Life course psychological distress and total mortality by middle age: birth cohort study

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Author contributions: GDB authors generated the idea for the present paper; the authors developed an analytical plan; MH built the dataset; CRG analysed the data and generated the table and figure; and GDB prepared a draft of the manuscript which all authors edited.

Abstract

Background: The onset of psychological distress most commonly occurs in adolescence and is time-varying across the life course, yet most studies of its association with mortality risk are conducted in middle- and older-aged populations with a single baseline assessment of this exposure. This may lead to an underestimation of the magnitude of this relationship.

Methods: We used data from the 1970 British Cohort Study, a prospective cohort study. Psychological distress and covariates were collected at ages 5, 10, and 26. Vital status was ascertained between ages 26 and 44 years.

Results: Eighteen years of mortality surveillance of 5901 individuals (3221 women) gave rise to 74 deaths. Net of confounding factors, relative to the no distress group, the presence of distress in childhood only was associated with a 50% elevation in mortality risk (hazard ratio; 95% confidence interval: 1.53; 0.86, 2.74), while distress in adulthood only was related to a doubling of risk (1.94; 0.85, 4.42). In people who reported persistent distress symptoms (childhood and adulthood) there was a tripling of death rates (3.07; 1.26, 7.49). As evidenced by the breadth of the confidence intervals, however, interpretation if these results is hindered somewhat by lower levels of precision.

Conclusion: The suggestion herein of a strong association between life course distress and death warrants replication in a study with a greater number of events.

Introduction

While pernicious in its own right,[1] it is also becoming increasingly well-documented that psychological distress – a combination of symptoms of depression and anxiety – is associated with elevated rates of future cardiovascular disease,[2-4] selected cancers,[5] intentional[6] and unintentional[7] injury, and premature mortality.[8] Distress in these studies is almost exclusively quantified in middle- and older-aged populations on a single, baseline occasion, yet, onset most commonly occurs in adolescence.[9] It is also the case that with around 40% of people who experience an episode of distress in childhood being symptom-free in adulthood,[10] a solitary assessment of this psychological characteristic will fail to capture its time-varying nature, potentially leading to an underestimate of its association with mortality.[11]

To the best of our knowledge, data from only one other study has been used to explore the impact of repeat assessments of distress from childhood through to adulthood on mortality experience.[12] To address this evidence gap, we used data from a birth cohort study with five decades of data collection. In accordance with evidence from cohort studies of middle- and older-aged groups,[13] we hypothesised that people with persistent distress across the early life course would experience the greatest risk of mortality followed by those reporting periodic episodes.

Methods

The 1970 British Cohort Study is a prospective investigation based on a representative sample of people born in the UK in a single week of that year.[14] For the purposes of the present analyses, we used distress responses from data collection sweeps administered at ages 5, 10, and 26. In

childhood, the parent-completed Rutter A scale was used to capture information about the behavioural and emotional problems of the study member.[15] The scale has been found to have utility for group comparisons and long term change in distress.[15]

In early adulthood, the Malaise inventory, which has been validated against psychiatric morbidity and service use,[16] was administered directly to the study members. At ages 5 and 10 years, values above the 80th centile denoted distress on the Rutter scale,[15] while at age 26 a score ≥90th centile on the Malaise inventory was used.[16] We then derived four distress groups: none (referent); childhood only (distress at age 5 and/or age 10); adulthood only (distress at age 26); or both (distress in childhood *and* adulthood). Additional data on paternal social class, birthweight, cognitive function at age 5, and hospital admission by age 5 were used as confounding factors. Vital status between ages 26 (1996) and 44 years (2014) was ascertained via linkage to a national registry and/or notifications by family members during fieldwork. Cox proportional hazards regression was used compute hazard ratios and accompanying confidence intervals;[17] there was no evidence that the proportional hazards assumption had been violated.

Results

Eighteen years of mortality surveillance of 5901 individuals (3221 women) gave rise to 74 deaths. As depicted in Table 1 and Figure 1, relative to the no distress group, in sex-adjusted analyses, the presence of distress in childhood only was associated with a 50% elevation in mortality risk (hazard ratio; 95% confidence interval: 1.48; 0.86, 2.54), while distress in adulthood only was related to a doubling of risk (2.00; 0.93, 4.32). In people who reported persistent distress symptoms (childhood *and* adulthood) there was a tripling of death rates (3.22;

1.50, 6.91). There was also a suggestion of a stepwise effect (p-value for trend: 0.001). This gradient was undiminished after separate adjustment for a series of confounding factors. These observations notwithstanding, as evidenced by the breadth of the confidence intervals, interpretation of results is somewhat hampered by lower levels of precision.

