A limit to frailty in very old, community-dwelling people: a secondary analysis of the Chinese longitudinal health and longevity study

**S. Bennett et al.**

**Abstract**

**Background:** It has been observed that a frailty index (FI) is limited by the value of 0.7. Whether this holds in countries with higher mortality rates is not known.

**Objectives:** To test for and quantify a limit in very old Chinese adults and to relate mortality risk to the FI.


**Subjects:** A total of 6,300 people from 22 of 31 provinces in China, aged 80-99 years at baseline and followed up to 7 years.

**Methods:** An FI was calculated as the ratio of actual to 38 possible health deficits. Frequency distributions were used to evaluate the limit to the FI. Logistic regression and survival analysis were used to evaluate the relationship between the FI and mortality.

**Results:** At each wave, a 99% submaximal limit to frailty was observed at FI = 0.7, despite consecutive losses to death. The death rate for those who were healthiest at baseline (i.e., those in whom the baseline FI = 0) increased from 0.18 at the 2-year follow-up to 0.69 by 7 years. At each wave, 100% mortality at 2 years was observed at FI close to 0.67. A baseline FI >0.45 was associated with 100% 7-year mortality.

**Conclusions:** A limit to frailty occurred with FI = 0.7 which was not exceeded at any age or in any wave. There appears to be a demonstrable limit to the number of health problems that people can tolerate.

**Keywords:** Ageing, frailty index, limit to frailty, mortality, China, older people
Introduction

Around the world, populations are ageing because more people are becoming older, and older people are living longer. China records the largest population of adults aged 60+ years in the world [1]. It has an average life expectancy of 73 years [2], with 12.0 million people aged 80+ years (9.2% of the older population). In China as elsewhere, although the mortality risk increases with age, not every one of the same age has the same risk of dying. This variable vulnerability to death and other adverse outcomes among people of the same age, known as frailty, can be operationalised in a frailty index (FI) [3]. For any individual, an FI can be calculated as a count of the number of health deficits they have accumulated, which is expressed as the proportion of health deficits considered [3]. For example, in a health survey that recorded 50 deficits, a person with no deficits would have an FI of 0/50 = 0; one who had accumulated 20 deficits would have an FI score of 20/50 = 0.40. An FI based on deficit accumulation has been independently validated by several groups and shown to be closely related to the risk of death [4–12].

In general, vulnerability to death and other adverse outcomes is said to arise from the ‘loss of physiological reserve’, which can be quantified according to a reliability theory of ageing that is rooted in engineering concepts [13, 14]. The body thus is seen as a complex system with significant redundancies that diminish as deficits accumulate. When redundancy is exhausted, the system can accumulate no new deficits without failure. Characteristically, redundancy exhaustion occurs at an FI value of ~0.7 [3, 15, 16]. The presence of such a quantifiable submaximal limit to frailty (i.e. a limit at FI < 1.0) is of considerable interest. If a quantifiable limit to frailty is verifiable, it has the potential to aid public health planning, as well as to assist clinical decision-making in being able to better estimate risks. The Chinese Longitudinal Health and Longevity Study (CLHLS) 1998–2005 data set allows for a severe test of the hypothesis of a limit to frailty, because it contains data on a large number of people, who at the age of 80+ years, have lived past the average life expectancy for their cohort, and who therefore would be candidates to exceed the limit to frailty. Another group has shown that levels of frailty increase exponentially in the CLHLS from ages 65 to 100 [11], indicating that the CLHLS is composed of people in whom worsening of health prior to death can be expected. In these community dwelling, very old Chinese people, our objectives were: to evaluate whether there is a quantifiable, submaximal limit to the number of health deficits that people can accumulate; to examine the behaviour of deficit accumulation close to this limit and to determine the relationship between frailty and mortality.

Methods

Participants and setting

This is a secondary analysis of data from the first four waves (1998, 2000, 2002 and 2005) of the 1998–2005 CLHLS. The data set contains baseline information on 9,093 community-dwelling respondents from 22 of China’s 31 provinces. The survey was designed to include as many centenarians as would participate, yielding 2,418 respondents over the age of 100. For this study, centenarians were omitted due to their disproportionate representation, potential problems with age verification and potentially suspect generalisability, which is a subject of a separate study by our group. A further 241 respondents were omitted due to incomplete baseline data. The four waves contain information on 6,300; 3,716; 2,164 and 912 eligible people, respectively, with mortality recorded in 1,909; 1,087 and 1,013 people at each respective wave. Death data were obtained through death certificates, next of kin or neighbourhood committees, and all mortality data were validated. Another 1,380 (675, 466, 239 at each respective follow-up) were lost to the follow-up. The CLHLS used questionnaires, completed by respondents and/or next of kin, to record data on personal, family and household characteristics, lifestyle and diet, economic resources, social support, and physical, cognitive and psychological conditions [11, 17].

