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Developing a Working Framework for Understanding Frailty

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Mrs. P. is a 71-year-old widow with 4 adult children. Her medical history includes diabetes and osteoarthritis. She lives alone, tends to be socially isolated and has mild depressive symptoms. Her nutritional intake is poor. She walks without aids but seems to have slowed down lately. Her cognition is normal and she is independent for activities of daily living.

Is she frail? What is frailty and how can it be identified? Is frailty inevitable if we all live long enough? What are the risk factors for its development? Are there interventions that effectively delay the onset of frailty and/or prevent adverse outcomes?

Frailty: An emerging and enigmatic concept

Frailty has emerged as an increasingly important concept from both the standpoint of the clinical care of older individuals and research on aging. Since the 1980's, there has been an exponential increase in the number of publications that refer to frailty, from 36 between 1986 and 1990 to over 1,100 between 2000 and mid-2004. Frailty has also received increasing interest in the lay press, including a full-page article in the *New York Times* (Kolata, 2002).

In the 1980's, frailty was equated with disability, the presence of chronic disease, extreme old age, or the need for geriatric services (Hogan, Macknight, & Bergman, 2003). More recently, there has been an uncoupling of frailty from these other concepts.

However, frailty remains an enigmatic concept. In clinical settings, the term frailty is often used to describe older persons "at risk" (or vulnerable) for all types of negative outcomes. Unlike their "non-frail" contemporaries, these individuals are seemingly unable to withstand "insults" like environmental stresses (e.g., heat, cold), injuries, and acute illness. These insults may provoke a downward spiral where the frail, older individual cannot recover and return to their baseline state. Clinicians often say, "I know frailty when I see it, but I can't define it". This is not surprising given that in spite of a growing body of knowledge, there is no widely accepted definition. The literature abounds with different models, criteria and definitions (Hogan et al., 2003).

A Complex Syndrome of Increased Vulnerability

Among those studying frailty, there is a growing consensus that frailty is a syndrome that can be identified and measured in both the clinical and community setting. It represents a state of reduced homeostasis and resistance to stress that leads to increased vulnerability and risk for adverse outcomes such as the progression of disease, falls, disability, and premature death. Frail individuals have higher rates of health care utilization with a greater need for continuing and long term care. There is growing agreement that frailty lies on a continuum, is age-related (though not uniformly present with aging), and at a biological level is the result of the impact of multiple system impairment (or multiple system reduction in reserve capacity). Some currently undefined threshold of impairments in the endocrine-metabolic, cardiovascular, musculoskeletal,

immunologic, and neurological systems is seemingly crossed. Frailty might well represent a dynamic, complex interaction of biological, psychological, cognitive, and social factors. There is an interplay of assets and deficits in a given individual within a given context (Lebel et al., 1999).

Frailty and disability are distinct but overlapping concepts (Fried, Ferrucci, Darer, Williamson, & Anderson, 2004). Disability often refers to the inability to independently carry out instrumental and basic activities of daily living. This may be on the basis of single or multiple impairments. Not all older persons with disabilities are frail and not all frail elders have disabilities (Fried et al., 2001). Disability, though, can be an adverse outcome of frailty and if frailty is the pathway to disability for an individual, they don't cease to be frail with the onset of disability.

Fried and her colleagues have developed the most coherent and clearly articulated approach to frailty to date. Central to their concept are neuromuscular changes (e.g., sarcopenia), neuroendocrine dysregulation, and immunologic dysfunction. Five characteristics of their "frailty phenotype" have been defined: weakness, poor endurance, reduced physical activity, slow gait speed, and unintentional weight loss over the past year. Individuals with three or more of these characteristics are classified as "frail" while those with one or two are labelled "prefrail". Using data from the Cardiovascular Health Study, Fried et al. (2001) showed that those meeting their frailty criteria were at significantly higher risk for falls, mobility and functional decline, hospitalization, and death within 3 years.

There are other approaches that attempt to capture the complexity of frailty and are also predictive of adverse outcomes. For example, Mitnitski, Song, and Rockwood (2004) developed a frailty index comprised of 40 self-reported variables representing symptoms, attitudes, illnesses, and function. Applied to a sample of 9,008 community-dwelling people aged 65 years and older in the Canadian Study of Health and Aging, the index showed an exponential increase with age and was strongly inversely correlated with survival.

The Canadian Initiative on Frailty and Aging

In all developed countries the absolute number and the proportion of the population aged over 65 is growing exponentially, as is that of the oldest old. Canada, which has one of the most rapidly aging populations, experienced a growth of 41% of those aged 80 and over between 1991 and 2001. A similar increase is also expected in the following ten years (Statistics Canada, 2002).

