Bed Rest
THE DANGERS OF GOING TO BED

BY

R. A. J. ASHER, M.D., M.R.C.P.

It is always assumed that the first thing in any illness is to put the patient to bed. Hospital accommodation is always numbered in beds. Illness is measured by the length of time in bed. Doctors are assessed by their bedside manner. Bed is not ordered like a pill or a purge, but is assumed as the basis for all treatment. Yet we should think twice before ordering our patients to bed and realize that beneath the comfort of the blanket there lurks a host of formidable dangers. In "Hymns Ancient and Modern," No. 23, Verse 3, we find:

"Teach me to live that I may dread
The grave as little as my bed."

It is my intention to justify placing beds and graves in the same category and to increase the amount of dread with which beds are usually regarded. I shall describe some of the major hazards of the bed. There is hardly any part of the body which is immune from its dangers.
Complications of bed rest
Musculoskeletal system

Pathophysiology: Loss of strength:
• Total inactivity: >10-20% decrease in muscle strength per week (1-3% per day)
• 3-5 weeks of complete immobilization can lead to a 50% decrease in muscle strength

Loss of muscle mass:
• 3% loss in thigh muscles within 7 days (bed rest alone does not completely unweight the bones, but elderly, deconditioned patient cant reposition).
• Involvement greatest in postural muscles (lower back and quads/glutes/soleus)
Musculoskeletal system

Contracture Involvement: Muscles That Cross Two Joints
- Muscle fibers & connective tissues are maintained in a shortened position (5-7 days)
- Muscle fibers & connective tissues adapt to the shortened length by contraction of collagen fibers and a decrease in muscle fiber sarcomers
- Loose connective tissue in muscles and around the joint gradually change into dense connective tissue (occurs in approximately 3 weeks)

Disuse Osteoporosis
- Causes: Loss of bone density due to increased resorption caused by the lack of weight bearing, gravity, and muscle activity on bone mass
- Pathophysiology: An increase in the excretion of calcium in the urine and stool; after 12 weeks of bed rest bone density is reduced by almost 50%
- Involvement: bones, especially the long bones; develops from the bone marrow outward
Cardiovascular changes with bed rest

• Increase in resting heart rate (4-15 beats within the first 3-4 weeks then plateaus)
• Decrease in blood volume (5% in 24 hours, 10% in 6 days, 20% in 14 days)

Major cardiovascular complications
• Fluid shifts
• Postural hypotension
• Increased risk of clot formation (DVT/PE)
Understanding Cardiovascular adaptations to bed rest

CONFINED TO BED REST
• 500 ml fluid shift from lower extremities to the thorax (also known as central fluid shift)
• Increased stroke volume/cardiac output/left end-diastolic volume

PROLONGED BED REST
• Depressed levels of aldosterone & antidiuretic hormone -> diuresis (net effect is decreased blood & plasma volume)
• Increased heart rate & stroke volume to maintain cardiac output
• Increased ORTHOSTATIC hypotension
Respiratory changes related to bed rest

- PFT Parameters reduced
  - Compliance change due to fluid shifts and Diaphragm splinting
- Muscle strength and endurance changes
- Impaired cough/secretions
- Mucus plugging/atelectasis
- Lung consolidation/infection
Metabolic and nutritional changes

- Decreased lean body mass
- Increased body fat
- Disorders of nitrogen balance
- Mineral and electrolyte loss
- Altered Glucose tolerance
  - Onset by day 3
  - Improved by isotonic leg muscle exercise
  - Takes two weeks to improve
Psychosocial complications of Immobility

• Depression
• Apathy/helplessness/ loss of motivation
• Changes in perception
  – Disorientation in time and space
  – Hallucinations
  – Change in pain threshold
  – Change in auditory threshold
• Changes in cognition
• Changes in behaviour
Complications of bed rest

- Muscle weakness
- Systemic inflammation
- Atelectasis
- Metabolism
- Thromboembolic disease
- Microvascular function
- Skin ulcers
- Changes in blood volume
Lets talk about Frailty

• How useful is the concept
• What is it
• What underpins Frailty
• How is it measured
• How does it affect the body
What is frailty?

“A medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual’s vulnerability for developing increased dependency and/or death.”


- “Easy to spot but hard to define”
- Has important prognostic significance in many areas of medicine
What does frailty look like?
Mr Burns’ Profile

• “Physically weak, he often has great difficulty performing the most basic physical tasks, such as giving a thumbs-up, receiving a hug, crushing a paper cup, or stepping on an insect. He is weak enough to be pushed over by an ant or a high-five, or pushed down by a sponge scrub on his head”
Lets talk about Frailty

How do we use information about Frailty Clinically?

• Prognosis
• Diagnosis
• Treatment

• Why does this matter?
  Future directions
What are the risks

• “Frail” older people are at greatest risk of adverse outcomes (worsening disability, institutionalisation and death) and are more likely to present with a geriatric syndrome (particularly delirium and falls).
Measurement of Frailty

• There are many validated tools to measure frailty as a clinical syndrome or phenotype

• Fried model which defines someone as frail if they meet 3 or more of 5 criteria: weight loss, exhaustion, weak grip strength, slow walking speed and low physical activity

• Edmonton Frailty Scale which derives a maximum score of 17 from assessments across 10 different domains.
Measurement of Frailty

• Frailty can be conceptualised as the failure of a complex system.

• Deficits accumulate with the passage of time leading to a loss of redundancy.
  – Over a critical threshold the system becomes vulnerable to failure
  – Measurement by the number rather than the nature of health problems.
Pathogenesis

• Frailty is strongly associated with a combination (rather than by a single measure) of immunological and physiological impairments
  – evidence linking inflammation with frailty
Falls

- Falling is strongly linked to frailty. When complex systems fail, they fail first with their higher order functions.
- The frail older person, on the threshold of failure, can present with falls in the face of seemingly minor stressor.
Therapeutic strategies

• Therapeutic strategies to prevent or reverse frailty remain incompletely explored
• Lifestyle behaviours including smoking and the development of obesity (particularly the accumulation of abdominal fat) increase risk
• Complex interventions such as optimisation of nutrition, better education and exercise have the potential to delay the onset of frailty.
Definition

• The term “frail” is intended to identify vulnerable older people at high risk of adverse outcomes including falls, worsening disability, institutionalisation and death.
Conceptual Framework

Reliability Theory of Ageing

• Progressive accumulation of random damage to a complex system composed of redundant parts
  – Defects accumulate with the passage of time (age) resulting in an increased risk of death (ageing).
  – As defects accumulate, lose redundancy
    • System with elements connected in series
    • System has no resilience
    • System vulnerable to external or internal stressors.
Frailty

- Definition
- Epidemiology
- Mechanisms, Interactions
- Assessment
- Prevention, Treatment
- Select References
Frailty is a clinical syndrome

- Frailty is a precursor to disability
- Frailty assumes vulnerability to stressors
- Sarcopenia and cachexia are integral to the progression
- Clinical presentation includes:
  - Exhaustion
  - Weakness, Slowness
  - Inactivity
  - Malnutrition
- Allostatic load and inflammation are present
- Marked unintentional weight loss may be seen in a subset of the frail population
A Reminder about the definition

‘a condition or syndrome which results from a multi-system reduction in reserve capacity to the extent that a number of physiological systems are close to, or past, the threshold of symptomatic clinical failure.

As a consequence the frail person is at increased risk of disability and death from minor external stresses’
Overlap

**Sarcopenia**
A syndrome characterized by progressive loss of skeletal muscle mass and strength associated with adverse outcomes [23, 22, 83].

**Cachexia**
A complex metabolic syndrome associated with underlying illness and characterized by loss of muscle and fat [84].

**Frailty**
Decreased physiologic reserve across multiple organ systems with impaired homeostatic reserve, reduced capacity to withstand stress and resultant adverse health outcomes [28, 85].

