Frailty: What to Measure? When to Measure? and Does It Add Any Value?

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Canada Research Chairs

Alberta Innovates Health Solutions

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

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- *I am not a geriatrician – nor necessarily an expert in frailty*

Objectives

1. Define and review the biologic of the concept of "frailty"
2. Understand the tools to capture frailty and identify a vulnerable population
3. Understanding the impact of frailty on outcomes after acute stress and critical illness

FRAILTY is a multi-dimensional "syndrome" or "state" related to ageing first described in elderly patients

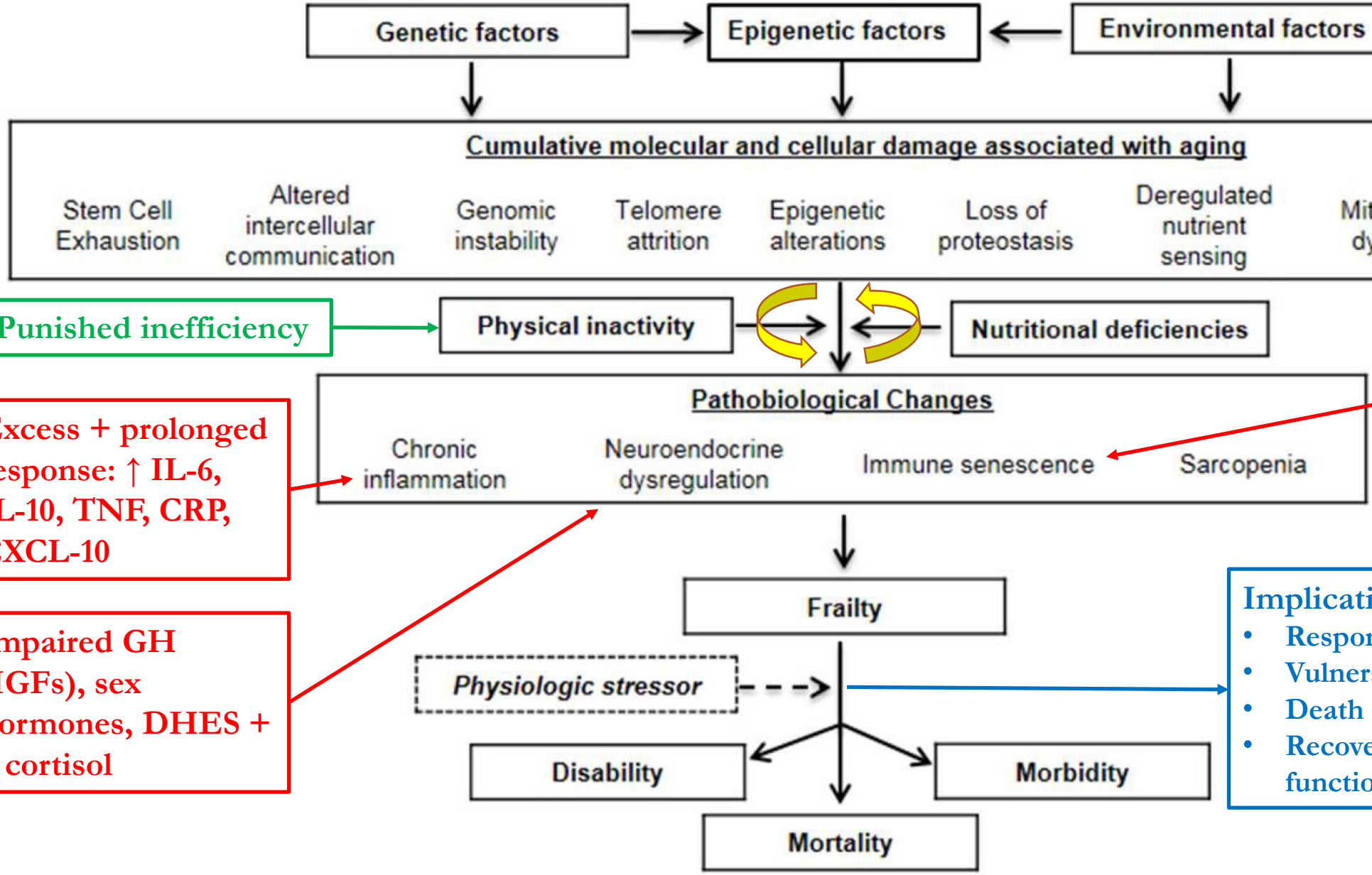
Characterized by:

Loss of reserve (energy, physical, cognitive, health) and the accumulation of "deficits"

(individually reversible but collectively insurmountable)

Consequence:

Heightened vulnerability or "state-at-risk" to adverse outcomes



Punished inefficiency

↓ stem cells, T-cell production, B-cell Ab response, phagocytic activity

Excess + prolonged response: ↑ IL-6, IL-10, TNF, CRP, CXCL-10

Impaired GH (IGFs), sex hormones, DHES + ↑ cortisol

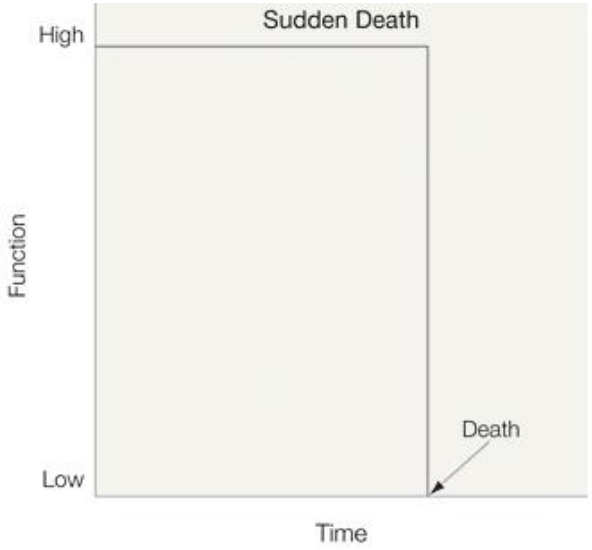
Implications for ICU settings:

- Response the therapy
- Vulnerability to complications
- Death
- Recovery → disability, impaired function, loss of autonomy

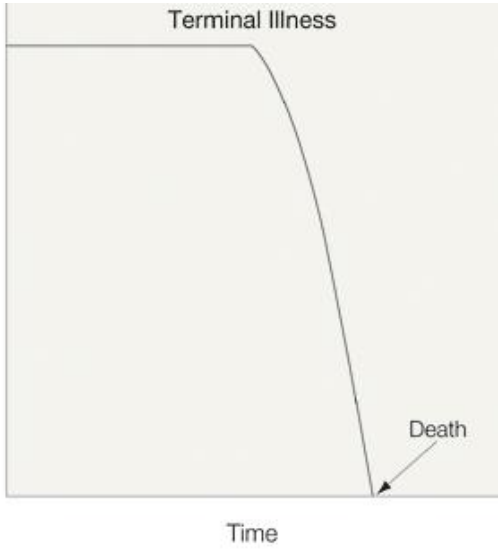
Singer J et al AATS 2016

Patterns of Functional Decline at End of Life

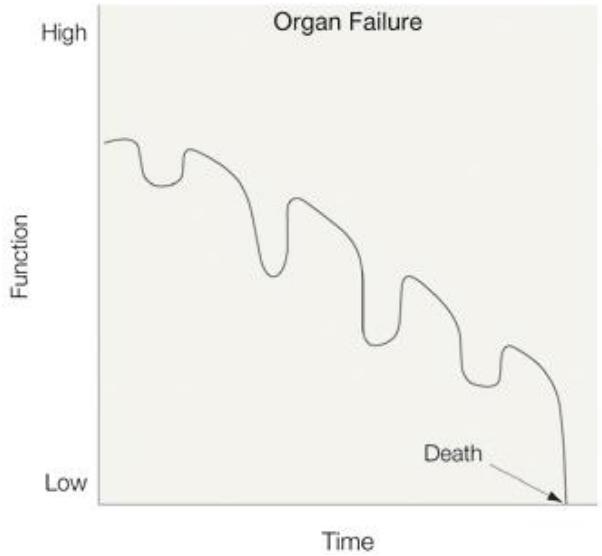
Sudden Death



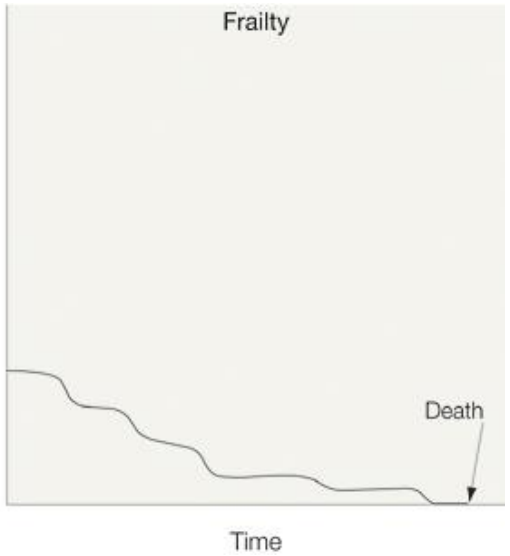
Terminal Illness



Organ Failure



Frailty



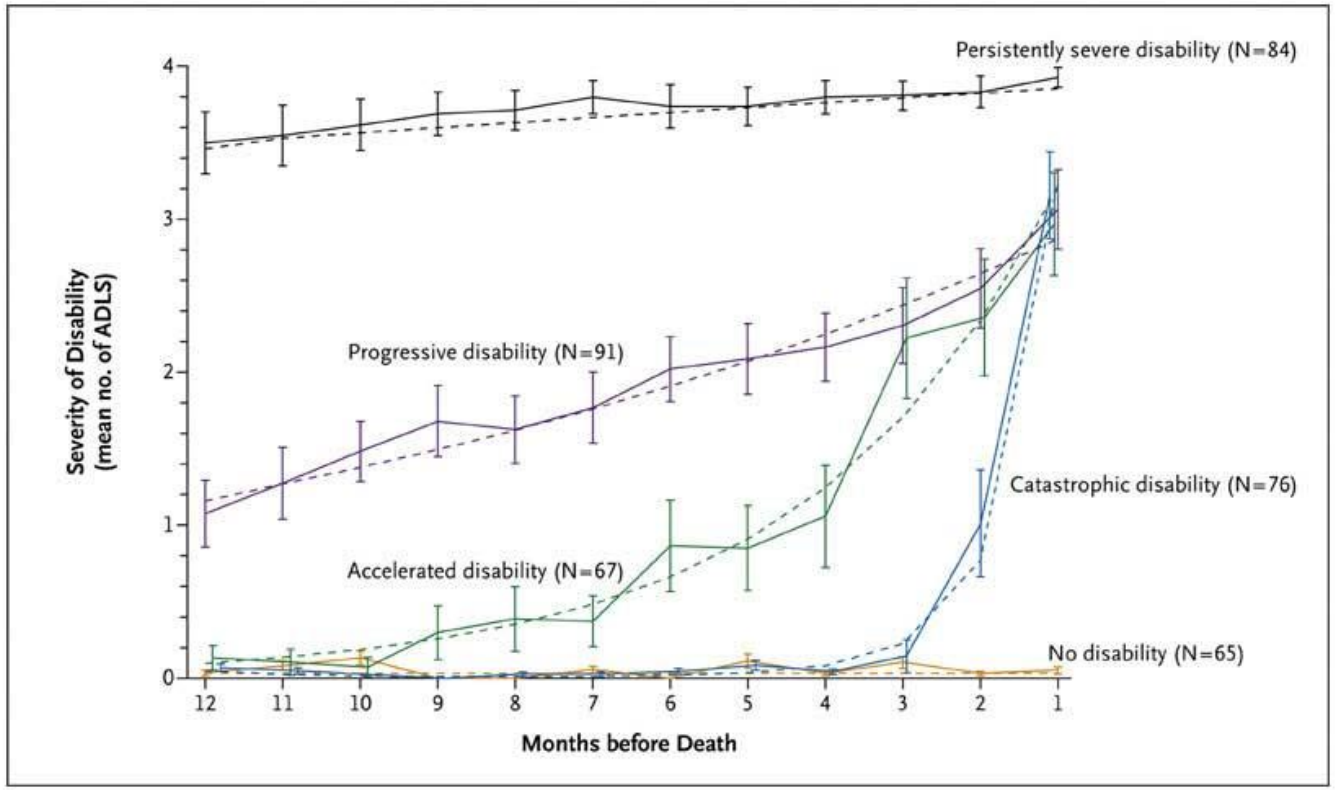
Definitions: Sudden death = cardiac arrest or trauma; Terminal illness = cancer; Organ failure = HF/COPD; Frailty: residence in nursing home