With the growth of the older population there has been increasing concern about its well-being, both from the perspective of the individual and that of society, which is faced with the challenges of meeting their health and social care needs. Functional decline is a major health problem, particularly in aging countries (Hébert, 1997). The prevalence of disabilities increases dramatically with age from 30% in those aged 65 to 74, to 50% in the 75-84 age group and 80% for those over 85 (Saucier, 1992). The annual

incidence of functional decline in community-dwelling people over 75 years of age is nearly 12% (Hébert, Brayne & Spiegelhalter, 1997). While the great majority of older people consider themselves to be in good health and lead independent lives, a significant proportion, 10-20% depending on the definition, would be classified as frail by health care providers and/or researchers.

The increasing interest in frailty parallels the growth in the numbers of elders, reflecting the growing impact of frailty and the potential to improve the health of a significant segment of the population. However, as previously described the term currently has no accepted definition, and has been used inconsistently even amongst researchers in the field.

It is in this context that the Canadian Initiative on Frailty and Aging was initiated with the overall goals of furthering our understanding of the causes, implications and trajectory of frailty and improving the lives of older persons at risk of frailty by dissemination knowledge on its prevention, detection and treatment as well as the cost-effective organisation of services.

The specific objectives of the Canadian Initiative on Frailty and Aging are:

- to summarize the present state of research on frailty in older persons in order to develop a working framework and identify research priorities which could be used to develop a program of enquiry;
- to make recommendations to primary health care providers and specialists on detection and care of older persons who become frail;
- to propose policy recommendations to decision-makers and administrators of the health care system and to develop greater public awareness of frailty and the potential for its prevention and treatment.

The systematic literature review

As part of the first phase of the initiative, a systematic review of the literature is being carried out. The approach is intended to be broad and integrative from a variety of perspectives. The review includes all aspects of frailty, from its biological antecedents to its social, economic, psychological and quality of life consequences. It is intended to be relevant to researchers, medical and social care professionals and the wider community, as well as informing health and social care policy. The involvement of investigators and collaborators from Canada, Europe, Israel, USA, Japan, Singapore, Latin America ensures its relevance across a variety of cultures. The research is starting from a broad and flexible perspective, without a hypothesis as to a frailty model. It is intended that a consensus on frailty will emerge through the process of the critical review of the existing evidence and exchanges between the investigators.

Objectives of systematic review

The objectives of the systematic literature review are to collate, critically review and synthesize the evidence and identify the gaps in the literature and in existing and emerging Canadian and international research. The results will be disseminated through the publication of a series of papers.

Methodology

Due to the vast and multidisciplinary nature of the literature on frailty, the systematic review was divided into 10 domains and research questions were developed for each, by experts in each field. Within each domain, the existing frailty literature was identified, and the quality of evidence assessed using standardised methods. The literature searches were conducted using Medline and Ageline and limited to literature published in English or French between 1997 and 2002. Search terms included “aged,” “frail,” “frailty,” “vulnerable,” “vulnerability,” “healthy aging,” “successful aging,” “disability,” “disability evaluation,” and “disabled persons,” combined with domain-specific terms such as “biomarkers,” “prevalence,” or “diagnosis”. Table 1 presents the domains and the domain-specific research questions.

Insert table 1 here

Domain	Research questions
Biological basis	What are the biological and physiological determinants of frailty and how can these determinants be used to define, predict and characterize frailty?
Social basis	How has frailty been conceptualized (defined, modeled) from a social perspective?
Prevalence	What is the prevalence of frailty in the community dwelling elderly? How does prevalence vary according to the definitions used?
Risk Factors	What factors have been shown to predict frailty, functional decline, disability, mortality or increased resource utilization? What factors have been shown to predict successful aging?
Impact	What impact does frailty have on affected individuals? What impact does frailty have on relatives of affected individuals? What impact does frailty have on the health care system?
Identification	Are there clinical markers that can be measured in the asymptomatic normal population that predict frailty in the future? What are the clinical operational diagnostic criteria? What are the tools for the screening and diagnosis, and investigation of frailty? Are there measures of severity of frailty?

Prevention & Management	Can interventions aimed at the general population prevent frailty? Can interventions aimed at the general population prevent the consequences of frailty e.g. death, institutional admission, etc? Can interventions aimed at those who are frail or at risk of frailty, prevent the consequences of frailty?
Environment & Technology	What technological interventions have been demonstrated to increase quality of life and safety technologies are not effective? What are the common characteristics of those technologies that have been found to be effective? What are the needs or opportunities for technologies to assist frail older adults and their caregivers that have not been adequately addressed?