"Most cachectic individuals are sarcopenic"  
"Some sarcopenic individuals are also frail"  
"Cachectic individuals are commonly frail"  
"Not all frail individuals are cachectic"  
"Most frail individuals are sarcopenic"
**Panel 2: The five phenotype model indicators of frailty and their associated measures**

**Weight loss**  
Self-reported weight loss of more than 4.5 kg or recorded weight loss of ≥5% per year

**Self-reported exhaustion**  
Self-reported exhaustion on US Center for Epidemiological Studies depression scale<sup>73</sup>  
(3–4 days per week or most of the time)

**Low energy expenditure**  
Energy expenditure <383 kcal/week (men) or <270 kcal/week (women)

**Slow gait speed**  
Standardised cutoff times to walk 4.57 m, stratified by sex and height

**Weak grip strength**  
Grip strength, stratified by sex and body-mass index
Mechanisms

Inflammation and lack of biological resilience are key markers. These markers include:

- Interleukins (IL-6)
- C-Reactive Protein (CRP)
- Tumor Necrosis Factor (TNF-α)
- Coagulation Factors
- Chemokines
- Neuropeptides
- Hormones (e.g. DHEA)
Pathophysiology

Inflammation changes protein kinetics:
- Increases degradation
- Decreases nitrogen balance
- Increases amino acid utilization for gluconeogenesis
- Decreases hematopoiesis and immune mediated memory cell activation
- Increases oxidation and glycation products
- Increases steatosis and atrophy
- Increases apoptosis and catabolism
Inflammatory cascades linked to frailty in older persons
Links with specific diseases

Anemia:
• 33% unexplained etiology
• 33% iron deficiency
• 33% anemia of chronic disease

Hypertension
• Most frequently associated with frailty in both genders
• Renin-Angiotensin receptor activation dysregulation
• Increased cytokines, oxidative stress, apoptosis
• Susceptible individuals have SNPs for exaggerated pro-inflammatory response

Cardiovascular Disease
• Prevalence in both genders is 3x, mortality is 2x
• Mortality is 8x in frail women of advanced age undergoing cardiac surgery
Epidemiology

Frailty is expected to increase rapidly in the following segments:

- Oldest old
- Poor minority groups
- Obese older adults

- Increased or worsening deficits herald disability and death (5x)
- Women are more likely to be frail
- Frailty is highly correlated with multi-morbidity
The slippery slope of frailty

- Genetic factors
- Epigenetic mechanisms
- Environmental factors
  - Cumulative molecular and cellular damage
    - Reduced physiological reserve
      - Brain
      - Endocrine
      - Immune
      - Skeletal muscle
      - Cardiovascular
      - Respiratory
      - Renal
    - Physical activity
    - Nutritional factors
      - Frailty
        - Stressor event
          - Falls
          - Delirium
          - Fluctuating disability
        - Increased care needs
          - Admission to hospital
          - Admission to long-term care

Lancet 2013; 381: 752-62
Frail people are vulnerable
Tools to identify frailty

• Two main schools of thought

1. Frailty phenotype model

2. The cumulative deficit model
Conceptual Framework

Reliability Theory of Ageing

• Progressive accumulation of random damage to a complex system composed of redundant parts
  – Defects accumulate with the passage of time (age) resulting in an increased risk of death (ageing).
  – As defects accumulate, lose redundancy
    • System with elements connected in series
    • System has no resilience
    • System vulnerable to external or internal stressors.
Measurement of Frailty in clinical practice

• Physical inactivity, weight loss, gait speed, peak expiration, hand grip, sitting position, visual impairment

• Inability to rise from a chair 5 times without using arms plus reduced energy level and

• FRAIL Scale
  • Fatigue, resistance, ambulation, illness, loss of weight
Measurement of Frailty in clinical practice

Fried phenotype
• Presence of ≥ 3 of 5 criteria:
  • Unintentional weight loss of ≥ 10lbs in the preceding year
  • Self-reported exhaustion,
  • Weak grip strength
Clinically coherent, reproducible
Identifies frailty as a wasting disorder with sarcopenia as a key pathophysiological feature.
Measurement of Frailty in clinical practice

“Vulnerable” older inpatients

• Unable to attempt performance based tests
• Cannot be stratified by phenotypic measures.

Omission of disorders of cognition and mood from these models is controversial:

– Frailty in the clinical setting consists of more than weakness, slowness and wasting
Edmonton Frail Scale

• Designed for geriatricians in both inpatient and outpatient settings

• Derives a maximum score of 17 from 10 sampled domains;
  – cognition, balance and mobility, mood, functional independence, medication use, social support, nutrition, health attitudes, continence and quality of life
Ageing

Concept

• The accumulation of deficits facilitates measurement of frailty as a multidimensional risk state quantified by number rather than nature of health problems.

Frailty Index (FI)

• Employs a well-defined methodology to create an index as a proportion of deficits
Frailty in Older Adults: Evidence for a Phenotype

Linda P. Fried,1 Catherine M. Tangen,2 Jeremy Walston,1 Anne B. Newman,3 Calvin Hirsch,4 John Gottdiener,5 Teresa Seeman,6 Russell Tracy,7 Willem J. Kop,8 Gregory Burke,9 and Mary Ann McBurnie2 for the Cardiovascular Health Study Collaborative Research Group

- This study used data from the Cardiovascular Health Study, a prospective, observational study of men and women > 65 yoa in the USA
- 5317 patients, followed up for 7 years
- Patients with a history of Parkinson’s disease, stroke, MMSE < 18, or taking anti-depressants were excluded
The frailty phenotype (CHS index)

5 criteria
1. Weight loss $\geq 4.5$ kg or $\geq 5\%$ of body weight in the prior year
2. Weakness – grip strength in lowest 20%
3. Exhaustion – self reported
4. Slowness - slowest 20% walking 5 metres
5. Low physical activity – lowest 20% kilocalories expended per week
The frailty phenotype (CHS index)

**Frail** = $\geq 3$ criteria present

**Pre-frail / Intermediate** = 1 or 2 criteria present

**Robust** = no criteria present
Prevalence of frailty

46% not frail, 47% pre-frail, 7% frail

Table 3. Prevalence of Frailty Phenotype Components in Percentages: Cardiovascular Health Study

<table>
<thead>
<tr>
<th>Frequency of Frailty Components</th>
<th>Total (N = 5317) %</th>
<th>Men (n = 3077) %</th>
<th>Women (n = 2240) %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exhaustion</td>
<td>17</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td>Weight loss</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Low activity (kcals)</td>
<td>22</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Slow walk (s)</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Grip strength (kg)</td>
<td>20</td>
<td>20</td>
<td>20</td>
</tr>
<tr>
<td>Number of Frailty Components Present</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>46</td>
<td>45</td>
<td>48</td>
</tr>
<tr>
<td>1</td>
<td>32</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>2</td>
<td>15</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>3</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>0.2</td>
<td>0.1</td>
<td>0.2</td>
</tr>
</tbody>
</table>
Often coexistent with disability and comorbidity but can be independent
Frailty correlates with poor outcome

- Increased risk of death, hospitalisation, falls and worsening disability
Is the CHS index too black and white?

• Is it too simplistic to say that someone either is frail or not?
• Would a cumulative deficit model of assessing frailty be more biologically sensible?
This study used data from the Canadian Study of Health and Aging, a prospective study of 2305 people over 70 years of age.

