

Sabato 7 aprile 2018

Aula Magna Nuovo Arcispedale S. Anna
Cona, Ferrara



Il Geriatra e gli aspetti della vulnerabilità (Fragilità) del paziente anziano con tumore operabile

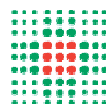
Stefano Volpato

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Università
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di Ferrara

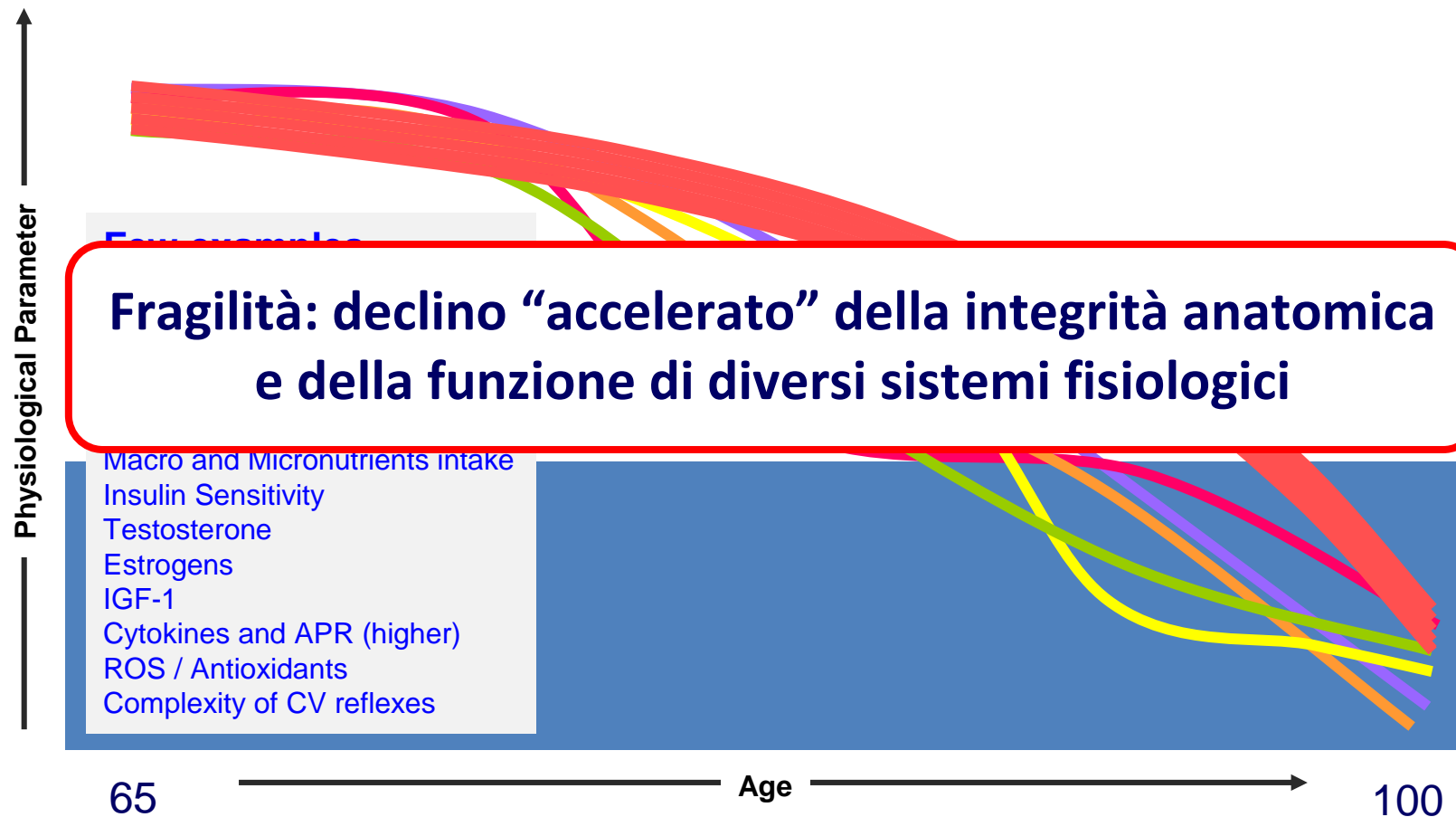
Dipartimento
di Morfologia, Chirurgia
e Medicina Sperimentale



SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Unità Sanitaria Locale di Ferrara

Invecchiamento, Meccanismi Omeostatici e Fragilità

Aging: Declino progressivo della integrità anatomica e funzionale di diversi sistemi fisiologici





Fragilità

“Una condizione di aumentata vulnerabilità allo stress dovuta alla riduzione età-correlate nella riserva funzionale di molteplici sistemi fisiologico e in particolare di quelli neuromuscolare, metabolico e immunitario”

American Geriatric Society 2004



“Sindrome medica, ad eziologia multifattoriale, caratterizzata da ridotta forza by diminished strength, resistenza, e diminuta funzione fisiologica, che aumenta la vulnerabilità del soggetto allo sviluppo di disabilità e/o morte”



Frailty Consensus: A Call to Action
J Am Med Dir Assoc 2013



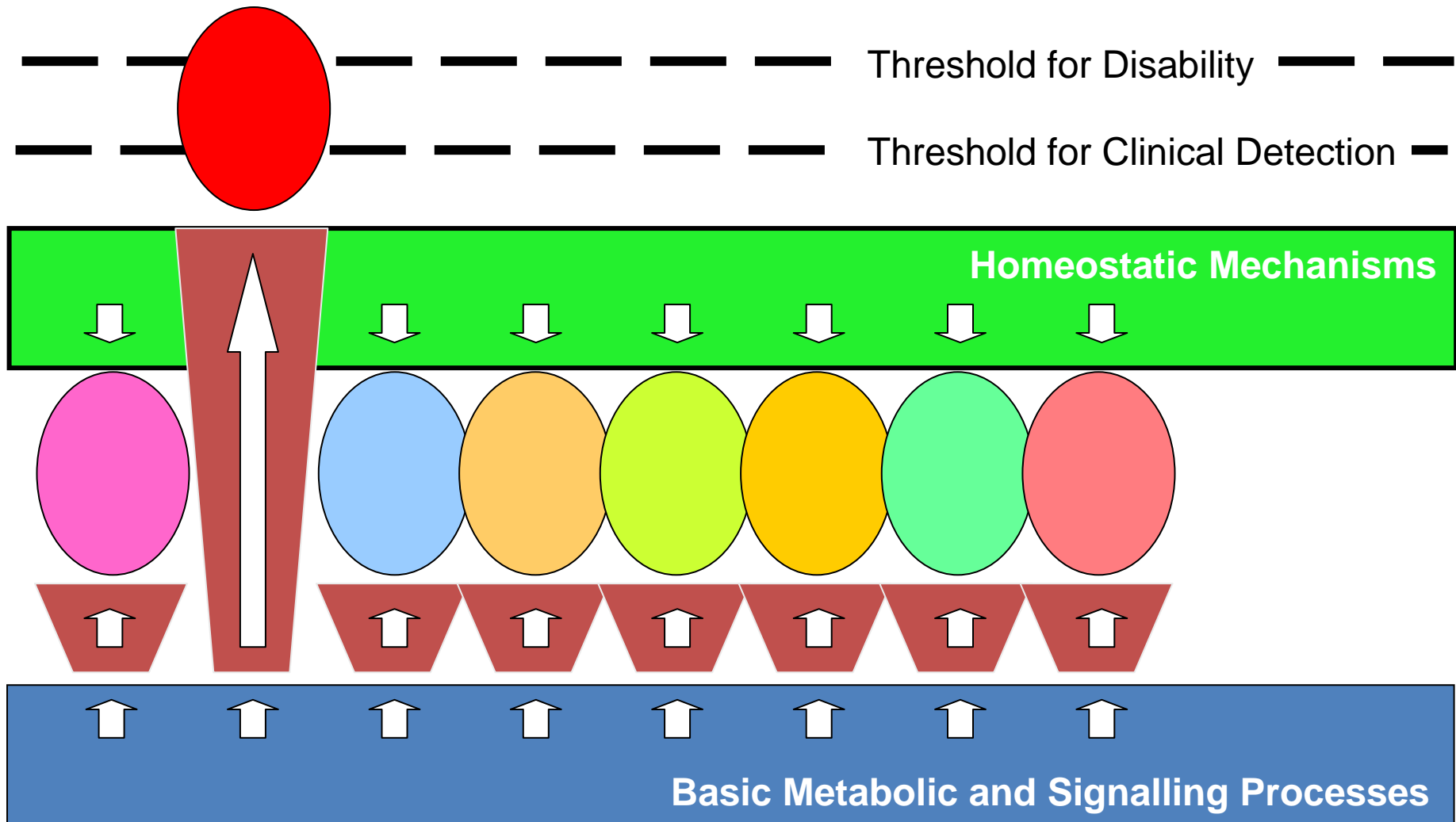
La Fragilità in Medicina Geriatrica

- La fragilità viene definita come una condizione dinamica caratterizzata da:
 1. *modificazioni fisiopatologiche età-correlate*
 2. *di natura multi-sistemica*
 3. *con aumentata vulnerabilità*
 4. *associata ad un aumentato rischio di outcome negativi come:*
 - *Disabilità*
 - *Cadute*
 - *Ospedalizzazione*
 - *Istituzionalizzazione*
 - *Morte*

