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THE INTERSECTION BETWEEN COMORIDITY, MULTIMORBIDITY AND FRAILTY

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New York University

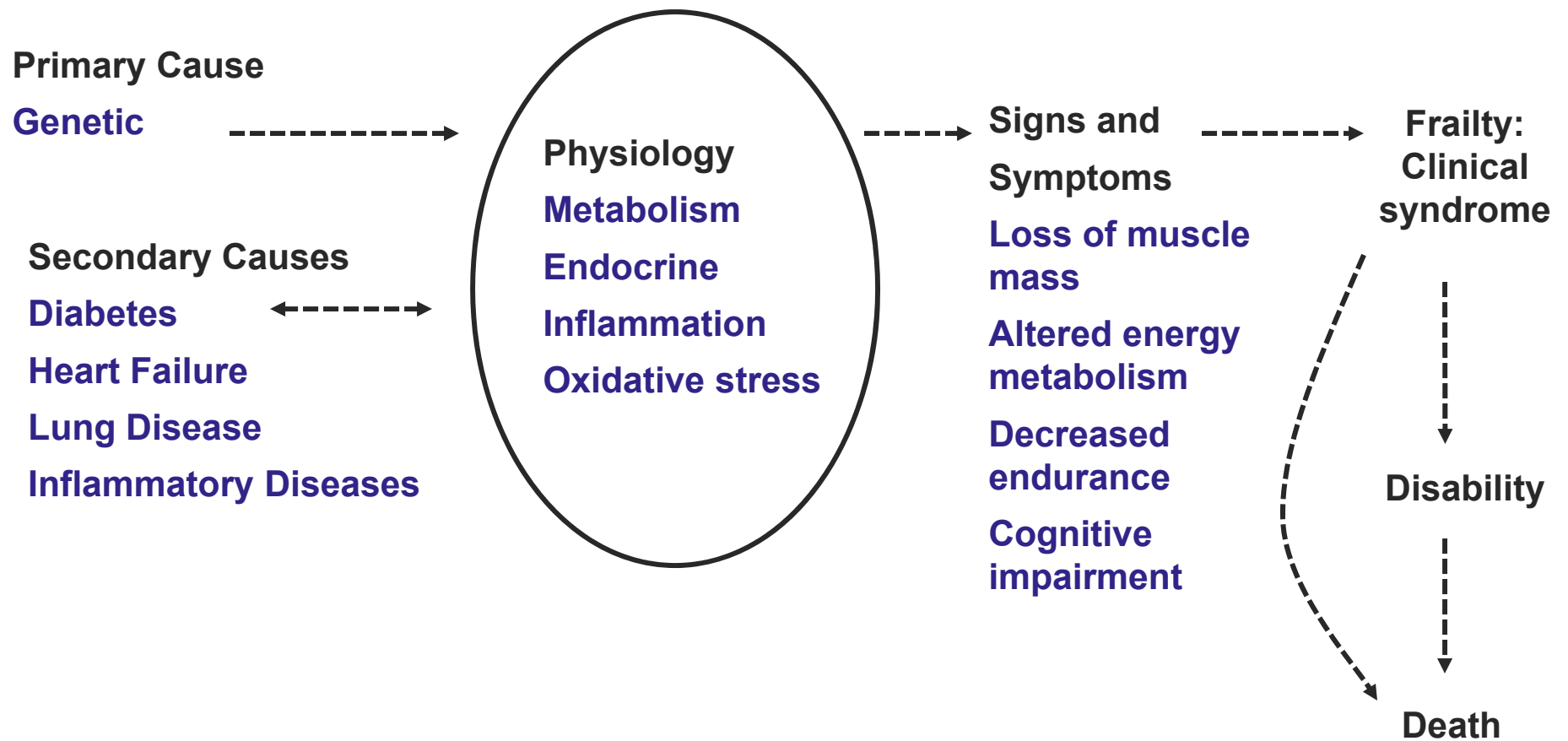*U13 Gemsstar Conference March, 2015*

Definitions

- Comorbidity: additional diseases beyond the index disease
- Multimorbidity: co-occurrence of multiple diseases
- Frailty: increased vulnerability to stressors and adverse outcomes

Goals of this Presentation

- Overview: Multiple Chronic Conditions
  - Disease specific
  - Geriatric conditions
- Multiple chronic conditions and frailty
- Links to theory in aging research
- Research gaps

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Frailty: A Conceptual Model

Primary Cause

Genetic ------>

Secondary Causes

Diabetes <------>

Heart Failure

Lung Disease

Inflammatory Diseases

Physiology

Metabolism

Endocrine

Inflammation

Oxidative stress

------>

Signs and Symptoms ------> **Frailty: Clinical syndrome**

Loss of muscle mass

Altered energy metabolism

Decreased endurance

Cognitive impairment

Disability

Death

"The most common chronic condition experienced by adults is multimorbidity, the coexistence of multiple chronic diseases or conditions."

Tinetti et al. JAMA 2012.

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It's Not Easy Living with Multimorbidity

Time	Medications	Non-pharmacologic Therapy	All Day	Periodic
7 AM	Ipratropium MDI Alendronate 70mg weekly	Check feet Sit upright 30 min. Check blood sugar	Joint protection Energy conservation Exercise (non-weight bearing if severe foot disease, weight bearing for osteoporosis) Muscle strengthening exercises, Aerobic Exercise ROM exercises Avoid environmental exposures that might exacerbate COPD Wear appropriate footwear Albuterol MDI prn Limit Alcohol Maintain normal body weight	Pneumonia vaccine, Yearly influenza vaccine All provider visits:Evaluate Self-monitoring blood glucose, foot exam and BP Quarterly HbA1c, biannual LFTs Yearly creatinine, electrolytes, microalbuminuria, cholesterol <u>Referrals:</u> Pulmonary rehabilitation Physical Therapy DEXA scan every 2 years Yearly eye exam Medical nutrition therapy <u>Patient Education:</u> High-risk foot conditions, foot care, foot wear Osteoarthritis COPD medication and delivery system training Diabetes Mellitus
8 AM	Eat Breakfast HCTZ 12.5 mg Lisinopril 40mg Glyburide 10 mg ECASA 81 mg Metformin 850mg Naproxen 250mg Omeprazole 20mg Calcium + Vit D 500mg	2.4gm Na, 90mm K, Adequate Mg, ↓ cholesterol & saturated fat, medical nutrition therapy for diabetes, DASH		
12 PM	Eat Lunch Ipratropium MDI Calcium+ Vit D 500 mg	Diet as above		
5 PM	Eat Dinner	Diet as above		
7 PM	Ipratropium MDI Metformin 850mg Naproxen 250mg Calcium 500mg Lovastatin 40mg			
11 PM	Ipratropium MDI			

Boyd et al. JAMA 2005;294:716-724

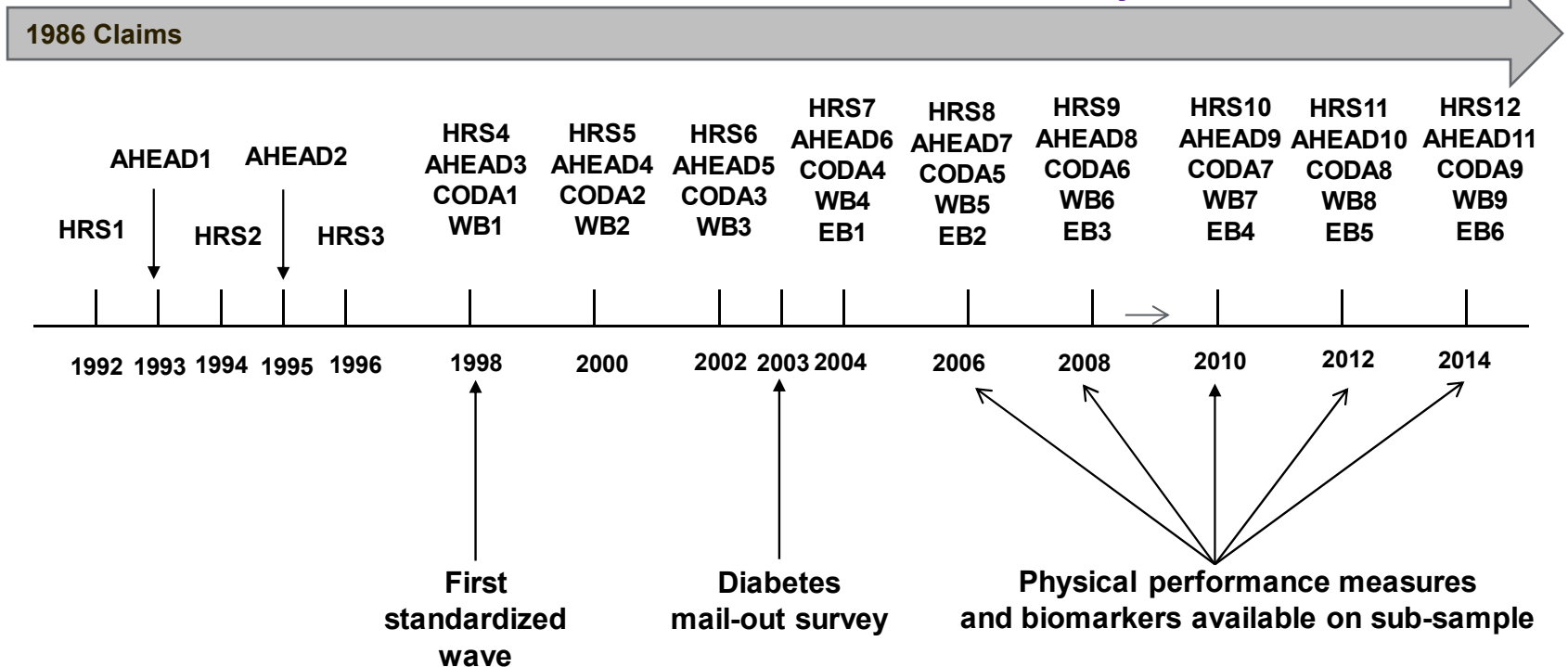**Figure 4.1** *Co-morbidity among Chronic Conditions for Medicare FFS Beneficiaries: 2010*

Slide Courtesy of R. Goodman, CDC
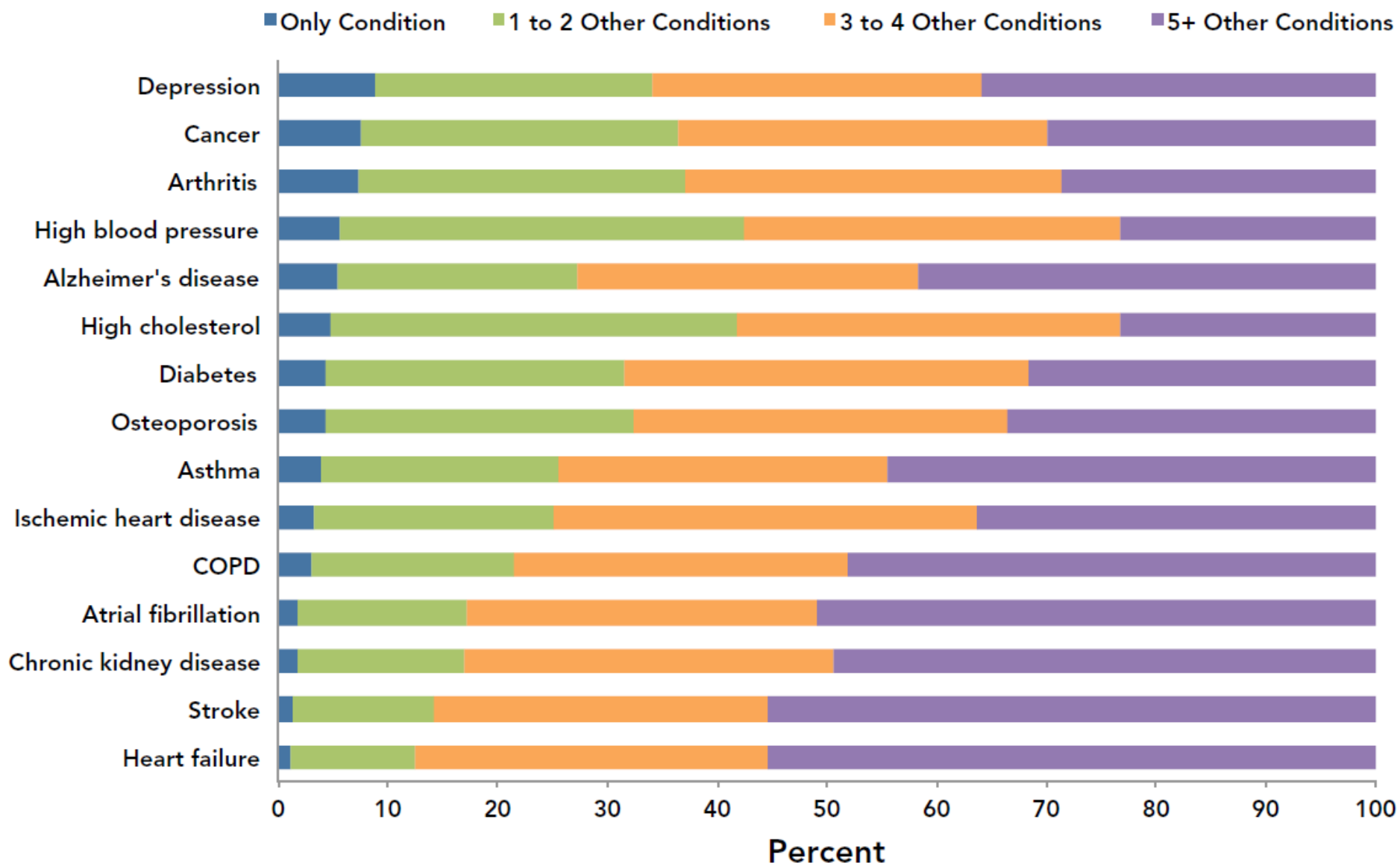
Geriatric conditions are associated with ADL dependency