- Included patients with cognitive impairment and patients in aged care facilities.
- Followed up for 5 years.
The frailty index

Appendix 1: List of variables used by the Canadian Study of Health and Aging to construct the 70-item CSHA Frailty Index

- Changes in everyday activities
- Head and neck problems
- Poor muscle tone in neck
- Bradykinesia, facial
- Problems getting dressed
- Problems with bathing
- Problems carrying out personal grooming
- Urinary incontinence
- Toileting problems
- Bulk difficulties
- Rectal problems
- Gastrointestinal problems
- Problems cooking
- Sucking problems
- Problems going out alone
- Impaired mobility
- Musculoskeletal problems
- Bradykinesia of the limbs
- Poor muscle tone in limbs
- Poor limb coordination
- Poor coordination, trunk
- Poor standing posture
- Irregular gait pattern
- Falls
- Mood problems
- Feeling sad, blue, depressed
- History of depressed mood
- Tiredness all the time
- Depression (clinical impression)
- Sleep changes
- Restlessness
- Memory changes
- Short-term memory impairment
- Long-term memory impairment
- Changes in general mental functioning
- Onset of cognitive symptoms
- Clouding or delirium
- Paranoid features
- History relevant to cognitive impairment or loss
- Family history relevant to cognitive impairment or loss
- Impaired vibration
- Tremor at rest
- Postural tremor
- Intention tremor
- History of Parkinson’s disease
- Family history of degenerative disease
- Seizures, partial complex
- Seizures, generalized
- Syncope or blackouts
- Headache
- Cerebrovascular problems
- History of stroke
- History of diabetes mellitus
- Arterial hypertension
- Peripheral pulses
- Cardiac problems
- Myocardial infarction
- Arrhythmia
- Congestive heart failure
- Lung problems
- Respiratory problems
- History of thyroid disease
- Thyroid problems
- Skin problems
- Malignant disease
- Breast problems
- Abdominal problems
- Presence of snout reflex
- Presence of the palmental reflex
- Other medical history
Frailty index

• Score = number of variables / 70
  ie. 7/70 = Frailty index of 0.10
• All patients had frailty index and CHS index calculated
• Reasonable correlation between the two
Median frailty index scores

Robust – 0.12

Pre-frail – 0.30

Frail – 0.44
- Frailty index (FI) not designed to be dichotomised into frail and robust however empirical cut-off point appears to be 0.25
- Five-year mortality much higher if (FI) > 0.25
Could frailty be assessed more simply?

This study used data from the Study of Osteoporotic Fractures (SOF), a prospective study of 6701 community dwelling women over 69 years of age followed up for 9 years.
SOF Index

1. ≥5% weight loss over 2 years
2. Inability to rise from a chair 5 times without using arms
3. Reduced energy level based on the question “Do you feel full of energy”

**Frail** = 2 or more of the above
**Intermediate or pre-frail** = 1 of the above
**Robust** = none of the above
SOF vs CHS index

Pretty good correlation between SOF and CHS

Frailty status concordant in 75%

Frail women had an increased risk of recurrent falls, disability, non-spine fracture, hip fracture and death
So how should we best measure frailty?

• Multiple tools have now been developed
• Unclear which one is best
• Correlation between methods is not great
*Substantial variation in the prevalence of frailty
Maybe we can diagnose frailty by the age old “end-of-the-bed-o-gram”? 
Frailty in Acute Cardiology: Comparison of a Quick Clinical Assessment Against a Validated Frailty Assessment Tool

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Background
 Increasingly frail patients are being referred for invasive cardiac interventions and cardiac surgery. We aimed to evaluate the utility of a quick clinical assessment of frailty against a validated frailty assessment tool in an acute cardiology setting.

Methods
 Forty-seven cardiology in-patients ≥70 years were recruited in this prospective study. All patients were first assessed by a senior cardiology registrar as either not-frail or frail. This was based on general observation and brief discussions. Following this, patients were administered the Reported Edmonton Frail Scale (REFS) questionnaire. After a registrar assessment, the foot-of-the-bed frailty assessment was independently repeated by one or two consultant cardiologists.

Results
 None of the three clinicians showed satisfactory similarity to the REFS score. When the two consultants were compared with the registrar, and with each other, the Cohen’s kappa was only above 0.7 for the comparison between Consultant 1 and the registrar. Consultant 1 and the registrar were also significantly more likely to disagree at higher REFS score with a mean REFS score of 8.8.

Conclusion
 A quick foot-of-the-bed clinical assessment is not a reliable way to determine frailty.
Frail patients require Complete Geriatric Assessment (CGA)

• It is a process of specialist elderly care delivered by a multidisciplinary team to establish an elderly person’s medical, psychological and functional capability, so that a plan for treatment and follow-up can be developed.

• This process, provided it is closely linked to interventions, is associated with superior outcomes.
Is identifying frailty important?
Pathophysiology of Frailty

Strongly associated with a combination of immunological and physiological impairments rather than a single biomarker

• Supports conceptualisation of ageing as progressive damage to a complex system resulting in loss of system redundancy.
Falls

Complex systems
• Able to withstand stresses because of the presence of multiple defences
• First processes to be compromised in the event of failure are higher-order functions
  — Because they require coordinated, integrated, and precise interaction between many components of the complex system.

Falls
• a macrostate indicator of complex system failure rather than a specific disorder of particular organs (such as the brain or heart).
Frailty- Prescribing

- Altered pharmacokinetic responses affect bioavailability of prescribed medications.
- Increases in body fat and reductions in lean body mass affect distribution of drugs.
- Low albumin levels reduce drug binding.
- Activity of enzymes of drug metabolism becomes impaired.
Delirium

• Older people taking 5 or more medications are at significantly higher risk of delirium and falls, independent of medication indications.

• In one study the median life expectancy for frail older adults with delirium was 88 days (95% CI: 5-171)
It seems to be quite common

- Systematic review of 21 studies of 61,500 people found that on average 10.7% of community-dwelling older adults are frail and 41.6% are pre-frail.
- Wide variability given different methods used of measuring frailty.
- Increased risk of frailty with increasing age and in women.
SHORT REPORTS

The risk of adverse outcomes in hospitalized older patients in relation to a frailty index based on a comprehensive geriatric assessment

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Design and setting: prospective cohort study. Inpatient medical units in a teaching, acute care hospital. Subjects: individuals on inpatient medical units in a hospital, n = 752, aged 75+ years, were evaluated on their first hospital day; to test reliability, a subsample (n = 231) was seen again on Day 3.

Conclusions: frailty, measured by the FI-CGA, was independently associated with a higher risk of death and other adverse outcomes in older people admitted to an acute care hospital.
Can it help us predict outcome?

- It seems clear that being frail is a risk factor for falls, disability and death
- Recent data would suggest that it is an important risk factor across multiple areas of medicine
133 general medical patients admitted to a private hospital were screened for frailty via the Reported Edmonton Frail Scale (REFS)

- Average age 86yoa, 60% female
### The Reported Edmonton Frail Scale

<table>
<thead>
<tr>
<th>Frailty domain</th>
<th>Item</th>
<th>0 Point</th>
<th>1 Point</th>
<th>2 Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognition</td>
<td>Please imagine that this pre-drawn circle is a clock. I would like you to place the numbers in the correct positions then place the hands to indicate a time of ‘ten after eleven’</td>
<td>No errors</td>
<td>Minor spacing errors</td>
<td>Other errors</td>
</tr>
<tr>
<td>General health status</td>
<td>In the past year, how many times have you been admitted to a hospital?</td>
<td>0</td>
<td>1–2</td>
<td>≥2</td>
</tr>
<tr>
<td>Functional independence</td>
<td>In general, how would you describe your health?</td>
<td>Excellent/Very good/Good</td>
<td>Fair</td>
<td>Poor</td>
</tr>
<tr>
<td>Social support</td>
<td>When you need help, can you count on someone who is willing and able to meet your needs?</td>
<td>Always</td>
<td>Sometimes</td>
<td>Never</td>
</tr>
<tr>
<td>Medication use</td>
<td>Do you use five or more different prescription medications on a regular basis?</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Nutrition</td>
<td>At times, do you forget to take your prescription medications?</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Mood</td>
<td>Have you recently lost weight such that your clothing has become looser?</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Continence</td>
<td>Do you often feel sad or depressed?</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Self-reported performance</td>
<td>Two weeks ago were you able to:</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(1) Do heavy work around the house like washing windows, walls or floors without help?</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(2) Walk up and down stairs to the second floor without help?</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(3) Walk 1 km without help?</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
</tbody>
</table>

