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Descriptive Finding

Frailty at death: An examination of multiple causes of death in four low mortality countries in 2017

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Contents

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Abstract

BACKGROUND
The increasing prevalence of frailty in ageing populations represents a major social and public health challenge which warrants a better understanding of the contribution of frailty to the morbid process.

OBJECTIVE
To examine frailty-related mortality as reported on death certificates in France, Italy, Spain, and the United States in 2017.

METHODS
We identify frailty at death for the population aged 50 years and over in France, Italy, Spain, and the United States. We estimate the proportions of deaths by sex, age group, and country using specific frailty-related ICD-codes on the death certificate, (1) as the underlying cause of death (UC), (2) elsewhere in Part I (sequence of diseases or conditions or events leading directly to death), and (3) anywhere in Part II (conditions that do not belong in Part I but whose presence contributed to death).

RESULTS
The age-standardized proportion of deaths with frailty at ages 50 and over is highest in Italy (25.0%) followed by France (24.1%) and Spain (17.3%), and lowest in the United States (14.0%). Cross-country differences are smaller when frailty-related codes are either the underlying cause of the death or reported in Part II. Frailty-related mortality increases with age and is higher among females than males. Dementia is the most frequently reported frailty-related code.

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CONCLUSIONS
Notable cross-country differences were found in the prevalence and type of frailty-related symptoms at death, even after adjusting for differential age distributions.

CONTRIBUTION
Strong similarities between countries were found that warrant monitoring frailty at death in low-mortality countries to complement information on frailty prevalence in the living population.

1. Introduction

Since the earliest studies on mortality, cause-of-death data have provided invaluable information describing the circumstances leading to death. From a public health perspective, understanding the circumstances in which people die is essential for planning interventions and services to improve end-of-life experiences, and more generally to deepen our knowledge of the morbid processes.

In ageing populations (Christensen et al. 2009) the high prevalence of frailty is an important and major societal and public health challenge (Manfredi et al. 2019). Frailty is defined as "a state of increased vulnerability to poor resolution of homeostasis after a stressor event, which increases the risk of adverse outcomes" (Fried et al. 2001). Frail individuals are less resistant to stressors because they lack the compensating mechanisms to recover from small health issues (Bottle et al. 2019; Fried et al. 2004; Fries 1983). A large body of literature on frailty prevalence, the frailty index, and related health outcomes exists for various populations (e.g., Amblàs-Novellas et al. 2018; Clegg et al. 2013; Hao et al. 2019; Kojima, Iliffe, and Walters 2018; Kulmala, Nykänen, and Hartikainen 2014; Lohman et al. 2020; Orfila et al. 2022), and a strong relationship between frailty and the risk of subsequent death has been documented (Hao et al. 2019; Kojima, Iliffe, and Walters 2018; Kulmala, Nykänen, and Hartikainen 2014; Lohman et al. 2020).

The extent to which frailty is reported on the death certificate by certifying physicians is poorly documented. One of the major obstacles in estimating frailty at death is the fact that frailty per se is not a disease in the International Classification of Diseases version-10 (ICD-10). Therefore, it is only possible to examine frailty-related mortality by identifying death certificates that include ICD10-codes related to frailty. In that regard, it is important to look at frailty-related codes among both underlying causes (UC) and contributing causes (CC) of death. The standard death certificate recommended by the World Health Organization (WHO) and implemented by most countries comprises two parts. Certifying physicians are expected to differentiate between the medical causes of

death that have been involved in the main process leading to death (reported in Part I of the death certificate) and all other diseases or conditions that may have adversely influenced the course of the morbid process but that were not a direct part of it (reported in Part II). A number of rules developed by the WHO determine which of all the causes listed on the death certificate is the underlying cause of death (UC). The WHO defines the UC as "the disease or injury which initiated the train of events leading directly to death, or the circumstances of the accident or violence which produced the fatal injury" (World Health Organization 1979). The UC is that typically reported in cause-of-death statistics as published by the WHO or National Statistics Offices. In most cases, it is selected from the conditions listed in Part I of the death certificate. The other causes reported in Part I are supposed to be direct consequences of the underlying cause; that is, they are part of the "train of events leading directly to death". In Part II the certifier is asked to report "any other significant condition that unfavorably influenced the course of the morbid process but is not related to the condition directly causing death" (instructions given on the WHO-recommended death certificate). Nevertheless, in some cases improper certification occurs and in practice, the WHO authorizes the selection of the UC from Part II in such cases. In the past, coding the causes mentioned on the death certificate according to the International Classification of Diseases and selection of the UC were carried out manually. Over the past few decades a growing number of countries have implemented automatic coding and UC selection, which has increased comparability of cause-of-death statistics over time and across countries.