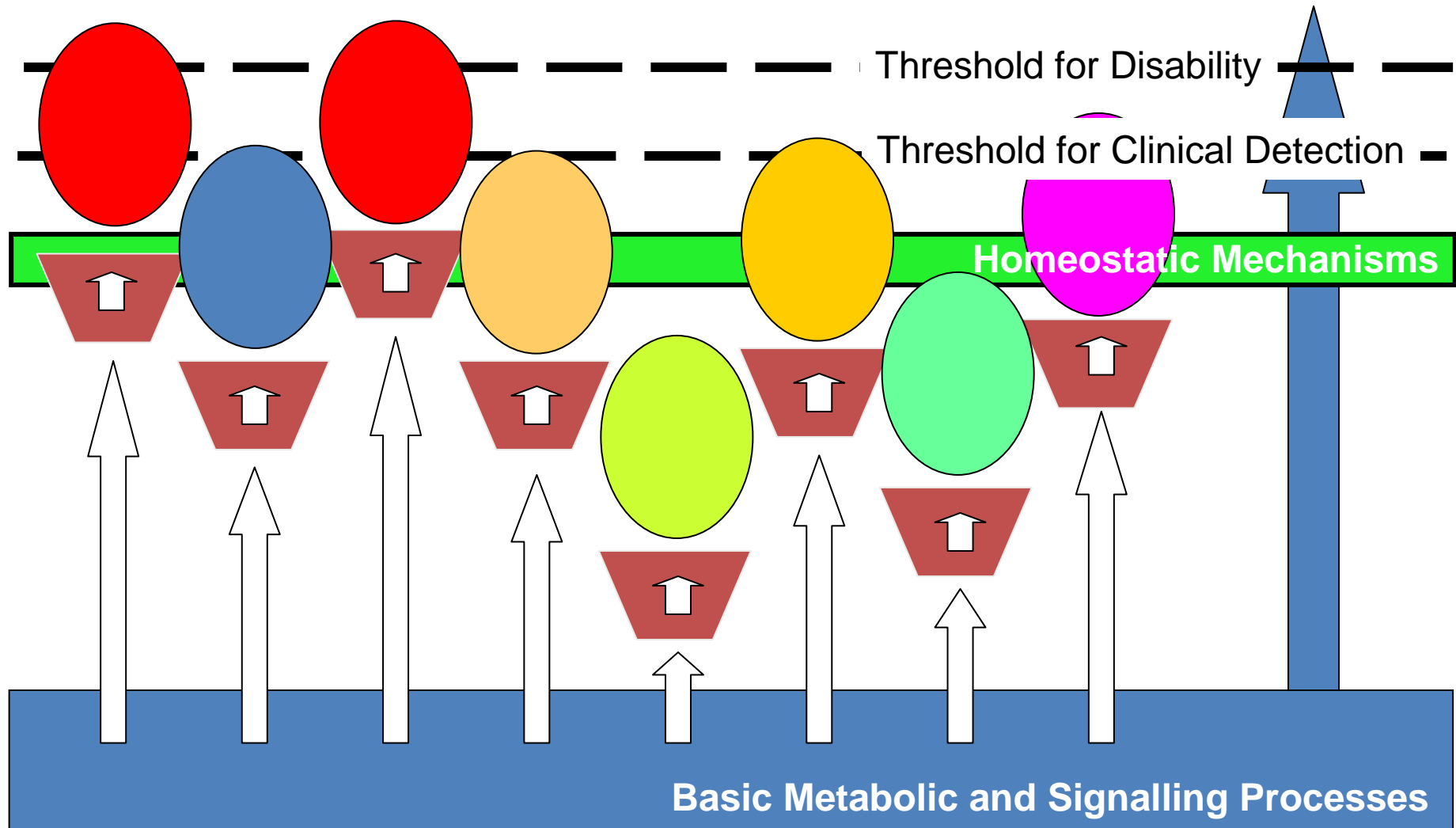


E' concettualmente diversa da comorbilità e disabilità

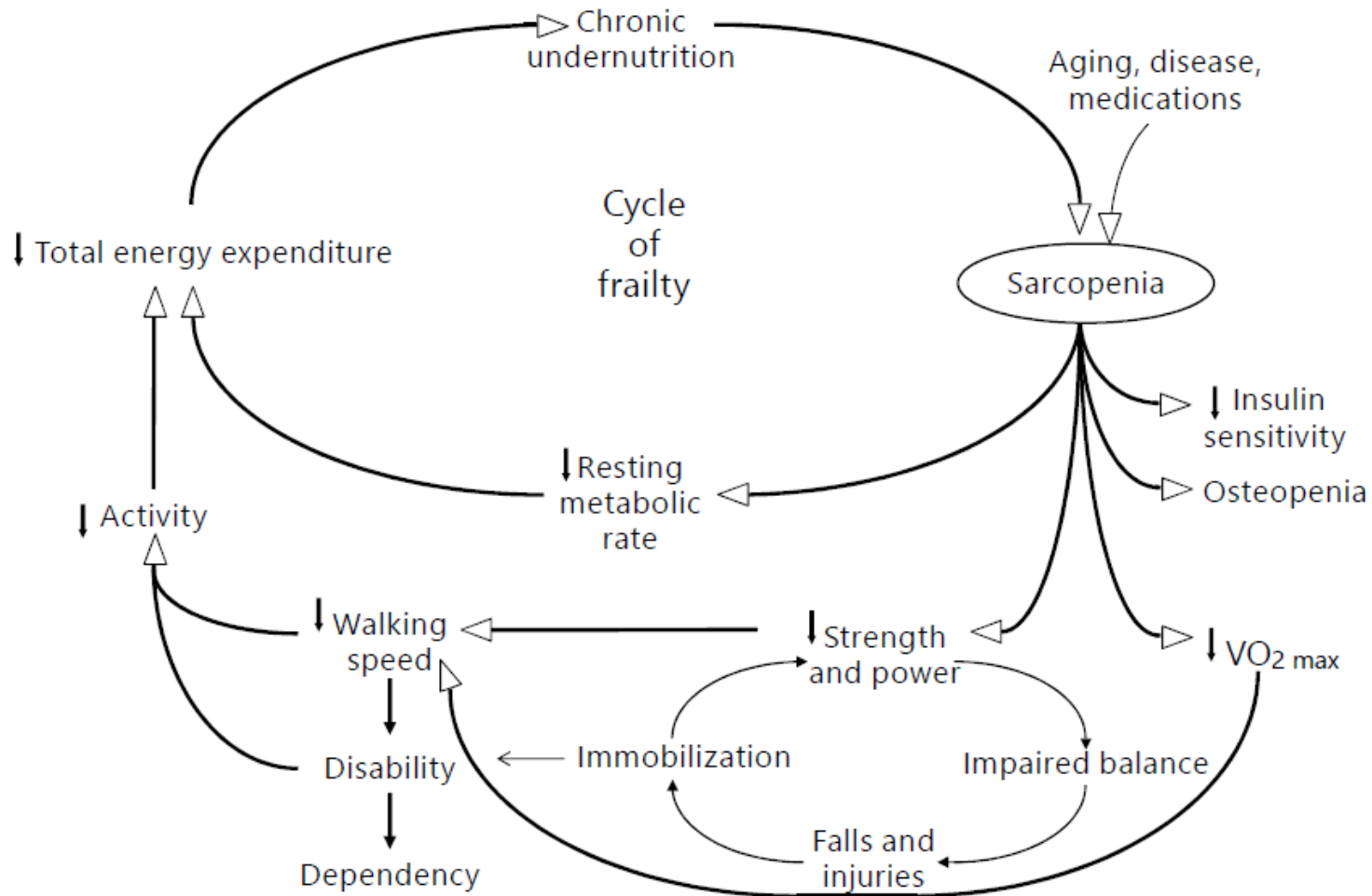
SINGOLA MALATTIA



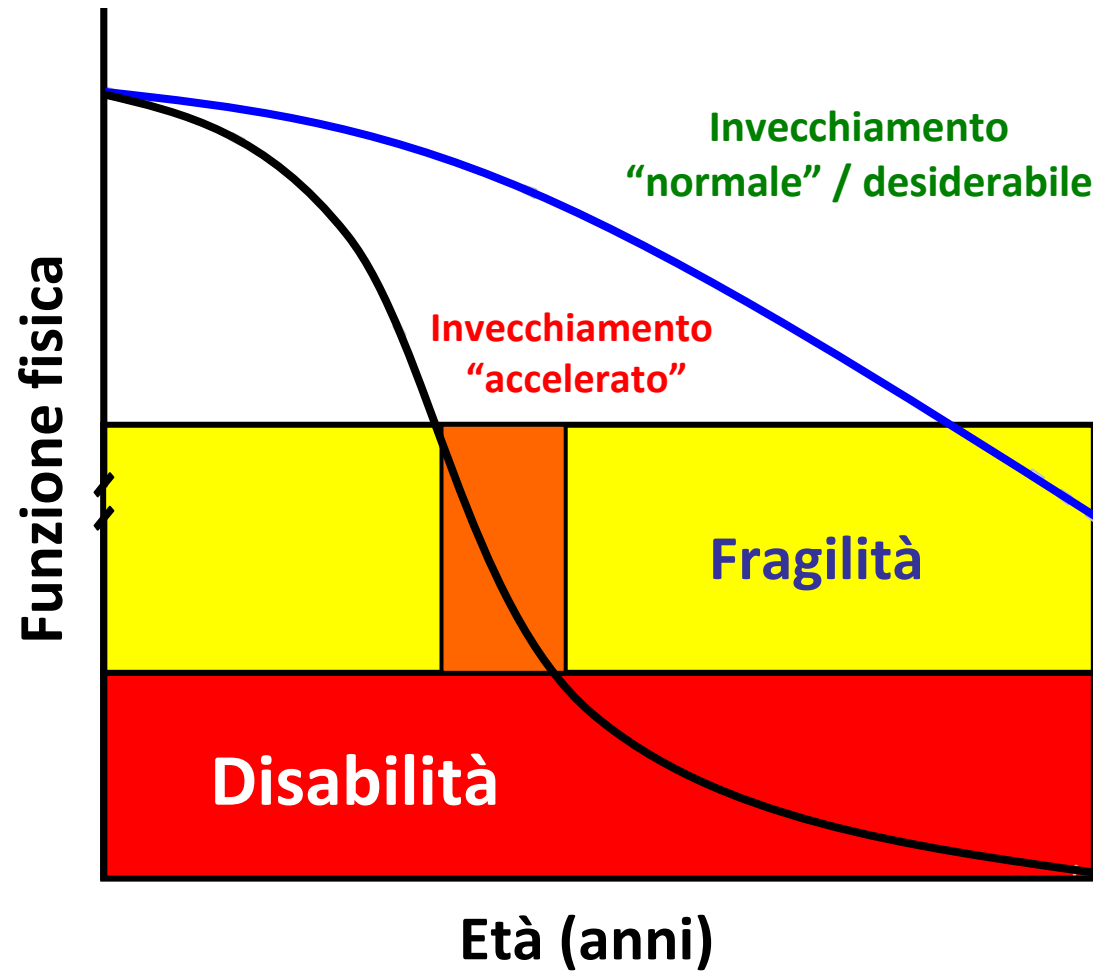
FRAGILITÀ



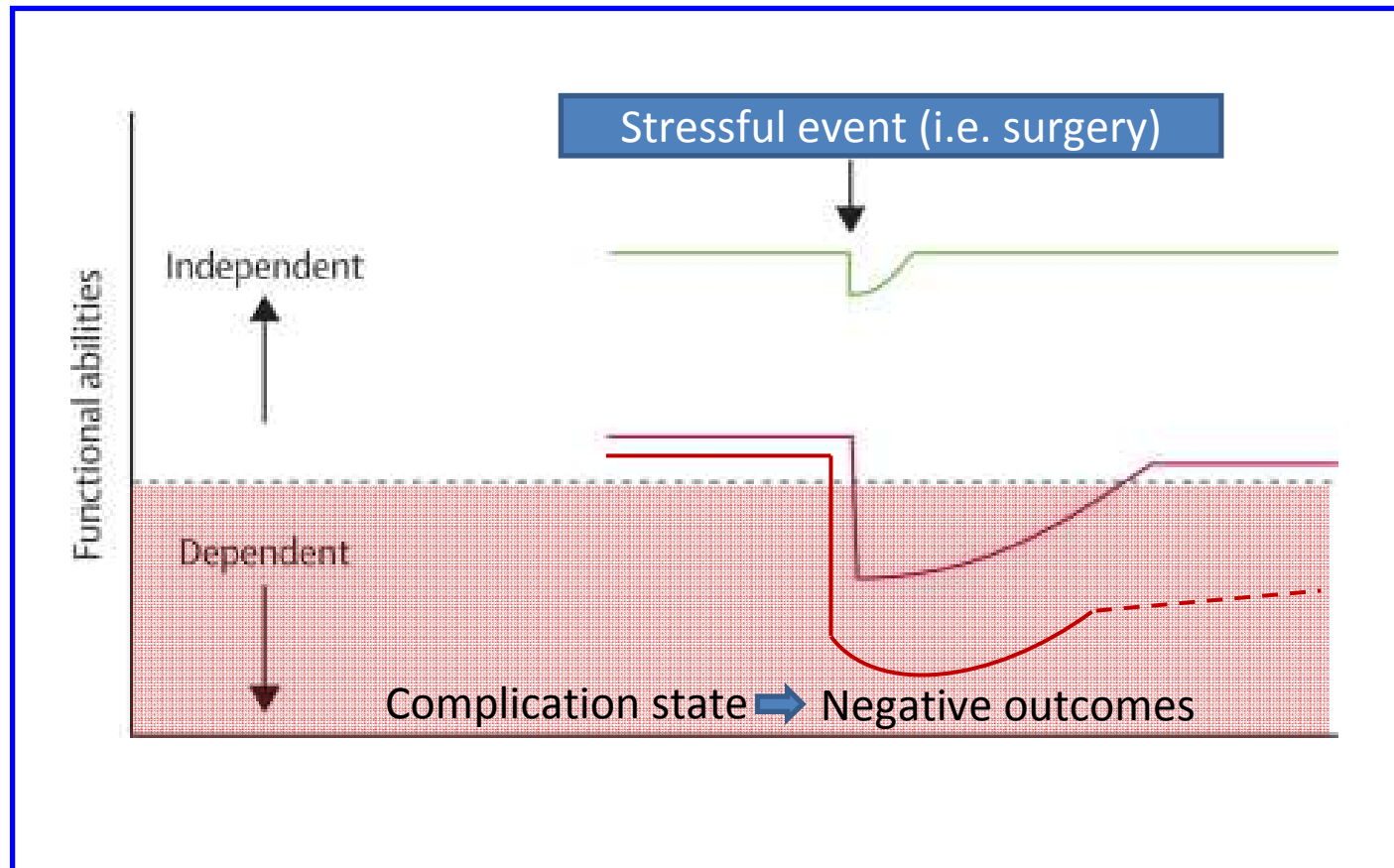
Il ciclo della Fragilità



Invecchiamento e declino funzionale



Vulnerability of frail elderly to a sudden change in health status after illness or stress



Fit/resilient

Pre-Frail

Frail



Frailty Problem



No single operational definition or simple assessment tool for frailty has been agreed upon either locally, nationally or internationally !!



Review Article

Frailty measurement in research and clinical practice: A review

Elsa Dent^{a,b,*}, Paul Kowal^{c,d}, Emiel O. Hoogendijk^{e,f}

Index	Country of origin	Time (min)	# items	Components	Frailty	Requirements of frailty measurements					Measurement used in the clinical or population setting?
						Data CGA ^b	Special equipment	Assessor training	Valid & reliable	Outcome prediction	
CHS	USA	<10	5	Weight loss, low physical activity, exhaustion, slowness, weakness	Frailty ≥ 3 items; pre-frail 1–2 items; Robust = none	x	✓	✓	✓	✓	Both
FI-CD	Canada	20–30	30+	Accumulated health deficits: score of 0 (no deficits) to 1.0 (all deficits)	A continuous score. Frailty cut-off suggested >0.25	✓	x	✓	✓	✓	Both
FI-CGA	Canada	<15	30+	10 domains, 52 items (originally 14): including ADL, IADL, Co-morbidities, Mood & Cognition	A continuous score. Frailty cut-off suggested >0.25	✓	x	✓	✓	✓	Clinical
SOF	USA	<5	3	Weight Loss, Exhaustion, Unable to Rise from Chair 5 times	Frailty ≥ 2 items; pre-frail = 1 item; robust = 0 items	x	x	x	✓	✓	Both
EPS	Canada	<5	9	Cognition, health (2×), hospitalisation, social support, nutrition, mood, function, continence	Frailty = scores ≥ 7	x	x	✓	✓	✓	Clinical
FRAIL	USA	<10	5	Fatigue, Resistance, Ambulation, Illness, Loss of Weight	Frailty ≥ 3 items; Pre-frail 1–2 items; robust = 0 items	✓	x	x	✓	More studies needed	Both
