Centenarian research in the past two decades

LW Poon1 PhD, SLK Cheung2 PhD

1 Institute of Gerontology, University of Georgia, Athens, Georgia, USA
2 Department of Social Work and Social Administration, The University of Hong Kong

Correspondence to: Dr Leonard W Poon, Institute of Gerontology, University of Georgia, Athens, Georgia, USA, 30606. E-mail: lpoon@uga.edu

ABSTRACT

Longevity research has increased in recent decades as the numbers of oldest old and centenarians have increased around the world. At the same time, the breadth of focus of longevity research has expanded and methodological approaches have become more robust. This paper reviews the demographic change seen in industrialised countries and the state of the literature on centenarian research, summarising findings from some of the major longitudinal studies.

Key words: Aging; Demography; Longevity

INTRODUCTION

Throughout history, there has been a search for the secrets of longevity. In Chinese culture, for example, happiness and longevity are regarded as important determinants of a high quality of life, well-being, and successful ageing. Elders are honoured and respected. These concepts are similar in most, if not all, cultures.

The scientific study of mechanisms that contribute to human longevity has emerged over the past 50 years. Four reasons account for the earlier lack of such studies. Firstly, the number of people aged over 100 years was small until the past several decades. The United States has the largest number of centenarians; there were 37,306 centenarians in 1990, 72,000 in 2000, 131,000 in 2010, and it is projected that there will be 834,000 in 2050. Early studies of these long-lived individuals were mostly descriptive. It was difficult to identify or replicate factors that contributed to longevity. Secondly, sample sizes of most early studies were small, precluding generalisation to the population of long-lived people overall. Thirdly, only a few isolated domains, such as health habits and presence of specific diseases, were investigated. These studies lacked power to compare or contrast hypotheses or mechanisms contributing to longevity. Fourthly, not until recent decades have there been systematic studies with sufficient sampling power and representative samples in order to test and contrast different multidisciplinary hypotheses of longevity and to generalise possible mechanisms and principles of longevity.

Pioneering studies of the oldest old tended to be small samples, descriptive in nature, and not driven by theories of longevity. Most longevity studies have been biologically based, with less than one-third of studies examining behavioural and social aspects of longevity.1 This paper aims to review demographic changes around the world that signify the emergence of centenarians as an important segment of the population. This development mandates new knowledge about the characteristics of this population, as well as information on adaptation and maintenance of quality of life. The literature on centenarians is also reviewed, and recommendations for the next era of longevity research are provided.

CHANGING DEMOGRAPHICS

In the past 2 decades, demographic features of all industrialised countries have changed significantly. People are living longer. In 2006, there were about 500 million people aged 65 years and older in the world. By 2030, over one billion or 1 in 8 people will be over 65 years of age. At the end of World War II, the average lifespan in Japan, Hong Kong, Singapore, and South Korea was about 45 to 50 years. Now, populations in these countries are among the longest-lived in the world.

The demographic profile of societies is also changing. The traditional demographic structure is similar to a pyramid, as the number of younger people is proportionally larger. The population pyramid is becoming a rectangle, owing to increased lifespan and decreased birth rate. The ‘rectangularisation’ of the population profile leads to a lower dependency ratio, with fewer in the working population supporting the non-working and retired populations. With very low birth and marriage rates, the population rectangle could become an inverted pyramid, in which the dependency ratio is so low that it would threaten the existence of a society. This could be an
impending crisis in some countries, such as China, that have fostered a one-child policy, with decreasing birth and marriage rates. The transformation of the population pyramid to a rectangle is an ongoing process in Asia.2

The rate of population ageing in different countries varies considerably. Among industrialised countries, populations in Asian countries are ageing fastest. France took 115 years (from 1865 to 1980) to increase its population aged ≥65 years from 7 to 14% of the total population. In the United States, the process is estimated to take 69 years (from 1944 to 2013). In Japan, it took merely 26 years (from 1970 to 1996). Those Asian countries that are experiencing a rapid increase in average lifespan are also experiencing rapid ageing of their population.3,4 The implication of these changes are significant in terms of economics, work production, worker age profiles, dependency ratios, family structures and relations, caregiving, institutionalisation, leisure, and policies associated with health care, welfare, and retirement. There is a need to better understand the biology, psychology, sociology, health and disease, survival, successful adaptation, and quality of life and well-being of the oldest old.