Whether frailty-related ICD codes are reported in the first or the second part of the death certificate thus points to two very different situations and as such has very different implications in term of public health. In the first situation (frailty as part of the morbid process), frailty is likely to correspond to end-of-life symptoms and does not necessarily reflect pre-existing frailty in the deceased. In the second situation (frailty as a contributing cause), frailty indicates vulnerability and it is more likely to reflect a situation pre-existing the process leading to death, a situation that might have increased the risk of dying but that was independent from the main morbid process.

Altogether, information on frailty involved in the morbid process is useful for guiding health policies aimed at improving health and survival in advanced societies with high life expectancy and high shares of older population. Approaching frailty from a death certificate perspective complements frailty-related research in the living population by providing information on the extent to which frailty is directly or indirectly related to a death. We are only aware of one study that assesses frailty at death using death certificate data (Grippo et al. 2020). In the study, frailty was mentioned in 25% of all deaths in Italy over age 50 and in 46% of those over age 95. At all ages, frailty was mentioned more frequently on female than on male death certificates.

We aim to shed new light on how frailty contributes to mortality in four countries: France, Italy, Spain, and the United States. These four countries have been selected for their high-quality, readily available mortality data, with information on all causes reported on the death certificate (Mikkelsen et al. 2015) and sufficiently large populations to make multiple cause-of-death analyses statistically meaningful. All four countries implement automated coding systems. The United States uses the MICAR-ACME system, or Mortality Medical Indexing, Classification, and Retrieval (2009 version – https://www.cdc.gov/nchs/nvss/mmds/about_mmds.htm), while France, Italy, and Spain use the IRIS system. Both systems are highly consistent.

We seek to measure the prevalence at death of frailty-related codes over age 50 and their distribution according to where they are located on the death certificate (as the underlying cause of death; as another mention in Part I of the death certificate; as a mention in Part II of the death certificate), by sex and age group across the four study countries, in order to identify similarities and differences in these low-mortality populations.

2. Data and methods

2.1 Data

We use all individual multiple cause-of-death records for the year 2017 for France, Italy, the United States, and Spain. All four countries use the standard medical certification form recommended by the World Health Organization (WHO) (World Health Organization 2004) to report causes of death. Data are collected and published by the National Institute for Health and Medical Research (INSERM) in France, the National Institute of Statistics (ISTAT) in Italy, the National Institute of Statistics (INE) in Spain, and the National Center for Health Statistics (NCHS) within the Centers for Disease Control (CDC) in the United States. As our classification aims at better describing the circumstances of death at higher ages, the analysis is restricted to deaths at age 50 and over (amounting to 555,861 deaths in France, 622,801 in Italy, 402,934 in Spain, and 2,514,491 in the United States), representing more than 94% of all deaths in each of the four countries (HMD 2022).

2.2 Methods

There is no agreement on an operational list of clinical entities – labelled as frailty symptoms or frailty syndromes – that perfectly reflects the concept of frailty (De Vries

et al. 2011; Rodríguez-Mañas et al. 2013). We use a list derived from Soong et al. (Soong et al. 2015), who were the first to attempt developing an operational definition of frailty-related codes based on the ICD. Of the nine groups of frailty syndromes identified by Soong et al. we selected the following types of frailty-related codes: dementia and other symptoms and signs involving cognitive functions and awareness (ICD-10 codes: F00–F03, G30, R41); organic amnesic syndrome and delirium not induced by alcohol and other psychoactive substances (F04–F05); incontinence (R15, R32); functional dependence and mobility problems (R26, R27, Z74); decubitus ulcer and pressure area (L89); and senility (R54). We excluded falls and fractures because they amalgamate a wide range of situations (from traffic accidents to accidental falls) and because we consider that they should be regarded as causes or consequences of frailty rather than frailty per se. We also excluded anxiety and depression, which we do not consider to be frailty syndromes, and we added malaise and fatigue (R53) and cachexia and protein-energy malnutrition (R64, E40–E46). In order to improve the visualization of some results, we combined incontinence (R15, R32), functional dependence, and mobility problems (R26, R27, Z74) and decubitus ulcer and pressure area (L89) into a single category labelled 'mobility problems'.

We classified all death certificates that mentioned frailty into three categories: (1) those where frailty is the underlying cause of death (UC), (2) those with other frailty-related codes in Part I, and (3) those with frailty-related codes in Part II (but other than the underlying cause). The three categories are not mutually exclusive since a single death certificate can include multiple mentions of frailty-related codes, so each death certificate can be classified in more than one category. For each country, sex, and 5-year age group, we computed the proportion of deaths in each of the three frailty categories as a share of all deaths. Age-standardized proportions were calculated using the direct method, with the age structure of the deaths combined over all four countries as the standard. We also differentiated by the type of frailty-related code by analysing the specific ICD codes mentioned on the death certificates. Ninety-five per cent confidence intervals for the proportions were computed using the Wald method (Agresti and Coull 1998).