(Cigolle, C, et al. Ann Intern Med 147, 2006)

	Model 1	Model 2	Model 3
# geriatric conditions			
1	3.0 (2.6-3.4)	2.6 (2.3-3.0)	2.2 (2.0-2.5)
2	7.3 (6.3-8.3)	5.4 (4.7-6.2)	3.9 (3.6-4.4)
≥3	16.9 (14.8-18.9)	11.5 (9.9-13.0)	7.5 (6.4-8.5)
# chronic diseases			
1	-	-	1.9 (1.8-2.1)
2	-	-	2.8 (2.6-3.1)
≥3	-	-	4.0 (3.5-4.5)

The Health and Retirement Survey: 1992-2012

1986 Claims

HRS1

AHEAD1   AHEAD2

HRS2   HRS3

HRS4
AHEAD3
CODA1
WB1

HRS5
AHEAD4
CODA2
WB2

HRS6
AHEAD5
CODA3
WB3

HRS7
AHEAD6
CODA4
WB4
EB1

HRS8
AHEAD7
CODA5
WB5
EB2

HRS9
AHEAD8
CODA6
WB6
EB3

HRS10
AHEAD9
CODA7
WB7
EB4

HRS11
AHEAD10
CODA8
WB8
EB5

HRS12
AHEAD11
CODA9
WB9
EB6

1992 1993 1994 1995 1996   1998   2000   2002 2003 2004   2006   2008   2010   2012   2014

First standardized wave

Diabetes mail-out survey

Physical performance measures and biomarkers available on sub-sample

Cohorts:	Birth Years	Baseline
Assets and Health Dynamics Among the Oldest Old (AHEAD)	1890-1924	1993
Children of the Depression (CODA)	1924-1930	1998
Original Health and Retirement Study (HRS)	1931-1941	1992
War Babies (WB)	1942-1947	1998
Early Boomers (EB)	1948-1953	2004
Middle Boomers (MB)	1953-1959	2012

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Common Comorbidities Among Older Adults: Diseases and Geriatric Conditions

HRS, representative of 35 million people 65 and older, 2004 (Lee et al, JAGS 2009:57;840)

Index Condition (%)	Weighted Prevalence (%) of Other Conditions Among Respondents Having Index Condition						
	CAD	CHF	Diabetes	UI	Falls	≥1 Other	≥2 Other
CAD (8.7)		17%	29%	29%	34%	67%	30%
CHF (4.8)	58%		37%	37%	43%	87%	56%
Diabetes (19.4)	24%	9%		28%	29%	57%	23%
UI (25.0)	19%	7%	22%		37%	58%	20%
Falls (23.2)	23%	9%	24%	39%		64%	23%

Incidence of Geriatric Conditions Among Adults With Diabetes Aged 51 and Older: HRS 2004 to 2006

(Cigolle, et al, JGIM, 2010)
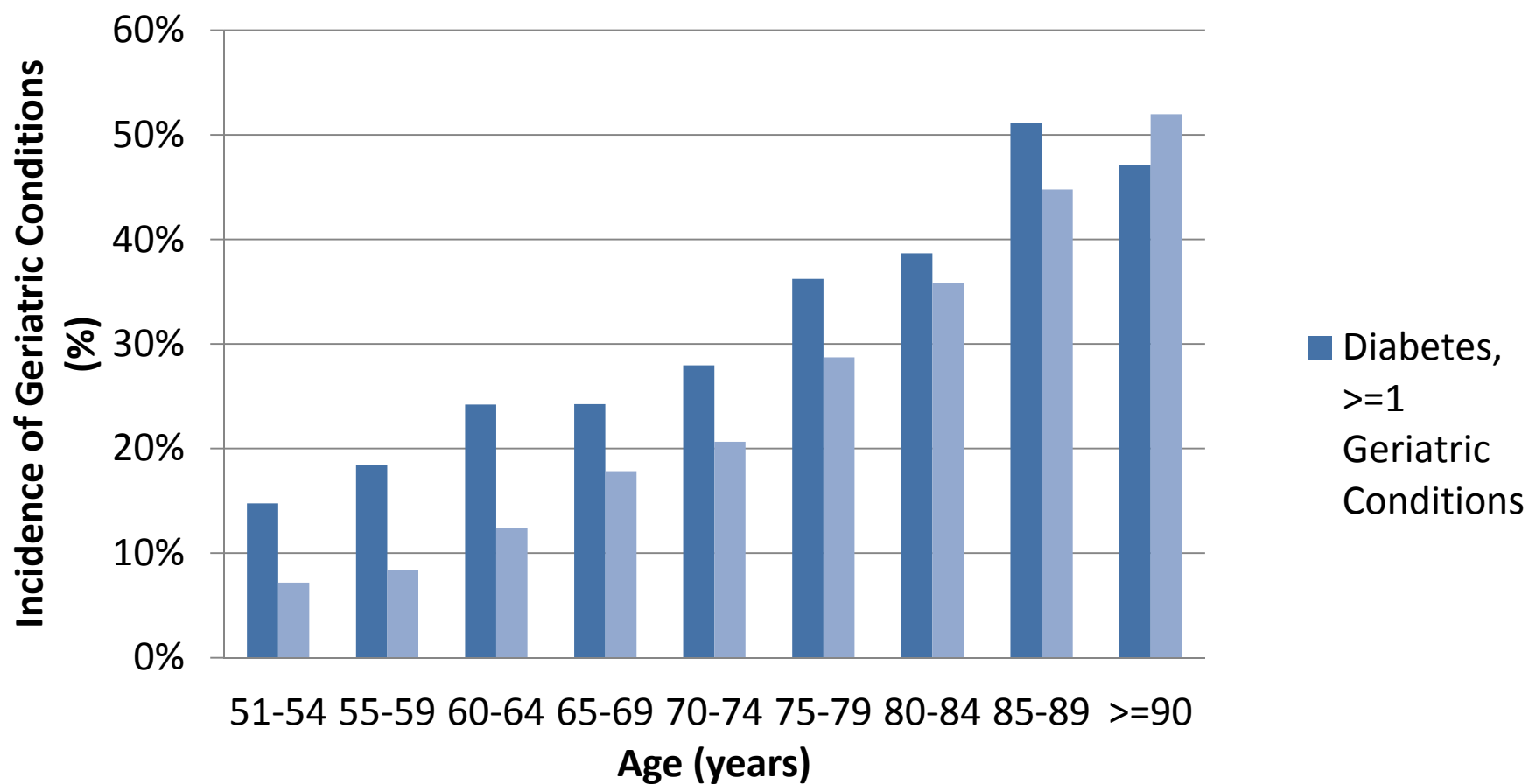
Framework for Considering Comorbid Conditions

<u>Clinically dominant comorbid conditions:</u>

so complex or serious that they eclipse the management of other health problems

– end-stage, severely symptomatic, recently diagnosed

e.g. heart failure

<u>Concordant conditions:</u>

represent parts of the same overall pathophysiologic risk profile and are more likely to be the focus of the same disease management plan (may include 'complicating')

- e.g. coronary atherosclerosis and hyperlipidemia

<u>Discordant conditions:</u>

not directly related in either their pathogenesis or management and do not share an underlying predisposing factor

- arthritis or urinary incontinence

Diabetes and Vascular Complications

IR,obesity
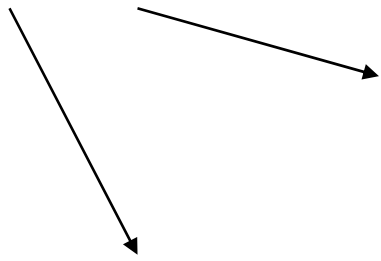
Modifiers: Blood pressure, lipids, physical activity, treatment
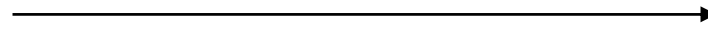
Diabetes
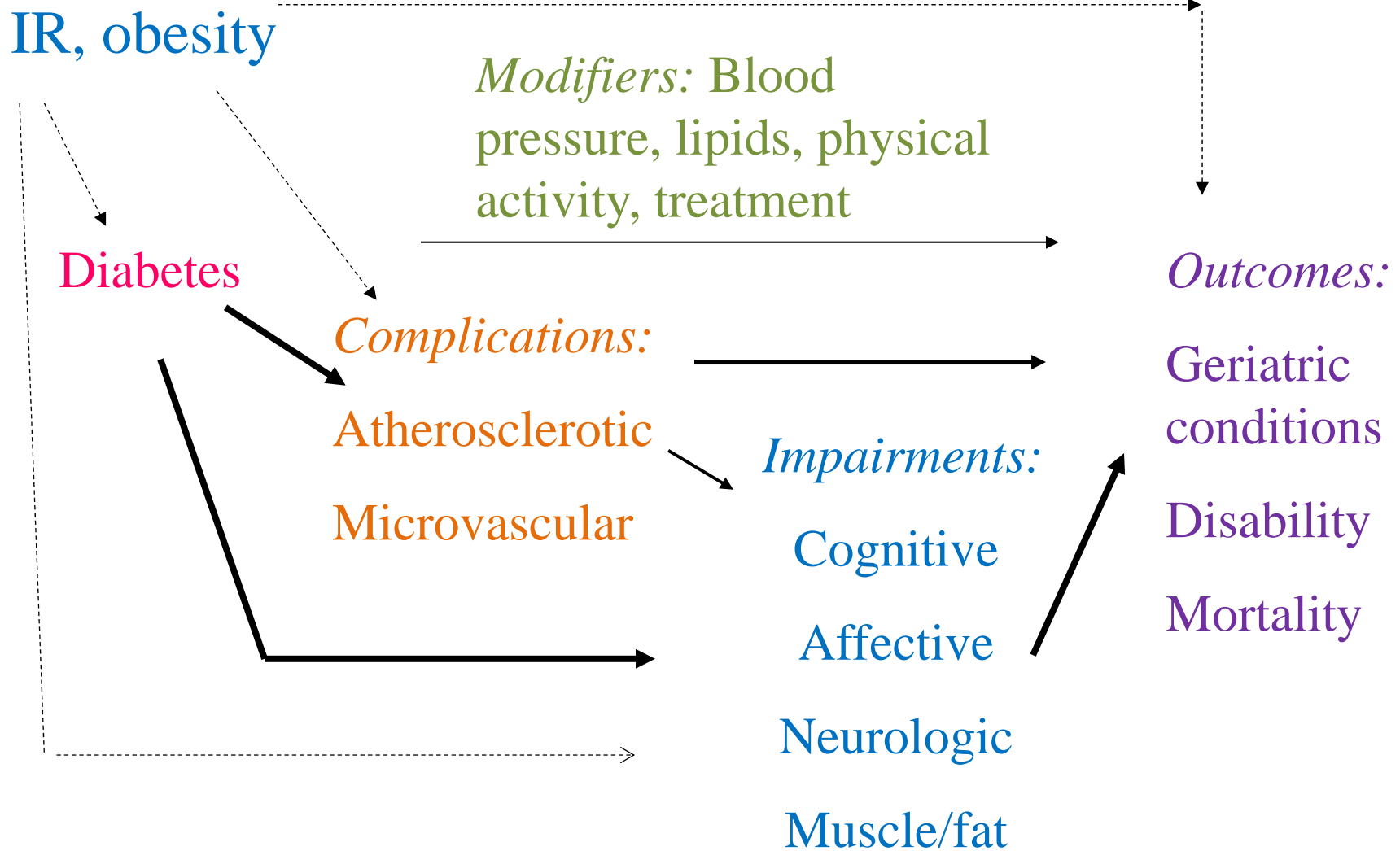
Complications:

