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A review of centenarian studies

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Abstract

Studying centenarians requires a 'positive biology' approach, where rather than focusing on disease, the research aims to understand the causes of positive phenotypes and explain biological mechanisms of health and longevity. This review outlines characteristics of the key centenarian studies. Variables that may relate to longevity of these oldest old are also described, including cardiovascular health, cognitive function, physical ability, mental and cognitive health, personality and the social circumstances of the centenarian.

Introduction

Studying centenarians requires a 'positive biology' approach, where rather than focusing on disease, the research aims to understand the causes of positive phenotypes and explain biological mechanisms of health and longevity. Healthy ageing and longevity is likely due to the interaction between genetics, environment and social factors, while it is the modifiable factors, such as diet, physical activity and other lifestyle or social changes that can be applied as public health strategies or interventions.^[1]

Successful ageing encompasses the domains specified in the revised Rowe and Kahn's model: maximise physical and mental abilities, minimise risk and disability, engage in active life and maximise positive spirituality.^[2] It is hoped that centenarian studies will clarify how to achieve successful ageing for the general population.

There are several potential challenges in carrying out centenarian studies: firstly the ages need to be verified through birth certificates. It may be difficult to arrange assessments due to frailty, illness or even death of the participants, with a need to consider their physical and mental state during the review. Hearing impairment may also cause difficulties in carrying out interviews. However, there are lessons from other centenarian studies, including protocols from various localities, such as the Sevilla and Castilla y Leon Centenarian Study.^[3]

Geographical Variation

Different countries have different levels of mortality selection based on a study of nonagenarians and centenarians living in the 5 low mortality countries (Denmark, France, Japan, Switzerland and Sweden). Based on the 5-Country Oldest Old Project (5-COOP), there are 3 levels of mortality selection: milder in Japan, stronger in Denmark and Sweden, and intermediary level in France and Switzerland. There is a need to study if there is a trade-off between the level of mortality selection and functional health status.^[4]

Two Centenarian studies in Portugal found regional differences in morbidity profiles and healthcare use. Among 241 centenarians, the predominantly urban participants had a higher average of 4.8 self-reported illnesses compared to the rural participants (2.96), who had lower levels of physical and cognitive impairment, and less people who had the three most common diseases leading to mortality (heart disease, non-skin cancer and stroke).^[5]

Physical, sensory and cognitive functions were compared between the Tokyo and Georgia centenarian studies (304 and 245 participants respectively) in terms of sensory impairment (vision and hearing) and physical function based on activities of daily living (eating, grooming, dressing, transporting, bathing and walking). The Georgia cohort had higher levels of functioning in all domains, with the Tokyo cohort showing a strong association between cognitive and sensory function with physical function.^[6]

Genetic Factors

There is a strong genetic component to longevity as shown in the Okinawa Centenarian Study, where their siblings had survival advantages (female siblings 2.58 fold and male siblings 5.43 fold) likelihood of reaching age 90 years and older compared to their birth cohorts. APOE lipoprotein genetic variants have been shown to consistently be associated with longevity, with a need to explore further relevant genetic contributors to this cohort.^[7] Four centenarian studies also suggested that specific FOXO3 single-nucleotide polymorphisms were also associated with longevity.^[8]

Key Centenarian Studies

The Georgia Centenarian Study was carried out in three phases:

Phase 1 (1988-1992): cross-sectional review of adaptation characteristics of community dwelling and cognitively intact older people (60-69, 80-89, 100+),

Phase 2 (1992-1998): Longitudinal follow-up of the three cohorts,

Phase 3 (2001-2007): Comprehensive, population based to identify longevity genes, assess neuropsychological and physical functioning, and characterise the resources and adaptations of centenarians. This paper describes methodological concerns and pitfalls, with an emphasis on the need for a multidisciplinary team to work across disciplines to resolve problems and issues.^[9]

The New England Centenarian Study evaluated 14 age-associated comorbidities, alcohol and tobacco usage as well as the Blessed Roth Memory-Concentration (BRMC) test for cognitive screening. The following comorbidities were asked: hypertension, congestive heart failure, heart attack, cardiac arrhythmia, diabetes, stroke, non-skin cancer, skin cancer, osteoporosis (including history of non-traumatic hip, wrist or spinal fracture after age 50 years), thyroid dysfunction, Parkinson's disease, dementia, COPD (emphysema / bronchitis and cigarette smoking 2 pack years or more), cataracts. Based on this, the centenarians were classified into three morbidity profiles:

- Survivors - diagnosis of age-associated illness prior to age 80 years (24% male, 43% female)
- Delayers - delayed onset of age-associated illness until at least age 80 (44% male, 42% female)
- Escapers - attained 100th year of life without age-associated illness (32% male, 15% female)^[10]