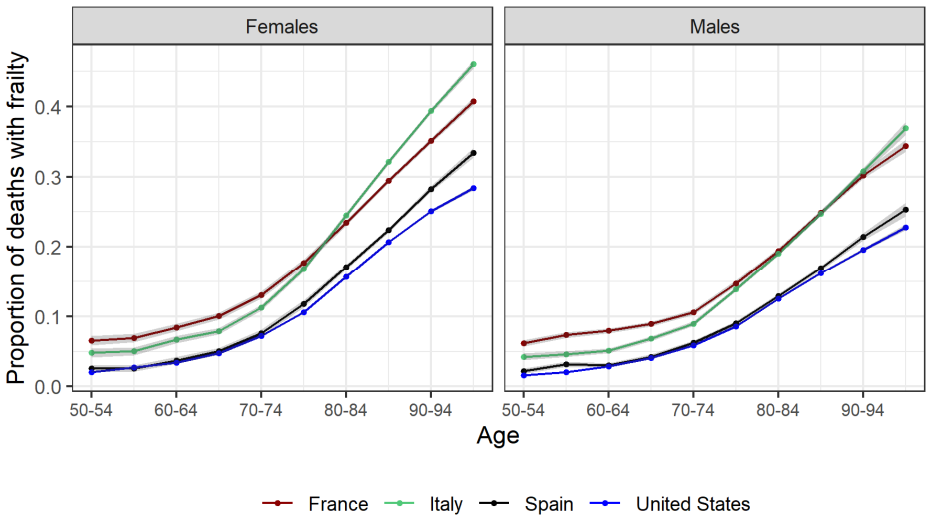
3. Results

3.1 General findings

Figure 1 shows the proportion of death certificates with a mention of frailty by age and sex and for each country. The proportion of deaths with frailty increases with age, especially after age 65. For example, frailty prevalence at death in Italy increased from 6.6% (95% CI: 6.1–7.2) at age 60–64 to 24.5% (24.1–24.8) at age 80–84 for women, and

from 5.1% (4.7–5.5) to 19.0% (18.6–19.4) for men; similar increases were found in the other study countries. Overall, the age-standardized proportion of deaths with frailty at ages 50 and over was the highest in Italy (25.0%), followed by France (24.1%) and Spain (17.3%), and lowest in the United States (14.0%). The share of deaths with frailty was higher in Italy and France than in Spain and the United States for both men and women, and higher for women than for men in all four countries, with a female-to-male standardized proportion of deaths-with-frailty-ratio ranging from 1.39 in Spain to 1.57 in the United States.

Figure 1: Country, sex, and age-specific proportion of deaths with any mention of frailty

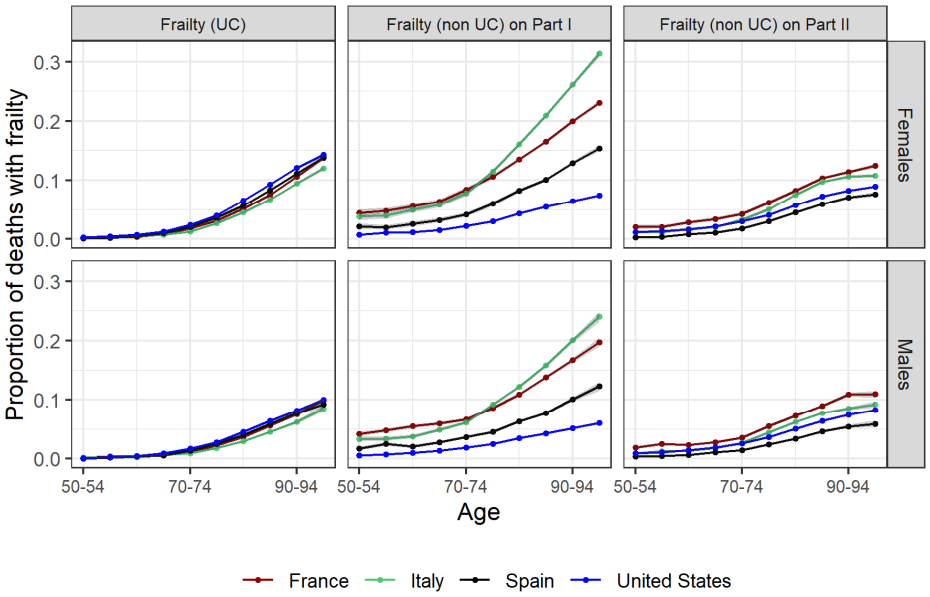


3.2 Frailty according to its position on the death certificate

The proportion of deaths with a mention of frailty increases over age for all three categories of frailty mentions (UC, non-UC Part I, and non-UC Part II), though the increase is sharper when frailty is recorded as either the underlying cause or another cause listed in Part I (Figure 2). When identified as the UC, frailty is reported most frequently on death certificates in Spain and least frequently in Italy (Table S1 in the supplementary material). At absolute levels, wider country differences are observed in frailty being

