



# Frailty: Searching for a Relevant Clinical and Research Concept

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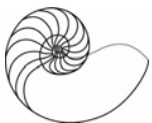
# The Challenge of Defining Frailty

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- ◆ 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

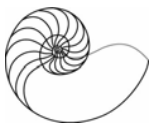


# Frailty: a proposed research and clinical entity

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- ◆ 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

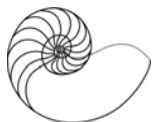
Hogan DB, et al. Aging Clin Exp Research. 2003



# Frailty General Agreement

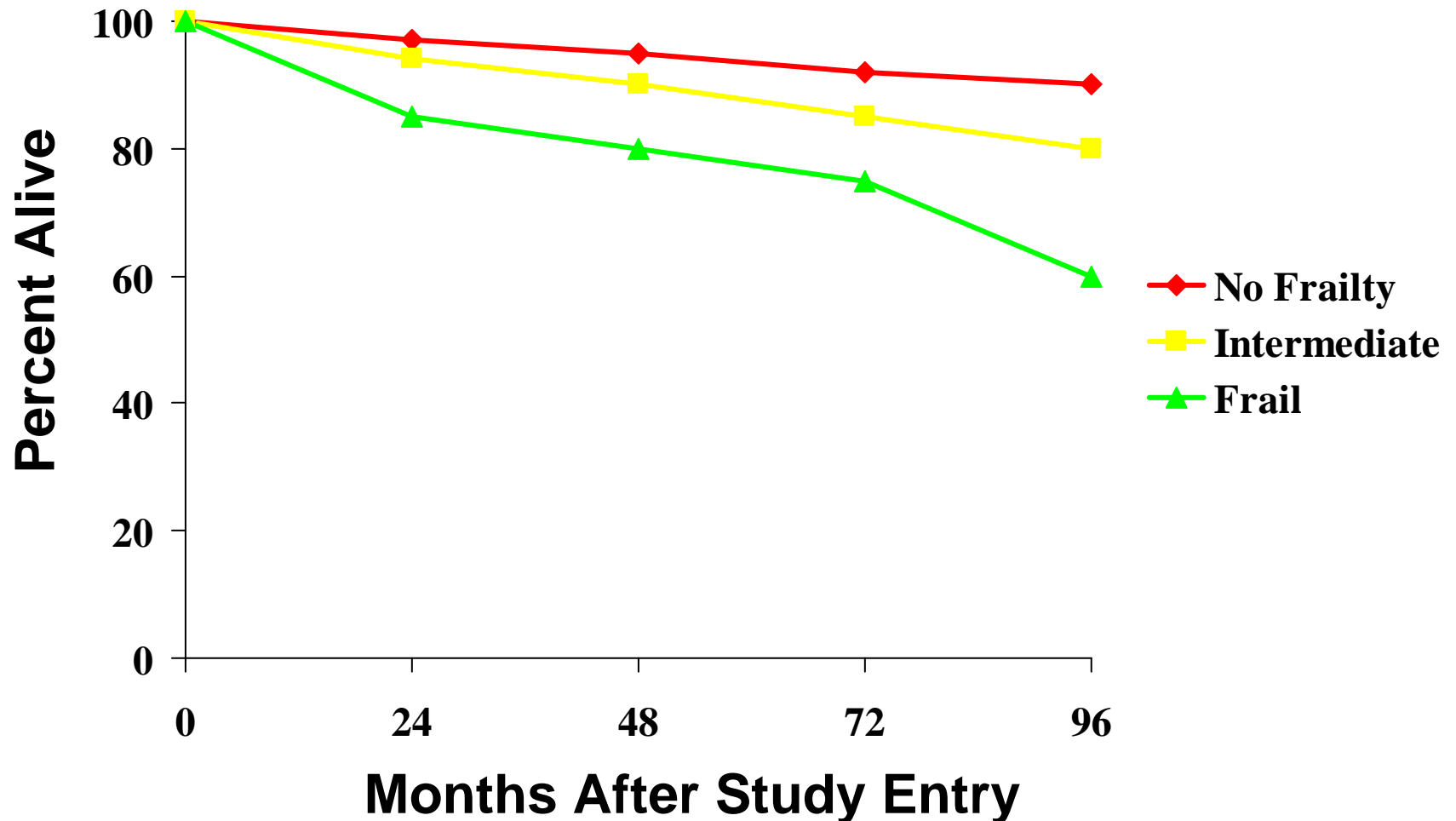
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- ◆ Core feature of frailty is increased vulnerability to stressors due to impairments in multiple, inter-related systems that lead to decline in homeostatic “reserve” and resiliency
- ◆ The main consequence is an increased risk for multiple adverse 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

