Changes in the severity and lethality of age-related health deficit accumulation in the USA between 1999 and 2018: a population-based cohort study

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Summary

Background With an ageing population, the number of people with frailty is increasing. Despite this trend, the extent to which the severity and lethality of frailty have changed over time is not well understood. We aimed to investigate how frailty severity and lethality have changed over an 18-year period in the USA.

Methods In this population-based observational study, we used data from the National Health and Nutrition Examination Survey (NHANES) to identify community-dwelling individuals (aged ≥20 years) in the USA between 1999 and 2018. We analysed data from a series of ten 2-year, nationally representative, cross-sectional, prospective studies (from 1999–2000 to 2017–18) from the NHANES. Frailty was measured by use of the deficit accumulation approach (ie, a 46-item frailty index). The proportion of individuals categorised as non-frail, or living with very mild frailty, mild frailty, moderate frailty, and severe frailty were compared across cohorts. Random-effects models were used to examine the association between frailty index score and sex, age, and cohort. Mortality status as of Dec 31, 2015, was ascertained by use of National Death Index data, and 5-year mortality was available in the first six cohorts (1999–2010). Cox regression models and Kaplan-Meier curves were used to estimate the association between frailty index scores and mortality.

Findings In total, 49 004 individuals were included in our study. Associations were mainly non-linear (quadratic), with frailty increasing at a faster rate in more recent cohorts. Between 1999 and 2018, the proportion of non-frail individuals decreased by 10·4% (from 2747 [63·8%; 95% CI 61·9–65·6] of 4307 to 2884 [53·4%; 51·3–55·5] of 5399), whereas the proportion of individuals with very mild frailty increased by 2·4% (from 987 [22·9%; 21·3–24·6] to 1365 [25·3%; 23·5–27·2]), by 2·7% (from 370 [8·6%; 7·7–9·6] to 609 [11·3%; 10·1–12·5]) in those with mild frailty, by 3·1% (from 140 [3·3%; 2·7–3·9] to 347 [6·4%; 5·6–7·4]) in those with moderate frailty, and by 2·1% (from 63 [1·5%; 1·1–1·9] to 195 [3·6%; 3·0–4·3]) in those with severe frailty. Being a woman, older, and from a more recent cohort were associated with higher frailty index scores (all p<0·0001). In more recent cohorts, mean frailty index scores increased more quickly with age (p<0·0001), and sex differences in mean frailty index scores decreased (p<0·0001). In men of all ages and in women aged 35 years or older, mean frailty index scores were higher in more recent cohorts, with larger increases in frailty in older age groups. In 28 692 individuals from the first six cohorts (1999–2000 to 2009–10) with linked mortality data, frailty index scores were significantly associated with mortality (hazard ratio 1·053 [95% CI 1·050–1·057] per 0·01 increase in frailty index score). The absence of an interaction between cohort and frailty index score (p=0·58) suggested that the association between frailty and mortality was similar for all cohorts.

Interpretation Increasing frailty levels in more recent cohorts of middle-aged and older adults combined with stable frailty lethality between 1999 and 2018, suggest a challenge to healthy longevity, with the proportion of individuals with a high degree of frailty continuing to increase.

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See **Comment** page e60

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Introduction

In most countries, the number of older people is increasing, and older people are living longer. This trend is also reflected in an increase in the prevalence of most chronic diseases, the number of years spent in poor health, and the increased use of health care.[1] Nevertheless, secular trends in overall health are unclear, with some evidence that younger generations have worse health than their ancestors.[2,3] The lack of clarity about health in ageing extends to research, in which age-related diseases are typically studied individually, despite occurring together.[4]

Frailty captures the combined effects of age-related diseases and is associated with an increased vulnerability to adverse health outcomes.[5] The deficit accumulation approach quantifies frailty by use of a frailty index, allowing a quantitative measure of frailty with strong biological underpinnings. By considering deficits across a range of domains, frailty indexes offer a summary indicator of health at various stages of life.[5] There is

Research in context

Evidence before this study

People of the same age have varying risks of adverse health outcomes, such as functional disability, hospitalisation (ie, admission to hospital), and death. People with higher levels of frailty are at a higher risk of these adverse health outcomes. A frailty index robustly grades risk of adverse outcomes as the ratio of the number of deficits an individual has accumulated to the total number of deficits considered (eg, in a survey or health record). As factors influencing health and ageing have changed in the past 20 years, we sought to understand how the severity and lethality of frailty have changed over a 20-year period.

We searched PubMed and Web of Science using the search terms "frailty" AND "cohort effect", with no language restrictions. We searched for any study published from database inception up to the date of each literature search that had investigated differences between cohorts in levels of frailty, lethality of frailty, or both. We found four studies involving older adults from the UK, Sweden, and the USA. All studies measured frailty with a frailty index; three studies used data from longitudinal cohort studies, and one study used administrative data. Three of the four studies reported increases in frailty in more recent cohorts, with two of these three studies reporting decreases in lethality.