mentioned in Part I (but not as the UC). For example, at ages 80–84 the proportion of female deaths with frailty reported in Part I (not as the UC) is 16.1% (15.8–16.4) in Italy, 13.6% (13.2–13.9) in France, 8.3% (8.0–8.6) in Spain, and 4.3% (4.2–4.4) in the United States. Death certificates with a frailty mention in Part II represent a much lower share of all deaths, although higher in France (8.3%, 95%CI: 8.0–8.5) and Italy (7.5%, 95%CI: 7.3–7.8) than in Spain (4.5%, 95%CI: 4.3–4.7) and the United States (5.8%, 95%CI: 5.7–5.8).

Figure 2: Country, sex, and age-specific proportion of deaths with frailty-related codes by location on the death certificate



*Non-exclusive groups, as any one death can include all three types of frailty mentions.

3.3 Specific frailty-related codes according to their position on the death certificate

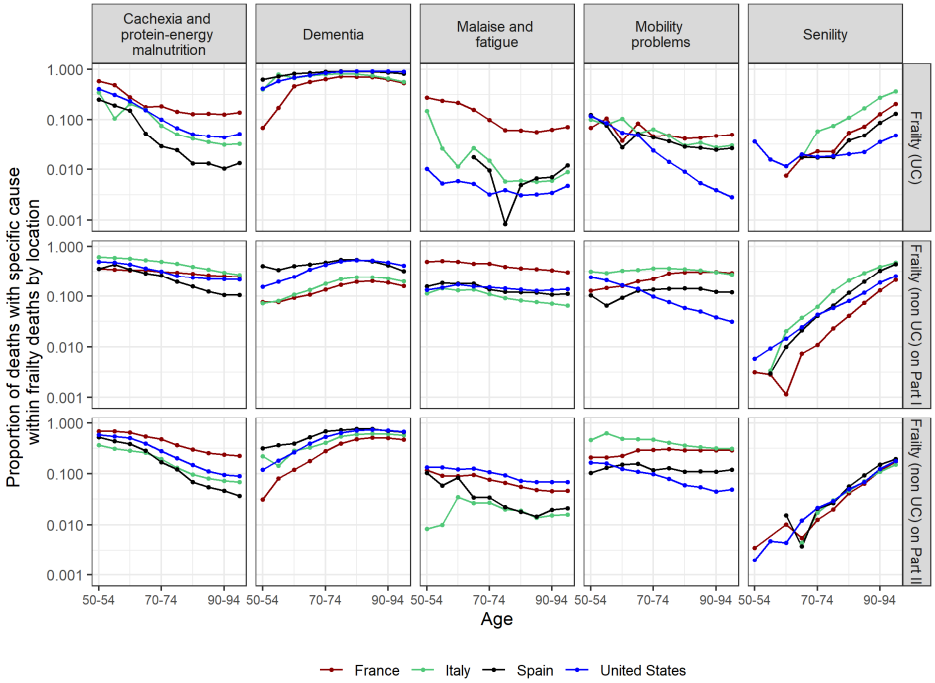
Figure 3 identifies more precisely which specific frailty-related codes are reported when frailty is mentioned as the UC, in Part I but not as the UC, or in Part II and not as the UC. The distribution among the corresponding deaths is provided by sex and age group.

Frailty as the UC: Dementia is the most frequent frailty-related code among all those selected as the UC in all countries and age groups. It represents at least 75% of all deaths, with a frailty ICD-code as the underlying cause in most age groups in Spain, the United States, and Italy. By contrast, in France the share of certificates with dementia as the UC is lower (ranging from around 20% at ages 55–59 to almost 75% at ages 75–79). However, compared to the three other countries, France reports cachexia and malaise and fatigue much more frequently as the UC; i.e., at least 10% for each condition, and above 25% at ages 50–59. Generally, with age, senility represents an increasing share of frailty mentions as the UC, particularly in Italy where values are close to 40% in the highest age group.