**Scoring the Reported Edmonton Frail Scale (/18):**

- Not Frail 0–5
- Apparently Vulnerable 6–7
- Mild Frailty 8–9
- Moderate Frailty 10–11
- Severe Frailty 12–18

*Validated to be used by non-geriatrician researchers*
Results

Non-frail – 32%
Apparently vulnerable – 17.3%
Mild frailty – 14%
Moderate frailty – 12%
Severe frailty – 24%

Frailty was associated with an increased LOS and more complex discharge planning
Frail patients are more likely to have complications post cardiac and non-cardiac surgery

They have an increased length of stay and greater mortality than non-frail patients

Frailty appears to be gaining traction in anaesthesia as an important peri-operative risk factor

Anaesthesia 2014, 69 (Suppl. 1), 26-34
Frailty index predicts severe complications in gynecologic oncology patients, Gynecol Oncol (2015).
Prevalence and impact of frailty on mortality in elderly ICU patients: a prospective, multicenter, observational study

• Prospective, observational study performed in 4 ICUs in France
• 196 patients ≥65yoa that were admitted to ICU for more than 24 hours
• Followed up for 6 months or until death
Frailty assessment

• Two methods were used
  a) Modified frailty phenotype (FP)
  b) Clinical Frailty Score (CFS)

• Score was calculated on admission to ICU by questioning the patient (31%), their relatives (61%) or both (8%)
# Modified Frailty phenotype

<table>
<thead>
<tr>
<th>Characteristics of frailty</th>
<th>Original scale [1]</th>
<th>Tools used in our study (adapted from [2])</th>
<th>Frailty score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Shrinking</td>
<td>Unintentionally (not due to dieting or exercise) weight loss ≥ 4.5 kg or more than 5% of body weight in the prior year</td>
<td>Unintentionally (not due to dieting or exercise) weight loss ≥ 4.5 kg or more than 5% of body weight in the prior year</td>
<td>Yes = 1; No = 0</td>
</tr>
<tr>
<td>Weakness</td>
<td>Handgrip strength measured by dynamometer (adjusted for gender and body mass index)</td>
<td>Difficulty rising from a chair</td>
<td>Yes = 1; No = 0</td>
</tr>
<tr>
<td>Slowness</td>
<td>Time to walk 15 feet, (adjusted for gender and standard height)</td>
<td>Slowed walking speed (during the last 6 months, with difficulties walking and with aid) and/or the occurrence of fall(s)</td>
<td>Yes = 1; No = 0</td>
</tr>
<tr>
<td>Low physical activity</td>
<td>Kilocalories expended per week.</td>
<td>Discontinued daily leisure activities such as walking or gardening and/or discontinued some sport activity per week.</td>
<td>Yes = 1; No = 0</td>
</tr>
<tr>
<td>Exhaustion</td>
<td>Feeling that everything the patient does is an effort and/or the feeling that he could not get going, as well as how often in the last 3 months she felt this way: rarely or not at all = 0, occasionally = 1, often = 2, usually = 3</td>
<td>Feeling that everything the patient does is an effort and/or the feeling that he could not get going, as well as how often in the last 3 months she felt this way: rarely or not at all = 0, occasionally = 1, often = 2, usually = 3</td>
<td>Answering 2 or 3 to either of these questions were considered frail (1 point) by exhaustion</td>
</tr>
</tbody>
</table>

Nonfrail: FP < 3; Frail: FP ≥ 3.
# Clinical Frailty Score

<table>
<thead>
<tr>
<th>Score</th>
<th>Frailty grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Very Fit</td>
<td>People who are robust, active, energetic and motivated. These people commonly exercise regularly. They are among the fittest for their age.</td>
</tr>
<tr>
<td>2</td>
<td>Well</td>
<td>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.</td>
</tr>
<tr>
<td>3</td>
<td>Managing well</td>
<td>People whose medical problems are well controlled, but are not regularly active beyond routine walking.</td>
</tr>
<tr>
<td>4</td>
<td>Vulnerable</td>
<td>While not dependent on others for daily help, often symptoms limit activities. A common complaint is being &quot;slowed up&quot;, and/or being tired during the day.</td>
</tr>
<tr>
<td>5</td>
<td>Mildly frail</td>
<td>These people often have more evident slowing, and need help in high order independence in activities of daily living (finances, transportation, heavy housework, medications). Typically, mild frailty progressively impairs shopping and walking outside alone, meal preparation and housework.</td>
</tr>
<tr>
<td>6</td>
<td>Moderately frail</td>
<td>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.</td>
</tr>
<tr>
<td>7</td>
<td>Severely frail</td>
<td>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).</td>
</tr>
<tr>
<td>8</td>
<td>Very severely frail</td>
<td>Completely dependent, approaching the end of life. Typically, they could not recover even from a minor illness.</td>
</tr>
<tr>
<td>9</td>
<td>Terminally Ill</td>
<td>Approaching the end of life. This category applies to people with a life expectancy &lt;6 months, who are not otherwise evidently frail.</td>
</tr>
</tbody>
</table>

Results

- 41% (FP) and 23% (CFS) were classified as frail
- SAPS II and SOFA scores were similar
Recognising frailty pre-operatively can affect outcome

- Retrospective review of all surgical palliative care referrals pre and post-implementation of a systemwide frailty-screening program
- Patients identified as frail (10% of patients), were encouraged to be referred to palliative care pre-op
- 310 referrals (160 pre, 150 post)
- Essentially all male patients (avg. age 70) undergoing elective surgery
- Conducted in a Veteran Affairs Hospital
Last Name________________________ Last four SSN_____
Date this Form completed_________________________
Date of Surgery-Anticipated_____________________
Proposed Operation_____________________________

AGE, SEX, AND CANCER:
1. Sex
   Female = 0/ Male = __5__

<table>
<thead>
<tr>
<th>Age</th>
<th>Score without cancer</th>
<th>Score with cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; + 69</td>
<td>2</td>
<td>20</td>
</tr>
<tr>
<td>70 - 74</td>
<td>3</td>
<td>19</td>
</tr>
<tr>
<td>75 - 79</td>
<td>4</td>
<td>18</td>
</tr>
<tr>
<td>80 - 84</td>
<td>5</td>
<td>17</td>
</tr>
<tr>
<td>85 - 89</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>90 - 94</td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>95 - 99</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>100+</td>
<td>9</td>
<td>13</td>
</tr>
</tbody>
</table>

MEDICAL CO-MORBIDITIES:
2. Age__________
   (Excluding skin cancer, except for melanoma)
   Score with Cancer ______
   OR
   Score without cancer ______

3. Have you had unintentional weight loss in the past 3 months (>10 lbs)? No/Yes __5__
4. Renal failure? No/Yes __6__
5. Chronic/congestive heart failure? No/Yes __4__
6. Poor appetite? No/Yes __4__
7. Shortness of breath (at rest)? No/Yes __8__
COGNITION, RESIDENCE, AND ACTIVITY OF DAILY LIVING:

Cognition and Activities of Daily Living:

7. Do you reside at a setting other than independent living? (listed below)
   No/Yes 8
   If YES, circle answer: Skilled Nursing Facility/ Assisted Living/ Nursing Home
   No/Yes

