# Clinical Utility of Frailty

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*WA RURAL HEALTH CONFERENCE 2023*

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# Summary

- “Disposable soma” and ageing – The theoretical basis of frailty
- What is frailty, what is different from what we currently use, and why is there more around than we think?
- What are some practical implications of the frailty model?

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- What are some practical implications of the frailty model?
- Some thoughts and concerns about using the frailty model for clinical practice

# Why do people age?

## Disposable soma theory (Kirkwood (2000)

(1) ageing is not pre-programmed; it results from accumulation of somatic damage, owing to limited investments in maintenance and repair;

(2) the accumulation of somatic damage is stochastic in type;

(3) adverse gene actions may occur at older age due to genes that escape the force of natural selection or from pleiotropic genes that trade benefit at an early age against harm at older ages.

**This works for cells, whole animals and humans**

Biogerontology
DOI 10.1007/s10522-013-9446-3

RESEARCH ARTICLE

# Assessing biological aging: the origin of deficit accumulation

Arnold Mitnitski · Xiaowei Song · Kenneth Rockwood

"In this paper, we have proposed a general and simple stochastic model to explain how the number of deficits present in individuals can be represented by the product of the intensity of environmental stresses to the average recovery time (in accordance with Little's Law). The exponential increase in the number of health deficits with age directly corresponds to the exponential increase of recovery time, as does the changes with age in the distributions of the deficits."

However, maybe our adaptations to previous insults actually increases the propensity to develop deficits with stable environmental stressors – e.g. hypertension and atherosclerosis

# Summary

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- What is frailty, what is different from what we currently use, and why is there more around than we think?
- What are some practical implications of the frailty model?

# Frailty: An Inevitable Consequence of Ageing

- Characterizes individuals at the limits of their physiological reserve in one or more of the major homeostatic systems such that any minor perturbation precipitates a cascade of events in multiple systems, leading to further illness and death (Walston et al 2006).
- Two major competing views of frailty

(a waste of time, what we are trying to do is capture information about physiological reserve of systems that are not our focus)

1) Older people acquire a specific "phenotype" of frailty, defined by 5 items, unintentional weight loss (5 kilos in past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity (Fried et al 2001) ("sarcopenic" frailty – muscle or nerves?).
2) Another approach has assumed a straightforward stochastic model, frailty is just simply an accumulation of deficits of multiple aetiologies (Rockwood & Minitski 2007).
3) More recently frailty "screens"

# Frailty (Cont'd)

- There is now evidence from observational studies that older people can improve, or become less frail, and decrease their risk of disability and death, highlighting the importance of targeted interventions (Mitnitski et al 2007).
- How do we identify the ”frail”? The challenge in formalizing the concept of frailty is to identify individuals at very high risk of an event that has not yet happened, and to do this in a way that is sensitive, specific, reliable and easy to use in clinical practice.
- What interventions do we use on this targeted group of individuals? The purpose of developing and applying this definition is to facilitate pre-emptive interventions that prevent the catastrophic unravelling that follows after the point of critical overload is reached.

- Practically The type of model that we have used has not been that important
- People with advanced frailty usually exhibit obvious disability and then we use our typical Geriatric Evaluation and Management model based loosely on the ICF framework.

# What we currently use
# CGA Comprehensive Geriatric Assessment

- In 1984, a randomised clinical trial of the effectiveness of a geriatric evaluation unit was reported. (Incidentally, this study was designed and funded in Australia but was never carried out here.)
  Rubenstein et al NEJM 1984;311 1664
- At one year, patients who had been assigned to the geriatric unit had much lower mortality than controls (23.8 vs. 48.3 per cent, P<0.005) and were less likely to have spent any time in a nursing home during the follow-up period (26.9 vs. 46.7 per cent, P<0.05).
- Patients in the geriatric unit were significantly more likely to have improvement in functional status and morale than controls. Direct costs for institutional care were lower for the experimental group, especially after adjustment for survival.

# Assessment & Rehabilitation in Aged Care - More Evidence

- Since that early study meta-analyses, have confirmed the benefits of inpatient geriatric assessment and rehabilitation with patients more likely to be alive at 6 months, odds ratio (OR) of 1.25 [1.11, 1.42], with benefits on decreased rates of institutionalisation, OR 0.79 [0.69, 0.88], and improved physical and cognitive function Cochrane 2011; Ellis
- Increased benefits were associated with medical control over recommendations and perhaps explains some of the heterogeneity between studies.
- Similarly organised inpatient stroke unit care has also shown benefits, with a reduction in death or institutionalisation of 0.76 [0.65, 0.90] and inpatient rehabilitation of older patients with proximal femoral fractures demonstrated a trend for benefits, OR of death and decrease in function of 0.89 [0.78, 1.01]. (Cochrane Library 2007 and 2009)

# Frailty - The Scientific Basis of Why Geriatric Interventions Work (Flicker BMJ 2008; 337:a516)

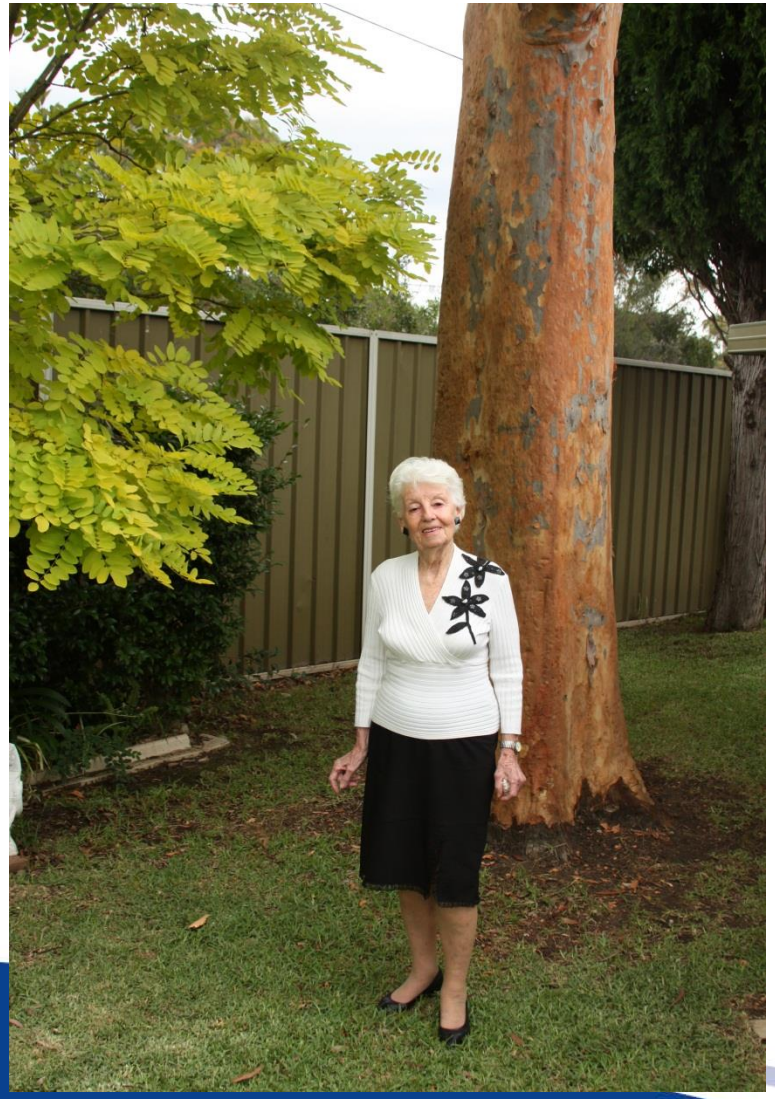
- Frailty is almost certainly mediated by physiological ageing? and multiple diseases associated with ageing converging to syndromes – dementia, falls, depression, incontinence……..
- The accumulation of multiple insults over time and consequent reduction of homeostatic reserve must be addressed by a comprehensive approach that includes all organ systems and focuses on functional effects.
- Loss of homeostatic reserve, and the necessity to treat multiple conditions concurrently will lead to an inevitable risk of iatrogenic complications.
- Deficit accumulation is not just confined to physical insults. Life course events may also increase susceptibility to illness and thus the need for "psychosocial' interventions.

# FRAIL Scale

- Assessed frailty at Waves 2 and 3 with the FRAIL scale (Abellen van Kan G et al JAMDA 2008; 9:71).
- Five domains are assessed in this screening tool: fatigue, resistance (ability to climb a single flight of stairs), ambulation (ability to walk one block), illnesses (more than five), and loss of weight.
- Fatigue, resistance and ambulation were assessed from SF-36.
- A deficit was recorded for illness if > 5 of the following: arthritis, diabetes, angina or myocardial infarction, hypertension, stroke, asthma, chronic bronchitis, emphysema, osteoporosis, colorectal cancer, skin cancer, depression or anxiety disorder, dementia and leg ulcers
- Participants scored positive for weight loss if their weight decreased by more than 5% between W1 and W2 or W2 and W3.