Frailty in Part I (but not as the UC): When frailty is mentioned in Part I but not as the UC, there is interesting cross-country variation in the types of conditions reported. Dementia is the main contributor in Spain and the United States, where it represents up to half of all frailty mentions in Part I (but not as the UC) at ages 75–84 years. Cachexia is more common in Italy across all age groups. Malaise and fatigue represent a higher share in France (ranging from 25% to 50%, depending on the age group). In all countries, the proportion of deaths with senility mentioned in Part I (but not as the UC) increases with age to reach values close to 25% in France and the United States and 50% in Spain and Italy at age 95 and over.

Frailty in Part II (and not as the UC): Among all deaths with a mention of frailty in Part II (not UC), dementia is the most prevalent frailty-related code, with proportions reaching 75% in Spain and the United States compared to 50% and 60% in France and Italy, respectively. In the latter two countries, mobility-related conditions are more prevalent, as well as cachexia in France. At substantially lower levels (15%), malaise and fatigue are slightly more prevalent in France and the United States than in Italy and Spain. Finally, senility represents a very similar proportion (about 20%–25% at ages 95 and over) of all Part II mentions of frailty in the four study countries.

Figure 3: Country and age-specific frailty-related codes by location on the death certificate (both sexes combined)



*Mobility problems include decubitus ulcer and pressure area, incontinence, and functional dependence.
** In this plot the denominators are the frailty-related death counts within each country and age group. Therefore, the sum of cause-specific results could be higher than 1, as some deaths may have more than one cause reported in Part II.
Note: For each panel the denominators are the number of deaths with frailty-related codes within each position on the death certificate for each country and age group.

4. Discussion

We examined frailty-related codes at death, extending a previous study by Grippo et al. (2020) in various directions: first, by comparing the situation in four low-mortality countries (France, Italy, Spain, and the United States); second, by distinguishing entries of frailty-related codes depending on their location on the death certificate (as the UC; in Part I but not as the UC; in Part II and not as the UC); and third, by measuring how frequently the various types of frailty are reported on the certificates.

In line with previous results, we find that frailty-related mortality increases systematically with age, and that the contribution of frailty to death is more frequent for females than for males at all ages in all four countries. A further comparison of our results and previous findings is challenging, due to the lack of studies based on mortality data. Most previous studies of frailty have relied on survey data with frailty identified in living individuals. Our population of interest (dead individuals) is a very selected population, which therefore could not be compared with the general (living) population. Additionally, our frailty measures are not the same as those used in surveys and healthcare databases in the living population (Amblàs-Novellas et al. 2018; Clegg et al. 2013; Hao et al. 2019; Kojima, Iliffe, and Walters 2018; Orfila et al. 2022; Rodríguez-Mañas et al. 2013; Silan et al. 2022). Consequently, our results describe the circumstances surrounding the deaths and not the health status of a population. With this consideration in mind, it is worth mentioning that the higher frailty prevalence at death that we found in women compared with men is consistent with results on frailty prevalence in the living population (Clegg et al. 2013; Fried et al. 2001; Manfredi et al. 2019).

The differences found in the prevalence at death of frailty-related codes across countries could reflect differences in either the underlying health status of the population or in death reporting and certifying practices. In general, frailty is most frequently reported on death certificates in Italy and France, and least frequently in Spain and the United States. However, the situation varies depending on the location of the frailty mentions on the death certificate.

In all four countries, frailty is most frequently reported in Part I of the certificate, but not as the underlying cause of death. Wider country differences are observed in that case, with similarly high levels in Italy and France and low levels in the United States and Spain. In the absence of precise rules governing the reporting of these end-of-life symptoms, we suspect that part of the variation is due to differences in certification practices, and in particular to the overall number of mentions reported on the death certificate, with a higher number of mentions driving the larger proportions of frailty mentions. We found, for instance, that the average number of mentions in Part I is above 3 in Italy but only slightly above 2 in the United States, consistent with the more frequent reporting of frailty in Part I of the certificate (Figure S1 in the supplementary material). However, the average number of entries in Part I is higher in Spain than in France, even though there are fewer mentions of frailty in the former than in the latter. Country variation in the propensity to report more or fewer causes on the death certficate could explain the differences we observed, but the relationship is not systematic. We suspect that frailty is underreported by certifying physicians, either because they consider almost everyone to be frail at the end of life, especially at higher ages, or because frailty syndromes are not considered valid causes of death. We thus acknowledge that our estimates of frailty at death are likely to be conservative. However, there is no reason

why reporting practices should lead to higher reporting of frailty among females or at higher ages, two characteristics of the uncovered patterns in all four populations that are likely to reflect actual differences in the prevalence of frailty at the end of life.

