**Parental lifespan and the likelihood of reaching the age of 90 years in the Netherlands Cohort Study**

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**Aim:** Growing evidence suggests an association between parental longevity and lifespan of subsequent generations. We aimed to reproduce earlier findings, showing a positive association between parental longevity and offspring’s longevity. Additionally, we investigated whether this is mainly driven by the maternal or paternal germline in male and female offspring.

**Methods:** For these analyses, data from the oldest birth cohort (1916–17) of the Netherlands Cohort Study was used. Participants filled in a baseline questionnaire in 1986 (at age 68–70 years). Follow up for vital status information until the age of 90 years (2006–07) was >99.9% complete. Multivariable-adjusted Cox regression analyses with a fixed follow-up time were based on 2368 men and 2657 women with complete parental survival data and relevant confounders to calculate risk ratios (RR) of reaching longevity.

**Results:** In age-adjusted models, paternal and maternal age at death were significantly positively associated with reaching 90 years in both male and female offspring. In male offspring, paternal age at death (≥90 years vs <80 years) showed the strongest association with survival to 90 years (RR 1.42, 95% CI 1.07–1.89), after confounder correction. In female offspring, maternal age at death (≥90 years vs <80 years) showed the strongest association with survival to 90 years (RR 1.20, 95% CI 1.04–1.40).

**Discussion:** After confounder adjustment, stronger and significant associations were observed between paternal lifespan and male offspring longevity, and maternal lifespan and female offspring longevity. Future research should investigate through which pathways a longer lifespan of parents is transmitted to their offspring.

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**Keywords:** aging, cohort study, longevity, parental lifespan, survival.

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**Introduction**

Several studies observed that parental longevity was significantly associated with the offspring’s lifespan. Furthermore, it was found that this association was primarily present for maternal longevity, and not for paternal longevity, and also more pronounced in female offspring.

Using data from the Netherlands Cohort Study (NLCS), we aimed to reproduce earlier findings, showing an association between parental longevity and offspring’s longevity. Additionally, we aimed to investigate if these relationships differ by sex, and whether it is mainly driven by the maternal and/or paternal germline in male and female offspring separately.

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**Methods**

**Population and study design**

For the present study, data from the NLCS were used. The NLCS was set up in September 1986 as a large prospective cohort study. Participants born in 1916 or 1917 were selected to form the longevity cohort for the current longevity analyses in the NLCS (i.e. aged 68–70 years at baseline), as has been done before in other NLCS longevity studies. Follow up for vital status of the longevity cohort until the age of 90 years (2006–2007) was 99.9% complete. The date of death was collected by record linkage to the “Centraal Bureau voor Genealogie” from 1986 until 1995, and the
“gemeentelijke basisadministratie voor persoensgegevens”. Seven participants were lost to follow up due to migration before reaching the age of 90 years. After exclusion of participants with missing information on both parental and maternal survival information (n = 946), and potential confounders (n = 1836), the analyses were based on 2368 men and 2657 women.

**Exposure assessment**

At baseline, participants completed an 11-page self-administered questionnaire on diet, lifestyle and other cancer risk factors, including information on paternal and maternal year of birth. Furthermore, they were asked in what year their mother and father had died and the cause of death. Parental age at death was computed by subtracting the year of birth from the year of death, for those parents who were deceased at baseline in 1986. Additional parental cause of death information was used to check whether the father and/or mother was still alive at baseline. Parental age at baseline was used to determine the minimum attained age for parents who were still alive at baseline in September 1986.

**Statistical analysis**

Reaching the age of 90 years (yes/no) was used as our main outcome variable. For the analyses, maternal and paternal age at death were categorized as: <80, 80 to <85, 85 to <90 or ≥90 years. Participants whose father and/or mother were still alive at baseline, according to cause of death information, were only included in categorical analyses if the parental age was >90 years at baseline, to avoid misclassification of the exposure. Furthermore, parental longevity was defined as having a parent who belonged to the top 10% of survivors of their birth cohort using a dichotomous variable (yes/no). The sex- and birth cohort-specific parental longevity cut-off ages were based on national Dutch population-based survival tables. Parental birth cohorts ranged from 1850 to 1906, cut-off ages were based on national Dutch population-based survival tables. Parental birth cohorts ranged from 1850 to 1906, cut-off ages were based on national Dutch population-based survival tables. Parental longevity was determined for the mother (yes, no), father (yes, no) and combined (none, only father, only mother, both).