For the main analyses, we applied published thresholds to denote distress for each of the two scales and these were then used to construct the life course distress categories, however, in the context of mortality risk, these thresholds are arbitrary and therefore contentious. We therefore explored the impact of using a further two, equally arbitrary classifications to signal distress at each of the data points: >50th versus >75th centile. Relative to the distress thresholds featured in the main analyses, while mortality rates remain elevated in the people with distress, the stepwise effect apparent across categories in the original analyses were lost (Table e1, Appendix). The highest mortality risk was now apparent in the group who experienced distress in adulthood only as opposed to childhood and adulthood. Again, however, these estimates are statistically unstable owing to the low number of deaths.

Discussion

We found support for our hypothesis that people with persistent distress across the early life course experienced the greater risk of death than those with single bouts. This gradient was not explained by adjustment for confounding factors, and was stronger than in meta-analyses of ten cohort studies with a single assessment of distress in middle- and older-aged people (age- and sex-adjusted hazard ratio; 95% confidence interval: 1.94; 1.66, 2.26).[8]

Existing studies

Investigators using extended mortality surveillance in the 1946 birth cohort study[12] provide

mixed support for our results. In that study, minimally-adjusted analyses showed a stepwise

effect, as we did. After multiple control for more than twenty covariates, however, individuals

who only experienced distress symptoms in adolescent actually had higher death rates than those

who reported mental health problems on as many as four occasions up until middle-age. There

was also a difference in the type of questionnaire used to assess adult distress in the present study

(Malaise inventory) relative to the 1946 birth cohort (Present State Examination). After the

original submission of the present manuscript, findings from the 1958 birth cohort study[18] were

published showing an increased risk of total mortality in study members with evidence of

chronic distress up to age 16 years only.

Study strengths and limitations

The rarity of the distress data across the life course is a distinguishing feature of the present

study, however, that different devices, and modes of administration (parent and study member),

were used to capture this phenotype is a potential shortcoming. Capturing childhood distress via

a third party is arguably preferable to the study members' own responses to questions that they

may not fully comprehend at 10 and certainly 5 years of age. Related, it is perhaps testament to

the predictive utility of these different measures of the same phenotype that, irrespective of the

mode of delivery and the threshold to denote distress, each reveals associations with mortality –

the only exception was childhood distress as denoted by scores above the 50th centile (table e1).

Further, in meta-analyses of cohort studies of adults which use a range of questionnaires to

assess symptoms of distress, however, this characteristic was consistently positively related to

the outcomes which most commonly comprise premature mortality in middle- and older-age populations, including coronary heart disease (incidence and prognosis)[4] and stroke.[19] As in these studies, we used an established threshold for denote distress 'caseness' which is the same approach taken in the other birth cohort study exploring this question[12] but, as we demonstrate herein, different thresholds denoting distress revealed somewhat different relationships with mortality.

In another potential weakness, there is evidence that life course distress is related to moderately unfavourable levels of biomarkers assessed in middle-age, such as blood pressure, blood lipids, and glycosylated heamoglobin.[20] Such biological data were also captured in the present cohort, and, in keeping with other data,[18] we found little suggestion of an association with life course distress[21] categorised in the same manner as the present study. Given the recency of the collection of these biological data – 2016-18 when study members were aged 46-8 years – we do not yet have sufficient deaths in this group to explore their potentially mediation role.

Attrition is inevitable in longitudinal studies, and we examined the early life characteristics of study members according to whether or not they had been included in the present analyses (Table e2, Appendix). As has been demonstrated in other studies of cohort member attrition,[22] the characteristics of individuals with missing data differed to those included in the analyses: they were more likely to be distressed, to have poorer socioeconomic backgrounds, lower birth eight, and lower childhood IQ, and a higher prevalence of hospital admissions. Mortality rates were also higher in study members who were excluded from our analyses relative to those who were not. We examined the impact of weighting to reduce bias due to attrition (for methodology,

see footnote to Appendix), and adding this attrition weight had a trivial attenuating effect on the hazard ratios for mortality relative to the unweighted effects (Table e3, Appendix).

Participants in our cohort study were followed into middle-age and it is likely that the distress–mortality gradient is driven by relationships with external causes of death such as suicide, a behaviour, rather than vascular disease, the culmination of a process occurring over several decades. There is currently no release date for the cause-specific death data for the present study, however (Personal communication – Matt Brown, Centre for Longitudinal Studies, UCL).

Lastly, unmeasured physical co-morbidity may be responsible for both elevated levels of distress and mortality risk in existing studies of older-aged individuals.[8] One of the strengths of our study therefore, is that, in capturing distress earlier in the life course when such co-morbidities are less prevalent, we have, to some degree, addressed this issue of reverse causality. An alternative approach to dealing with reverse causality is prolonged followed up of participants in randomised controlled trials that successfully led to a reduction in depression symptoms in the intervention arm. The two of which we are aware reveal discordant findings, with a lower risk apparent in one using general practices as the unit of assessment[23] and no effect in another in which individual patients with existing cardiovascular disease were recruited.[24] Studies of patient groups are more commonplace than those based on the general population but are characterised by modest quality and have yielded disappointing results.[25]

In conclusion, distress measured at various points across the early adult life course was associated with elevated rates of mortality, and the magnitude of this association was greatest in study members for whom distress symptoms persisted.

