

**Cancer: Are offspring of long-lived siblings both robust and resilient?**

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Resilience is one of the components for successful aging and is related to wellbeing in late life. Studies have shown that older people living alone have low resilience. However, most of these studies were mainly conducted on unhealthy participants. The aim of this study is to examine the factors that contribute to resilience of healthy older adults living alone. Older people living alone who are not subject to public health care service provided to the economically or physically challenged or depressed people were recruited. Data collected from 295 participants were used to conduct hierarchical multiple regression analyses, controlling demographic characteristics, level of cognitive and physical functions, and emotional status. A self-reported questionnaire, UCLA Loneliness Scale, Lubben Social Network Scale (LSNS), and Multidimensional Individual and Interpersonal Resilience Measure (MIIRM) were used to measure study variables. A hierarchical model accounted for 48.8% of the variance in resilience. In model 1 (demographics), the religion ( $\beta=.178$ ,  $p<.001$ ) and the perceived economic status ( $\beta=-.176$ ,  $p<.001$ ) variables were significantly related to resilience. The subjective health ( $\beta=-.109$ ,  $p=.038$ ) in model 2 (level of function) and the loneliness ( $\beta=-.379$ ,  $p<.001$ ) in model 3 (emotional status) had a significant effect on resilience. In model 4, the size ( $\beta=-.115$ ,  $p=.029$ ) and the frequency ( $\beta=.160$ ,  $p=.003$ ) of social networks significantly predicted resilience. The results showed that protecting older adults' social networks could lead to promote their health and wellbeing. What can be inferred from this finding is that even though the members are small, the social network they often have contact with is important for the resilience of older adults living alone.

#### CANCER: ARE OFFSPRING OF LONG-LIVED SIBLINGS BOTH ROBUST AND RESILIENT?

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Background: The mechanisms underlying clustering of longevity in families are unclear. We have previously shown a low cancer incidence in offspring of long-lived siblings, i.e. cancer robustness. Here we test whether such offspring are also more resilient in terms of survival after cancer diagnosis. Methods: Identification of offspring from long-lived families was undertaken in three nationwide, consecutive Danish studies (DOS, GeHA, LLFS). Cancer cases were identified through linkage with the Danish Cancer Registry. Each offspring cancer case was matched with two control cancer

cases from the 5% random sample of the Danish population. Matching criteria were birth year, sex, year of diagnosis and cancer site. The main outcome was overall survival. Factors studied were sociodemographic, health-related and cancer-related. Survival analyses were performed using stratified Cox proportional hazards models based on the matching data. Results: Among the 5,377 offspring of the 634 families, 465 offspring of long-lived siblings with first primary cancer were included, along with 930 controls. Offspring of long-lived siblings had a significantly better survival than controls (HR=0.64 95%CI=[0.52-0.78]). The association attenuated only slightly after adjustment of marital status, education, Charlson Comorbidity Index, and number of prescribed drugs (HR=0.66 95%CI=[0.54-0.81]). Conclusion: Our results suggest that in addition to being more robust to cancer risk, offspring of long-lived siblings are also more resilient to cancer after its diagnosis and show better overall survival compared to individuals with cancer from general Danish population. Funding: The LLFS study is funded by the US National Institute on Aging / National Institutes of Health.

#### BIOLOGICAL AGING IS ASSOCIATED WITH INCREASED MONOCYTE INFLAMMATORY ACTIVITY IN OLDER ADULTS

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Chronic inflammation is thought to play a central role in biological aging. However, the causes of chronic inflammation are not fully elucidated. We hypothesized that a dysregulation in monocyte inflammatory activity may contribute to chronic inflammation and biological aging. There are no validated methods for Biological Age (BA) estimation. Therefore, we also hypothesized that older adults with a recent ED (Emergency Department) admission had a higher BA compared to age-matched older adults without a recent ED admission. Two groups of older adults were enrolled: a "high BA"-group who were discharged from the ED four weeks preceding data collection (n=52), and a "low BA"-group consisting of age and sex matched participants without ED admission within the two years preceding data collection (n=52). We assessed NF- $\kappa$ B phosphorylation (Ser529) and NLRP3 inflammasome levels in monocytes using flow cytometry staining of whole blood. Preliminary analyses showed that participants had a median age of 74.8 (IQR: 70.7–82.0) years, 48% were women. Participants in the high-BA group had reduced lower body strength (30 seconds chair stand test  $p=0.02$  and 4 meters gait speed  $p=0.001$ ) and cognitive function (Digit Symbol Substitution Test  $p=0.001$  and Trail Making Test  $p=0.002$ ) compared to the low-BA group. Monocytes of participants in the low BA group had lower constitutive p-NF- $\kappa$ B ( $p<0.0001$ ) and NLRP3 ( $p=0.0001$ ) median fluorescence intensity compared to the high BA group. Increased monocyte inflammatory activity assessed by p-NF- $\kappa$ B and NLRP3 was associated with a higher BA. We will investigate associations between monocyte inflammatory activity and markers of chronic inflammation.