Exploring Frailty and its Domains – Systematic Mapping of the Literature

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Summary

Background: ‘Frailty’ has no consensual definition till date, although the term occupies a pivotal role in geriatric medicine. A bibliometric analysis of the literature serves to capture the keyword cooccurrences and linkages, co-citations, author collaborations, research trends and to present the extant research in a nutshell. Objective: To explore the usage of frailty, its domains in medical research and the evolution of the term to other disciplines through systematic mapping by bibliometric analysis. Methods: Literature search was done in the Scopus database using a pre-formed search strategy. 2629 documents were retrieved. Co-occurrence citation analysis using keywords and link strength was obtained using the VOSViewer ver.1.6.16. A three-field plot was constructed using ‘biblioshiny’ package of the R-studio to identify the various domains of frailty. Descriptive statistics were applied to identify the trends in frailty research, number of contributions from countries, fields of research involving frailty. Results: Total of 3739 publications were observed, with the USA having most number of contributions (740, 20%) as single country, while India has only 19 contributions (0.5%) in the past 20 years. As a region, Europe and Central Asia contributed to the maximum (1714, 46.4%), most of them being from the high-income countries. Research on frailty has steadily increased over the past two decades, with most of the researches being conducted in the fields of Medicine, Biochemistry and Genetics. Co-occurrence citations and three-field plots indicate the evolving usage of frailty in other domains, such as cognition, mental health, indicators of survival, risk assessment, mortality, and quality of life. Conclusion: Upon exploring frailty, it also makes one wonder if frailty could be the cause for what is known as death due to ‘natural causes’ or ‘old age’. The implementation of extension codes in the ICD-11 related to ‘Ageing’ (XT9T) and ‘Old Age’ (MG2A), paves way for researchers to further explore ‘frailty’ as a cause of mortality.

Key words: Aging, bibliometric analysis, co-occurrence network map, frailty

INTRODUCTION

History suggests that the term “frailty” has been in use in the medical field for about three decades. Woodhouse and associates, in 1988, defined a frail elderly as “those more than 65 years of age, who depended on others for the activities of daily living and were often under institutional care.”¹ Starting from that point in time, “frailty” has had umpteen definitions to its name, becoming a part of the language of geriatric medicine.

Frailty, with its origin rooted in demography,² was only considered as a tool to quantify the variability of risk of adverse outcomes for the same degree of exposure among the elderly, with an aspiration to explain the paradox of low risk of deaths at extreme old age.³ Today, translational works studying epigenetic changes based on animal models, provide an insight on the physiologic mechanisms of frailty, its influence on disease and interventions to mitigate the syndrome. Frailty is being employed in understanding the sub cellular mechanisms of damage and repair, providing new knowledge on the molecular basis of ageing.⁴,⁵

It is interesting to note that no consensual definition for the term has yet been arrived at, though every definition identifies people at risk, but not the same people. Among a wide range of definitions, experts categorise use of “frailty”

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under two approaches, viz., “syndromic” as defined by Fried et al.\(^6\) and “clinical” as explained by Mitnitski et al.,\(^7\) the two pioneers of frailty research. Fried et al.\(^6\) defined frailty as a syndrome characterized by functional dependence (loss of strength, speed, or weight, sense of lack of energy, or the inability to perform demanding activities). This “frailty phenotype,” defined an elderly to be frail if a combination of at least three of the features in the definition were present. To the contrary, Rockwood et al.\(^7\) expressed frailty as age-related deficit accumulation, by the “frailty index.” It is expressed as a ratio of deficits present to the total number of deficits considered.

Despite wide differences, both these approaches are widely used in identifying the elderly at risk for adverse outcomes and predicting the mortality. Both these approaches are used in various settings, and also among various groups of populations, depending on the research question posed and the subject area that is involved. Either way, frailty fits in the bio-psycho-social model of primary care and provides caregivers a focus for targeting resources at an aging population.\(^9\)

A traditional review of the literature helps in quantifying the amount of research done on frailty, the various scales used for assessing frailty, the prevalence, and incidence of frailty among populations, but misses out on the diversity of its utilisation in medical research under different domains. Fried et al.\(^6\) defined frailty only using components of the physical domain, but in recent times, the definitions used for frailty indicate the evolution of the term beyond a single domain and also to various subject areas. A bibliometric analysis of the literature serves to capture this essence by analyzing the keyword co-occurrences and linkages, co-citations, author collaborations, and research trends.