8. Have your cognitive skills or status deteriorated over the last 3 months?  No/Yes

9. Activities of Daily Living Chart:
   Without cognitive decline
   With cognitive decline
   TOTAL SCORE
   PERCENT

<table>
<thead>
<tr>
<th>Mobility/locomotion</th>
<th>Eating</th>
<th>Toilet use</th>
<th>Personal hygiene</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 Independent</td>
<td>0 Independent</td>
<td>0 Independent</td>
<td>0 Independent</td>
</tr>
<tr>
<td>1 Supervised</td>
<td>1 Supervised</td>
<td>1 Supervised</td>
<td>1 Supervised</td>
</tr>
<tr>
<td>2 Limited assistance</td>
<td>2 Limited assistance</td>
<td>2 Limited assistance</td>
<td>2 Limited assistance</td>
</tr>
<tr>
<td>3 Extensive assistance</td>
<td>3 Extensive assistance</td>
<td>3 Extensive assistance</td>
<td>3 Extensive assistance</td>
</tr>
<tr>
<td>4 Total dependence</td>
<td>4 Total dependence</td>
<td>4 Total dependence</td>
<td>4 Total dependence</td>
</tr>
</tbody>
</table>

INDEPENDENT = No help or oversight – OR = help or oversight provided only 1 or 2 times in last 7 days
SUPERVISED = Oversight, supervision or easing provided 3 or more times during the last 7 days.
LIMITED ASSISTANCE = patient highly involved in activity, but received physical help in guided maneuvering of limbs or other non weight bearing assistance 3 or more times in the last 7 days.
EXTENSIVE ASSISTANCE = while patient performed part of activity over last 7 day period, help was provided for the following: weight bearing support OR full staff performance during part of the past 7 days.
TOTAL DEPENDENCE = full staff performance during the past 7 days.
TOTAL DEPENDENCE = full staff performance during the past 7 days.

<table>
<thead>
<tr>
<th>12- ADL POINTS SCORE</th>
<th>ADL POINTS SCORE WITH COGNITIVE DECLINE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>ADL score -2</td>
</tr>
<tr>
<td>1,2</td>
<td>ADL score -1</td>
</tr>
<tr>
<td>3,4</td>
<td>ADL score 0</td>
</tr>
<tr>
<td>5,6,7</td>
<td>ADL score +1</td>
</tr>
<tr>
<td>8,9</td>
<td>ADL score +2</td>
</tr>
<tr>
<td>10,11</td>
<td>ADL score +3</td>
</tr>
<tr>
<td>12,13</td>
<td>ADL score +4</td>
</tr>
<tr>
<td>14,15,16</td>
<td>ADL score +5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Points = percent</th>
<th>Points = percent</th>
<th>Points = percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5 = 4%</td>
<td>6-10 = 4%</td>
<td>16-20 = 11%</td>
</tr>
<tr>
<td>26-30 = 27%</td>
<td>31-35 = 30%</td>
<td>41-45 = 58%</td>
</tr>
<tr>
<td>56-60 = 89%</td>
<td>38-40 = 47%</td>
<td>45-50 = 69%</td>
</tr>
<tr>
<td>61-65 = 90%</td>
<td>41-45 = 58%</td>
<td>50-60 = 88%</td>
</tr>
<tr>
<td>66-70 = 93%</td>
<td>45-50 = 69%</td>
<td>71-75 = 100%</td>
</tr>
</tbody>
</table>
Patient demographics

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before Implementation (n = 160)</th>
<th>After Implementation (n = 150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>157 (98.1)</td>
<td>150 (100.0)</td>
</tr>
<tr>
<td>Cancer history</td>
<td>124 (77.5)</td>
<td>107 (71.3)</td>
</tr>
<tr>
<td>Recent weight loss</td>
<td>57 (35.6)</td>
<td>49 (32.7)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>18 (11.3)</td>
<td>21 (14.0)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>21 (13.1)</td>
<td>25 (16.7)</td>
</tr>
<tr>
<td>Poor appetite</td>
<td>52 (32.5)</td>
<td>45 (30.0)</td>
</tr>
<tr>
<td>Short of breath at rest</td>
<td>36 (22.5)</td>
<td>29 (19.3)</td>
</tr>
<tr>
<td>Not living independently</td>
<td>26 (16.3)</td>
<td>35 (23.3)</td>
</tr>
<tr>
<td>Age, mean (SD), y</td>
<td>68.3 (11.2)</td>
<td>71.3 (10.6)</td>
</tr>
<tr>
<td>ADL score, mean (SD)</td>
<td>1.2 (3.9)</td>
<td>1.9 (4.4)</td>
</tr>
<tr>
<td>Preoperative RAI score, mean (SD)</td>
<td>28.8 (9.6)</td>
<td>28.8 (9.1)</td>
</tr>
<tr>
<td>VASQIP, 30-d mortality score, mean (SD)</td>
<td>6.5 (9.7)</td>
<td>6.0 (7.1)</td>
</tr>
</tbody>
</table>

Patients were considered frail if scored ≥ 21 points
Implementation of the screening program was associated with an OR of death of 0.37 (CI 0.22-0.62)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before Implementation (n = 160)</th>
<th>After Implementation (n = 150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual consultation rate, mean (SD), consults/y</td>
<td>32 (20)</td>
<td>56 (8)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Died within</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 d</td>
<td>51 (31.9)</td>
<td>32 (21.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>180 d</td>
<td>113 (70.6)</td>
<td>66 (44.0)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>360 d</td>
<td>126 (78.8)</td>
<td>99 (66.0)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Died during study</td>
<td>145 (90.6)</td>
<td>104 (69.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mean survival, d</td>
<td>295 (492)</td>
<td>314 (296)</td>
</tr>
<tr>
<td>PCC timing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before surgery</td>
<td>42 (26.3)</td>
<td>78 (52.0)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>After surgery</td>
<td>118 (73.8)</td>
<td>72 (48.0)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>PCC referring service</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>121 (75.6)</td>
<td>65 (43.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Surgery</td>
<td>39 (24.4)</td>
<td>85 (56.7)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Surgery status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did not have surgery</td>
<td>9 (5.6)</td>
<td>29 (19.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Had surgery</td>
<td>151 (94.4)</td>
<td>121 (80.7)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Abbreviation: PCC, palliative care consultation.
Sarcopaenia

= age-related loss of muscle mass

• Begins 30-35 yoa and is slowly progressive

Caused by: ↑ apoptosis, oxidative stress
mitochondrial dysfunction
↓ neuronal stimulation of muscle
pro-inflammatory cytokines
loss of hormone production
poor nutrition, sedentary lifestyle
chronic diseases
Other factors

• Sarcopaenia is a key component of the frailty syndrome, but not the only one

• Other factors include
  • Endocrine
  • Inflammation
  • Oxidative stress
  • Nutrition
Endocrine

- Sex hormone production declines with age, especially in women post menopause – unclear relationship with frailty
- DHEA (Dehydroepiandosterone) falls in patients with frailty
- GH and IGF-1 levels are lower in frail patients
- Ghrelin (Growth Hormone Release Inducing), a neuropeptide that stimulates feeding, is part of a feedback loop with GH and IGF-1 and has been found to be decreased in frail older patients
Inflammation and Oxidative stress

- Increased pro-inflammatory cytokines such as IL-6 and TNF-α in frailty
- Decreased anti-inflammatory cytokines
- Frailty is associated with high levels of oxidised glutathione and malonaldehyde, both indicators of increased oxidative stress
- Smoking (which generates oxidative stress) increases the risk of frailty

*Current Pharmaceutical Design, 2014, Vol. 20, No. 18*
Data are from a prospective study of 727 non-frail participants ≥ 65yoa who were followed for 3 years.

Those with Vitamin D levels <15ng/mL were more likely to become either pre-frail or frail.
Diet may be important

Major dietary patterns and risk of frailty in older adults: a prospective cohort study

Luz M León-Muñoz, Esther García-Esquinárez, Esther López-García, José R Banegas, and Fernando Rodríguez-Artalejo

Abstract

Background: There is emerging evidence of the role of certain nutrients as risk factors for frailty. However, people eat food, rather than nutrients, and no previous study has examined the association between dietary patterns empirically derived from food consumption and the risk of frailty in older adults.