Frailty index

The FI was created following a standard procedure [18]. Symptoms, signs, disabilities and diseases were considered as health deficits, if they: were associated with the health status; had a prevalence >1%; generally increased with age, recognising that some age-related adverse conditions become less common in extreme old age due to survivor effects; did not saturate (i.e. were found to be present in most people at an early age, quantified here as a prevalence of 80%) and in their aggregate, represented several physiological systems [18]. Each variable was re-coded as 0 (absence of deficit), 1 (presence of deficit) or missing. The 1998–2005 CLHLS data set included 45 deficits, 29 of which had been used by another group to construct an FI [11, 19]. We considered all 29 of these, plus 16 other variables that met the above criteria. Of these 45 variables, 4 were excluded due to saturation, 2 because they were not age related and 1 (‘Feel lonely and isolated’) because it was considered to reflect social vulnerability more than frailty. For each individual, the FI score was calculated by summing the deficits present and dividing by the 38 deficits considered (Supplementary data are available in Age and Ageing online, Appendix A). No individual at baseline had >5% missing data. For individuals in whom variables had missing data, we excluded the variables from the denominator and the numerator. Outcomes were described using all data points for four cycles (over 10 years). The recorded date of death was verified by police registry and death certificate upon availability. The data were obtained from Duke University, Center for the Study of Aging and Human Development [17].
Statistical analysis

To identify the upper limit to frailty, for each wave, the distributions of the FI, its maximal value and the 0.95 and 0.99 quantiles were identified. The rate of deficit accumulation was calculated as the slope of the least squares mean value of the FI (on a logarithmic scale) in relation to age. To evaluate whether the rate of deficit accumulation slows with increasing frailty, the best fit log of the FI was evaluated in relation to age, having separated the data into 95 and 99th percentiles, as detailed elsewhere [15].

Binary logistic regression was used to evaluate the relationship between the baseline FI and mortality at each wave. Kaplan-Meier analysis was used to estimate the 7-year survival in relation to the FI. To compare the impact of age, sex and frailty on mortality, Cox proportional hazards regression models were employed. Proportionality of hazards assumption was tested by correlating corresponding sets of scaled Schoenfeld residuals with a suitable transformation of time for each estimate. All analyses were performed using SPSS version 15.0 for Windows or codes developed using Matlab version 7.1 (MatSoft, Inc.).

Discussion

In the CLHLS 1998–2005 data set, we quantified frailty in people aged 80–99 years as the accumulation of deficits and evaluated the behaviour of deficit accumulation in relation to mortality so that we could test whether a limit to frailty was present. In this high-risk group of very old adults, a 99% limit to frailty was observed at an FI value of 0.7, with little change in the shape of the distribution of the FI over 7 years. Consistent with earlier analyses [14], we observed deceleration in deficit accumulation in relation to age with increasing FI scores. The data showed a consistent and non-trivial increase in the death rate as a function of the FI, as well as the expected acceleration in mortality at each wave. Even so, in this evidently high-risk group of very old adults, the hypothesised limit to frailty was never exceeded.

In addition to the consistent limit, the distributions of the FI wave were characteristically skewed [20] and showed a marked decrease in the area under the curve with each subsequent wave (Figure 1A). Despite the substantial numbers who died with each subsequent wave, the

Table 1. Demographic characterisation of respondents categorised by levels of the frailty index

<table>
<thead>
<tr>
<th>Frailty index groupings</th>
<th>FI ≤ 0.05</th>
<th>0.05 &lt; FI ≤ 0.15</th>
<th>0.15 &lt; FI ≤ 0.25</th>
<th>0.25 &lt; FI ≤ 0.35</th>
<th>0.35 &lt; FI ≤ 0.45</th>
<th>FI &gt; 0.45</th>
<th>People lost to follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>948</td>
<td>3,350</td>
<td>1,274</td>
<td>422</td>
<td>206</td>
<td>100</td>
<td>1,380</td>
</tr>
<tr>
<td>Age</td>
<td>87.3 (5.5)</td>
<td>88.3 (5.7)</td>
<td>89.8 (5.8)</td>
<td>91.8 (5.5)</td>
<td>92.4 (5.7)</td>
<td>91.7 (5.4)</td>
<td>87.6 (5.6)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>47.2</td>
<td>51.7</td>
<td>55.7</td>
<td>61.8</td>
<td>63.1</td>
<td>57.0</td>
<td>53.8</td>
</tr>
<tr>
<td>No formal education (%)</td>
<td>54.1</td>
<td>60.9</td>
<td>65.0</td>
<td>66.7</td>
<td>74.1</td>
<td>66.0</td>
<td>53.7</td>
</tr>
<tr>
<td>Married (%)</td>
<td>24.9</td>
<td>21.9</td>
<td>19.0</td>
<td>16.8</td>
<td>11.0</td>
<td>2.1</td>
<td>25.6</td>
</tr>
</tbody>
</table>

Data presented are mean ± standard deviation, otherwise as specified.