# Non Frail

# Pre Frail



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# Frail

# Very Frail

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# Identifying Frailty

## Clinical Frailty Scale*

1 **Very Fit** – People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.

2 **Well** – People who have **no active disease symptoms** but are less fit than category 1. Often, they exercise or are very **active occasionally**, e.g. seasonally.

3 **Managing Well** – People whose **medical problems are well controlled,** but are **not regularly active** beyond routine walking.

4 **Vulnerable** – While **not dependent** on others for daily help, often **symptoms limit activities.** A common complaint is being "slowed up", and/or being tired during the day.

5 **Mildly Frail** – These people often have **more evident slowing,** and need help in **high order IADLs** (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.

6 **Moderately Frail** – People need help with **all outside activities** and with **keeping house.** Inside, they often have problems with stairs and need **help with bathing** and might need minimal assistance (cuing, standby) with dressing.

7 **Severely Frail** – **Completely dependent for personal care**, from whatever cause (physical or cognitive). Even so, they seem stable and not at high risk of dying (within ~ 6 months).

8 **Very Severely Frail** – Completely dependent, approaching the end of life. Typically they could not recover even from a minor illness.

9. **Terminally Ill** - Approaching the end of life. This category applies to people with **a life expectancy <6 months**, who are **not otherwise evidently frail.**

**Scoring frailty in people with dementia**

The degree of frailty corresponds to the degree of dementia. Common **symptoms in mild dementia** include forgetting the details of a recent event, though still remembering the event itself, repeating the same question/story and social withdrawal.

In **moderate dementia**, recent memory is very impaired, even though they seemingly can remember their past life events well. They can do personal care with prompting.

In **severe dementia**, they cannot do personal care without help.

* 1. Canadian Study on Health & Aging, Revised 2008.
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489–495.



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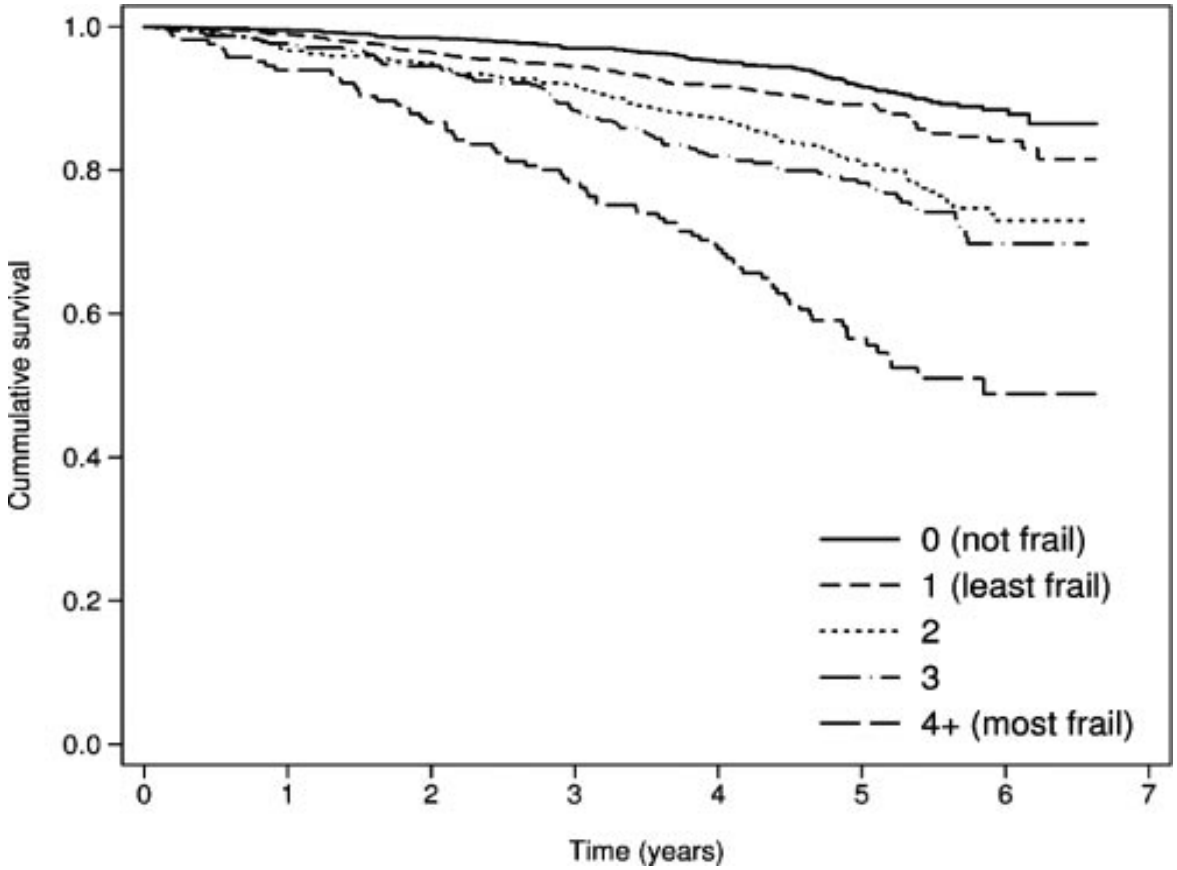
# Validation of FRAIL scale




Association between FRAIL scale at Wave 2 and subsequent all-cause mortality.

After adjustment for age, BMI, medical comorbidity, and smoking, frailty (3+ on FRAIL scale) at W2 was associated with increased odds of disability at W3 [OR: 3.95, 2.73–5.72; p<0.001].

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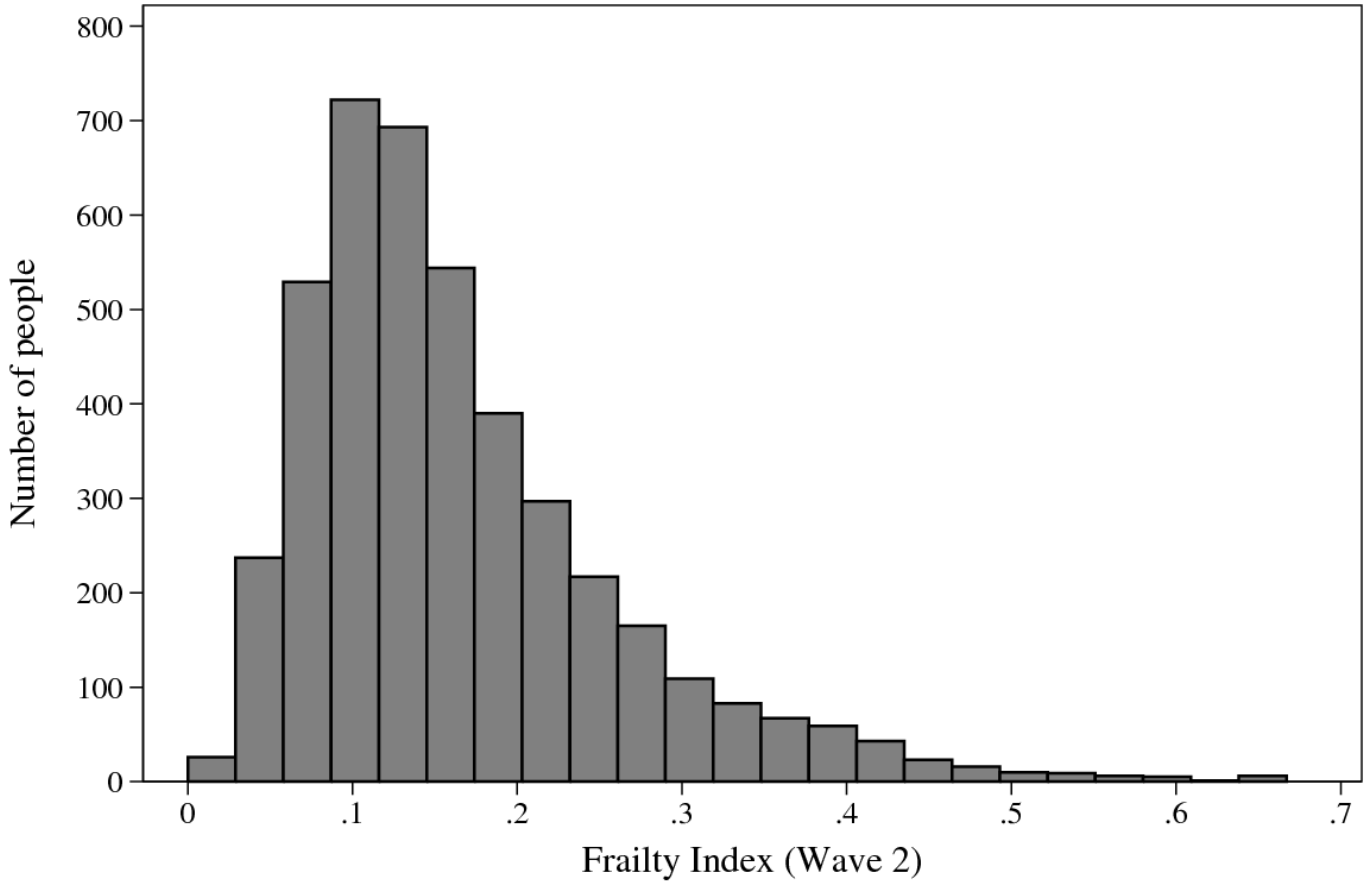
# Frailty Index – Multiple deficits approach 34 items

