FRAILTY

an emerging concept for clinicians

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Case Presentation

Case 1

An 82-year old man with a history of heart failure, knee osteoarthritis, and hypertension presented for elective knee replacement.

Brown C. Frailty in Older adults [Power Point Slides]. Retrieved from *www.lhl.uab.edu/uabgecfsp/wp-content/uploads/.../**Frailty**-Part-1.**ppt***

Case Presentation

Case 2

An 82-year old man with a history of heart failure, knee osteoarthritis, and hypertension presented for elective knee replacement.

Brown C. Frailty in Older adults [Power Point Slides]. Retrieved from *www.lhl.uab.edu/uabgecfsp/wp-content/uploads/.../**Frailty**-Part-1.**ppt***

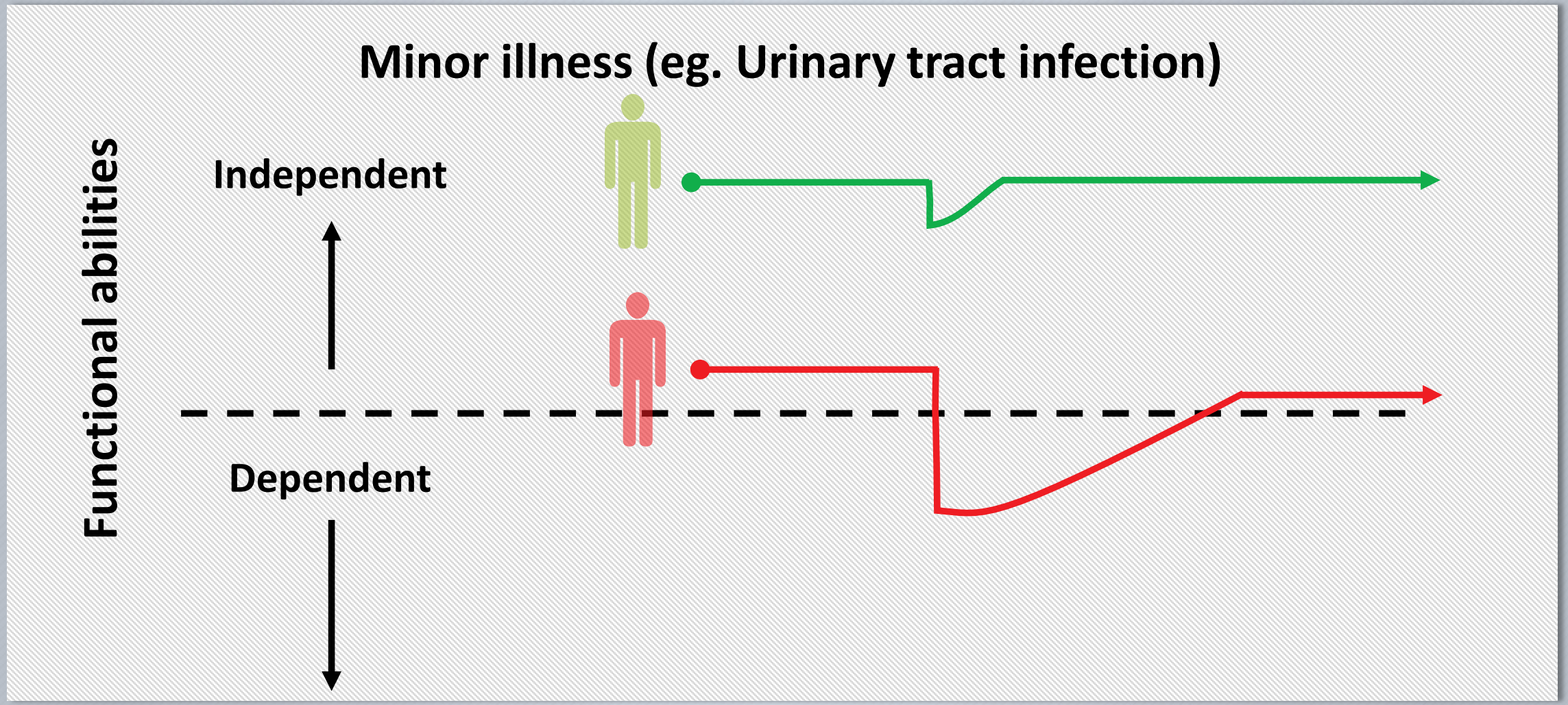
Case Presentation

Case 3

An 82-year-old man with a history of heart failure, knee osteoarthritis, and hypertension presented to the ED after being found by a neighbor on the floor.

Brown C. Frailty in Older adults [Power Point Slides]. Retrieved from *www.lhl.uab.edu/uabgecfsp/wp-content/uploads/.../**Frailty**-Part-1.**ppt***

Patterns of vulnerability



Adapted from Clegg et al., 2013

Defining frailty

FRAILTY

- How would you define the term “frail”?
- What makes a person frail?
- Are there key components to frailty?

Frailty Definitions

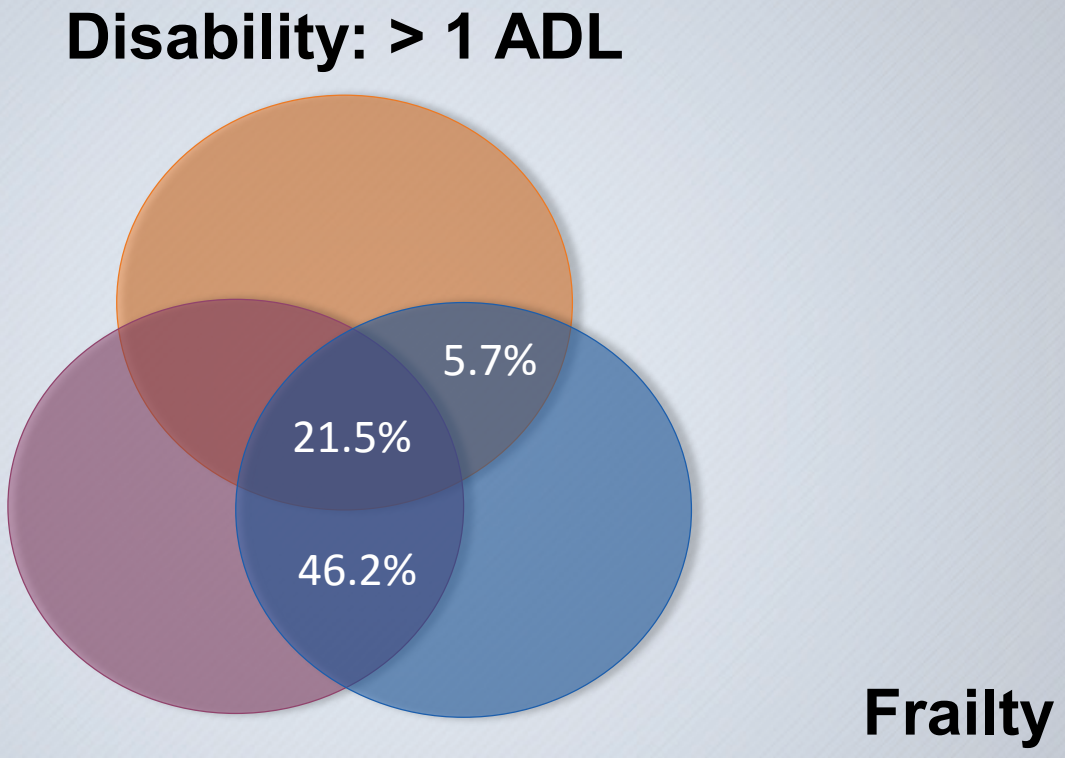
FRAILTY

A variety of definitions have been used defining frailty as synonymous with:

Disability **Comorbidity** **Advanced Old Age**

However, while there is some overlap, frailty appears to encompass more than disability or comorbidity.

