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Incidence of frailty: a systematic review of scientific literature from a public health perspective

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Abstract

Introduction. Because of the dynamic nature of frailty, prospective epidemiological data are essential to calibrate an adequate public health response.

Methods. A systematic review of literature on frailty incidence was conducted within the European Joint Action ADVANTAGE.

Results. Of the 6 studies included, only 3 were specifically aimed at estimating frailty incidence, and only 2 provided disaggregated results by at least gender. The mean follow-up length (1-22.2 years; median 5.1), sample size (74-6306 individuals), and age of participants (≥ 30-65) varied greatly across studies. The adoption of incidence proportions rather than rates further limited comparability of results. After removing one outlier, incidence ranged from 5% (follow-up 22.2 years; age ≥ 30) to 13% (follow-up 1 year, age ≥ 55).

Conclusions. Well-designed prospective studies of frailty are necessary. To facilitate comparison across studies and over time, incidence should be estimated in person-time rate. Analyses of factors associated with the development of frailty are needed to identify high-risk groups.

Key words
- frailty
- aging
- epidemiology
- public health
- systematic review

INTRODUCTION

The scientific and public health importance of frailty has become increasingly relevant over the past decades. Frailty is now considered one of the major challenges of global population aging, causing suffering and harm to individuals and their families, and threatening the long-term sustainability of current health care systems [1-3].

Much effort has been made to reach a clear definition of frailty and to understand both its aetiology and the potential for prevention. A common classification for research and clinical practice is yet to be achieved [4] but the conceptual and theoretical bases of frailty as a syndrome are well established [3, 5, 6]. One of the major achievements of recent research is the increased recognition that frailty is not part of the natural aging process. It is distinct from disability or multi-morbidity, although strictly related to them, and it is a complex, multifaceted, dynamic process [7].

In 2015, the World Health Organization summarized the background knowledge on frailty defining it

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as a "progressive age-related decline in physiological systems that results in decreased reserves of intrinsic capacity, which confers extreme vulnerability to stressors and increases the risk of a range of adverse health outcomes" [8]. The adverse outcomes related to frailty include disability, falls, hospitalization, and mortality [9]. Since frailty is a dynamic condition along a continuum from normal aging to disability, during which transitions between frailty states are common, and recovery, although not frequent, is possible [10, 11], there is ample potential for prevention aimed at maintaining homeostasis and limiting the vulnerability to endogenous and exogenous stressors that lead to the adverse health related outcomes [1, 2, 9, 12].

The European Union met this public health challenge by supporting and co-financing the Joint Action (JA) ADVANTAGE "A comprehensive approach to promote a disability-free advanced age" in the framework of the Third Programme of Community Action in the field of Health. Its aim is to mobilize Member States (MS) to cooperate and work towards the uptake, exchange and development of a common approach to frailty prevention and management. ADVANTAGE is a 3-year Joint Action (2017-2019) involving 22 MSs, represented by 33 organizations. The project is structured around eight work packages. One of them has the specific objective of exploring the current state of knowledge on the epidemiology of frailty, analysing available data on prevalence, incidence, and transitions between discrete frailty states [13].

Understanding the real burden of frailty, its characteristics and progression in the population is essential to calibrate an adequate public health response, balancing available resources against individual and collective needs. Detailed and reliable epidemiological findings are necessary to inform resource planning, prioritisation of interventions addressed to groups of people at higher risk, and to evaluate the effectiveness of prevention programmes. Current epidemiological evidence on frailty usually focuses on prevalence and little is known on the prospective aspects of frailty in the population. The purpose of the present study was to carry out a systematic review of literature on the incidence of frailty, with a special focus on the public health implications of retrieved results.

MATERIALS AND METHODS

Data sources and search strategy

As part of the European JA ADVANTAGE [14] on prevention and management of frailty, a systematic search of published and unpublished studies concerning the frequency of frailty in the general population was carried out using two parallel approaches. First, we searched for scientific literature using PubMed, Embase, CINAHL, MEDLINE, Opengrey and the Cochrane Library databases. Second, an opportunistic search for unpublished data was conducted among the JA partners, asking them for research projects ongoing in their own countries that explicitly addressed the epidemiology of frailty.