CFS	Canada	<5	1	Visual and written chart for frailty with 9 graded pictures. 1 = very fit; 9 = terminally ill	A continuous score. Frailty cut-off point ≥ 5	x	x	✓	✓	✓	Clinical
MPI	Italy	<15	8	Co-morbidity, Nutrition, Cognition, Polypharmacy, Pressure Sore Risk, Living Status, ADL, IADL	Frailty > 0.66; Pre-frailty = 0.34–0.66; robust < 0.34	✓	x	✓	✓	More studies needed	Both
TFI	The Netherlands	<15	15	Self-reported in 3 domains: physical, psychological and social	Frailty = scores ≥ 5	x	x	x	✓	More studies needed	Population-level screening
PRISMA-7	Canada	<10	7	Self-reported: age (>85 years), male, social support and ADLs	Frailty = scores ≥ 3	x	x	x	✓	More studies needed	Population-level screening
GFI	The Netherlands	<15	15	Self-reported in 4 domains: physical, cognitive, social and psychological	Frailty = scores ≥ 4	x	x	x	x	More studies needed	Population-level screening
SPQ	Canada	<5	6	Self-reported: living alone, polypharmacy, mobility, eyesight, hearing, memory	Frailty = scores ≥ 2	x	x	x	x	More studies needed	Population-level screening
GFST	France	<5	6	2 parts: (i) self-report (lives alone, weight loss, fatigue, mobile, memory, gait) (ii) clinical judgement	Identified by clinical judgement, after screening	x	x	✓	x	More studies needed	Population-level screening
KCL	Japan	<10	25	25 items from CGA, scoring as per FI-CGA	A continuous score. Frailty cut-off suggested >0.25	✓	x	✓	✓	More studies needed	Population-level screening

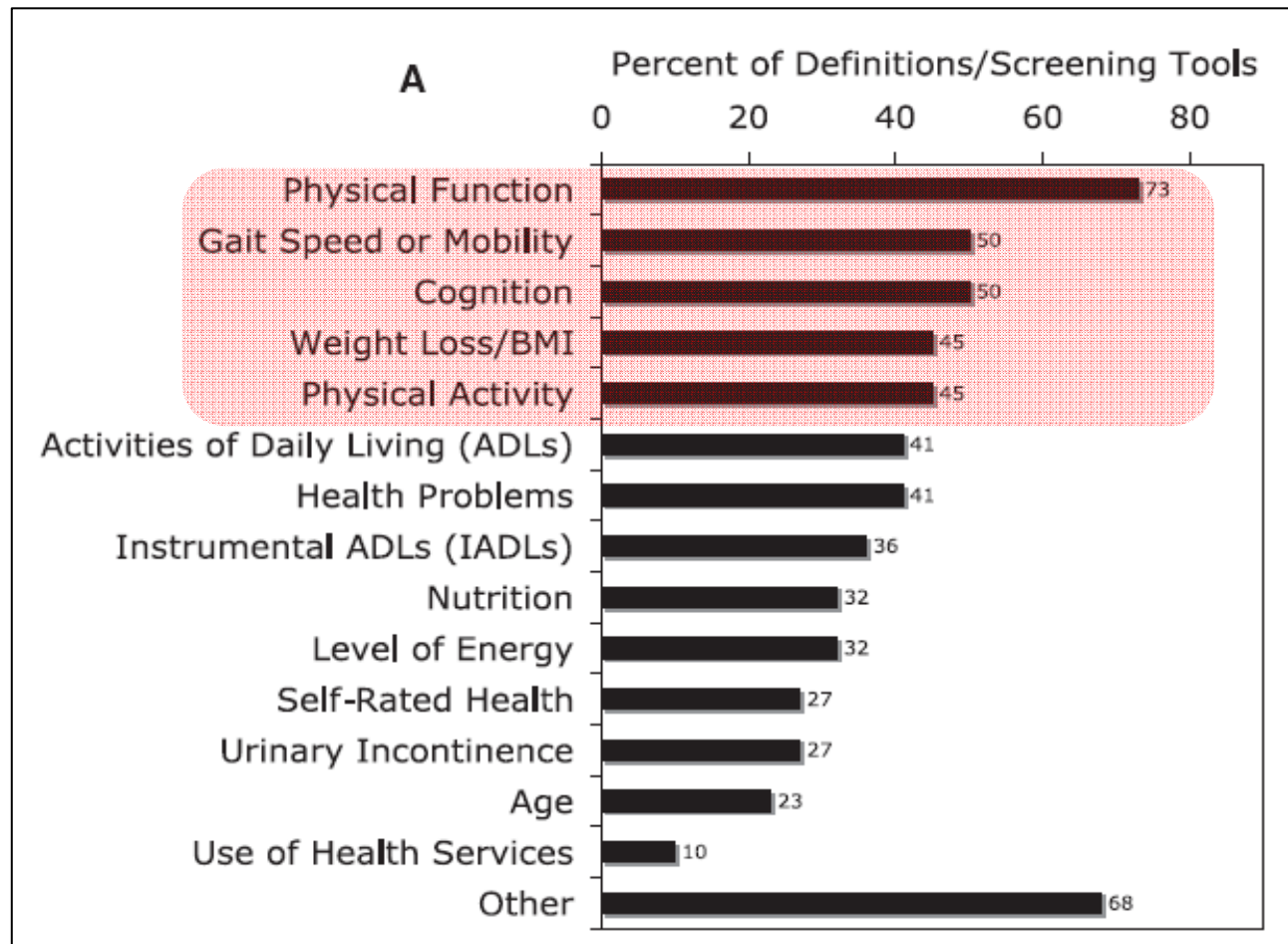
Abbreviations: CHS = Cardiovascular Health Study Index (Fried's Frailty Phenotype); FI-CD = Frailty Index of Accumulated Deficits; FI-CGA = Frailty Index derived from Comprehensive Geriatric Assessment; SOF = Study of Osteoporotic Fracture (SOF) Index; EPS = Edmonton Frailty Scale; FRAIL = Fatigue, Resistance, Ambulation, Illness and Loss of Weight Index; CFS = Clinical Frailty Scale; MPI = Multidimensional Prognostic Index; TFI = Tilburg Frailty Index; GFI = Groningen Frailty Indicator; SPQ = Sherbrooke Postal Questionnaire; GFST = GÉrontopôle Frailty Screening Tool (GFST); KCL = Kihon Check-list.