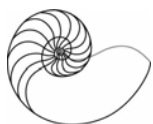
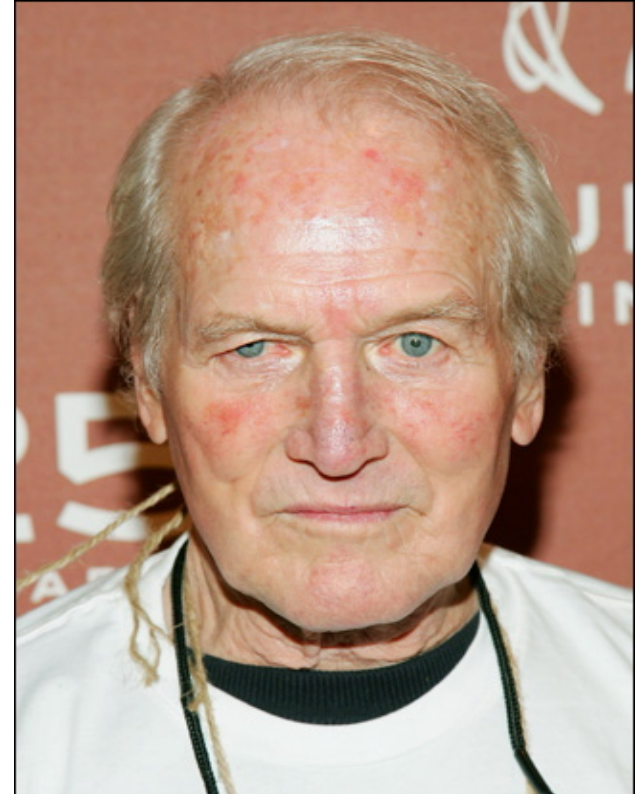
## Cardiovascular Health Study



Fried et al, J. Gerontology Med Sci, 2001

# Aging ...or Frailty

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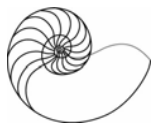


# Issues/Controversies

## Frailty and Aging

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- ◆ 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.

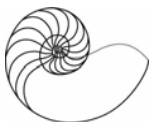


# Issues/Controversies

## Frailty and Chronic Disease

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- ◆ 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

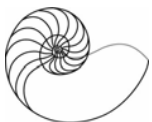
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- ◆ A clinical syndrome with specific manifestations linked to an underlying biological pathway
- ◆ neuroendocrine and immune dysfunction, sarcopenia
- ◆ Grip strength; exhaustion/fatigue; less physically active; slow gait; unintentional weight loss

## 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

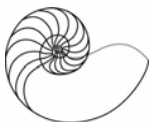


# The Frailty Index

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- ◆ 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

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- ◆ 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

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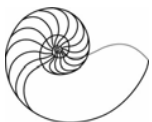
- ◆ Tested in different populations through secondary analysis of large databases; consistently found that the increase in number of deficits increases the risk of mortality
- ◆ Components and number of components are highly variable
  - The more things you have wrong with you, the worse you are
  - 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

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- ◆ 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

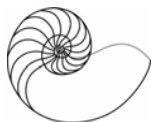
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- ◆ Improves our understanding of the aging process and ability to characterise the heterogeneity of older persons
- ◆ At population and clinical level: characterises health and functional status beyond disability and co morbidity
  - Interventions 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



# Explosion of frailty models

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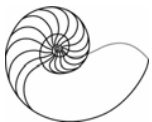
- ◆ The single analysis and the single meeting models
- ◆ In the last three months of 2008 alone, several new models of frailty have been proposed in the literature:
  - Prognostic score for frailty (Ravaglia et al, 2008)
  - The “FRAIL” scale (van Kan et al, 2008)
  - SOF index (Ensrud et al, 2008)
- ◆ 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

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- ◆ 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

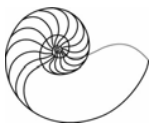


# Further Research

## Preliminary (very) results

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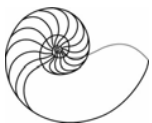
- ◆ International Data Base Inquiry on Frailty (FrData): comparable approach to 13 international data base
  - Number of markers predictive for disability and mortality
  - Specific markers eg nutrition
- ◆ Clinical research:
  - cancer treatment : Grip strength, cognition
  - cardiac surgery: gait speed



# Conclusion

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- ◆ 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

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