Overlap of Frailty with ADL Disability and Comorbidity



Adapted from Fried at el ., 2001

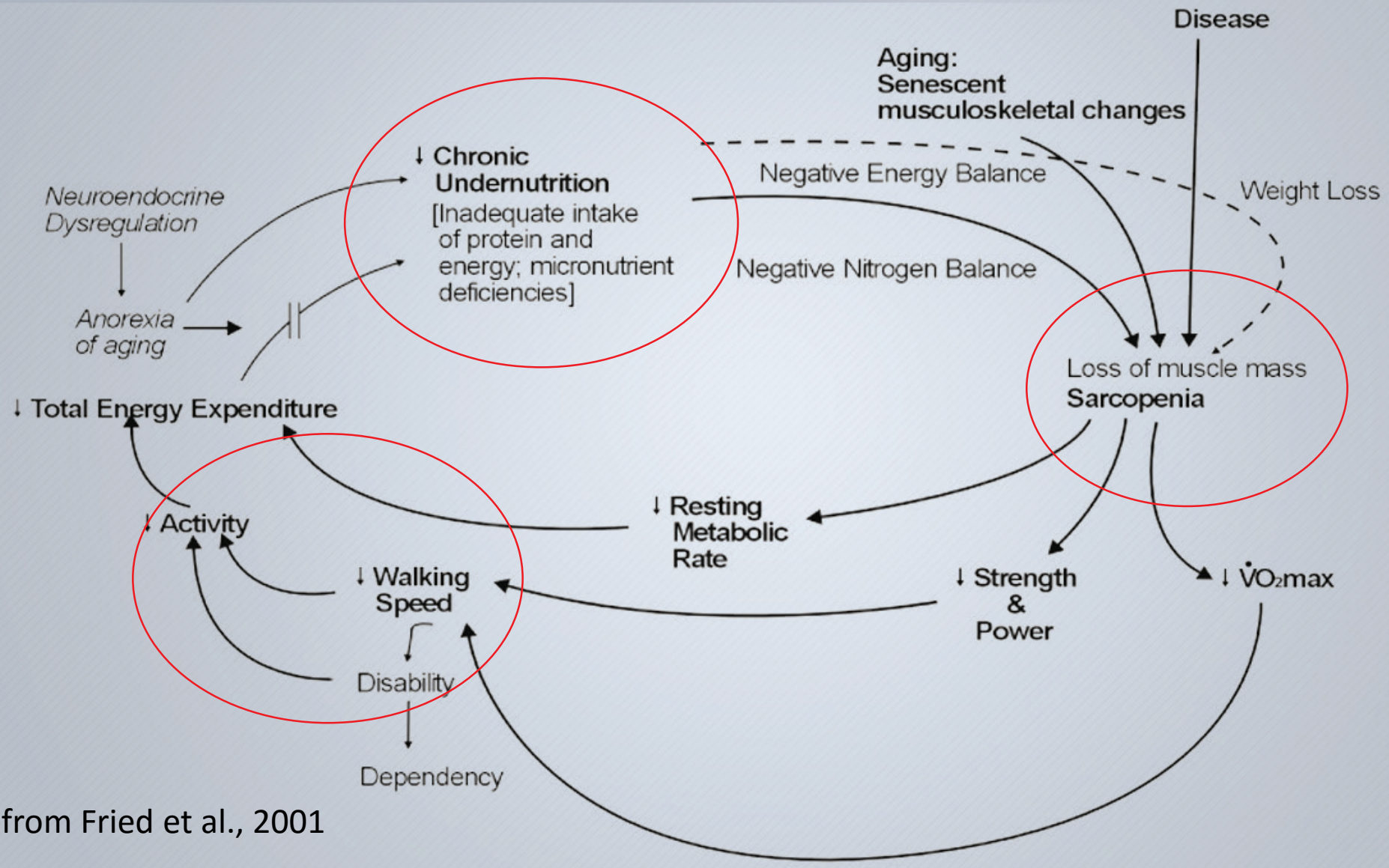
Frailty Definition

Clinicians have begun to define frailty as:

> ***"a syndrome of decreased reserve and resistance to stressors, that result in cumulative declines across multiple physiologic systems, causing vulnerability to adverse outcomes."***

It has been postulated that there are key components of frailty, and multiple components must be present to constitute frailty.

Fried's Model of Frailty



Adapted from Fried et al., 2001

Operational definitions

FRAILTY

CHS index

Unintentional weight loss

(>10 lbs or ≥5% of body weight in 1 year)

Exhaustion

(self report of exhaustion)

Weakness

(grip strength in the lowest 20% by gender and BMI)

Slow walking speed

(gait speed in the lowest 20% by gender and height)

Decreased physical activity

(Kcals/week in the lowest 20% by gender)

Fried et al., 2001

CHS Index or Fried's phenotype

	7% frail	47% pre-frail	46% no frail
Mortality at 7 years	**43%**	**23%**	**12%**

HR for mortality was 1.63
(95% CI 1.27-2.08)
for frail group

Operational definitions cont.

FRAILTY

Study of Osteoporotic Fractures (SOF) index

Weight loss

(≥ 5% between examinations)

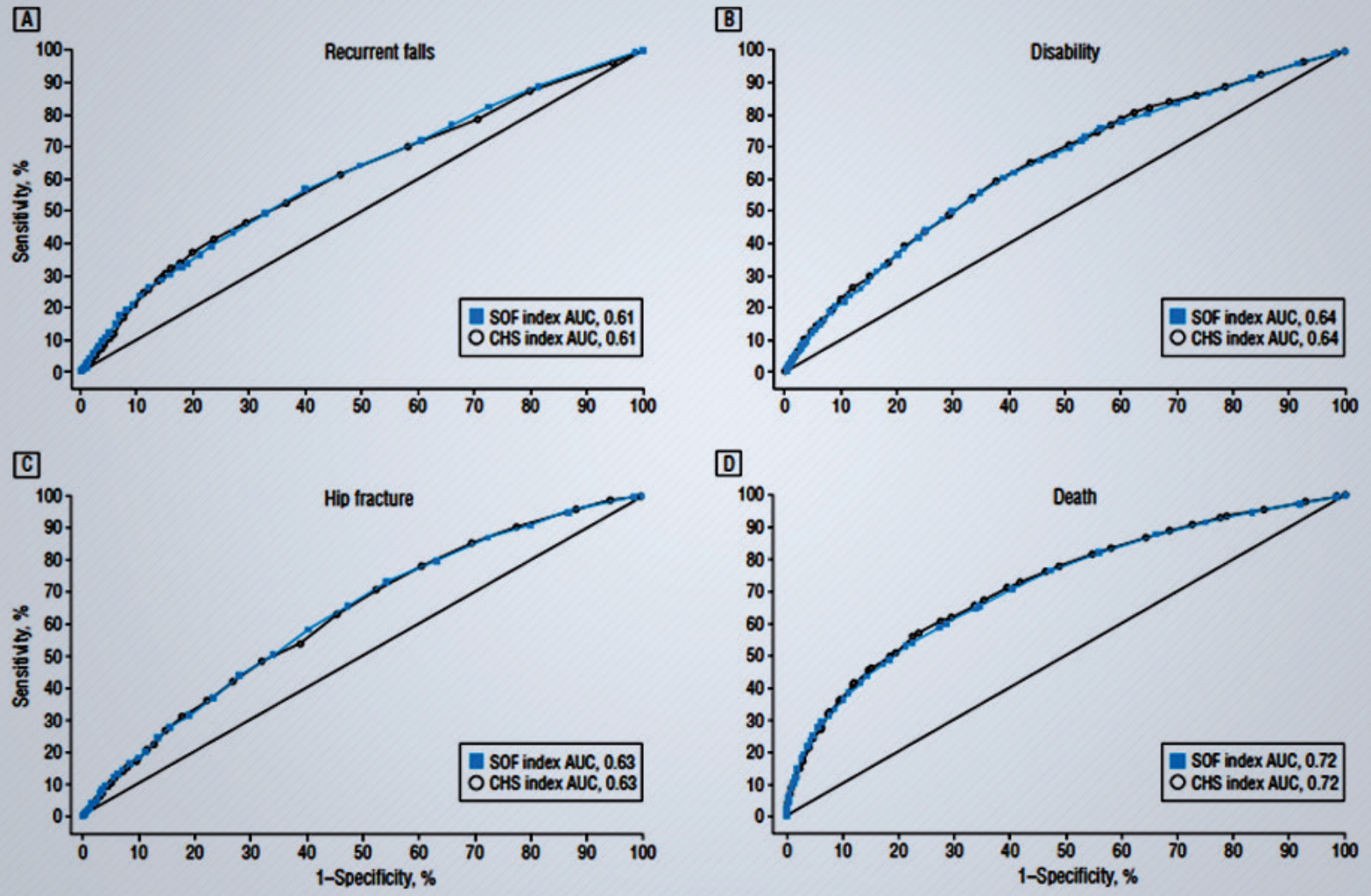
Poor energy

(A "no" response to the question: "Do you feel full of energy?")

Inability to rise from a chair five times without use of arms

Ensrud et al., 2008

Comparing CHS and SOF indexes



Adapted from Ensrud et al., 2008

Operational definitions (cont.)

FRAILTY

Women's Health Initiative (WHI) index

Unintentional weight loss

(≥5 percent of body weight between examinations)

Exhaustion

(SF-36 Vitality Scale score<55)

Low Physical Function

(2 points) (SF-36 Physical Function Subscale score<75)

Decreased physical activity

(Kcal spent per week in the lowest 25%)

Woods et al., 2005

Comparing CHS and WHI indices

	Harrell's C statistics					
	Mortality	**P value for comparison**	**Hip Fracture**	**P value for comparison**	**Falls**	**P value**
CHS	0.62 (0.59-0.65)	0.84	0.64 (0.57-0.70)	0.59	0.54 (0.52-0.57)	0.83
WHI	0.62 (0.59-0.65)		0.65 (0.58-0.71)		0.54 (0.51-0.57)	

Zaslavsky et al (under review)

Operational definitions (cont.)