- **Self reported diseases**: Arthritis, diabetes mellitus, angina, hypertension, stroke, heart attack, asthma, chronic bronchitis, emphysema, osteoporosis, prostate cancer, bowel cancer, melanoma, skin cancer, depression, anxiety or nervous disorder, dementia.
- Major surgery
- Injury following a fall in last year, fractured a bone in last year
- Difficulty hearing, difficulty with sight.
- Treatment for depression, sleep problems, poor self rated health, poor health compared with a year ago
- Limitations in general activities, managing finances, shopping, stair climbing, walking and bathing, Depression scale positive, Cognitive screen positive.

# Frailty Index distribution at Wave 2

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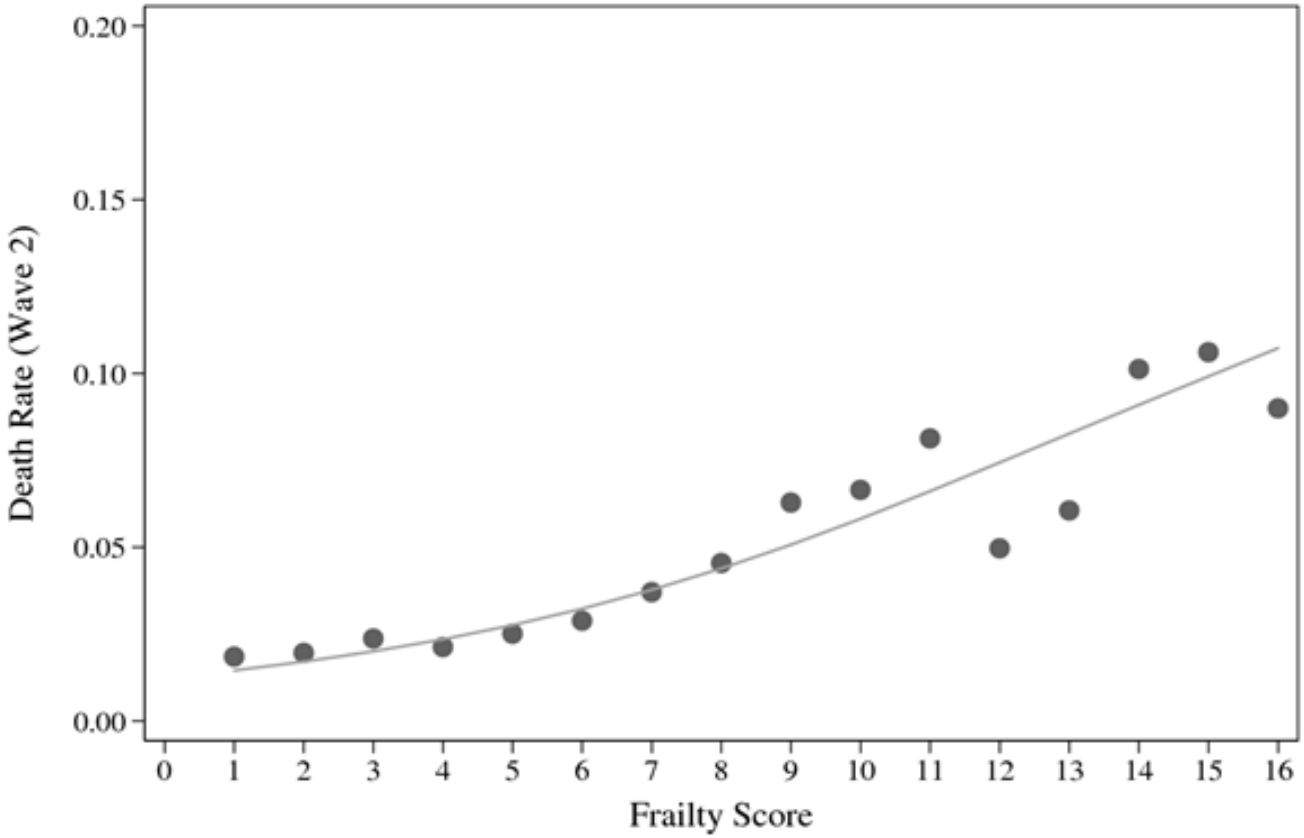
# Mortality rate by Frailty Index at Wave 2




Frailty index of 0.25 = 8.5

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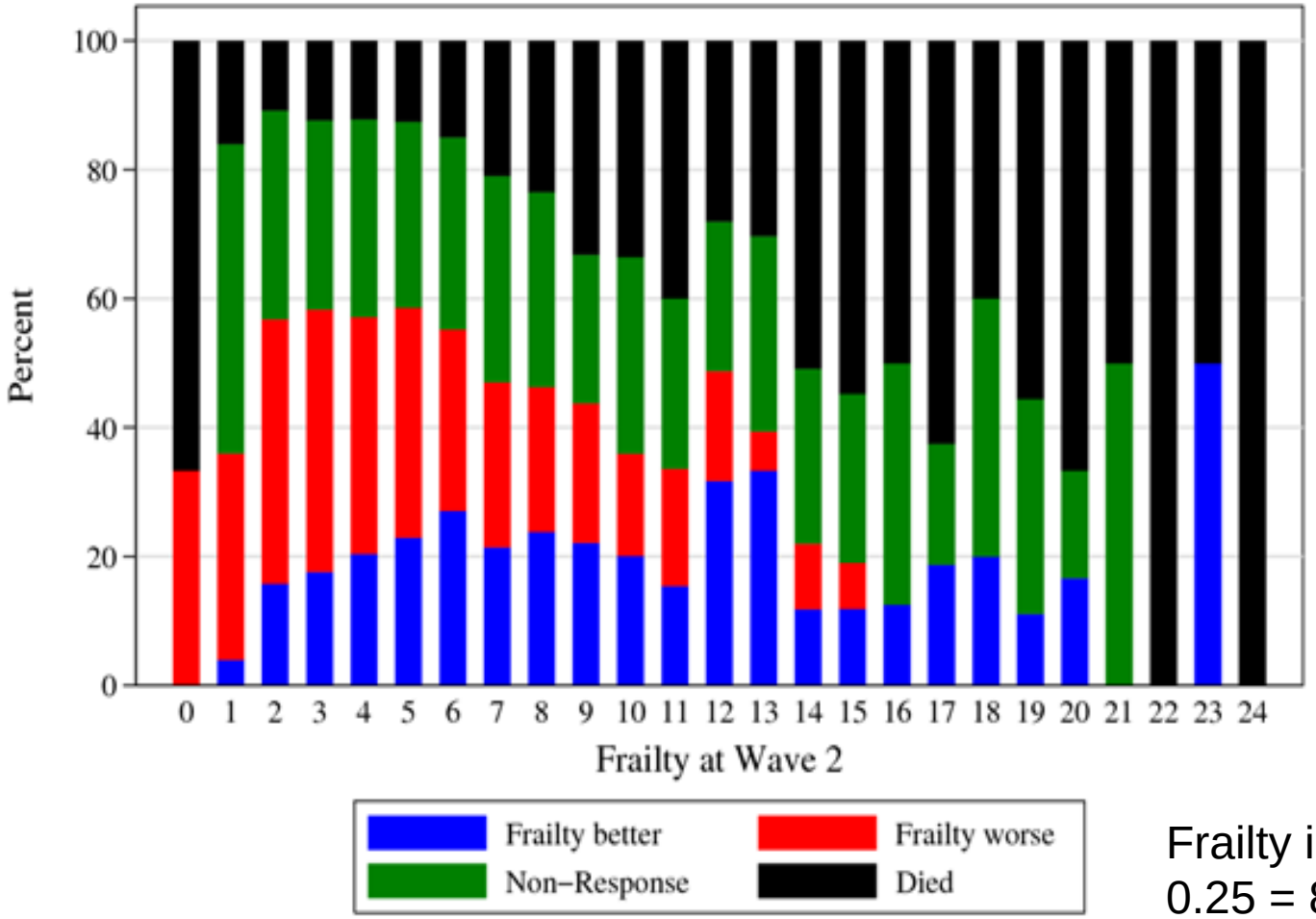
# Distribution of all outcomes at Wave 3 by Frailty Index at Wave 2