^a Frailty measurements are evaluated by clinical or research staff, unless otherwise indicated (for example, by patient self-report). All frailty measurements were based on a biological theory, with the exception of the CFS.

^b 'Data CGA' implies that the data for the frailty measurement is obtainable readily from a Comprehensive Geriatric Assessment (CGA).



Prevalence of *Identifying Factors* for frailty in definitions and screening tools

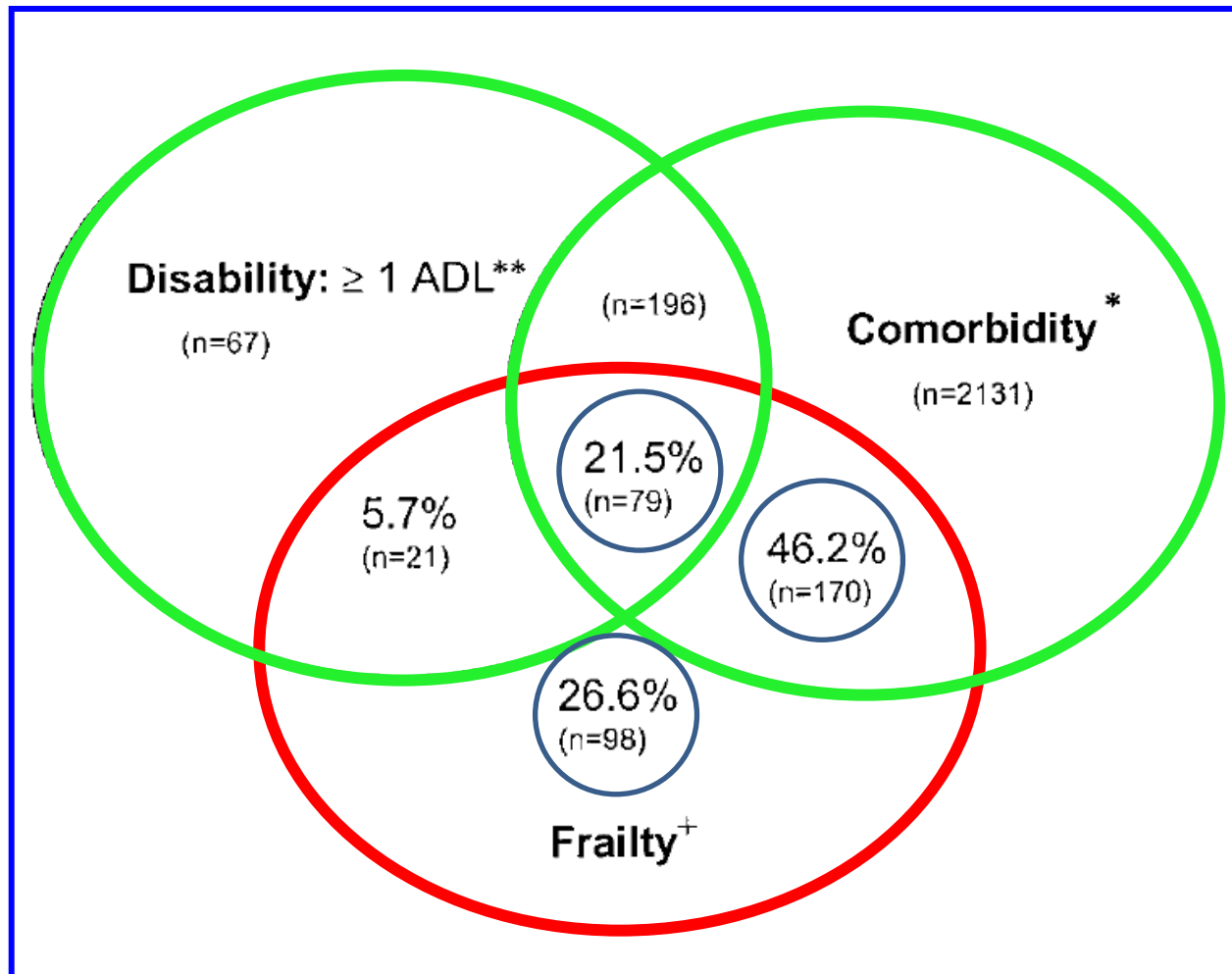


La Sindrome Clinica della Fragilità: fenotipo clinico

1. **Perdita di Peso:** >10 “pounds” nell’ultimo anno (involontaria)
2. **Debolezza:** “grip strength”, aggiustata per sesso e BMI
3. **Esaurimento/affaticabilità:** autoriferita
4. **Lentezza:** velocità del cammino sui 4 metri, aggiustata per sesso e altezza
5. **Ridotta attività fisica:** Kcals/settimana, stratificata per sesso

Fragilità è presente se sono soddisfatti 3/5 criteri

Rapporto tra Fragilità, Disabilità e Comorbidità



Mortality Risk Along the Frailty Spectrum: Data from the National Health and Nutrition Examination Survey 1999 to 2004

Table 2. Frailty Components and rates

Frailty Components	Five-Component Model	Four-Component Model ^a
	n (weighted %)	
Difficulty walking between rooms	586 (10.0)	
Body mass index <18.5 kg/m ²	59 (1.3)	
Less activity than peers	735 (14.1)	
Gait speed <0.8 m/s ^b	1,865 (31.3)	n/a
Difficulty lifting 10 pounds	1,455 (27.1)	
Number of components		
0	2,246 (50.4)	3,063 (67.0)
1	1,486 (27.7)	1,026 (21.7)
2	709 (12.6)	414 (7.8)
3	371 (6.4)	189 (3.4)
4	167 (2.7)	5 (0)
5	3 (0)	n/a
Frailty status		
Robust	2,246 (50.4)	3,158 (65.4)
Prefrail	2,195 (40.3)	1,561 (30.2)
Frailty	541 (9.2)	263 (4.5)

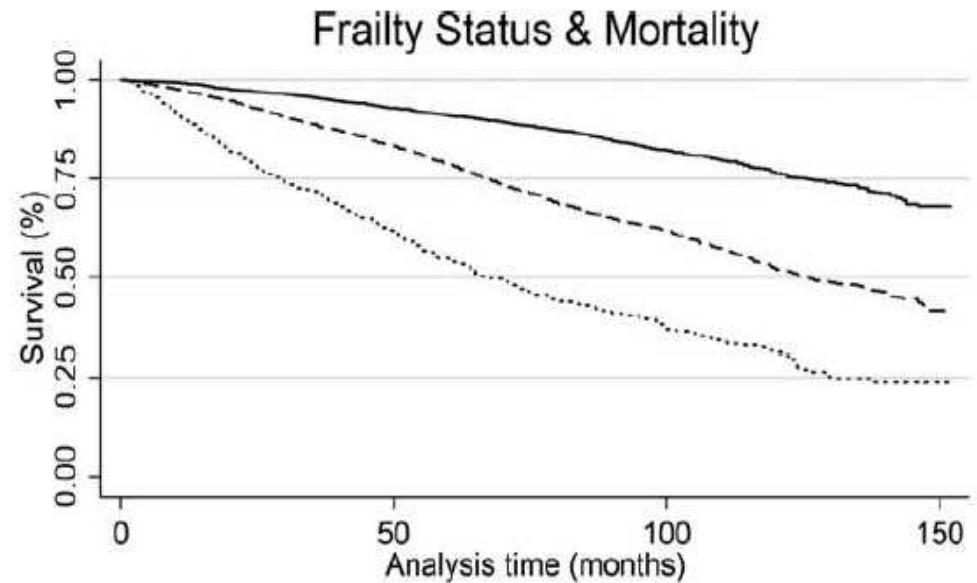


Table 3. Association Between Frailty and Overall and Cardiovascular Mortality

Mortality	Model 1	Model 2	Model 3
	Hazard Ratio (95% Confidence Interval)		
Overall			
Prefrail	2.40 (2.16–2.67)	1.79 (1.60–2.01)	1.64 (1.45–1.85)
Frail	4.97 (4.34–5.69)	3.89 (3.36–4.51)	2.79 (2.35–3.30)
Cardiovascular			
Prefrail	2.82 (2.28–3.48)	2.07 (1.65–2.60)	1.84 (1.45–2.34)
Frail	3.72 (2.85–4.87)	4.79 (3.61–6.34)	3.39 (2.45–4.70)



Association of a Cancer Diagnosis With Vulnerability and Frailty in Older Medicare Beneficiaries

Supriya Gupta Mohile, Ying Xian, William Dale, Susan G. Fisher, Miriam Rodin, Gary R. Morrow, Alfred Neugut, William Hall

Characteristic	Cancer group, Noncancer group,		P‡
	No. (%)†	No. (%)†	
Functional limitations			
ADL limitations	794 (31.9)	2959 (26.9)	<.001
Bathing or showering	335 (13.3)	1172 (10.2)	<.001
Dressing	212 (8.4)	728 (6.4)	<.001
Eating	81 (3.3)	271 (2.5)	.033
Getting in or out of bed or chair	352 (14.2)	1369 (12.5)	.022
Walking	671 (27.0)	2570 (23.2)	<.001
Using toilet	146 (5.7)	586 (5.3)	.373
IADL limitations	1220 (49.5)	4606 (42.3)	<.001
Using telephone	218 (8.2)	812 (6.9)	.023
Doing light housework	424 (17.2)	1562 (13.9)	<.001
Doing heavy housework	1083 (44.0)	4035 (36.9)	<.001
Preparing meals	409 (15.9)	1540 (13.5)	.003
Shopping	443 (17.2)	1716 (14.9)	.007
Managing money	266 (10.0)	1086 (9.5)	.434
Geriatric syndromes	1456 (60.8)	5661 (53.9)	<.001
Dementia and memory loss	288 (11.5)	1190 (10.5)	.181
Depression	614 (26.1)	2481 (23.8)	.039
Falls	633 (25.9)	2288 (21.6)	<.001
Incontinence	375 (15.6)	1220 (11.1)	<.001
Osteoporosis	593 (24.3)	2103 (19.8)	<.001
Vulnerability or frailty			
Vulnerability (VES-13 \geq 3)	1184 (45.8)	4513 (39.5)	<.001
Frailty§	1910 (79.6)	7722 (73.4)	<.001
Poor or fair self-rated health status	661 (27.4)	2191 (20.9)	<.001

Impact of frailty on outcomes after discharge in older surgical patients: a prospective cohort study

Yibo Li BMSc, Jenelle L. Pederson MSc, Thomas A. Churchill PhD, Adrian S. Wagg MBBS, Jayna M. Holroyd-Leduc MD, Kannayiram Alagiakrishnan MD, Raj S. Padwal MD MSc, Rachel G. Khadaroo MD PhD

CMAJ 2018 February 20;190:E184-90. doi: 10.1503/cmaj.161403

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.