FRAILTY

Rockwood frailty index

This index uses 30-70 variables that range from medical conditions to functional decline

The higher the score,
the more frail the individual

Rockwood et al., 2007

Rockwood Frailty Index

FRAILTY

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 palmomental reflex
- Other medical history

Adopted from
Rockwood et al., 2007

What definition should I use?

FRAILTY

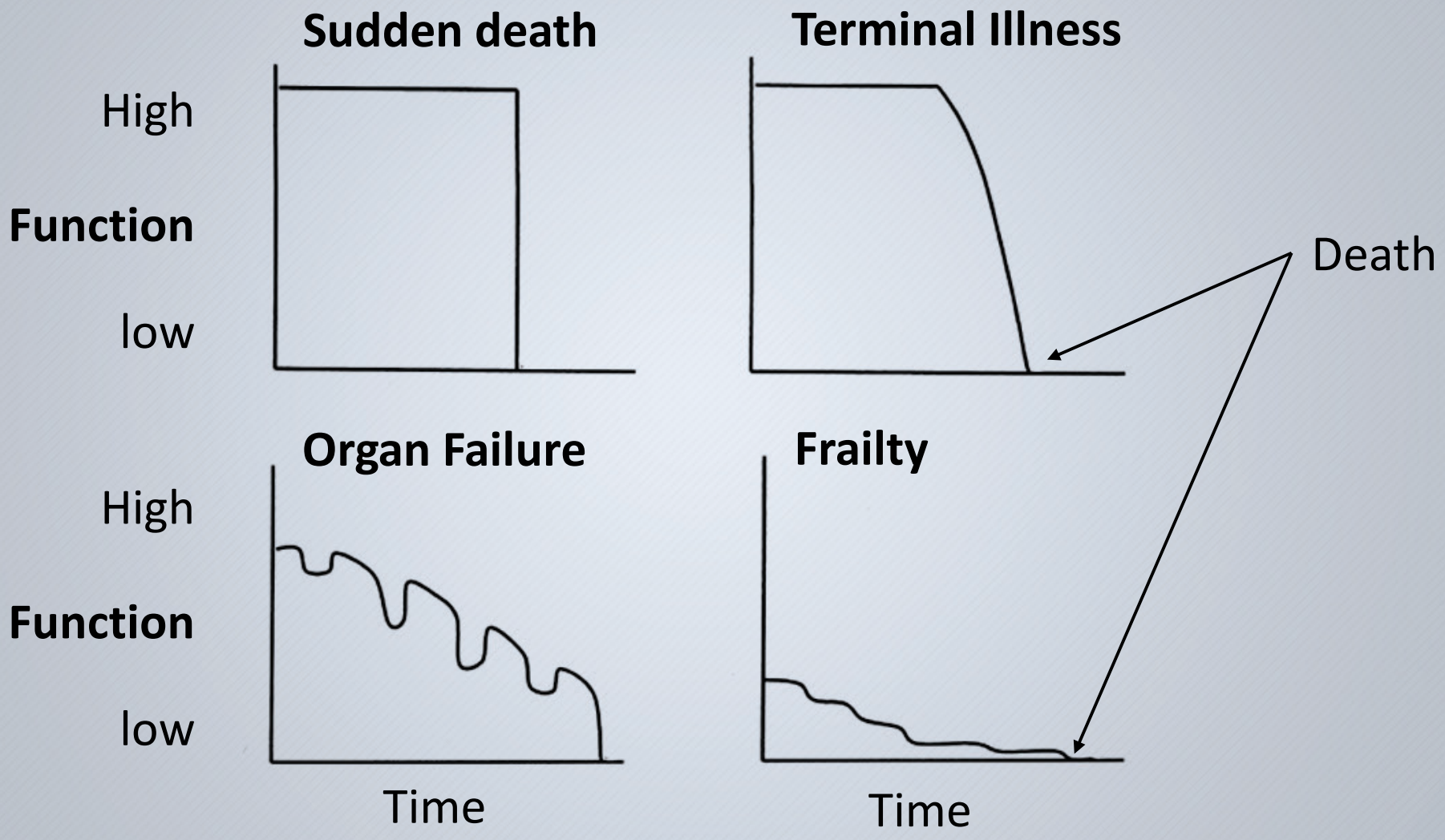
CHS index

SOF index

WHI index

Rockwood index

Epidemiology



Gill et al., 2010

Epidemiology

FRAILTY

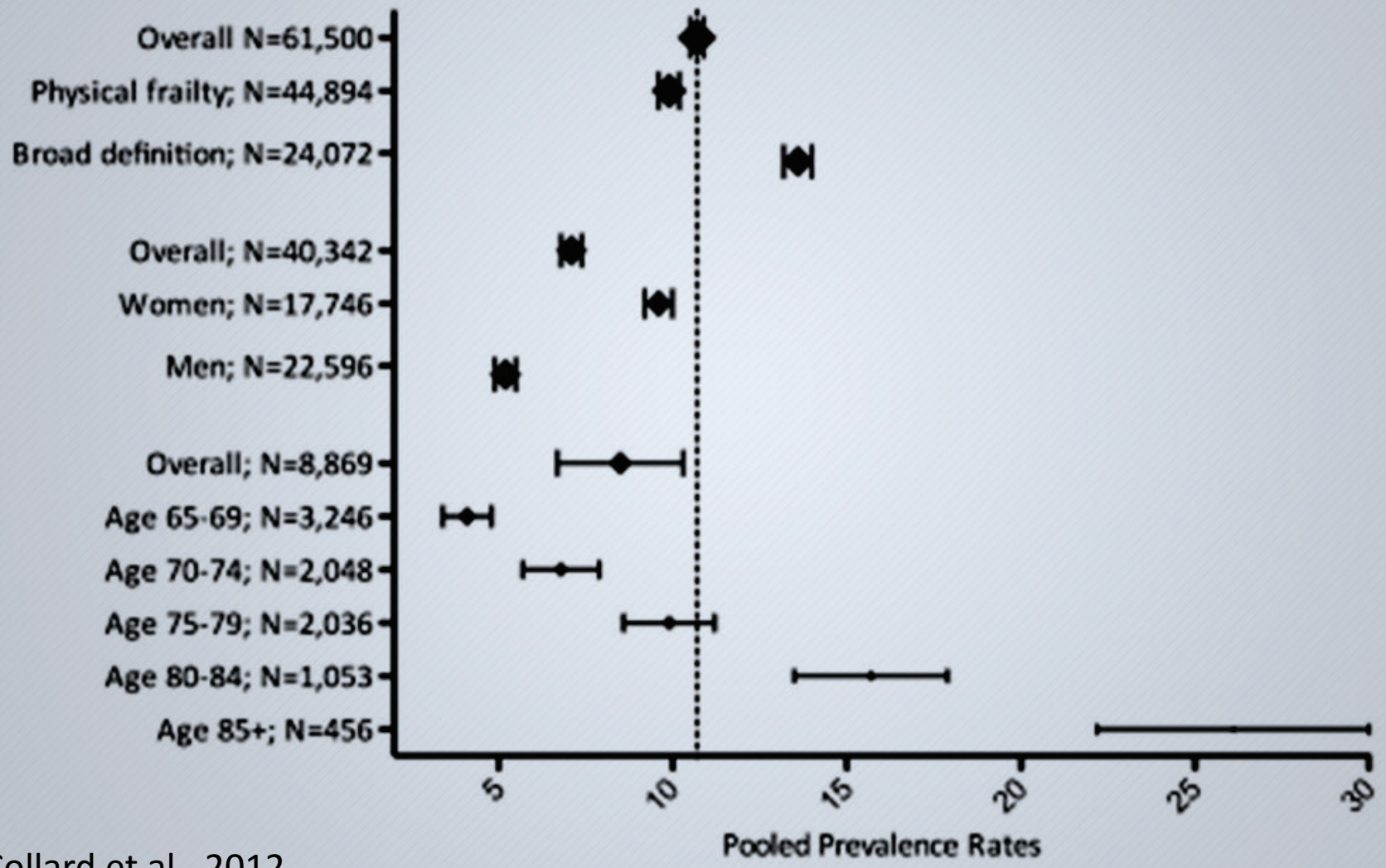
- **The overall weighted prevalence of frailty was 10.7%** (95% confidence interval (CI) = 10.5-10.9; 21 studies; 61,500 participants).

