Canadian Initiative on Frailty and Aging
Initiative canadienne sur la fragilité et le vieillissement
www.frail-fragile.ca

Developing a working Framework for Understanding Frailty

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Frailty: an emerging concept

Adapted from Swine, Age & Ageing 1998, 27:411-13
Frailty: an enigmatic concept

Frailty is like pornography: You can’t define it but you recognize it when you see it.

an anonymous clinician
Frailty: an enigmatic concept

“Frailty is one of those complex terms – like independence, life satisfaction, and continuity – that trouble gerontologists with multiple and slippery meanings”

Frailty: an enigmatic concept

◆ Models
  – Demographic and mathematical
  – Aging
  – Genetic
  – Primary pathways
  – Concurrent dysfunction of multiple biological systems
  – Combined bio-medical/psychosocial

◆ 30 criteria for identifying frailty or predicting frailty

Early definitions

- Disability caused by chronic diseases and their sequelae
- Comorbidity
- Defined by eligibility for specialized geriatric programs

NIH Consensus Development Conference on geriatric assessment methods (1988)
The Uncoupling of Disability and Frailty

- Population data on decreasing disability
- Interest in healthy/successful aging and the potential for prevention
- Data from longitudinal and intervention studies
  - markers of frailty in healthy individuals
  - not all persons with disability are frail
  - not all frail persons have disabilities
  - there is potential for prevention
Growing body of knowledge

- Basic biological mechanisms (genetic (APOE4); inflammatory (IL-6, IGF-1, C-Reactive Protein); hormonal, oxidative stress)
- Socio-economic factors
- Early and midlife experiences
- Prevalence and risk factors
- Markers for early detection and diagnosis
- Population health and social interventions
- Clinical interventions (detection, prevention, treatment & rehabilitation)
- Use of assistive technology and modification of the environment
- Organisation of services
Growing consensus

- Frailty: state of increased vulnerability
  - Vulnerability to what?
  - Components?
  - Trajectories?
  - Determinants/risk factors?
  - Prevention/management?

Hypothesized Pathway to Frailty

Determinants and pathways → “Partial” components/manifestations → Clinically observable syndrome → Adverse* outcomes

Robust → Pre Frail
Resilient → Frail

*Disability, morbidity, hospitalization, institutionalization, mortality
FRAILTY - Models/Approaches - are they competing?

Hogan, MacKnight, Bergman. Aging: Clinical and Experimental Research, Sept. 2003

- Accelerated or advanced aging
- A physiologic syndrome with specific pathway(s)
- A complex syndrome with biological, social, psychological determinants across the life-course
Accelerated or Advanced Aging

Fig. 1 - Trajectories of performance over the life span. The 2 curves represent “normal” aging and “accelerated” aging. Areas of “full performance”, “frailty” and “disability” are indicated with different shades of grey.

Ferrucci 2002
A Physiologic Syndrome

- A physiologic syndrome characterized by decreased reserve and resistance to stressors, resulting from cumulative decline across multiple physiologic systems, and causing vulnerability to adverse outcomes

(Fried et al. 2003)
Primary Causes of Frailty: Changes in gene expression, Oxidative DNA damage, Telomere shortening

Secondary Causes of Frailty: Depression, Cancer, Chronic Infection, CHF

Neuroendocrine Dysregulation → Sarcopenia → Immune Dysfunction

Clinical Syndrome of Frailty

Figure 116-9  Hypothetical causal pathway of frailty focused on primary, age-related mechanisms, and secondary disease-related mechanisms. We hypothesize that both mechanisms can trigger the physiology of frailty, and that there is substantial interaction between primary and secondary mechanisms.
Figure 116-6 The cycle of frailty. Key components of frailty that appear to underlie its phenotypic manifestations in a negative cycle are chronic undernutrition; sarcopenia; declines in strength, power, and exercise tolerance; and declines in activity and total energy expenditure. Factors that could precipitate or exacerbate this core cycle are indicated with dashed lines. Factors in which a relationship is hypothesized are indicated in italics.
The Life Course approach

◆ An integrative approach that includes the biological, social, clinical (including cognitive), psychological and environmental determinants which interact across a person’s lifespan and which may promote healthy aging and either delay or promote the emergence of frailty
  – The contribution of early life factors jointly with later life factors to identify risk and protective processes
  – Integrate biological and social risk processes rather than draw false dichotomies

(Adapted from: Ben-Shlomo and Kuh, 2002)
Examples of risk factors/markers across the life span

- Low birth weight associated with
  - Grip strength 53 years later (Kuh 2002)

- Decreased grip strength in mid life
  - Risk of functional decline and disability 25 years later (Rantanen, Guralnik 1999)

