



Frailty: Searching for a Relevant Clinical and Research Concept

Howard Bergman, MD

www.solidage.ca

Groupe de recherche
Université de
Montréal/McGill sur la
fragilité et le
vieillessement

McGill/Université de
Montréal Research
Group on Frailty and
Aging

The Dr. Joseph Kaufmann Professor of Geriatric Medicine,
Professor of Medicine, Family Medicine and Oncology,
McGill University and Jewish General Hospital

Vice-président et directeur scientifique
Fonds de la Recherche en Santé du Québec

IAGG 1.7...09



Hôpital général juif
Jewish General Hospital



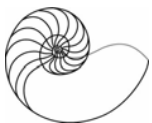
McGill
University

The Challenge of Defining Frailty

- ◆ Frailty is like pornography: Clinicians can't define it but they recognize it when they see it.
an anonymous clinician

Clinicians and researchers

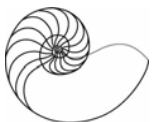
- ◆ don't know how to define it
- ◆ are not sure if it is different from disability
- ◆ cannot position frailty in the spectrum of health status
- ◆ don't know whether it is a reversible condition or not
- ◆ don't know how much it is physiological aging and how much is the result of diseases
- ◆ don't know where social factors fit in



Frailty: a proposed research and clinical entity

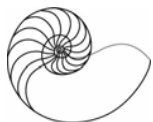
- ◆ Progressively dissociated from disability
- ◆ Models
 - Demographic and mathematical
 - Ageing
 - Genetic
 - Primary pathways
 - Concurrent dysfunction of multiple biological systems
 - Combined bio-medical/psychosocial
- ◆ 30 criteria for identifying frailty or predicting frailty