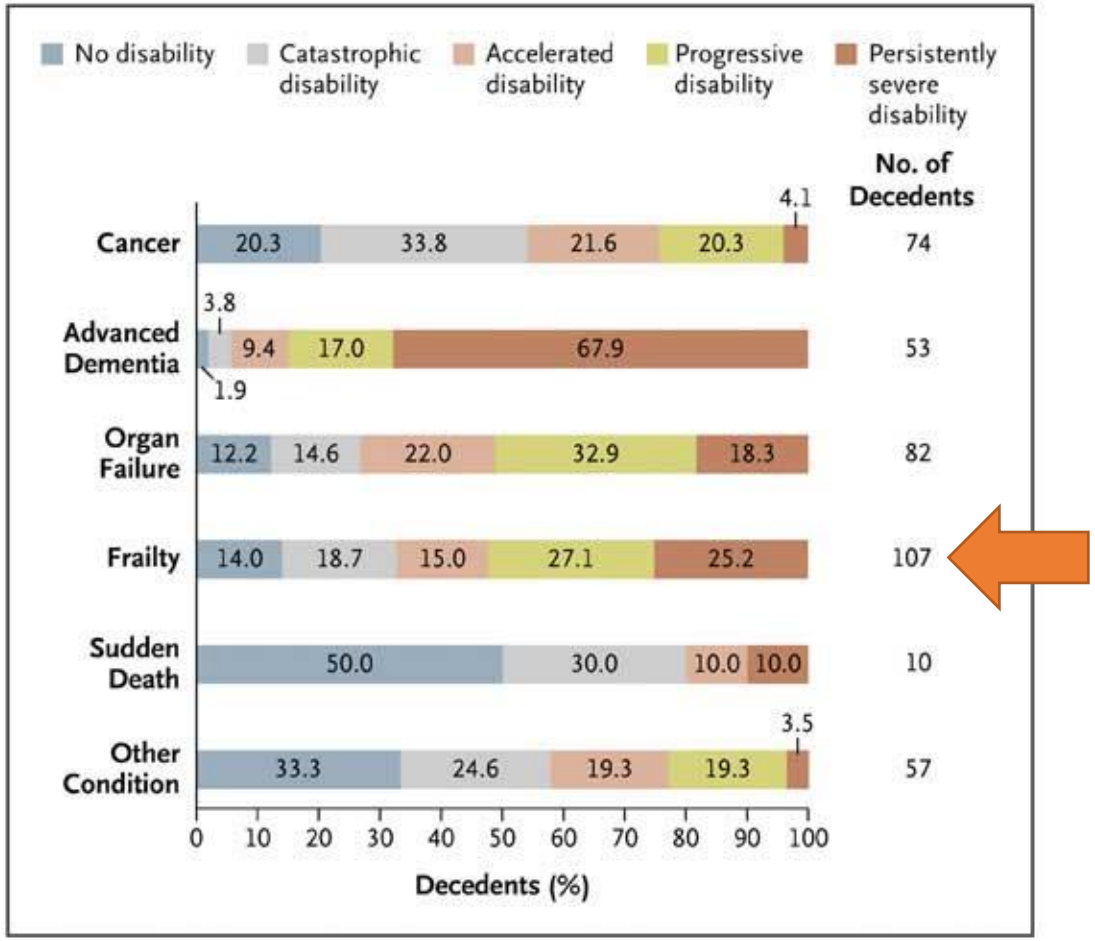
Lunney JR et al JAMA 2003

Trajectories of Disability in the Last Year of Life

Thomas M. Gill, M.D., Evelyne A. Gahbauer, M.D., M.P.H., Ling Han, M.D., Ph.D., and Heather G. Allore, Ph.D.

n=383 elderly decedents





FRAILTY ~ most common condition leading to death

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Gill TM et al. N Engl J Med 2010;362:1173-1180

Cumulative Deficit Model

CSHA captured 92 variables such as symptoms, signs, laboratory values, disease states and disabilities – collectively termed **"deficits"**

- 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 palmomental reflex
- Other medical history

Frailty Index (FI) = # deficits / total variables

Frailty represents the "cumulative effects of individual deficits"

Reinforces the concept of "physiologic/homeostatic reserve" and "biological gradation"

FI strongly correlated with risk of death and institutionalization

Jones et al J Am Ger Soc 2004

Physical Phenotype Model

Frailty Characteristics	CHS Measure
Shrinking, weight loss (unintentional), sarcopenia	>10 lb lost unintentionally in prior 1 year
Weakness	Grip strength: lowest 20% (by sex, BMI)
Poor endurance, exhaustion, slowness	"exhaustion" (self-reported); walking time/15 ft: slowest 20% (by sex, height)
Low activity	Kcal/week: lowest 20% (males <383 Kcal/wk; females <270 Kcal/wk)

1. **Shrinking**: weight loss, unintentional, of ≥10 lbs in prior year)
2. **Weakness**: grip strength in lowest 20% at baseline (age/BMI)
3. **Poor endurance/energy**: self report of exhaustion (CES-D scale)
4. **Slowness**: slowest 20% at baseline for time to walk 15 ft (sex/height)
5. **Low physical activity**: lowest quintile of physical activity (gender)

Frail ≥ 3

Vulnerable 1-2

Not Frail 0

Fried et al (Cardiovascular Health Study)_J Gerontol Biol Sci Med Sci 2001

Domains to Define, Measure and Operationalize

Domain	Operational Measures
General Health Status	Hospitalizations, global assessment of functioning scale, self-rated health
Physical Function	BADL, IADL, functional independence measure (FIM)
Cognitive Function	MMSE, Montreal Cognitive assessment, clock drawing test
Mobility	Short physical performance battery, gait speed, TGUG, chair rise, mobility aid
Strength	Grip strength, stair climb, subjective assessment of weakness
Energy	Fatigue severity scale, subjective assessment of exhaustion or fatigue
Nutritional Status	BMI, weight, albumin/prealbumin, mini-nutritional assessment, weight loss
Skeletal Muscle Mass	Anthropometry, bioelectrical impedance, MRI/CT/ultrasound
Mood	Geriatric depression scale, HADS, self-reported depression/anxiety
Social relations/support	Availability of social resources, subjective assessment of loneliness or isolation
Laboratory Markers	Inflammatory mediators (IL-6, IL-1, TNF, CRP), oxidized LDL, creatinine

Rajabali et al Can J Cardiol 2016; De Vries et al Ageing Research Reviews 2011

Methods to Screen and "Diagnose" Frailty

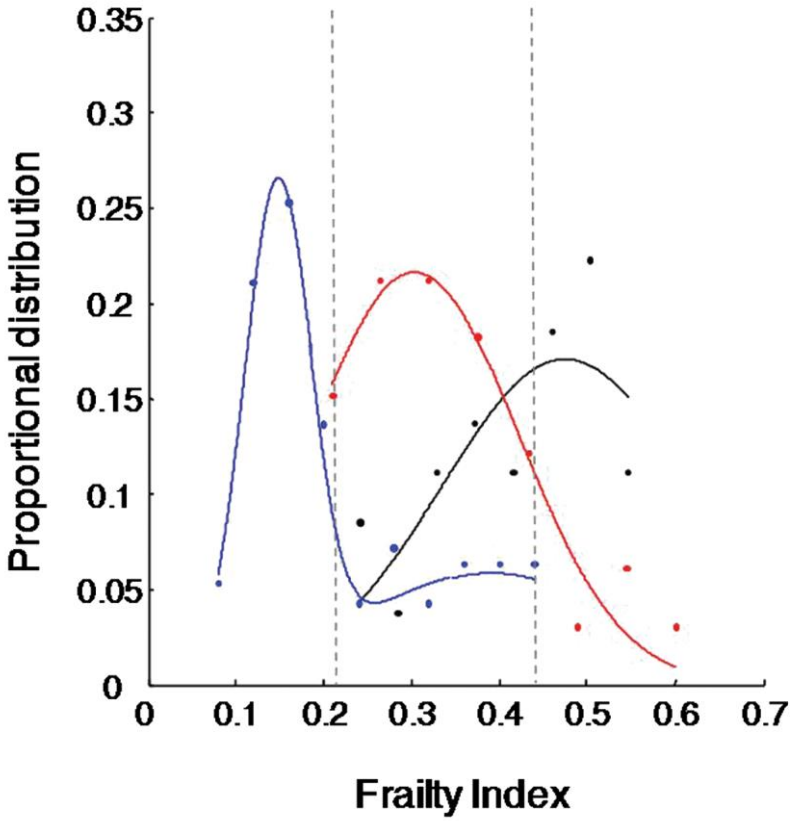
Method	Description	Items	Example	Evaluated in ICU
Frailty Index (FI)	Deficit accumulation	30-70	CSHA FI (70 items)	YES
Physical phenotype	≥ 3 physical features	3-5	Fried (CHS) criteria	YES
Physical performance measures	Single measure	1	Gait speed, grip strength, chair stand	NO
Judgement-Based tools	Global subjective assessment	1	Clinical Frailty Scale	YES
Multidimensional tools	Battery of assessments across domains	5-20	EFS, FRAIL, CAF, Groningen Frailty Indicator	NO
Sarcopenia	Imaging to assess skeletal muscle	1	CT scan psoas or rectus femoris	YES

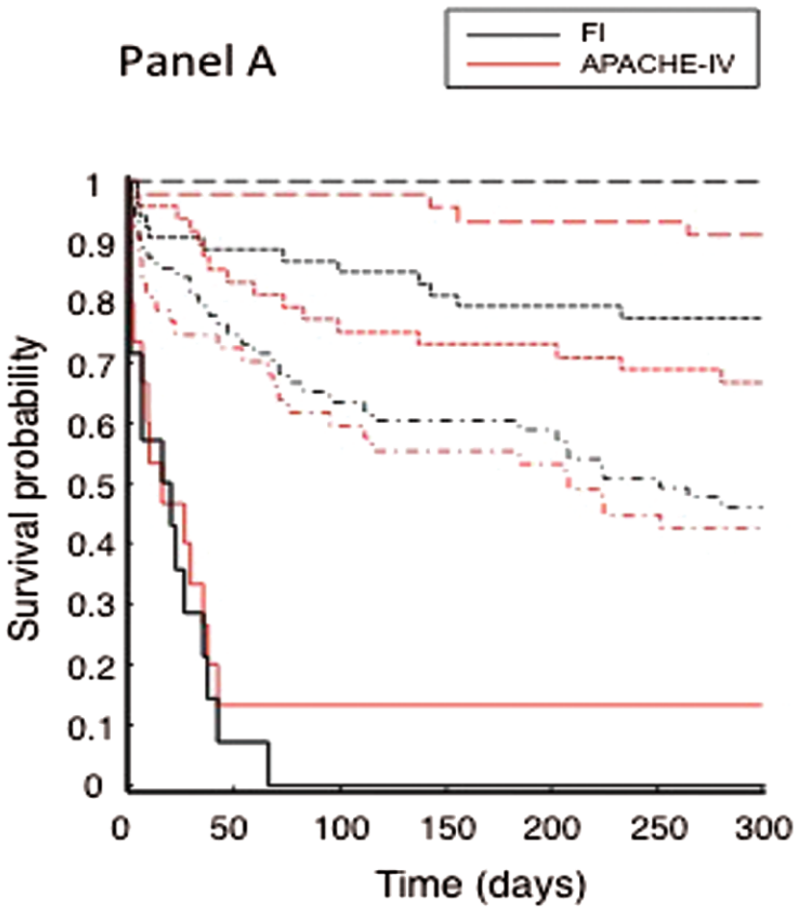
Gold Standard: Comprehensive Geriatric Assessment (CGA)

Rajabali et al Can J Cardiol 2016

Mortality in Relation to Frailty in Patients Admitted to a Specialized Geriatric Intensive Care Unit

- Single "geriatric" ICU in China (mean age 82 yr)
- Novel FI based on 52 variables (23 chronic + 31 acute)
- All patients who died had FI > 0.46
- All patients who survived 30-days had FI <0.22





Each 1% ↑ in FI associated with 11% ↑ in 30-day mortality (OR 1.11; 95% CI, 1.07-1.15)

n=155

Zeng et al J Genrontol A Biol Sci Med Sci 2015

Frailty as a Predictor of Surgical Outcomes in Older Patients

n=594	Non-Frail (58.2%)	Intermediate (31.3%)	Frail* (10.4%)
Age (yr)	71 (67-94)	75 (65-92)	76 (65-94)
Female Sex (%)	67.6	52.7	41.9
Post-operative complications	1.0	2.06 (1.2-3.6)	**2.54 (1.1-5.8)**
Length of stay	1.0	1.49 (1.2-1.8)	**1.69 (1.3-2.2)**
Institutionalized	1.0	3.2 (1.0-9.9)	**20.5 (5.5-76)**

