Cardiovascular Research – Research Letter

Life course psychological distress and cardiovascular disease risk factors in middle-age: birth cohort study

G. David Batty,[a] PhD, DSc (Email. david.batty@ucl.ac.uk; ORCID: 0000-0003-1822-5753)
Mark Hamer,[b] PhD (m.hamer@ucl.ac.uk; 0000-0002-8726-7992)
Catharine R. Gale,[c] PhD (crg@mrc.soton.ac.uk; 0000-0002-3361-8638)

[a]Department of Epidemiology & Public Health, University College London, UK
[b]Institute of Sport, Exercise & Health, University College London, UK
[c]MRC Lifecourse Epidemiology Unit, University of Southampton, UK

Corresponding author: David Batty, Department of Epidemiology & Public Health, University College London, 1-19 Torrington Place, London, WC1E 6BT, UK. E. david.batty@ucl.ac.uk

Conflict of interest: The authors declare no conflict of interest.

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

Funding: GDB is supported by the Medical Research Council (MR/P023444/1) and the US National Institute on Aging (1R56AG052519-01; 1R01AG052519-01A1), MH through a joint award from the Economic Social Research Council and Medical Research Council (RES-579-47-0001).

Manuscript statistics: 947 words, 7 references, 1 table

Recent findings suggest that psychological distress in childhood – a combination of symptoms of anxiety and depression – particularly when persistent across the life course, is related to an elevated rate of cardiovascular disease mortality in older age.[1] Several mechanisms have been potentially implicated in this observation. One possibility is that people who experience distress in early life, and particularly its recurrence across the life course, may become more susceptible to vascular disease via differences in physiological development. There is, however, a paucity of studies holding data on early distress and biological risk factors for cardiovascular disease in adulthood.

To the best of our knowledge, only two studies have examined these pathways. In an extended follow-up of the National Collaborative Perinatal Project, a small US prospective study,[2] there was a suggestion that a single measurement of poor emotional functioning at age 7 was associated with the activation of the inflammatory system as indicated by higher levels of C-reactive protein at age 42 years. Further, in a large study of a UK population,[3] investigators explored the links between psychological distress across the life course and an amalgamation of cardio-metabolic risk factors in middle-age which included blood pressure and glycosylated haemoglobin. Psychological distress at any point across the life course was associated with a less favourable risk profile in middle-age, although effects were typically modest.

Given the rarity of data in this area, we tested the hypothesis that individuals who reported persistent distress across the life course will experience the most unfavourable levels of cardiovascular disease risk factors, including inflammatory indices, glucose metabolism, and lipids, some of which are also important health outcomes in their own right.

The 1970 British Cohort Study is an on-going, prospective cohort study. Based on a representative sample of people born in the UK in a single week of that year,[4] for the purposes of the present

analyses, we used distress data from sweeps administered at ages 5, 10, and 26. In childhood, the Rutter A scale was used to ask teachers and parents about the behavioural and emotional problems of the study member.[5] In adulthood, the Malaise inventory, which has been validated against psychiatric morbidity and service use,[6] was administered directly to the study members. At ages 5 and 10 years, values above the 80th centile denoted distress on the Rutter scale,[5] while at age 26 a score of ≥8 on the Malaise inventory was used.[6] 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. Mediating variables at age 34 were educational attainment, smoking status, and frequency of drinking alcohol and of taking exercise. Parents (5 and 10 year surveys) and cohort members (26, 34, and 46 year surveys) provided informed consent. The age 46 survey was approved by the National Research Ethics Service Committee for Brighton & Sussex (Ref 15/LO/1446).

Between 2016 and 2018 (ages 46-48 years), for the first time, cohort members participated in a nurse-administered, home-based clinical examination (N=8,581; 51.8% of the original sample).[7] This included an assessment of blood pressure using the automated Omron HEM-907 device, standard measurement of height and weight, and the drawing of non-fasting blood samples for analysis of blood lipids, C-reactive protein, and glycated haemoglobin. We used multiple imputation by chained equations to impute missing covariate and psychological distress data. In all, 30 imputation datasets were created for analysis of each outcome.