Frailty index of 0.25 = 8.5

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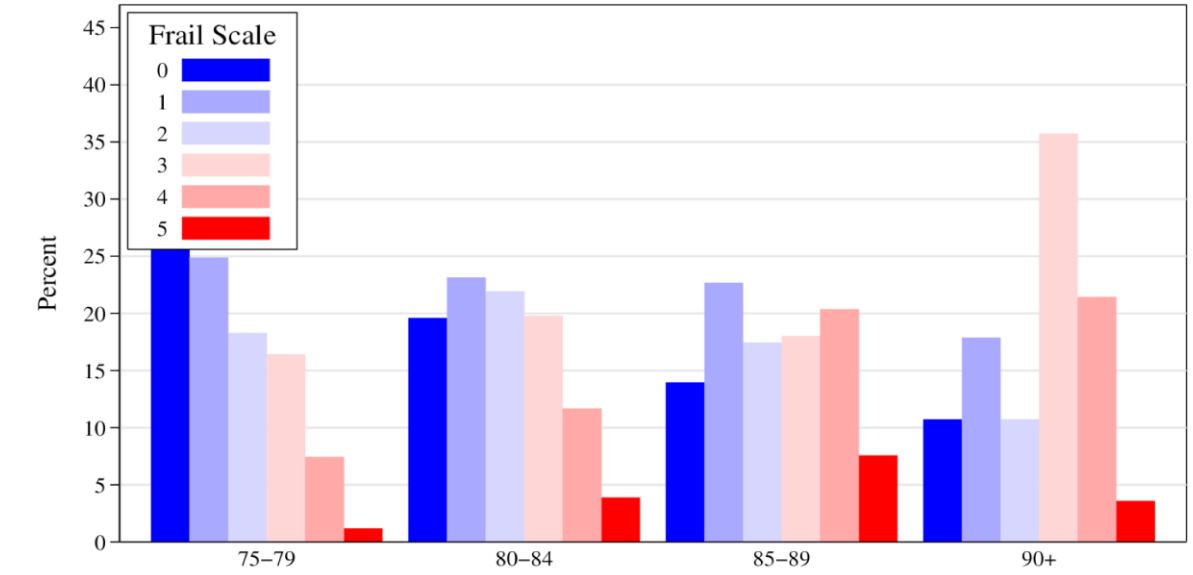
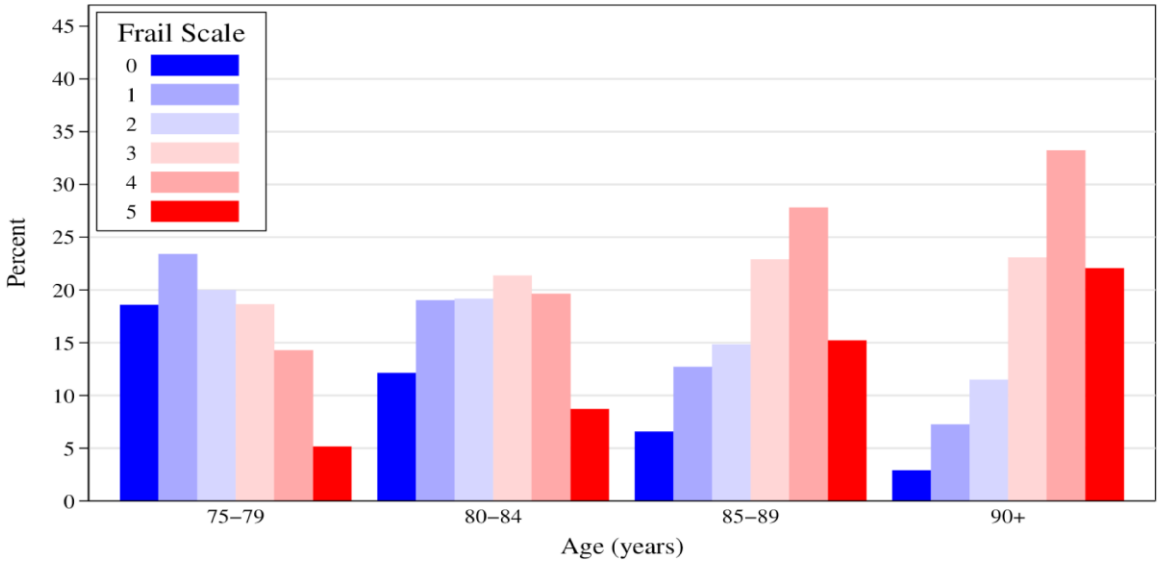
# Observed and imputed prevalence of Frailty at Wave 3

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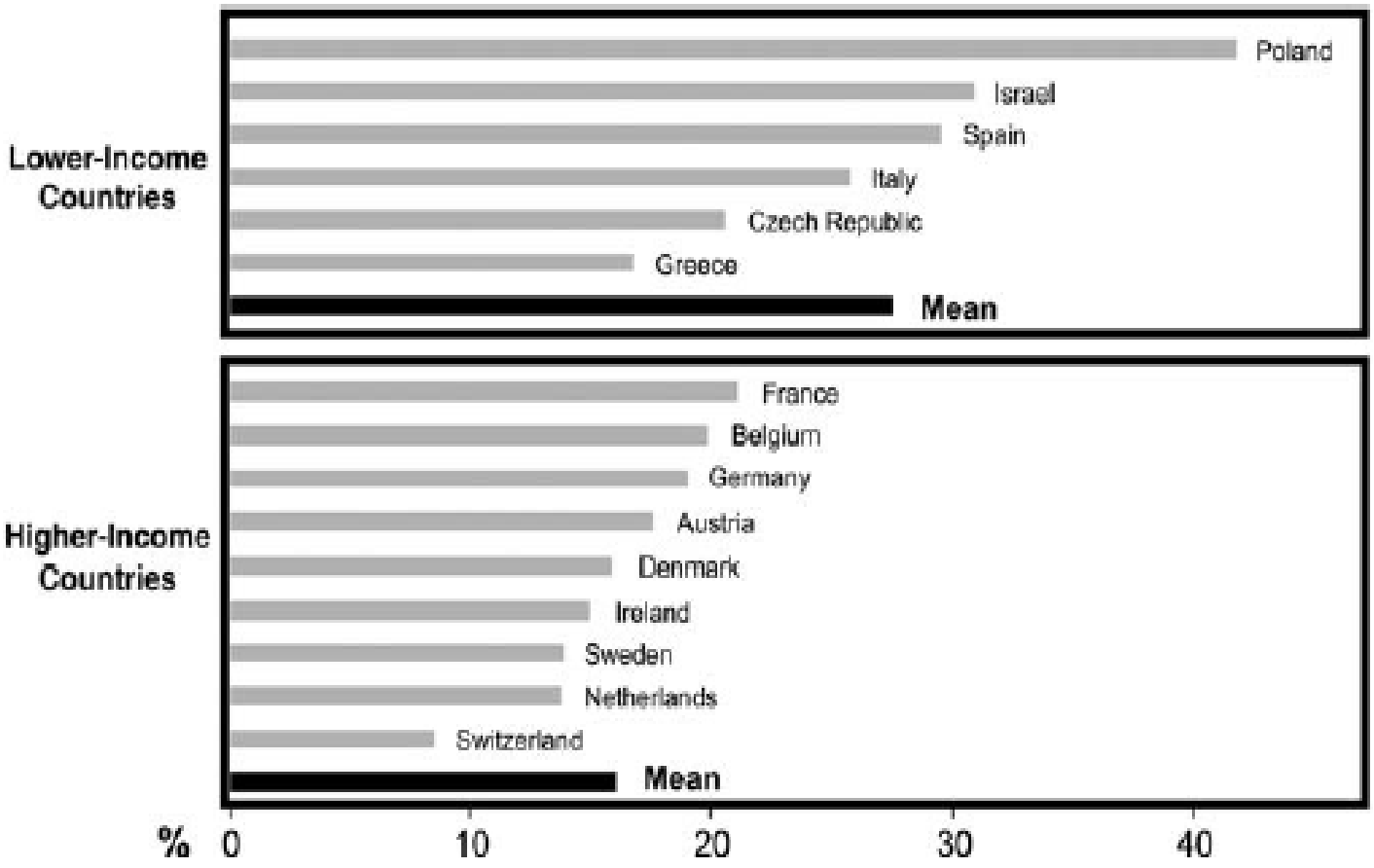
# Prevalence of Frailty by Country
## (Theou et al Age & Ageing 2013)




