HDFS649: Multidisciplinary Gerontology Discussion Presentation

Old Age Frailty: Mechanisms, Antecedents, and Mortality

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Frailty

Broad definitions:

- Decline in physiological systems and ability to regulate stressors [Yang et al., 2024]
- Diminished ability to carry out important practiced social activities of daily living under stressful conditions [Morley et al., 2006]

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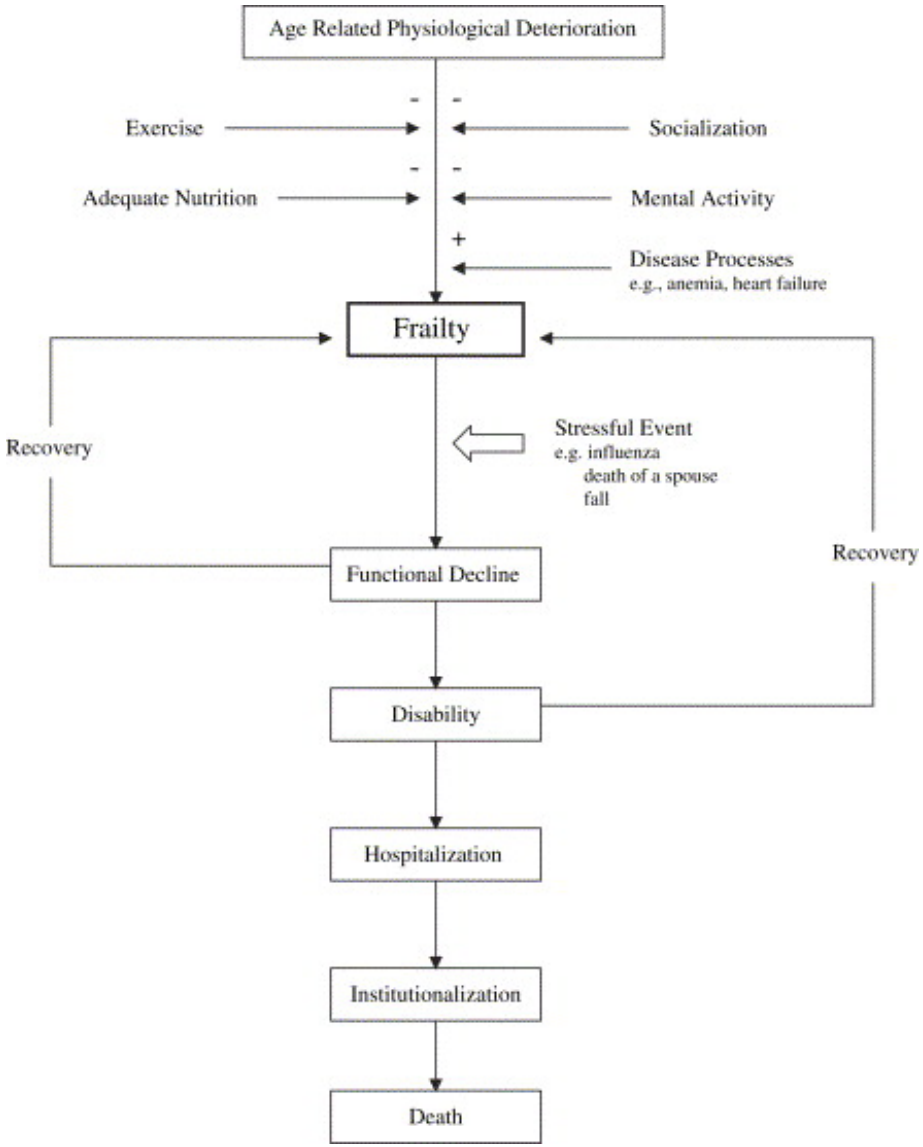
Risks of Frailty

1. Individual level
   - $RR_{mortality}$: $1.8 - 2.3$
   - $RR_{hospitalisation}$: $1.2 - 1.8$
2. Aggregate level
   - Cost burden of frailty $\approx 40 - 76\%$ of total healthcare costs
   - Heavier burden on working population



Frailty 'Cascade':

- Age-related stressors precipitates individuals into frailty
- Excess loss of functional muscle related to decline in executive function
- *But non-linear process and reversible

Conceptual Models

How has frailty been conceptualised in the literature?

1. Reliability Theory
2. Allostatic Load
3. Complexity Theory

How do different conceptualisations translate into operationalisations of frailty?

1. Frailty Index (FI)
2. Rockwood's Clinical Frailty Scale (CFS)
3. 5-item Frailty Scale
4. Various Biomarkers

Reliability Theory

Underlying Hypothesis

- Humans as being born in a 'defective' state in need of constant maintenance
- Possess limited biological resources (e.g., cells) to maintain *homeostasis*
- Exposure to stressors deplete these resources through a process of *deficit accumulation*

Deficit accumulation model of Frailty

Subcellular deficits $\rightarrow$ Higher order disorders $\rightarrow$ Frailty onset

Reliability Theory

Senescence: the gradual deterioration of physiological functions and cellular processes in living organisms as they age

- We have encountered this concept earlier on in the semester!
- Expressed formally:

$$R(t) = Pr\{T > t\} = \int_t^{\infty} f(x)dx$$

where $f(x)$ is the failure PDF, t is the length of time, and $R(t)$ is the probability that the body will survive past time t

Some would also recognise this to be the **survival function** in survival analysis!