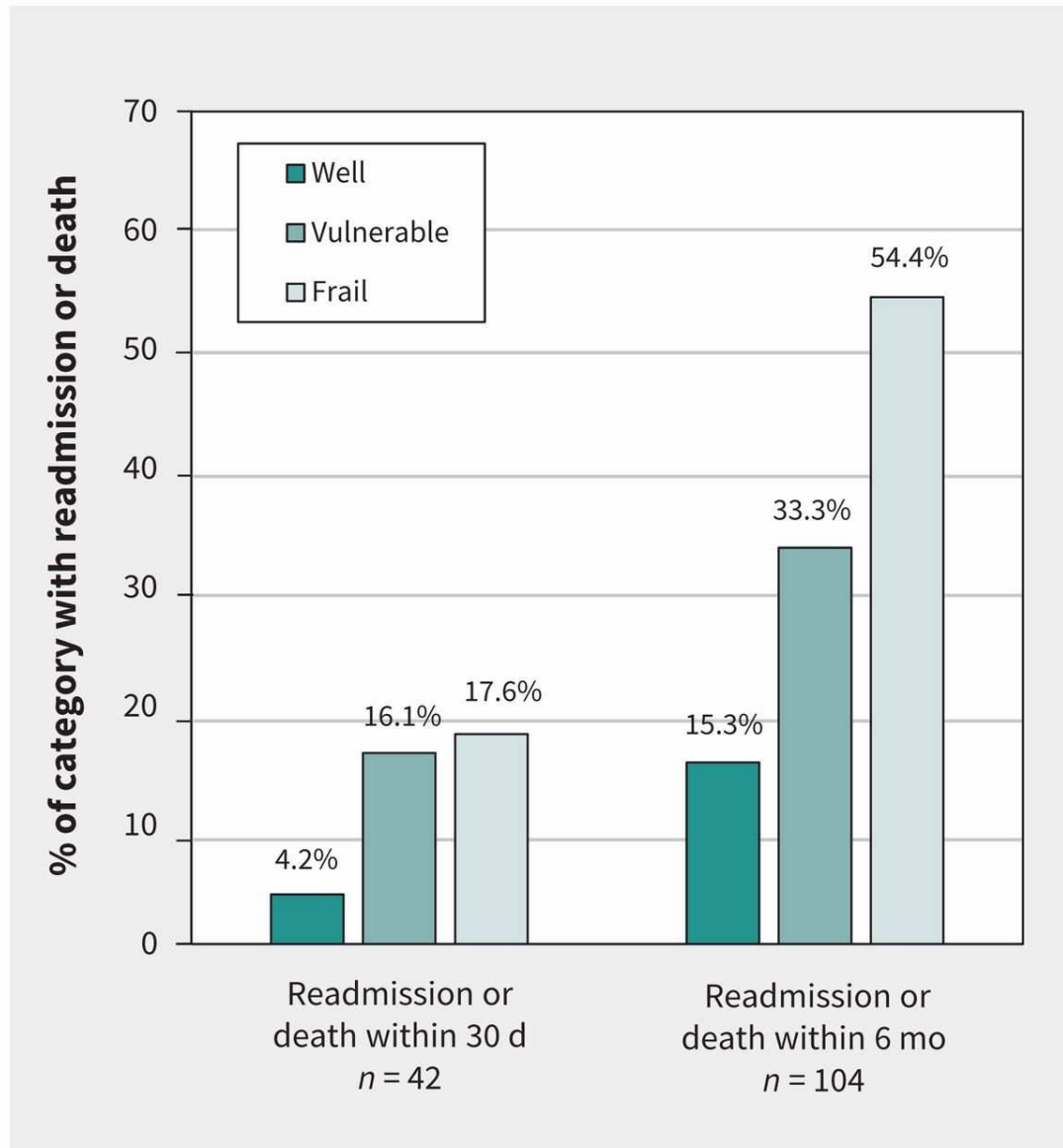
2. K. Rockwood et al. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

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Table 1: Baseline characteristics of older patients discharged from hospital after emergency abdominal surgery

Characteristic	Preadmission level of frailty*; no. (%) of patients†			p value‡
	Well n = 72	Vulnerable n = 168	Frail n = 68	
Age, yr, mean ± SD	73.9 ± 7.0	75.2 ± 6.7	79.9 ± 9.2	< 0.001
Sex, female	30 (41.7)	75 (44.6)	35 (51.5)	0.2
Ethnicity, white	57 (79.2)	122 (72.6)	52 (76.5)	0.7
Marital status, married or common-law§	52 (72.2)	122 (72.6)	37 (54.4)	0.03
Charlson Comorbidity Index, median (IQR)§	0 (0–1)	1 (0–2)	2 (1–3)	< 0.001
BMI, mean ± SD	26 ± 4.5	27.6 ± 6.4	26.9 ± 6.5	0.4
No. of admission medications, mean ± SD	1.3 ± 0.5	1.5 ± 0.6	2.0 ± 0.7	< 0.001
Laboratory results in normal range on admission				
Hemoglobin§	57 (79.2)	115 (68.5)	37 (54.4)	0.003
Sodium	60 (83.3)	138 (82.1)	50 (73.5)	0.1
Potassium§	64 (88.9)	133 (79.2)	57 (83.8)	0.3
Creatinine§	61 (84.7)	113 (67.3)	36 (52.9)	< 0.001
Type of initial surgery				0.01
Colon	7 (9.7)	25 (14.9)	11 (16.2)	
Small intestine	19 (26.4)	44 (26.2)	24 (35.3)	
Hernia	10 (13.9)	23 (13.7)	9 (13.2)	
Open cholecystectomy–appendectomy	10 (13.9)	9 (5.4)	4 (5.9)	
Closed cholecystectomy–appendectomy	23 (31.9)	52 (31.0)	11 (16.2)	
Other	3 (4.2)	15 (8.9)	9 (13.2)	
ASA class, median (IQR)§	2 (2–3)	3 (2–3)	3 (3–4)	< 0.001

Pre-admission frailty and outcome after discharge



Pre-admission frailty and outcome after discharge

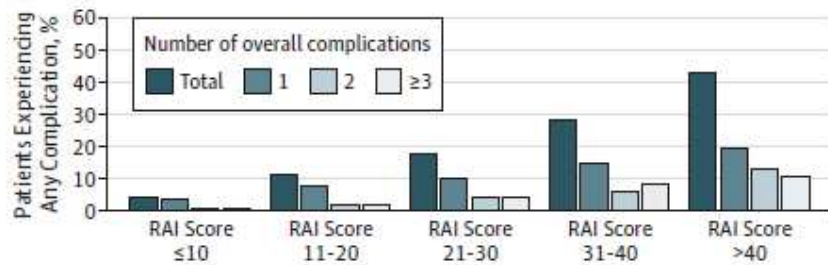
Outcome*	Preadmission level of frailty†		
	Well n = 72	Vulnerable n = 168	Frail n = 68
30-day readmission or death‡			
No. (%) of patients	3 (4.2)	27 (16.1)	12 (17.6)
Crude OR (95% CI)	1.00 (ref)	4.40 (1.29–15.02)	4.93 (1.33–18.33)
Adjusted OR (95% CI)	1.00 (ref)	4.60 (1.29–16.45)	4.51 (1.13–17.94)
30-day readmission‡			
No. (%) of patients	3 (4.2)	26 (15.5)	11 (16.2)
Crude OR (95% CI)	1.00 (ref)	4.21 (1.23–14.49)	4.44 (1.18–16.68)
Adjusted OR (95% CI)	1.00 (ref)	4.23 (1.20–14.97)	3.97 (1.00–15.78)
6-month readmission or death§			
No. (%) of patients	11 (15.3)	56 (33.3)	37 (54.4)
Crude OR (95% CI)	1.00 (ref)	2.77 (1.35–5.68)	6.62 (2.97–14.73)
Adjusted OR (95% CI)	1.00 (ref)	2.15 (1.01–4.55)	3.27 (1.32–8.12)
6-month readmission§			
No. (%) of patients	11 (15.3)	55 (32.7)	33 (48.5)
Crude OR (95% CI)	1.00 (ref)	2.70 (1.32–5.54)	5.23 (2.35–11.63)
Adjusted OR (95% CI)	1.00 (ref)	2.20 (1.04–4.62)	3.03 (1.23–7.49)

Note: CI = confidence interval, OR = odds ratio.
 *Age, sex and type of surgery were forced into all models. Additional variables meeting the statistical criteria for confounding are detailed in separate footnotes for the individual models.
 †Level of frailty based on Canadian Study of Health and Aging Clinical Frailty Scale.¹⁵
 ‡For the 30-day model, the following variables met the statistical criteria for confounding: hemoglobin level on admission, postoperative recovery on ward, postoperative use of total parenteral nutrition and Charlson Comorbidity Index. The final 30-day model was adjusted for age, sex, type of surgery, hemoglobin level on admission and postoperative use of total parenteral nutrition.
 §For the 6-month model, the following variables met the statistical criteria for confounding: creatinine and hemoglobin levels on admission, postoperative use of total parenteral nutrition, intraoperative ostomy creation and Charlson Comorbidity Index. The final 6-month model was adjusted for age, sex, type of surgery, hemoglobin level on admission, intraoperative ostomy creation and the Charlson Comorbidity Index.