Frailty score > 0.25

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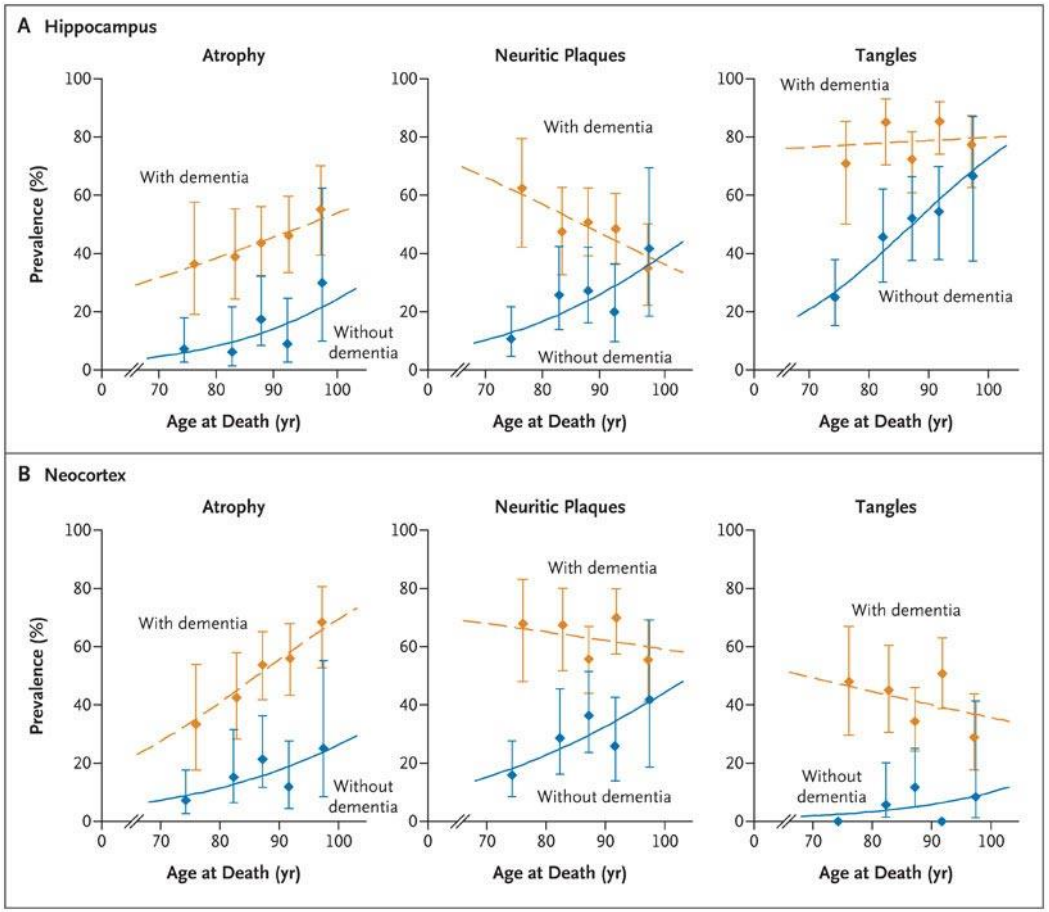
# Dementia or Cognitive Frailty?

Age, neuropathology and dementia Savva et al N Engl J Med 2009; 360:2302

**The association between the presence of dementia and Alzheimer pathology decreases with age**




- 5 separate pathologies associated with "Alzheimers-type dementia"
- Plaques and tangles
- Microvascular Lesions
- Atrophy
- Hippocampal sclerosis
- Cortical Lewy Bodies

(White L 2009)

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# Dementia or Cognitive frailty?

**Normal**

**Mild neurocognitive Disorder**

**Dementia**

**Mild** **Moderate** **Severe**

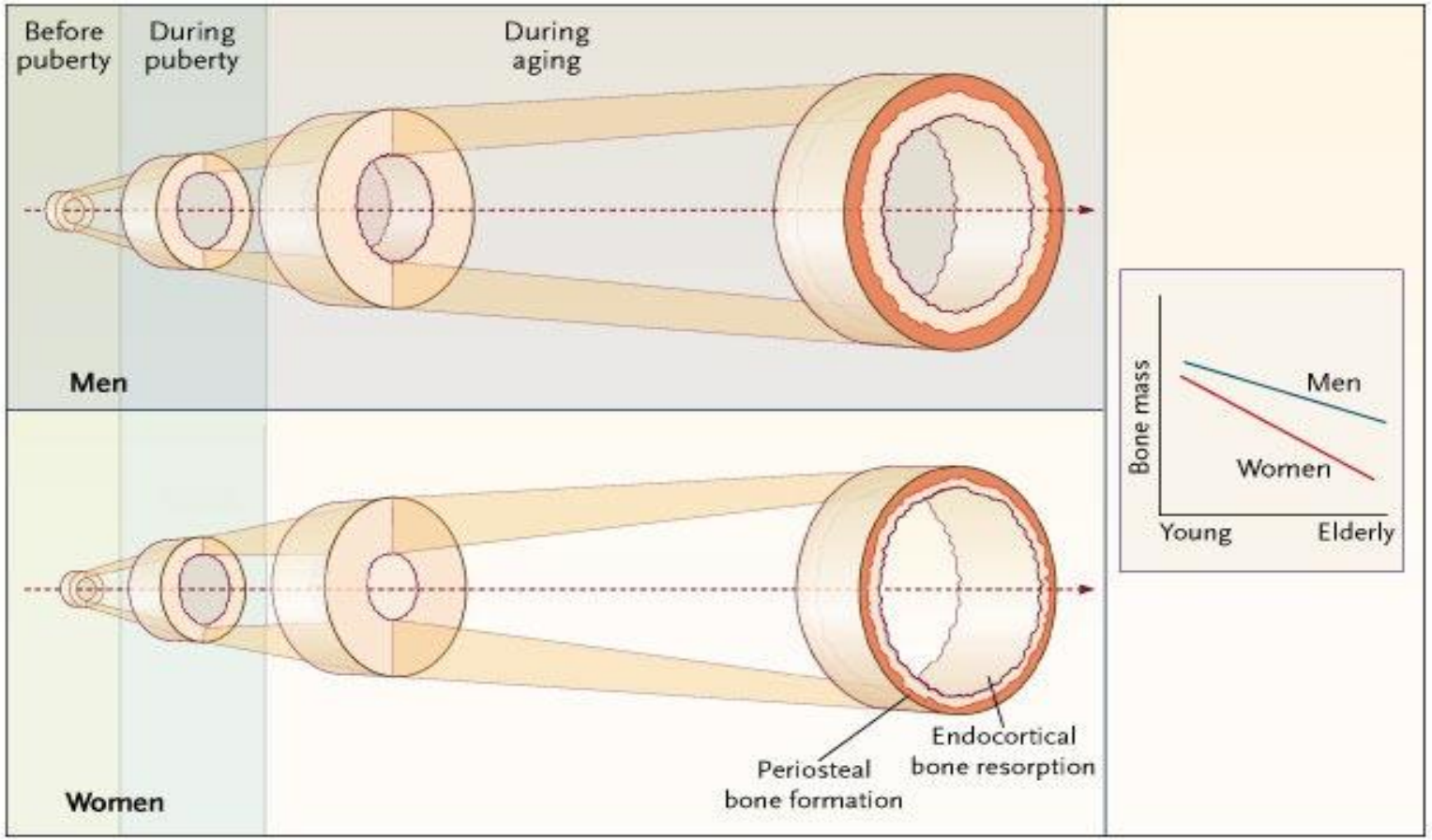
**INCREASING COGNITIVE FRAILTY**

**Increasing amounts and types of pathology - Alzheimers, Lewy Body and Vascular identified over 20 years ago and 4 relatively new common pathologies.**

**Delirium (potentially reversible)**

# Bone Frailty

Differences between Men and Women in Periosteal Apposition and Net Bone Loss during Ageing. Seeman NEJM 2003; 349:320



# Low Free Testosterone Predicts Frailty in Older Men: The Health in Men Study

Zoë Hyde, Leon Flicker, Osvaldo P. Almeida, Graeme J. Hankey, Kieran A. McCaul, S. A. Paul Chubb, and Bu B. Yeap