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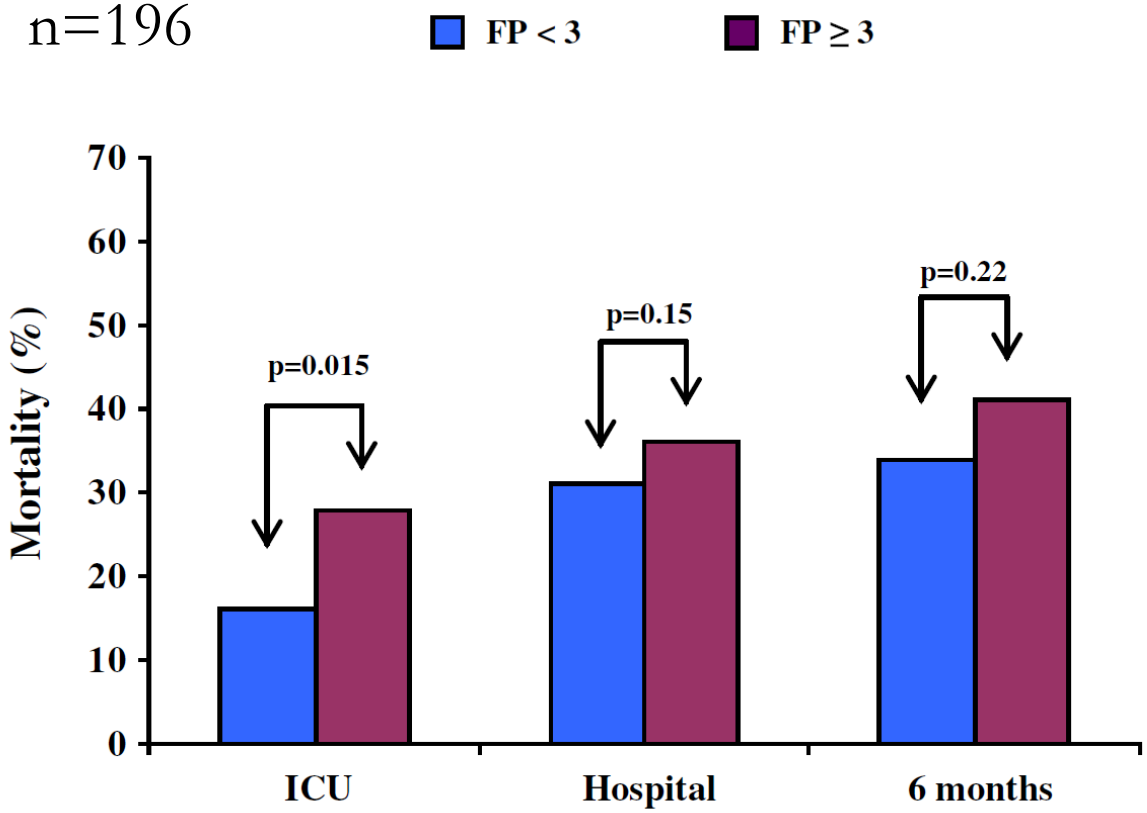
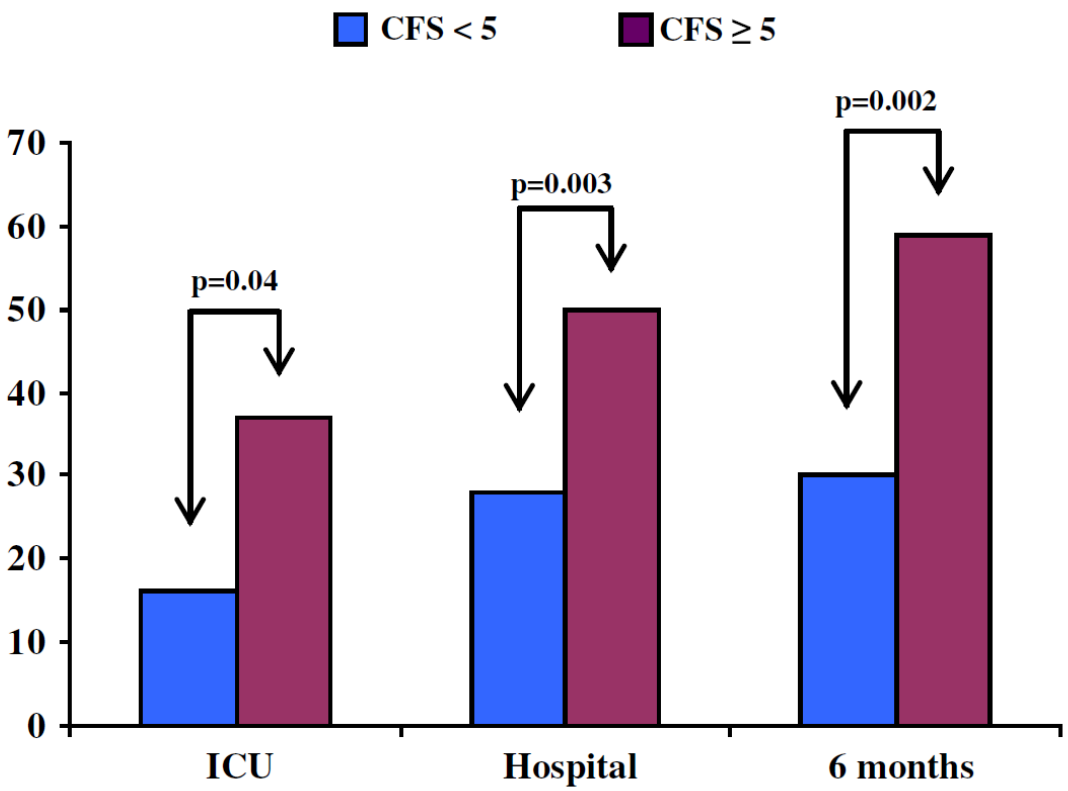
* FRAILTY defined by the physical phenotype criteria proposed by Fried

Makary et al JACS 2010

Prevalence and impact of frailty on mortality in elderly ICU patients: a prospective, multicenter, observational study

n=196





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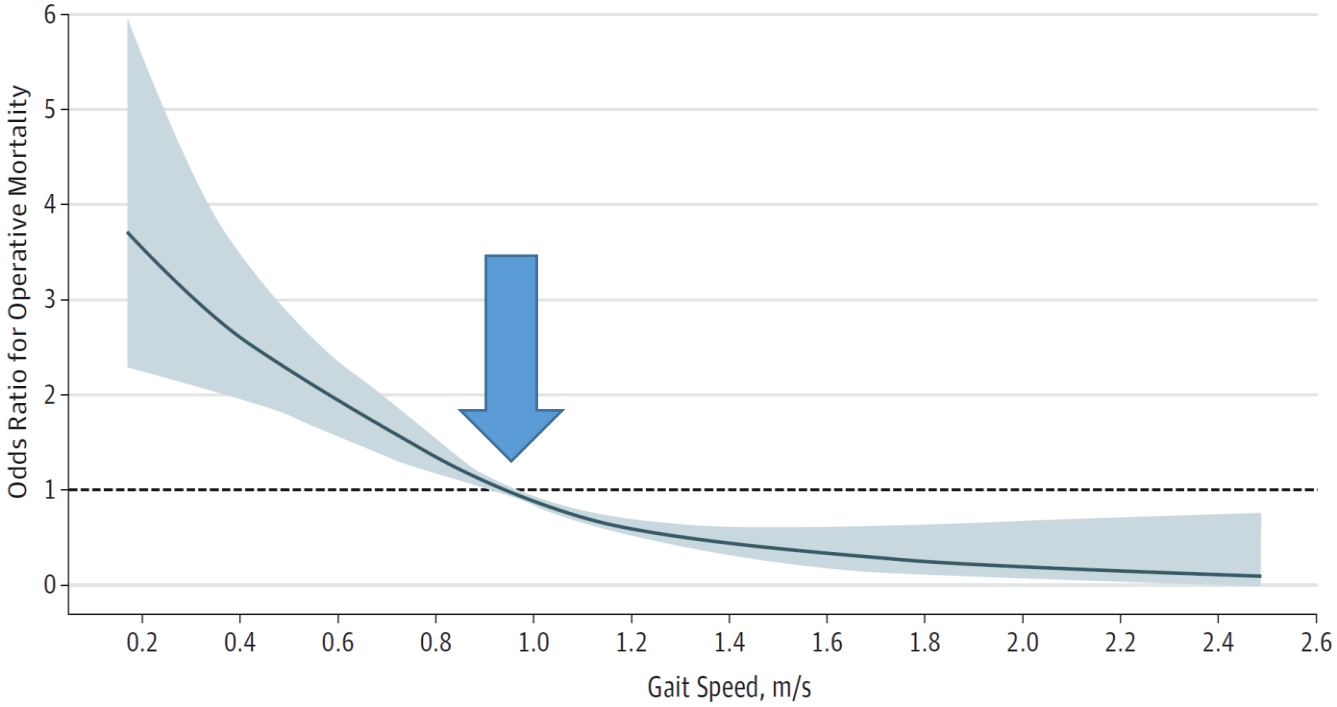
Le Maguet et al ICM 2014

Gait Speed and Operative Mortality in Older Adults Following Cardiac Surgery

Prospective multicenter cohort study of 15,717 patients undergoing cardiac surgery (STS Adult Cardiac Surgery Database)



Outcome	No. (%) Slow Tertile (<0.83 m/s) (n = 4588)	Middle Tertile (0.83-1.00 m/s) (n = 5717)	Fast Tertile (>1.00 m/s) (n = 4866)	*P* Value
Primary end point				
Operative mortality	154 (3.4)	108 (1.9)	52 (1.1)	<.001
Secondary end point and components[a]				
Composite mortality and morbidity	767 (16.7)	685 (12.0)	474 (9.7)	<.001
Reoperation for bleeding	109 (2.4)	144 (2.5)	117 (2.4)	.88
Reoperation for graft occlusion	8 (0.2)	7 (0.1)	9 (0.2)	.68
Reoperation for valve dysfunction	0 (0.0)	2 (0.03)	3 (0.06)	.26
Reoperation for other cardiac cause	26 (0.6)	21 (0.4)	15 (0.3)	.18
Reoperation for noncardiac cause	104 (2.3)	82 (1.4)	51 (1.1)	<.001
Permanent stroke	83 (1.8)	92 (1.6)	74 (1.5)	.52
Acute kidney injury	156 (3.4)	156 (2.7)	79 (1.6)	<.001
Deep sternal wound infection	23 (0.5)	7 (0.1)	8 (0.2)	<.001
Prolonged mechanical ventilation	496 (10.8)	406 (7.1)	246 (5.1)	<.001

Slowest tertile (<0.83 m/s) OR 3.2 (95% CI, 2.3-4.3) for 30-day all-cause mortality

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Afilalo et al JAMA Cardiol 2016

A global clinical measure of fitness and frailty in elderly people

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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Table 2: Cox proportional hazard ratios (HR) for time until death and until the requirement for institutional care

Factor	Death, HR (95% CI)	Entry into institution, HR (95% CI)
Age	1.08 (1.07–1.08)	1.15 (1.10–1.13)
Sex	0.83 (0.78–0.89)	1.38 (1.21–1.58)
Education level*	0.98 (0.97–0.99)	0.98 (0.97–0.99)
Modified Mini-Mental State Examination	0.84 (0.82–0.86)	0.65 (0.60–0.70)
Cumulative Illness Rating Scale	1.14 (1.11–1.17)	1.22 (1.16–1.27)
CSHA measuring tools		
Rules-based definition of frailty	1.17 (1.13–1.20)	1.27 (1.19–1.35)
Frailty Index	1.26 (1.24–1.29)	1.56 (1.48–1.65)
Function Scale	1.16 (1.13–1.20)	1.29 (1.20–1.39)
Clinical Frailty Scale	1.30 (1.27–1.33)	1.46 (1.39–1.53)

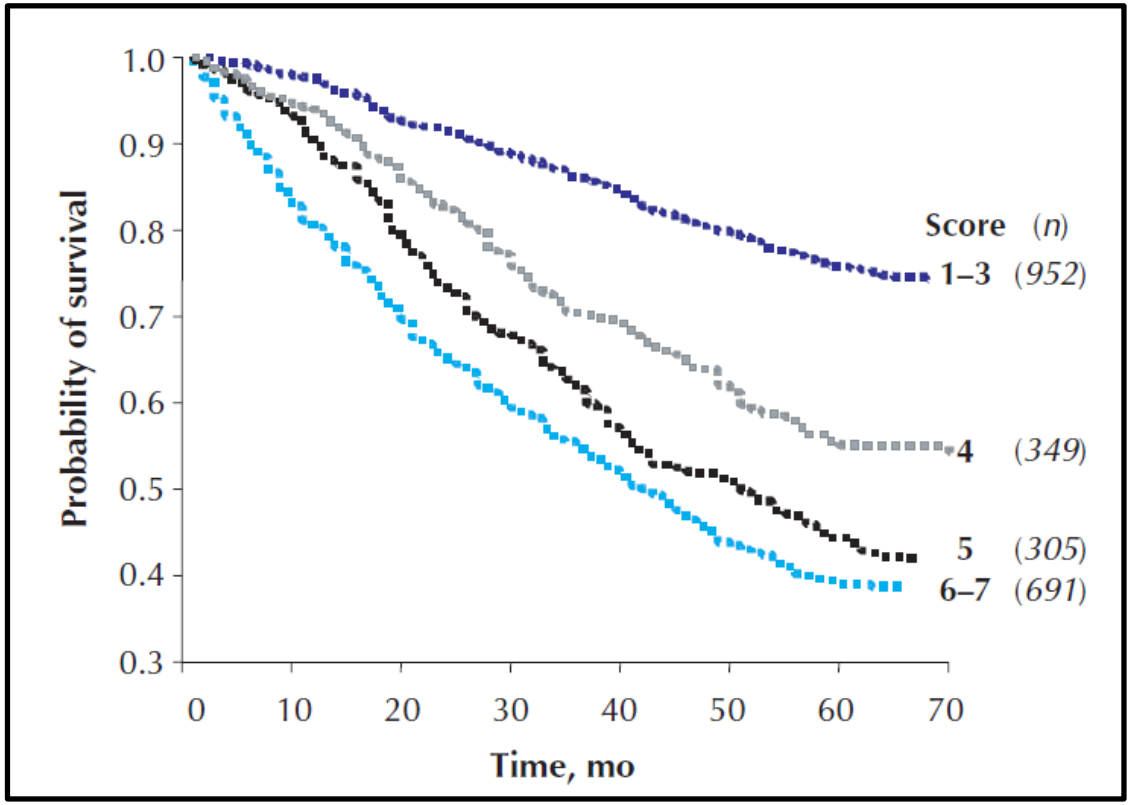
CFS score and mathematically derived FI highly correlated (Pearson 0.80, $p<0.01$)