Hogan DB, et al. Aging Clin Exp Research. 2003



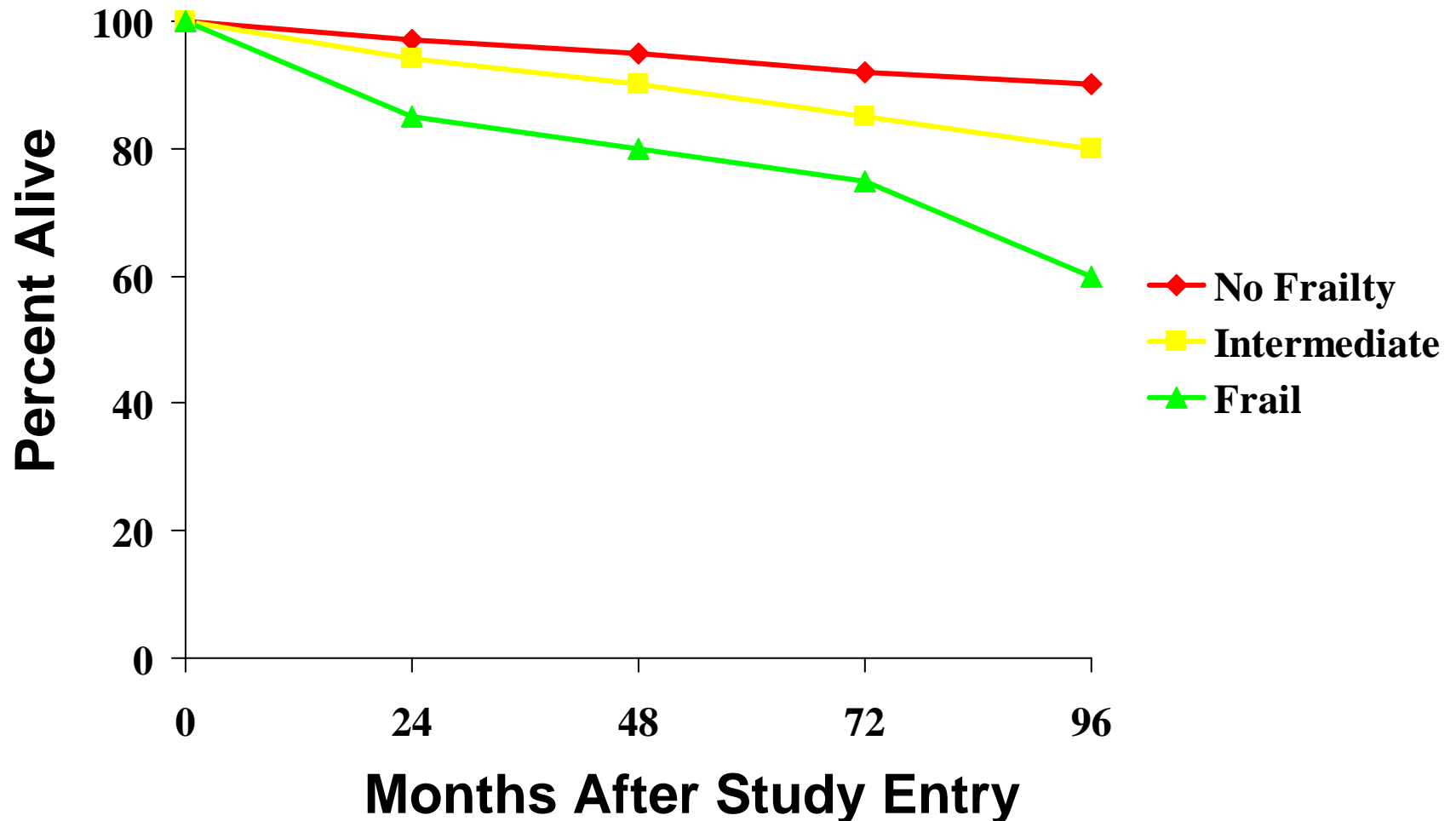
Frailty General Agreement

- ◆ Core feature of frailty is increased vulnerability to stressors due to impairments in multiple, inter-related systems that lead to decline in homeostatic “reserve” and resiliency
- ◆ The main consequence is an increased risk for multiple adverse health-related outcomes
 - disability, morbidity, falls, hospitalisation, institutionalisation, death
- ◆ a syndrome encountered in older persons with diverse predisposing, precipitating, enabling and reinforcing factors
- ◆ Frailty and disability: while related and with overlap, are distinct concepts



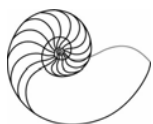
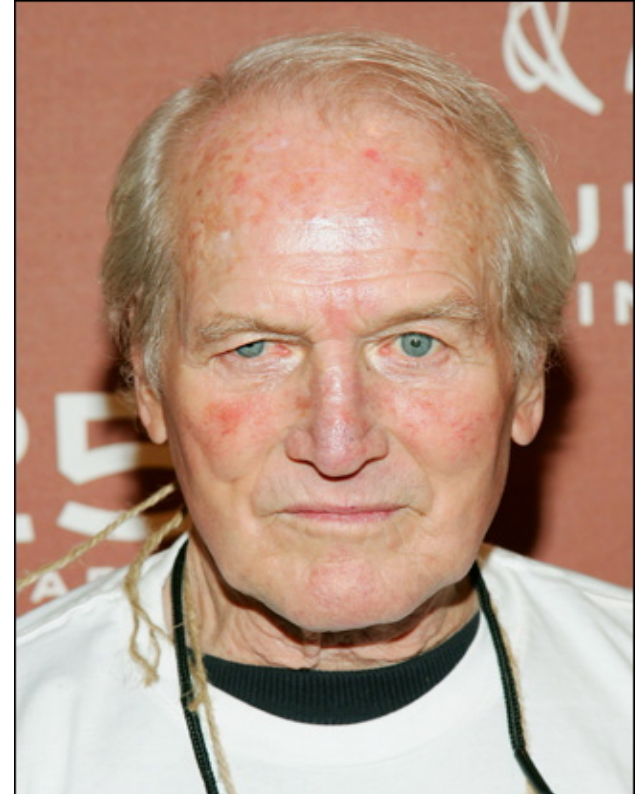
Survival According to Frailty Status

Cardiovascular Health Study



Fried et al, J. Gerontology Med Sci, 2001

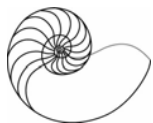
Aging ...or Frailty



Issues/Controversies

Frailty and Aging

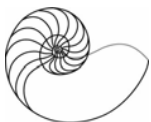
- ◆ Many of the attributes of frailty also apply to aging
 - ◆ Some degree of functional impairment/vulnerability inevitable with very old age
- Deiana L et al. Aging 1999; Gondo Y et al. J of Gerontol: Med Sci 2006
- ◆ An arbitrarily defined point on a continuum of increased vulnerability with age
 - ◆ Inevitable part of the aging process/flip side of healthy aging
 - ◆ Nevertheless, the conceptualization of frailty may help in understanding the heterogeneity of functional decline observed with chronological aging.
 - Chronological age alone is only a rough proxy of a person's vulnerability to adverse outcomes.
 - Some people appear to be frail (however defined) at age 70, while others only reach this state in their 90s.