Atherosclerotic

Microvascular

Diabetes and Distal Complications

IR, obesity

Modifiers: Blood pressure, lipids, physical activity, treatment

Diabetes

Complications:

Atherosclerotic

Microvascular

Impairments:

Cognitive

Affective

Neurologic

Muscle/fat

Outcomes:

Geriatric conditions

Disability

Mortality

Most frequently co-occurring chronic conditions, women 65+ in community (WHAS screenees)

- Arthritis, visual impairment   44%
- Visual Impairment, HBP   40%
- Arthritis, HBP   34%
- Heart disease, visual imp.   17%
- Visual imp, hearing imp   15%
- Heart disease, arthritis   14%
- Heart disease, HBP   13%
- Arthritis, hearing imp   12%
- Diabetes, visual imp   12%

Heart Failure and Cognition

(Gure, TR et al, JAGS 60,2012)

	No heart failure	Heart disease but low probability heart failure	High probability heart failure
TIC's score: mean ± sd, (range 0-27)	14.5 ± 4.3	13.7 ±4.6	12.7 ±4.3
Normal cognition	71 (70-71)	68 (65-70)	61 (57-65)
MCI % (confidence interval)	21 (19-22)	22 (22-24)	24 (21-28)
Mod-severe cognitive impairment	8 (7-9)	10 (9-11)	15 (12-18)

Changes in ADL/IADL with time in respondents with and without diabetes in HRS (51 and over)
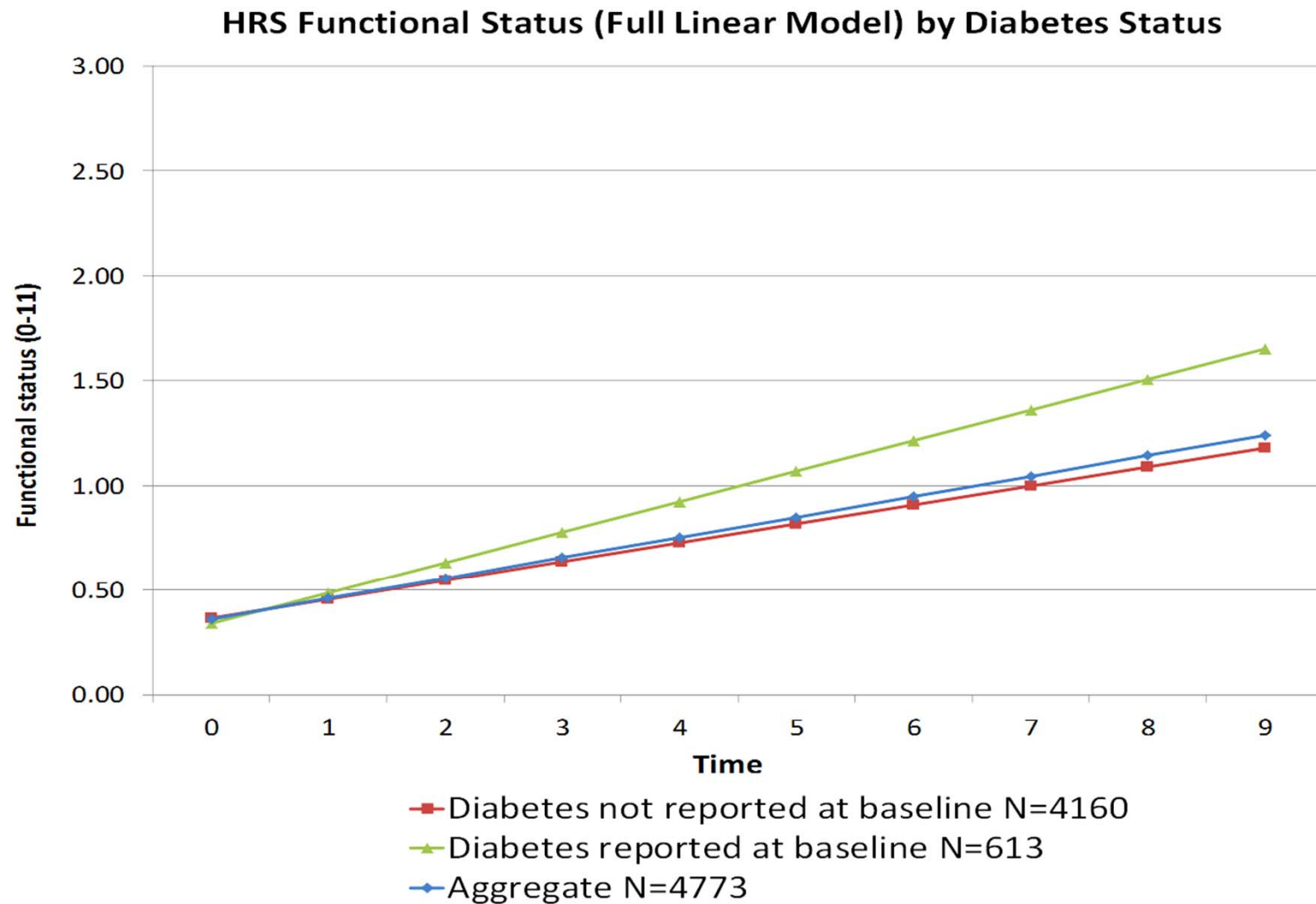
HRS Functional Status (Full Linear Model) by Diabetes Status

- Diabetes not reported at baseline N=4160
- Diabetes reported at baseline N=613
- Aggregate N=4773

ADL/IADL with time by diabetes and hypertension (HRS, ages 51 and up)

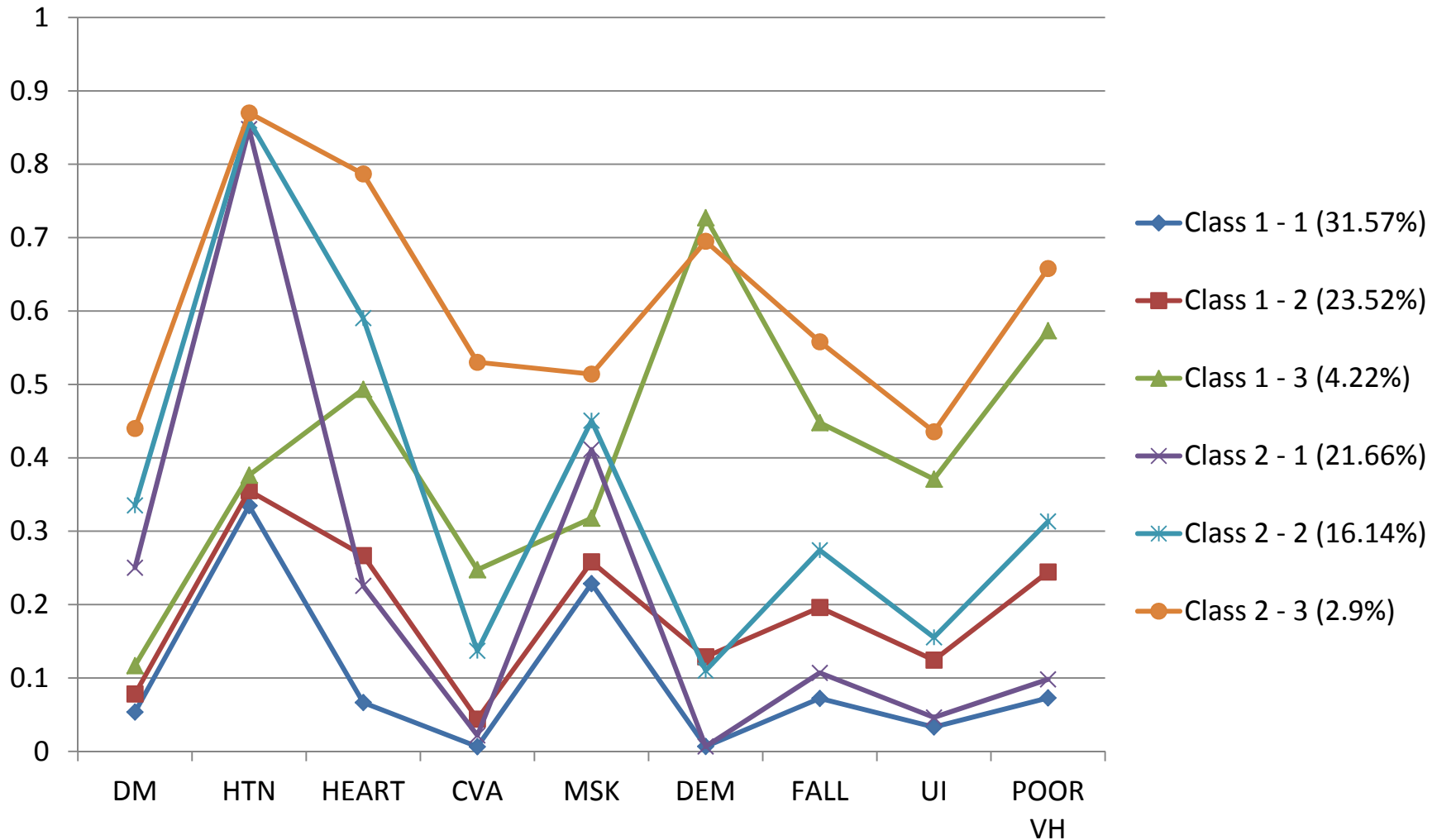HRS Functional Status by Diabetes by High Blood Pressue Interaction

Competing risks in older adults with diabetes: falls and strokes (Min,L, preliminary data)