- **9.9% for physical frailty** (95% CI = 9.6-10.2; 15 studies; 44,894 participants)

- **13.6% for the broad phenotype of frailty** (95% CI = 13.2-14.0; 8 studies; 24,072 participants)

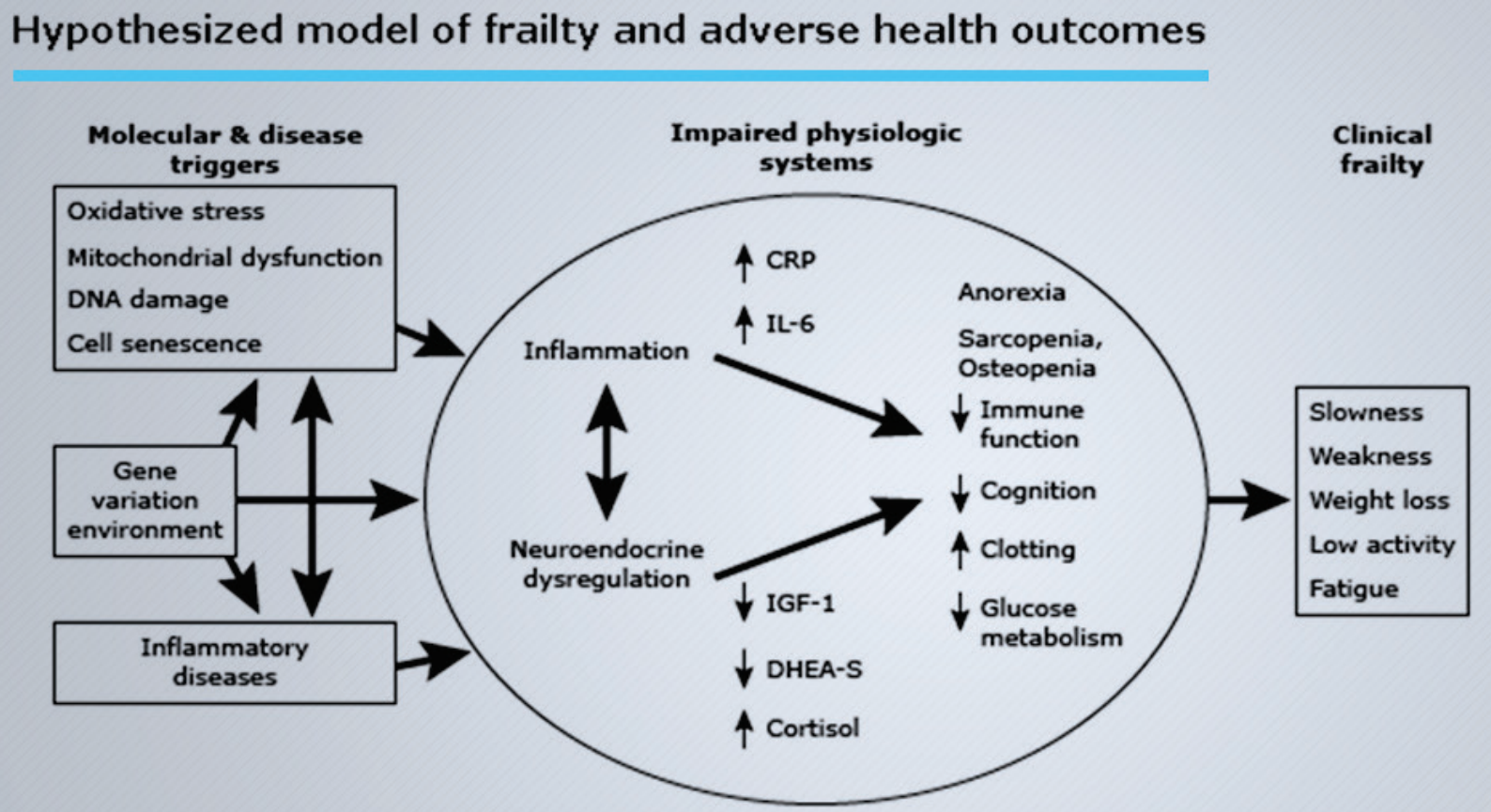
Collard et al., 2012

Epidemiology



Adapted from Collard et al., 2012

Pathophysiology



Pathophysiology

FRAILTY

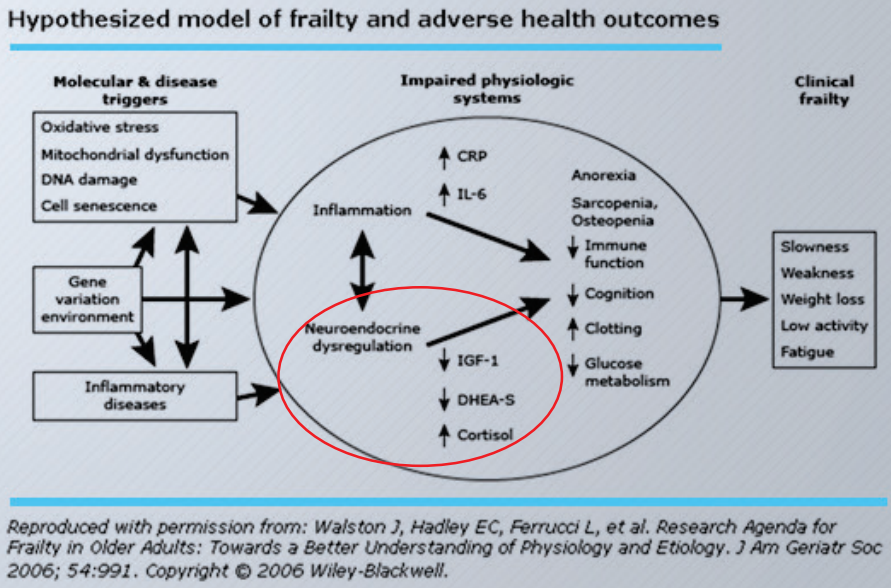
IGF-1 levels

Sex steroids

DHEA-S levels

25(OH)D

Cortisol levels



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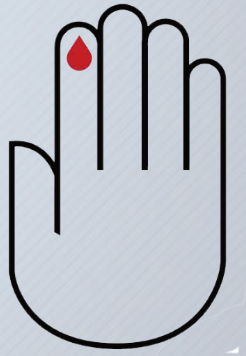
Capolla et al., 2003; Leng et al., 2004;
Varadhan et al., 2008; Puts et al., 2005

Study aims

To test the hypothesis that diabetes and higher glucose levels are associated with risk of frailty



Zaslavsky et al. (under review)

Outcome ascertainment

FRAILTY

Modified version of the CHS index:

Weakness

(Low grip strength stratified by sex and BMI)

Slow walking speed

<0.6 m/s in a timed 10-foot walk test

Low physical activity

(Fewer than 3 times per week)

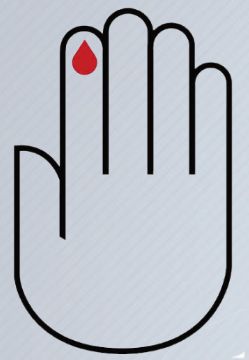
Exhaustion

(Self report)

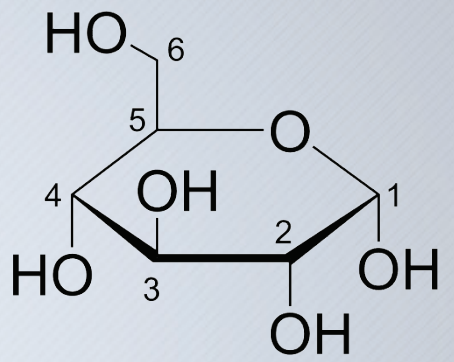
Weight loss

(>7.5% between ACT visits)