CENTENARIAN RESEARCH

A search of the literature (using the PubMed database) identified 1402 articles on the oldest old in the year 2000. In 2011, the number of publications increased by more than 500 to 1952. There is a need for new information for the care and welfare of the emerging oldest-old populations. In Europe, 17 countries have conducted oldest-old or centenarian research. These are Azerbaijan, Belgium, Denmark, Finland, France, Georgia, Germany, Greece, Hungary, the Netherlands, Poland, Italy, Russia, Spain, Sweden, Switzerland, and the United Kingdom. In Asia, such studies have been reported from Mainland China, Hong Kong, India, Japan (including Okinawa), South Korea, and Taiwan. In the United States, such studies have been reported in the states of California, Florida, Georgia, Iowa, Idaho, Louisiana, New England, New York, and Utah. In Australia, 3 centenarian studies have been reported. In South America, such studies have been initiated.5

The largest survey of centenarians was started in 1990 by the IPSEN Foundation in France.5 During January 1990 to April 1991, of 910 subjects enrolled, 800 were verified as centenarians and underwent medical examination.5 In addition, the familial aggregation of longevity was studied in the relatives of the longest-lived woman, Jeanne Calment, who died in Arles, France on August 4, 1997, at the age of 122 years and 164 days. Genealogical data were collected, and 62 of her immediate ancestors were noted to live longer than the matched controls.5

Previous studies have been affected by methodological shortcomings such as a cross-sectional design, convenience sampling, and lack of appropriate controls.6 In Denmark, in the longest longitudinal population-based study, centenarians from the 1905 cohort were identified through the Danish Civil Registration System from 1977 to 2004. There were 40 355 individuals alive in the cohort. The Danish centenarians experienced fewer hospitalisations and hospital days than their shorter-lived contemporaries did.7 The Longitudinal Study of Danish Centenarians from 1995 to 1996 (the 1895 cohort) included 276 centenarians, whereas the Danish 1905 Cohort Survey included 225 centenarians. The 1905 cohort displayed better self-reported activities of daily living (ADL) than the 1895 cohort did.8 Exceptional longevity in the 1905 cohort was not associated with excessive level of disability.9 Of 207 centenarians, 20% of women and 44% of men were able to perform all selected ADL independently.10 Although the prevalence of common chronic diseases was high, a minor proportion of centenarians remained cognitively and functionally intact.11

In Italy, 38 centenarians (mainly residing in Padua) were interviewed between October 1992 and July 1995.12 Their cognitive function was reasonably preserved and they had lower scores for anxiety and depression than subjects in the 2 younger groups. They considered themselves as religious and satisfied with their financial situation. They reported greater satisfaction with life and with social and family relations than less elderly individuals did. Protective factors that may contribute to healthy longevity were investigated. Nonetheless, the study had methodological shortcomings such as small convenience samples from one homogeneous geographical area.

In the AKEA study in Sardinia13 and the AKEA study in the province of Mantova (northern Italy),14 the sociodemographic, clinical and genetic characteristics of near-centenarians and centenarians were identified using multidimensional home interviews. The long-standing isolation, low immigration rate, high endogamy, and rather uniform lifestyle of Sardinia has enabled study of genetic traits associated with extreme longevity and successful ageing. Biomarker and genetic analysis associated with longevity has been performed.15,16 The Mantova oldest old were quite heterogeneous, likely owing to genetic and/or environmental and lifestyle factors. From 1997 to 2003, 53 persons aged ≥105 years from 44 municipalities on Sardinia were identified (the AKeA2 project). Familial determinants affecting the longevity of Sardinian centenarians were studied; longevity occurred among the ascendants of a particular family branch, although the findings were provisional.18

In epidemiological studies conducted as part of the Italian Multicenter Studies on Centenarians (IMUSCE), 602 centenarians were enrolled from various regions of Italy. They were in good health, autonomous, had good physical and cognitive capacity, but not engaged in social or productive activities.19 Compared to Italian oldest olds in Calabria,20 gender-specific healthy longevity characteristics were highlighted. Males had better physical performance and lower co-morbidity than females.
Ultra-nonagenarians had a lower incidence of diabetes, osteoporosis, and gastric ulcer.20