Reliability Theory

Frailty Index (FI)

- Takes a value of $0 - 1$
- Sum of individual deficits at the point of evaluation, divided by total number of symptoms, signs, and impairments under consideration

Rockwood et al.'s Clinical Frailty Scale (CFS)

- Categorise individuals into $7 - 9$ categories based on physiological function across domains of disease pathology, physical activity, ability to engage in daily activities, and need for caretaking

Allostatic Load

'Wear and tear' of physiological systems

- Fried et al.'s Frailty Scale
  1. Unintentional weight loss $\geq$ 4.5kg or 5% body weight
  2. Fatigue levels
  3. Reductions in grip strength (adjusted for gender and BMI)
  4. Low levels of physical activities
  5. Low gait speed
- Allostatic load index
  1. Biomarkers of cardiovascular, metabolic, endocrine, and inflammatory regulatory systems

Predictive of various physiological problems (e.g., inflammation & endocrine misbalance; age-related disease) [Dowd et al., 2024; Ding et al., 2019]

Complexity Theory

Underlying hypothesis

- Interaction between biological systems to produce compensatory mechanisms to counteract physiological abnormalities
- Impaired interactions between physical systems compromise ability to adapt to stressors
- Less studied in the literature, but *sometimes* operationalised as heart rate variability [Zaslavsky et al., 2012; Beckers et al., 2006]

Cumulative Risk

Much support in the literature

- Every additional adversity associated with increased risk of frailty by 38% [Yang et al., 2024]
- Cumulative adversity exposure positively associated with greater risk of frailty across various countries [Dimitriadis et al., 2023; Wang, 2023; Van Der Linden et al., 2020]
- *Cumulative risk* of adversity exposure, rather than other life course models (*recency; sensitive periods*), most strongly associated with frailty [Baranyi et al., 2022]

Cumulative Risk

Gender differentiated effects?

- Accumulated adversity for women (but not men) positively related to greater frailty risk and steeper trajectories of frailty [Tao et al., 2024; Wang, 2023; Mian et al., 2021]
- *Little evidence of female-disadvantage in cumulative adverse experience [Bornscheuer et al., 2024]
- *Early-life stress related to frailty risk among men but not women in Finland [Haapanen et al., 2018]

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Differences in political economic contexts? Female disadvantage largely detected in neoliberal regimes where weaker socioeconomic positions of women are related to poorer health and healthcare access

Sensitive Periods

The Long Arm of Childhood

- Elevated levels of brain plasticity during developmental phases in young ages
- Stressors and shocks experienced sensitive periods exert *pronounced* and *enduring* effects on individuals
- Early stressors affect outcomes even as late as old-age health and age-at-death [Pakpahan et al., 2017]

Sensitive Periods

Sensitive periods differed by age

- Males most susceptible to adversity during childhood
- Females most vulnerable during mid-adulthood

Potentially due to differential brain structure, gonadal hormones, and neuroendocrine functioning between men and women during stress response

- Men undergo overall suppression of HPA axis after puberty – dampened stress-response effect in later life
- Fluctuations in orbitofrontal cortex (brain region crucial to stress regulation) for women across the menstrual cycle in response to emotional stimuli

Recency

Understudied and little support

- Recency model only salient among girls when considering exposure to financial stress [Marini et al., 2018]
- Other forms of adversities (e.g., abuse; psychopathy; instability) were associated with sensitive period hypothesis

All-cause Mortality

Frailty status is associated with greater mortality risk

- Associated with loss of 5.71 years of life by age 45 [Hou et al., 2022]
  - **Men:** Loss of 4.82 years by age 65
  - **Women:** Loss of 4.96 years by age 65
- 3-year survival rates lowest among *frail* (74.2%) compared to pre-frail (85.7%) and non-frail (92.6%) [Lee et al., 2021]
- Robust across alternate operationalisations of frailty status ($OR = 3.95 - 7.96$)

All individual measures of frailty also related to shorter life expectancy

- Slow walking pace predicted greatest loss of life (1.49 years) by age 65 [Hou et al., 2022]

Cause-specific Mortality

Frailty status most predictive of respiratory-related mortality

- Respiratory illness: $OR = 3.48$
- Heart disease: $OR = 2.96$
- Cancer: $OR = 2.82$
- Dementia: $OR = 2.87$

Proposed Mechanism

- Multidimensional health behaviours (body mass, tobacco and alcohol consumption) mediated $\approx 5.1\%$ of relationship between frailty and respiratory illness specific mortality

Cause-specific Mortality

- Cardiovascular disease
  - **Male:** Hazard ratio = 1.69
  - **Female:** Hazard ratio = 1.91
- Geriatric conditions
  - **Malnutrition:** OR = 2.83 – 5.25
  - **Dysmobility:** OR = 3.58 – 7.97
  - **Disability:** OR = 2.18 – 4.46
  - **Impaired Cognition:** OR = 2.36 – 5.25

Frailty impinges on health and mortality through a broad spectrum of diseases

Office of Interdisciplinary Graduate Programs' Spring Reception

Much apologies for shameless promotion...

Office of Interdisciplinary Graduate Programs' Spring Reception

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- I will be doing a poster building on my MPhil thesis!
  - Which life course model (*sensitive periods; cumulative risk; recency*) best explains the relationship between childhood adversity and epigenetic ageing?
  - How does accelerated epigenetic ageing affect (physical/mental) health and life history outcomes?
  - Does epigenetic ageing mediate the relationship between childhood adversity and health/life history outcomes?

I could really use all of your brilliant ideas and feedback! :)

Office of Interdisciplinary Graduate Programs' Spring Reception

- **Where:** North & South Ballrooms, PMU
- **When:** 7th May 2025, 9:30 a.m– 3:30 p.m

Thank you for your attention!

Please feel very free to reach out anytime for any questions, comments, or coffee (preferably tea)!

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Github: https://github.com/wesleywj/Multi-Gerontology

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