Diabetes and Glucose levels



Treated diabetes
- GH pharmacy dispensing data

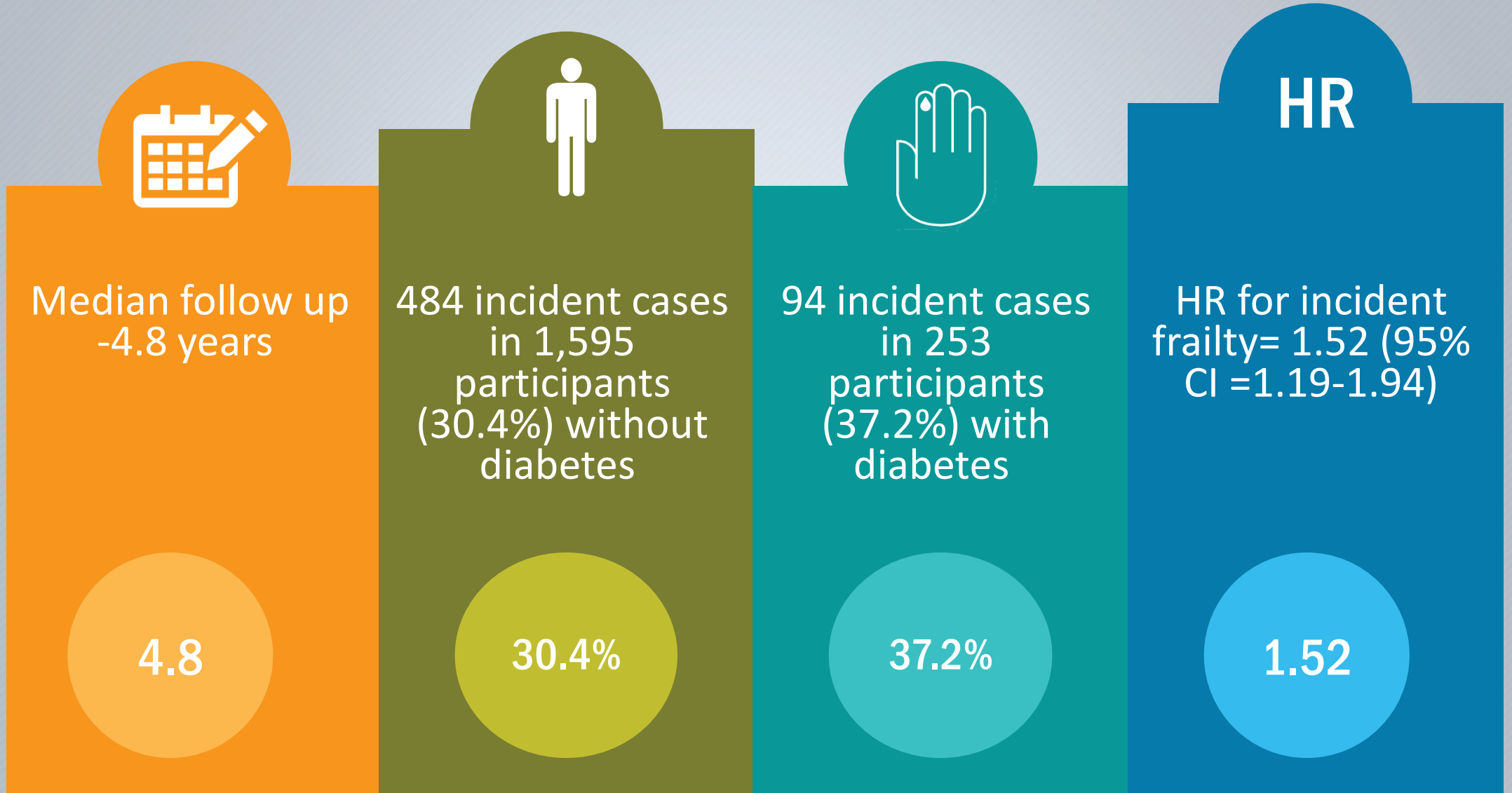


Fasting or random glucose and glycated hemoglobin
– computerized laboratory databases

Results

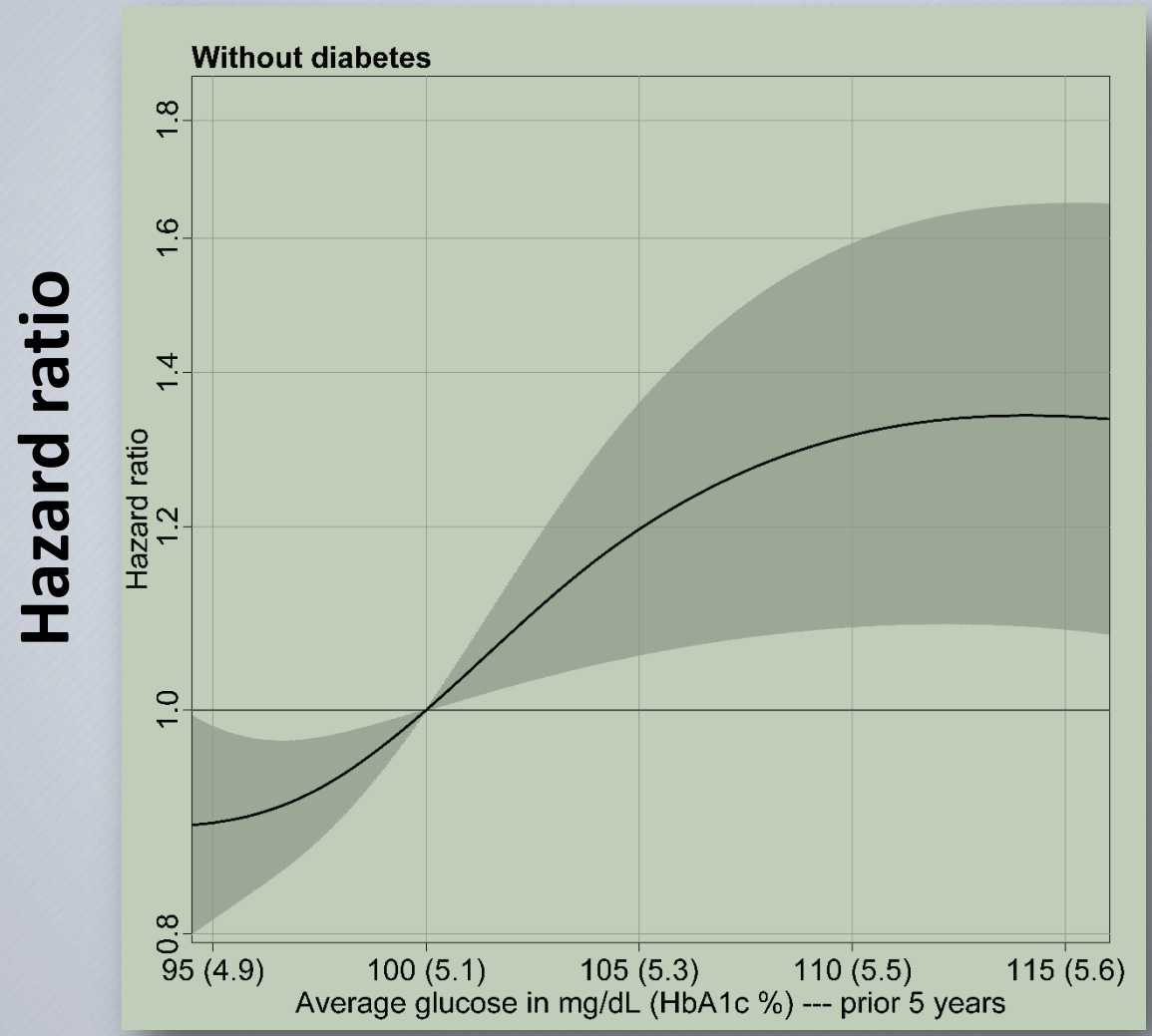
	Without diabetes (N=1,648)	With diabetes (N=200)
Average glucose level in mg/dL, median (25^{th}, 75^{th}) in HbA1c%, median (25^{th}, 75^{th})	 100 (96, 107) 5.1 (5.0, 5.4)	 168 (153, 187) 7.5 (7.0, 8.1)
Age, median (25^{th}, 75^{th})	76 (72, 81)	75 (72, 80)
Female	59%	52%
Non-white	7%	14%
At least some college	66%	58%
CHF	5%	7%
CAD	25%	34%
COPD	12%	15%
Current or former smoker	52%	56%
Obese (BMI 30+)	22%	40%

Results (cont.)