A systematic, transparent, and reproducible review process based on the statistical measurement of science, scientists, or scientific activity is produced by a bibliometric analysis.\(^{10-11}\) Bibliometrics become useful, especially amidst overwhelming volume of researches in a field and conceptual developments. This type of analysis provides a structure to large information, to infer time-trends, themes of research, shifts in the boundaries of the disciplines, to detect the prolific scholars and institutions, and subsequently, to present the “big picture” of extant research.\(^{12}\) With this background, this study is designed with an objective to explore the usage of frailty, its domains in medical research, and the evolution of the term to other disciplines.

**Materials and Methods**

The articles were retrieved from the Scopus Database up to January 5\(^{th}\), 2021. The retrieval strategy was as follows: (TITLE-ABS-KEY [frailty AND syndrome] OR TITLE-ABS-KEY [frailty AND phenotype]) AND (LIMIT-TO [DOCTYPE, “ar”]). Based on this strategy, a total of 2629 documents were retrieved. For keyword co-occurrence network analysis, the search was limited by years (2016–2020), language (English), and publication stage (final), which yielded a total of 1587 articles [Figure 1].

**Software used for analysis**

VOSviewer version 1·6·16,\(^{13}\) “bibliometrix” package of R-Studio,\(^{14}\) and Microsoft Excel.

CSV files were generated for the retrieved articles and were fed into the software for further analysis. Descriptive analysis was done in Microsoft Excel using the citation information. Keyword co-occurrence network visualization map was built using the VOSviewer version 1·6·16 and the three-field plot showing the evolution of frailty under various domains was built using the “bibliometrix” package of R-Studio.

**Results**

**Trends in research progress and publications**

An increasing trend in research interest has been observed in “frailty” in the last decade. Among the 2629 articles that were retrieved, it was found that majority (1778, 67%) of the articles were published only in the last 5 years (2016–20). In 2020, there were a total of 596 articles published. Before 2005, there were <10 articles published per year (not marked in the figure) [Supplementary Figure 1].

**Journal distribution**

In the study, we identified 160 academic journals covering topics related to frailty. The top five journals, ranked according to the total publications were: Journal of the American Geriatrics Society (Impact Factor [IF] 2019 = 4·388, 94 papers), Journals of Gerontology Series A Biological Sciences and Medical Sciences (IF 2019 = 4·598, 89 papers), Journal of Nutrition Health and Aging (IF 2019 = 2·996, 83 papers), Journal of the American Medical Directors Association (IF 2019 = 5·325, 67 papers), BMC Geriatrics (IF 2019 = 3·02, 64 papers). These journals enlisted above,
have published almost 15% of the total research articles in this domain.

**Profiling of countries**
The retrieved articles were from 88 countries/regions. Although the total number of articles retrieved from the search strategy was only 2629, the contributions from each country summed to 3739, which indicates a high collaboration among the research teams in these Countries/Regions. As a single country, the United States of America (740, 20%) accounted for the most number of citations related to frailty. However, among the seven regions of the World, as classified by the World Bank, countries in the Europe and Central Asia region accounted for almost half of the citations (1714, 46.4%) in frailty research. On the other hand, countries in the sub-Saharan Africa (22, 0.6%) and the South Asian regions (23, 0.6%) have contributed the least. The top ten countries involved in the frailty research are shown in Supplementary Figure 2.

The high-income countries across all the seven regions have made the maximum number of citations in frailty (3104, 84%), whereas the other income groups have together contributed to only 16% (577). Among the lower-middle income countries, India has contributed to around 19 studies out of the total 43 (45%), which is the maximum by a country in this group. While there have been no much contributions from the South Asia, sub-Saharan Africa, and the Middle East and North Africa, high-income countries from the other regions (except Latin America and Caribbean) have proportionately contributed most to the research in frailty [Supplementary Figure 3].

The country-wise contributions, classified based on income and regions of the World (according to the World Bank Classification) are showed in Table 1 and Supplementary Figures 4 and 5.

**Domains of frailty**

**Subject areas of frailty research**
It is observed that most of the studies on frailty have been done in the field of Medicine (55%), followed by biochemistry, genetics, and molecular biology (16%). While the other fields have contributed very less in the frailty research, it can be seen that frailty has been researched as a prominent tool in nursing (13%) and social sciences (4%). Some of the uncommon fields where frailty has been researched include Psychology, Pharmacology, Toxicology and Pharmaceutics, Environmental Science, Computer Science, Decision Science, Arts and Humanities, Veterinary, Dentistry, Earth and Planetary Sciences, Economics, Econometrics and Finance (clubbed as Others in the figure) [Supplementary Figure 6].

