Reviewer's report

Title: 10-year follow-up of the Super-Seniors Study: Compression of morbidity and genetic factors

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Reviewer: Irene Maeve Rea

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The authors have presented a short manuscript of follow-up assessments of a range of comparative functional, clinical, biometric and genetic variables in Super Seniors (those who at the age of 85 have had no evidence of major age-related diseases) compared with initial assessments made 10-14 years previously at recruitment. The effect of extra years' survival was compared for cognitive function (MMSE), functional activity (IADL), Time to get up and go Test (TUG) and Geriatric Depression Score (GDS), together with clinical measurements of Body Mass Index (BMI), systolic and diastolic Blood Pressure (BP) and ApoE and FOX3 genotype frequencies.

Cognitive function, mobility and ability to take part in activities of daily living showed apparent decreases while depression scale measurement appeared somewhat higher values in the followed-up Super Seniors. Systolic and diastolic blood pressure and BMI showed lower values in the 13 surviving participants. This group of 13 centenarians appeared to show an accentuation of the ApoE2 allele with a reciprocal decrease in the ApoE4 allele and a marginal increase in the FOX3 gene frequency.

Issues

The authors should be applauded for taking on the follow-up study of Super Agers up to 10-14 years after initial recruitment, and obtaining consent for those able to be assessed, albeit in a small number of subjects. Other authors have previously noted the difficulty in following up Super Agers, centenarians and supercentenarians, many of whom have had several changes of residence, recurrent episodes of illness or death records may not have been found, and research within these very elderly groups are well known to be very demanding for research teams, participants and their families (samuelson et al. 2008). A flow chart would be helpful in visualizing the decision processes for the Super Seniors' follow-up strategy.
Assessments

Centenarians and supercentenarians are a difficult group to assess or re-assess because of the increase in visual and hearing difficulties in this group, even when mental and physical function is maintained. An amended MMSE that takes these factors into consideration has been suggested and used in several studies ie Bennati et al. 2010

Statistics

From the initially recruited 480 Super Seniors only 13 follow-up participants were alive and willing and able to be consented for inclusion in this follow-up study of the effect of increased age on the quality of life and biometrics of extreme longevity. The small number of followed-Super Seniors involved in the follow-up is disappointing and it could be argued to make statistical comparisons unreliable and consideration should be given as to whether these changes should be reported as observational in nature rather than statistically significant.

As the authors report the findings on the clinical and functional results and the changes in genetic frequency in ApoE 2 and 4 and FOX3 frequencies do agree with findings from previous authors who have carried out research into the survival phenotype of nonagenarians, centenarians and supercentenarians. The authors have documented some of these studies in the discussion -noted omissions are the original publication on French nonagenarians' ApoE gene frequency - Schachter 1994, Jylhä et al 1999, Rea et al., ApoE, 2001, Bennati et al 2010 Wilhemsen, 2015 on follow-up nonagenarians and centenarians. (see additional possible references below).

Meta-analysis

It would be of interest to consider the possibility of including a quantitative or a narrative tabular analysis of available centenarians or supercentenarian studies with suitable functional, clinical, biometric and genetic data. This would add to the findings from a single study and give a broader global view of the phenotype of long-lived centenarian groups.

Collerton J et al. BMC Geriatr 2007, 7:7-14
Kerse N, Int J Epidemiol 2015; 44: 1823-32
Lennartsson C et al., Int J Epidemiol 2014; 434: 732-8
Willcox DC et al., Curr Gerontol Geriatr Res 2010; 1-6


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Yes

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