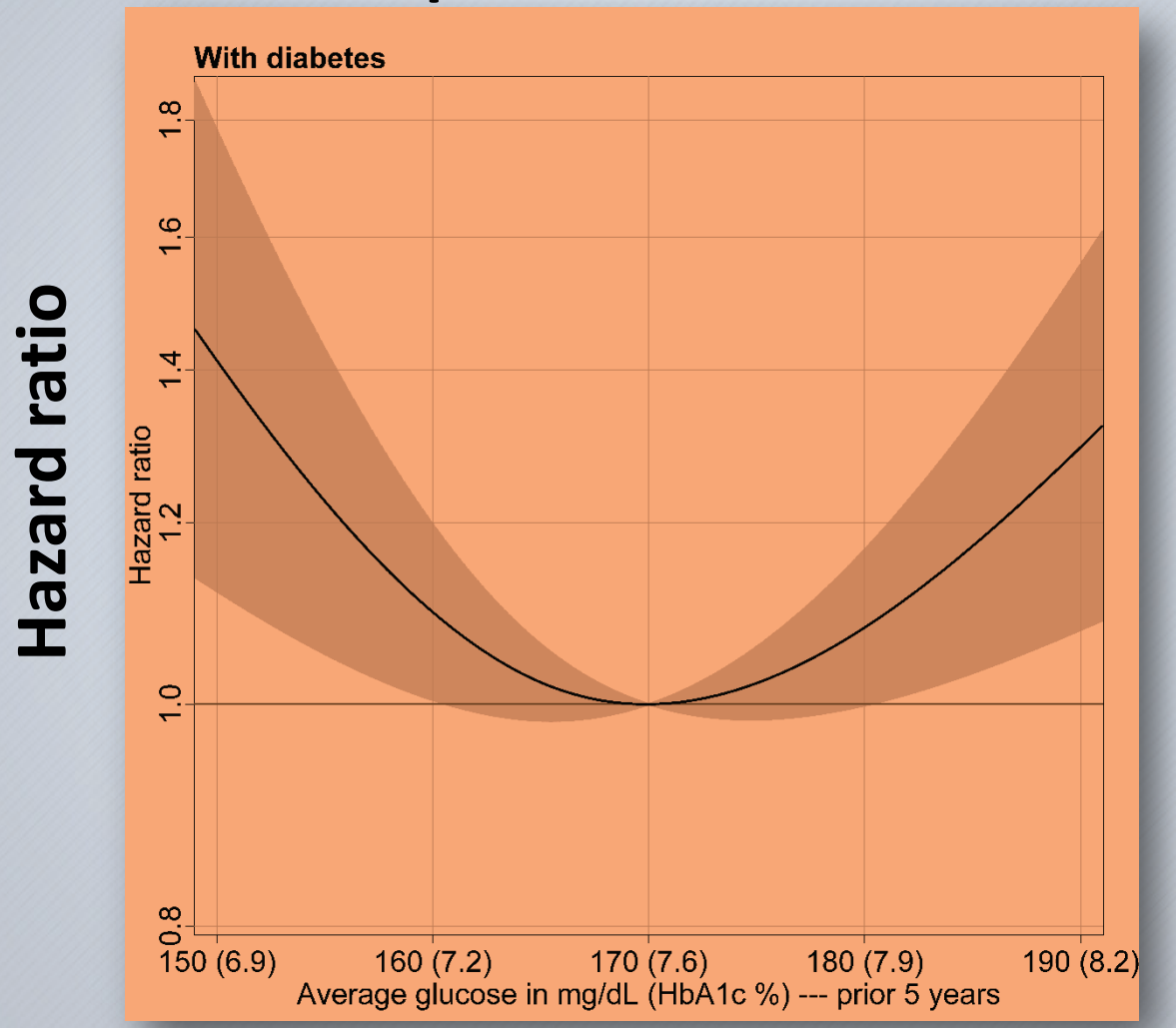
Results (cont.)

Participants without diabetes



Results (cont.)

Participants with diabetes



Conclusions

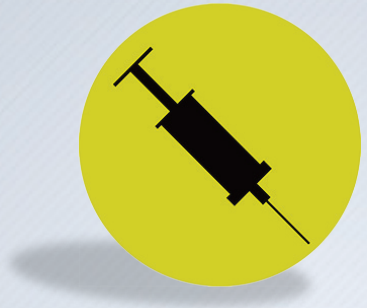
- Diabetes is a frailty risk factor
- Higher glucose levels, based on a recent 5-year average, are associated with an increased risk of frailty in older adults free of diabetes
- Risk estimated to increase(nonlinearly) across glucose levels of 95-115 mg/dL

Conclusions

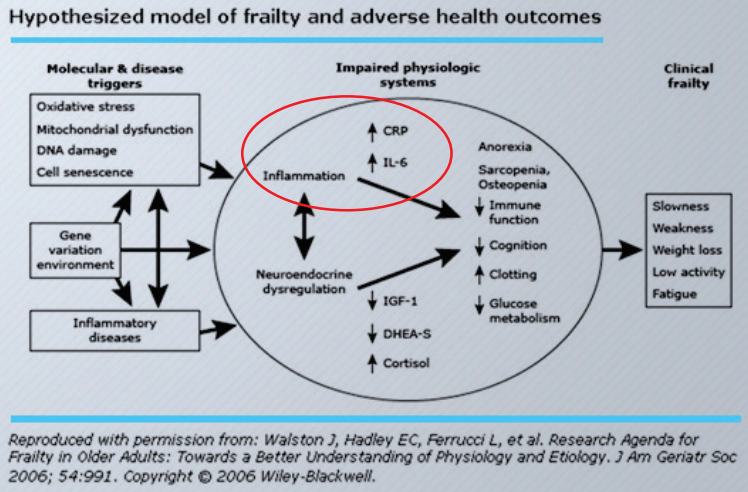
In persons with diabetes a U-shape relationship emerged
with the lowest hazards at glucose levels
of about 170 mg/dL

Inflammation

Elevated serum levels of the pro-inflammatory cytokines and C-reactive protein (CRP)



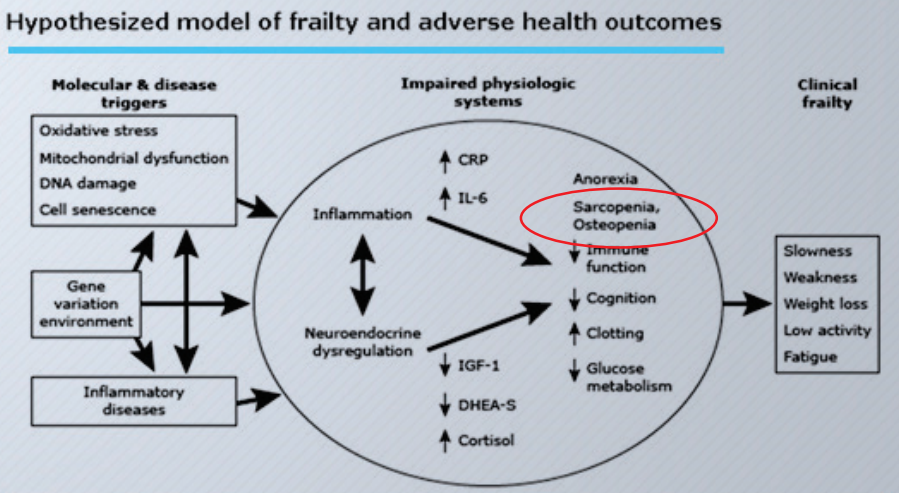
Impaired immune response to vaccination



Leng et al., 2004; Puts et al., 2005; Walston et al., 2002; Leng et al., 2009

Sarcopenia

Progressive loss of skeletal mass, strength and power



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Interventions

Exercise

Interventions

FRAILTY

Nutritional

Objectives

Examine association between currently recommended categories of BMI and the risk of all-cause mortality among frail women ages 65 and older

Zaslavsky et al. (accepted for publication)

Frailty defined

Unintentional weight loss

Exhaustion

Low physical function

Low physical activity

BMI categories

Underweight
(BMI <18.5 kg/m^2)

Normal weight
(BMI 18.5-24.9 kg/m2)

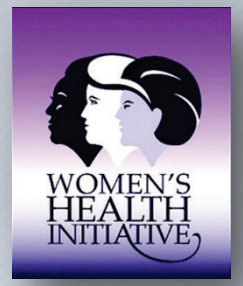
Overweight
(BMI 25-29.9 kg/m2)

Obese I
(BMI 30-34.9 kg/m2)

Obese II
(BMI 35-39.9 kg/m2)

Obese III
(BMI 40 kg/m2)

Mortality



- Mortality data was based on all discoverable death index (December 2013)

- For women no longer followed, or with the lost of follow up, mortality data were sought by linkage with the National Death Index (the latest search through 2011)