**Keyword co-occurrence network map**
A 5-year span of publications (2016–2020) in English was taken into consideration for constructing this map [Figure 2a]. This map shows the extensive connections of frailty with other medical headings. It can be observed that “frailty” is mostly associated with the terms defining an older person (“aged,” “very elderly,” “aged, 80 and over”), thereby indicating that it is evolving as an important tool in geriatrics.

As seen for the domains in which frailty is considered [Figure 2b], it can be observed that “frailty” has strong links with terms related, but not limited to, mobility and transfers (“daily life activity,” “falling,” “body mass index,” “sarcopenia,” “physical activity,” “walking speed”). Other domains where “frailty” is linked includes “nutritional status,” “cognition,” “comorbidity indices,” “socioeconomics” and chronic diseases (“cardiovascular,” “chronic kidney disease,” “diabetes,” “hypertension,” “dementia,” “cancer,” “musculoskeletal”).

It can be observed that “frailty” also has reasonable link strengths with terms such as “risk factor,” “follow-up,” “survival,” “outcome,” “disease severity,” “complication,” “risk assessment,” “hospitalisation.” All these links indicate the broadening use of “frailty” in research, denoting the importance of including frailty as a tool in monitoring, evaluation and follow-up of an elderly person with a disease.

The associations with “biomarkers,” “pathology,” and “genetics” demonstrate the expanding reach of “frailty” and can be extrapolated to state that even at the cellular stage, frailty induces changes. Social factors such as “independency,” “socioeconomic status,” “community-dwelling,” “educational status,” and “quality of life” are also closely linked to “frailty” and changes to any of these factors might influence the frailty status of an individual.

With the “geriatric assessment” highlighted [Figure 2c] in the network, it is visualized that it is strongly linked with “frailty” indicating its use as one of the prominent tools in the assessment. The links to the “geriatric assessment” in the network closely resemble the variables included in the comprehensive geriatric assessment (“nutritional status,” “physical activity,” “disability,” “activities of daily living,” “falls,” “cognitive defect,” “dementia,” “depression,” “quality of life,” and “poly-pharmacy”).

**Evolution of frailty in various domains**
Though in the past, frailty research was confined to the physical domain and ageing, it can be observed from Figure 3 that “frailty” has expanded its branches to be considered under various domains. Frailty is included as a part of co-morbidity studies, geriatric assessment, studies at the cellular level (biomarkers and inflammatory markers), predictor of mortality, survival and disease or treatment outcomes. Similarly, the term “frail elderly” is also applied beyond “physical frailty,” to include “malnutrition,” “quality of life,” “comorbidity.”

**Discussion**
The objective of the study was to explore the usage of frailty and its domains in medical research, given the propensity of the term to be utilised in various fields.
The trend analysis of the literature shows that most of the studies published on “frailty” have happened in the last 5 years, signifying the changing trends of focus on research. This can be attributed to the phenomenon of population ageing (6% elderly in 1990–9% in 2019) across the globe, which necessitates the need for identifying tools that can be used for comprehensive assessment of an elderly for the health status. “Frailty,” although considered as an age-independent marker of disability, fits in this frame, as it evaluates an elderly on various domains with functional status at its core. The total elderly population is projected to reach 1·5 billion in 2050 (which is double the current population).

Population aging is considered one of the four global “mega-trends,” which carves a focus for geriatric health. It is opined that policies and programs that consider the demographic trends and population dynamics of the region are required to progress toward attainment of the sustainable development goals.

Based on the profiling of 88 countries/regions, it was found that the USA (20%) and the countries in the Europe and Central Asia region (46%) accounted for about two-thirds citations related to frailty. This can be ascribed to their higher proportion of older population and the stage of demographic transition of the countries in the region. The increased longevity of life in...
Table 1: Contributions among the countries of the World based on income groups (as classified by the World Bank for the fiscal year 2021)

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<th>Income</th>
<th>East Asia and Pacific</th>
<th>Europe and Central Asia</th>
<th>Latin America and the Caribbean</th>
<th>Middle East and North Africa</th>
<th>North America</th>
<th>South Asia</th>
<th>Sub-Saharan Africa</th>
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these countries is accompanied by multiple co-existing chronic morbidities and psychosocial dysfunctioning. The “functional limitation” in an old person is considered a social process. This disability is caused by the lifelong accrual of deficits from various domains and remains the most potent indicator of health status and prognosis.\[16\] In that respect, an elderly has to be assessed in as many domains as possible with functional status at the core, which brings in “frailty” as the most suitable tool for the purpose, similar to the Comprehensive Geriatric Assessment, yet simpler and hence justifying an increased magnitude of research in this field.