When frailty-related codes are mentioned as either the underlying cause of death or in Part II, differences across countries are small. The prevalence of frailty mentions in Part II (and not UC), which identifies a state of vulnerability that increases the risk of adverse events, ranged from 4.0% in Spain and 4.4% in the United States to 6.2% in Italy and 6.7% in France. The notable role played by mobility issues in France and Italy and by cachexia and nutritional deficiencies in France must be highlighted. However, dementia, with a higher prevalence in Spain and the United States than in the other two countries, turns out to be the most common type of frailty reported in all four countries at higher ages. Wilkins et al. (1999) propose an interesting interpretation of this phenomenon, suggesting that the care provided to people with dementia may not be the same as the care provided to other elderly patients: "People whose general health is compromised by the physical effects of dementia are presumably less resistant to ailments that might otherwise not result in death. As well, pharmaceutical and other treatments for these conditions might be prescribed with less stringency to people with dementia than to those not so affected" (p. 30). This implies that the observed country differences in frailty-related codes reported in Part II may result from cross-country heterogeneity in the provision of healthcare (Sezgin et al. 2019), an issue that should be further explored.

Dementia is also the most frequently cited frailty-related code when frailty is the UC. Frailty as the UC ranged from 4.1% in Italy to 6.0% in the United States (Table S1 in the supplementary material). A clinical study of death over age 65 in France and Italy provides some relevant indications of these morbid processes (Désesquelles et al. 2014). On death certificates with an entry of dementia as a contributing cause, the top three underlying causes of death were diseases of the circulatory system (e.g., cerebrovascular diseases) (Désesquelles et al. 2014). When dementia was the UC, diseases of the circulatory system and pneumonia were the most frequently reported contributing conditions. This study also shows a strong association of dementia with other frailty-related codes such as nutritional deficiencies and mobility problems, and especially bed confinement. In their 2001 paper, Fried and colleagues note that "there is a growing consensus that […] multiple components must be present clinically to constitute frailty" (Fried et al. 2001). In this study, we have examined the presence of frailty-related codes on the death certificates, to further disentangle key components of the higher mortality risks among frailty individuals (Kulmala et al., 2014; Lohman et al., 2020). In this study, we have examined the presence of all frailty-related codes on death certificates. Yet, more work needs also to be done relating frailty-specific symptoms to morbidity status and underlying causes of death. For example, previous studies in Australia and the Netherlands found that dementia was reported in the death certificate in 52% and 75% of

the deceased with dementia, respectively (Klijs et al. 2021; Xu et al. 2022). Similarly, we acknowledge our inability to assess the extent to which under-reporting differs across countries, as over the last decade dementia has been found to be increasingly reported in Part I in Australia and the United States (Adair et al. 2022).

Our study comes with some limitations. We acknowledge that our results are sensitive to the frailty codes we have selected, and therefore comparison with other studies on frailty-related health outcomes should be made with extreme caution. However, to facilitate comparison we provide results for each frailty-related code (type of frailty). In principle, and though frailty measures are not the same across study types, it is expected that the prevalence of frailty derived from either health registers or health surveys (in the living population) is somewhat reflected in the prevalence of frailty derived from death certificates, in spite of frail people's differential risk of dying. Finally, in our view the concept of senility, which in medical terms corresponds to a global cognitive decline associated with old age, is a good indicator of old-age frailty. For the statisticians in charge of cause-of-death statistics, senility (R54 code in the ICD10) has long been considered a garbage code that is used when the physician does not know what the person has died from. In fact, we find that senility is often reported as a contributing cause in either Part I or Part II of the death certificate, potentially associated with well-defined causes of death. This finding suggests that for the physician, senility represents an actual meaningful condition to be considered within the circumstances surrounding the morbid process. For this reason, at a time when a new revision of the ICD (the 11th) is about to be implemented, we plead in favour of maintaining a specific code in the classification that allows for the reporting of senility. Alternatively, to identify a pre-existing vulnerability in the deceased a new 'frailty' code could be introduced to allow statistics on such conditions, as well as others (Banerjee et al. 2021; Muscedere 2020). The ICD-11 provides an extension code (XT9T "ageing-related diseases") which will be very useful for analysing specific diseases reported as "ageing-related"; nevertheless a code is needed for situations where ageing-related frailty is reported on death certificates without mention of specific diseases.

In conclusion, this study highlights similarities and differences in the prevalence of frailty at death in four countries: France, Italy, Spain, and the United States. Further research should explore the role played in these cross-country differences by certification practices and should further examine the associations between frailty and other causes of death in order to shed more light on cross-national differences in the prevalence and the nature of frailty at death. In a context of ageing populations and increasing numbers of frail individuals, our study provides a basis for further monitoring frailty in low-mortality countries using a widely available and highly comparable source of information.