Available at: http://geriatricresearch.medicine.dal.ca/clinical_frailty_scale.htm

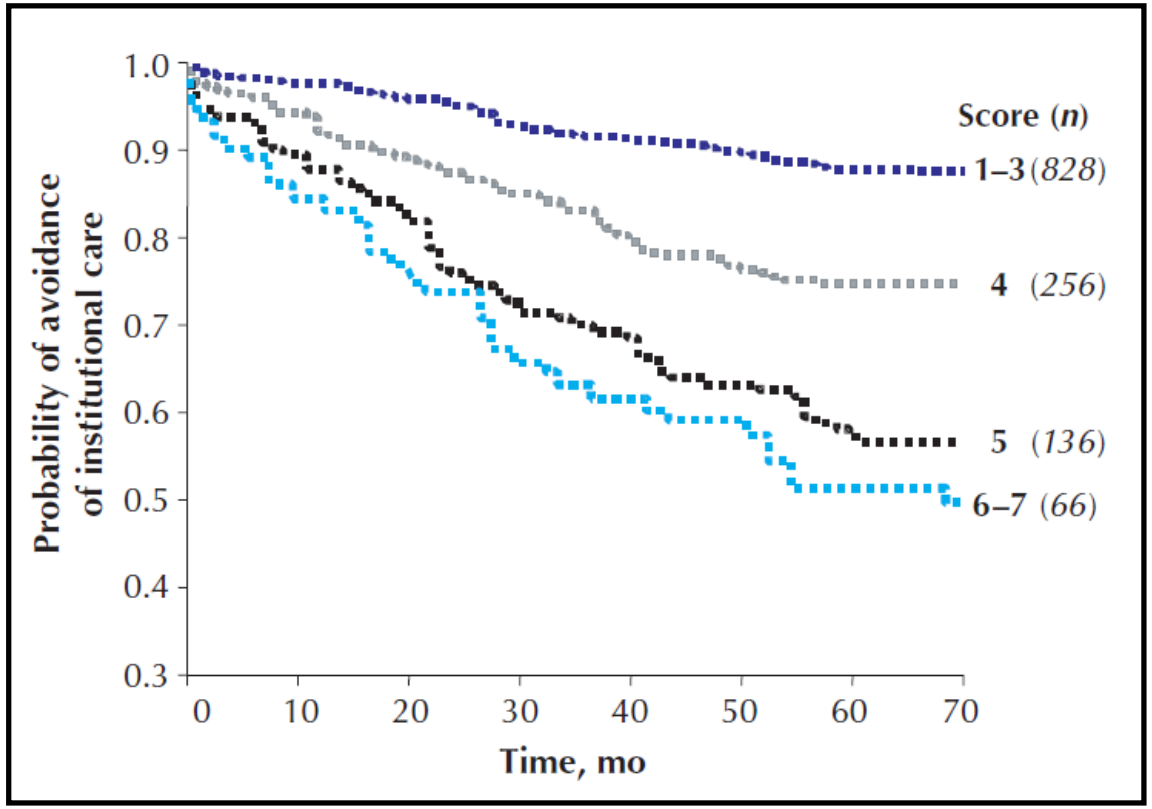
Rockwood et al CMAJ 2005

A global clinical measure of fitness and frailty in elderly people

Survival



Institutionalization



For each 1-category ↑ in CFS score ~ 21.2% ↑ death and 23.9% ↑ institutionalization

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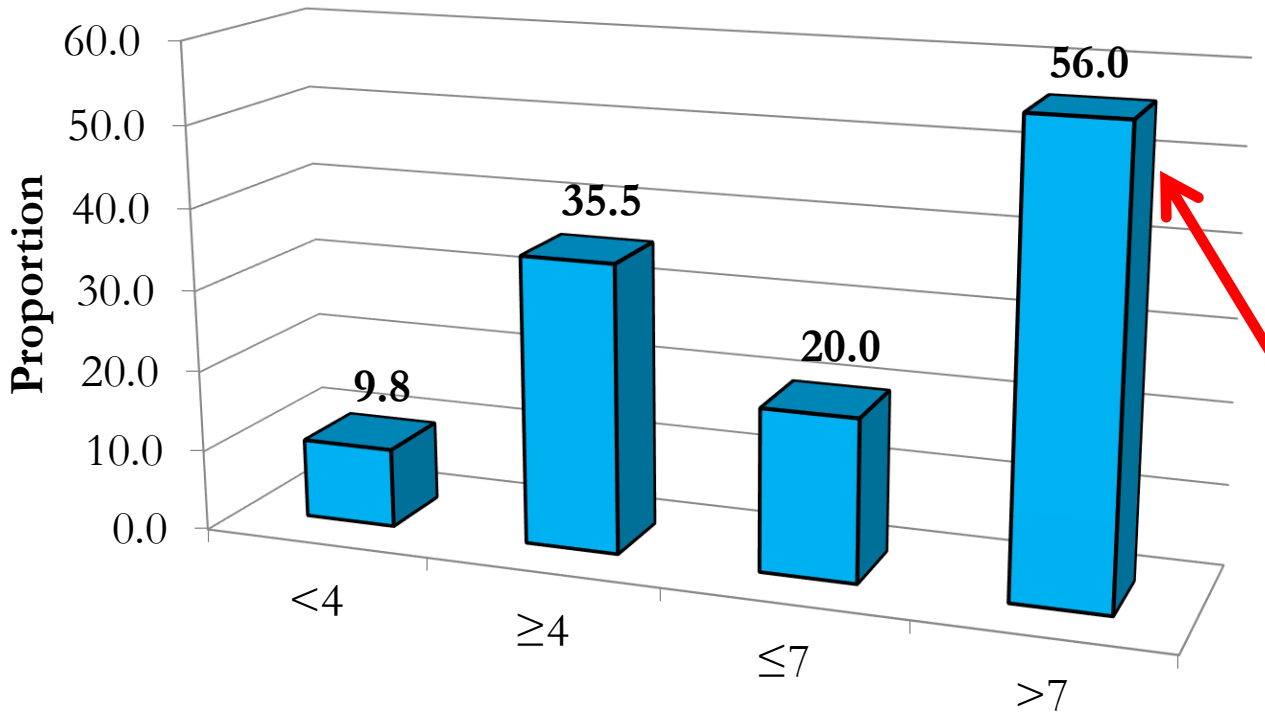
Rockwood et al CMAJ 2005

Frailty is associated with postoperative complications in older adults with medical problems

Monidipa Dasgupta [a,*], Darryl B. Rolfson [b], Paul Stolee [c,d], Michael J. Borrie [e], Mark Speechley [d,f]

Post-operative Complications



Edmonton Frail Scale score

Prospective cohort (n=125); aged > 70 yr; pre-op clinic; referred for elective non-cardiac surgery

Age-adjusted OR complications 5.02 (95% CI, 1.5-16.3)

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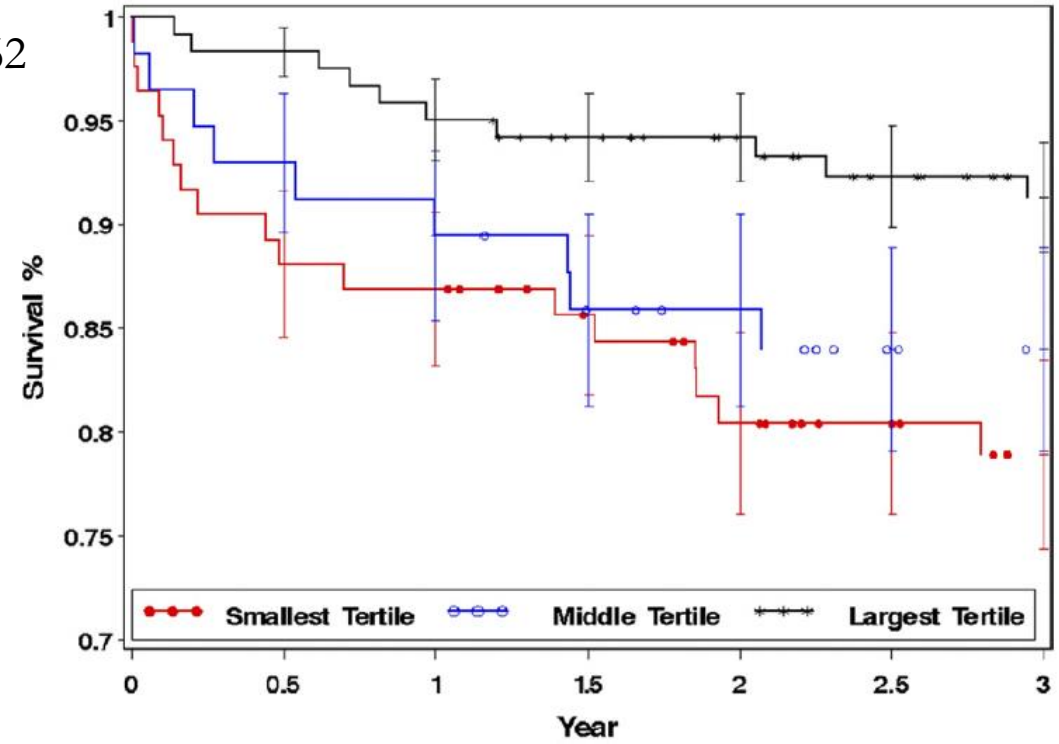
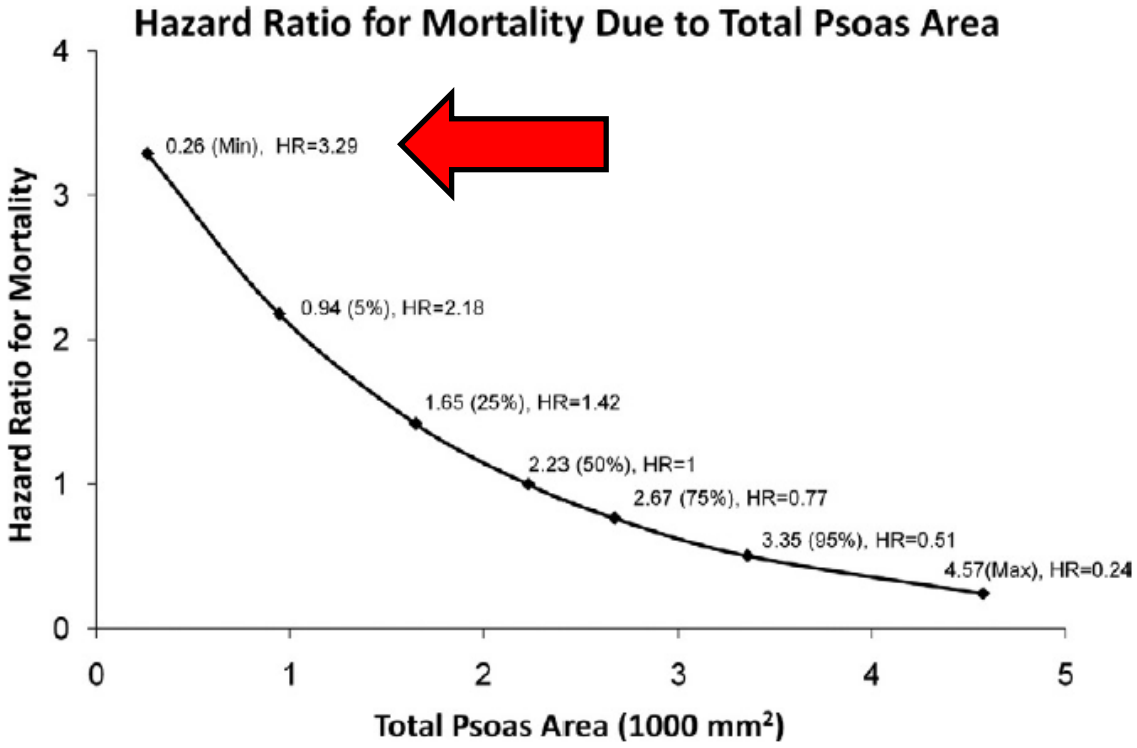
Dasgupta et al Arch Ger Ger 2009

Frailty, core muscle size, and mortality in patients undergoing open abdominal aortic aneurysm repair

n=262





Psoas core muscle size (i.e. sarcopenia) by pre-op CT ~ objective surrogate for FRAILTY

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Lee et al J Vasc Surg 2011

Frailty – The "What" and "When"

Rapid Case Finding

- CFS
- FI (eFI)
- Gait Speed

→

Define Frailty Components

- Multi-dimensional assessment (i.e. EFS)