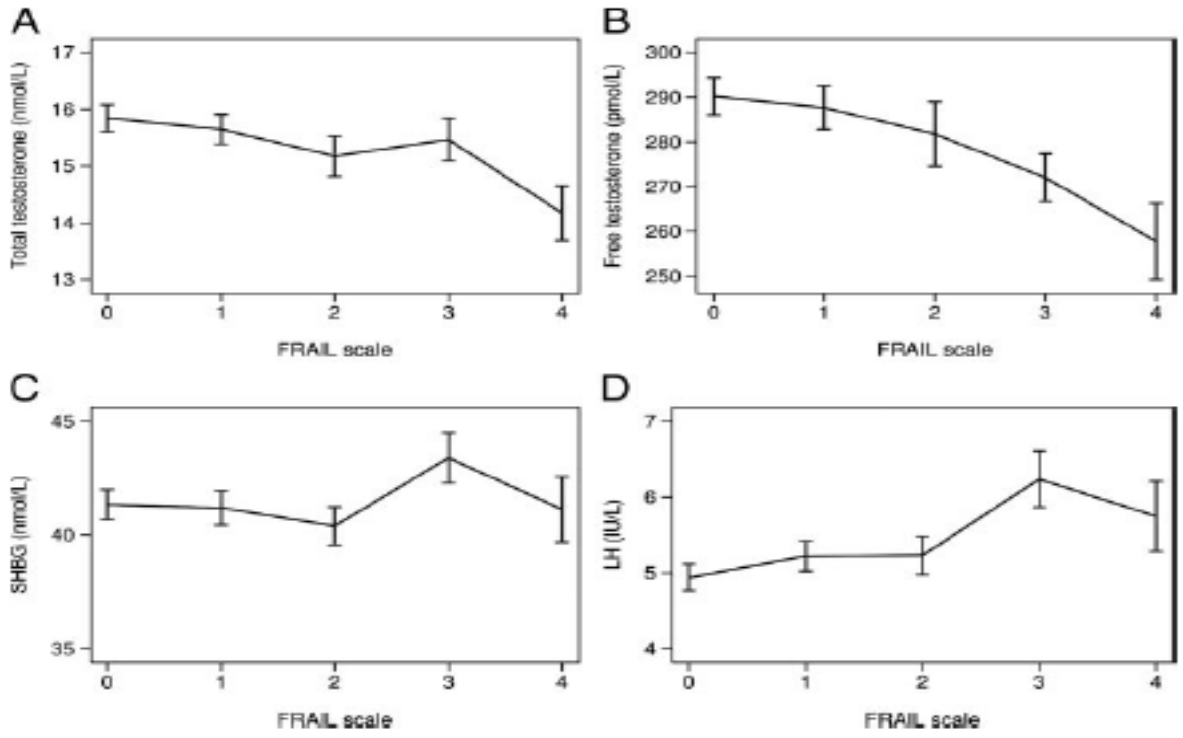



**FIG. 3.** Mean (±1 SEM) total testosterone (A), free testosterone (B), SHBG (C), and LH (D) measured at W2, stratified by FRAIL scale at W3. Higher scores indicate greater frailty. Men with four or more deficits were combined into a single category.

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# Low Vitamin D Status Is an Independent Predictor of Increased Frailty and All-Cause Mortality in Older Men: The Health in Men Study

Yuen Y. E. Wong, Kieran A. McCaul, Bu B. Yeap, Graeme J. Hankey, and Leon Flicker

J Clin Endocrinol Metab 98: 3821–3828, 2013

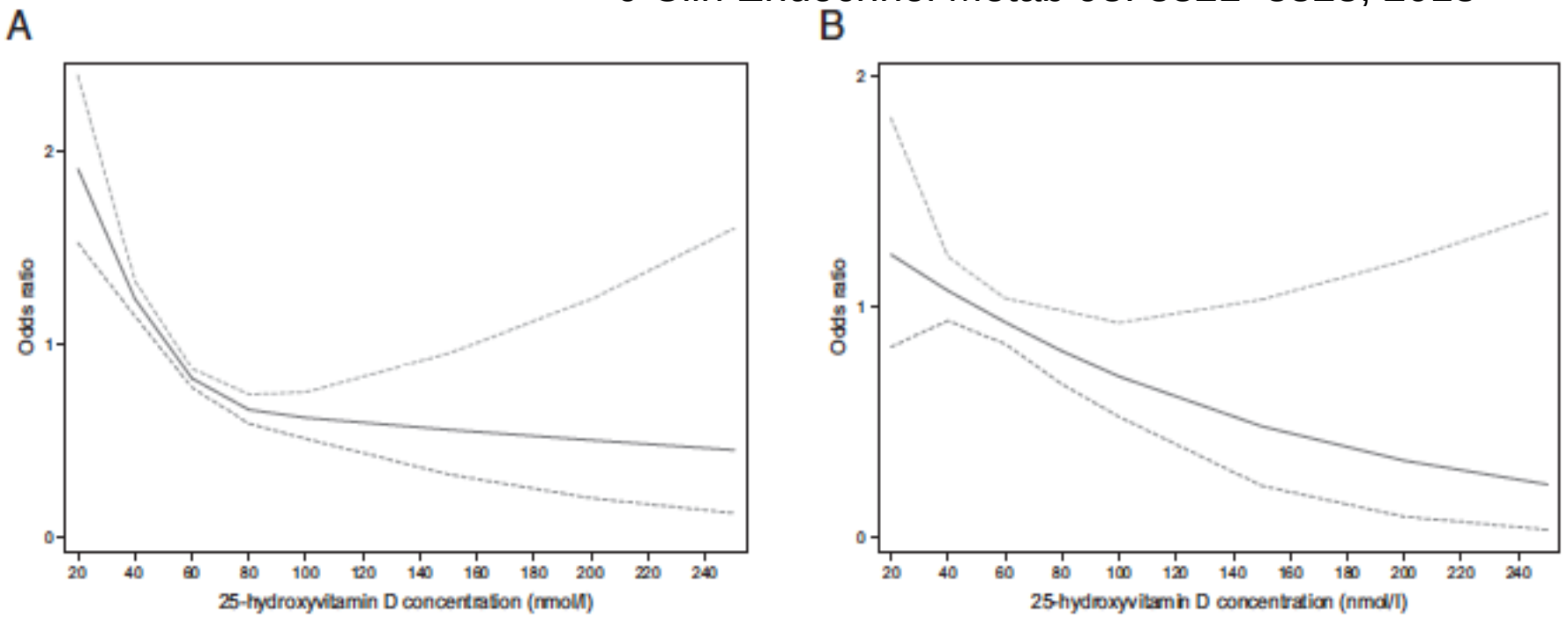


**Figure 1.** OR of prevalent and incident frailty during wave 2 (A) and wave 3 (B), respectively, with changing serum 25(OH)D levels. 25(OH)D are entered into the models as restricted cubic splines (3 knots) with a reference value of 50.0 nmol/L. Dashed lines denote 95% CI.

JAMDA 16 (2015) 296–300

JAMDA

journal homepage: www.jamda.com

Original Study

# Depression, Frailty, and All-Cause Mortality: A Cohort Study of Men Older than 75 Years

Osvaldo P. Almeida MD, PhD[a,b,c,*], Graeme J. Hankey MD[d,e], Bu B. Yeap MBBS, PhD[e,f], Jonathan Golledge MChir[g,h], Paul E. Norman DS[i], Leon Flicker MBBS, PhD[b,d,j]

*Results:* 558 participants died during mean period of follow-up of 4.2 ± 1.1 years. The annual death rate per thousand was 50 for men without depression, 52 for men with past depression, and 201 for men with major depressive symptoms at baseline. The crude mortality hazard was 4.26 (95% confidence interval = 2.98, 6.09) for men with depression at baseline compared with never depressed men, and 1.79 (95% confidence interval = 1.21, 2.62) after adjustment for frailty. Further decline in mortality hazard was observed after adjustment for other measured factors.

*Conclusions:* Current, but not past, depression is associated with increased mortality, and this excess mortality is strongly associated with frailty. Interventions designed to decrease depression-related mortality in later life may need to focus on ameliorating frailty in addition to treating depression.