Cumulative Incidence of Injurious Fall vs Stroke
N=365 Diabetics Aged 65+

With Competing Risk of Death
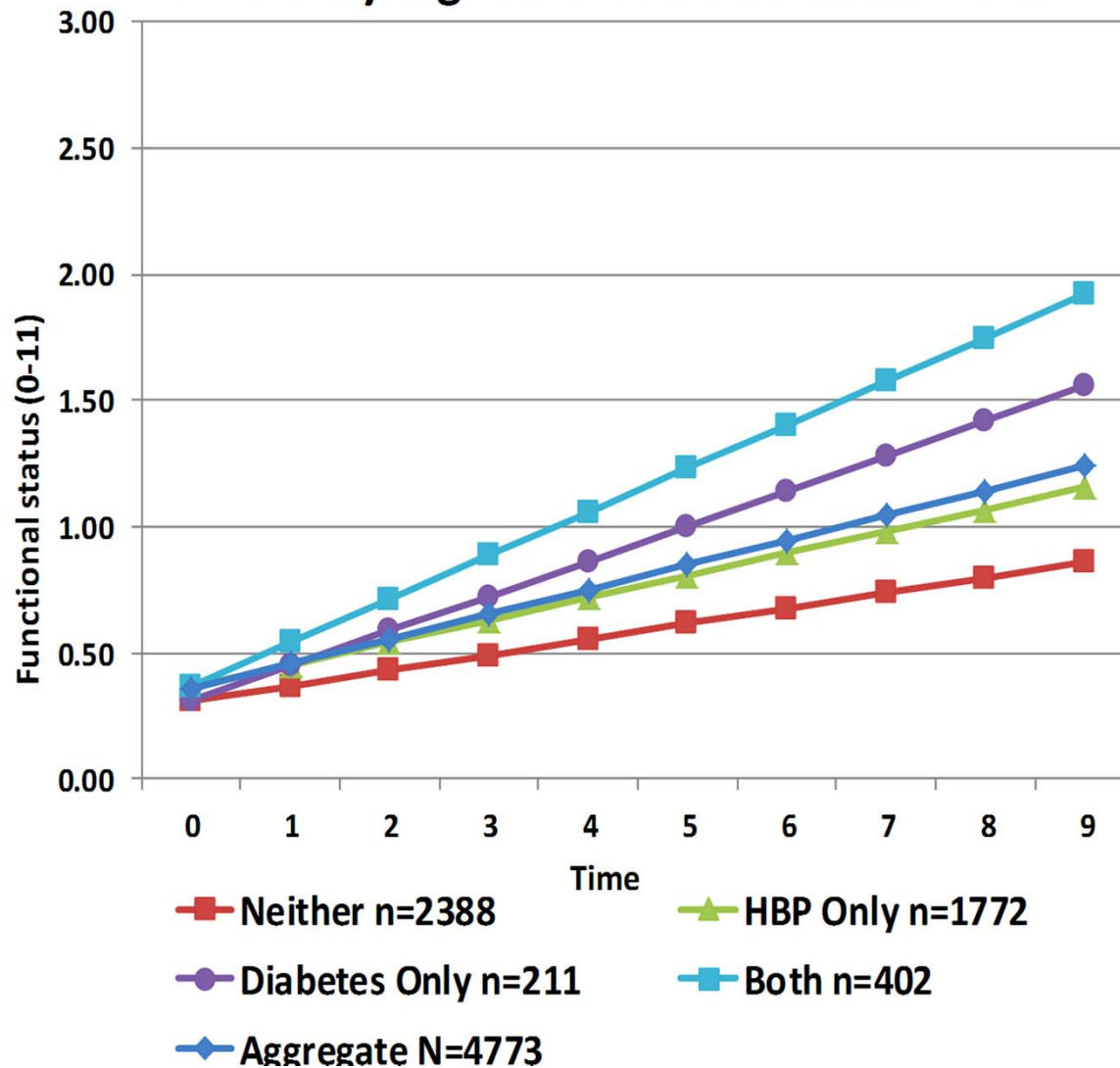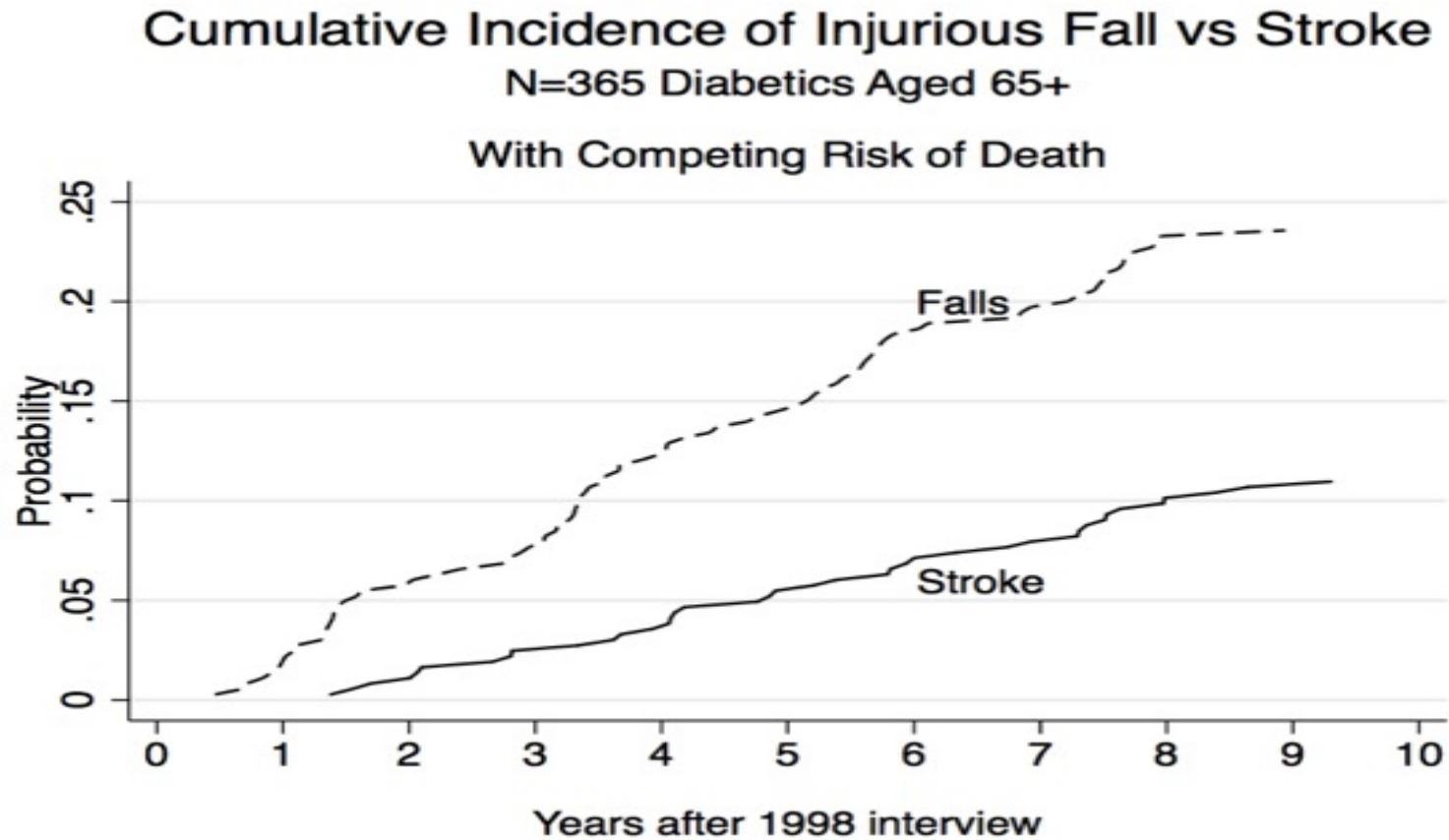
Grouping Chronic Diseases and Geriatric Conditions: The HRS

(Cigolle, Ha, et. al, 2012, JGIM paper presentation)

Legend:
- Class 1 - 1 (31.57%)
- Class 1 - 2 (23.52%)
- Class 1 - 3 (4.22%)
- Class 2 - 1 (21.66%)
- Class 2 - 2 (16.14%)
- Class 2 - 3 (2.9%)

X-axis: DM, HTN, HEART, CVA, MSK, DEM, FALL, UI, POOR VH

RESULTS: Disability and Mortality Outcomes

	Healthy BP, MS	BP, CV, MS, falls	Ger cond, dementia	Healthy DM, MS, BP	DM, CV	All
New ADL dependency at 2 years (%)	3.0	7.7	42.0	7.8	10.0	26.3
New IADL dependency at 2 years (%)	5.1	13.9	60.2	11.5	15.3	53.2
Mortality at 2 years (%)	4.8	13.7	44.4	6.4	13.0	35.5
Mortality at 4 years (%)	10.3	25.7	73.3	13.8	24.2	59.8

Goal-Oriented Patient Care

Measurement Domain	Examples of Diseases	Traditional Outcomes	Goal-Oriented Outcomes
		Comparison of Traditional Disease-Specific and Goal-Oriented Outcomes.*	
Survival	Cancer, heart failure	Overall, disease-specific, and disease-free survival	None if survival not a high-priority goal; survival until personal milestones are met (e.g., grandchild's wedding)
Biomarkers	Diabetes, COPD	Change in indicators of disease activity (e.g., glycated hemoglobin level, CRP level, and pulmonary-function tests)	None (not a meaningful outcome observed or felt by patient)
Signs and symptoms	Heart failure, COPD, arthritis	Inventory of disease-specific signs and symptoms (e.g., dyspnea, edema, and back pain)	Symptoms that have been identified as important by the patient (e.g., control of dyspnea or pain sufficient to perform an activity such as bowling or walking grandchild to school)
Functional status, including mobility	Cancer, heart failure, COPD	Usually none or disease-specific (e.g., Karnofsky score, NYHA functional classification, and 6-minute walk test)	Ability to complete or compensate for inability to complete specific tasks identified as important by the patient (e.g., ability to get dressed without help)

* COPD denotes chronic obstructive pulmonary disease, CRP C-reactive protein, and NYHA New York Heart Association.

Tinetti and Reuben NEJM 2012

Multiple Chronic Conditions in Context

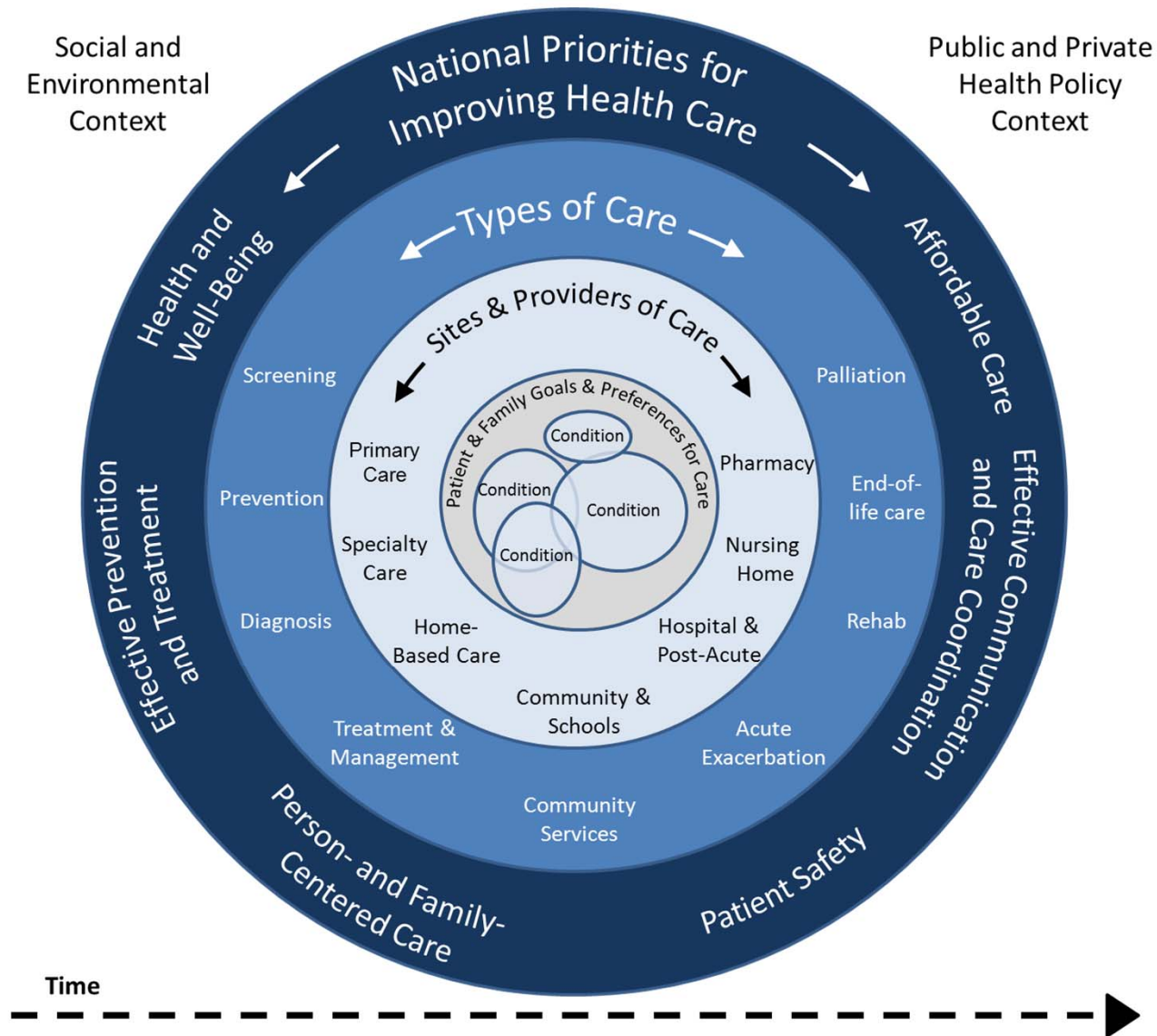Moving from "What is the matter?" to **"What Matters to You?"**

Key contextual factors: public policy, community, health care systems, family, and person, to sub-personal cellular and molecular levels (where most medical knowledge currently is generated)