The study of Danish centenarians involved an interview (sociodemographic characteristics, activities of daily living, living conditions, need of assistance from other people, former health and current diseases, current medication) and a clinical examination (dementia screening test, heart and lung auscultation, neurological assessment, height and weight, electrocardiogram, arm and ankle blood pressure, assessment of hearing and vision capacity, a short physical performance test, bio-impedance, lung function test, blood test). This study found that among 207 centenarians, there was a high prevalence of diseases and chronic conditions, with 25 autonomous (functioning well physically living at home without dementia) and 182 nonautonomous centenarians^[11]

The China Hainan Centenarian Cohort Study (CHCCS) coordinated an interdisciplinary research team to conduct a longitudinal observational study of centenarians from Hainan, China. Among the 1811 centenarians present in their registry, 1002 participated in this study. The comprehensive baseline data collection included sociodemographics, functional capacity, cognitive function, mental health, behaviours, habitual diet (11-item Semi-Quantitative Food Frequency Questionnaire), sleep quality (Pittsburgh Sleep Quality Index - PQSI), quality of life (EQ-5D), family information, social support / relations, environment, economic status, health service use and reproductive history. The medical or clinical examination included health conditions, anthropometric measurements, falls, general pain, physical function, physical examination, ECG, ultrasonography and dental examination. Biological specimens taken included blood analysis, saliva DNA, hair analysis for trace elements, faeces examination and a gynaecological check-up. This study aims to evaluate their physical, mental and social situations, as well as establish healthy ageing indicators that may be used to plan and implement population-wide health interventions.^[12]

Cardiovascular health and cognitive functioning

A study of Tokyo centenarians found that 95% had chronic diseases - hypertension, heart disease, stroke, fractures, cataracts. However, diabetes mellitus was relatively uncommon.

Among Georgian centenarians, there were 2 clusters:

1. cardiovascular disease, pneumonia, osteoporosis, anaemia, cancer;
2. dementia, psychiatric disorders, neurological disorders

The Danish study identified a relatively high rate of vascular risk factors: hypertension (52%), myocardial infarction (27%) and stroke (22%).

However, a study based in Australia identified a low prevalence of osteoporosis, dementia, cardiovascular disease, respiratory illness, cancers, anxiety and depression.^[13]

The Longitudinal Study of Danish Centenarians evaluated participants within 3 months of their 100th birthday. This involved a sociodemographic interview, evaluating the family background, education, occupation, lifestyle. Assessment of ADLs included Katz's ADL index and IADLs (Lawton and Brody). Cognitive function was assessed with the MMSE. A proxy was interviewed regarding short and long term memory, ability to recognise other people, find their way home, recall time of the year, understand messages and make decisions. Specific questions regarding health conditions were also asked. Physical examination included the neurological examination, blood pressure and ECG. This study found that 51% of the centenarians had mild to severe dementia; of which 12% had diseases contributing to dementia (Vitamin B12 or folate deficiency, hypothyroidism, Parkinson's disease), and 0% had at least one or more cardiovascular and cerebrovascular risk factors.^[14]

Physical Abilities

The Georgia Centenarian Study assessed physical performance to identify normative data for the Short Physical Performance Battery (SPPB), which consists of three standing balance measures, five continuous chair stands and a 2.44 metre walk. For those who are physically weak or immobile, the items on the Physical Performance Mobility Exam (PPME) not included in the SPPB was used - this included bed mobility (lying to sitting), transfer from sitting on the edge of the bed to sitting on a chair, and stepping up one step with or without use of a bed handrail. The GCS Composite Scale, Direct Assessment of Functional Status (DAFS), grip strength and knee extensor strength were also assessed. This found that the GCS Composite Scale performed better than SPPB or PPME, correlating with performance on ADLs, IADLs, grip strength, leg extensor strength and predictive of longer time to mortality.^[15]

Mental Health

The Fordham Centenarian Study carried out in New York City assessed the physical, cognitive, social and mental health in near-centenarians and centenarians. They were interviewed based on physical functioning (number of diagnosis, subjective health and functional status), cognitive functioning (MMSE, Global Deterioration Scale), social resources (6-item Social Network Scale) and their mental health (Geriatric Depression Scale, 5-item Satisfaction with Life Scale). This

study found that despite limited physical function and social resources, they were in good mental health, suggesting high resilience and ability to adapt to age-associated challenges. A large proportion still living in the community highlighted their desire for leading an autonomous life.^[16]

In Hong Kong, a quantitative study of 153 near-centenarians and centenarians exploring biopsychosocial correlates of health and 'living long' used two validated tools: the Chinese Longitudinal Healthy Longevity Survey and the Elderly Health Centre questionnaire.^[17] From this group, they identified six community dwelling participants, who were physically and cognitively well for a qualitative study. Four themes were identified: positive relations with others, positive events and happiness, hope for the future and a positive life attitude.^[18]