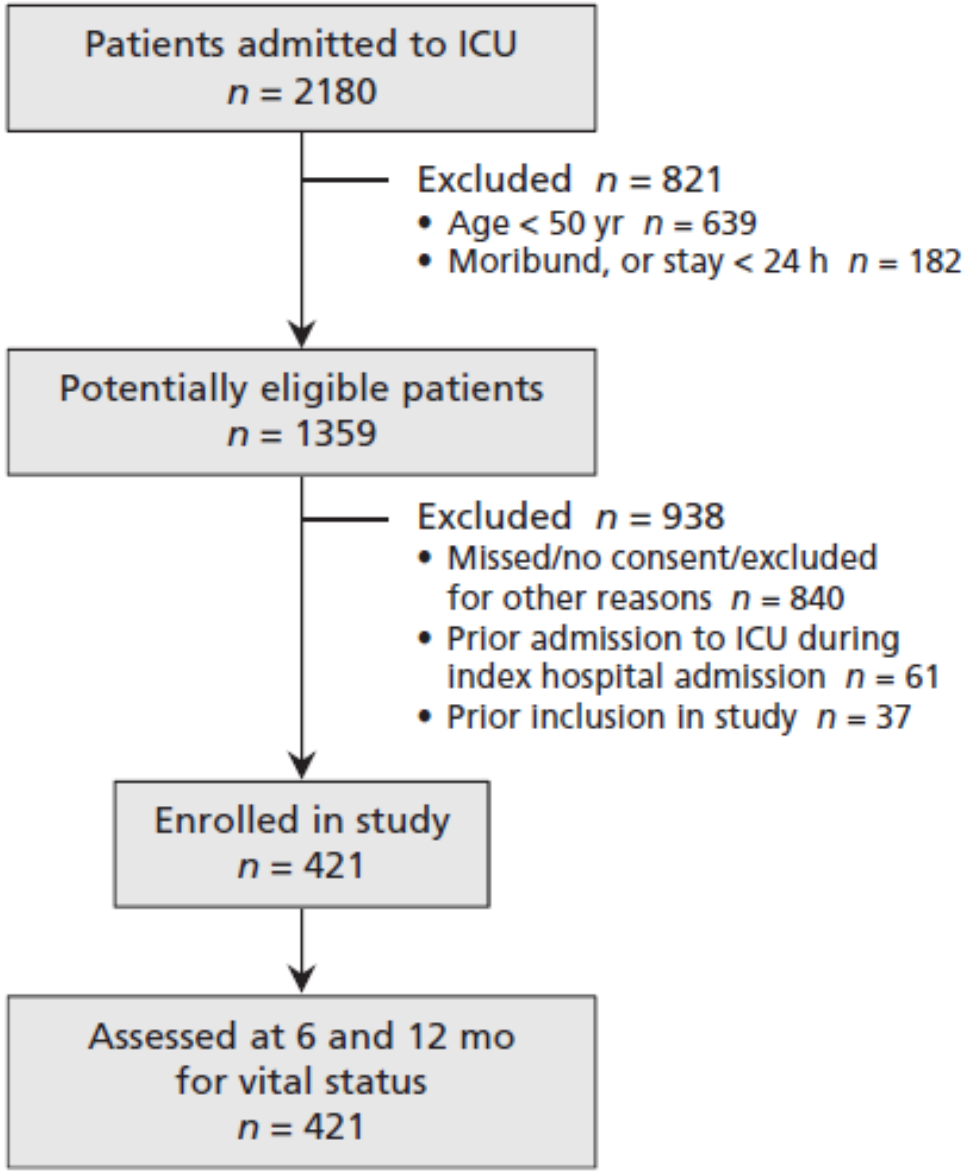
→

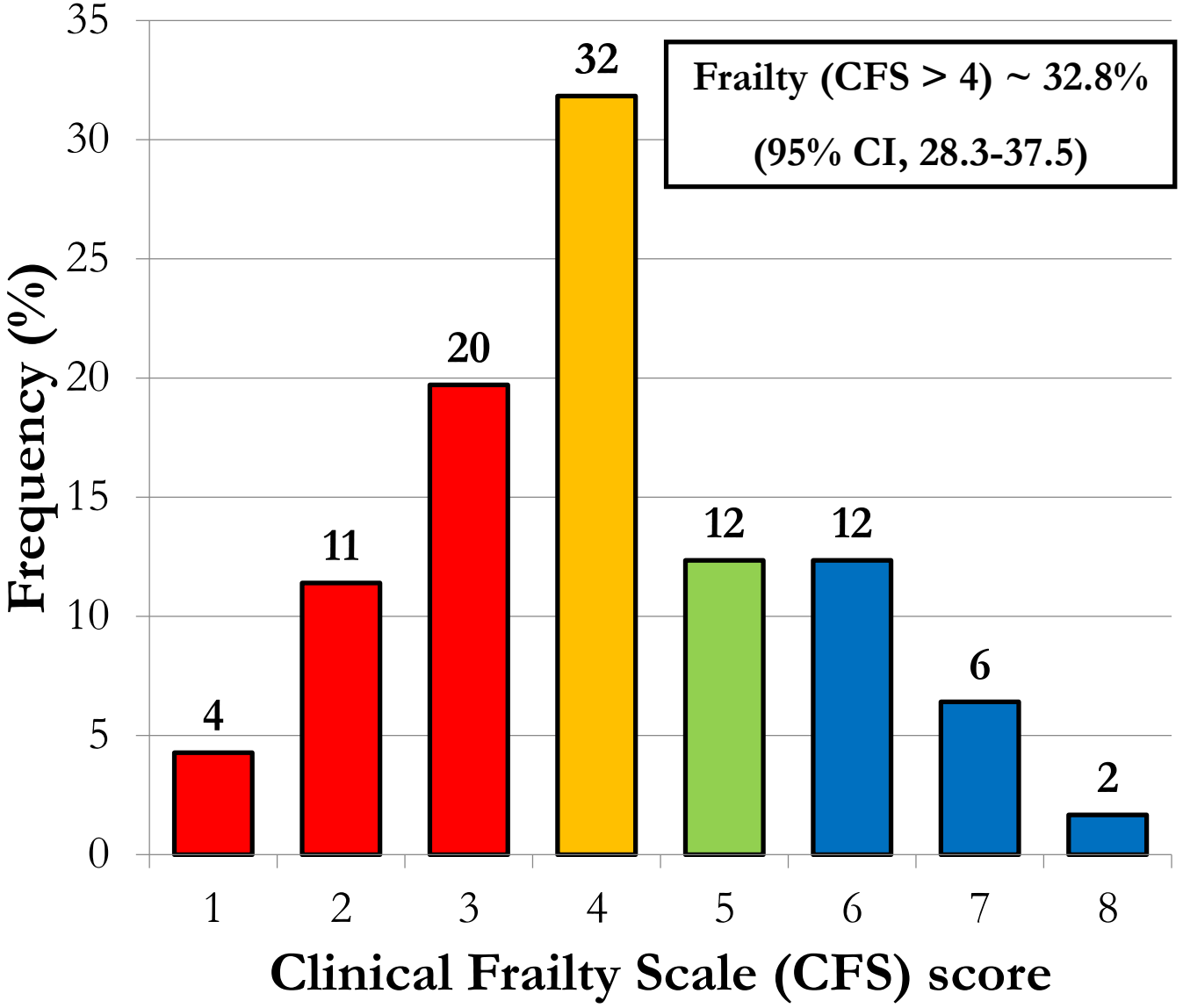
Address Components

- Informed decision-making

ICU admission → → Identify Contributors → → Precision Recovery

Adapted from D. Rolfson





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Bagshaw et al CMAJ 2014

↑ vulnerability

↑ risk for death

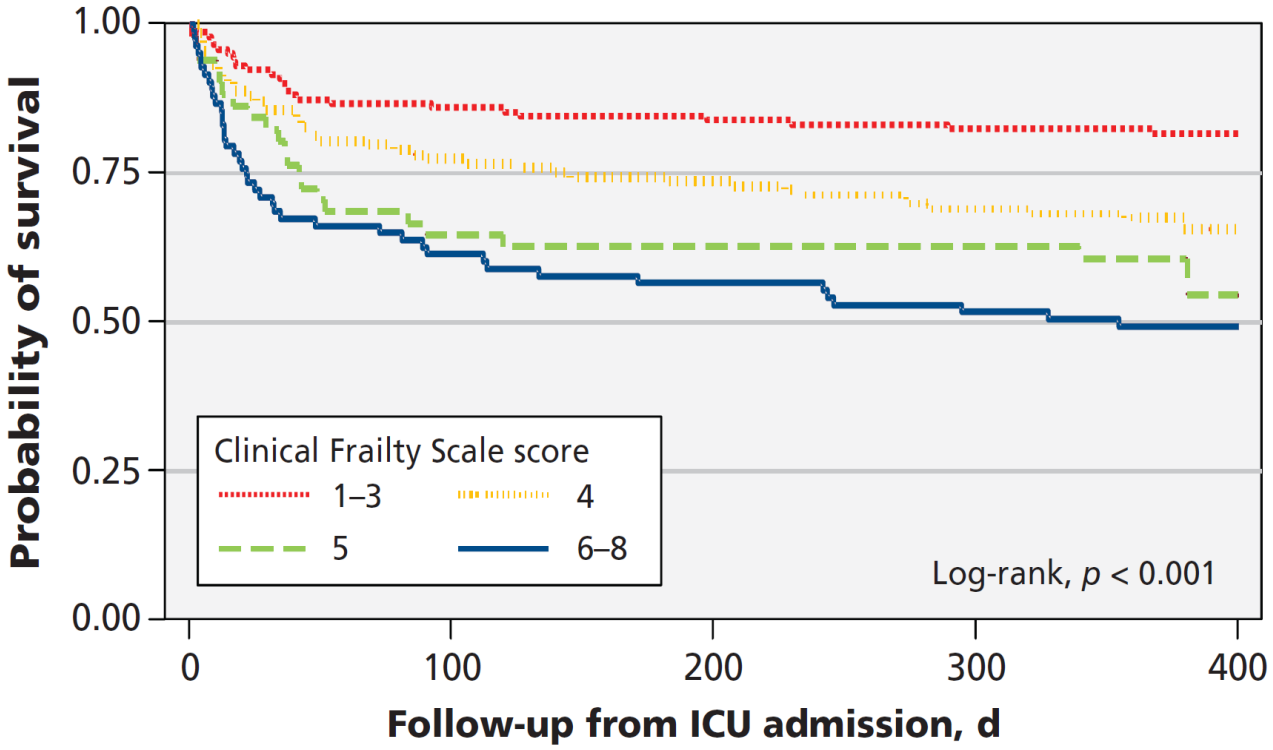
↑ time for recovery

↑ functional impairment

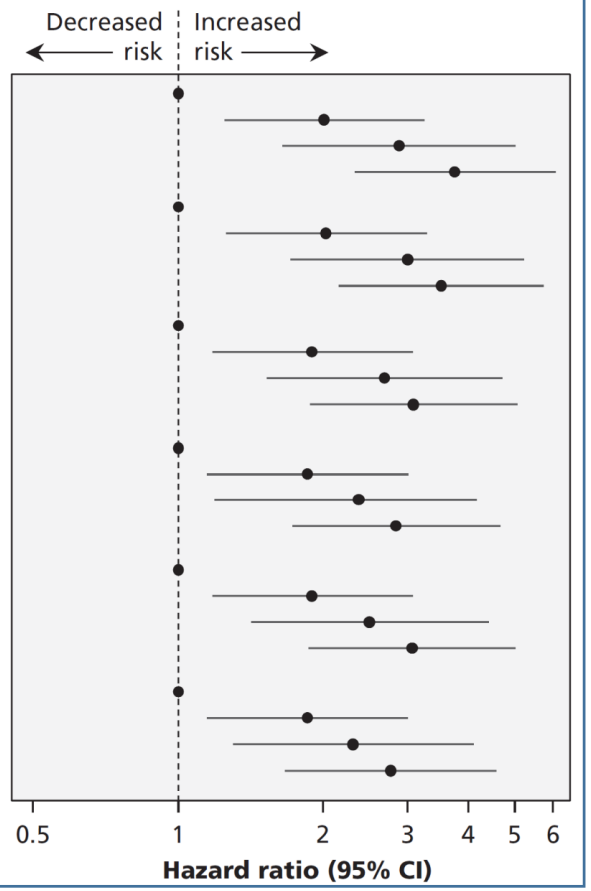
Outcome	Group; no. (%) of patients*		Association, OR (95% CI) or difference in medians (*p* value†)
	Frail *n* = 138	Not frail *n* = 283	
Adverse event‡	54 (39.1)	83 (29.3)	1.54 (1.01–2.37)
Death			
In ICU	16 (11.6)	27 (9.5)	1.37 (0.72–2.62)
In hospital	44 (31.9)	45 (15.9)	1.81 (1.09–3.01)
Duration of stay, d, median (IQR)			
In ICU	7 (4–13)	6 (3–10)	1 d (0.02)
In hospital	30 (10–64)	18 (10–40)	12 d (0.02)
Discharge disposition§	*n* = 91	*n* = 235	
Home, living independently	20 (22.0)	104 (44.3)	0.35 (0.20–0.61)
Home, living with help	33 (36.3)	58 (24.7)	1.67 (1.00–2.81)
Other¶	38 (41.8)	73 (31.1)	1.51 (0.92–2.48)
Discharged newly dependent**	24 (70.6)	96 (51.6)	2.25 (1.03–4.89)
Hospital readmission§	51 (56.0)	92 (39.1)	1.98 (1.22–3.23)