In the Swedish Centenarian Study, 100 centenarians born in 1887 to 1891 from southern Sweden were interviewed.21 The centenarians were characterised as more responsible, capable, easygoing and less prone to anxiety than the population in general, although the variation in performance DSM III-R was wide.21 Individual characteristics (physiological reserve, health and functional status) and chance appear important for centenarian survival.22 Levels of survival-promoting (salutogenic) and survival-reducing (pathogenic) markers play an important role in determining the outcome at exceptional ages.22 Stochastic determinants such as ‘accidental’ risk factors for death may dominate over programmed factors (family longevity) in determining survival.22

Summary of centenarian studies conducted in Europe are shown in the Table.5,10-13,14,20,23-36 Centenarian studies have ranged from unstructured interviews with a few selected participants to systematic studies of biology, clinical medicine, psychology, sociology, and anthropology of ageing processes with population-based samples. Examples of long-standing centenarian studies are the Longitudinal Study of Danish Centenarians,6,10,11 the Okinawa Centenarian Study,37 the US Georgia Centenarian Study,38,39 and the US New England Centenarian Study.40

Apart from centenarian studies, there are oldest-old studies in Switzerland, the United Kingdom, and Sweden. In Switzerland, family contacts and the presence of a close friend have been shown to assist in the maintenance of good functional health.41 The family environment may also prevent further disability among the oldest old in the future.41 In the United Kingdom, the capability and levels of dependency of the cohort were diverse. A remarkably high proportion of the oldest old remain independent, particularly men.42 However, a considerable proportion of this population require 24-hour care at home or in care homes.43 In Sweden, oldest-old studies such as the SWEOLD,44,45 the Kungsholmen Project,46 the Umea 85+,47 Octogenarian Twins study (OCTO-Twin),48 and Good Aging in Skane49,50 have examined health status, living conditions, and factors affecting quality of life and survival in terms of health, finances, housing, social relationships, activities, political resources, etc.

To uncover replicable mechanisms that contribute to longevity and successful adaptation, a broad perspective of ageing theories, methods, data, history, and interdisciplinary approaches is needed, as is understanding the paradox that living longer is different from living well and that life is only worth living to a second century if it comes with satisfactory levels of health, autonomy, and functioning. Investigators need to adapt an interdisciplinary ‘biopsychosocial’ approach in order to understand primary and interactive factors across the spectrum of group and individual differences in biological, sociological, and psychological adaptive functions. Different studies from different countries have different aims. Coordinated efforts across studies or countries or the comparison and contrast of theoretical positions remain limited, with the exception of the Genetics of Healthy Aging in Europe study and the 5-Country Oldest Old Project (including Denmark, France, Japan, Switzerland, and Sweden).

REVIEWS OF CENTENARIAN RESEARCH

In the 2007 Annual Review of Gerontology and Geriatrics, the ‘biopsychosocial’ approach to longevity was adopted.1 This review began with the quote: “Though exceptional human longevity has captured the imagination for millennia, it has been only in the past 15 years or so that some of the secrets to very long lives are finally giving way to scientific inquiry.” This annual review took into account the methodological and design dilemmas and pitfalls faced in conducting centenarian research. It then offered potential methodological cautions and solutions to problems that had plagued earlier studies. The review offered guidance in locating literature and data sources for primary and secondary information on centenarians and the oldest old. A list of the world’s oldest old was included, and difficulties in compiling such a list were discussed. The review then focused on the biology and genetics of longevity. This section outlined questions relating to the stochastic processes in ageing, lifespan extension, the contribution of nature and nurture in exceptional longevity, and the benefits of focusing on centenarians’ offspring for longevity research. The review then focused on new findings from psychological perspectives on longevity. This section updated findings on the impact of personality and coping skills, social support and cognitive function on survival and longevity. The review then focused on research methodologies. This section examined data quality of available datasets, qualitative methods, development of models, and a discussion of methodological issues and considerations by using the Georgia Centenarian Study as a case study. A primary contribution of this review was to reveal problems and issues of earlier studies and to recommend methodologies for preventing potential pitfalls. This review adopted multidisciplinary and interdisciplinary approaches in testing hypotheses regarding nature and nurture contributions to extreme longevity.