Added value of this study

To our knowledge, this study of 49 004 individuals from the USA is the first to use a nationally representative sample (from the National Health and Nutrition Examination Survey) to assess changes in frailty severity and lethality between 1999 and 2018 across all ages of the adult life course. In men aged 20 years and older and women aged 35 years and older, both preclinical and clinical frailty levels increased over this time period. However, we found that the lethality of frailty has not changed over the past 20 years. Notably, frailty appeared to decrease in young women (ie, those aged 20–34 years), which could only be partially explained by the novel finding of higher laboratory-based frailty scores in pregnant women.

Implications of all the available evidence

An increase in mean frailty levels in all age groups of men and women aged 35 years and older, combined with stable frailty lethality between 1999 and 2018, suggests that the prevalence of frailty will continue to increase. These findings have important public health implications as the number of older adults continues to increase globally.

conflicting evidence of changes in frailty across cohorts between countries, with higher levels of frailty in more recent cohorts (assessed in 2010) than in earlier cohorts (assessed in 2002) of the English Longitudinal Study of Ageing,[6] but no changes in levels of frailty between Swedish cohorts born in 1901–02 and in 1930.[7] Similarly, reports vary on whether the lethality of frailty has decreased[7,8] or remained stable[9] over time.

Properties of the frailty index are well established, including higher frailty index scores in women, and increases in frailty index scores with age.[10–12] Although studies done in the UK and Sweden have reported stable sex differences in frailty over time,[6,7,9] no US study has examined whether these differences have changed over time. Additionally, these studies focused on older adults (ie, those aged ≥50 years, ≥65 years, and ≤70 years),[6–9] despite an improved understanding that frailty is a consequence of deficits that arise across the adult life course.[13] The frailty index has been validated in young and middle-aged adults (ie, those aged 15–65 years) adults,[11–14] which could provide opportunities for early, targeted interventions. Finally, frailty indexes consisting of laboratory-based deficits have shown different properties to frailty indexes based on self-reported deficits, such as greater deficit accumulation at younger ages, and similar frailty levels between men and women.[15,16] Most notably, both self-reported and laboratory-based frailty indexes have shown independent contributions of frailty to mortality risk.[11,17] Frailty indexes consisting of many items using multiple types of measures (eg, self-reported, test-based measures and laboratory-based measures, and tests for other biomarkers) have better predictive ability for mortality risk than a single type of frailty index.[11,16,18] This observation suggests that all possible deficits should be considered to best identify frailty level in order to predict poor outcomes. However, there could be utility in examining different types of frailty index deficits; for example, self-reported frailty indexes might capture clinically visible deficits, whereas laboratory-based frailty indexes might capture subclinical aspects of frailty.

How frailty severity and lethality have changed in the US population over time is not well understood. Using a nationally representative cohort study of community-dwelling individuals in the USA, we aimed to investigate how the severity of age-related deficit accumulation (ie, frailty index scores) and its lethality have changed between 1999 and 2018. Additionally, within each objective, we sought to understand how effects differ between women and men, across age groups, and between laboratory-based deficits and self-reported deficits. We hypothesised that mean frailty levels would increase over time, with a corresponding decline in lethality. These changes were expected to be similar between men and women and between laboratory-based frailty indexes and self-reported frailty indexes, but larger in older age groups, compared to younger age groups.

Methods

Data sources and study population

In this population-based observational study we used data from the National Health and Nutrition Examination

Survey (NHANES) to identify community-dwelling individuals (aged ≥20 years) in the USA between 1999 and 2018. We analysed data from a series of ten 2-year (1999–2000, 2001–02, 2003–04, 2005–06, 2007–08, 2009–10, 2011–12, 2013–14, 2015–16, and 2017–18) studies from the NHANES. This survey is a series of cross-sectional, prospectively ascertained studies, that are nationally representative of community-dwelling individuals in the United States. Individuals aged younger than 20 years and those with insufficient data on frailty were excluded from the analyses. Changes in sample design and in survey response rates across NHANES cohorts have been documented in detail on the NHANES website. NHANES provides statistical weights that account for survey design (including oversampling), survey non-response, and post-stratification adjustment to ensure that estimates are representative of the non-institutionalised civilian population in the USA.

The mortality status (as of Dec 31, 2015) of study participants was ascertained by use of National Death Index data.

NHANES protocols have been approved by the Institutional Review Board of the Centers for Disease Control and Prevention and, at all waves, study participants provided written informed consent. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

Construction of frailty index

A 46-item frailty index, consisting of 27 self-reported items and 19 laboratory-based items from blood tests, was produced according to standard procedures.[19] Building on previously published NHANES frailty indexes, only items available in all ten cohorts were included.[11,13] Each item was assigned a score between 0 and 1, such that 0 indicated no deficits (eg, no memory problems) and 1 indicated the presence of a deficit (eg, self-reported memory problems; appendix p 5). Intermediate scores were also possible if a deficit had multiple levels of severity (eg, a score of 0 indicated no overnight stay in hospital, a score of 0·5 indicated 1–2 nights in hospital, and a score of 1 indicated three or more nights in hospital). The frailty index score for each participant was calculated as the number of deficits present divided by the total number of deficits considered.[19] The robust properties, generalisability, and validity of the frailty index has been established in many community-dwelling and clinical sample populations. Additionally, tests of sensitivity of frailty index items show that the sum of deficits present is more important than the nature of individual deficits.[19,20] To compare differences between self-reported and laboratory-based frailty indexes, a self-reported frailty index (27 items) and a laboratory-based frailty index (19 items from blood tests) were separately generated. Consistent with standard criteria,[13,19] a frailty index could only be calculated for individuals who had data on at least 37 (80%) of 46 items.