Issues/Controversies

Frailty and Chronic Disease

- ◆ A complex relationship-almost all frail persons have chronic disease but most persons with chronic disease are not frail
- ◆ Increasing prevalence of frailty with increasing chronic disease
- ◆ Is frailty a manifestation diagnosed and undiagnosed chronic disease; a secondary condition rather than an underlying state?



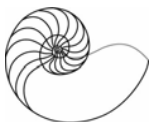
The Frailty Phenotype

- ◆ A clinical syndrome with specific manifestations linked to an underlying biological pathway
- ◆ neuroendocrine and immune dysfunction, sarcopenia
- ◆ Grip strength; exhaustion/fatigue; less physically active; slow gait; unintentional weight loss

Cardiovascular Health Study

- ◆ Prevalence 6.9%, 4 year incidence 7.2%
- ◆ Predictive of falls, mobility/ functional decline, hospitalization, and death (within 3 years); adjusted HRs 1.3-2.2

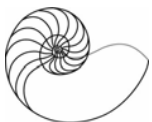
Fried LP et al. J Gerontol: Med Sci 2001



The Frailty Index

- ◆ Identified 40 self-reported variables representing symptoms, attitudes, illnesses, and function
- ◆ strongly correlated with mortality; NH placement; exponential increase of frailty with age
- ◆ Based upon secondary analysis of the Canadian Study on Health and Aging

Mitnitski, Song, Rockwood, (2004). The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences, 59A(6), 627-632.



Spectrum of frailty models

Common features: Age-related vulnerability to stressors, clinically identifiable, multi-system impairment

Medical syndrome

- Hypothesis-driven
- Limited number of components linked to defined underlying biologic/physiologic pathway
- Medical syndrome: aggregate of Sx and signs associated with morbid process constituting picture:
Cushing

Risk factor approach

- Variable pathway and pathophysiology
- Unlimited number of deficits
 - Geriatric syndrome: accumulated effects of impairments in multiple domains resulting in a particular adverse outcome: falls

The Frailty Phenotype Replicated

- ◆ Several studies have tested the properties of the frailty phenotype in other populations; predictive validity has been consistent; dissociation from ADL disability and co morbidity has been consistent
- ◆ all studies are secondary analyses
- ◆ Confusion and variability over characteristics, measures and cutoffs
 - Eg energy measured by question from depression questionnaire
- ◆ Not clear why those 5 components were designated
 - May not capture the complexity
 - Role of cognitive and psychological factors
 - Link with social and environmental factors

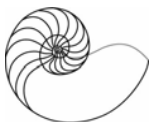
The Frailty Index Replicated

- ◆ Tested in different populations through secondary analysis of large databases; consistently found that the increase in number of deficits increases the risk of mortality
- ◆ Components and number of components are highly variable
 - The more things you have wrong with you, the worse you are
 - Includes disability which is also an outcome
 - Does not help understand underlying mechanisms
 - Hard to see as a clinical tool

The Down Side of a Frailty Syndrome

Missing the Trees for the Forest

- ◆ Lack of attention when only one component is present and definition of syndrome not met
- ◆ Misclassification-persons with diseases/conditions that mimic frailty may be erroneously considered as frail
- ◆ Simple measure(s) of vulnerability may be adequate
 - Gait velocity, grip strength
- ◆ If frailty is really “just” the non specific impact of aging, chronic disease and other risk factors, the inappropriate “labeling” can
 - Alter self-concept; change others’ perceptions; affect decision making inappropriately