For practical purposes and to minimize oversight and inadvertent omissions, the search for relevant articles was not limited to incidence but extended to prevalence, as prevalence studies on frailty, which are far more common, may also include information on incidence. The following search query was adopted: [("Elderly" OR "Aged" OR "Older adult$" OR "Older person$" OR "Geriatric$") AND ("Frailty" OR "Frail") AND ("Population-based" OR "Population based") AND ("Prevalence" OR "Incidence", OR" Epidemiology") NOT Search # ("Frailty model" OR "Frailty survival model")]. Results relating to frailty incidence were then singled out and presented in the present paper, whereas findings concerning the prevalence of frailty are reported in another paper of the present journal issue [15].

The review was carried out in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16]. The adopted protocol was registered on the international prospective register of systematic reviews PROSPERO (University of York, Centre for Reviews and Dissemination; Reference number CRD42017071866) [17].

Inclusion criteria

Papers were included if they explicitly addressed frailty, irrespective of the definition or diagnostic instrument used. As a rough guide to reviewers, in order to discriminate between pertinent/irrelevant papers, frailty was defined as a state of increased vulnerability to endogenous and exogenous stressors that exposes the individual to a higher risk of negative health-related outcomes [3]. Incidence was defined as the number of new cases of frailty per population in a given time period.

All studies published from January 2002 to April 2017, with participants aged 18 or more (no maximum age limit), in English or any other language of JA partners were eligible for inclusion in the systematic review. The reference sections of papers meeting the inclusion criteria were manually examined to find additional articles not identified through the database searches. Papers published before 2002 were included if deemed relevant to the review.

Original papers reporting studies conducted either on community dwelling or hospitalized/institutionalized participants (regardless of the reasons of admission) were eligible, provided that the findings could be extended to the general population, and not restricted to a segment affected by particular diseases or conditions. Other reasons for exclusion were: replicated data, Randomized Controlled Trials, letters to the editor, abstract only publications, conference proceedings, non-systematic reviews, and editorials.

Data selection and analysis

The screening of abstracts was conducted independently by two reviewers. The full text of papers selected as potentially relevant by one or both of them was retrieved for in-depth evaluation. Disagreements were settled by a third reviewer. Data from articles assessed as eligible for inclusion in the systematic review were extracted and analysed by expert reviewers. Data extraction from articles written in languages different from English was done by a native speaker from a JA partner country.

Due to the limited number and heterogeneous characteristics of the available literature, data obtained through the systematic search were not pooled or meta-analysed to produce an overall quantitative estimate, but synthesized and compared using a narrative and tabular approach [18].

The methodological quality of selected papers was assessed by two independent critical appraisers using the Joanna Briggs Institute (JBI) critical assessment tool for prevalence and incidence studies [19]. Discrepancies in the evaluation were discussed and resolved through consensus. The quality appraisal was not merely aimed to assign a score for inclusion/exclusion of papers, but to ascertain the extent to which the possibility of bias in the study design, conduction and analysis had been addressed. The results of the evaluation were incorporated in the synthesis and interpretation of the systematic review results.

RESULTS

We found 2948 papers on prevalence and/or incidence of frailty through the literature search. Twenty-nine additional records, 6 of them potentially relevant only for incidence, were identified by reading references of selected papers. The opportunistic search for unpublished data provided no additional result. Out of the 2185 abstracts screened after duplicates removal, 1859 were excluded, most because they were unrelated to the topic (84.6%) or not reporting original data (10.0%). A total of 326 full-text articles were assessed for eligibility and 260 of them excluded (43.1% for replicated data), resulting in 66 potentially relevant articles. Those reporting only prevalence findings were singled out and examined separately [15]. Ultimately, 6 independent studies met the full inclusion criteria and provided pertinent population-based information on the incidence of frailty.

Description of retrieved studies

The main characteristics and findings of the six papers selected are summarized in *Table 1*.