Baseline characteristics are presented by offspring survival status using the mean with standard deviation (SD) for continuous variables, and using frequencies (n) and percentages (%) for categorical variables. Cross-tabulations were used to examine the distribution of environmental factors according to parental survival status. Age- and multivariable-adjusted risk ratios (RR) of reaching 90 years with 95% confidence intervals (95% CI) were estimated using Cox regression models with a fixed follow-up time. Standard errors were calculated using the robust Huber–White sandwich estimator to account for underdispersion. Restricted cubic spline regression analyses were used for modeling continuous relationships between parental and maternal age at death and the chance of reaching the age of 90 years. For these analyses, three knots were used at the 10th, 50th and 90th percentile. The median ages at death of the reference category in categorical analyses were used as a reference in continuous analyses. Some additional sensitivity analyses were carried out to assess the association between dichotomous exposure variables (parental survival to 85 years [yes/no], 90 years [yes/no] and survival to top the 10% of their birth cohort [yes/no]) and offspring survival to the age of 90 years.

Confounder selection was based on earlier studies examining parental longevity and offspring’s longevity and directed acyclic graphs, using a disjunctive cause criterion approach. Confounders used for these analyses included: cigarette smoking status (never smoker/former smoker/current smoker), number of cigarettes smoked per day (continuous; centered), cigarette smoking duration (in years; continuous; centered), alcohol consumption (<0.1, ≥0.1–5, ≥5–15, ≥15–30 and ≥30 g/day), non-occupational physical activity (c ≤30, >30–60, >60–90, >90 min/day), total energy intake (kcal; continuous), body mass index at baseline (<18.5, ≥18.5–<25, ≥25–<30 and ≥30 kg/m^2), educational level (primary/lower vocational education, junior/senior high school and higher vocational/university), marital status (never married/married/divorced/widowed), number of (selected) diseases at baseline and, depending on the exposure, mutually adjusted for parental or maternal survival. Selected diseases at baseline included hypertension, heart attack, angina pectoris, stroke, any type of cancer excluding skin cancer, asthma, chronic bronchitis and diabetes. All analyses were carried out with Stata 15.0 (2017; Statacorp, College Station, TX, USA).

**Results**

Survival to the age of 90 years was more common in women (35.0%) compared with men (17.1%; Table 1). In men, those who survived to the age of 90 years were more often a never smoker (15.8% vs 8.9%), had a higher average non-occupational physical activity level (85.0 vs 72.4 min/day), more often had a higher vocational or university degree (25.3% vs 17.2%) and were more often married (90.4% vs 87.6%) compared with those who died before the age of 90 years. In women, we observed similar patterns, except for physical activity levels, which were comparable for both survivors and non-survivors (56.0 vs 55.9 min/day; Table 1).

In male offspring, paternal age at death showed a significantly positive association with survival to the age of 90 years in both age-adjusted (P-trend = 0.002) and multivariable-adjusted analyses (P-trend = 0.011; Table 2). In multivariable-adjusted analyses, men whose father died after the age of 90 years had a significantly higher chance of reaching the age of 90 years themselves (RR 1.42, 95% CI 1.07–1.89) compared with those whose father died before the age of 80 years. Compared with maternal age at death <80 years, maternal age at death ≥90 years was significantly positively associated with male offspring survival to 90 years in the age-adjusted model (RR 1.32, 95% CI 1.01–1.72) but not in the multivariable-adjusted model (RR 1.15, 95% CI 0.87–1.51). A significantly increased chance of reaching the age of 90 years was observed when only the father reached longevity (RR 1.30, 95% CI 1.02–1.65), and a somewhat weaker non-significantly increased chance when only the mother reached longevity (RR 1.16, 95% CI 0.88–1.42) compared with those of which none of the parents reached longevity. Having both parents reaching longevity was not associated with an increased chance of reaching the age of 90 years for male offspring (RR 1.04, 95% CI 0.63–1.73).