New knowledge needed involves moving from a predominant disease focus toward a person-driven, goal-directed research agenda
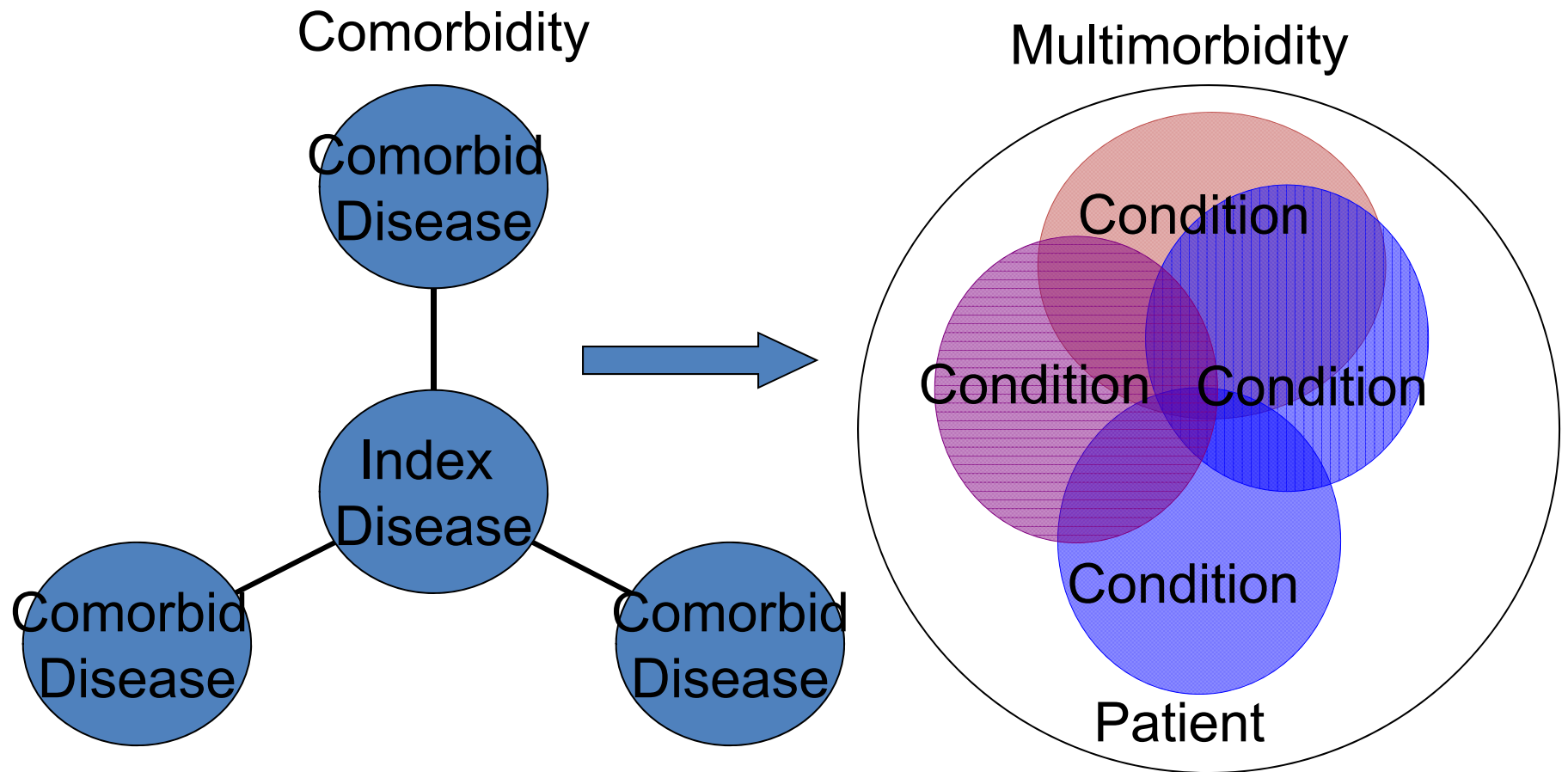
NIH/PCORI Meeting on Multiple Chronic Conditions in Context, Feb. 2013

Quality Framework for People with MCC's
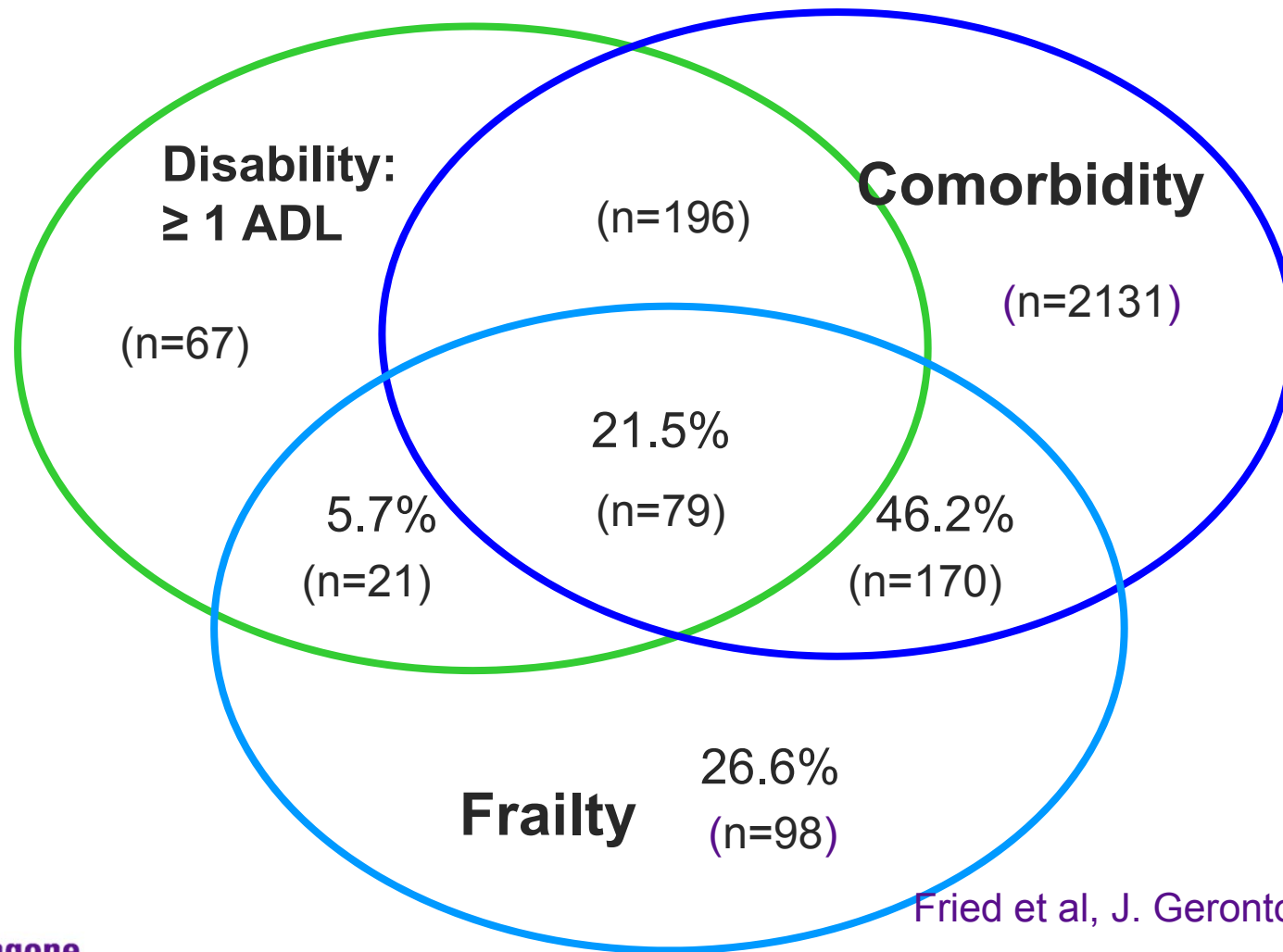## (Giovannetti, ER, et al. Am J Man Care 19, 2013)

Conceptual Framework

Comorbidity

Comorbid Disease

Index Disease

Comorbid Disease

Comorbid Disease

Multimorbidity

Condition

Condition   Condition

Condition

Patient

Boyd, CM, Fortin M. Public Health Reviews, 2011.

Frailty: A Conceptual Model

Primary Cause

Genetic

Secondary Causes

Diabetes

Heart Failure

Lung Disease

Inflammatory Diseases

Physiology

Metabolism

Endocrine

Inflammation

Oxidative stress

Signs and Symptoms

Loss of muscle mass

Altered energy metabolism

Decreased endurance

Cognitive impairment

Frailty: Clinical syndrome

Disability

Death
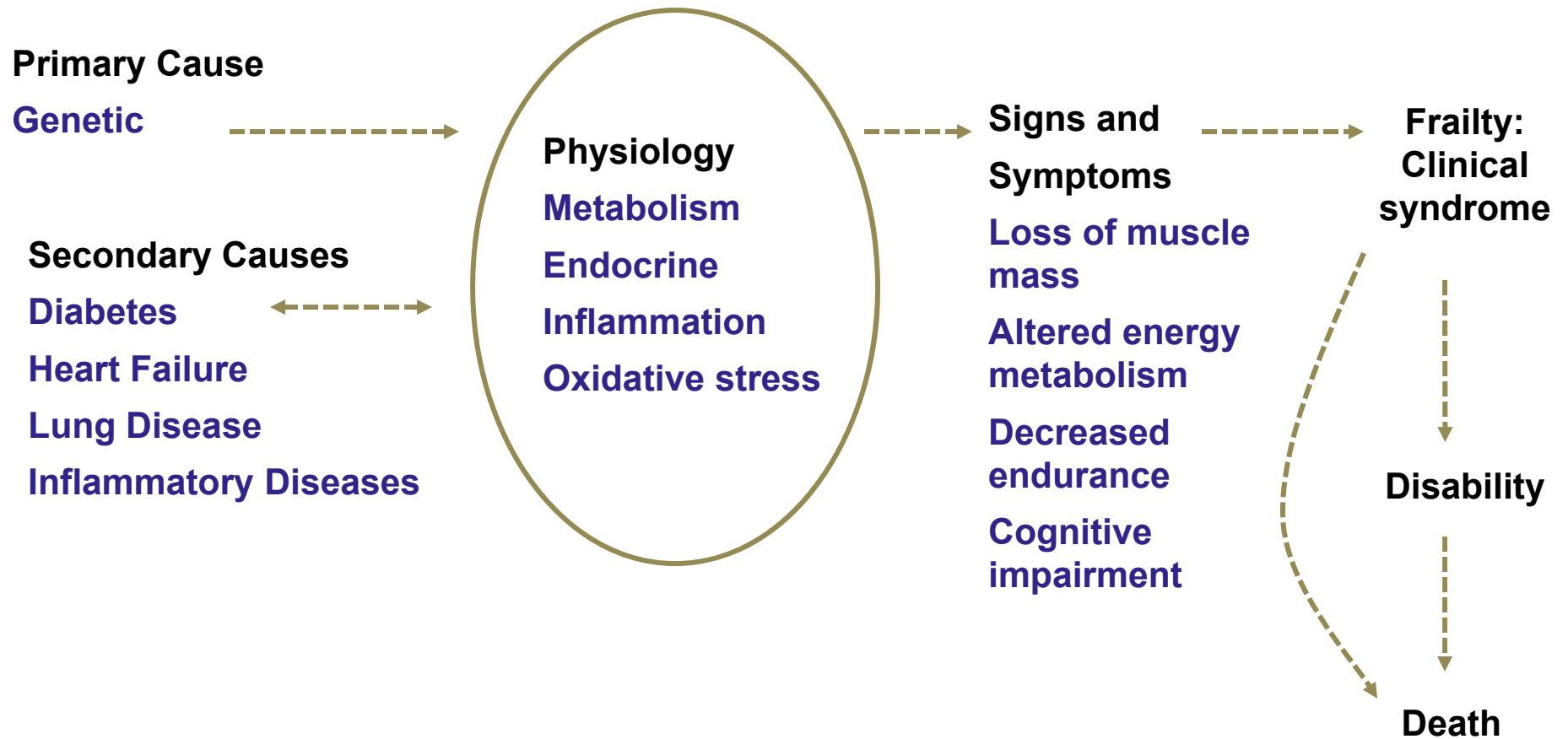
Frailty is distinct from comorbidity and disability

Disability:
≥ 1 ADL

Comorbidity

(n=196)

(n=2131)

(n=67)

21.5%

5.7%
(n=21)

(n=79)

46.2%
(n=170)

26.6%
Frailty (n=98)

Fried et al, J. Gerontology MS, 2001.

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Frailty Models
(Cigolle, C et al, JAGS 57, 2008)

- Frailty has been modeled in different ways, reflecting different theoretical understandings of the concept.
  - **Biologic Syndrome model** (Fried et al.)[1]: frailty phenotype - defined in terms of 5 components
    .

    - Frailty-defining criteria: weight loss, exhaustion, low energy expenditure, slowness, weakness.
    - Not cognition (excluded in original study)

[1]Fried et al., Frailty in older adults: evidence for a phenotype, *J Gerontol A Biol Sci Med Sci* 2001.

Frailty Models

- **Burden model**[2]: frailty index (FI) - a measure of an older adult's cumulative burden of symptoms, diseases, conditions, disability, etc.
- **Functional Domains** model[3]: deficiencies in four domains of functioning (physical, nutritive, cognitive, and sensory).

.

[2]Rockwood et al., A global clinical measure of fitness and frailty in elderly people, *Cmaj* 2005.

[3]Strawbridge et al., Antecedents of frailty over three decades in an older cohort, *J Gerontol B Psychol Sci Soc Sci* 1998.

