reliability. The factor scores of Xu et al. for emotional problems were standardised with z-scores at ages 13 and 15 years, and then summed to create a single measure of adolescent affective symptoms.

We generated a three-category ordinal variable based on previously used cut-off points. Study members between the 1st and 50th percentiles were classified as having mild or no symptoms, those between the 50th and 90th percentiles were classified as having moderate symptoms and those between the 91st and 100th percentiles were classified as having severe symptoms. The cut-off point for severe symptoms is in keeping with 12-month prevalence rates for adolescent anxiety and depressive disorders reported in samples in Europe and the USA (6.9–9.5% for anxiety and 2.1–3.4% for depressive disorders).

Confounding factors

Potential confounders were identified a priori as childhood social, psychological and physical health factors associated with lifetime mental health and mortality in other studies, including the NSHD. These were prospectively measured childhood social class (based on the occupation of the study member’s father at age 11 years, or if this was unknown, at age 4 or 15 years, and coded into six groups according to the Registrar-General’s classification), childhood cognition at age 8 years (derived from tests designed by the National Foundation for Education Research and described in detail elsewhere), teacher-rated adolescent externalising behaviour at ages 13–15 years (derived from factor analysis by Xu et al.), birth weight (in kilograms, obtained from birth records), childhood sickness absence (0–4 weeks, 4–10 weeks and 10+ weeks, obtained from school records spanning ages 6–12 years) and childhood hospital admission at ages 0–5 years, 6–10 years and 11–15 years (obtained from parental interviews, school attendance records, medical examinations and hospital in-patient records). Schizophrenia was ascertained by questionnaire, interview, and hospital and general practitioner contact data up to age 43 years. Health behaviours and other adult psychiatric or psychological problems were not included as potential confounders because we considered these variables to be potential mediators on the causal pathway.

Analyses

We used Kaplan–Meier graphs to compare the survival probability of those with mild or no, moderate and severe affective symptoms over the follow-up period, and tested the equality of survival curves with a log-rank test. Cox proportional hazards models were used to test the relationship between adolescent affective symptoms and all-cause mortality rates. Models were first adjusted for gender. The gender-adjusted hazard ratios for affective symptoms were then adjusted for each potential confounder in turn, with childhood sickness absence and hospital admissions grouped to represent physical health. A further model included all variables. The analyses were repeated using competing-risks analyses, to examine whether associations between affective symptoms and mortality were observed across different causes of death (cardiovascular, cancer, externalising and all other causes).

Gender interactions were tested using joint Wald tests; however, there was no evidence that associations differed in males and females (P = 0.86 for all-cause mortality and P = 0.19–0.54 for cause-specific mortality).

The proportional hazards assumption was checked by including an interaction term between log-time and affective symptoms. Associations were robust to sensitivity analyses, which included the use of a less stringent cut-off point to classify severe symptoms (84th–100th percentile) (see supplementary Table 1, available at https://doi.org/10.1192/bjp.2018.90), and the exclusion of people with schizophrenia (n = 24) to examine whether associations were driven by concurrent mental disorder.

Sample

Eligible participants included all those who had complete data on affective symptoms at ages 13 and 15 years and who were linked with the National Health Service Central Register. Of the original birth cohort (n = 5362), 250 died and 838 refused participation in the study, emigrated or were unable to be traced before age 15 years. A further 342 had missing data on affective symptoms at ages 13–15 years, and 48 had non-linked mortality data, leaving 3884 study members in the analytical sample. To minimise data loss, multiple imputation with chained equations was used to impute missing data on the following covariates: birth weight (n = 17, 0.4%), childhood social class (n = 55, 1.4%), childhood cognition (n = 165, 4.2%) and childhood sickness absence (n = 647, 16.7%). The imputation analyses contained all study variables, including factors that have been shown to predict non-response in the NSHD, such as manual social class and poor childhood cognition. Analyses were run across 20 imputed data-sets. On visual inspection, the imputed results were very similar to those using observed values (see supplementary Table 2 for non-imputed results, and supplementary Fig. 1 for fully adjusted survival curves based on non-imputed data; the Kaplan–Meier function is not currently supported for imputed data). All analyses were carried out in STATA version 13.1.