Methods: This is a prospective cohort study of 1,872 non-institutionalized individuals aged ≥60 years recruited between 2008 and 2010. At baseline, food consumption was obtained with a validated diet history and, by using factor analysis, two dietary patterns were identified: a ‘prudent’ pattern, characterized by high intake of olive oil and vegetables, and a ‘Westernized’ pattern, with a high intake of refined bread, whole dairy products, and red and processed meat, as well as low consumption of fruit and vegetables. Participants were followed-up until 2012 to assess incident frailty, defined as at least three of the five Fried criteria (exhaustion, weakness, low physical activity, slow walking speed, and unintentional weight loss).

Results: Over a 3.5-year follow-up, 96 cases of incident frailty were ascertained. The multivariate odds ratios (95% confidence interval) of frailty among those in the first (lowest), second, and third tertile of adherence to the prudent dietary pattern were 1.064 (0.37–1.12), and 0.40 (0.22–0.81), respectively; P-trend = 0.009. The corresponding values for the Westernized pattern were 1.53 (0.85–2.75), and 1.61 (0.85–3.03); P-trend = 0.14. Moreover, a greater adherence to the Westernized pattern was associated with an increasing risk of slow walking speed and weight loss.

Conclusions: In older adults, a prudent dietary pattern showed an inverse dose-response relationship with the risk of frailty while a Westernized pattern had a direct relationship with some of their components. Clinical trials should test whether a prudent pattern is effective in preventing or delaying frailty.

Keywords: Cohort study, Diet, Frailty, Older adults, Spain

Can anything be done to reverse or at least halt the progression of frailty?
Prevention

Epidemiological data exploring factors associated with frailty development provide information on potential interventional strategies.

• Start here
  • Cardiovascular disease
  • Obesity
  • Diabetes
  • Alcohol
  • Cigarettes
Physical activity

- Decreases abdominal fat
- Endurance exercise training stimulates mitochondrial biosynthesis.
- Reduced abdominal adiposity and increased oxidative activity may underlie physical activity’s benefit to function independent of its effects on weight reduction

May modify the accumulation of deficits across many systems
• The assessment of frailty syndrome in the pre-operative evaluation has been recently associated with post-surgical outcomes.

• Severity of frailty correlated with post-surgical mortality rates and to some complications.

• These relationships emerge in different type of surgical procedures and patients’ features.

• There is a need of a standardized diagnostic tool to assess frailty in pre-operative risk assessment.
Frail patients require Complete Geriatric Assessment (CGA)

• It is a process of specialist elderly care delivered by a multidisciplinary team to establish an elderly person’s medical, psychological and functional capability, so that a plan for treatment and follow-up can be developed

• This process, provided it is closely linked to interventions, is associated with superior outcomes
Exercise

- Exercise influences protein metabolism in skeletal muscle and leads to muscle hypertrophy in the setting of adequate protein intake.
- Resistance training helps aging muscle to retain fibre strength, decrease fatty infiltration and increase metabolic function.

*Pharmaceutical Interventions for Frailty and Sarcopenia*

Exercise (contd.)

• 16 RCTs published

In summary
• Exercise training interventions do appear to improve physical performance tests in frail people
• These improvements may not persist without ongoing exercise therapy
• Home-based exercises appear to be effective with less risk of regression after cessation of the intervention than supervised programs
Exercise (contd.)

• Moderate intensity exercise is better than low intensity programs
• People who are less frail achieve better results than those with severe frailty
Pharmacological therapy

• This requires an understanding of the likely mechanisms of frailty
Nutrition

• Adequate protein intake +/- amino acid supplementation (eg. carnitine) may be helpful
• Carnitine supplementation appears to improve myocyte atrophy and anorexia
• Vitamin D supplementation especially in those already deficient
## Completed RCTs

<table>
<thead>
<tr>
<th>Trial</th>
<th>Inclusion Criteria</th>
<th>Age Range (Mean)</th>
<th>N</th>
<th>Time Frame</th>
<th>Intervention(s)</th>
<th>Control</th>
<th>Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neto 2013</td>
<td>Grip strength &lt; Fried cutoff</td>
<td>60–75 (68)</td>
<td>17</td>
<td>3 m</td>
<td>Symbiotic (1 x/d)</td>
<td>Placebo</td>
<td>Inflammatory cytokines: no difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Muscle mass: no difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Grip strength: no difference</td>
</tr>
<tr>
<td>Villareal 2001</td>
<td>Women with 2/3: modified PPT score 18–18 mL/kg/min</td>
<td>≥75 (82)</td>
<td>67</td>
<td>9 m</td>
<td>Conjugated estrogens (0.625 mg/d) + trimonthly medroxyprogesterone (5 mg/d)</td>
<td>Conjugated estrogens</td>
<td>Bone mineral density: improved</td>
</tr>
<tr>
<td></td>
<td>VO2max 10–18 mL/kg/min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(0.625 mg/d) + Placebo</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Difficulty with ≥1 ADL or ≥2 IADL</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Muller 2006</td>
<td>Weak grip strength and leg extension power Men</td>
<td>≥70 (78)</td>
<td>100</td>
<td>36 w</td>
<td>Atametane (100 mg/d) + placebo DHEA (50 mg/d) + placebo atametane (100 mg/d) +</td>
<td>Placebo + placebo</td>
<td>Physical performance tests: no difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Androgel (5 mg/d)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kenny 2010</td>
<td>Frail or pre-frail (Fried) Men total testosterone &lt; 350 ng/dL or less or atrophic fracture</td>
<td>≥60 (77)</td>
<td>131</td>
<td>1–2 y</td>
<td></td>
<td>Placebo</td>
<td>Bone mineral density: increased at femur and lumbar spine*, decreased</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>at radius*</td>
</tr>
<tr>
<td>Papanicolau 2013</td>
<td>MMI &lt; Baumgartner cutoff Women SPB ≤ 9 Self-reported mobility limitation</td>
<td>≥65 (76)</td>
<td>170</td>
<td>6 m</td>
<td>Selective androgen receptor modulator MK-0773 (50 mg 2 x/d)</td>
<td>Placebo</td>
<td>Physical performance tests: no difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lean body mass: increased by 1 kg*</td>
</tr>
<tr>
<td>Srinivas- Shankar 2010</td>
<td>Frail or pre-frail (Fried) Men total testosterone ≤ 12 nmol/L or free testosterone ≤ 250 pmol/L</td>
<td>≥65 (74)</td>
<td>274</td>
<td>6 m</td>
<td>Testogel (50 mg/d)</td>
<td>Placebo</td>
<td>Muscle strength: no difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Gait speed: no difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>SPB: no difference</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Isometric knee extension peak torque: improved*</td>
</tr>
<tr>
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<td></td>
<td></td>
<td>Lean body mass: increased*</td>
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<td>PPTs: trend improved**</td>
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<td>6-minute walk: trend improved**</td>
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<td></td>
<td>Physical activities: no difference</td>
</tr>
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<td></td>
<td></td>
<td>Muscle strength: increased in both exercise groups*</td>
</tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td>*<em>Muscle type II fibers: increased in both rhGH groups</em></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Bone mineral density: no difference</td>
</tr>
<tr>
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<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>SFPB score: improved*</td>
</tr>
<tr>
<td>Hennessey 2001</td>
<td>PPT score 12–28</td>
<td>(71)</td>
<td>31</td>
<td>6 m</td>
<td>rhGH (SQ qhs) + resistance training 1 h 3 × w rhGH (SQ qhs) alone</td>
<td>Placebo + resistance</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>training 1 h 3 × w Placebo alone</td>
<td></td>
</tr>
<tr>
<td>Kenny 2010</td>
<td>Frail or pre-frail (Fried) Women DHEA &lt; 550 ng/dL</td>
<td>≥65 (77)</td>
<td>99</td>
<td>6 mo</td>
<td>DHEA (50 mg/d) + yoga DHEA (50 mg/d) + aerobics</td>
<td>Placebo + yoga placebo +</td>
<td></td>
</tr>
<tr>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>aerobics</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** ADL, activities of daily living; DHEA, dehydroepiandrosterone; IADL, instrumental activities of daily living; PPT, physical performance test; rhGH, recombinant human growth hormone; SD, standard deviation; SFPB, short physical performance battery.  
* P < 0.05.  
** P = 0.05–0.10.
Current or unpublished RCTs