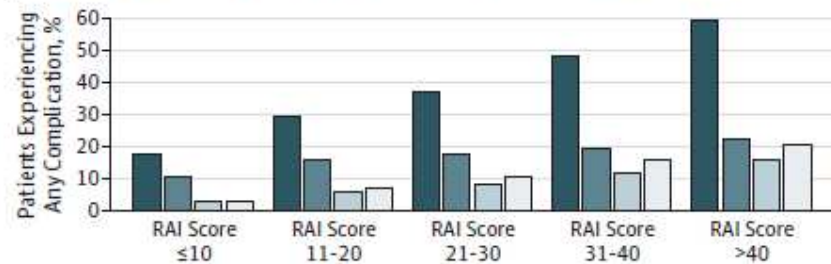
Association of Frailty With Failure to Rescue After Low-Risk and High-Risk Inpatient Surgery

The RAI was adapted from the Minimum Data Set Mortality Risk Index–Revised (MMRI-R). The RAI was validated prospectively predicts post-operative mortality and morbidity-with as good or better predictive ability than other existing measures of frailty, such as the MMRI-R and the modified Frailty Index (mFI).

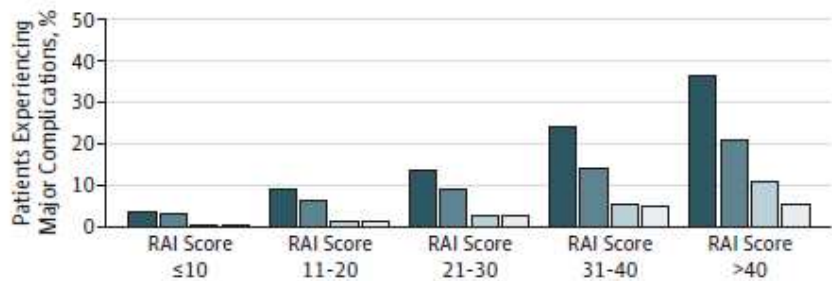
A Any complications rates, stratified by RAI score, in low-risk procedures



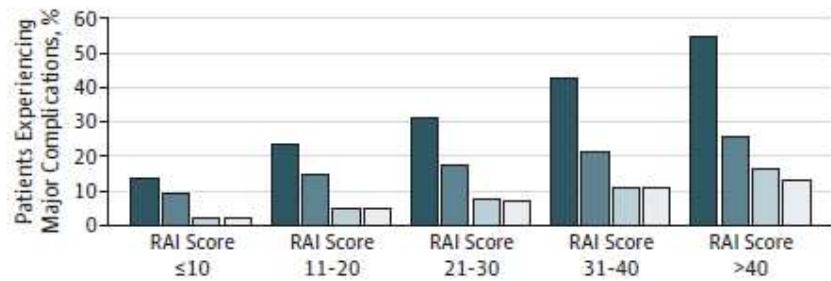
B Any complications rates, stratified by RAI score, in high-risk procedures



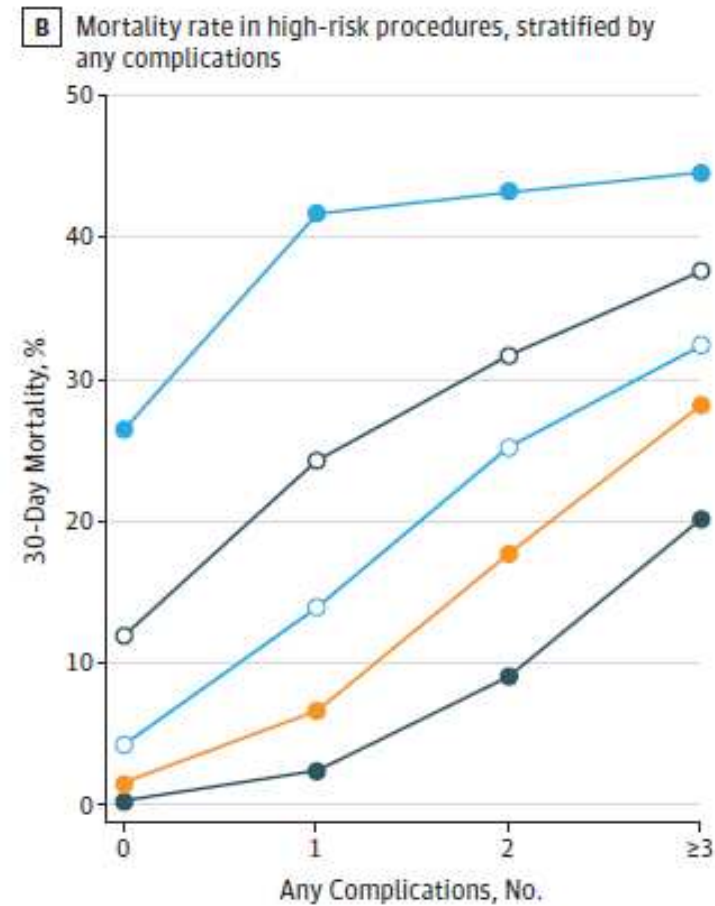
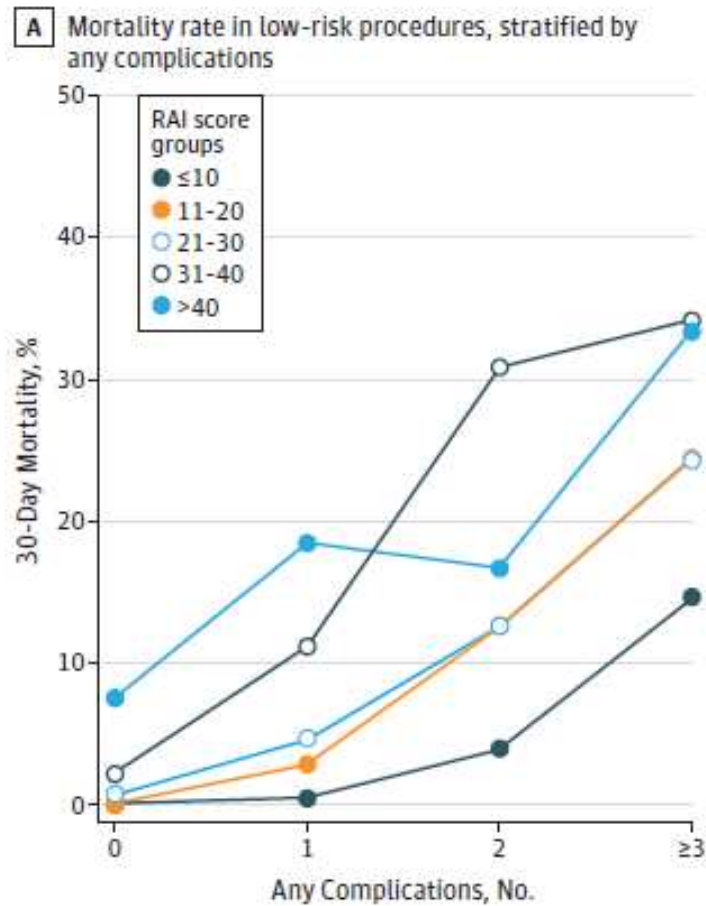
C Major complication rates, stratified by RAI score, in low-risk procedures



D Major complication rates, stratified by RAI score, in high-risk procedures



Association of Frailty With Failure to Rescue After Low-Risk and High-Risk Inpatient Surgery



High preoperative modified frailty index has a negative impact on short- and long-term outcomes of octogenarians with gastric cancer after laparoscopic gastrectomy

Frailty Definition

- Albumin <3.4 g/dl
- Haematocrit <35%
- Creatinine <2 mg/dl

Table 1 Clinicopathological characteristics

Characteristics	HPMFI (n=43)	LPMFI (n=76)	P value
Age, years	82.1 ± 2.7	82.0 ± 2.3	0.758
Sex			0.052
Male	39 (90.7%)	58 (76.3%)	
Female	4 (9.3%)	18 (23.7%)	
BMI, kg/m ²	22.0 ± 1.8	22.0 ± 3.1	0.976
ALB, g/dl	32.4 ± 4.6	35.8 ± 4.5	<0.001
Cr, mg/dl	1.2 ± 0.4	0.8 ± 0.2	<0.001
Hct < 35%			0.007
Yes	28 (65.1%)	30 (39.5%)	
No	15 (34.9%)	46 (60.5%)	
ASA status			<0.001
1	0 (0.0%)	5 (6.6%)	
2	11 (25.6%)	65 (85.5%)	
3	32 (74.4%)	6 (7.9%)	

High preoperative modified frailty index has a negative impact on short- and long-term outcomes of octogenarians with gastric cancer after laparoscopic gastrectomy