A working framework

Although the literature review is not yet complete, a tentative working framework has emerged (www.frail-fragile.ca). A complex entity such as frailty is likely to have a complex etiology. The Canadian Initiative considers that the biological, psychological, social, and environmental factors that interact across the life course are the determinants of frailty. The life course approach to chronic disease (Ben Shlomo & Kuh, 2002) provides an attractive framework for understanding frailty and its determinants. As applied to frailty, it is an integrative approach that considers biological, social, clinical, cognitive, psychological, and environmental factors interacting across a person's lifespan that may either promote healthy aging or the emergence of frailty. Both early and late life factors are important to consider in identifying risk/protective factors for the development and progression of frailty. Rather than creating false dichotomies, biological and social risk factors are integrated.

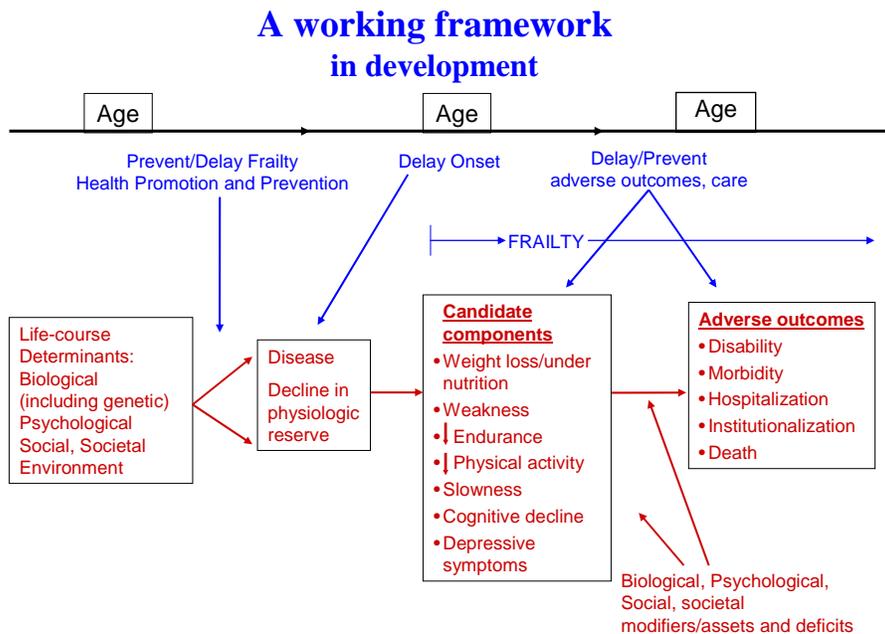
Studies of risk factors for frailty or characteristics associated with frailty support the use of this approach. For example, data from the 1946 British birth cohort study showed that low birth weight was associated with decreased grip strength and increased risk of diabetes and cardiovascular disease some 50 years later (Kuh et al., 2002; Aboderin et al., 2001). Other studies have examined risk factors in mid and late life. In a systematic review, Stuck et al. (1999) identified several biological, psychological, and social factors (cognitive impairment; depression; disease burden; increased/decreased BMI; lower extremity function limitation; decreased social contacts; low physical activity; no compared to moderate alcohol consumption; poor self-perceived health; smoking; vision impairment) that were predictive of later life functional decline.

Strawbridge and colleagues used data from a 30-year longitudinal study to identify risk factors associated with subsequent frailty (Strawbridge, Shema, Balfour, Higby, & Kaplan, 1998). These included heavy drinking, physical inactivity, poor perceived health, having two or more chronic symptoms and having one or more chronic conditions. Among the demographic variables assessed, increasing age and having less than 12 years of education were significantly associated with being frail.

In developing a working framework, the Canadian Initiative on Frailty and Aging considers that frailty is a measurable syndrome (clinically and in community) that can be identified in older persons with a combination of some or all of a number of candidate components that need to be considered in the study of frailty. Certainly, Fried's work has identified the core of those components. These are weakness, poor endurance, reduced physical activity, slow gait, and unintentional weight loss. In addition, we hypothesise that cognitive decline and depressive symptoms may also be among the core components of frailty.

The pathway from frailty to its adverse outcomes is affected by various biological, psychological, social, and societal modifiers which have been described as the assets and deficits of an individual in their specific context (Lebel, 1994; Rockwood, 1994).