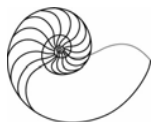
Relevance of the Frailty Syndrome

- ◆ Improves our understanding of the aging process and ability to characterise the heterogeneity of older persons
- ◆ At population and clinical level: characterises health and functional status beyond disability and co morbidity
 - Interventions to delay onset of disability
- ◆ Identifies a subset of vulnerable older adults at high risk of *adverse outcomes*
 - Targeting risk in non disabled older persons with chronic disease

Cacciatore et al. Eur J Clin Invest 2005

Ferrucci et al. Reviews in Oncology/Hematology 2003

Retornaz et al: JGeron med sci 2008



Canadian Initiative on Frailty and Aging / Initiative canadienne sur la fragilité et le vieillissement

www.frail-fragile.ca

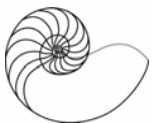
Explosion of frailty models

- ◆ The single analysis and the single meeting models
- ◆ In the last three months of 2008 alone, several new models of frailty have been proposed in the literature:
 - Prognostic score for frailty (Ravaglia et al, 2008)
 - The “FRAIL” scale (van Kan et al, 2008)
 - SOF index (Ensrud et al, 2008)
- ◆ Extensive literature that is difficult to interpret:
 - Range of the reported crude prevalence of frailty based on a systematic review: 1% to 98%

Further Research

Projects and Methodologies

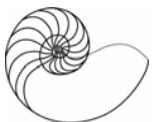
- ◆ Design of novel longitudinal studies with a priori hypotheses
 - Frele, CLSA, NuAge
 - Lausanne cohort
 - Kuh et al: Life course approach to healthy aging nine UK life course cohort studies.
- ◆ Systematic review-Canadian Initiative on Frailty and Aging (Karunanathan, Hogan, Wolfson, etc)
- ◆ Secondary analyses: International Data Base Inquiry on Frailty (FrData): comparable approach to 13 international data base (Sourial, Bergman, Wolfson)
- ◆ Clinical research: natural “experiments: cancer treatment (Martine Puts), cardiac surgery (Jonathan Afilalo), ED utilisation (Anita Au), general surgery (Simon Bergman)
- ◆ Montreal Consortium for the Study of Aging and Chronic Disease from bench to bedside to function to society
 - Biology in humans; animal models
 - Clinical characteristics, cognitive and physical performance and function



Further Research

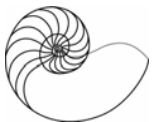
Preliminary (very) results

- ◆ International Data Base Inquiry on Frailty (FrData): comparable approach to 13 international data base
 - Number of markers predictive for disability and mortality
 - Specific markers eg nutrition
- ◆ Clinical research:
 - cancer treatment : Grip strength, cognition
 - cardiac surgery: gait speed



Conclusion

- ◆ Frailty research and debate has opened new horizons in understanding
 - the aging process and the heterogeneity of older persons and
 - the potential to identify independent vulnerable older adults and prevent/delay adverse consequences
- ◆ Still working towards an understanding of frailty; too early to close the debate
 - Not yet a clinical instrument
 - Frailty vs aging; which model
 - » Cannot be based on one study or discussion among friends
 - Frailty markers as markers of vulnerability in independent older persons may be more important than a model
 - » Number of markers; different markers depending on pathway
 - » Disability: an outcome, not a component or marker of frailty
- ◆ Ultimately will only be relevant we succeed in identifying effective health promotion, prevention, treatment, rehabilitation, and care interventions.



“I had come to an entirely erroneous conclusion, which shows my dear Watson, how dangerous it always is to reason from insufficient data.”

Sherlock Holmes in “The speckled band”

Acknowledgements: The Team

- ◆ Christina Wolfson PhD
- ◆ François Béland PhD
- ◆ Johanne Monette MD, MSc
- ◆ David Hogan MD
- ◆ Simon Bergman
- ◆ Jonathan Afilalo

- ◆ Sathya Karunanathan MSc
- ◆ Nadia Sourial MSc
- ◆ Michelle Monette MSc
- ◆ Bin Zhu MSc
- ◆ Audrey Attia MSc

- ◆ Martine Puts PhD (post doc)
- ◆ Frederique Retornaz MD
- ◆ Chek Wong MD

- ◆ Debbie Weiss PhD cand
- ◆ Jacqueline Quail PhD cand

- ◆ and Canadian and international collaborators