Bagshaw et al CMAJ 2014

Survival 1-year after ICU Admission



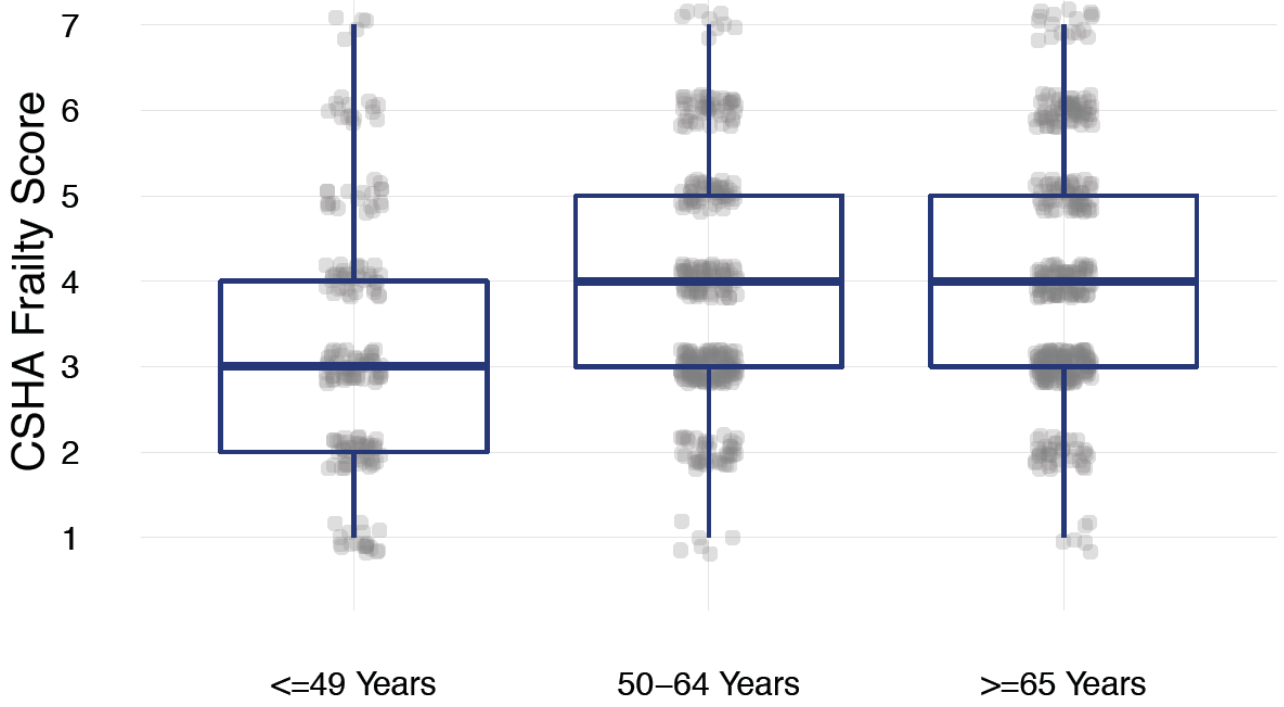
Model	Frailty score	HR (95% CI)
Unadjusted	1–3	1.00 (ref)
	4	2.01 (1.25–3.24)
	5	2.88 (1.65–5.02)
	6–8	3.76 (2.33–6.07)
Model 1	1	1.00 (ref)
	4	2.03 (1.26–3.28)
	5	3.00 (1.71–5.22)
	6–8	3.52 (2.16–5.73)
Model 2	1–3	1.00 (ref)
	4	1.90 (1.18–3.07)
	5	2.69 (1.53–4.71)
	6–8	3.08 (1.88–5.06)
Model 3	1–3	1.00 (ref)
	4	1.86 (1.15–3.01)
	5	2.37 (1.19–4.17)
	6–8	2.84 (1.73–4.66)
Model 4	1–3	1.00 (ref)
	4	1.90 (1.18–3.07)
	5	2.50 (1.42–4.41)
	6–8	3.06 (1.87–5.01)
Model 5	1–3	1.00 (ref)
	4	1.86 (1.15–3.00)
	5	2.31 (1.30–4.10)
	6–8	2.77 (1.67–4.58)



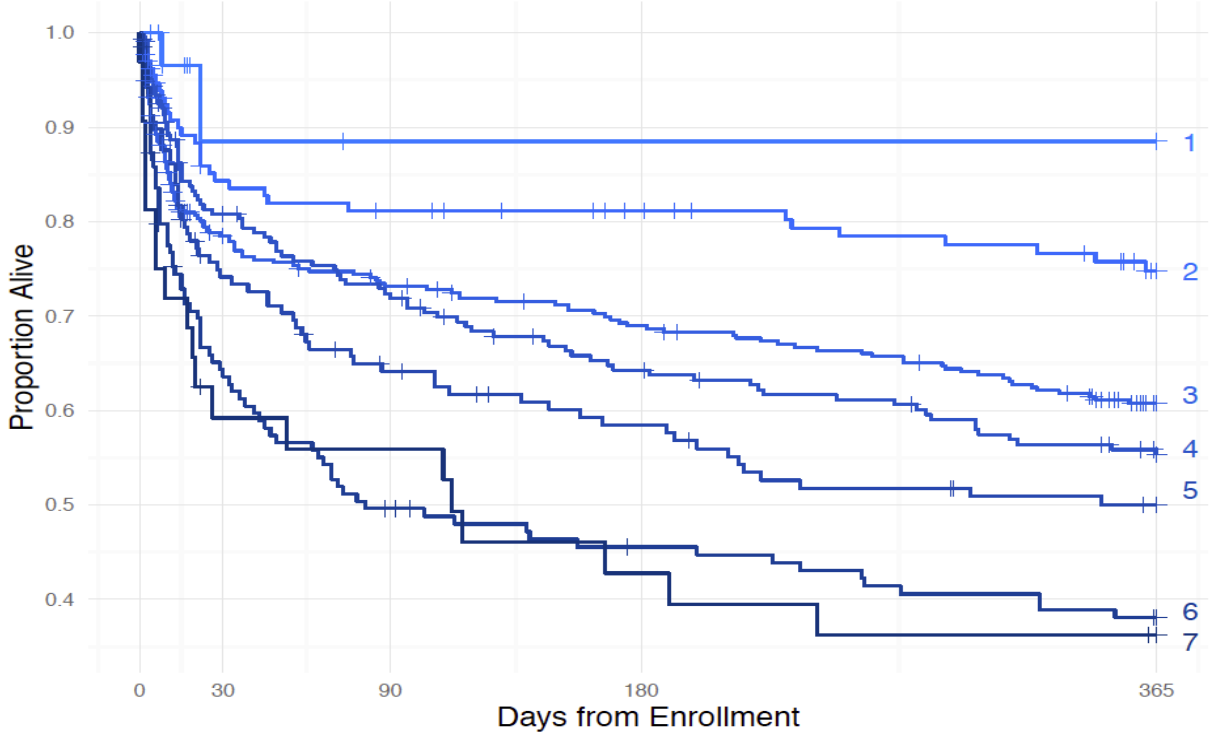
Bagshaw et al CMAJ 2014

Secondary Analysis of BRAIN/MIND ICU Studies

CFS Scores Stratified by Age



Mortality Stratified by CFS Score



Prevalence of frailty 30% (n=307) (50% age < 65 years)

↑ CFS score associated with ↑ mortality, ↑ disability in IADL and worse physical (not mental) HRQL

CFS scores not associated with disability in BADL or cognition

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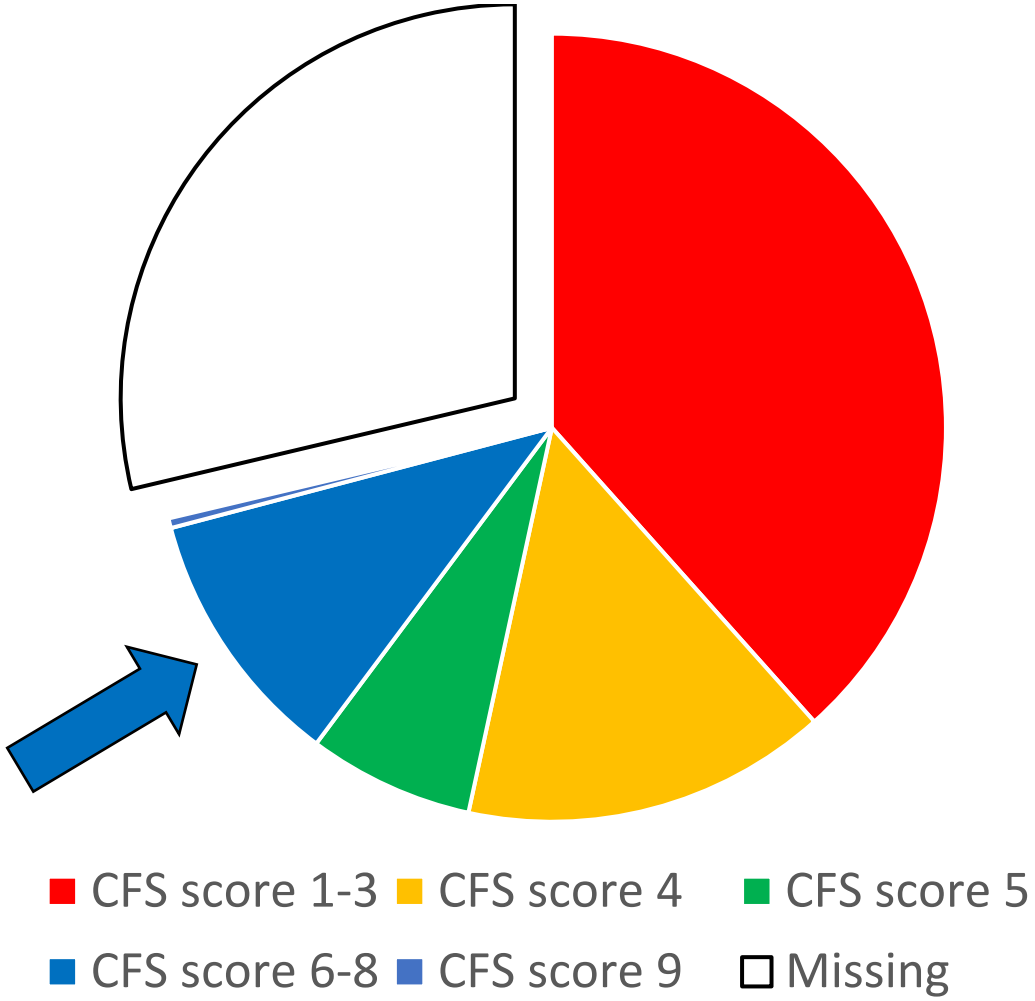
n=1040

Courtesy of Brummel N et al In Press

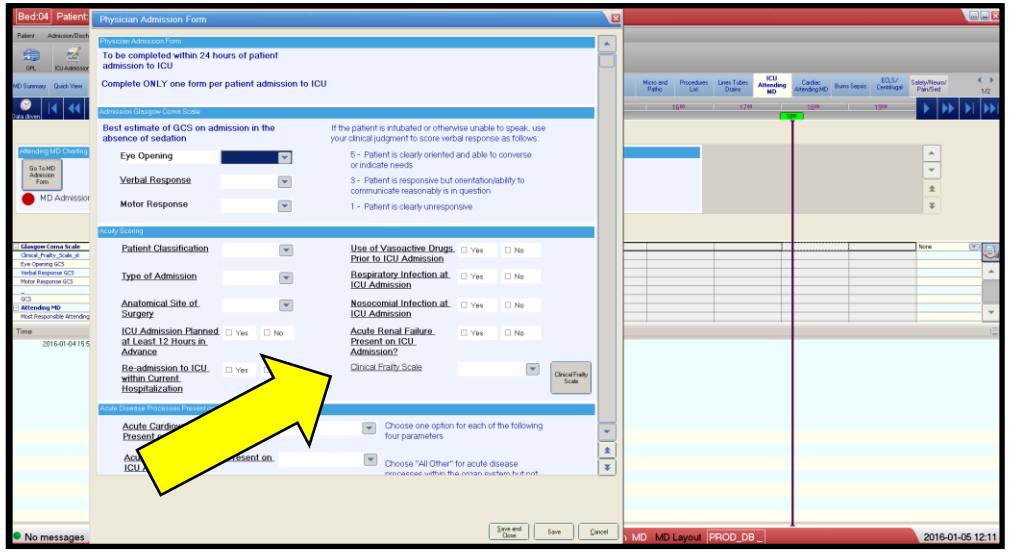
CFS Implementation: Preliminary Data



- 9,080 unique admissions to 15 Alberta ICUs between Jan 1 – Sept 9 2016
- All patients screened for frailty with CFS (28.7% missing)
- Prevalence ~ 17.5% (frail)
- Undertaking further validation work and dissemination performance reports

Frailty Measure eCritical (CIS) Implementation Pilot

1.