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COMPARING MODELS OF FRAILTY:
THE HEALTH AND RETIREMENT STUDY
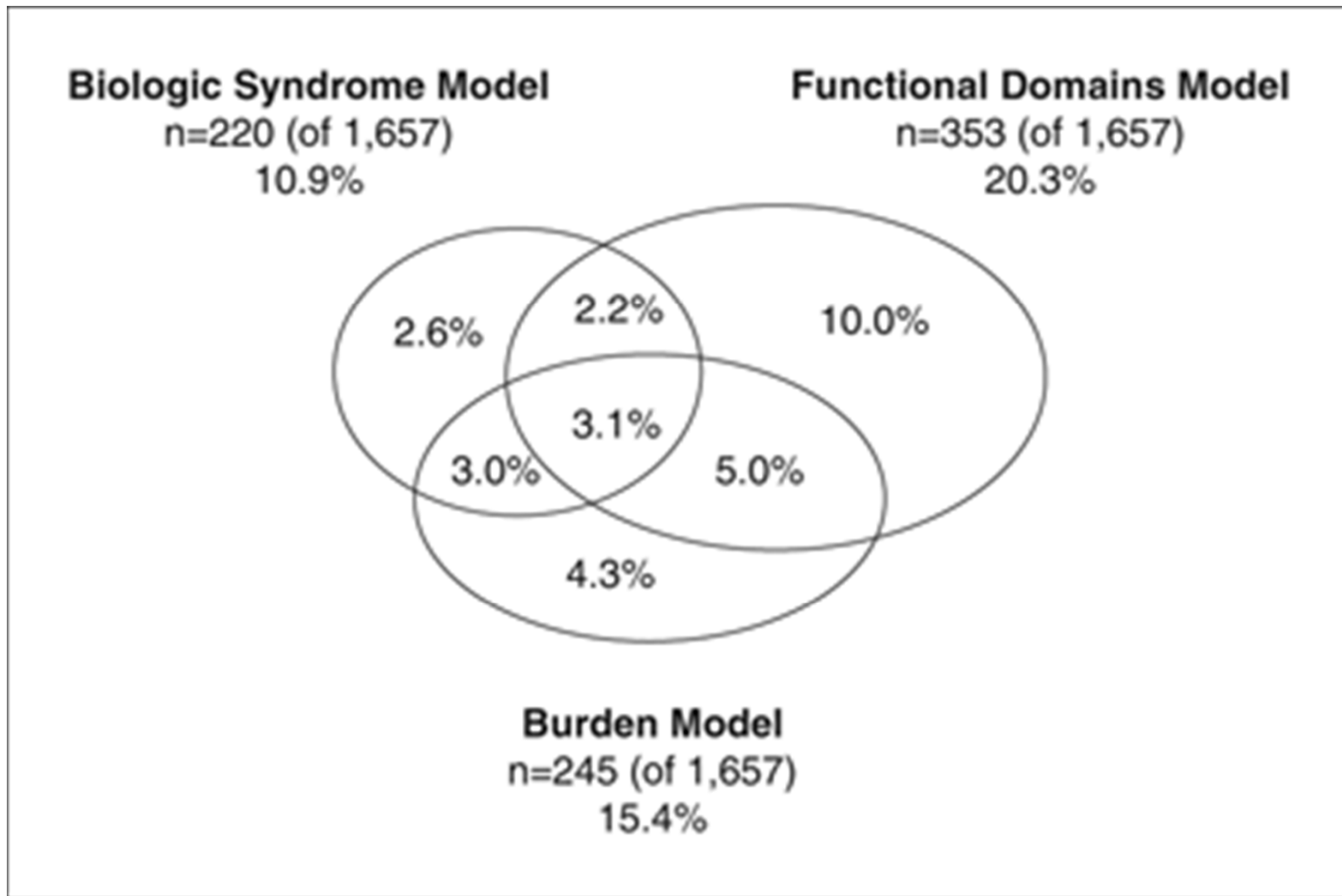
Two-Year Functional Decline by Frailty Model
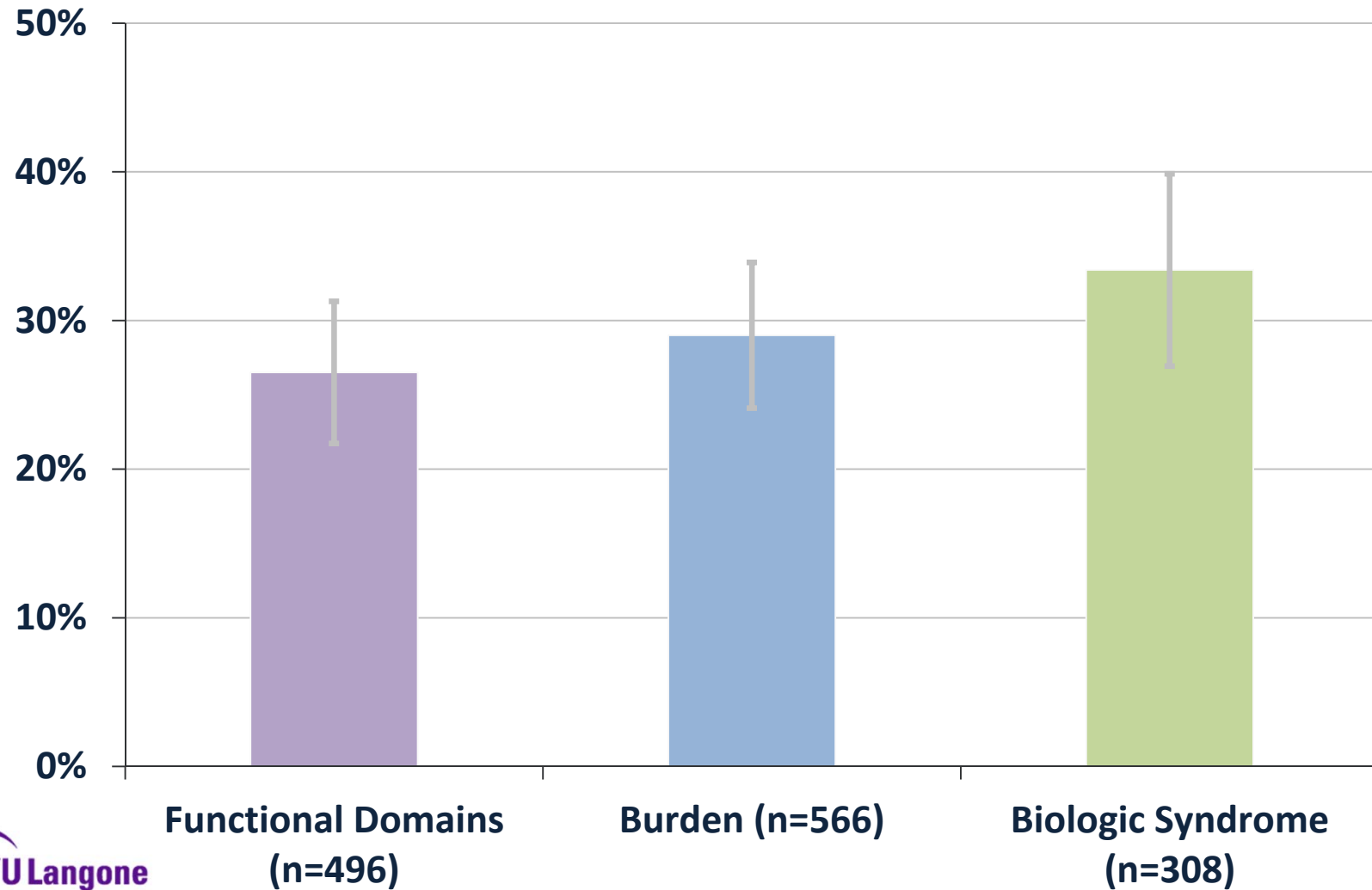
Baseline Association of Diseases and Frailty (CHS)

(Fried, et al. J Gerontology, 2001)
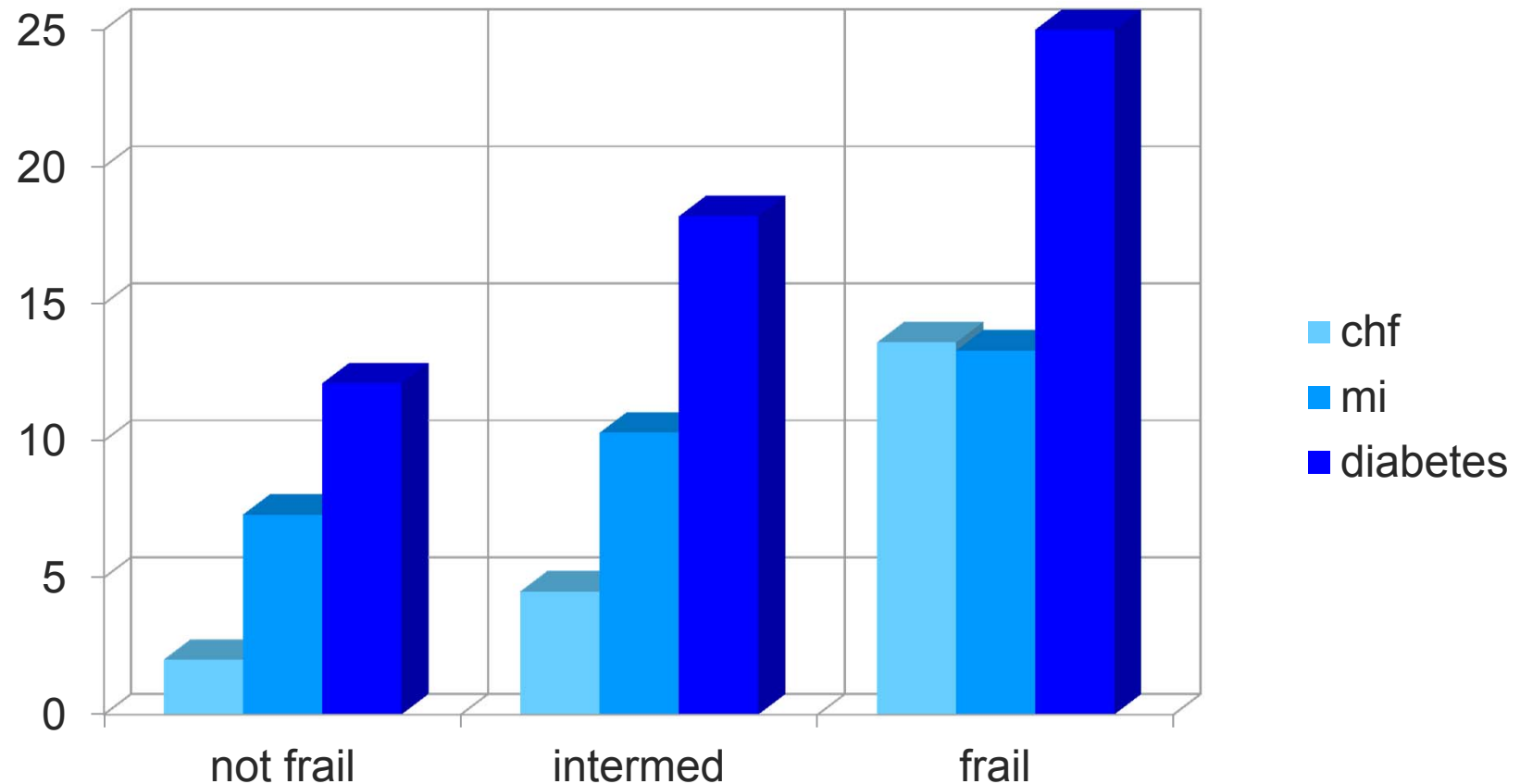
# Diseases associated with increased risk of frailty

- Congestive Heart Failure
- ESRD
- Diabetes
- Dementia
- Depression
- Advanced cancers
- COPD
- Chronic inflammatory diseases
- Hip fractures
- Pressure ulcers and chronic wounds
- AIDS, Tuberculosis, other chronic infections

Conditions Related to Frailty

- Sarcopenia: loss of muscle mass
- Weight loss/undernutrition
- Decreased strength, exercise tolerance
- Slowed motor processing, performance
- Slow gait speed, poor mobility
- Decreased balance
- Low physical activity
- Cumulative illness
- Cognitive impairment
- Increased vulnerability to stressors
- Psychosocial stressors