Half of the studies were carried out in Europe. These three papers presented incidence data but their main goal was to explore the prospective association between the onset of frailty and: adherence to the Mediterranean diet (MD) [20], midlife overweight and obesity [21], serum levels of vitamin D [22]. The three non-European studies were specifically aimed at estimating and examining characteristics of the incidence of frailty in the population. Two of them, conducted in Texas (USA) [23] and Australia [24], investigated particular ethnic groups, providing an insight into the complex relationship between frailty incidence and socio-economic factors. The remaining study examined a large sample of Chinese population [25].

All the selected studies were community-based and had a prospective design. Participants with frailty at baseline were excluded from the follow-up sample, in order to measure the occurrence of new cases in the population at risk of developing frailty during the specified period. The mean follow-up length (range 1-22.2 years; median 5.1 years), the sample size (range 74-6306 individuals), and the age of participants (range ≥ 30-65 years) varied greatly across studies.

Assessment of methodological quality

The critical assessment performed according to JBI criteria showed a satisfactory level of methodological quality, with all selected papers receiving a positive appraisal of at least 5 of the 9 evaluated aspects. The most critical issue identified was the analytical approach and statistical method used to measure frailty incidence. Five of the studies presented results in terms of incidence proportions, or cumulative incidence (percentage of new cases on the population at risk over the investigated period), and one as absolute number of incident cases [20]. None of the papers provided an estimate of the incidence rate, or person-time rate (ratio of the number of new cases to the total time each person in the population is at risk of developing the condition). This methodological weakness was accompanied by an overall lack of specific analysis by age, sex, and other relevant risk conditions and possible predictors of frailty.

Incidence of frailty

Four studies [20-23] adopted slightly modified versions of the Cardiovascular Health Study (CHS) phenotype criteria to classify frailty [9]. The remaining two studies, both non-European [24, 25], were based on the deficits accumulation method [26, 27] and used a Frailty Index (FI) with 20 and 34 items, respectively. In addition to the two studies adopting a FI, incidence was estimated using the dichotomous variable (robust/frail) also in other two of the studies using the CHS criteria [20, 23]. The articles applying the trichotomous CHS classification (robust/pre-frail/frail) reported an incidence proportion of pre-frailty that varied from 21.2% [22] to 36% [21]; the first result was obtained on older subjects (≥ 65 years) observed for about 3 years, the second on adults (≥ 30 years) followed for a longer period (mean 22.2 years).

As shown in *Table 1*, results for incidence varied substantially across studies, reflecting the degree of heterogeneity of objectives, follow-up duration, classification instruments and sample characteristics. The relevance of this heterogeneity appeared intensified by the incidence measure adopted, since incidence proportion is highly influenced by the time of observation and it steadily increases in relation to length of follow-up. This might account for the rather high cumulative incidence of frailty (5%) found in a Finnish sample of relatively young people (mean age 43.6 years) followed over a period of about 22 years [21], the longest follow-up duration documented in our literature search.

The Chinese article [25] was the only one that presented both crude (13.0%; 95% CI 12.2-13.9) and standardized incidence results (10.8%; 95% CI 10.0-11.6), properly accompanied by the relative 95% Confidence Intervals (CI). Moreover, this paper provided sex-specific results and identified subgroups of subjects at greater risk of developing frailty over time. A higher probability with increasing age, female sex, urban residence, lower education, presence of ≥ 3 diseases, and assumption of ≥ 4 medications per day was reported [25]. As pointed out by the authors, their 1-year incidence result was slightly higher than in previous studies based on the Fried mod-

Table 1
Characteristics of the studies included in the systematic review of the literature on frailty incidence