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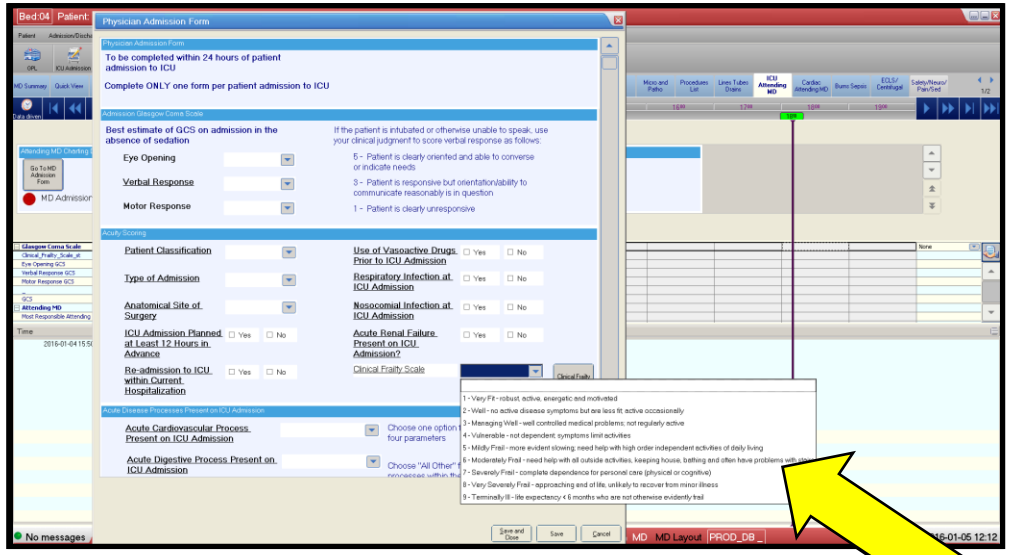

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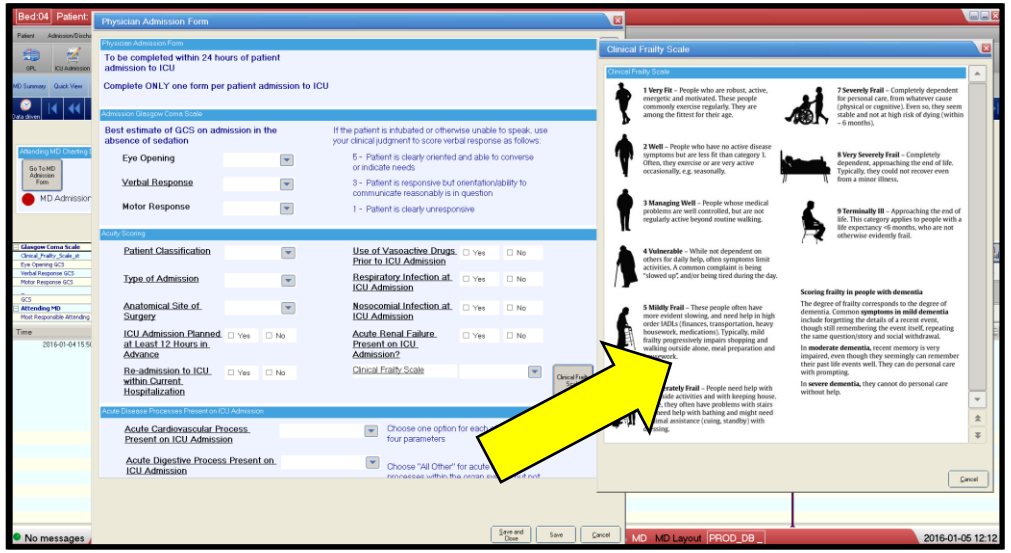

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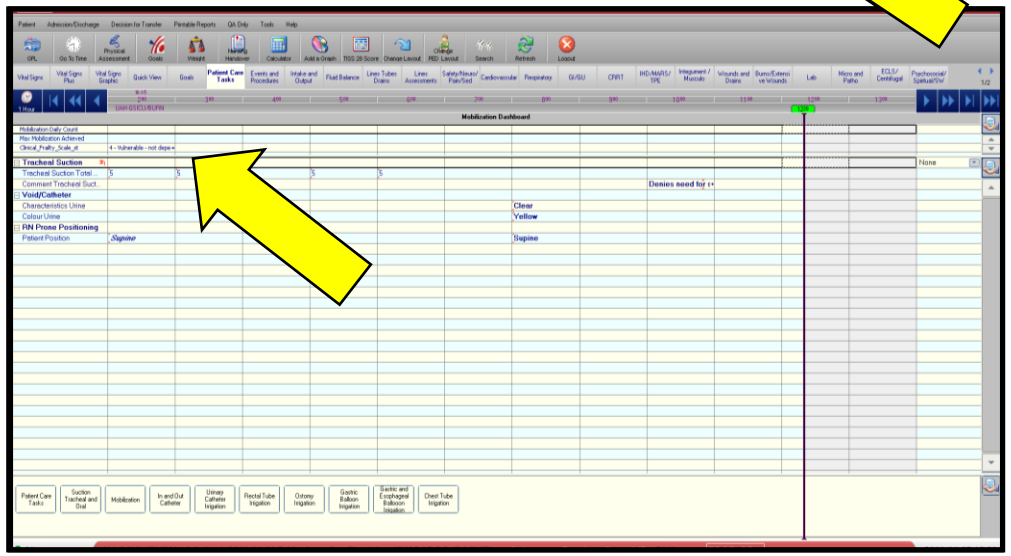

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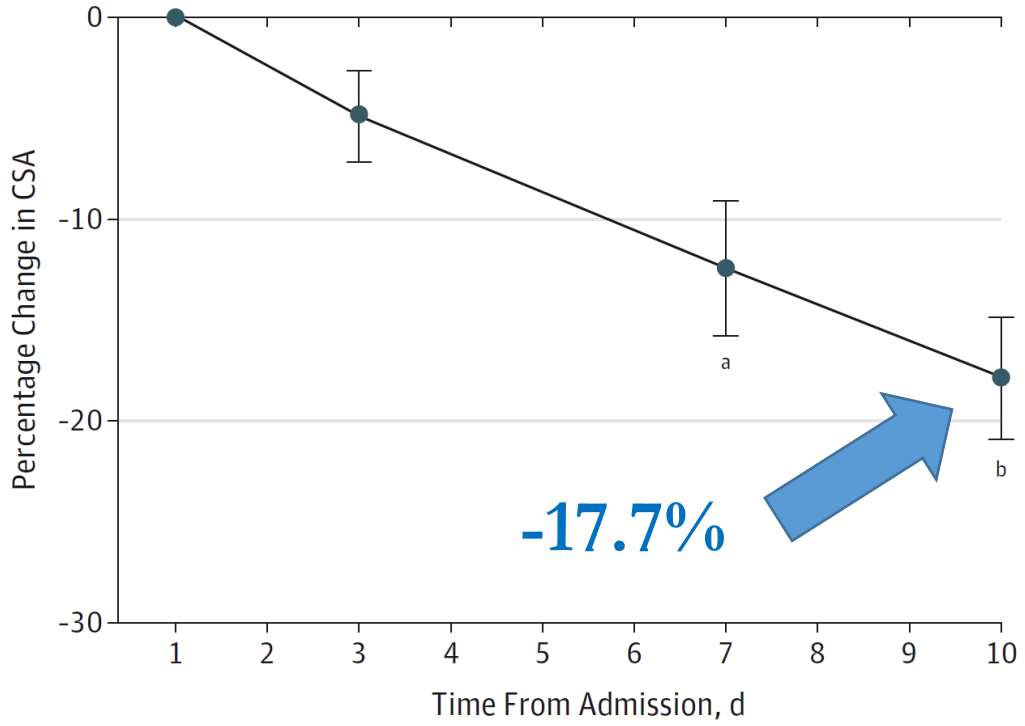
But…Does It Add Value?

1. **Better informed triage decisions ~**
   - Regarding to suitability and likely benefit for ICU support
2. **Guide and inform patient-centered decision-making ~**
   - Regarding scope/duration of ICU support (i.e., time-limited trials)
   - Regarding establishing/revisiting goals of care
   - Regarding managing post-ICU survivorship expectations and experience (i.e., impact on HRQL, new disability, institutionalization, rehospitalization)

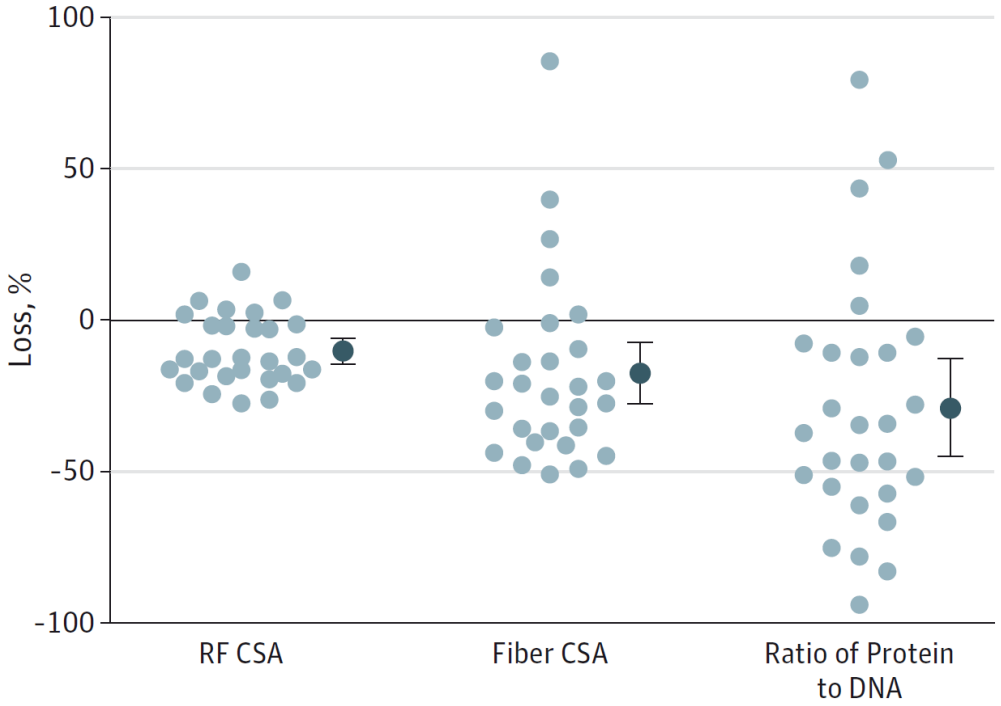
Acute Skeletal Muscle Wasting in Critical Illness

63 critically ill mechanically ventilated patients (age 54.7; APACHE II 23.5)

A Change in rectus femoris (RF) cross-sectional area (CSA) over 10 d

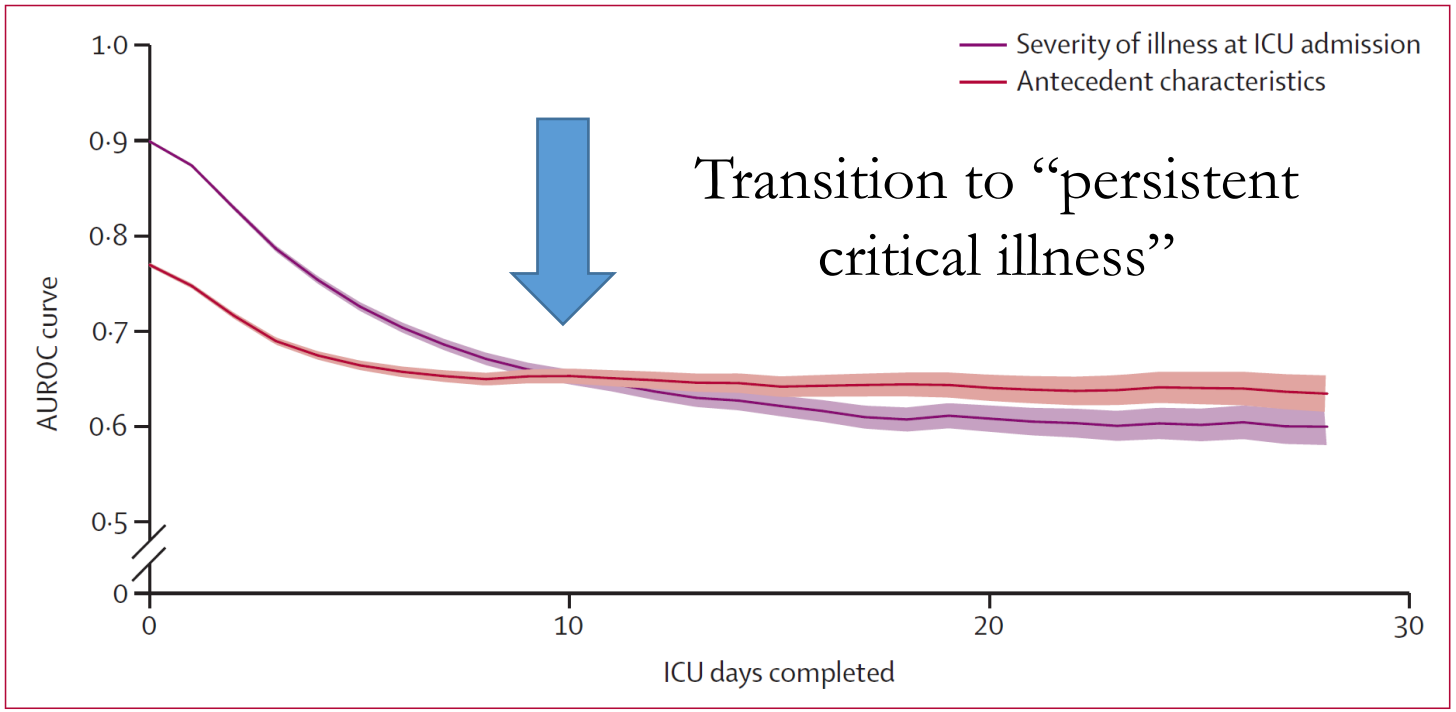


B Measures of muscle wasting in patients assessed by all 3 measures on both day 1 and day 7 (n = 28)



Puthucheary et al JAMA 2014

Timing of onset and burden of persistent critical illness in Australia and New Zealand: a retrospective, population-based, observational study



At ~ 10 days after ICU admission, acuity did not predict mortality better than antecedent characteristics (age, sex, comorbid disease) (variable transition point by case-mix and acuity)

Prevalence only 5.0% but accounted for 32.8% of ICU-bed days and only 46.5% returned home

Iwashyna et al Lancet Resp Med 2016

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An initiative of the ABIM Foundation

Critical Care Societies Collaborative - **Critical Care**

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AMERICAN THORACIC SOCIETY 1905 ATS® *We help the world breathe®* PULMONARY • CRITICAL CARE • SLEEP

Society of Critical Care Medicine The Intensive Care Professionals

Five Things Physicians and Patients Should Question

5

Don't continue life support for patients at high risk for death or severely impaired functional recovery without offering patients and their families the alternative of care focused entirely on comfort.