Results

Table 1 shows the characteristics of the original (non-imputed) data and imputed study sample were similar. Mean follow-up for mortality after age 15 years was 48.8 years (range 3.4–53.0), with a total of 189 609 person-years and 472 deaths. Males had a slightly higher mortality rate than females (2.75 compared with 2.21 per 1000 person-years, respectively). For both genders, the most common cause of death was cancer, followed by cardiovascular disease and externalising causes (violent, accidental or suicidal deaths). All other causes of death comprised diseases of the respiratory system (33.0%), digestive system (23.0%), nervous system (16.5%) and all other miscellaneous causes (27.5%). Affective symptoms were more commonly reported in females than males, with 10.5% of females and 7.6% of males rated as having severe symptoms.

Fig. 1 shows that study members rated with severe adolescent affective symptoms had the lowest survival probability throughout the follow-up period, followed by those with moderate and those with mild or no symptoms (the log-rank test showed that there was a difference in survival curves: χ²(2) = 14.1, P < 0.001). Markedly, the
survival curve for severe symptoms continued to diverge for the duration of the follow-up period; the proportional hazards assumption was not violated ($P = 0.58$). By age 68 years, 18.6% of the severe group had died compared with 10.8% in the mild or no problem group.

Table 2 shows the association between adolescent affective symptoms and all-cause mortality, adjusted for potential confounders.

After adjustment for gender, severe affective symptoms were associated with a higher rate of mortality compared with those with mild or no symptoms. There was no evidence of an association between severe affective symptoms and externalising causes of death (subdistribution hazard ratio 1.52, 95% CI 1.00–2.33), compared with those with mild or no symptoms. There was no evidence of an association between severe affective symptoms and externalising causes of death; however, reliable estimates could not be generated in this subgroup as there were only four from externalising causes deaths (one of which was suicide) among those with severe symptoms.

After adjustment for all potential confounders, an association remained between severe affective symptoms and other causes of death (subdistribution hazard ratio 2.03, 95% CI 1.07–3.85), but all other associations were attenuated to non-significance. The gender-adjusted subdistribution hazard ratios for cardiovascular mortality were attenuated by childhood social class (subdistribution hazard ratio 1.76, 95% CI 1.01–3.06), cognition (subdistribution hazard ratio 1.61, 95% CI 0.92–2.82), and childhood sickness absence and hospital admissions (subdistribution hazard ratio 1.82, 95% CI 1.06–3.16), whereas the gender-adjusted subdistribution hazard ratios for other causes were attenuated only by cognition (subdistribution hazard ratio 2.31, 95% CI 1.26–4.24) and childhood sickness absence and hospital admissions (subdistribution hazard ratio 2.21, 95% CI 1.20–4.05) (see supplementary Table 3). Estimates for cancer and externalising causes did not change with these adjustments (not shown).

![Fig. 1](https://example.com/fig1.png)  
Fig. 1 Gender-adjusted Kaplan–Meier survival curves for all-cause mortality by adolescent affective symptoms, based on 472 deaths ($n = 3884$).
In this large, UK population-based cohort, we found that severe adolescent affective symptoms were associated with a 61% increase in premature mortality over a 53-year follow-up period compared with those who had mild or no symptoms (hazard ratio 1.61, 95% CI 1.20–2.15, P < 0.05; equivalent to an additional 66 deaths per 1000 people). Notably, this relationship persisted for the duration of the follow-up period and was independent of a wide range of potential confounders, including parental social class, childhood hospital admissions, sickness absence and cognition, and adolescent externalising behaviour. There was also evidence to suggest that associations were observed across multiple causes of death.