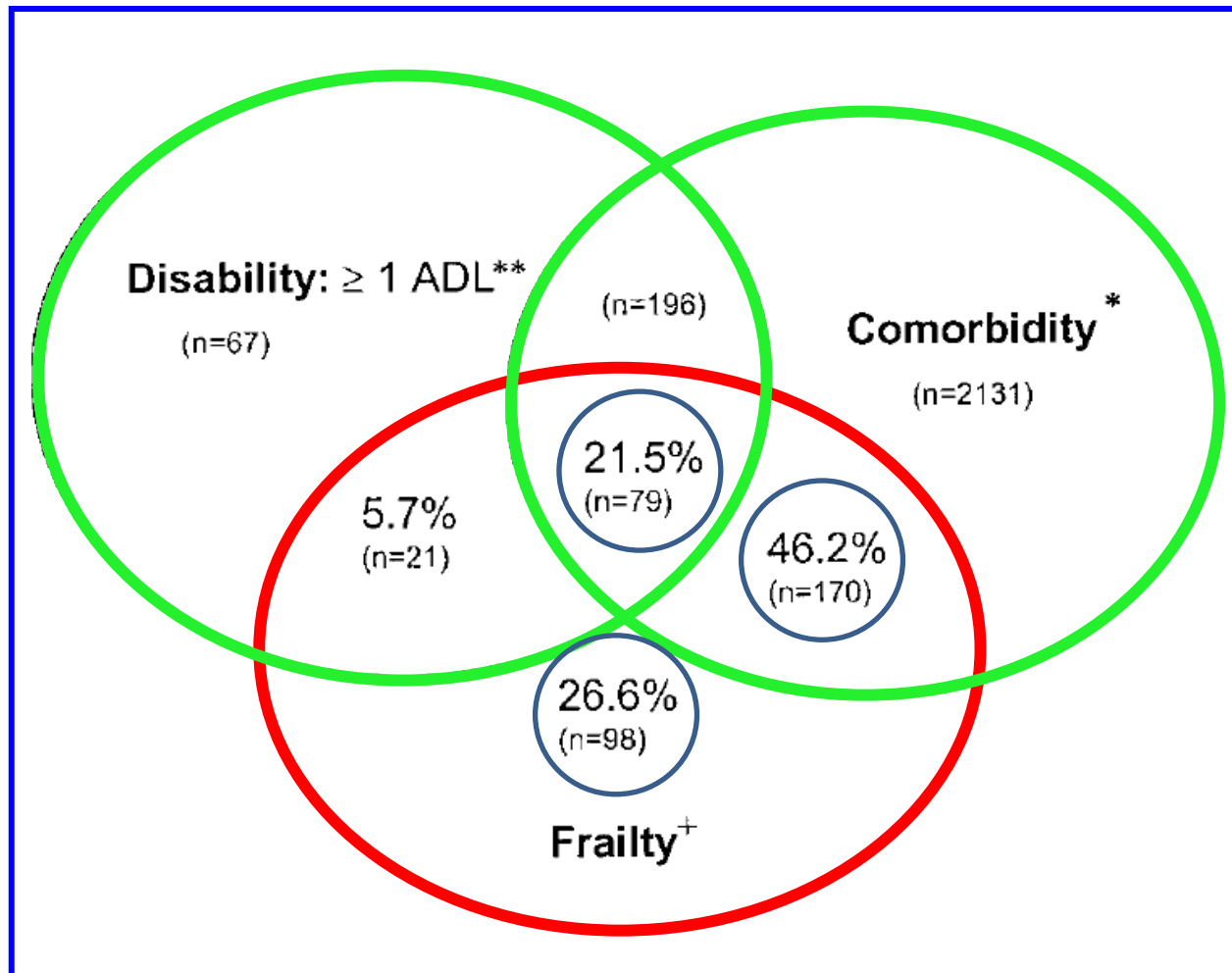
Variables	HPMFI (<i>n</i> =43)	LPMFI (<i>n</i> =76)	<i>P</i> value
Operation time (min)	174.4 ± 53.3	154.5 ± 47.2	0.037
Blood loss (ml)	134.2 ± 228.1	66.6 ± 56.5	0.062
Time to ambulation (days)	2.3 ± 0.8	2.3 ± 0.9	0.914
Time to first flatus (days)	4.1 ± 1.0	3.8 ± 1.1	0.145
Time to soft diet (days)	6.9 ± 6.0	5.4 ± 3.6	0.082
Postoperative hospital stay (days)	16.5 ± 8.1	14.6 ± 14.5	0.432
Number of dissected LNs	25.2 ± 8.2	26.2 ± 4.3	0.978
Complication rate (%)	55.8 (24/43)	30.3 (23/76)	0.006

LPMFI low preoperative modified frailty index, *HPMFI* high preoperative modified frailty index

Variable	Univariate analysis OR (95% CI)	<i>P</i> value	Multivariate analysis adjusted OR (95% CI)	<i>P</i> value
Sex (male)	1.508 (0.859–2.646)	0.153		
ASA (3 vs. 1 or 2)	2.218 (0.947–4.880)	0.052		
BMI (≥ 25 kg/m ²)	1.835 (1.025–3.349)	0.041	1.829 (1.008–3.320)	0.047
Comorbidities	1.060 (0.792–1.419)	0.694		
PMFI (high vs. low)	2.925 (1.627–3.363)	0.013	2.506 (1.113–5.643)	0.027
Operating time (≥ 240 min)	3.672 (1.129–2.478)	0.010	2.862 (1.120–2.466)	0.012
EBL (≥ 200 ml)	0.945 (0.620–1.440)	0.945		
Adjuvant chemotherapy (yes vs. no)	1.066 (0.511–2.223)	0.865		



Rapporto tra Fragilità, Disabilità e Comorbidità

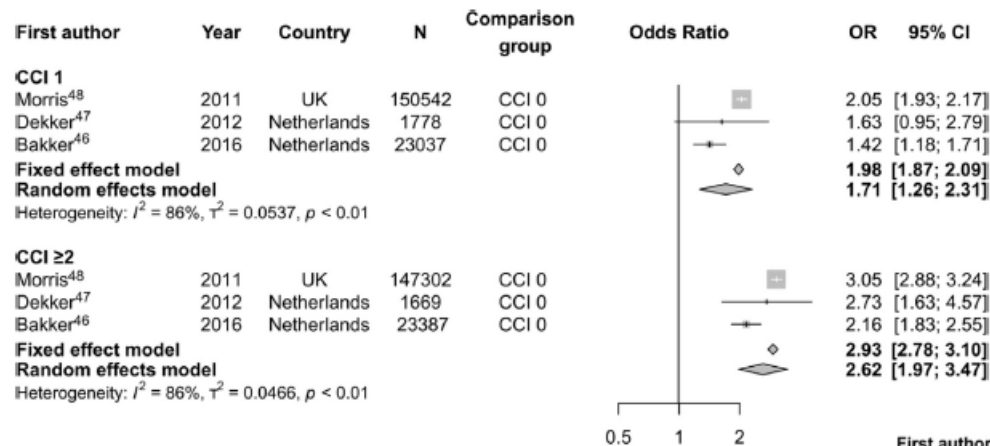


Systematic or Meta-analysis Studies

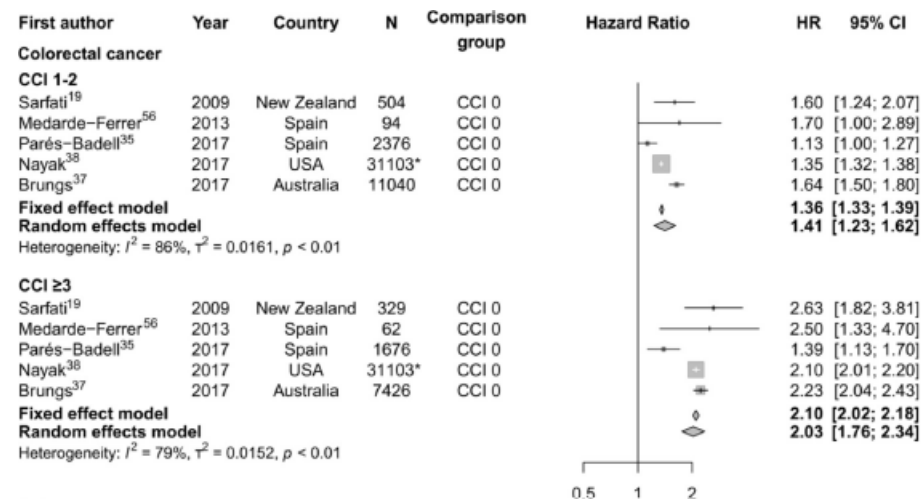
Impact of comorbidity and frailty on prognosis in colorectal cancer patients: A systematic review and meta-analysis

Daniel Boakye^a, Bettina Rillmann^{a,b}, Viola Walter^a, Lina Jansen^a, Michael Hoffmeister^a, Hermann Brenner^{a,c,d,*}

Comorbidity and 30-day mortality in colorectal cancer patients.



Comorbidity and overall mortality in colorectal and colon cancer patients.

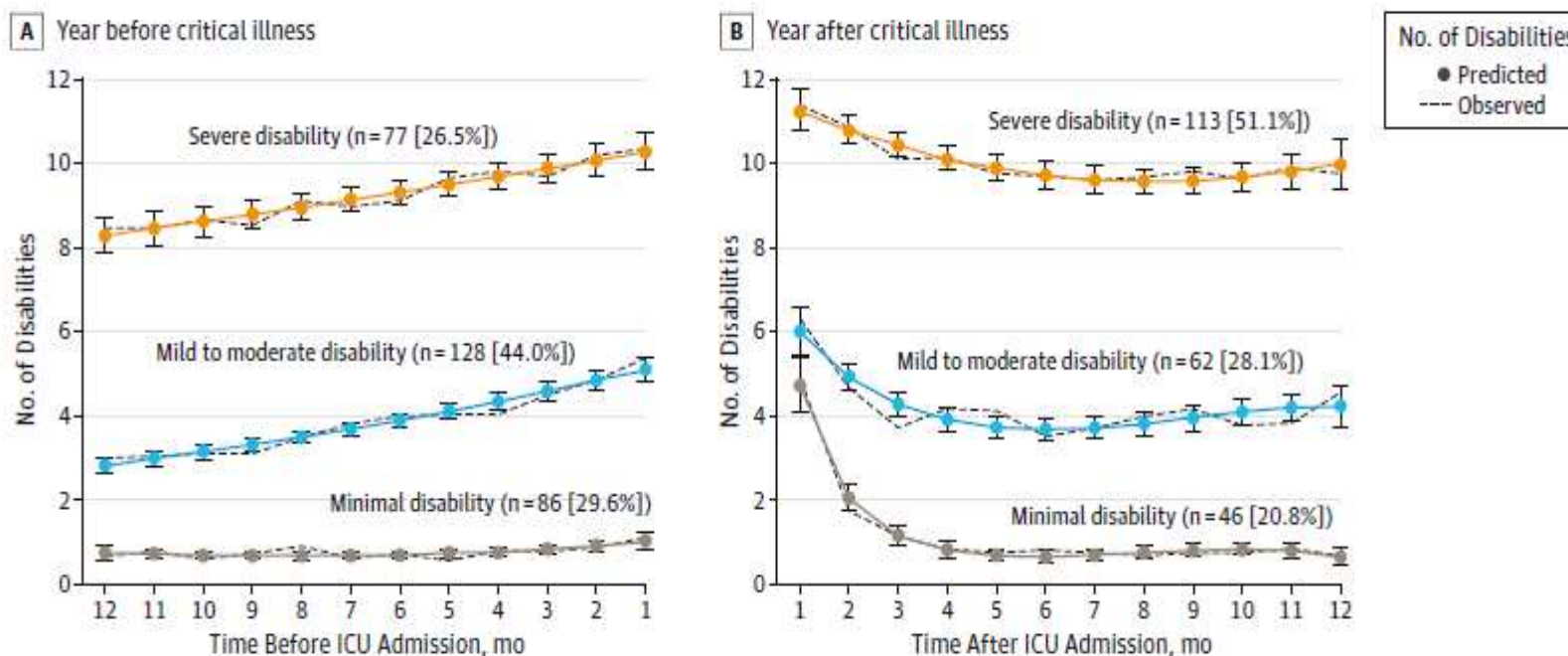


Functional Trajectories Among Older Persons Before and After Critical Illness

Lauren E. Ferrante, MD; Margaret A. Pisani, MD, MPH; Terrence E. Murphy, PhD; Evelyne A. Gahbauer, MD, MPH; Linda S. Leo-Summers, MPH; Thomas M. Gill, MD *JAMA Intern Med.* 2015 April ; 175(4): 523–529