Patients and their families often value the avoidance of prolonged dependence on life support. However, many of these patients receive aggressive life-sustaining therapies, in part due to clinicians' failures to elicit patients' values and goals, and to provide patient-centered recommendations. Routinely engaging high-risk patients and their surrogate decision makers in discussions about the option of foregoing life-sustaining therapies may promote patients' and families' values, improve the quality of dying and reduce family distress and bereavement. Even among patients pursuing life-sustaining therapy, initiating palliative care simultaneously with ongoing disease-focused therapy may be beneficial.

5

Fields MJ, Cassel CK. Approaching death, improving care at the end of life. Washington, D.C.: National Academy Press; 1997. 437 p.

Angus DC, Barnato AE, Linde-Zwirble WT, Weissfeld LA, Watson RS, Rickert T, Rubenfeld GD; Robert Wood Johnson Foundation ICU End-Of-Life Peer Group. Use of intensive care at the end of life in the United States: an epidemiologic study. Crit Care Med. 2004;32(3):638–43.

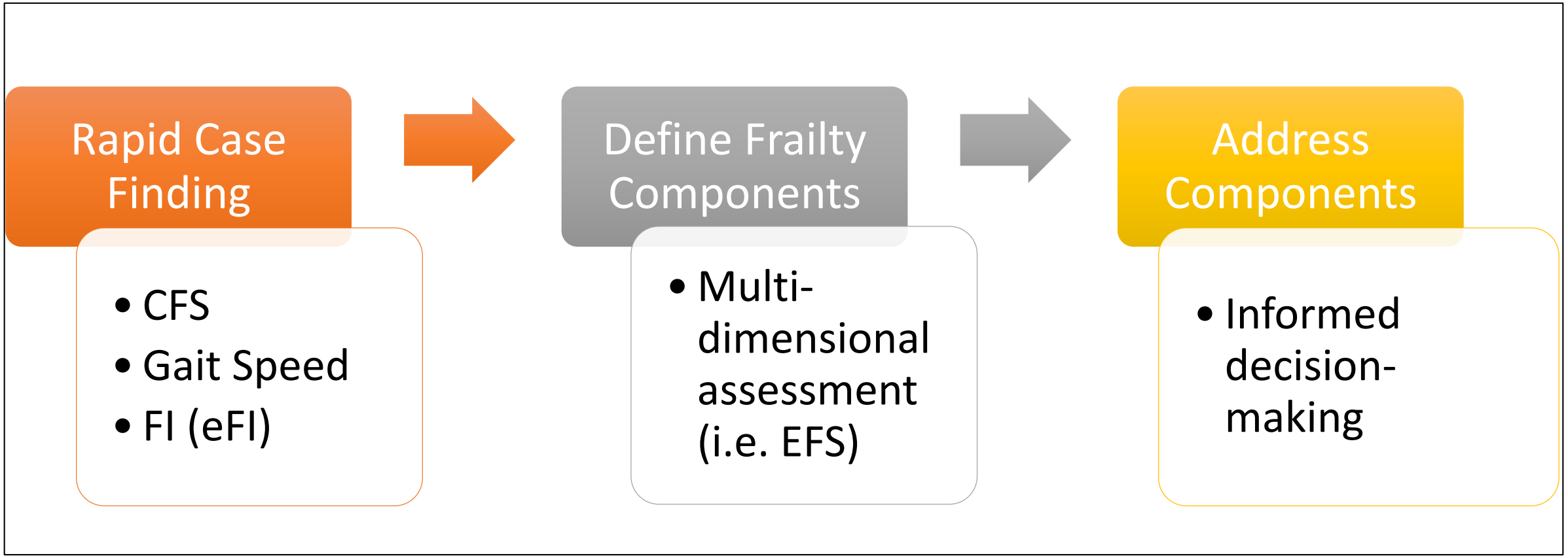
Curtis JR, Engelberg RA, Wenrich MD, Shannon SE, Treece PD, Rubenfeld GD. Missed opportunities during family conferences about end-of-life care in the intensive care unit. Amer J Respir Crit Care Med. 2005;171:844–9.

Gries CJ, Engelberg RA, Kross EK, Zatzick D, Nielsen EL, Downey L, Curtis JR. Predictors of symptoms of posttraumatic stress and depression in family members after patient death in the ICU. Chest. 2010;137(2):280–7.

And…How Else May It Add Value?

3. **Transitions of care ~**
   - Priorities/specialized needs for transition from ICU to ward setting
   - Priorities/specialized needs for hospital to community (i.e., CGA)
4. **Interventions (recognizing vulnerability)~**
   - Focused on maximizing physical recovery (i.e., minimizing avoidable disability)
   - Focused on cognitive, psycho-social, and emotional recovery
   - Focused on care-giver burden/experience
   - Focused strategy towards palliation

Frailty – An Integrated Model

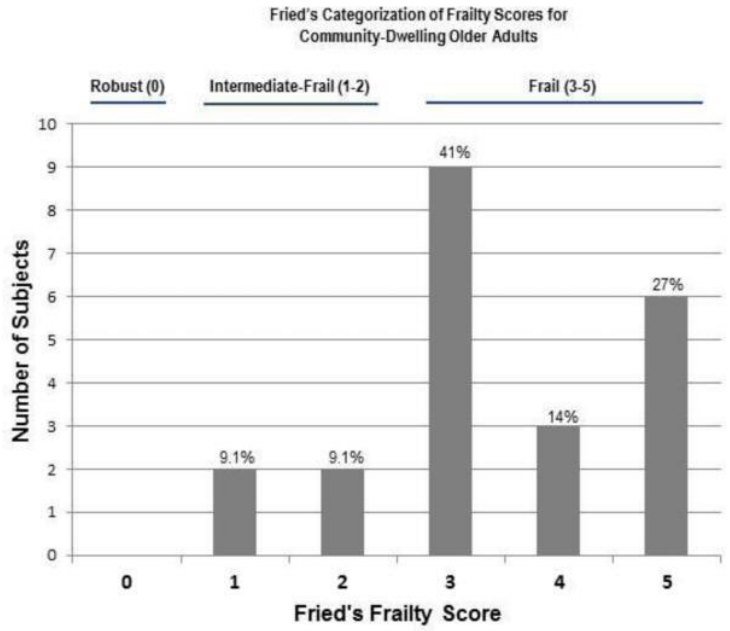


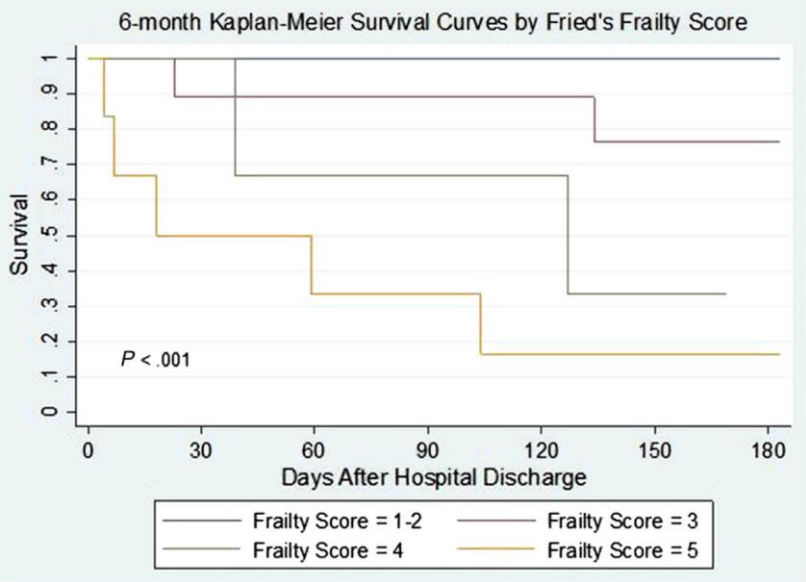
ICU admission → → ICU Transition → → Community Transition

The feasibility of measuring frailty to predict disability and mortality in older medical intensive care unit survivors ☆

Matthew R. Baldwin, MD, MS [a,*], M. Cary Reid, MD, PhD [b], Amanda A. Westlake, MD [a], John W. Rowe, MD [c], Evelyn C. Granieri, MD, MPH, MSEd [d], Hannah Wunsch, MD, MSc [e,f], Thuy-Tien Dam, MD [e], Daniel Rabinowitz, PhD [g], Nathan E. Goldstein, MD [h], Mathew S. Maurer, MD [i], David J. Lederer, MD, MS [a,e]

- Prospective cohort study of ICU survivors aged >= 65 years (n=22)
- Frailty assessed 4 day prior to hospital discharge using Physical Frailty Phenotype
- Prevalence 82% (n=18)
- Frailty associated with increased (unadjusted) rate of disability (1-month) and death (6-mon)
- Showed feasibility of "ward-based" assessment





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Baldwin MR et al Chest

Summary

- **Frailty** is a multi-dimensional syndrome contributing to vulnerability to adverse events:
  - can be measured in critically ill patients
  - is associated with ↑ risk adverse events, death, re-hospitalization
  - is associated with ↓ HRQL, new disability and ↑ functional dependence
  - identifies a vulnerable population
- **Frailty Assessment**
  - at ICU admission should focus on "case-finding" for near-term prognostication, guiding clinical care and decision-making and
  - after ICU should start to focus more comprehensive assessments, care transitions and specialist referral

Acknowledgements:

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Coordinators: Tracy Davyduke, Maliha Muneer, Nadia Baig, Barbara Artiuch, Kristen Reid, Gwen Thompson, Robin Scheelar, Jennifer Barchard, Dawn Opgenorth

Questions?

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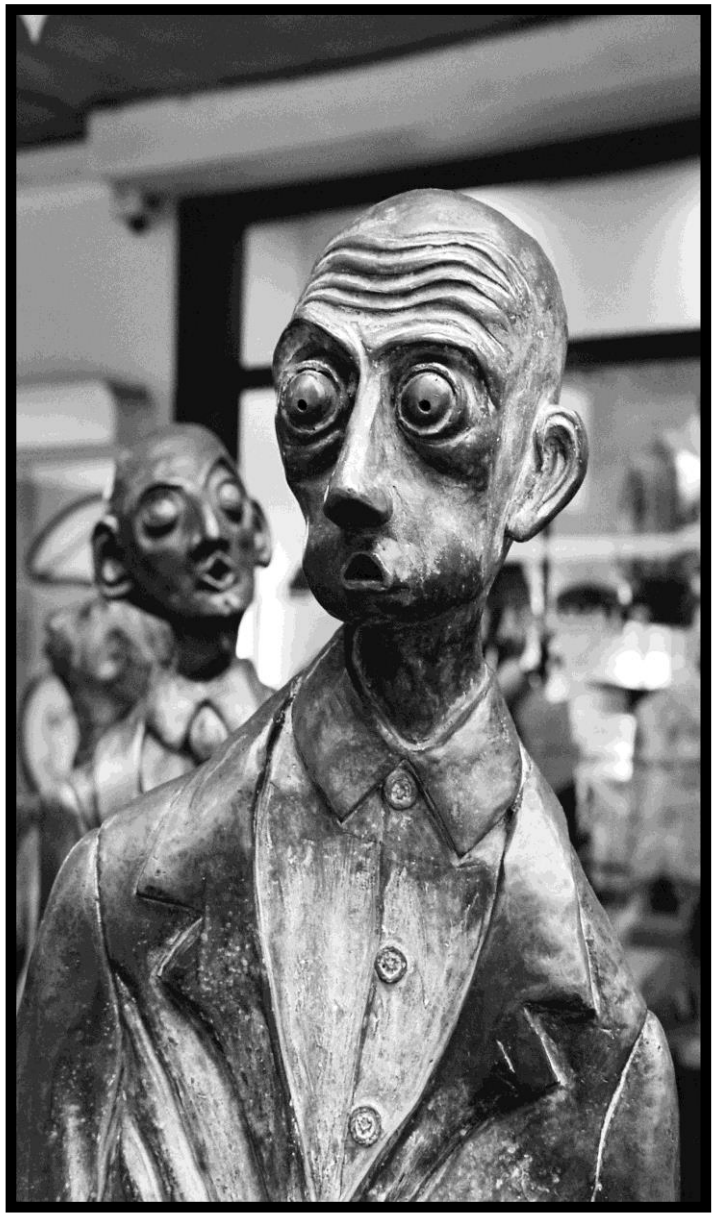

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University Hospital Foundation

CICF Canadian Intensive Care Foundation — Life from Knowledge

CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

University of Alberta

You never see it coming (frailty)

But maybe you can – consider how fit one is at age 60 years and that:

You are unlikely to be more fit at 80 years than you are at 60 years