Statistical analysis

The proportion of individuals classified as non-frail (frailty index score ≤0·1), or living with very mild frailty (frailty index score >0·1 to ≤0·2), mild frailty (frailty index score >0·2 to ≤0·3), moderate frailty (frailty index score >0·3 to ≤0·4), and severe frailty (frailty index score >0·4), were compared across the ten cohorts. Our first main objective was to examine if frailty index scores had changed over time (ie, between cohorts), and to establish whether these changes differed by sex, age, or by the type of frailty index (ie, self-reported or laboratory-based deficits). In accordance with suggestions by Yang and Land,[21] we used random-effects models to examine this association. Individual frailty index scores (level 1) were clustered by cohort (level 2); the intercept (cohort 1999–2000) and slopes for sex (men or women) and age group (20–34 years, 35–49 years, 50–64 years, 65–79 years, and ≥80 years) were modelled as random effects in the initial model. Quadratic terms, together with age, sex, and cohort interactions, were assessed. Analyses were stratified when significant interaction terms were identified. Each β coefficient indicates the change in mean frailty score for each additional cohort (ie, cohorts two [2000–01] to ten [2017–18]) compared with the baseline cohort (1999–2000). Our second main objective was to examine whether the lethality of frailty (ie, the association between frailty index scores and mortality) had changed over time. Cox regression models and Kaplan-Meier curves were used to examine frailty scores and mortality hazard ratios (HRs). To ensure sufficient time for follow-up, the 5-year mortality of participants (up to 2015) was considered in the first six cohorts (from 1999–2000 to 2009–10).

We did several sensitivity analyses. First, associations between frailty index scores and cohort were examined separately for the self-reported frailty index and the laboratory-based frailty index. Differences in self-reported frailty index scores between participants with a valid laboratory-based frailty index score and those with missing data for 20% or more laboratory-based frailty index items were compared. Similarly, differences in laboratory-based frailty index scores between participants with a valid self-reported frailty index score and those missing data on 20% or more self-reported frailty index items were compared. Given the possible effects of pregnancy on blood tests and subsequent laboratory-based frailty index scores, pregnant women were excluded from analyses examining associations between laboratory-based frailty index scores and cohort. Finally, Cox regression models examined the association between laboratory-based and self-reported frailty index scores and mortality, and estimated the overall HR in a subsample of individuals aged 50 years and older. Analyses were weighted by use of NHANES sample weights.

Statistical analyses were done in Stata 15.1. An α level of 0·05 was used to indicate statistical significance.

For more on the **National Health and Nutrition Examination Survey** see https://www.cdc.gov/nchs/nhanes/index.htm

See **Online** for appendix

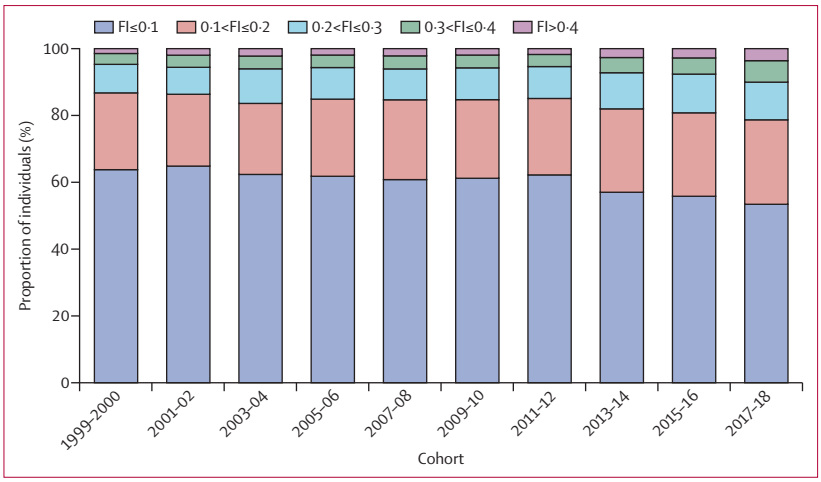

Figure 1: **Proportion of individuals in each frailty index score category by cohort (1999–2018)**
FI=frailty index.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, interpretation of the secondary data, or writing of the report.