# Kimberley Healthy Aboriginal Project
# Prevalence of frailty and disability by age group at W1 and W2 (%)

| | Frailty W1 (n=363) | Frailty W2 (n=182) |
|---|---|---|
| 45-59 | 54.9 | - |
| 50-59 | 63.7 | 60.8 |
| 60-69 | 64.8 | 64.3 |
| 70-79 | 71.6 | 73.7 |
| 80+ | 83.3 | 87.0 |
| | Disability W1 (n=352) | Disability W2 (n=131) |
| 45-49 | 2.9 | - |
| 50-59 | 8.5 | 14.5 |
| 60-69 | 18.8 | 20.7 |
| 70-79 | 19.7 | 37.9 |
| 80+ | 53.3 | 72.2 |

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# Kimberley Healthy Adults Project n= 289
# Rates of common geriatric syndromes, by age group

| Age | 45-49 (45; 16%) | 50-59 (111; 38%) | 60-69 (61; 21%) | 70-79 (47; 16%) | 80+ (25; 8%) |
|---|---|---|---|---|---|
| Trouble walking: (118; 42%) | 15 (34%) | 40 (37%) | 25 (44%) | 24 (51%) | 14 (61%) |
| Fall last yr: (82; 32%) | 10 (23%) | 29 (31%) | 16 (29%) | 20 (46%) | 7 (39%) |
| Urinary incont: (71; 26%) | 8 (18%) | 26 (24%) | 12 (21%) | 13 (30%) | 12 (52%) |

# Summary

- “Disposable soma” and ageing – The theoretical basis of frailty
- What is frailty, what is different from what we currently use, and why is there more around than we think?
- What are some practical implications of the frailty model?

JAMDA

journal homepage: www.jamda.com

2017

Special Article

# The Asia-Pacific Clinical Practice Guidelines for the Management of Frailty

Objective: To develop Clinical Practice Guidelines for the screening, assessment and management of the geriatric condition of frailty.

Recommendations: Strong recommendations were

(1) use a validated measurement tool to identify frailty;

(2) prescribe physical activity with a resistance training component; and

(3) address polypharmacy by reducing or deprescribing any inappropriate/superfluous medications.

# Asia Pacific guidelines for frailty (cont'd)

Conditional Recommendations were

1) screen for, and address modifiable causes of fatigue

2) For persons exhibiting unintentional weight loss, screen for reversible causes and consider food fortification and protein/caloric supplementation; and

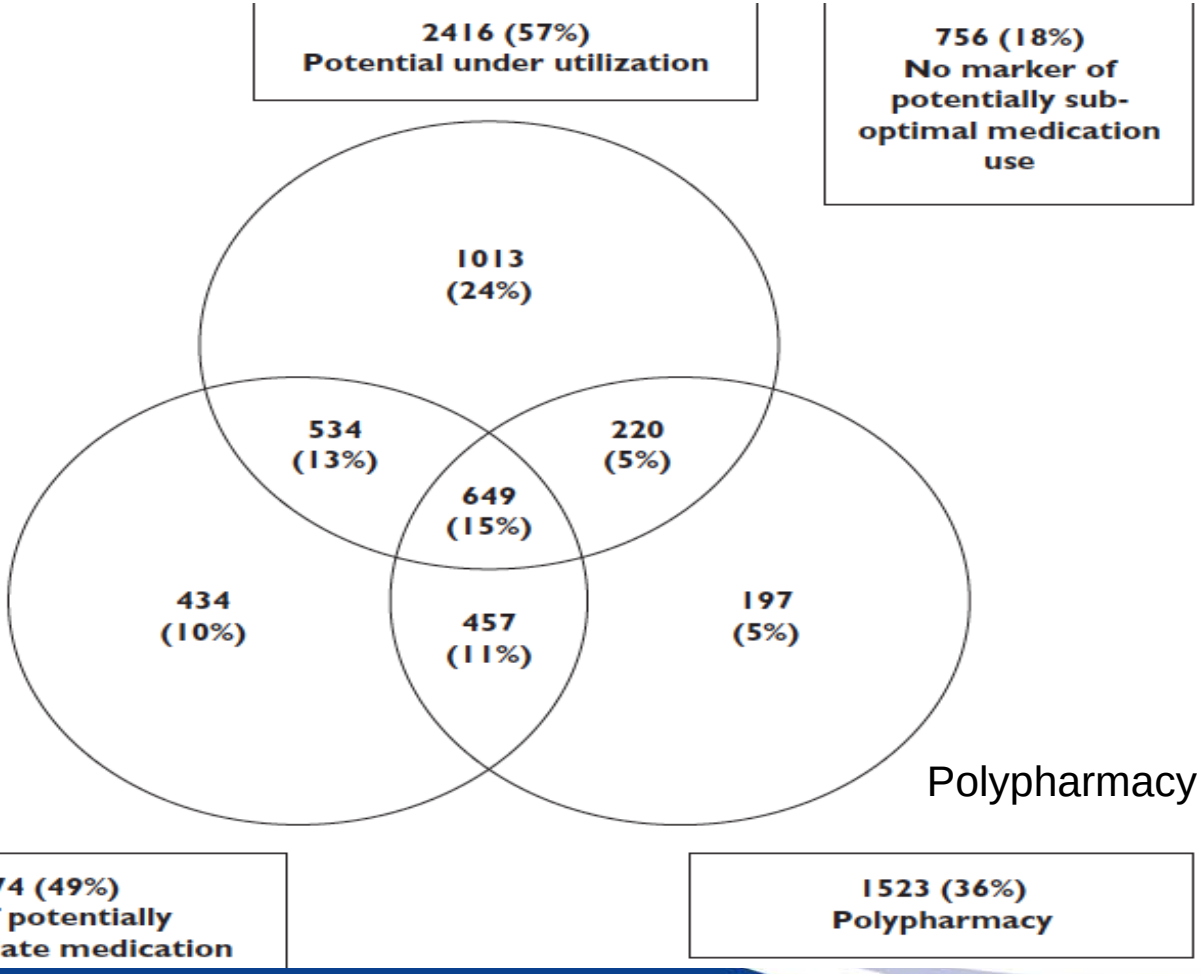
(3) prescribe vitamin D for individuals deficient in vitamin D.

No recommendation was given regarding the provision of a patient support and education

# Frailty and Medications

- Most drugs have been evaluated on younger people with predominantly single diseases
- However, many users of medications are older people, with multiple chronic illnesses and multiple drug treatments. Multiple chronic illnesses result in loss of physiological reserve
- This results in increased risk of
  - Drug-Drug interactions
  - Drug-Disease interactions
- This leads to a narrowing of the therapeutic window. Most of the major problems are pharmacodynamic in type rather than pharmacokinetic
- However, as older people have the highest absolute risk of disease, if the relative benefit of a medication is maintained, they may receive the greatest benefits from medication- OP

# Quality use of medicines and health outcomes among a cohort of community dwelling older men: an observational study (Beer et al Br J Clin Pharmacol 71:592–599)




Polypharmacy ≥ 5 medications

# Deprescribing

- **Data on the effects of deprescribing are scarce.**
- **Small observational studies and a few randomised trials have examined withdrawing a single class of medication in older people.**
- **Antihypertensives, benzodiazepines and psychotropic agents can usually be stopped without causing harm Iyer S, Naganathan V, McLachlan AJ, Le Conteur DG. Drugs & Aging 2008; 25:1021**
- **Data from observational studies suggest that serious adverse drug withdrawal effects are rare, the majority of adverse reactions are caused by only a few types of medication, and adverse effects are easily treated by restarting the withdrawn medication**

# The war against Polypharmacy: A New Cost-Effective Geriatric-Palliative Approach for Improving Drug Therapy in Disabled Elderly People

Doron Garfinkel MD[1], Sarah Zur-Gil MA[2] and Joshua Ben-Israel MD[3] 2007

**Methods: The study group comprised 119 disabled patients in six geriatric nursing departments; the control group included 71 patients of comparable age, gender and co-morbidities in the same wards.**

**Results: A total of 332 different drugs were discontinued in 119 patients (average of 2.8 drugs per patient) and was not associated with significant adverse effects. The overall rate of drug discontinuation failure was 18% of all patients and 10% of all drugs. The 1 year mortality rate was 45% in the control group but only 21% in the study group (P < 0.001, chi-square test).**

**Successful discontinuation of all target drugs in 82% of patients. Antidepressants and antipsychotics were the most difficult drugs to cease, with failure of withdrawal in 26% and 31% of patients respectively.**

# Frailty, Falls and Medications Drugs Aging. 2014; 31:225

METHODS:

Patients ≥60 years of age admitted with a fall to a tertiary referral teaching hospital in Sydney

RESULTS:

A total of 204 patients were recruited (mean age 80.5 ± 8.3 years), with 101 robust and 103 frail. On admission, compared with the robust, frail participants had significantly higher mean number of fall-risk-increasing drugs (FRID), **frail 3.4±2.2 vs**. **robust 1.6±1.5**, total number of medications **9.8± 4.3 vs. 4.4±3.3**,, and drug-drug interactions exposure, **35% vs. 5%.**

CONCLUSION:

Exposure to FRIDs and other measures of high-risk medication exposures is common in older people admitted with falls, especially the frail. Number of FRIDs and to a lesser extent total number of medicines at discharge were associated with recurrent falls.