The maximum analytical sample was 6932 men and women. In Table 1 we show the relation between life course distress and biomarkers in mid-life. In age- and sex-adjusted analyses, with the exception of systolic blood pressure, there was some evidence that distress was related to each of

the adult biomarkers. Thus, for high-density lipoprotein, triglycerides and C-reactive protein, the least favourable levels were apparent in study members who reported having experienced persistent psychological distress, that is, in both childhood *and* early adulthood. There was also some evidence of dose-response effects across these endpoints (p[trend]<=0.014). In general, however, the magnitude of these relationships was weak and individual beta coefficients rarely attained statistical significance at conventional levels. There was some attenuation of these associations after sequential adjustment for confounding and mediating factors, such that, in multiply-adjusted analyses, there was a suggestion that only for triglyceride was the highest level seen in the persistent distress group. To further test the robustness of the distress–triglyceride association, we also controlled for adult body mass index. This had essentially no impact on the existing result. These estimates were essentially unchanged when analyses were based on the non-missing dataset (N=3178).

Our main finding that experience of persistent episodes of psychological distress across the early life course showed only weak relationships with selected biomarkers in middle-age did not provide support for our hypothesis for a deleterious effect of distress accumulation. Alongside the similarly modest associations in the few other studies of childhood distress,[2,3] this raises the suggestion of other explanations for the apparent impact of distress on mortality which include indirect effects via health behaviours, socioeconomic status, and a continuation of mental health problems into middle-age. These inter-relationships require further exploration.

While our study has a degree of novelty and is unusually well characterised across the life course, it is not without its shortcomings. The array of biomarkers captured in middle-age is modest; we had data on distress symptoms only rather than a clinical diagnosis; different questionnaires were used

to capture distress at different time points; and, inevitably for a cohort study, there was study member attrition.

In conclusion, we found little evidence of a relation of distress across the childhood and early adult life course with biomarkers in middle-age. Other candidate mechanisms linking early life disease and adult cardiovascular disease mortality should be considered.

References

1. Archer G, Kuh D, Hotopf M, Stafford M, Richards M. Adolescent affective symptoms and mortality. *The British journal of psychiatry : the journal of mental science* 2018; **213**(1): 419-24.
2. Appleton AA, Buka SL, McCormick MC, et al. Emotional functioning at age 7 years is associated with C-reactive protein in middle adulthood. *Psychosomatic Medicine* 2011; **73**(4): 295.
3. Winning A, Glymour MM, McCormick MC, Gilsanz P, Kubzansky LD. Psychological Distress Across the Life Course and Cardiometabolic Risk: Findings From the 1958 British Birth Cohort Study. *J Am Coll Cardiol* 2015; **66**(14): 1577-86.
4. Elliott J, Shepherd P. Cohort profile: 1970 British Birth Cohort (BCS70). *International journal of epidemiology* 2006; **35**(4): 836-43.
5. Elander J, Rutter M. Use and development of the Rutter parents' and teachers' scales. *International Journal of Methods in Psychiatric Research* 1996; **6(2)**: 63-78.
6. Rodgers B, Pickles A, Power C, Collishaw S, Maughan B. Validity of the Malaise Inventory in general population samples. *Soc Psychiatry Psychiatr Epidemiol* 1999; **34**(6): 333-41.
7. University of London IoE, Centre for Longitudinal Studies. 1970 British Cohort Study: Forty-Six-Year Follow-Up, 2016-2018 (http://doi.org/10.5255/UKDA-SN-8547-1): UK Data Service; 2019.