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Authors' contributions: STL: Data analysis, methodology, visualization, writing original draft, review, and editing. MB: Conceptualization, writing original draft, review, and editing. VE, LF, FM, and MP: Conceptualization, review, and editing. FG: Conceptualization, data analysis, methodology, software, review, and editing. AD: Conceptualization, methodology, writing original draft, review, and editing.

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References

Adair, T., Temple, J., Anstey, K.J., and Lopez, A. D. (2022). Is the rise in reported dementia mortality real? Analysis of multiple-cause-of-death data for Australia and the United States. *American Journal of Epidemiology* 191(7): 1270–1279. doi:10.1093/aje/kwac047.

Agresti, A. and Coull, B.A. (1998). Approximate is better than 'exact' for interval estimation of binomial proportions. *The American Statistician* 52(2): 119–126. doi:10.1080/00031305.1998.10480550.

Amblàs-Novellas, J., Martori, J.C., Espaulella, J., Oller, R., Molist-Brunet, N., Inzitari, M., and Romero-Ortuno, R. (2018). Frail-VIG index: A concise frailty evaluation tool for rapid geriatric assessment. *BMC Geriatrics* 18(1): 1–12. doi:10.1186/s12877-018-0718-2.

Banerjee, D., Mukhopadhyay, S., Rabheru, K., Ivbijaro, G., and de Mendonca Lima, C.A. (2021). Not a disease: A global call for action urging revision of the ICD-11 classification of old age. *The Lancet Healthy Longevity* 2(10): e610–e612. doi:10.1016/S2666-7568(21)00201-4.

Bottle, A., Kim, D., Hayhoe, B., Majeed, A., Aylin, P., Clegg, A., and Cowie, M.R. (2019). Frailty and co-morbidity predict first hospitalisation after heart failure diagnosis in primary care: Population-based observational study in England. *Age and Ageing* 48(3): 347–354. doi:10.1093/ageing/afy194.

Christensen, K., Doblhammer, G., Rau, R., and Vaupel, J.W. (2009). Ageing populations: The challenges ahead. *The Lancet* 374(9696): 1196–1208. doi:10.1016/S0140-6736(09)61460-4.

Clegg, A., Young, J., Iliffe, S., Rikkert, M.O., and Rockwood, K. (2013). Frailty in elderly people. *The Lancet* 381(9868): 752–762. doi:10.1016/S0140-6736(12)62167-9.

De Vries, N.M., Staal, J.B., Van Ravensberg, C.D., Hobbelen, J.S.M., Rikkert, M.O., and Nijhuis-van der Sanden, M. (2011). Outcome instruments to measure frailty: A systematic review. *Ageing Research Reviews* 10(1): 104–114. doi:10.1016/j.arr.2010.09.001.

Désesquelles, A., Demuru, E., Salvatore, M.A., Pappagallo, M., Frova, L., Meslé, F., and Egidi, V. (2014). Mortality from Alzheimer's disease, Parkinson's disease, and dementias in France and Italy: A comparison using the multiple cause-of-death

approach. *Journal of Aging and Health* 26(2): 283–315. doi:10.1177/0898264313514443.

Fried, L.P., Ferrucci, L., Darer, J., Williamson, J.D., and Anderson, G. (2004). Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 59(3): M255–M263. doi:10.1093/gerona/59.3.M255.

Fried, L.P., Tangen, C.M., Walston, J., Newman, A.B., Hirsch, C., Gottdiener, J., Seeman, T., Tracy, R., Kop, W.J., and Burke, G. (2001). Frailty in older adults: Evidence for a phenotype. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences* 56(3): M146–M157. doi:10.1093/gerona/56.3.M146.

Fries, J.F. (1983). The compression of morbidity. *The Milbank Memorial Fund Quarterly. Health and Society* 61(3): 397–419. doi:10.2307/3349864.

Grippo, F., Désesquelles, A., Pappagallo, M., Frova, L., Egidi, V., and Meslé, F. (2020). Multi-morbidity and frailty at death: A new classification of death records for an ageing world. *Population Studies* 74(3): 437–449. doi:10.1080/00324728.2020.1820558.

Hao, Q., Zhou, L., Dong, B., Yang, M., Dong, B., and Weil, Y. (2019). The role of frailty in predicting mortality and readmission in older adults in acute care wards: A prospective study. *Scientific Reports* 9(1): 1207. doi:10.1038/s41598-018-38072-7.

HMD (2022). Human Mortality Database. Max Planck Institute for Demographic Research (Germany), University of California, Berkeley (USA), and French Institute for Demographic Studies (France). Available at www.mortality.org.