Results

We identified 55 081 community-dwelling individuals aged 20 years and older from the NHANES, 49 871 (90·5%) of whom had blood tests taken. Among these individuals, 49 004 (98·3%) had sufficient data for inclusion in the main analyses. The average sample size in each cohort was 4900 (range 4121–5680), with a mean age of 46·9 years (SD 16·9) and an equal distribution of men and women (26 355 [51·8%] of 49 004 individuals were women). Mean frailty index scores were 0·11 (SD 0·10) in men and 0·12 (0·11) in women. Mean frailty index scores were highest in non-Hispanic Black individuals (0·12 [0·12]) and White individuals (0·11 [0·10]), and lowest in Mexican Americans (0·09 [0·09]).

Between 1999 and 2018, the proportion of non-frail individuals decreased by 10·4% (from 2747 [63·8%; 95% CI 61·9–65·6] of 4307 to 2884 [53·4%; 51·3–55·5] of 5399). Conversely, the proportion of individuals in all frailty categories increased. Between 1999 and 2018, the proportion of individuals with very mild frailty increased by 2·4% (from 987 [22·9%; 21·3–24·6] of 4307 to 1365 [25·3%; 23·5–27·2] of 5399), by 2·7% (from 370 [8·6%; 7·7–9·6] to 609 [11·3%; 10·1–12·5]) in those with mild frailty, by 3·1% (from 140 [3·3%; 2·7–3·9] to 347 [6·4%; 5·6–7·4]) in those with moderate frailty, and by 2·1% (from 63 [1·5%; 1·1–1·9] to 195 [3·6%; 3·0–4·3]) in those with severe frailty (figure 1). These increases were similar in men and women, and across each 15-year age group (appendix p 1).

In the random-effects models, being a woman, older, and from a more recent cohort were all associated with higher frailty index scores (all p<0·0001; appendix p 6). Interaction terms suggested that in more recent cohorts, frailty index scores increased significantly with age (p<0·0001) and sex differences in frailty decreased (p<0·0001). Due to the significant three-way cohort–sex–age interaction (p=0·004), analyses were first stratified by sex and age group.

In men of all ages and in women aged 35 years or older, frailty index scores were higher in more recent cohorts than in earlier cohorts, with larger increases in frailty index scores in older age groups than in younger age groups (figure 2; appendix p 7). Exponential increases in frailty index scores with each subsequent cohort predominated, with linear increases observed in both men and women aged 35–49 years and aged 80 years and older. For example, in both men and women aged 80 years and older, those from the most recent cohort (2017–18) had a 0·08 (95% CI 0·05–0·10) higher mean frailty index score compared with the 1999–2000 cohort (calculated as 10 [cohort waves]$\times\beta$ of 0·0075 in men and 10$\times\beta$ of 0·0076 in women; figure 2, appendix p 7). Conversely, women aged 20–34 years had lower frailty index scores in each subsequent cohort (figure 2A).

Analyses were stratified by cohort and age group to assess how sex differences in frailty index scores changed over time (eg, between cohorts). In individuals aged 20–34 years, sex differences decreased over time from a difference of 0·022 (95% CI 0·017 to 0·028; p<0·0001) in 1999–2000 to –0·006 (–0·012 to 0·0002; p=0·057) in 2017–18 (figure 3). Sex differences in frailty index scores did not change over time in all other age groups (appendix p 2).

Among individuals from the first six cohorts (1999–2000 to 2009–10), 28 692 (99·9%) of 28 726 individuals had 5-year mortality data; the remaining 34 individuals were ineligible for linkage because of insufficient identifying data. No difference in mean frailty index scores between individuals with mortality data (0·13 [SD 0·11]) and those without mortality data (0·12 [0·14]) was observed (p=0·78). 1994 (weighted 4·5%) of 28 692 individuals died within 5 years, ranging from 74 (weighted 0·7%) of 7575 individuals aged 20–29 years to 768 (weighted 35·2%) of 2102 individuals aged 80 years and older. In Cox regression models, frailty index scores were significantly associated with mortality (HR 1·053 [95% CI 1·050–1·057] per 0·01 increase in frailty index score; figure 4). Interactions between cohort, frailty index score, sex, and age were not significant. Notably, the absence of interaction between cohort and frailty index score (p=0·58) suggested that the association between frailty and mortality was similar across all cohorts (appendix p 8).

A sensitivity analysis of the random-effects models examined associations of frailty index scores and cohorts separately for laboratory-based and self-reported deficits. More recent cohorts consistently showed both higher laboratory-based and self-reported frailty index scores (appendix pp 3, 9). Associations between frailty index score and cohort were primarily quadratic for the

laboratory-based index, and primarily linear for the self-reported index. Similar rates of increase in laboratory-based and self-reported frailty index scores across cohorts were observed in both men and women aged 50 years and older, whereas differences emerged in individuals aged 20–49 years. In men aged 35–49 years, increases in self-reported frailty index scores were small (0·0013 [95% CI 0·0004 to 0·0021] per cohort, p=0·004), with no significant difference in self-reported frailty index observed between cohorts in women (0·0007 [–0·0003 to 0·0016] per cohort, p=0·16). Conversely, laboratory-based frailty index scores decreased exponentially over time in women aged 20–34 years (linear term –0·0172 [–0·0203 to –0·0141]; quadratic term 0·0010 [0·0009 to 0·0015]), but increased exponentially over time in men aged 20–34 years (linear term –0·0051 [–0·0079 to –0·0023]; quadratic term 0·0006 [0·0004 to 0·0009]; appendix p 3).