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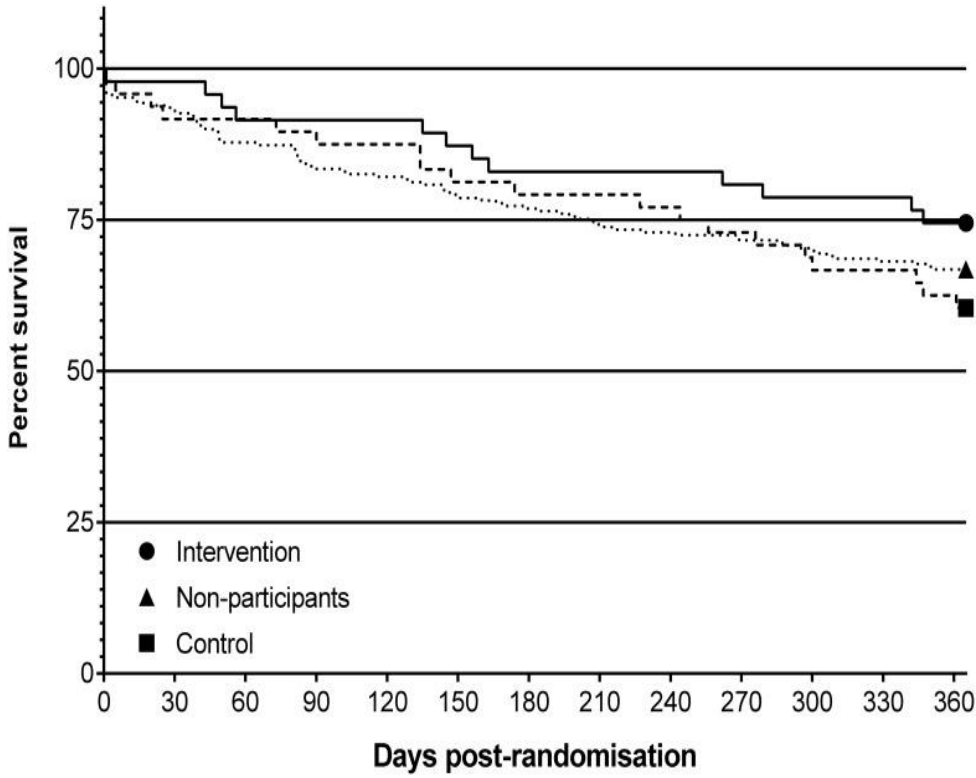
RESEARCH ARTICLE

# Deprescribing in Frail Older People: A Randomised Controlled Trial

Kathleen Potter[1,3]*, Leon Flicker[1,2,3], Amy Page[1], Christopher Etherton-Beer[1,2,3]

Ninety-five people aged over 65 years living in four RACF in rural mid-west Western Australia randomised in an open study. The intervention group (n = 47) received a deprescribing intervention, planned cessation of non-beneficial medicines. The control group (n = 48) received usual care.

Mean age 84.3±6.9
Intervention group consumed mean 9.6±5.0 and control group 9.5±3.6 unique regular medicines at baseline.
Mean change in no. regular medicines at 12 months was -1.9±4.1 in intervention group and +0.1±3.5 in control group

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# JAMA Internal Medicine

## RCT: Effect of Routine Invasive vs Conservative Strategy in Older Adults With Frailty and Non–ST-Segment Elevation Acute Myocardial Infarction (NSTEMI)

### POPULATION

**79 Men, 88 Women**

Adults ≥70 y with NSTEMI and frailty defined by ≥4 points on the Clinical Frailty Scale

**Mean age, 86 y**

### SETTINGS / LOCATIONS

**13 Hospitals in Spain**

### INTERVENTION

**167** Participants randomized and analyzed

**84 Routine invasive management**
Coronary angiography and revascularization if deemed appropriate

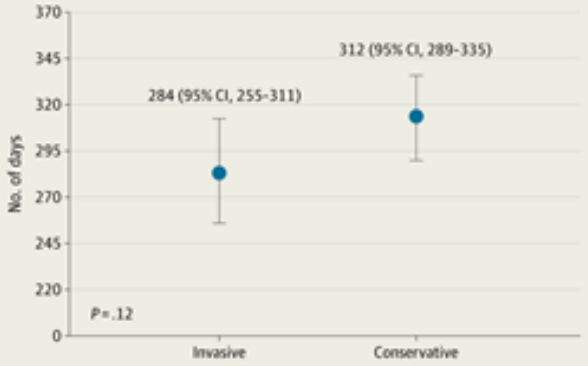
**83 Conservative management**
Medical therapy with coronary angiography only if recurrent ischemia

### PRIMARY OUTCOME

The primary end point was the number of days alive and out of the hospital (DAOH) between discharge from the index hospitalization to 1 y

### FINDINGS

There was no significant difference in DAOH between the routine invasive management and conservative management groups




Routine invasive management: 284 d; 95% CI, 255-311 d
Conservative management: 312 d; 95% CI, 289-335 d; *P* = .12

Sanchis J, Bueno H, Miñana G, et al. Effect of routine invasive vs conservative strategy in older adults with frailty and non-ST-segment elevation acute myocardial infarction: a randomized clinical trial. *JAMA Intern Med*. Published online March 6, 2023. doi:10.1001/jamainternmed.2023.0047



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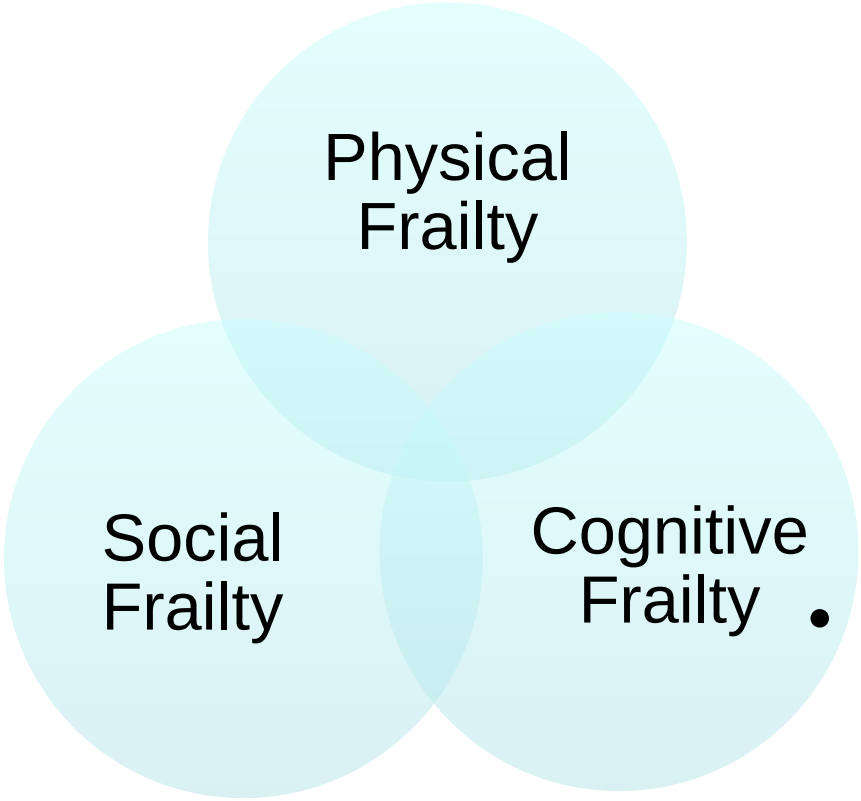
# Frailty – One Giant 3 domains




- Physical Frailty
  - Sarcopenia
  - Falls
  - Immobility
  - Incontinence
  - Susceptibility to iatrogenesis (esp drugs)
- Cognitive frailty
  - Dementia
  - Mild neurocognitive disorder
  - Delirium
- Social Frailty
  - Can be defined as a continuum of losing, or lost, resources that are important for fulfilling social needs during the life span. (Bunt, Eur J Ageing (2017) 14:323

# Conclusions

- The concept of frailty is exciting as it potentially taps into the scientific basis of ageing
- There are probably more people with greater frailty in older age groups than revealed in surveys.
- Business is Booming! If only we knew what to do about it.
- The risks for us to embark on unproven interventions is that it will be based on opportunism