In female offspring, increasing paternal age at death was significantly positively associated with reaching longevity in the age-adjusted model (P-trend = 0.007), but not in the multivariable-adjusted model (P-trend = 0.069; Table 2). Although not significantly, paternal age at death ≥90 years pointed toward a positive association (RR 1.16, 95% CI 0.97–1.38) with offspring longevity in the multivariable-adjusted model compared with paternal age at death <80 years (Table 2). Maternal age at death was significantly positively associated with reaching the age of 90 years in both the age-adjusted (P-trend <0.001) and the multivariable-adjusted model (P-trend = 0.003). In multivariable-adjusted analyses, women whose mother had died after the age of 90 years had a significantly higher chance of reaching the age of 90 years (RR 1.20,
Parental lifespan and longevity

Table 1 Baseline characteristics of the cohort members overall and by survival status in a birth cohort of 1916–17 in the Netherlands Cohort Study on diet and cancer (1986–2007)

|                      | Men                          | Women                        |
|----------------------|------------------------------|------------------------------|
|                      | Survived to 90 years         | Died before age 90 years     |
|                      |                              |                             |
| n (%)                | 404 (17.1)                   | 1964 (82.9)                  |
| Year of birth (%)    |                              |                              |
| 1916                 | 23.5                         | 22.9                         |
| 1917                 | 76.5                         | 77.1                         |
| Smoking status (%)   |                              |                              |
| Never smoker         | 15.8                         | 8.9                          |
| Former smoker        | 56.2                         | 50.5                         |
| Current smoker       | 28.0                         | 40.6                         |
| Body mass index, kg/m^2 (mean ± SD) | 24.7 ± 2.5       | 24.9 ± 2.7                   |
| Physical activity, min/day (mean ± SD) | 85.0 ± 73.2     | 72.4 ± 59.5                  |
| Alcohol consumption, g/day | 14.1 ± 14.8     | 13.8 ± 15.8                  |
| Total energy intake, kcal (mean ± SD) | 2120 ± 469    | 2034 ± 448                   |
| Educational level (%)|                              |                              |
| Primary/lower vocational | 40.4             | 45.5                         |
| Junior/senior high school | 34.4           | 37.4                         |
| Higher vocational/university | 25.3          | 17.2                         |
| Marital status (%)   |                              |                              |
| Married              | 90.4                         | 87.6                         |
| Widow(er)            | 5.0                          | 7.2                          |
| Divorced             | 2.0                          | 2.1                          |
| Never married        | 2.7                          | 3.2                          |
|                      | Survived to 90 years         | Died before age 90 years     |
|                      | 929 (35.0)                   | 1728 (65.0)                  |

95% CI 1.04–1.40) compared with those whose mother died before the age of 80 years. Non-significant positive associations were observed with reaching the age of 90 years, for only father, only mother or both parents reaching longevity (Table 2).

For the total population, in multivariable-adjusted analyses, paternal age at death (P-trend = 0.003) and maternal age at death (P-trend = 0.001) were both significantly positively associated with reaching longevity in age-adjusted and multivariable-adjusted analyses, respectively. No statistically significant interaction was observed by sex in the multivariable adjusted analyses for the relationship of paternal age at death (P-interaction = 0.468), maternal age at death (P-interaction = 0.859) and parental longevity (P-interaction = 0.728) with reaching offspring longevity.

Restricted cubic spline analyses showed a positive association between paternal and maternal age at death and reaching age 90 years in both male and female offspring (Fig. 1). All figures showed a gradually increasing slope from the age of death ≥73 years, with steeper and statistically significant slopes observed for paternal age at death in men, and maternal age at death in women.

Discussion

In the present large prospective cohort study, we observed that parental survival to age ≥80 years pointed toward an increasing likelihood of reaching the age of 90 years in both male and female offspring compared with parental age at death ≤80 years, in age-adjusted analyses. After further adjustment for offspring environmental factors and disease history, paternal survival in male offspring and maternal survival in female offspring in particular were still significantly positively associated with an increased likelihood of reaching the age of 90 years.