Klijs, B., Mitratza, M., Harteloh, P.P., Moll van Charante, E.P., Richard, E., Nielen, M. M., and Kunst, A.E. (2021). Estimating the lifetime risk of dementia using nationwide individually linked cause-of-death and health register data. *International Journal of Epidemiology* 50(3): 809–816. doi:10.1093/ije/dyaa219.

Kojima, G., Iliffe, S., and Walters, K. (2018). Frailty index as a predictor of mortality: A systematic review and meta-analysis. *Age and Ageing* 47(2): 193–200. doi:10.1093/ageing/afx162.

Kulmala, J., Nykänen, I., and Hartikainen, S. (2014). Frailty as a predictor of all-cause mortality in older men and women. *Geriatrics and Gerontology International* 14(4): 899–905. doi:10.1111/ggi.12190.

Lohman, M.C., Sonnega, A.J., Resciniti, N.V., and Leggett, A.N. (2020). Frailty phenotype and cause-specific mortality in the United States. *The Journals of Gerontology: Series A* 75(10): 1935–1942. doi:10.1093/gerona/glaa025.

Manfredi, G., Midão, L., Paúl, C., Cena, C., Duarte, M., and Costa, E. (2019). Prevalence of frailty status among the European elderly population: Findings from the Survey of Health, Aging and Retirement in Europe. *Geriatrics and Gerontology International* 19(8): 723–729. doi:10.1111/ggi.13689.

Mikkelsen, L., Phillips, D.E., AbouZahr, C., Setel, P.W., de Savigny, D., Lozano, R., and Lopez, A.D. (2015). A global assessment of civil registration and vital statistics systems: Monitoring data quality and progress. *The Lancet* 386(10001): 1395–1406. doi:10.1016/S0140-6736(15)60171-4.

Muscedere, J. (2020). The need to implement frailty in the International Classification of Disease (ICD). *The Journal of Frailty and Aging* 9(1): 2–3). doi:10.14283/jfa.2020.2.

Orfila, F., Carrasco-Ribelles, L.A., Abellana, R., Roso-Llorach, A., Cegri, F., Reyes, C., and Violán, C. (2022). Validation of an electronic frailty index with electronic health records: EFRAGICAP index. *BMC Geriatrics* 22(1): 1–10. doi:10.1186/s12877-022-03090-8.

Rodríguez-Mañas, L., Féart, C., Mann, G., Viña, J., Chatterji, S., Chodzko-Zajko, W., Gonzalez-Colaço Harmand, M., Bergman, H., Carcaillon, L., and Nicholson, C. (2013). Searching for an operational definition of frailty: A Delphi method based consensus statement. The frailty operative definition-consensus conference project. *Journals of Gerontology Series A: Biomedical Sciences and Medical Sciences* 68(1): 62–67. doi:10.1093/gerona/gls119.

Sezgin, D., O'Donovan, M., Cornally, N., Liew, A., and O'Caoimh, R. (2019). Defining frailty for healthcare practice and research: A qualitative systematic review with thematic analysis. *International Journal of Nursing Studies* 92: 16–26. doi:10.1016/j.ijnurstu.2018.12.014.

Silan, M., Signorin, G., Ferracin, E., Listorti, E., Spadea, T., Costa, G., and Boccuzzo, G. (2022). Construction of a frailty indicator with partially ordered sets: A multiple-outcome proposal based on administrative healthcare data. *Social Indicators Research* 160(2): 989–1017. doi:10.1007/s11205-020-02512-7.

Soong, J., Poots, A.J., Scott, S., Donald, K., Woodcock, T., Lovett, D., and Bell, D. (2015). Quantifying the prevalence of frailty in English hospitals. *BMJ Open* 5(10): e008456. doi:10.1136/bmjopen-2015-008456.

Wilkins, K., Parsons, G.F., Gentleman, J.F., and Forbes, W.F. (1999). Deaths due to dementia: An analysis of multiple-cause-of-death data. *Chronic Diseases and Injuries in Canada* 20(1): 26–35.

World Health Organization (1979). *Medical certification of cause of death: Instructions for physicians on use of international form of medical certificate of cause of death*. Geneva: World Health Organization.

World Health Organization (2004). *The International Statistical Classification of Diseases and Health Related Problems ICD-10: Tenth revision. Volume 1: Tabular list* (Vol. 1). Geneva: World Health Organization.

Xu, Z., Hockey, R., McElwee, P., Waller, M., and Dobson, A. (2022). Accuracy of death certifications of diabetes, dementia and cancer in Australia: A population-based cohort study. *BMC Public Health* 22(1): 902. doi:10.1186/s12889-022-13304-8.