Mean self-reported frailty index scores were significantly higher in individuals without a valid laboratory-based frailty index score (0·13 [SD 0·16]; n=3480) than in those with a valid laboratory-based frailty index score (0·11 [0·13]; n=48 865; p<0·0001); this difference was consistent across cohorts, except the 2017–18 cohort. Mean laboratory-based frailty index scores were significantly higher in individuals without a valid self-reported frailty index score (0·23 [0·13]; n=43) than in those with a valid self-reported frailty index score (0·12 [0·10]; n=48 865; p<0·0001).

In the 1999–2000 cohort, 208 (weighted 5·9%) of 1186 women aged 20–49 years were pregnant during data collection, decreasing to 37 (weighted 3·3%) of 1173 in the 2017–18 cohort. No pregnancies were reported in women aged 50 years or older in any cohort. Mean laboratory-based frailty index scores in pregnant women were significantly higher than those in non-pregnant women in all cohorts. For example, in the 1999–2000 cohort, the mean laboratory-based frailty index score in pregnant women aged 20–49 years was 0·19 (SD 0·08) compared with 0·09 (0·08) in non-pregnant women, and in the 2017–18 cohort, the mean laboratory-based frailty index score was 0·16 (0·10) in pregnant women compared with 0·09 (0·08) in non-pregnant women. There were no differences in self-reported frailty index scores between pregnant and non-pregnant women in any cohort (eg, in the 1999–2000 cohort, the mean self-reported frailty index score in pregnant women was 0·05 [0·04] *vs* 0·06 [0·08] in non-pregnant women, and in the 2017–18 cohort, the mean self-reported frailty index score in pregnant women was 0·07 [0·06] *vs* 0·07 [0·09] in non-pregnant women). When pregnant women were excluded from the analyses, associations between cohort and laboratory-based and self-reported frailty index scores in women in the 20–34 years and 35–49 years age groups remained, and sex differences in frailty index scores showed the same trend over time (ie, decrease) as when pregnant women were included in the analyses (appendix p 4).

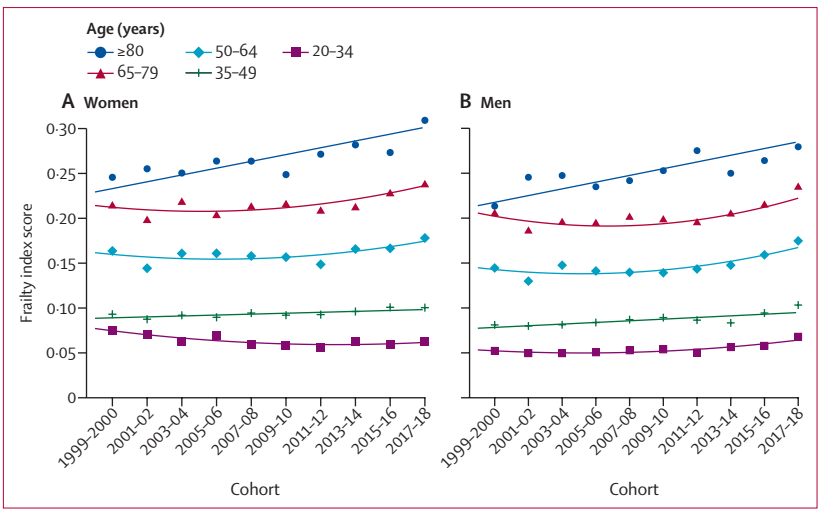

Figure 2: **Association between cohort and frailty index score, stratified by age group, in women (A) and men (B)**

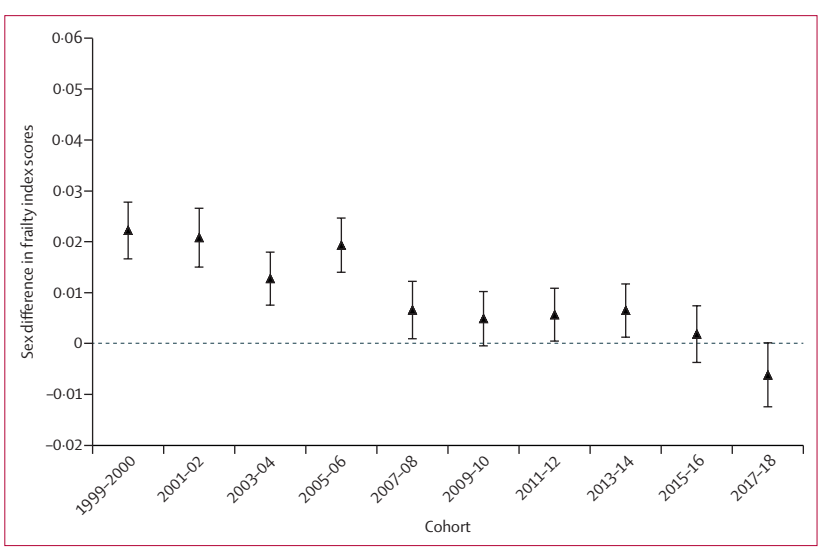

Figure 3: **Sex differences in frailty index scores in individuals aged 20–34 years by cohort**
Data are the differences (β values and 95% CIs) in frailty index scores between men and women. A β value of greater than 0 indicates that women have higher frailty index scores than men. Sex differences in frailty index scores for other age groups are shown in the appendix (p 2).