Several studies have investigated the parent–offspring heritability of longevity with varying study designs and results. Most studies used cross-sectional analyses comparing multiple cohorts or cases with younger controls using historical genealogical data,15–17 as summarized by van den Berg et al.18 Of these, parental lifespan showed positive associations with offspring lifespan in all 12 studies investigating this relationship.18 When examining patterns of inheritance, most evidence was observed for the presence of a mother–daughter longevity relationship (positive association, n = 13; no association, n = 3), and least evidence for a father–daughter relationship (positive association, n = 6; no association, n = 10).18

Similar to the present study, several studies have used a prospective cohort design to study the parent–offspring longevity relationship.1–5 Three studies observed no significant association between parental age and death and male offspring longevity after confounder adjustment.1,2,4 In analyses from the Honolulu Heart Program, a significant association was observed between maternal age at death ≥80 years and male offspring survival to 90 years (OR 1.84, 95% CI 1.37–2.47) and 100 years (OR 2.26, 95% CI 1.04–4.90), respectively, but not for paternal age at death.5 However, the effect estimates were not shown.5

Regarding female offspring, in the personnes âgées QUID study, women had a significantly increased chance of reaching the age of 90 years if their mother had reached the age of 85 years or older. However, the effect estimates were not shown.5
Table 2  Age- and multivariable-adjusted risk ratios for reaching longevity according to parental survival in a birth cohort of 1916–17 in the Netherlands Cohort Study (1986–2007)