Definizione di disabilità

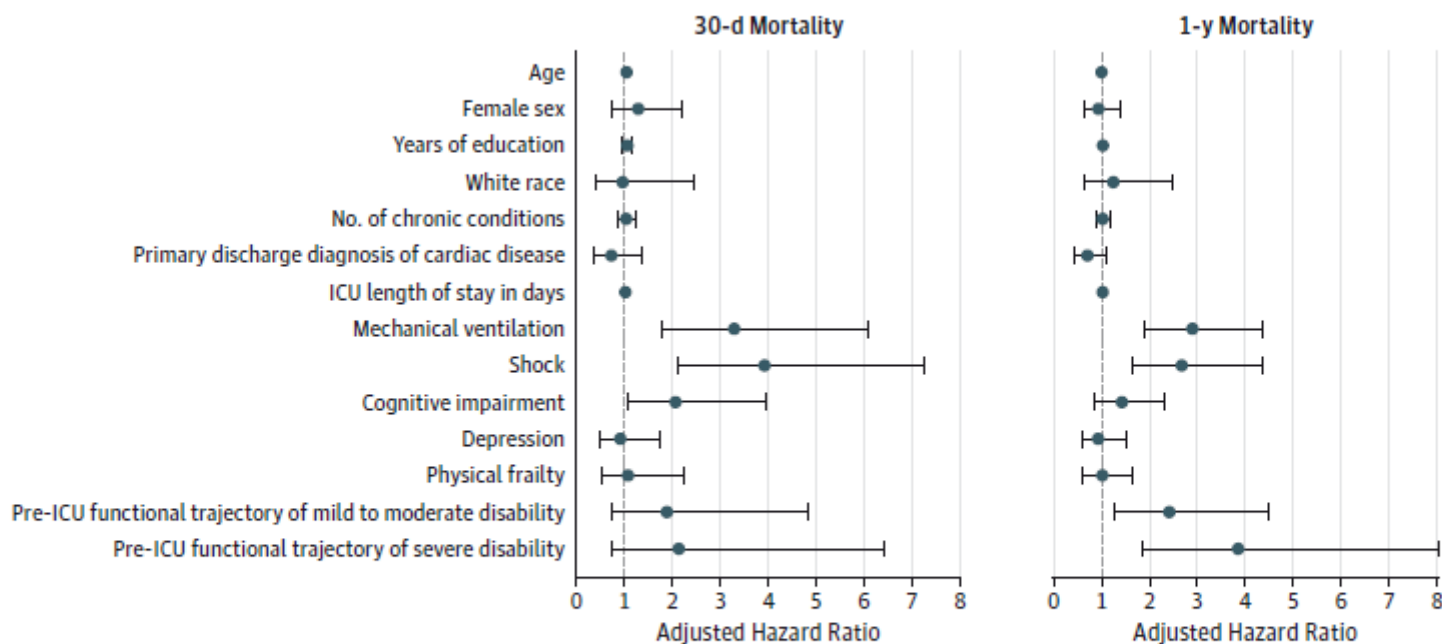
- “At the present time, do you need help from another person to complete the task?”
- 4 BADL(bathing, dressing, walking across a room, and transferring from a chair),
- 5 IADL(shopping, housework, meal preparation, taking medications, and managing finances),
- 3 mobility activities (walk a quarter mile, climb a flight of stairs, and lift or carry 10 lb).
- Disability was operationalized as the need for personal assistance or an inability to perform the task.



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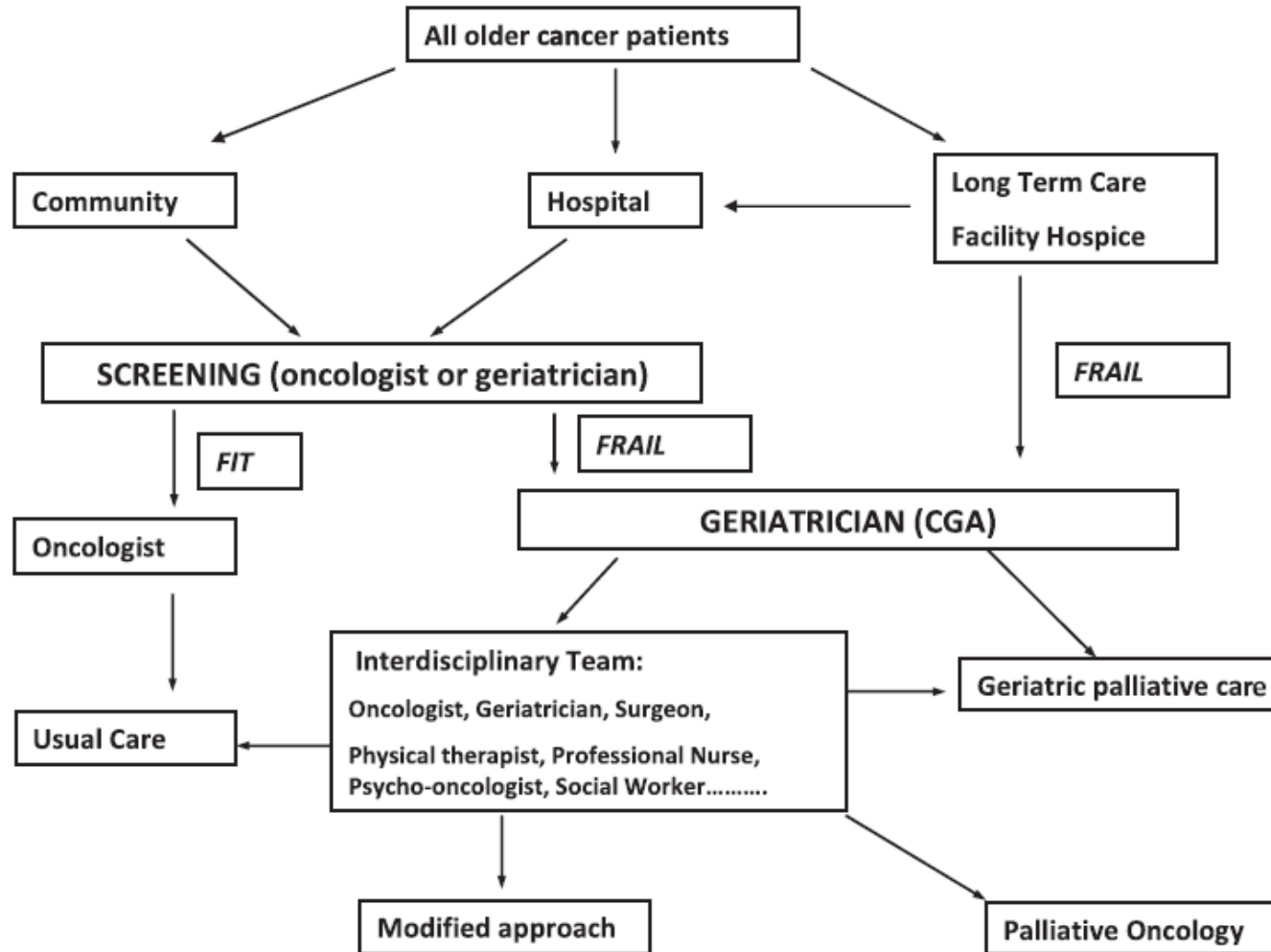
Figure 2. Factors Associated With Short-term and Long-term Mortality After Critical Illness in Older Persons



The pre-intensive care unit (ICU) functional trajectory of minimal disability served as the reference group. The Cox proportional hazards regression model was adjusted for the first 12 factors listed in the figure. Time to death was measured from the day of hospital admission, and survivors were censored at 30 days and 1 year, respectively, for the short-term and long-term mortality models. The point estimates are accompanied by 95% CIs.



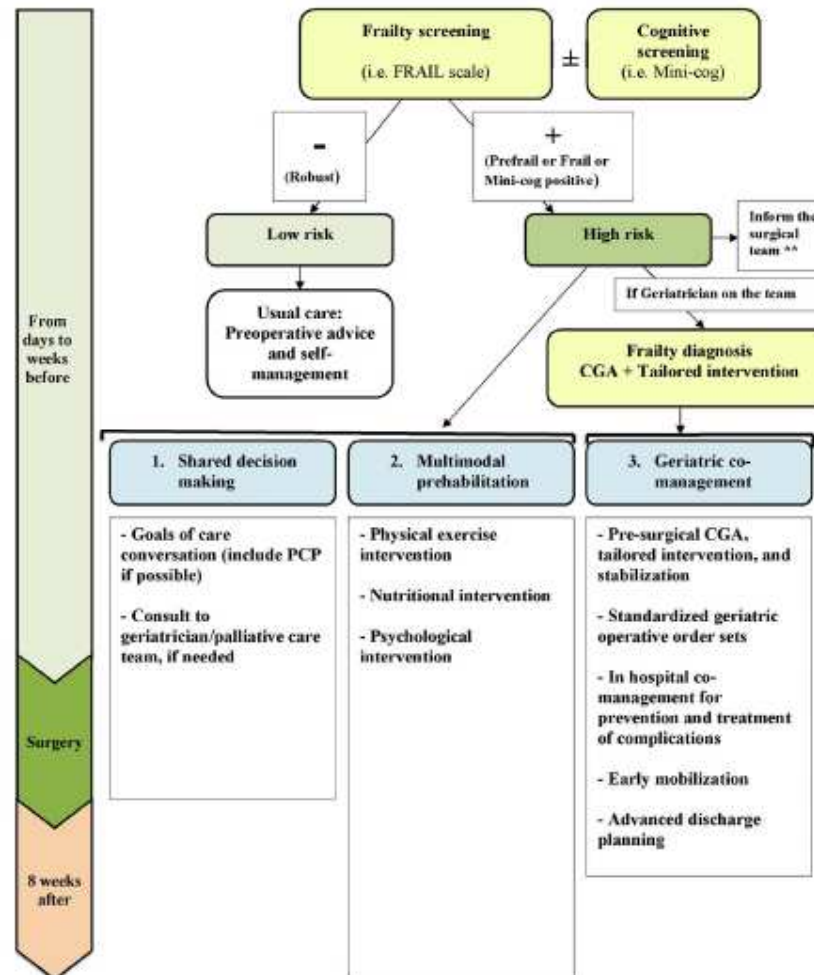
Assessment and treatment of elderly patients with cancer





Original Contribution

Recommendations for Preoperative Management of Frailty from the Society for Perioperative Assessment and Quality Improvement (SPAQI)[☆]





**Elderly
people**