Author(s) Year	Country	Study name	Setting	Number of participants	Age (years) Women (%)	Follow up length mean ± SD	Frailty definition	Frailty Incidence	Other relevant results
EUROPEAN STUDIES									
León-Muñoz *et al.* 2014 [20]	Spain	Seniors-ENRICA	Community	1815	≥ 60 y *Unavailable*	3.5 y	CHS	Frailty 7.5% *	Increasing adherence to Mediterranean diet was associated with decreasing risk of frailty.
Stenholm *et al.* 2014 [21]	Finland	Mini-Finland Health Examination Survey	Community	1119	≥ 30 y 43.6 ± 9.7 W 58%	22.2 ± 0.82 y	CHS	Prefrailty 36% Frailty 5%	Evidence that development of frailty may start in midlife. Being overweight or obese at baseline increased the risk of pre-frailty and frailty at follow-up, after adjusting for age, sex, lifestyle factors and chronic conditions.
Vogt *et al.* 2015 [22]	Germany	KORA-Age Study	Community	727	≥ 65 y W 49.1% of tot. sample (954)	2.9 ± 0.1 y	CHS	Prefrailty 21.2% Frailty 3.9%	After multivariable adjustment, participants with very low 25(OH) D levels had a significantly higher odds for pre-frailty and pre-frailty/frailty combined (not significant for frailty alone).
NON-EUROPEAN STUDIES									
Espinoza *et al.* 2010 [23]	Texas USA	San Antonio Longitudinal Study of Aging (SALSA) + Oldest group of San Antonio Heart Study (SAHS) cohort	Community	606 (301 MAs; 305 EAs)	≥ 65 y W 57.9%	9.9 y (range 7.4-12.5 y) **	CHS	Frailty 7.8% (6.6% MA; 8.9 EA)	After covariate adjustment, frailty incidence was 60% lower in MAs than in similarly aged EAs (Hispanic Paradox). High education and income were significantly associated with lower incident frailty. Men seemed more likely to become frail (not significant).
Hyde *et al.* 2016 [24]	Australia	/	Community	74 (aboriginal people)	≥ 45 y 60.7 ± 11.9 W 54.5%	6.7 ± 0.7 y	FI	Frailty 51.4%	Very high incidence of frailty and disability at a much younger age than observed in the general population. Frailty was a strong predictor of all-cause mortality, but not disability.
Zheng *et al.* 2016 [25]	China	Beijin Longitudinal Study of Aging II (BLSA-II)	Community	6306	≥ 55 y 70.5 ± 7.8 W 61.3% of tot. sample (10039)	1 y (median 12.7 months)	FI	Frailty 13.0% (age- and sex-standard. 10.8%)	A significant increasing trend of incidence with increasing age was found. Subgroups at high risk of developing frailty were women, urban residents, older adults, less educated subjects, and those with comorbidities or polypharmacy.

CHS = Cardiovascular Health Study; FI = Frailty Index; MAs = Mexican Americans; EAs = European Americans.
* No incidence rate or proportion provided; percentages in the Table based on reported number of incident cases (137).
** Three follow-up examinations between 2000 and 2005, 18 months apart. Incident cases at previous follow-up were not excluded from the 2nd and 3rd waves. For this reason, only frailty incidence at the end of follow-up period (mean 9.9 years), estimated on non-frail at baseline, is presented in the Table.

el. This might be attributable to the characteristics of the FI that takes into account not only physical frailty but also cognitive impairment, depression, and comorbidity and is a more sensitive instrument.

However, the high variability of results was also evident in studies that shared the same definition of frailty (CHS) and were conducted on relatively similar samples in terms of age (≥ 60-65). The reported incidence proportions ranged from 3.9% for a follow-up of about 3 years [22] to about 8% over periods from 3.5 [20], to 9.9 years [23].

The 7-year frailty incidence registered among Australian aboriginal people aged 45 years and over is clearly an outlier [24]. The extraordinarily high probability of developing frailty (51.5%) found in this sample is attributable to the peculiar features of this indigenous population, characterized by the presence of deficits in almost all areas of health, poor life styles and psychosocial stressors. This result, based on a FI, is particularly interesting because it supports the hypothesis of a multifactorial aetiology of frailty, likely resulting from accumulated insults to the body, together with other external factors.