| Male offspring | median | n   | Survival | Age-adjusted RR (95% CI) | Multivariable-adjusted RR (95% CI) |
|----------------|--------|-----|----------|--------------------------|-----------------------------------|
| Male offspring |        |     |          |                          |                                   |
| Paternal age at death |        |     |          |                          |                                   |
| <80 years       | 69     | 1392| 208      | Reference                | Reference                         |
| 80–84 years     | 82     | 404 | 78       | 1.29 (1.02–1.64)         | 1.28 (1.01–1.62)                  |
| 85–89 years     | 87     | 298 | 55       | 1.23 (0.94–1.62)         | 1.16 (0.89–1.52)                  |
| ≥90 years       | 92     | 213 | 48       | 1.51 (1.14–2.00)         | 1.42 (1.07–1.89)                  |
| P-trend         |        |     |          | 0.002                    | 0.111                             |
| Maternal age at death |        |     |          |                          |                                   |
| <80 years       | 69     | 1233| 183      | Reference                | Reference                         |
| 80–84 years     | 82     | 405 | 78       | 1.30 (1.02–1.65)         | 1.19 (0.94–1.51)                  |
| 85–89 years     | 87     | 365 | 72       | 1.33 (1.04–1.70)         | 1.25 (0.97–1.60)                  |
| ≥90 years       | 92     | 297 | 58       | 1.32 (1.01–1.72)         | 1.15 (0.87–1.51)                  |
| P-trend         |        |     |          | 0.007                    | 0.112                             |
| Parental longevity (top 10% of birth cohort) |        |     |          |                          |                                   |
| None            | 1551   | 242 | Reference | Reference                |                                    |
| Only father     | 334    | 69  | 1.33 (1.04–1.69) | 1.30 (1.02–1.65) |
| Only mother     | 254    | 49  | 1.24 (0.94–1.63) | 1.16 (0.88–1.42) |
| Both            | 68     | 13  | 1.22 (0.74–2.02) | 1.04 (0.63–1.73) |
| Female offspring |        |     |          |                          |                                   |
| Paternal age at death |        |     |          |                          |                                   |
| <80 years       | 69     | 1653| 549      | Reference                | Reference                         |
| 80–84 years     | 82     | 423 | 157      | 1.12 (0.97–1.29)         | 1.10 (0.95–1.27)                  |
| 85–89 years     | 87     | 304 | 115      | 1.14 (0.97–1.34)         | 1.07 (0.92–1.26)                  |
| ≥90 years       | 92     | 216 | 88       | 1.23 (1.03–1.46)         | 1.16 (0.97–1.38)                  |
| P-trend         |        |     |          | 0.007                    | 0.069                             |
| Maternal age at death |        |     |          |                          |                                   |
| <80 years       | 68     | 1365| 435      | Reference                | Reference                         |
| 80–84 years     | 82     | 487 | 175      | 1.13 (0.98–1.30)         | 1.11 (0.96–1.28)                  |
| 85–89 years     | 87     | 397 | 157      | 1.24 (1.07–1.43)         | 1.19 (1.03–1.37)                  |
| ≥90 years       | 93     | 323 | 136      | 1.32 (1.14–1.53)         | 1.20 (1.04–1.40)                  |
| P-trend         |        |     |          | <0.001                   | 0.003                             |
| Parental longevity (top 10% of birth cohort) |        |     |          |                          |                                   |
| None            | 1803   | 606 | Reference | Reference                |                                    |
| Only father     | 334    | 128 | 1.14 (0.98–1.33) | 1.11 (0.96–1.29) |
| Only mother     | 290    | 114 | 1.17 (1.00–1.37) | 1.11 (0.95–1.29) |
| Both            | 64     | 27  | 1.25 (0.94–1.68) | 1.10 (0.34–1.47) |
| Total population |        |     |          |                          |                                   |
| Paternal age at death |        |     |          |                          |                                   |
| <80 years       | 3045   | 757 | Reference | Reference                |                                    |
| 80–84 years     | 827    | 235 | 1.17 (1.03–1.32) | 1.14 (1.01–1.29) |
| 85–89 years     | 602    | 170 | 1.16 (1.01–1.34) | 1.10 (0.96–1.26) |
| ≥90 years       | 429    | 136 | 1.31 (1.13–1.52) | 1.23 (1.06–1.43) |
| P-trend         |        |     |          | <0.001                   | 0.003                             |
| P-interaction (sex) |        |     |          | 0.539                    | 0.468                             |
| Maternal age at death |        |     |          |                          |                                   |
| <80 years       | 2598   | 618 | Reference | Reference                |                                    |
| 80–84 years     | 892    | 253 | 1.18 (1.04–1.33) | 1.14 (1.01–1.29) |
| 85–89 years     | 762    | 229 | 1.27 (1.12–1.43) | 1.21 (1.06–1.37) |
| ≥90 years       | 620    | 194 | 1.32 (1.16–1.51) | 1.19 (1.04–1.36) |
| P-trend         |        |     |          | <0.001                   | 0.001                             |
| P-interaction (sex) |        |     |          | 0.767                    | 0.859                             |
| Parental longevity (top 10% of birth cohort) |        |     |          |                          |                                   |
| None            | 3355   | 848 | Reference | Reference                |                                    |
| Only father     | 668    | 197 | 1.20 (1.05–1.36) | 1.17 (1.03–1.32) |
increased odds of reaching the age of 90 years compared with maternal or paternal survival to age 70–79 years. To increase statistical power, additional analyses were carried out in which men and women were combined. In these analyses, maternal age at death and paternal age at death were significantly positively associated with offspring reaching longevity. Furthermore, the test for interaction was not statistically significant, which might indicate that the relationship of paternal and maternal survival with reaching longevity is similar in both sexes.

Based on the existing literature and the results of our age-adjusted analyses, an older age at death of the parents seems to increase the likelihood of reaching old age in offspring. However, the observed relationship between parental longevity and offspring longevity is probably no direct causal relationship. The survival advantage of parents is most likely transferred to their offspring by...
Figure 2  A simplified conceptual representation of the relationship between parental longevity and offspring longevity.