Association of BMI and Frailty

(Blaum, CS, et al, JAGS53, 2005.)
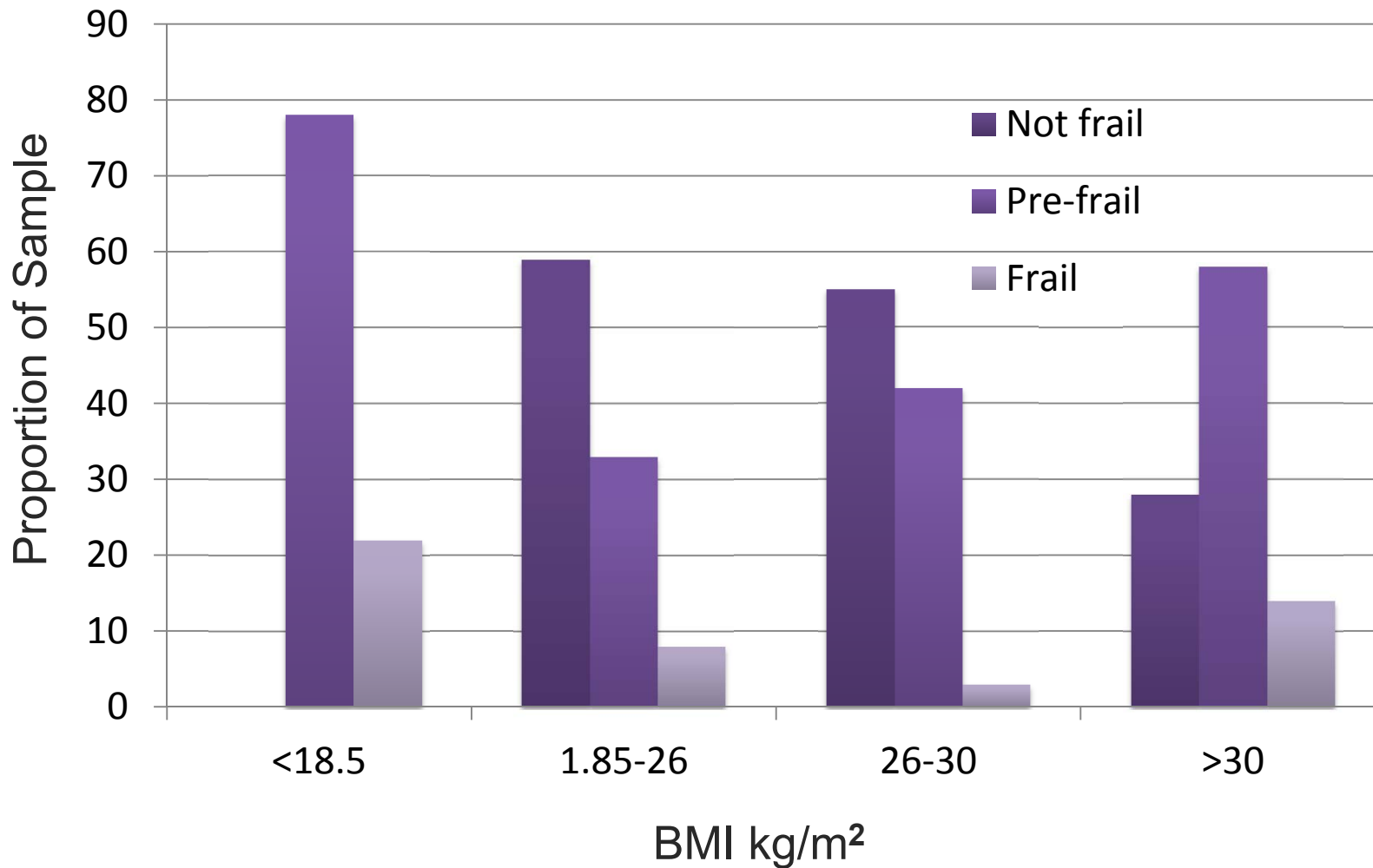
Prevalence Of Frailty Based On Cognitive Function
(Cigolle C, GSA paper presentation 2012)

Prevalence of Frailty	Cognitive Function		
	Normal (n=3,328)	Mild Cognitive Impairment (n=894)	Dementia (n=231)
Robust (%)	40.2	16.4	5.2
Pre-Frail (%)	47.6	54.1	52.8
Frail (%)	12.2	29.4	42.0

Cognition and Frailty

- Over 50% of older adults with mild cognitive impairment and over 70% of older adults with dementia are classified as frail.

- Over 60% of older adults classified as frail have mild cognitive impairment or dementia.

Results: How Frailty-defining Criteria Sort
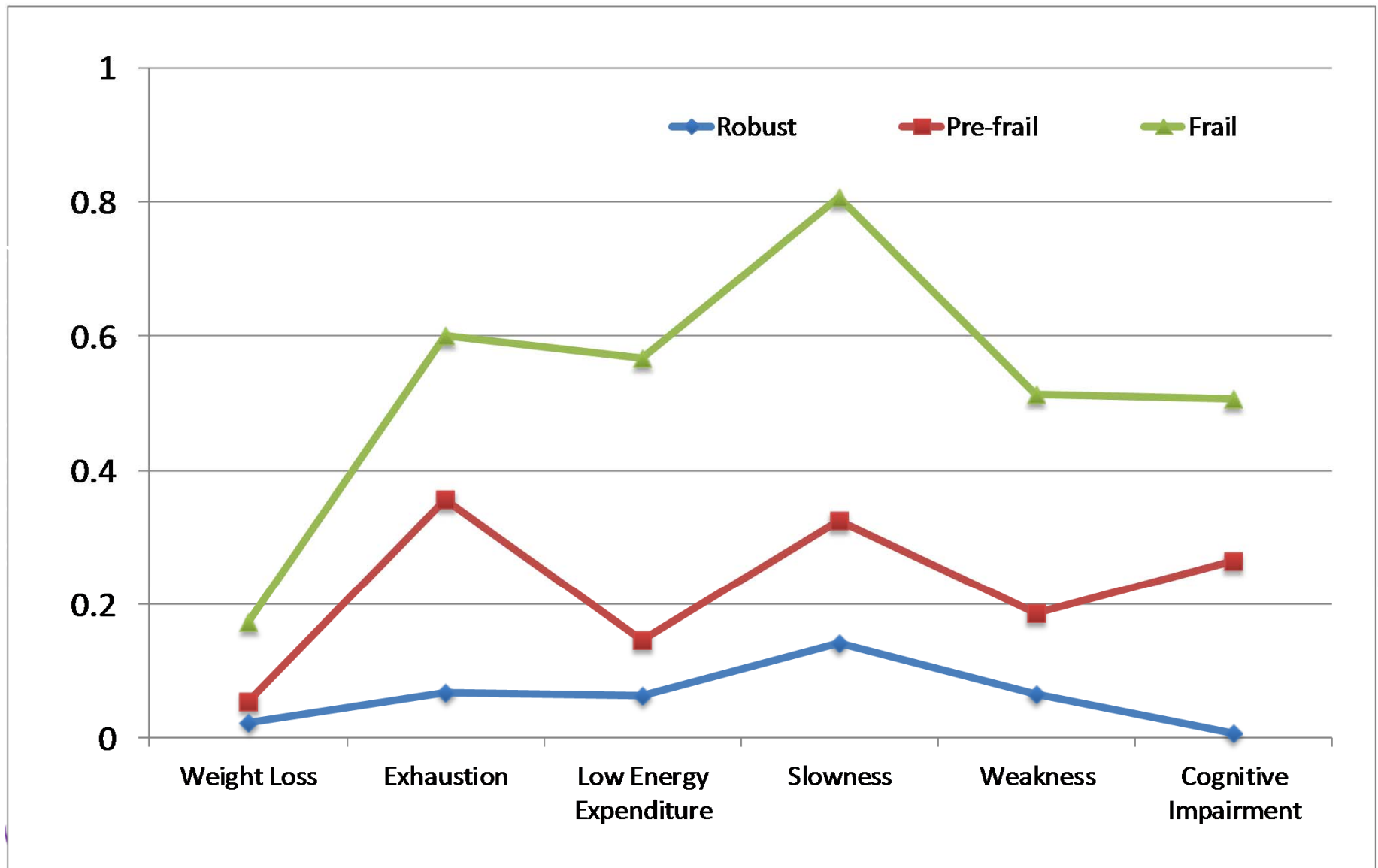
AREAS FOR RESARCH

Research Questions: Clinical

- How can we prevent frailty?
- Does frailty help in prognostication for specialists – oncology, elective surgery?
- How do we manage people with frailty?
- What are the competing risks?
- Should it have a clinical definition?

PREVENTION
PROGNOSTICATION

Diabetes and Distal Complications

IR, obesity

Modifiers: Blood pressure, lipids, physical activity, treatment

Diabetes

Complications:

Atherosclerotic

Microvascular

Impairments:

Cognitive

Affective

Neurologic

Muscle/fat

Outcomes:

Geriatric conditions
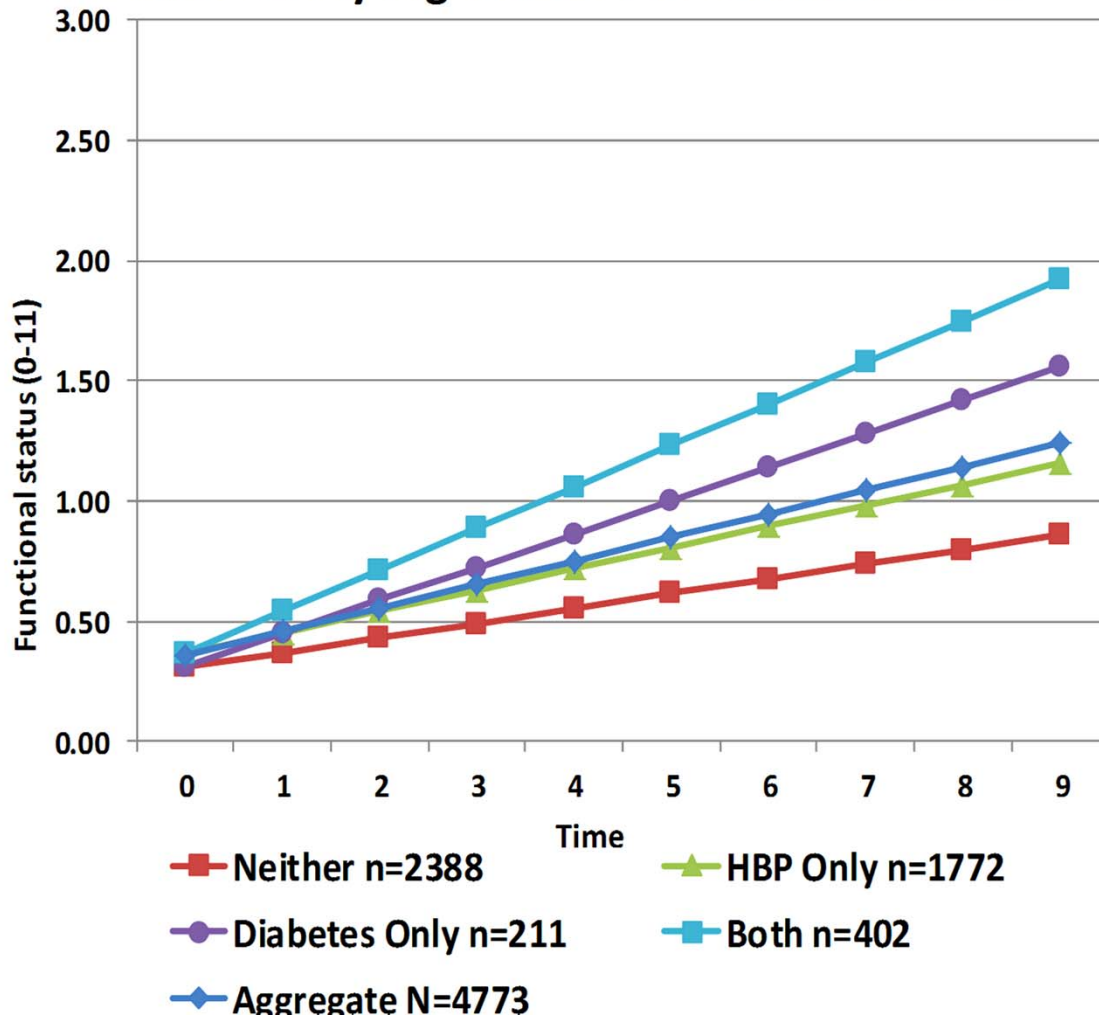
Disability

Mortality

Research questions: pathways

- Does frailty result from accumulating comorbidities or is it the underlying pathophysiological disruption that causes comorbidity accumulation, frailty and disability development?

- Is frailty a consequence of comorbidity, or is it causal?