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Figure 1. Lifecourse psychological distress by age 26 and risk of mortality by age 44 years
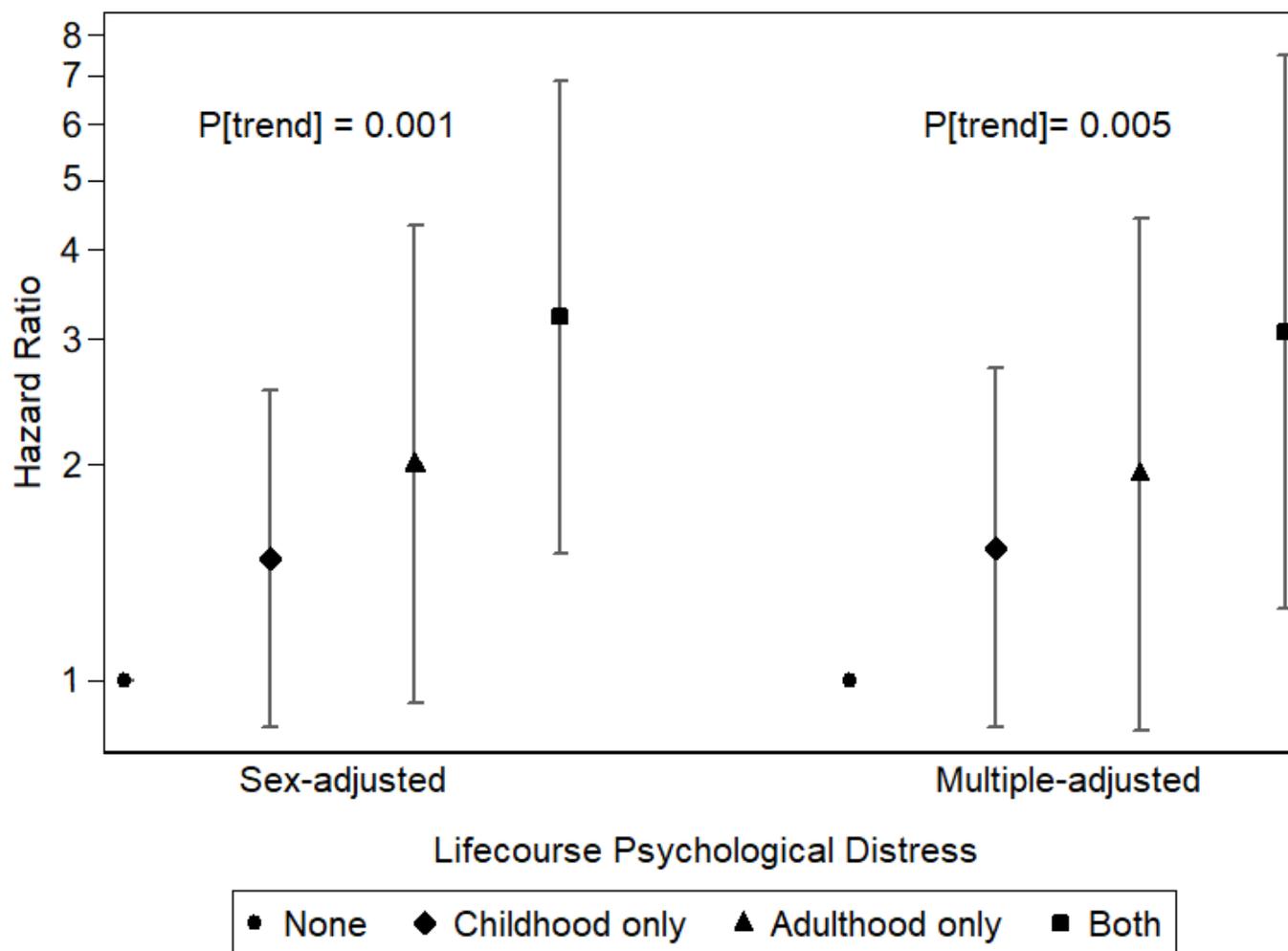
Cox proportional hazards regression analyses was used to compute hazard ratios with accompanying 95% confidence intervals to summarise the relationship between the distress groups and mortality rates. Confounder-adjusted hazard ratios are adjusted for sex, paternal social class at age 5, birthweight, cognitive function at age 5, and history of hospital admission by age 5. The number of people at risk, number of deaths, and point estimates are given in the appendix (Table e4).