**Discussion**

Our study is the most comprehensive examination of the relationship between adolescent affective symptoms and premature mortality to date; we build on existing studies by extending mortality follow-up by at least 15 years, providing more rigorous control for potential confounding factors and using a stronger measure of affective problems. The findings are largely consistent with previous studies examining the association between adolescent affective symptoms and mortality. Lee et al. found that associations were attenuated to non-significance after adjustment for adolescent externalising behaviour and other covariates such as cognitive ability and father’s social class. This could be partly attributed to the study’s measure of exposure (the ‘under-reaction’ dimension of the Bristol Social-Adjustment Guide), which the author’s note, could be considered related to, but not a direct measure of internalising.

**Comparison with other studies**

Our study extends the follow-up period of Jokela et al. by almost 20 years, which could be important because causes of death vary by age; for instance, deaths from cancer and other causes.
Affective symptoms strongly predicts adult mental disorder in data were handled with multiple imputation. Our measure of follow-up was particularly low because of their effect on educational attainment and subsequent negative social, psychological and behavioural factors. Because these factors are wide-ranging, it is understandable that we observed associations with mortality across several different causes of death. In particular, we found associations with deaths from cancers and cardiovascular disease after adjustment for gender; although the strongest associations were with deaths from other causes (predominantly diseases of the respiratory, digestive and nervous systems), which held after full adjustment for confounders. We did not have adequate power to examine the association between affective symptoms and deaths from other causes in more detail; however, the results are consistent with existing studies that have used mixed-age community-based samples, and have shown that depression and anxiety disorders are associated with multiple causes of death, including diseases of the metabolism, respiratory and nervous systems, and external causes such as accidents and suicide.

A key criticism of existing literature examining affective symptoms and mortality is a general failure to account for potential confounding with concurrent physical and mental health. Schizophrenia and adolescent externalising behaviour have demonstrated strong associations with premature mortality in the NSHD and elsewhere; however, our results were not attenuated by controlling for externalising behaviour, nor were they explained by excluding people with schizophrenia. Likewise, we found little evidence that the associations between affective symptoms and mortality were due to confounding with poor physical health, as controlling for factors relating to poor physical health in childhood, including hospital admissions, sickness absence and birth weight, did little to attenuate associations.

Strengths and limitations

Methodological strengths of our study include an exceptionally long follow-up period and prospectively obtained data on a wide range of potential confounding variables, although the possibility of residual confounding cannot be excluded. Loss to follow-up was particularly low as there were only 49 study members with non-linked mortality data, and missing covariate data were handled with multiple imputation. Our measure of affective symptoms strongly predicts adult mental disorder in the NSHD, suggesting good construct validity; furthermore, teacher-rated data have been shown to better predict psychiatric disorder than self-report data in other measures of child and adolescent emotional problems, as shown by the Strength and Difficulties Questionnaire.

Limitations of this study include low power to detect small effects, and so it was difficult to draw strong conclusions about moderate symptoms and estimates regarding cause-specific mortality. Also, the generalisability of the study may be limited because of differences in social and health challenges faced by study members compared with today’s children; for example, study members grew up in a post-war economy and in the era of serious childhood diseases such as polio and measles, which have since been effectively eradicated. Likewise, there have been considerable improvements in mental health awareness and treatment since the 1960s, which may buffer the effect of mental health problems on educational and behavioural outcomes associated with mortality; nevertheless, access to adolescent mental health services remains poor, with only around a quarter of young people in the UK getting the help they need.

In conclusion, we have shown that severe adolescent affective symptoms are associated with premature mortality irrespective of a range of potential confounders, including childhood social disadvantage, childhood illness and other mental health problems. Remarkably, the effect of severe adolescent affective symptoms on mortality persisted for the duration of follow-up – over 50 years; however further research is needed to elucidate the role of accumulation and potential mediating mechanisms. There was suggestive evidence of an association between affective symptoms and mortality across multiple causes of death, especially other causes, which warrants more detailed investigation with larger samples as these causes are rare. Given the prevalence of adolescent affective disorder, our findings highlight the importance of early intervention and treatment to prevent associated declines in mental and physical health, and subsequent early mortality. Early identification could be facilitated by routine assessment of mental health during medical check-ups or at school, and enhanced mental health training for health and education professionals.


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