FI, frailty index.
The distributions of the FI values stayed about the same (Figure 1B). Over 7 years, there was little change in the mode, and a small decrease in the proportion of people with FI = 0 (the so-called ‘zero state’ of frailty). This appears to reflect the nature of system failure and properties of the limit. Without a limit, it might be expected that an increased mean FI would arise from the mode shifting to the right and the maximum value approaching unity. Instead, the distribution shows that even though there is a small increment in the FI mode, and a small decrement in people with FI = 0, there is no corresponding increase in the proportion with the highest FI values. That is due to complete mortality as the limit is approached (at 2 years, with FI = 0.67). This is also in keeping with a report from Canada on adults aged 70+ years at baseline [14].

As before, the average rate of deficit accumulation decelerated in relation to age as the FI increased [3, 14, 20]. In other words, as respondents became frailer, they accumulated deficits at a slower rate. This result supports the concept of physiological redundancy exhaustion [13, 14], understood as follows. Any system with a large amount of accumulated damage can only tolerate a finite amount of additional damage without failure. In consequence, slopes of deficit accumulation in relation to age eventually attenuate to zero because further deficit accumulation is not possible. This is not because of a lower risk of death, but rather due to higher one: the alternative to further deficit accumulation is less likely improvement than it is death.

Mortality, as it relates to frailty, has been examined in CLHLS data before and showed, as here, that deficit accumulation is tightly linked to the risk of death, indicating that frail adults are more likely to die [11, 19]. What this study adds is the exploration of the limit. Note too, that as we used an older sample (the youngest respondents here were 15 years older than in other CLHLS studies) the death rates were notably higher, even for those fittest at baseline and particularly for the 7-year outcomes. Another recent report from China found a similarly high mortality rate for adults aged 85 and older from the Beijing Longitudinal Study of Aging (BLSA) database [21]. These reports suggest that at this age, at least in China during the time periods observed, high levels of deficit accumulation were lethal.

Our data must be interpreted with caution. The baseline cohort included 36% who were centenarians, whom we...
We demonstrated a limit to the number of health deficits that people can tolerate, estimated by a FI = 0.7. Additional analyses of this group also showed a consistent limit to the FI at 0.7 (data not shown); even so, the study of centenarians appears to be especially susceptible to local influences, sex compositions and familial effects, making generalisation uncertain [22, 23].

For these reasons, we have focused on this more restricted, but still very elderly sample. The data also chiefly come from self or informant reports, although in work on other aspects of the FI, we have found no difference between estimates based on self-reported, observer-assessed or test data, as long as the usual criteria for selecting health deficits are applied [24]. Despite these limitations, important properties of the FI (high correlation with age, highly associated with mortality and a submaximal limit at 0.7) held here [1, 3, 11, 24–28]. Many readers will be more familiar with frailty defined by a frailty phenotype [29]. How these findings can be applied to the phenotype requires additional investigation; the data here do not allow the phenotype to be identified. In any case, a recent report suggests that difficulties in operationalising the frailty phenotype limit its utility in the very old [30].

The high death rates and the empirical limit to frailty have important implications for understanding health in older adults. Previously, we have considered frailty chiefly in younger samples (mostly 55+ years) from several nations. Important properties of frailty observed there also seem to hold here. Notable results of this study include what did not happen in a large sample with a high mortality rate; the distribution changed little and the limit was not exceeded. Instead, with time, fewer people survived and even fewer had little wrong with them. Especially for healthcare delivery systems which view as normative patients with just one single illness, as exemplified in ideas such as diagnostic parsimony and the ‘most responsible diagnosis’, this increase in frailty will pose important challenges. The FI quantifies the vulnerability to adverse outcomes of people with many health problems. It also affords a systems approach to frailty, allowing a fuller understanding of patients with complex needs.

Acknowledgements

Data collection was supported by NIA/NIH grants, UNFPA, China Social Sciences Foundation, the Max Planck Institute for Demographic Research, China Natural Sciences Foundation and the Hong Kong Research Grants Council (RGC). Researchers are independent from sponsors.

Authors’ contributions

S.B. prepared the data, performed statistical analysis and drafted the initial manuscript. X.S. helped with the analysis design and assisted with data analysis and result interpretation. A.M. directed and assisted data analysis and result interpretation, and revised the manuscript. K.R. initiated and designed the study, re-drafted parts of the introduction and discussion, revised the paper, assisted in interpreting the results and finally approved the version to be published. All authors had full access to the CLHLS data and can take responsibility for the accuracy of the analysis. All authors also edited and approved the final manuscript.

Conflicts of interest

Data for these analyses were obtained from Duke University through the agreement between the Center for the Study of Aging and Human Development and Geriatric Medicine Research at Dalhousie University, Canada.

Funding

This work was supported by operating grants from the Canadian Institute for Health Research (CCI92216) and the Fountain Innovation Fund of the Queen Elizabeth II Health Sciences Research Foundation. K.R. receives career support through the Dalhousie Medical Research Foundation as the Kathryn Allen Weldon Professor of Alzheimer Research.

Supplementary data

Supplementary data mentioned in the text are available to subscribers in Age and Ageing online.

References

Limit to frailty in very old, community-dwelling people


Received 5 July 2012; accepted in revised form 6 September 2012