In the 2010 special issue of Current Gerontology and Geriatrics Research on ‘Centenarian studies: important contributors to our understanding of the aging process and longevity’,51 selected longitudinal and longevity studies were reviewed: the Okinawa Centenarian Study,37 the Honolulu Heart Program,52 and the Framingham Heart Study.53 The longest-running American centenarian study, the Georgia Centenarian Study,54 in 2008 presented papers from the Ashkenazi Jewish, Chinese, Danish, French, Georgia, Hawaii, Korean, New England, Okinawa
TABLE

Summary of centenarian studies in Europe

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<th>Study</th>
<th>Method</th>
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<tr>
<td>Belgium</td>
<td>Center on Demographic Studies for Public Administration, Catholique de Louvain, Belgium&lt;sup&gt;23&lt;/sup&gt; Using the Belgian Centenarian data</td>
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<td>Denmark</td>
<td>University of Southern Denmark and Epidemiology, Institute of Public Health, University of Southern Denmark, Odense&lt;sup&gt;10,11&lt;/sup&gt; Participants accessed through the Danish Civil Registration System</td>
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<td>Finland</td>
<td>Centenarian Study in Finland by the Second Department of Medicine, University of Helsinki&lt;sup&gt;24&lt;/sup&gt; Visited 185 centenarians based on the Finnish National Population Registry</td>
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<td>France</td>
<td>‘In search of the secret of centenarians’ by the IPSEN Foundation, INSERM&lt;sup&gt;5&lt;/sup&gt; During 1990-1991, 29 669 medical and geriatric doctors were visited to estimate the number of centenarians in France</td>
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<td>Georgia</td>
<td>Georgian Longevity Study; National Centre of Therapy, Research Institute of Experimental and Clinical Therapy, Tbilisi&lt;sup&gt;25&lt;/sup&gt; 136 long-lived persons aged ≥90 years were interviewed since 2004</td>
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<td>Germany</td>
<td>Heidelberg Centenarian Study by the University of Heidelberg&lt;sup&gt;26&lt;/sup&gt; Based on the city registries in Germany, 91 centenarians and near-centenarians were accessed in face-to-face interviews during 2000-2001</td>
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<td>Greece</td>
<td>Ilaria, Greece Study on oldest old (&gt;80 years) by the First Cardiology Clinic, School of Medicine, University of Athens&lt;sup&gt;27&lt;/sup&gt; 89 men and 98 women aged ≥80 years were interviewed</td>
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<td>Greek centenarians by the Laboratory of Cell Proliferation and Ageing, Institute of Biology, Athens&lt;sup&gt;28&lt;/sup&gt; All 489 centenarians and their proxies/caregivers were interviewed by health professionals at their domicile</td>
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<td>The Netherlands</td>
<td>Leiden 85+ Study by the Section of Gerontology and Geriatrics, Department of General Internal Medicine, Leiden University Medical Center&lt;sup&gt;30,31&lt;/sup&gt; Data were obtained from 599 participants aged ≥85 years (response rate, 87%) in Leiden with 27 qualitative in-depth interviews</td>
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<td>Poland</td>
<td>Polish centenarians programme by the International Institute of Molecular and Cell Biology, Warsaw&lt;sup&gt;29&lt;/sup&gt; 364 subjects aged ≥100 years were visited, biological material was collected from 285 subjects, and 153 lymphocyte cell lines were immortalised</td>
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<td>Department of Neurosurgery, Medical Research Center, Polish Academy of Sciences, Warsaw&lt;sup&gt;30&lt;/sup&gt; The selected centenarian group (n=10) and a reference group (n=20)</td>
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<td>Italy</td>
<td>Sardinian Centenarian Study (AKEA study) by the Department of Biomedical Sciences, University of Sassari, Italy&lt;sup&gt;13&lt;/sup&gt; 233 potentially eligible centenarians were traced from the entire territory</td>
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<td>Italian Multicenter Study on Centenarians (IMUSCE) by the Psychogeriatric Service, University of Padua&lt;sup&gt;13&lt;/sup&gt; Personal records of 38 people aged ≥100 years residing in Padua and Pordenone were supplied by the data processing centre of their municipalities under local health unit ULSS 13</td>
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<td>Calabria oldest old descriptive study by the University of Calabria&lt;sup&gt;13&lt;/sup&gt; Two specific questionnaires were used, one for subjects aged ≥90 years (n=400) and another for subjects aged 85 to 86 years (n=453)</td>
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<td>MALVA Study in Mantova, North Italy by the University of Bologna&lt;sup&gt;14&lt;/sup&gt; 117 subjects aged ≥98 years (39 were centenarians) were traced in 1998</td>
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<td>Russia</td>
<td>Centenarian Studies in Russia by the Russian Institute of Public Health, Moscow&lt;sup&gt;14&lt;/sup&gt; Genealogical data on longevity in European royal and noble families. 8409 records for men and 3741 records for women</td>
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<td>Spain</td>
<td>Spanish centenarians (100-108 years) by the Universidad Europea de Madrid, Madrid, Spain&lt;sup&gt;35&lt;/sup&gt; Centenarians aged 100 to 108 years (n=64, 57 women) versus young healthy controls aged 21±2 years (n=283, 67 women)</td>
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<td>Sweden</td>
<td>Stockholm University Swedish Centenarian Study by Lund University&lt;sup&gt;36&lt;/sup&gt; 164 centenarians born in 1887-91 who lived in southern Sweden were asked to participate. Of the 143 survivors, 100 agreed</td>
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<td>Europe</td>
<td>Genetics of Healthy Aging in Europe (GEHA) (2003-2008) coordinated by Claudio Franceschi from the University of Bologna, Italy&lt;sup&gt;14&lt;/sup&gt; 25 partners (24 from Europe and 1 from China) involving 11 European countries. Long-lived 90+ sibpairs (n=2650) versus younger ethnically matched controls (n=2650)</td>
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and Tokyo centenarian studies. The emergence of scientific studies of centenarians around the world demonstrates the advancement in the study of longevity. This 2010 review highlighted conceptual and methodological areas: (1) demographic issues relating to age verification among the oldest old and the trade-off between longevity and morbidity in different parts of the world, (2) methods in selecting predictors of longevity using established longevity datasets, (3) assessment of functional capacities among the very old, (4) the biological phenotype of longevity, and (5) the psychosocial dynamics of longevity. These studies have adopted scientific methodology on age verification, sampling, statistical power, and multivariate modelling hypothesis testing, compared to earlier descriptive studies with small samples.