- Amino acid supplementation
- Vitamin D
- Ghrelin
- Testosterone
- Allopurinol – xanthine oxidase inhibitor (xanthine oxidase is one of the major sources of oxidant production)
- Bimagrumab - mAb that binds receptors that mediate the growth of skeletal muscle and can induce muscle hypertrophy
Surgical Palliative Care Consultations

Original Investigation | ASSOCIATION OF VA SURGEONS

Surgical Palliative Care Consultations Over Time in Relationship to Systemwide Frailty Screening

Katherine F. Ernst, BS; Daniel E. Hall, MD, MDiv, MHSc; Kendra K. Schmid, PhD; Georgia Seever, RN; Pierre Lavedan, MD; Thomas G. Lynch, MD, MHA; Jason Michael Johanning, MD, MS

Frailty and Surgery

No consensus about how to obtain an appropriately timed palliative consultation in surgical patients.

Frailty identifies patients (regardless of age) at increased risk of dying within 6 months to 5 years

“Diagnosing frailty is to diagnose dying”

Authors implemented screening process to identify frail patients considering elective surgery.

• Developed a screening tool for use in surgical patients:
  — Risk analysis index (RAI)
• Validated its ability to discriminate frail patients from non frail patients
  — Data from National Surgery Quality Improvement Project and local administrative databases.
OBJECTIVE To examine surgical palliative care consultations over time and their relationship to the initiation and implementation of a systemwide frailty-screening program.

DESIGN, SETTING, AND PARTICIPANTS We reviewed all surgical palliative care consultations performed between January 1, 2006, and August 31, 2013, and abstracted the referring service (medicine/surgery), date of surgery (if any), date of death (if any), and all variables required to calculate a frailty score using the risk analysis index. We examined changes in mortality and referral patterns before and after implementation of the frailty-screening program using multivariable logistic regression.

CONCLUSIONS Surgical palliative care consultations, including frailty screening.
Methods

10% of all patients scheduled for elective surgery identified as frail (RAI score, ≥21).
• Frail patients encouraged to undergo preoperative palliative care consultation.
• A template consultation note completed addressing end-of-life care issues including do not resuscitate, power of attorney, and goals of care

Calculated a frailty score using the RAI and the Veterans Affairs Surgical Quality Improvement Project (VASQIP) postoperative risk calculators for each specialty type.

• For patients undergoing procedures after the implementation of frailty screening, the RAI score was calculated prospectively

• For patients undergoing procedures before implementation of the screening, frailty scores were calculated retrospectively based on preoperative data available in the medical record.
Results

From January 2006 to August 2013,
• 310 palliative care consultations:
  – 160 occurring before the initiation and implementation of the screening program
  – 150 occurring after implementation

• Implementation of the screening program was associated with a significantly reduced odds of death (odds ratio[OR], 0.37; 95%CI, 0.22-0.62; P < .001),
  – after controlling for age, frailty, surgery status (had surgery or did not have surgery), timing of consultation (before or after surgery), and ordering service (medicine or surgery).
  – 70.6% mortality at 180 days before implementation of the frailty-screening program
  – 33% reduction in the relative risk of dying,
  – NNS to prevent 1 death at 180 days was 4.24.

• Strongest association with reduced mortality was when surgeons (not internists) ordered a preoperative palliative care consultation (OR, 0.27),
  – 1 death was prevented for every 3 surgeon-ordered preoperative consultations.
  – Controlled for age, frailty (RAI score), and whether the patient received the surgical procedure associated with the palliative care consultation.
Bottom Line

Screen for frailty in surgical candidates
• If frail consider Palliative Care first
• If in doubt- refer
• Works best if surgeons refer

What we want to hear
• Stops you doing surgery on people who will die anyway
• Surgery rate went down from 94.4% to 80.0%
<table>
<thead>
<tr>
<th>Variable</th>
<th>Before Implementation (n = 160)</th>
<th>After Implementation (n = 150)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Annual consultation rate, mean (SD), consults/y</td>
<td>32 (20)</td>
<td>56 (8)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Died within</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 d</td>
<td>51 (31.9)</td>
<td>32 (21.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>180 d</td>
<td>113 (70.6)</td>
<td>66 (44.0)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>360 d</td>
<td>126 (78.8)</td>
<td>99 (66.0)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Died during study</td>
<td>145 (90.6)</td>
<td>104 (69.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mean survival, d</td>
<td>295 (492)</td>
<td>314 (296)</td>
</tr>
<tr>
<td>PCC timing</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before surgery</td>
<td>42 (26.3)</td>
<td>78 (52.0)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>After surgery</td>
<td>118 (73.8)</td>
<td>72 (48.0)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>PCC referring service</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>121 (75.6)</td>
<td>65 (43.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Surgery</td>
<td>39 (24.4)</td>
<td>85 (56.7)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Surgery status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Did not have surgery</td>
<td>9 (5.6)</td>
<td>29 (19.3)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Had surgery</td>
<td>151 (94.4)</td>
<td>121 (80.7)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>
What next?

• Should we be screening for frailty?
• If so, who should we be screening and how?
• What should we then do with this information?
• Given the multiple factors contributing to frailty it seems unlikely we will find a “magic bullet”
Utility of screening

• **Diagnosing** pre-frail / vulnerable patients in whom interventions may be of most benefit

• **Early identification** of patients likely to require complex discharge planning, allied health input

• **Risk assessment** of patients undergoing procedures / surgery / chemotherapy

• **Useful trigger** for advanced care planning / palliative care referral
Screening (contd.)

• General Medicine has a large proportion of frail patients but also has excellent allied health resources (especially in the AAU) and has easy access to the Rehab and Aged Care Liaison Service (RALS)
• Medical specialty/Surgical units may also have significant proportions of frail patients
• Screening for frailty in these patients could potentially be useful in the early identification of patients requiring RALS
Who should do it?

• Frailty assessment provides you with a fairly comprehensive social history
• It is generally quick to perform
• It could easily be incorporated into a medical +/- surgical admission
• It potentially has a role in the pre-admission clinic to screen patients prior to elective surgery
What is being done elsewhere?
Geriatric assessment unit (GAU)

- NHS Grampian
- All patients screened for frailty on presentation to ED
- If met the frailty criteria, patients were transferred to a 25-bed GAU where a multidisciplinary team carried out a Comprehensive Geriatric Assessment (CGA)
Step 1: Would this person benefit from Comprehensive Geriatric Assessment?
Aged 75 and over/age 65+ from nursing or residential care or admitted from community hospital

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Functional impairment in context of significant multiple conditions (new or pre-existing)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Resident in a care home</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Acute confusion (Think Delirium), for example the 4AT screening tool - Is there a diagnosis of dementia or a history of chronic confusion?</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Immobility or falls in last 3 months</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>List of six or more medicines (polypharmacy)</td>
<td></td>
</tr>
</tbody>
</table>

Are any of the above criteria met?
If YES to any of the above, move to Step 2

Step 2: For those potentially being referred for Comprehensive Geriatric Assessment
Would this person be better managed by another specialty team at present?
Indicator for care by another acute specialty regardless of age