While the country profiling can be linked to the population dynamics of the country/region, the income profiling of the countries can be coupled to the epidemiological transition and the economic old-age dependency ratio\[15\] of the country/region. The high-income countries across all the seven regions of the world have contributed to a majority (84%) of citations in frailty. As a country/region conquers the communicable and nutrition-related diseases, the focus of research in the country/region shifts towards morbidity or disability related diseases that reduce the functional ability of a patient, instead of causing mortality. This can be ascertained by the increase in funding and collaboration of institutes for frailty research, in recent past years. The need for extending health services to the ageing population is realised at this juncture, but the extension of a “disease-specific approach” as for other groups of populations, is considered a threat to the sustainability of the health system.\[17\]

“Frailty” fits in as a bio-psycho-social model of care,\[8\] helping to assess a geriatric patient beyond just a disease. On the other hand, developing countries like India and other lower or lower-middle income countries, undergoing the epidemiological transition and stuck with dual burden of both communicable as well as the noncommunicable diseases in the general population, have contributed very less in the field of frailty research, though the United Nations projects that these countries or regions are expected to have the largest (+312 million persons in Eastern and South-East Asia) and fastest increase (+226% in North Africa and Western Asia) of the elderly population in over the next three decades.\[15\]

In analysing the keyword co-occurrence network map, strong links were found to terms of the physical domain. This can be...
ascribed to the works of Fried et al.\cite{fried1999} and Mitnitski et al.\cite{mitnitski2002} who considered frailty as a cornerstone in geriatric health and operationalized it for clinical practice, mainly using objective components of the physical domain. Beyond the physical domain, frailty is also linked strongly to various domains (social, nutritional, psychological, and cognitive), indicating the expanding use of “frailty” in medical research and thereby its importance as a tool at various levels of prevention (screening, early diagnosis, disability limitation, and rehabilitation).

In the recent years, it has been observed that frailty, despite being studied in medical research, has also been studied in the fields of biochemistry, genetics and molecular biology, which signifies its possible association with changes at the cellular level. As observed from the subject areas, it is interesting to note the research done on frailty in veterinary science. The animal models such as the guinea pigs or mice, are studied to understand the changes that frailty could lead to. A frailty index which was developed for use in mice, based on the blood work and hemodynamic measures (FI-LAB),\cite{rockwood2018} has shown to predict mortality in the people.\cite{howlett2019} This has emphasised the importance of predicting frailty across life courses. Linkage of “frailty” with various other domains and its expansion of usage in recent years, as shown by the three-field plot, adds up to emphasise the importance of frailty in geriatric health and also to be considered as a factor among other morbidities.

**Conclusion**

Understanding the domains of frailty in research and the co-occurrences of terms in the literature helps in identifying lacunae and unmet gaps. The study indicated the growing importance of frailty in medical research, ascertained by the magnitude of publications in the past decade and also by the extensive collaborations of authors and institutes. Though “frailty” is strongly linked to the terms of the physical domain, the results indicate that it has grown beyond them to have its roots in other domains and other subject areas, as well. Upon exploring frailty, it also makes one wonder if frailty is the cause for what is known as death due to “natural causes” or “old age.” The implementation of extension codes in the international classification of diseases - 11th revision related to “Ageing” (XT9T) and “Old Age” (MG2A),\cite{vaupel1979} paves way for researchers to further explore “frailty” as a cause of mortality and in the development of interventions that can be used in the prevention and management of frailty or age-related diseases.

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Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**

Supplementary Figure 1: Trend-line showing the increase in magnitude of research in "frailty" in the past years.

Supplementary Figure 2: Top 10 countries that contributed to publications in frailty research (The status of frailty research in Indian context is added as a comparative measure).

Supplementary Figure 3: Component bar diagram showing the proportional contribution of every income-group across the 7 regions of the world.

Supplementary Figure 4: (A) Pie chart showing the distribution of publications among the 7 regions of the world. (B) Pie chart showing the distribution of publications based on income-group of the countries. Both the classifications are as per the world bank.
Supplementary Figure 5: Heat map showing the proportion of publications in the 7 regions of the world among various income groups (according to the world bank classification).

Supplementary Figure 6: Pie chart showing the various fields in which frailty research has been done.