Table 1. Lifecourse psychological distress by age 26 in relation to biomarkers at age 45

	Regression coefficients (95% confidence intervals		
	Adjusted for age and sex	**Adjusted for age, sex, & other confounders[a]**	**Adjusted for age, sex, other confounders & adult mediators**
Body mass index (kg/m^2) n=6827			
No distress (n=4474)	Reference	Reference	Reference
Distress in childhood only (n=1540)	0.48 (0.06, 0.91)	0.29 (-0.14, 0.72)	0.24 (-0.18, 0.67)
Distress in adulthood only (n=512)	1.08 (0.37, 1.80)	0.95 (0.23, 1.67)	0.84 (0.13, 1.55)
Distress in both childhood & adulthood (n=301)	1.07 (0.04, 2.11)	0.76 (-0.31, 1.82)	0.62 (-0.50, 1.72)
P for trend	<0.001	0.006	0.024
Systolic blood pressure (mm Hg) n=6932			
No distress (n=4546)	Reference	Reference	Reference
Distress in childhood only (n=1569)	0.94 (-0.16, 2.05)	0.06 (-062, 1.86)	0.36 (-0.74, 1.47)
Distress in adulthood only (n=521)	0.56 (-1.41, 2.52)	-0.41 (-2.05, 1.81)	-0.03 (-2.07, 2.00)
Distress in both childhood & adulthood (n=296)	0.83 (-1.91, 3.57)	-0.44 (-3.08, 2.20)	-0.16 (-2.92, 2.61)
P for trend	0.232	0.630	0.930
High-density lipoprotein (mmol/l) n=5575			
No distress (n=3713)	Reference	Reference	Reference
Distress in childhood only (n=1257)	-0.05 (-0.09, -0.01)	-0.03 (-0.07, 0.01)	-0.03 (-0.07, 0.01)
Distress in adulthood only (n=390)	-0.04 (-0.10, 0.02)	-0.03 (-0.09, 0.03)	-0.01 (-0.07, 0.05)
Distress in both childhood & adulthood (n=215)	-0.06 (-0.15, 0.03)	-0.04 (-0.13, 0.05)	-0.02 (-0.11, 0.07)
P for trend	0.014	0.106	0.337
Triglycerides (mmol/l) n=3131			
No distress (n=2070)	Reference	Reference	Reference
Distress in childhood only (n=725)	0.26 (0.11, 0.42)	0.23 (0.07, 0.39)	0.20 (0.03, 0.36)
Distress in adulthood only (n=221)	0.20 (-0.07, 0.48)	0.19 (-0.09, 0.46)	0.12 (-0.16, 0.39)
Distress in both childhood & adulthood (n=115)	0.44 (0.12, 0.76)	0.41 (0.09, 0.73)	0.32 (-0.004, 0.64)
P for trend	<0.001	0.001	0.013
Glycated haemoglobin (mmol/mol) n=5535			
No distress (n=3673)	Reference	Reference	Reference
Distress in childhood only (n=1267)	0.92 (0.03, 1.81)	0.60 (-0.30, 1.51)	0.52 (-0.39, 1.42)
Distress in adulthood only (n=385)	1.30 (-0.16, 2.76)	1.09 (-0.38, 2.55)	0.82 (-0.69, 2.33)
Distress in both childhood & adulthood (n=210)	0.49 (-1.76, 2.74)	0.20 (-2.04, 2.44)	-0.23 (-2.47, 2.01)
P for trend	0.040	0.155	0.391
C-Reactive Protein (log units) n=3096			
No distress (n=2037)	Reference	Reference	Reference
Distress in childhood only (n=718)	0.04 (-0.01, 0.10)	0.02 (-0.04, 0.07)	0.01 (-0.05, 0.06)
Distress in adulthood only (n=221)	0.07 (-0.02, 0.17)	0.06 (-0.04, 0.16)	0.05 (-0.05, 0.14)
Distress in both childhood & adulthood (n=120)	0.10 (-0.01, 0.21)	0.08 (-0.04, 0.19)	0.05 (-0.06, 0.17)
P for trend	0.013	0.087	0.237

[a]Paternal social class, birthweight, history of hospital admission by age 5, and cognitive function at age 5.
[b]Educational attainment, smoking status, and frequency of drinking alcohol and of taking exercise at age 34.
Systolic blood pressure, high-density lipoprotein, triglycerides, and glycated haemoglobin are all corrected for medication use. Participants (N=110) with a C-reactive protein level >10 mg/L were excluded from analysis of this biomarker as this level is indicative of acute infection.