Further sensitivity analyses, in which Cox regression models were used to estimate the association between laboratory-based and self-reported frailty index scores and mortality in those aged 50 years and older, showed that there was no difference from the main results. The pattern of similar HRs for mortality across cohorts remained (frailty index score–cohort interaction terms, p=0·96 in individuals aged ≥50 years; p=0·39 for the laboratory-based frailty index; and p=0·97 for the self-reported frailty index).

Discussion

By use of a nationally representative dataset of individuals living in the US, this study showed that age-related deficit

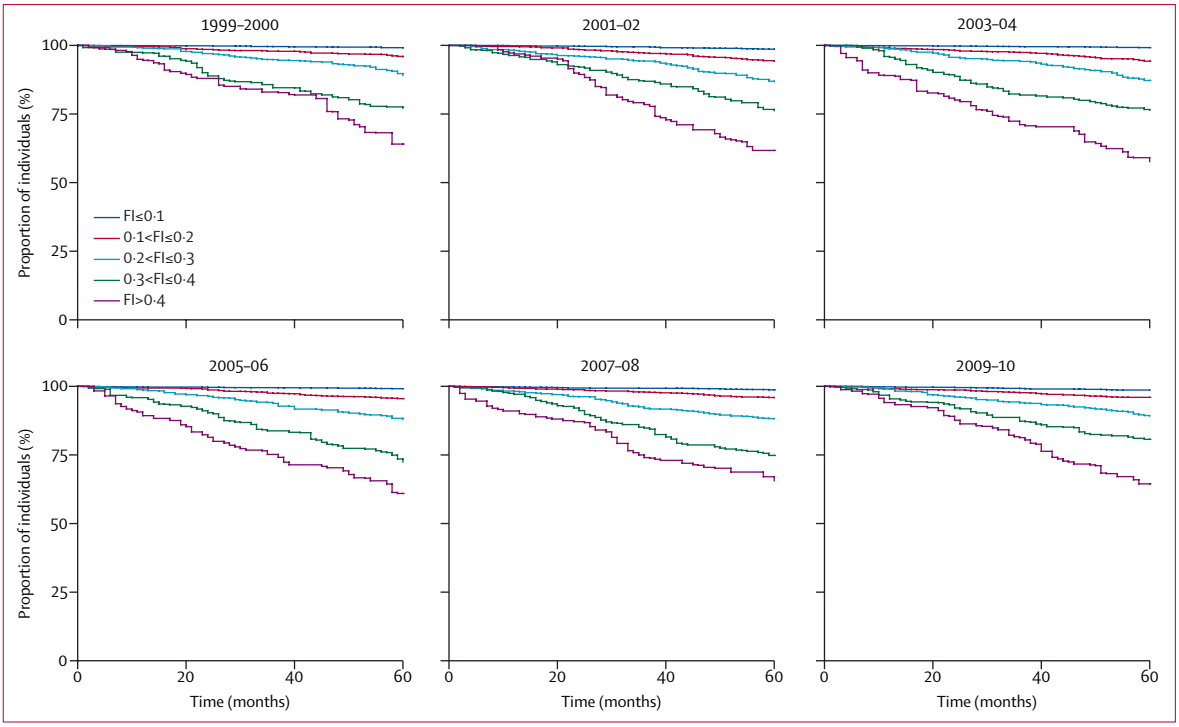

Figure 4: **Kaplan-Meier curves showing 5-year survival by frailty index category, stratified by cohort (1999–2010)**
FI=frailty index.

accumulation has increased between 1999 and 2018 in men of all ages. In women, age-related deficit accumulation increased between 1999 and 2018 in those aged 35 years and older, whereas women aged 20–34 years showed less deficit accumulation in more recent cohorts, compared to earlier cohorts. This observation appeared to be driven by a decline in the number of laboratory-based deficits (ie, a reduction in laboratory-based frailty index scores over time) in women aged 20–34 years, which contributed to the attenuation of sex differences in deficit accumulation in this age group over time. We found that the lethality of frailty did not change between 1999 and 2010. Together our results suggest that, as populations continue to age, and should frailty lethality continue to stay the same, the prevalence of frailty will continue to increase.