A 2011 review on understanding well-being in the oldest old\(^4\) acknowledged the rapid increase in the number of oldest old: “This segment of the population tends to suffer physical and cognitive decline, and little information is available to describe how their positive and negative distal experiences, habits, and intervening proximal environmental influences affect their well-being and how social and health policies can help meet the unique challenges they face.” This 2011 review described 4 stages in gaining an understanding of the oldest-old population. The first stage was the building of theories of well-being research. This section outlined the concepts of well-being and the pursuit of happiness, lessons learned from across the ageing spectrum, and the building of models to test adaptation hypotheses. The second stage examined the unique contributions of experiences and trauma over one’s lifetime that impact on the current status of an individual. Most centenarian studies have examined the current state of the individual while ignoring their histories. This section examined the unique experiences of Holocaust survivors and soldiers with posttraumatic stress disorders to illustrate how past traumas may influence current behaviours. The third stage focused on the impact of moderating and mediating processes on well-being including resources, nutrition, health, cognitive function, vitality, social relationships, spirituality, religiosity, and leisure activities. The fourth stage focused on how well-being can be measured with reliability and validity. This 2011 review provided a thorough understanding of the qualitative aspects of longevity and ageing well.

In the 2012 special issue on extreme longevity by the Journal of Gerontology Biological Sciences,\(^5\) with- and between-species study of extreme longevity was reported. It provided guidance to longevity researchers in the use of human and animal models in terms of longevity model building and hypothesis testing.

**CONCLUSION**

Recent reviews on longevity research have focused on the importance of both quantitative and qualitative methodologies, replication of mechanisms, interdisciplinary and systems perspectives, and generalisability of results. Researchers should be conversant with ageing theories and models in order to increase the specificity of research on the oldest old. Longevity is not only adding years to life but also adding life to years.

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