- Low education
  - Increased risk of Alzheimer disease not mediated by adult SES or SES mobility (Karp 2004)
Examples of risk factors/markers across the life span

◆ Longitudinal studies of aging: strong associations between lifestyle risks factors and the incidence of disability
  – Exercise, normal body mass index, non-smoker in mid and late years (Vita, 1998)
    » increased survival; postponement (7.75 years) of age of onset of disability- compression of disability
  – Physical activity (Leveille, 1999)
  – Prospective cohort study-runners vs community controls (Wang, 2002)
    » Postponement and compression of disability (12.8 years)
  – High risk factors: more disability throughout and surge in last 2 years (Hubert, 2002)
Examples of risk factors/markers across the life span

- **Risk factors for frailty**
  - Age, low education
  - 30 year cumulative predictors: heavy drinking, cigarette, physical inactivity, depression, poor perceived health, 2 or more chronic symptoms, 1 or more chronic conditions, social isolation
  
  (Strawbridge 1998 Alameda County Study)

- **Risk factors (in adult or late life) for functional decline**
  - 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
  
  » Evidence for an association among biological, psychological and social risk factors
  
  (Systematic review, Stuck et al 1999)
Biological and psychosocial exposures across the life course in relation to frailty and its adverse outcomes

(Adapted from Ben-Shlomo, Kuh 2002)
A working framework in development

Prevent/Delay Frailty
Health Promotion and Prevention

Delay Onset
Delay/Prevent adverse outcomes, care

Life-course Determinants:
Biological (including genetic)
Psychological
Social, Societal Environment

Disease
Decline in physiologic reserve

Candidate components
• Weight loss/under nutrition
• Weakness
• Endurance
• Physical activity
• Slowness
• Cognitive decline
• Depressive symptoms

Adverse outcomes
• Disability
• Morbidity
• Hospitalization
• Institutionalization
• Death

Biological, Psychological, Social, societal modifiers/assets and deficits
A possible working framework

An identifiable and measurable syndrome (clinically and in the population)
A combination of **some or all** of the following components:

- Decreased physical activity
- Weakness
- Decreased endurance
- Slowness
- Under-nutrition (weight loss)
- Cognitive decline
- Depressive symptoms
- Impairment in (I)ADL

A dynamic complex process
- Interaction of biological, psychological, cognitive and social factors
- Complex interplay of assets and deficits of a given individual in a given context (effect modifiers)

Reduced homeostasis and resistance to stress leading to increased risk of adverse outcomes
- Morbidity
- Disability { increased health/social service utilization
- Mortality

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A possible working framework

- **Age-related but not uniformly present in aging**
  - On a continuum
  - Chronic and progressive

- **Result of impact of multiple system impairment (or multiple system reduction in reserve capacity)**
  - Critical mass of changes
  - Particularly in metabolic, cardiovascular, musculoskeletal and neurological systems

- **Underlying biological and social determinants/risk factors throughout the life course**

- **Potential for prevention/delay of onset of frailty and adverse outcomes; potential for management/treatment**
Issues/Questions

◆ Does Frailty exist
  – or simply “accelerated” aging. Flip side of healthy aging

◆ Is Frailty
  – a specific biological entity with defined pathway
  – a syndrome with biological, psychological and cognitive characteristics and multiple pathways

◆ Relationship between biological, psychological and cognitive components; role of social and environmental factors

◆ Understanding Frailty as an entity or syndrome but also as a state of risk for adverse outcome eg metabolic syndrome X

◆ How do we study candidate determinants, components, mediating factors with a working framework?
Challenge:
From a working framework to a model

1. Systematic review—understand/assess quality of evidence
2. Identification of candidate components
3. Agreement on candidate components
   – Clinician and expert consensus
4. Study
   – How do the components cluster—do they present together more often than you would expect if they were independent?
   – Which candidate components do you maintain
   – What is the relative importance of the components
Perspectives

- Complete the systematic review
- International working meeting
- Develop a working framework through this process
- Move ahead the Research agenda
  - Opportunity to study frailty in developing longitudinal studies in Europe, Canada, USA; Canadian Longitudinal Study on Aging with an embedded study on frailty
  - Exploitation of existing databases
  - Funding and collaboration opportunities for biological, clinical and population studies e.g., CIHR, NIA, other
What if it doesn't work?

What if it all blows up in our faces?

What if somebody sees?

What happens if it works all too well?

What happens ten years down the line?

Then what?

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Immortality

Rather than achieve immortality through his films, Woody Allen stated: I would rather achieve immortality by not dying.
References


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References


