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Letters

Longer-Lived Parents and Cardiovascular Outcomes

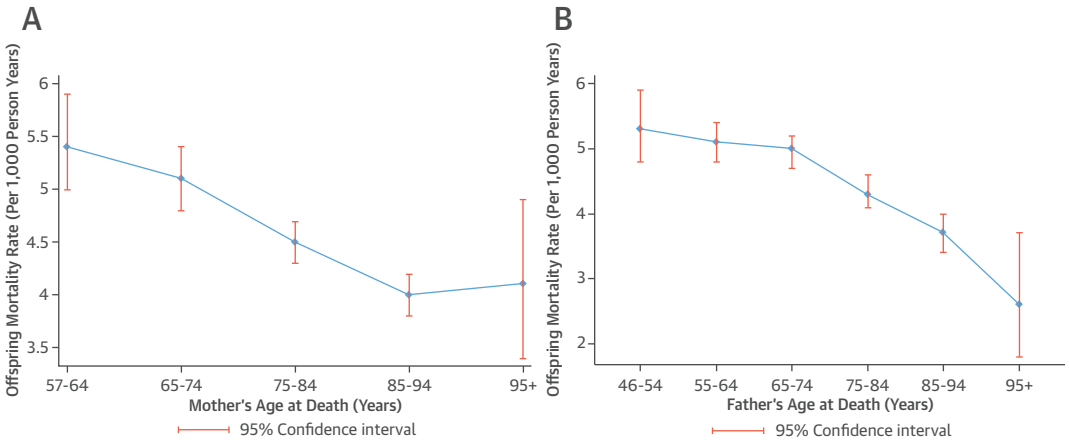
8-Year Follow-Up In 186,000 U.K. Biobank Participants

Cardiovascular risk assessment currently identifies higher risk individuals through parental histories of early onset myocardial infarction. However, having relatively long-lived parents is associated with markedly lower coronary heart disease (CHD) risks and longer survival (1,2). Parental longevity associations with other common cardiovascular outcomes are little studied. We estimated associations between parents' age at death and common incident conditions plus mortality in a large middle-aged cohort.

We included 186,151 nonadopted UK Biobank participants with deceased parents, recruited between 2006 and 2010 from England, Wales, and Scotland. We included participants 55 years of age to the recruited maximum of 73 years of age to ensure that parents' mean ages were >80 years old and that participants were above the age associated with incidence of early onset cardiovascular disease. We excluded "outlier" premature deaths (>2 standard deviations [SDs] below the mode; mothers <57 years of age; fathers <46 years of age). Follow-up data were from hospital admission records (for National Health Service hospitals in England and Scotland) and UK-wide death records (mean 6 and 5.5 years, respectively; maximum >8 years for both). We plotted the relationships between the offspring's unadjusted mortality rate and the mother's and the father's attained age, separately. Mother's and father's ages at death were also z-transformed (accounting for higher mother's age at death) and summed. Cox proportional hazards models assessed associations of parental longevity and risk of incident disease (excluding self-reported disease ascertained by baseline interview or prior inpatient data; International Statistical Classification of Diseases and Related Health Problems [rev. 10] codes from 1996) and mortality, adjusted for age, sex and risk factor differences at baseline.

At baseline (mean age: 62.8 ± 3.9 years; 53.4% female), increasing parental longevity was associated with more participant education, higher income, more physical activity, lower prevalence of smoking, and obesity. Age of mother's death and age of father's death showed inverse relationships with offspring's unadjusted mortality rate (n = 4,705 deaths) (Figure 1). Associations remained after adjustment for

FIGURE 1 Parents' Ages at Death and Offspring's Rate of All-Cause Mortality



Unadjusted rates of all-cause mortality (per 1,000 person years) in the offspring by **(A)** mother's and **(B)** father's age at death.

age, sex, ethnicity, education, income, smoking, alcohol use, physical activity, and body mass index; with increasing mother's and father's survival (≥70 years), all-cause mortality declined 16% (hazard ratio [HR]: 0.84; 95% confidence interval [CI]: 0.79 to 0.89) and 17% per decade (HR: 0.83; 95% CI: 0.78 to 0.89). Combined parental longevity was inversely associated with all-cause mortality (HR per SD increase in parents' age at death: 0.91; 95% CI: 0.89 to 0.94) and CHD mortality (HR: 0.83; 95% CI: 0.78 to 0.89) but less strongly with cancer mortality (HR: 0.92; 95% CI: 0.90 to 0.95). CHD mortality declined 20% and 21% per decade increase with mother's (HR: 0.80; 95% CI: 0.68 to 0.95) and father's (HR: 0.79; 95% CI: 0.63 to 0.98) survival ≥70 years, respectively.

Offspring of longer-lived parents had lower incidence of multiple circulatory conditions including peripheral vascular disease (HR per SD increase in parents' age at death: 0.82; 95% CI: 0.76 to 0.87), heart failure (HR: 0.86; 95% CI: 0.81 to 0.91), stroke (HR: 0.88; 95% CI: 0.83 to 0.93), hypertension (HR: 0.88; 95% CI: 0.86 to 0.91), CHD (HR: 0.91; 95% CI: 0.88 to 0.94), anemia (HR: 0.91; 95% CI: 0.86 to 0.96), hypercholesterolemia (HR: 0.93; 95% CI: 0.90 to 0.96) and atrial fibrillation (HR: 0.94; 95% CI: 0.90 to 0.97). For cancer incidence, associations were smaller, except for lung cancer. There were no significant associations with incident diabetes, colorectal/breast/prostate cancer, chronic obstructive pulmonary disease, asthma, hypothyroidism, or depression accounting for multiple statistical testing ($p < 0.002$). These results were very similar for prevalent disease.

Using UK Biobank data, we recently showed that offspring of longer-lived parents had fewer common genetic risk alleles (lower genetic risk scores) for coronary artery disease, systolic blood pressure, body mass index, cholesterol, and triglyceride levels (3). The consistency between the incident cardiovascular disease associations and the genetic findings suggest that the disease associations are causal. Overall, the results suggest that parental longevity may be a useful marker for the combined inheritance of multiple genetic and environmental/behavioral factors for common cardiovascular outcomes. To our knowledge, this is the first study that shows a protective association between parental longevity and incident peripheral vascular disease, heart failure, or atrial fibrillation. Previous studies, although with much smaller sample sizes, have also shown similar associations for all-cause and cardiovascular disease mortality, incident CHD, and stroke, and a more favorable cardiovascular risk profile in middle-aged offspring (1,2,4). Limitations include the fact that this volunteer cohort might not have been representative of the population and the limited offspring age range studied (oldest age at follow-up was 80 years). In addition, disease incidence (but not mortality) might have been underestimated for the 4% of the sample from Welsh assessment centers because hospital data were from England and Scotland only, and for diseases not strongly related to hospital admissions, e.g., hypertension. However, these underestimates are only likely to have biased results toward the null. Further work is needed to establish whether parental longevity is helpful for assessing risks for circulatory outcomes.

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