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This framework points to the potential for health promotion, prevention and management. Observational studies on aging suggest associations between several lifestyle factors (e.g., exercise, nutrition, education, socioeconomic status, social/intellectual activity) and the onset of frailty. These findings provide opportunities for the development of interventions to promote healthy aging, reduce the incidence of frailty, delay its onset and/or reduce the number of years of dependency (Fries, 2002). Secondary prevention with early detection and treatment of certain chronic conditions such as hypertension, diabetes, heart disease, osteoporosis, etc. could play an important role.

Effective programs for the care of frail individuals can minimize the impact on the individual, their families, and society. Evidence suggests that comprehensive, integrated health and social service interventions for the frail elderly population may have an important impact on health, quality of life, satisfaction, caregiver burden, pattern of health care utilization and cost (Bergman, Béland, & Perreault, 2002). Continuing functional decline is not inevitable in frail older people. Exercise and rehabilitation have the potential to improve their functional state (Gill et al., 2002). The introduction of assistive technologies for physically or cognitively impaired people could have an important impact on the quality of life of both caregivers and care-receivers.

Issues and questions

A certain number of key issues have arisen in discussion around the development of a framework. The first issue is that of the distinction between frailty and aging. Is frailty a distinct entity? Does frailty represent a form of “accelerated” aging and is it simply the flip-side of healthy or successful aging. In other words, is it a useful concept from a clinical and population point of view?

If it is a distinct entity, is it a specific syndrome with a unique pathway or is it a syndrome with complex biological, cognitive and psychological characteristics with multiple pathways?

What is the role of social factors and their relationship with the biologic, psychological and cognitive factors? Are they determinants, components or modifiers, or all three? And what specifically are these social factors?

Can frailty be understood as a syndrome but also as a state of risk much like the Metabolic Syndrome X? The metabolic syndrome is a multifaceted clinical entity produced by genetic, hormonal and lifestyle factors. It is not a disease but a clustering of metabolic abnormalities – truncal obesity, glucose intolerance or non-insulin dependent diabetes mellitus, dyslipidemia and essential hypertension – that has been found to be associated with a risk of coronary heart disease, stroke, and cardiovascular mortality greater than that of its individual components (Grundy et al, 2004). Likewise, frailty has been described as a clustering of physical and/or psychological dysfunctions that are associated with several adverse outcomes.

Another important challenge in the study of frailty is determining the methodology, the data and the approach necessary in order to resolve the above mentioned issues and arrive at a consensus on the characteristics of frailty, its components as well as the determinants and modifiers.

Opportunities to study frailty

The current work by the Canadian Initiative on Frailty and Aging is leading towards a working framework for studying healthy aging and frailty. Other opportunities to study frailty include the exploitation of existing databases, biological and clinical

studies, particularly of effective interventions, as well as population studies. Longitudinal studies of aging in Europe, Canada, and the USA will allow the antecedents and trajectories of frailty to be determined. One such study is the Canadian Longitudinal Study of Aging (<http://www.fhs.mcmaster.ca/clsa/>), which is anticipated to begin recruitment in 2008. The sample will include 50,000 individuals aged 40 or more who will be followed over 20 years, allowing aging to be studied as a dynamic process. Participating researchers come from diverse disciplines including the basic, social and clinical sciences, which is essential to determine the inter-relationships between biological and psychosocial factors.

Frailty will be studied as one of the constructs within the Canadian Longitudinal Study of Aging. In particular, the goal will be to identify the components of frailty, the relationships between them as they evolve over time, and the social, psychosocial and physiological factors that promote the emergence of frailty. Of particular interest are the trajectories of frailty through the aging process and the consequences of frailty with respect to psychological, physical and social well-being, as well as access to socio-economic resources. The study will also obtain estimates of utilization and costs of health and social care attributable to frailty.

Conclusion

Although there continues to be active debate on the exact nature of frailty, there is no disagreement about its impact on the older individual, their family and in particular those involved in care giving as well as society as a whole. It is clear that further study is necessary in order to advance the quality and strength of the evidence on frailty across the biological, clinical, population, and social domains. Certain key issues need to be addressed including the difference between frailty and aging, its determinants and pathophysiology, the identification of its core components, modifiers of its progression, and the relationship between the biological, cognitive, psychological, and social factors.

The multi-factorial aspects of frailty reflect the essence of care for older persons. It moves away from an organ-by-organ to an integrative approach. Ultimately, work on frailty will be relevant to clinicians, older individuals, and society by identifying effective health promotion, prevention, treatment, rehabilitation, and care interventions.

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History, concept and current definitions

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