Not taking into account the extreme outlier presented in the Australian study [24], the incidence proportions found in our systematic review ranged from 5% [21] to 13% [25], with very different follow-up times and participants' ages.

DISCUSSION

This systematic review shows an overall paucity of data on the incidence of frailty. The few incidence studies available showed a considerable heterogeneity of findings and a substantial lack of analysis of those factors, such as the basic socio-demographic characteristics, potentially influencing the development of new cases of frailty. The adoption of incidence proportions (or cumulative incidence), rather than incidence rates, highly influenced by the duration of follow-up, is a further obstacle to the comparability of results.

We know that frailty is very common among older people, roughly affecting about 10% of the population over 65 years of age [28], increases with age, is higher in women than men, is associated with lower education and income, poorer health, higher rates of comorbid chronic conditions and disability [9]. Increasing evidence of an association between frailty, cognitive impairment and dementia is emerging [3, 29]. A north-south gradient has also been suggested, with a higher prevalence in southern than in northern European countries [30]. All these findings – underlining the importance of integrating socioeconomic factors when studying the epidemiology of frailty – are based on cross-sectional, prevalence studies; while only two studies [23, 25] from the present systematic review reported incidence proportions specific by sex and other possible risk or protective factors. It might be argued that the associations observed by means of cross-sectional studies could be the same as those found through longitudinal studies, but this is not exactly correct. Incidence deals with the transition from health to disease, whereas prevalence focuses on the period of time that a person lives with a disease. From an analytic point of view, cross-sectional studies are weaker than cohort or prospective studies because they usually cannot disentangle risk factors associated with the occurrence of a disease/condition (incidence) from those related to the survival with that disease/condition [31]. This distinction is pivotal to provide a useful and reliable scientific base of knowledge to inform and prioritize cost-effective services, treatments and interventions, and is even more relevant for conditions, such as frailty, with a fluctuating nature over time.

The difficulty in comparing results, due to the great variability of follow-up lengths and sample characteristics across studies, might also be affected by the adoption of incidence proportions rather than incidence rates as measure of the frequency of frailty. In contrast with incidence rate (or person-time rate), which put the disease/condition in the perspective of the size of the population and incorporates time directly into the denominator, incidence proportion (or cumulative incidence) takes the perspective of what happens over an accumulation of time. As a consequence, the cumulative incidence increases each year as the cases continue to accumulate but the denominator, composed of the initial population at risk, remains fixed, thus limiting the comparability of findings, especially in case of great variability of follow-up durations. Incidence rates describe how quickly a disease occurs in a population and are the best instrument to evaluate the effectiveness of prevention programmes. However, although the use of cumulative incidence may be considered a methodological weakness, it is necessary to take into account that it is very often used because it is easier to calculate and understand. The adoption of incidence proportion can be plausible in studies not having incidence estimates as their main goal, like the majority of those identified through the present systematic review.

From a public health perspective, the scarce and rather unequal data available on the occurrence of frailty over time reduce the possibility of drawing a conclusion about the number of new cases we can reasonably expect in the future. In addition, the substantial lack of in-depth prospective analyses including predictors and risk factors involved in frailty development and progression prevents from reaching the clear and unambiguous base of knowledge that is essential to plan a responsive health care system focused on the actual needs of older subjects.

CONCLUSIONS

Well-designed and methodologically sound prospective studies of frailty are necessary to overcome the overall paucity of data regarding the occurrence and progression of this dynamic condition over time. To facilitate comparison of frailty incidence in different locations, at different times or among different groups of persons from potentially different populations, it should be estimated in terms of incidence rate (or person-time rate), instead of incident proportion (or cumulative incidence). A careful longitudinal investigation of major health and socioeconomic factors potentially involved in the development of new cases, and in the progression

of existing ones, is of utmost importance to understand the underlying causes of frailty in the population, and if possible, reverse it. Large-scale and up-to-date population-based studies of frailty incidence are urgently needed to inform resource planning and the prioritization of interventions to overcome the current inadequacy of health care systems to meet the multiple and complex needs of frail older people.

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Conflict of interest statement

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