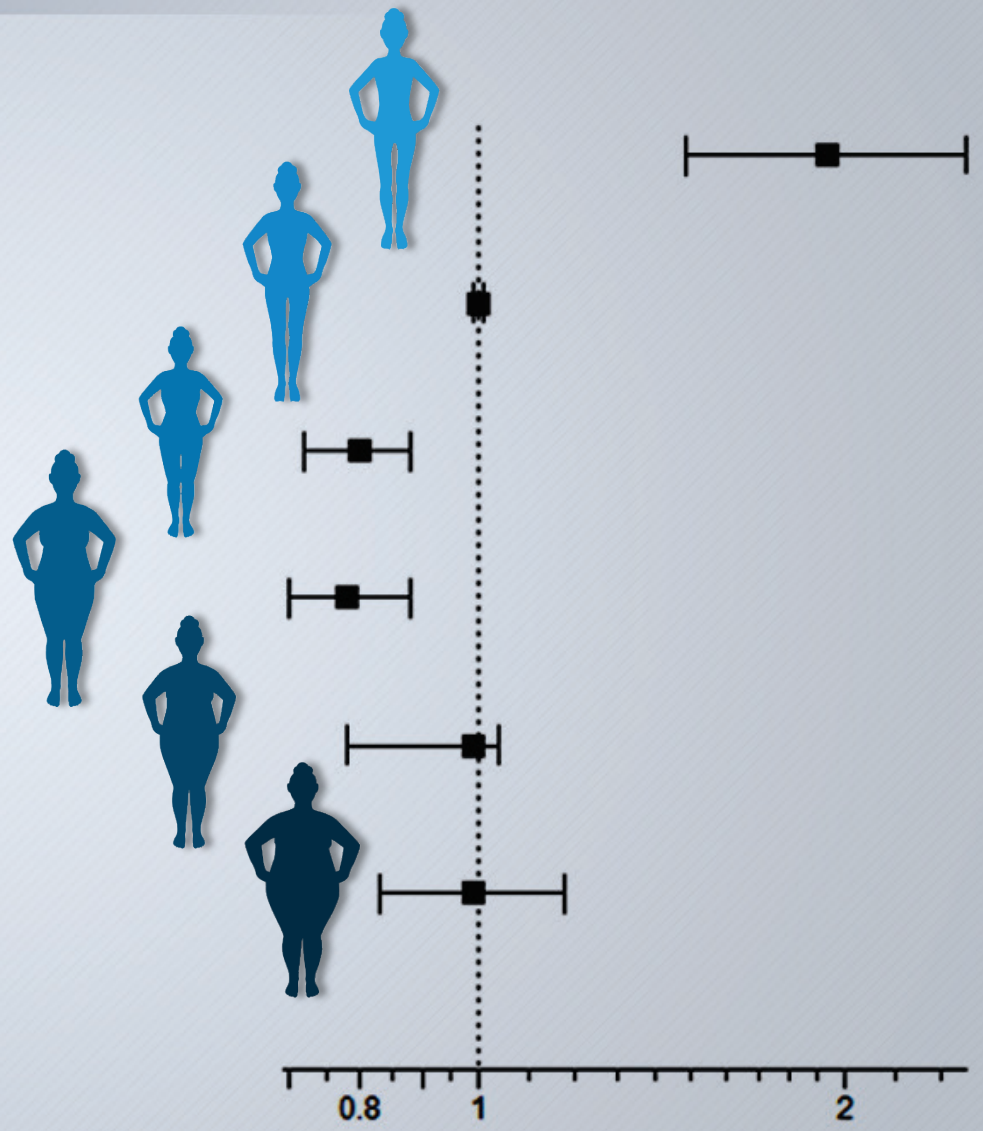
Selected Baseline … by BMI

FRAILTY

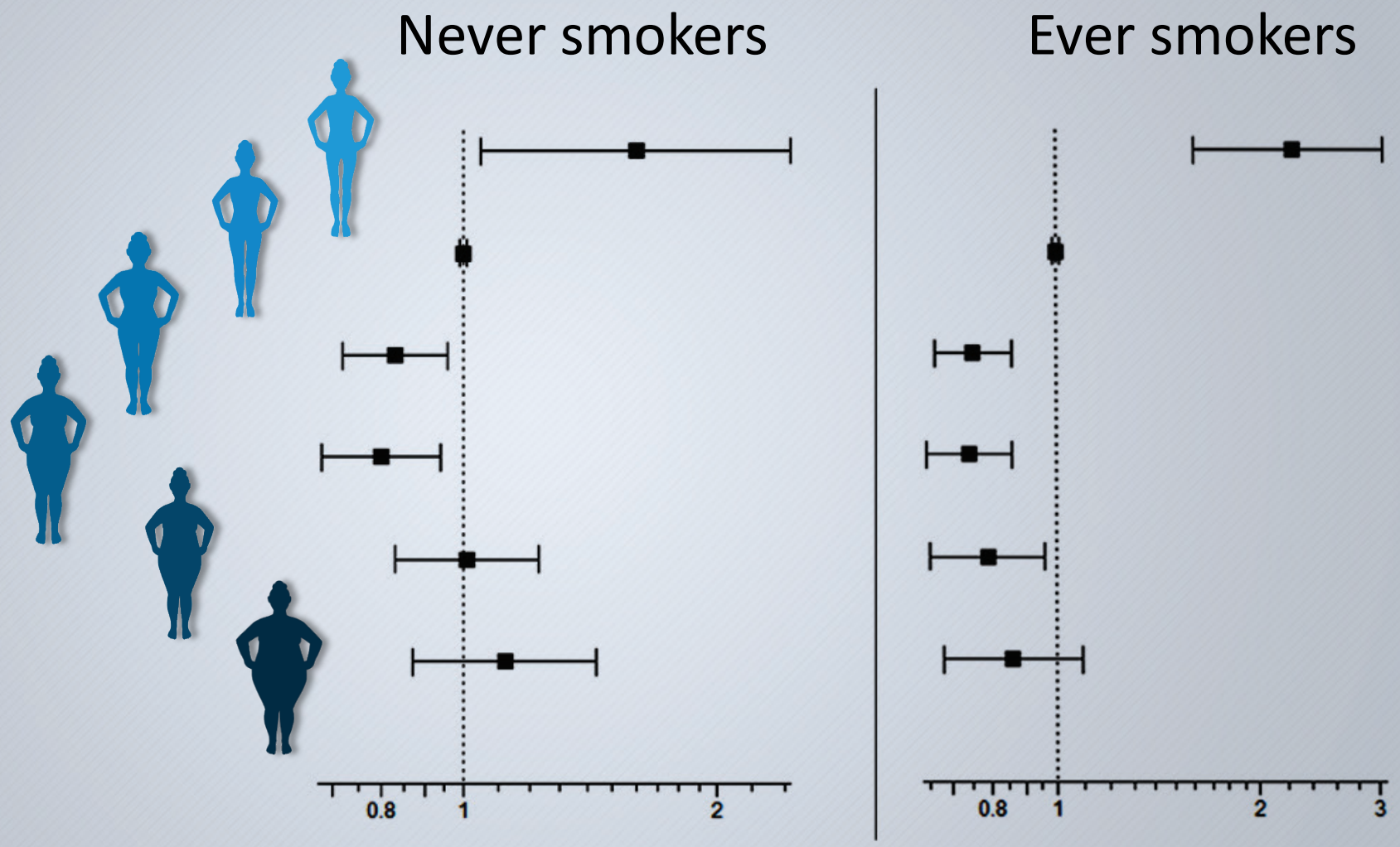
	Underweight	Normal Weight	Overweight	Obesity I	Obesity II	Obesity III
No. of participants	143	2,714	3,702	2,581	1,163	690
Age, yr	74.1 (4.3)	73.5 (4.6)	72.9 (4.5)	72.1 (4.4)	71.4 (4.3)	70.1 (4.1)
BMI , kg/m^2	17.2 (1.1)	22.6 (1.6)	27.4 (1.4)	32.2 (1.4)	37.2 (1.4)	44.8 (4.9)
White, n (%)	115 (80.4)	2,402 (89.0)	3,177 (86.1)	2,183 (84.7)	972 (84.0)	548 (79.5)
Smoking Status, %						
Never	66 (47.5)	1,393 (52.2)	1,885 (51.6)	1,307 (51.3)	620 (54.1)	347 (51.0)
Past	51 (36.7)	1,037 (38.8)	1,538 (42.1)	1,107 (43.4)	489 (42.7)	301 (44.2)
Current	22 (15.8)	241 (9.0)	228 (6.2)	136 (5.3)	37 (3.2)	33 (4.9)