Cognitive Health

In terms of cognitive performance, the Georgia Centenarian Study administered the Mini-Mental Status Exam, Severe Impairment Battery (for significantly cognitively impaired individuals or lower levels of performance) and Behavioural Dyscontrol Scale (executive function). There was a greater variation and dispersion in performance, as well as a stronger association between age and performance for centenarians.^[19]

In the US New England Centenarian Study, a neuropsychological test battery was used, including the MMSE, Mattis Dementia Rating Scale, Boston Naming Test (CERAD), Trail-Making Test A & B, Clock Drawing, Drilled Word Span Test, Cowboy Story (Boston-Rochester Test), Presidents since Franklin Roosevelt, Geriatric Depression Scale, Telephone Interview for Cognitive Status (for visual impairment), Test for Severe Impairment (if score 10 or less on MMSE), Tactile Naming (for visual impairment, unable to see the Boston Naming Test), Informant Cognition and Health History, Informant Psychiatry history, NEO-Five Factor Inventory (self-report and observer report), Clinical Dementia Rating Scale and Spiers' Calculations. The Hachinski scale was used to estimate the risk of vascular dementia. Of the 43 centenarians, 64% had some degree of dementia. CDR scores correlated significantly with Barthel Index scores.^[20]

The Sydney Centenarian Study was interested in brain health and sought to identify the cognitive profile of centenarians, relate cognition to brain imaging (MRI) and neuropathology (brain donors) and to establish a centenarian phenotype from neuropsychiatric, medical, nutritional and lifestyle perspectives. This was done in several phases, starting with a brief cognitive assessment, including the Addenbrooke Cognitive Examination Revised (ACE-R), an in-depth neuropsychological assessment, informant-based assessments, as well as utilisation of health services. MRI brain scans, blood tests, follow-up neuropsychological and medical assessments six-monthly as well as possible brain donation for neuropathology evaluation.^[21]

A study of centenarians correlating the pre-mortem cognitive tests and neuropathology identified on postmortem found a wide range of AD-type neuropathological changes on both dementia and non-dementia participants. While AD-type

pathology was associated with severe dementia and poor cognition, the heterogeneity of pathophysiological findings suggest the complexity and interaction of other variables for cognitive impairment in centenarians.^[22]

The International Centenarian Consortium - dementia (ICC-dementia) is a consortium that aims to harmonise global centenarian studies to describe the cognitive and functional profiles of the oldest-old, the prevalence and incidence of dementia and to identify their trajectories of decline. This should enable pooling of a large, heterogenous group to understand protective and harmful factors for brain health across diverse ethnoracial and sociocultural populations.^[23]

Personality

The Australian Centenarian study applied the NEO Five Factor Inventory (NEO-FFI), Connor-Davidson Resilience Scale (CD-RISC) and Life Orientation Test Revised (LOT-R) to evaluate different dimensions of the participant's personalities. They found that centenarians were low in openness and extraversion, high in neuroticism; with cognitively intact participants having higher levels of agreeableness. It is unclear whether these reflect their background personalities or changed due to their advanced age, psychosocial factors and changes in life circumstances. However, these may facilitate positive health behaviours contributing to their longevity.^[24]

The Tokyo Centenarian study similarly applied the NEO-FFI and found that their cohort had higher openness, with females having higher conscientiousness and extraversion. The authors suggested that these personality traits contribute to longevity by having positive effects on health-related behaviours, stress reduction and improved adaptation to problems.^[25]

Social Support

Second Heidelberg Centenarian Study measured socio-demographic characteristics, subjective health, number of health conditions (Health Conditions subscale of the MAI), functional competence (ADL, IADL using modified OARS Multidimensional Functional Assessment Questionnaire), cognitive impairment (Global Deterioration Scale), core social network, residence, living arrangements, daily help sources and types. Among the 112 centenarians, children were the main source of support while those without children were more likely to have friends or neighbours involved.^[26]

100-plus study (www.100plus.nl) is a prospective cohort study of cognitively well Dutch centenarians, their first-degree family members and respective partners. Demographics, life history, medical history, genealogy, neuropsychological data and blood samples were collected, in addition to optional PET-MRI scans, faeces donation and post-mortem brain donation. This study found that these centenarians had higher levels of education, higher socioeconomic background, higher socioeconomic status and had more children. A third carried the APO-E2 allele.^[27]

Quality of Life

An Italian centenarian study compared the quality of life between centenarians with participants aged 75 to 85, and 86 to 99 years. The Profile of Elderly Quality of Life (PEQOL) and the LEIPAD quality of life assessment instruments were used. This study found that although centenarians had greater functional disability, they complained less spontaneously about their health, had well-preserved cognitive function, scored lower for anxiety and depression, and had greater satisfaction with their social and family relations and life in general.^[28]

Conclusion

There are many aspects to learn from centenarians, ranging from geographical variation, genetic and lifestyle factors, physical and cognitive function, personality traits, available social support and quality of life.

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