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a combined effect of behavioral, environmental and genetic influences, as proposed in Figure 2. Health conditions, such as blood pressure and diabetes, seem to cluster within families. Furthermore, it has been suggested that offspring whose parents have an unfavorable lifestyle characteristic, such as smoking or obesity, have a higher chance of having this unfavorable lifestyle characteristic themselves. When adjusting for several offspring behavioral/environmental factors and history of (selected) diseases, the causal explanation by a common behavior/environment (pathway A) and a common vulnerability for disease (pathway C) becomes partially blocked. In these analyses, we observed that the father–son and mother–daughter longevity relationship showed somewhat stronger and significant effect estimates compared with the effect estimates of the mother–son and father–daughter longevity relationship. This could imply that genetic or residual confounding factors of the “A” and “C” pathway have a more prominent role in the heritability of old age survival between fathers and sons, and mothers and daughters. Based on earlier studies, it is estimated that approximately 20–30\% of human longevity can be attributed to genetic factors, of which single-nucleotide polymorphisms in the apolipoprotein E gene and the forhead box O3A gene are the most important genetic alterations associated with longevity.

In contrast to the current study, other prospective cohort studies observed no significant father–son longevity relationship; however, no effect estimates were shown. Among the aforementioned genealogical studies, eight observed a father–son longevity association, whereas an equal number (\(n = 8\)) observed no association. Therefore, more studies are required to investigate whether the present findings can be replicated in other cohorts as well.

More consistent evidence exists for a mother–daughter longevity relationship. The consistent sex-specific findings between mother and daughter could hint toward an important role of variations in inherited mitochondrial DNA (mtDNA) in the process of reaching longevity, which is transmitted through the maternal germline only. Several studies have found an association between longevity and mtDNA variants of haplogroup J in several European countries, and with mtDNA variant haplogroup D in Japan. In these studies, it was observed that these haplogroups were more common among centenarians than in ethnically matched younger controls. However, these findings could not be replicated in other geographical populations, which indicates that the effect of certain mtDNA variations depends on the individual-specific genetic background.

In analyses of the Framingham study, an increased odds of reaching the age of 75 years was observed per one parent increase in survival to 75 years. In the Iowa-established populations for epidemiological study of the elderly study, women were more likely to reach the age of 97 years when one or both parents survived to the age of 85 years compared with none of the parents surviving to 85 years. In the Women’s Health Initiative (WHI) trial, both parents surviving to 90 years was associated with an increased odds of reaching 90 years in female offspring. We did not observe an additional increased chance of reaching 90 years when both parents reached longevity in both men and women. A similar relationship was observed in analyses where men and women were combined. However, the absolute number of participants of which both parents reached longevity was very small, which makes it difficult to draw any conclusions based on this finding. We also observed a notably higher percentage of current smokers in these specific groups, which might have also altered the present results (Table S1).

The current analyses confirm the hypothesis that the chance of reaching longevity is related to parental lifespan. However, the causal explanation for this relationship remains unclear. Future studies should explore potential pathways through which longevity can be passed on by earlier generations.

Strength of the present study were the prospective study design, which limited the risk for selection and information bias, and the detailed information collected on confounding factors. Furthermore, the study population was very homogenous with respect to age, making confounding by age unlikely.

There were some limitations to the present study. First, the men and women included for our analyses had already survived to an advanced age, which might have led to survivorship bias. Second, only limited information on parental vital status was available for participants with missing data on parental age at death, including those whose parents were still alive at baseline. Because these parents most likely survived to older ages, this might have led to a higher dropout rate of participants whose parents survived to
advanced ages. Finally, all causes of death of the parents and offspring were taken into account for these analyses, instead of natural causes of death only. These biases might have led to an underestimation of the true relationship between parental lifespan and offspring lifespan.

In conclusion, we observed that paternal age at death was significantly positively associated with reaching the age of 90 years in men, and maternal age at death was significantly positively associated with reaching the age of 90 years in women. Weaker, non-significantly, positive associations were observed between maternal age at death and reaching 90 years in male offspring, and between paternal age at death and reaching 90 years in female offspring. Regarding parental longevity, paternal longevity showed the strongest association with reaching the age of 90 years in male offspring.

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Disclosure statement

The authors declare no conflict of interest.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher’s website:

Table S1 Baseline characteristics of the cohort members by survival status of parents in a birth cohort of 1916–17; Netherlands Cohort Study on diet and cancer (1986–2007).

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