Hazard Ratios

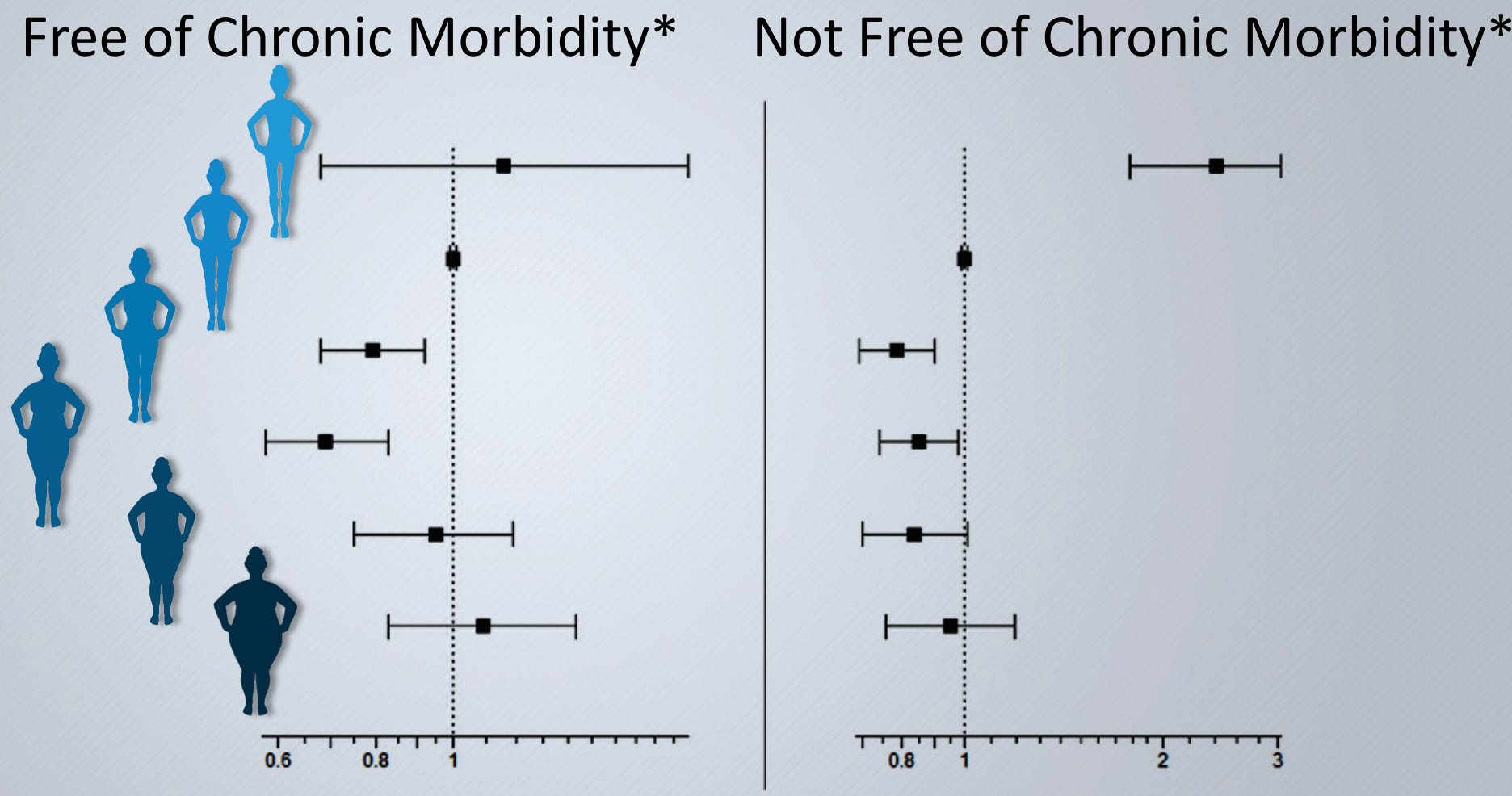
for All-Cause Mortality
among Frail Women,
according to BMI categories



Stratification by smoking status



Stratification by smoking status



*History of diabetes, CVD, stroke, cancer or emphysema

Conclusion

- Overweight and grade I obesity are associated with reduced risk for all-cause mortality compared with women of normal weight
- Grade II and III obesity are not associated with an increased risk for mortality
- Stratification by chronic morbidity, smoking status, exclusion of women with early death and unintentional weight loss did not substantially change the main findings

Interventions

FRAILTY

Pharmacological interventions

Onder et al., 2002; Sumukadas et al., 2007;
Basaria et al., 2010; Friedlander et al., 2001;

Future directions

FRAILTY

Clinical sensibility

Palliative practices

Objectives

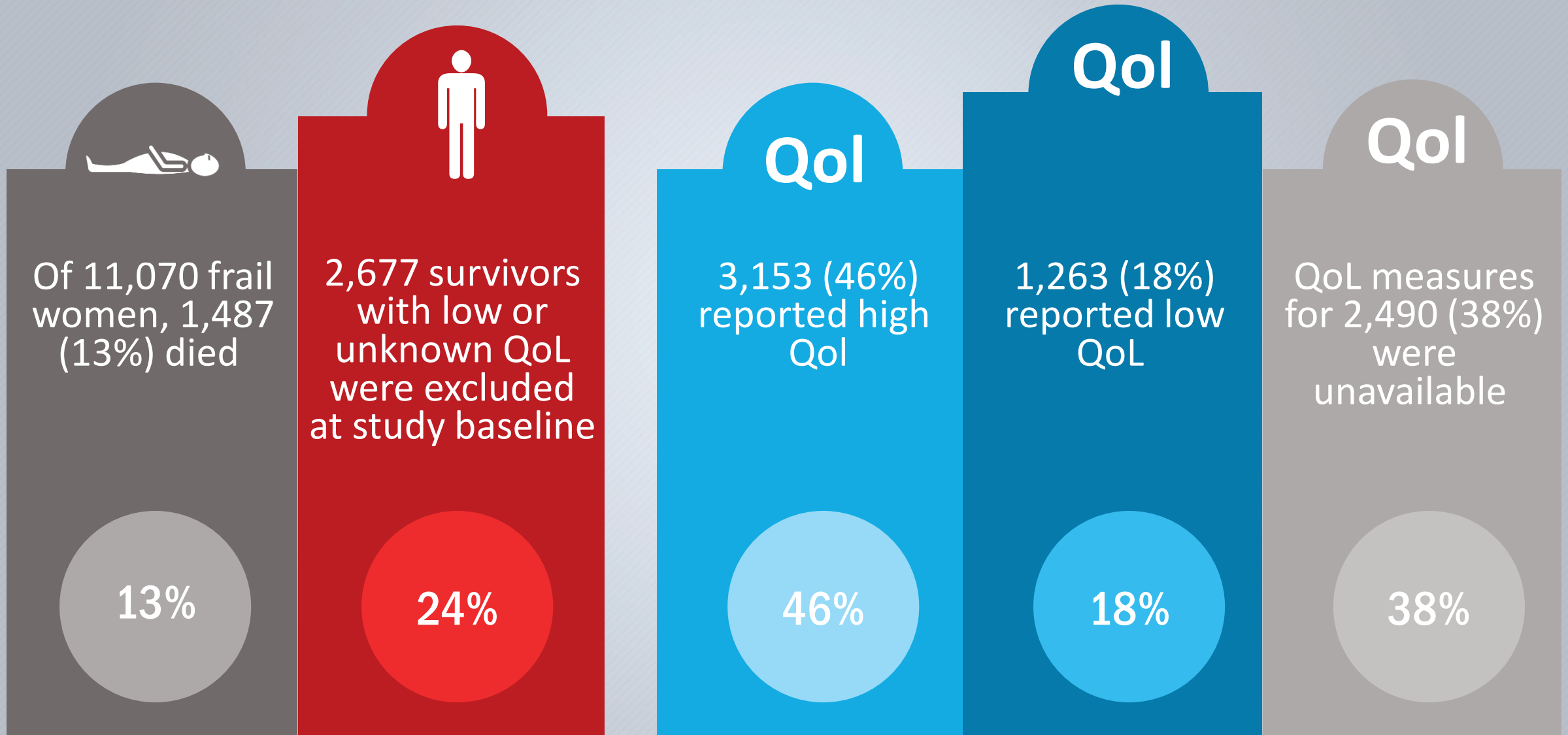
To identify potentially modifiable factors associated with overall and low-quality-of-life (QoL) survival among physically frail older women.

Zaslavsky et al. (accepted for publication)

Measurements

- Frailty was defined using WHI index.
- Overall and low-QoL survival
  (score <7 on global QoL scale) indicated study outcomes.
- Risk factors were measured at the first follow-up
  clinic visit for WHI OS participants in 1997-2001.

Results


Of 11,070 frail women, 1,487 (13%) died
13%
2,677 survivors with low or unknown QoL were excluded at study baseline
24%
QoI
3,153 (46%) reported high QoI
46%
QoI
1,263 (18%) reported low QoL
18%
QoI
QoL measures for 2,490 (38%) were unavailable
38%

Results (cont.)

- Older age
- History of cardiovascular disease
- Diabetes
- Low self-rated health
- BMI < 25 kg/m^2
- Waist circumference > 88cm
- Systolic blood pressure >140 mmHg
- High somatic symptoms
- Smoking
- Low education

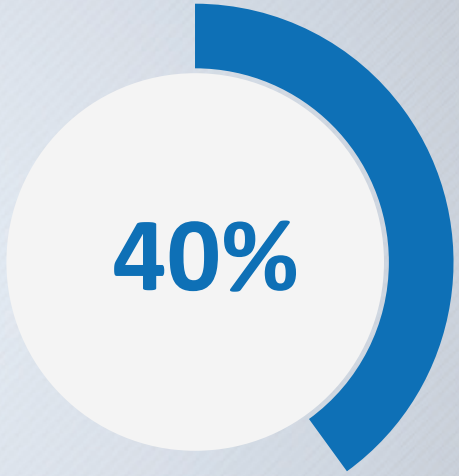
were associated
with a greater likelihood of low- versus high-QoL survival.

Results (cont.)

The probability of low-QoL survival

0 - 2 risk factors

(95% CI 15%–22%)



6≧risk factors

(95% CI 15%–22%)

Conclusion