The observed increases in frailty in more recent cohorts are consistent with other studies showing higher frailty levels in more recent cohorts.[6,8,9] However, these previous studies measured frailty levels in older adults (mean age 65–75 years) over periods of 10–30 years, and did not consider how the accumulation of health-related deficits might have changed across early or midlife. We show that trends of increasing frailty levels over time occur in men as young as 20 years old and women as young as 35 years. This finding contradicts evidence from the English Longitudinal Study of Ageing (ELSA), which reported no changes in frailty index scores over an 8-year period in individuals aged 50–69 years.[6] Data from the ELSA suggested greater increases in frailty from the age of 70 years. Using data from the NHANES, this pattern was also observed across all age groups in the current study apart from in women aged 20–34 years. NHANES data indicated that increases in frailty index scores in older age groups, particularly the 80 years and older age group, were greater than those of previous studies, which reported differences of 0·01 over a 20-year period in the UK (increase in mean frailty index score of 0·18 [95% CI 0·17–0·18) in 1991 to 0·19 [0·19–0·20] in 2011), 0·02 over an 8-year period in the UK (increase in mean frailty index score of 0·16 [SD 0·12] in 2002 to 0·18 [0·13] in 2010), and 0·03 over a 10-year period in the US (increase in median frailty index score of 0·16 [IQR 0·13] in 2002 to 0·19 [0·23] in 2012).[6,8,9] Changes in frailty severity are clinically detectable with a difference in frailty index score of approximately 0·03.[22] Men and women aged 80 years and older had 0·08 (95% CI 0·05 to 0·10) higher frailty index scores over a 20-year period, which equates to a clinically visible difference after 8 years. As the number of older adults continues to rise, this clinically significant increase in frailty levels could have important implications for health-care utilisation and costs.[23]

Changes in frailty index scores over time (ie, frailty cohort trends) are cumulative, such that changes in one cohort are influenced by changes in previous cohorts. Additionally, frailty cohort trends are expected to differ across different countries and cultures, given geographical disparities in health outcomes, life expectancy, and mortality risks. The

studies compared above[6,7,8,9] used cohorts from high-income countries (the UK, Sweden, and the USA), which both enables a reasonable comparison with our study and identifies a clear need for an investigation of changes in frailty severity and lethality over time in other cultures and geographical regions, to see if these trends hold in low-income and middle-income countries.

Previous studies have reported conflicting changes in frailty lethality over time. Although frailty lethality has been shown to have declined in Swedish cohorts over a 30-year period,[7] data from UK cohorts suggest that associations between frailty and mortality have remained stable over a 20-year period.[9] With advances in medical technology and health-care services, frailty lethality could be expected to decrease as a result of improved medical care and prognoses for individuals with high frailty levels. Conversely, our findings suggest that the lethality of frailty has remained stable over a 12-year period. Further assessment of this trend over a longer period might be necessary to identify small changes in frailty lethality over time. At present, stable frailty lethality and increased frailty levels at younger ages suggest that the rising frailty levels are not only a result of the increased survival of individuals with higher levels of frailty. If frailty prevalence is posited to be a function of incidence and survival, rising frailty levels across all age groups and stagnant frailty lethality could forecast a rise in the prevalence of frailty alongside changes to a rapidly ageing population.

As frailty prevalence and life expectancies increase, understanding the impact of rising frailty levels on outcomes other than mortality becomes a priority. How do recent rises in frailty affect institutional-free survival, disability, and health-care costs? Frailty severity is strongly associated with disability-adjusted life-years;[24] an increase in the number of years spent in poor health can have consequences at a population health resource level. The deficit accumulation approach recognises that age-related diseases are not independently accumulated.[5,13] Consequently, increasing frailty at all ages over time suggests greater phenotypic expression of morbidities across different stages of the life course. This trend is important from a life-course perspective, as identification of meaningful age-related variations in health at mid-life could provide better screening opportunities and interventions before clinical disease endpoints arise.[11,25]

As the NHANES is representative of the community-dwelling population in the USA, the observed increases in frailty index scores over time, which were largest in those aged 80 years and older, might indicate that the proportion of older adults with high frailty who remain in the community has increased over time. US census data shows that the proportion of individuals aged 65 years and older who live in nursing homes has declined from 5·1% in 1990, to 4·5% in 2000, to 3·1% in 2010, and from 24·5% in 1990, to 18·2% in 2000, to 10·4% in 2010 in those aged 85 years and older.[26,27] Although these numbers suggest that older adults are increasingly less likely to enter an assisted living facility, further understanding of how this might differ between those with different degrees of frailty is needed. An increasing desire to remain in independent living contributes to increased levels of frailty in the community, and could reflect a greater need for community-based care. Exploring how frailty levels in individuals in nursing or long-term care facilities might have changed over time could help to accurately capture frailty levels that are representative of the general population.

We found some differences in the accumulation of preclinical (ie, laboratory-based frailty index) and clinical (ie, self-reported frailty index) deficits. Laboratory-based frailty index deficits primarily showed a quadratic increase over time, with a slower increase in earlier cohorts and an acceleration in more recent cohorts. Given the potential translation of preclinical to clinical deficits,[13] this trend could indicate that clinical deficits will continue to increase over time. The intercept of laboratory-based frailty index deficits was higher than that of self-reported index deficits across all age groups, which might permit the detection of deficits at an earlier stage to identify at-risk individuals. Further research should consider how higher laboratory-based frailty index scores in more recent cohorts might provide an opportunity for earlier intervention. Laboratory-based frailty index scores have shown an association with mortality risk, independent of self-reported clinical deficits.[17] This association could suggest that, in addition to being precursors to clinical frailty, laboratory-based deficits might contribute to mortality via cellular or tissue pathways.