<table>
<thead>
<tr>
<th></th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Need for HDU / ITU (including non-invasive ventilation)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Suspected new stroke or TIA, consider thrombolysis and care in stroke unit</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Trauma with suspected fracture</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Head injury with loss of consciousness</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Acute abdominal pain with collapse</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Chest pain with suspected MI</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Clear need for other specialty input, for example flare-up of known chronic condition</td>
<td></td>
</tr>
</tbody>
</table>

Are any of the above criteria met?
If YES to anything in Step 2:
  - please ask for specialist multidisciplinary review while in their current unit, but do not transfer directly to the geriatric assessment service
If NO to the list in Step 2:
  - prioritise for transfer of care to specialist geriatric assessment service
Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Woodend Hospital (Dec 11 – Mar 12, before early CGA)</th>
<th>ARI Geriatric Assessment Unit (Dec 12 – Mar 13)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>83.6</td>
<td>83.9</td>
</tr>
<tr>
<td>Mean length of stay (days)</td>
<td>22.5</td>
<td>7.9</td>
</tr>
<tr>
<td>Discharge within 24 hours (%)</td>
<td>3</td>
<td>17</td>
</tr>
<tr>
<td>Discharge within 48 hours (%)</td>
<td>9</td>
<td>36</td>
</tr>
<tr>
<td>Readmitted within 7 days (%)</td>
<td>3.9</td>
<td>5.6</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>15.4</td>
<td>10.3</td>
</tr>
<tr>
<td>Care home discharge (%)</td>
<td>13.1</td>
<td>8.8</td>
</tr>
</tbody>
</table>

The slight increased trend in readmissions is not statistically significant (p=0.15).

Changes in mean length of stay, mortality and care home discharge are statistically significant (p<0.05).
Safe, compassionate care for frail older people using an integrated care pathway:

Practical guidance for commissioners, providers and nursing, medical and allied health professional leaders

38-page document published in Feb, 2014
Good acute hospital care of the frail patient

Good acute hospital care when (and only when) needed:

- A simple referral system with a single point of access for frail older people.
- Expert decision makers are available at the front door of the acute hospital from 8am to 8pm, seven days a week. Specialist assessment should be available within 12 hours of admission, seven days a week.
- An identified Frailty Unit/Service should be available with staff trained how to look after frail focusing on rapid assessment, treatment and rapid discharge.
- The presence of one or more frailty syndromes should trigger a comprehensive geriatric assessment.
Summary

• Frailty is common and portends a poor prognosis
• It can be identified fairly easily, however we should only look for it if we intend to intervene
Possible interventions once frailty has been identified

• Triggers a Comprehensive Geriatric Assessment (CGA) for patients admitted to hospital
• Help guide decision making regarding resuscitation / transfer to ICU
• Pre-operative risk assessment
Identifying frailty should not be a “heart sink moment” but rather seen as an opportunity to intervene.

Increased risk of falls, disability, long-term care and death. We also know that frailty is a graded abnormal health state which ranges from the majority who are mildly frail and need supported self-management, through those who are moderately frail and would benefit from interventions such as case finding/case management, to those who have advanced frailty where anticipatory care planning and end-of-life care may be appropriate interventions.

So frail people should not be perceived as a problem to the system but, rather, clinicians should support people with living with frailty to maintain their own health for as long as possible.
Thankyou for listening

Questions?
A bit about muscles
DEFINITION

• Skeletal muscle mass index
  – Appendicular skeletal muscle mass (ASM), evaluated by DEXA, divided by body height squared (ASM/ht²).

• Another definition uses a percentage of skeletal muscle index
  – (SMI%, total muscle mass/body mass x 100).

• affects postural muscles > non-postural ones
  – DEXA can underestimate limb body mass by up to 20%.
Changes with age/ gender

From 20’s to 70’s, total lean body mass (LBM) declines
• 18% in men and 27% in women.
• Thigh muscles:
  – 24–27% of muscle mass
  – 25% of muscle cross-sectional area
• TBM increases between 18 and 40%
Women’s LBM is about 64% that of men.
• When accelerated by disuse, disease or anorexia, loss of muscle mass may place women at greater risk of falling below the level of critical muscle mass essential for mobility and independent living.
Myosteatosis in Sarcopenia

Loss of muscle tissue accompanied by fat and connective tissue infiltration
- Net contractile muscle mass $<\text{CSA}$

In older women and men
- 15% muscle CSA
- 2.5X $>\text{in young controls (6%)}$.

Inversely related to level of physical activity
- Doubling level of physical activity halves the amount of myosteatosis.

Combined with obesity: sarcopenic obesity
- of particular concern in older individuals
- Prevalence rises from 2% aged 60–69 years to about 10% in those aged $>80$
- Associated with accelerated functional decline and high risk of diseases and mortality.
- Macrophage infiltration mediated-release of pro-inflammatory cytokines (such as TNF-a, IL-6, IL-1) and adipokines (leptin, adiponectin and resistin) from adipocytes.
Muscle Mass decrease in Sarcopenia

- decrease in muscle fibre size (atrophy) and number (hypoplasia).
- (disuse atrophy involves only a decrease in fibre size not number
- The number of motor units remains almost constant up to 60 years
  - rapid decline thereafter 3%/year,
  - By age 80 represents a 60% loss of MUs.

With ageing type II fibres are more vulnerable to atrophy than type I fibres
- Greater loss of type II fibres may occur up to the late 70s,
- past 80 years type I fibres are also lost and a new ‘balance’ between the two types of fibres is reached

Morphological changes of sarcopenia also involve remodelling muscle architecture.
- Since muscle power is the product of force and velocity, changes in muscle architecture play a role in loss of muscle force and power
Mechanisms

Hormonal and immunological alterations
• Withdrawal, or resistance to anabolic factors (decreased levels of GH, IGF-1, testosterone)
• Increased catabolic activity (increased levels of IL-1, IL-6, TNF-a, myostatin)

Differences in protein synthesis in response to feeding and exercise, a blunted response to anabolic stimuli.
• Older people show a lower increase in muscle protein synthesis in response to amino acid feeding (approx 40%) and in response to acute bout of exercise (approx 30%)

Sarcopenia not only due to blunted anabolic response (reduced sensitivity and responsiveness) to amino acid feeding but also to a reduced sensitivity to inhibitory effect of insulin on protein breakdown.
Force and power

Isometric force and peak power of older individuals
• 40% difference in isometric force
• 60% difference in peak power
Decline in muscle power > force has consequences
• Quality of life of older people ADL’s require power.
• Worse in SO
  – Less muscle mass
  – Heavier
  – Have to generate extra-power, and thus use more energy
• Case
• Bed rest
• Ageing
• Frailty
• What is it
• Pathophysiology
• Evidence that it is a useful construct
• Surgery
• ICU
• Medical
• Can we prevent it
• Can we treat it
Conclusion

Sarcopenia has a complex aetiology
• Neuronal, hormonal, immunological, nutritional and physical activity mechanisms.
Women at greater risk of losing functional independence than men
• Lower muscle mass
• Greater blunting of the anabolic response to exercise and
• Greater blunting of the antiproteolytic effect of insulin.

Muscle mass loss in old age due to
• Reduced anabolism and increased catabolism,
• Reduced capacity of muscle regeneration.

Increased prevalence of obesity gives rise to SO
• contributes to loss of muscle mass, mobility and independence
Sepsis-induced myopathy

- Characterized by reductions in muscle force-generating capacity, atrophy (loss of muscle mass), and altered bioenergetics.
- Muscle wasting occurs later
  - Results from increased proteolytic degradation as well as decreased protein synthesis.
- Sepsis produces marked abnormalities in muscle mitochondrial functional capacity.
- Mechanisms leading to sepsis-induced changes in skeletal muscle
  - Pro-inflammatory cytokines
  - Free-radical generation
  - Activation of proteolytic pathways.