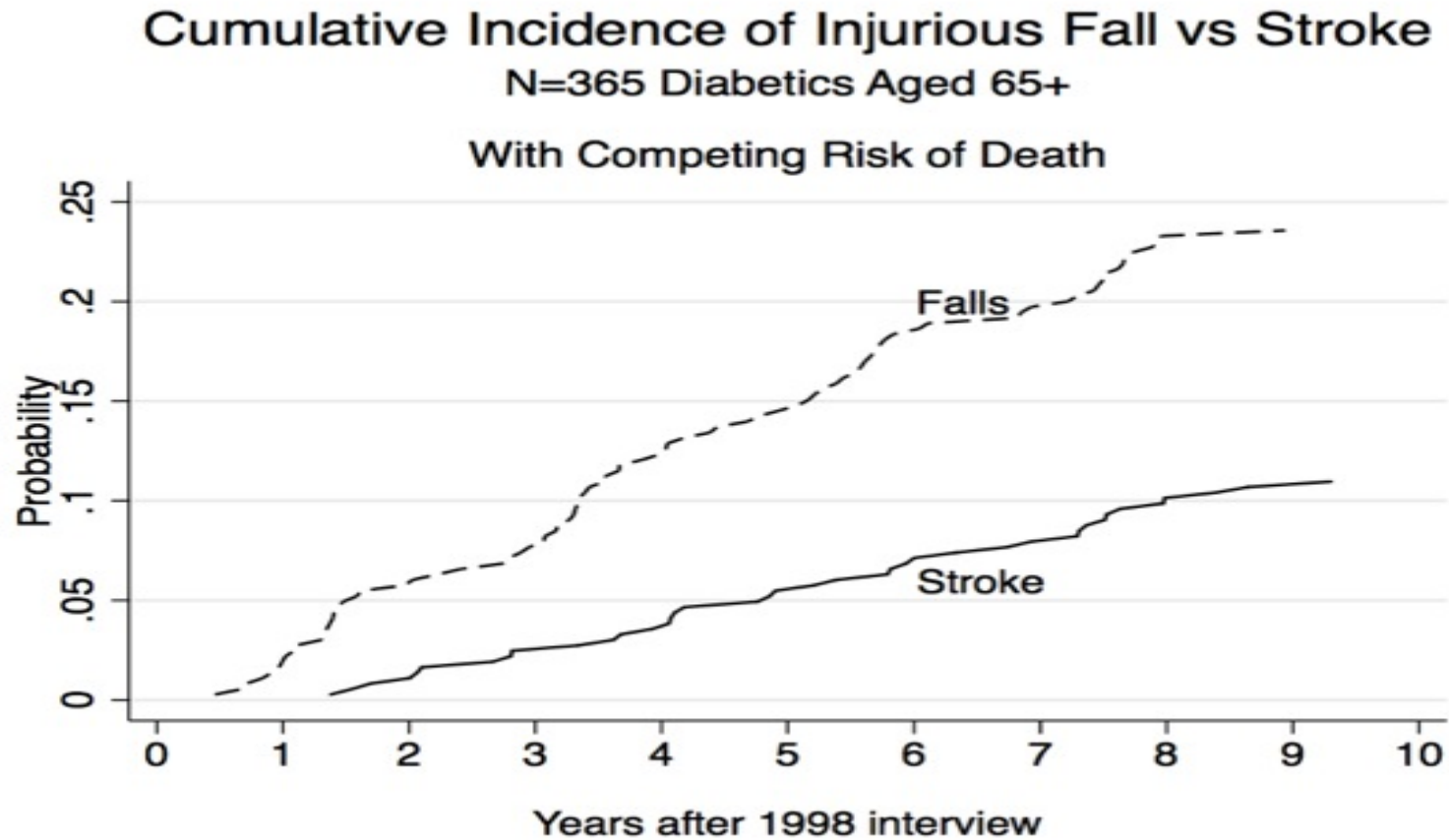# Diabetes, multiple chronic conditions, and health outcomes
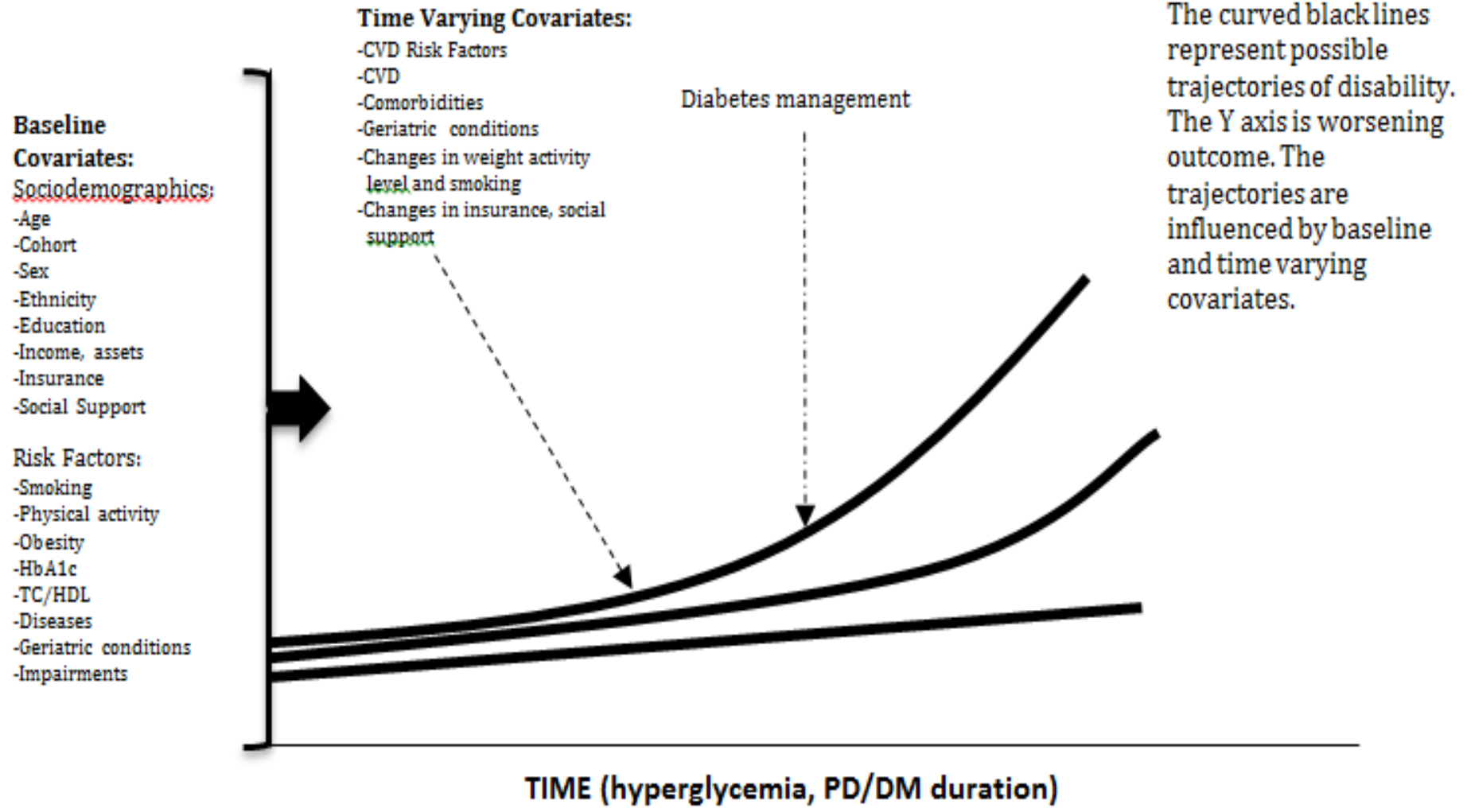
ADL/IADL with time by diabetes and hypertension (HRS, ages 51 and up)

HRS Functional Status by Diabetes by High Blood Pressue Interaction

Competing risks in older adults with diabetes: falls and strokes (Min,L, preliminary data)

Cumulative Incidence of Injurious Fall vs Stroke
N=365 Diabetics Aged 65+
With Competing Risk of Death

Research Questions: Aging

- People with multimorbidity at higher risk of getting 2 or more new diseases than those with no disease (van den Akker 1998)

- The Longevity Dividend; slow aging and slow the development of many chronic diseases. (Goldman, D et al. Health Affairs 32, 2013)

Research Collaborators and Support

University of Michigan

- Chris Cigolle
- Tanya Gure
- Lillian Min
- Pearl Lee
- Jinkyung Ha
- Jeffrey Halter
- Jersey Liang
- Ken Langa
- Mary Beth Ofstedal
- John Piette
- Michele Heisler
- Eve Kerr
- Mary Rogers
- Kathy Ward
- David Weir

Johns Hopkins

- Cynthia Boyd
- Erin Giovinetti
- Jennifer Wolfe
- Jeremy Walston
- Xian Li Xue
- Richard Semba

NQF

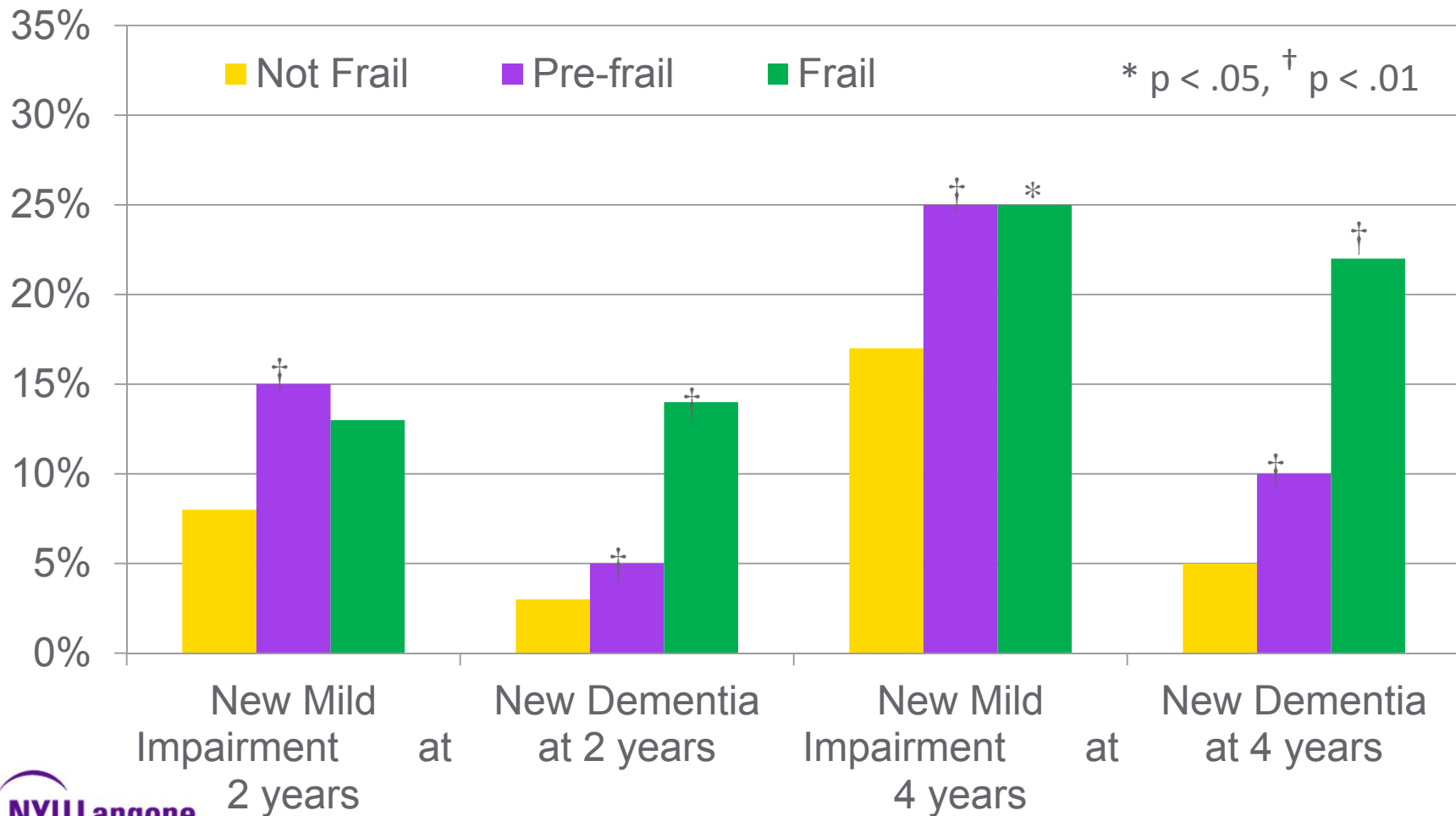- Karen Adams
- Aisha Pittman

NYULMC

- Ben Han
- Judy Zhong
- Rosie Ferris
- John Dodson
- Corita Grudzen

Research Support

- National Institute on Aging (K08, ROI)

- UM Claude D. Pepper Older American's Independence Center (NIA) (PESC)

- MICHR (Translational research pilot)

- VA Rehabilitation Research and Development Merit Awards

- Ann Arbor VA GRECC

- AHRQ Complex Patient Grant Program R21 and R24 (ARRA)

- John A. Hartford Foundation

- Diane and Arthur Belfer Research Endowment

- PCORI

Cumulative Incidence Of Mild Impairment And Dementia at Two-years and Four-years