In contrast to the observed increases in frailty in other age groups, women aged 20–34 years showed an opposing pattern of frailty improvements (ie, lower levels of frailty) in more recent cohorts; the declining frailty index scores over time were primarily driven by decreases in laboratory-based frailty index deficits. As laboratory-based frailty index scores were higher in pregnant women, a lower prevalence of pregnancies over time could partially explain these declining scores; however, this pattern remained in sensitivity analyses excluding pregnant women. These findings contrast with evidence from an Australian cohort study, which suggested that women aged 18–23 years born in 1973–78 are in poorer health than those born in 1990–95.[28] Further consideration of differences in health behaviours between countries is needed. Perhaps due to the recent (ie, within the past 5–10 years) application of frailty index approaches in a younger age demographic, to our knowledge, this is the first study to investigate and show that laboratory-based frailty index scores are higher in pregnant women than in non-pregnant women. The many adaptive physiological changes that occur during pregnancy often result in laboratory test results being outside the normal range. Notably, few clinical laboratories provide reference ranges for blood tests during pregnancy; therefore,

normal physiological adaptations that occur during pregnancy can be misinterpreted as pathological. Future work with a life-course perspective could improve our understanding of whether these laboratory abnormalities have any cumulative effect in later life. When laboratory-based frailty index approaches are used in women who could be pregnant, adjusted reference ranges might be needed to account for the effects of hormones. Even though frailty has widely been examined in older adults, extension of deficit accumulation approaches to younger adults is showing promising results.[11,12,14] Further studies should focus on frailty in younger adults, as the data could provide opportunities for early intervention and primary prevention.

To our knowledge, this study is the first to investigate differences in frailty severity and lethality across cohorts in a large nationally representative sample of nearly 50 000 community-dwelling individuals in the USA. Although the NHANES is representative of the community--dwelling population, individuals living in long-term care facilities are not included; therefore, the results of this study could underestimate any improvements in frailty lethality in the oldest age groups in these settings. Additionally, self-reported frailty index scores were higher in excluded individuals with data missing for 20% or more laboratory-based deficits, and laboratory-based frailty index scores were higher in those with missing data on self-reported deficits. Previous investigations of health survey data suggest that the amount of missing data tends to be higher in individuals with a poorer health status.[29] Therefore, exclusion of these individuals from the analyses might have underestimated frailty severity. To ensure a sufficient follow-up period, mortality data was only considered for six cohorts, spanning a 12-year period. This is a relatively short comparison period and should therefore be taken into account when interpreting the observed absence of differences in frailty lethality between cohorts.

For more on **The National Health and Nutrition Examination Survey data** see https://www.cdc.gov/nchs/nhanes/index.htm

In conclusion, this study identified that across all age groups, apart from women aged 20–34 years, the degree of frailty has increased in more recent cohorts. With an ageing population, an increase in frailty severity, and no change in frailty-associated mortality, the prevalence of frailty will continue to increase. An improved understanding of the precursors to frailty and how they might change over time is crucial in preparing for the shift in the ageing population. This improved understanding could include changes over time in the associations between demographic or socioeconomic indicators, related health inequalities, or health behaviours and levels of frailty. For example, racial differences in frailty were briefly shown in this study. Future research should aim to better understand these racial disparities and assess how they change over time. The consequences of rising frailty levels should also be better understood, as they are expected to include greater numbers of individuals living with disabilities and chronic diseases, and a corresponding increase in care responsibilities at both individual and population levels.

Contributors

JMB statistically analysed the data and wrote the first draft of the manuscript. JMB and OT accessed and verified all the data. All authors contributed to the conception and design of the study, data interpretation, and manuscript revision, and all authors read and approved the submitted paper. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

KR asserts copyright of the Clinical Frailty Scale through Dalhousie University's Industry, Liaison, and Innovation Office; is a co-founder of Ardea Outcomes (formerly DGI Clinical), which has had contracts with pharmaceutical and device manufacturers (Biogen, Shire, Hollister, Novartis, Nutricia, Roche, and Takeda) on individualised outcome measurement in the last 5 years; attended an advisory board meeting on dementia with Lundbeck in 2017; chaired a Scientific Workshop and Technical Review Panel on frailty for the Singapore National Research Foundation in 2020; received personal fees directly from event organisers for invited guest lectures, rounds, academic symposia, and presentations on frailty; and is an Associate Director of the Canadian Consortium on Neurodegeneration in Aging, which is funded by the Canadian Institutes for Health Research, the Alzheimer Society of Canada, and several other charities. JMB and OT declare no competing interests.

Data sharing

The National Health and Nutrition Examination Survey data is publicly accessible and available for download.

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