Frailty Measurement: Where We Stand

Karen Bandeen-Roche, Ph.D.
Professor of Biostatistics, Medicine & Nursing
The Johns Hopkins University

Research and Career Development Retreat
Johns Hopkins Older Americans Independence Center
February 6, 2006

Introduction
Whither "frailty measurement"?

- "Geronmetrics"
  - a.k.a.: econometrics, psychometrics, biometrics
  - e.g.: generalized inflammation; frailty; aging
- Essential to
  - Sensitivity, specificity for genetic, other discovery
  - Theory operationalization, testing
  - Correctly targeted, evaluated interventions
- Is frailty worth measuring?
  - If not, pursuing items under the last bullet makes little sense

Geronmetric Measurement

- Proposition: Most effective when attacked "from both ends"
  - Mechanisms / basic science
  - Phenotype / validity
    - Face
    - Content
    - Predictive / Criterion
    - Construct: Convergent, Divergent
      Internal, External

Frailty phenotype
Where we stand: Strengths

- Face validity
  - Criteria reflect geriatric impression
  - WHAS I: prevalence increases with age
  - WHAS: prevalence higher among more disabled (25.4%) than overall (11.3%)
- Cross validity
  - Prevalence similar across cohorts (11.3% in WHAS; 11.6% in age-matched CHS women)

Frailty phenotype
Where we stand: Strengths

- Criterion / Predictive validity
  - Phenotype strongly predicts adverse geriatric outcomes: severe disability onset; falls; NH admission; death
  - Phenotype predicted by signs of systemic dysregulation: inflammatory, immunological, hormonal, nutritional

Frailty phenotype
Where we stand: Strengths

- Convergent internal construct validity
- Criterion onset—Drs. Fried & Xue
- Criteria manifestation is syndromic

  "a group of signs and symptoms that occur together and characterize a particular abnormality"

  –Method: Latent class analysis

Syndrome validation
Latent class analysis

- Seeks clinically homogeneous subgroups
- Features that characterize each group
  - Prevalence in overall population
  - Percentage manifesting each criterion
- If criteria characterize syndrome:
  - At least two groups (otherwise, no co-occurrence)
  - No subgrouping of symptoms (otherwise, more than one abnormality characterized)

Table 3
Conditional Probabilities of Meeting Criteria in Latent Frailty Classes
WHAS

Criterion	2-Class Model		3-Class Model		
	CL. 1 NON-FRAIL	CL. 2 FRAIL	CL. 1 ROBUST	CL. 2 INTERMED.	CL. 3 FRAIL
Weight Loss	.073	.26	.072	.11	.54
Weakness	.088	.51	.029	.26	.77
Slowness	.15	.70	.004	.45	.85
Low Physical Activity	.078	.51	.000	.28	.70
Exhaustion	.061	.34	.027	.16	.56
Class Prevalence (%)	73.3	26.7	39.2	53.6	7.2

Bandeen-Roche et al., 2006

Frailty phenotype
Where we stand: Content validity

- Missing pieces?
  - Cognitive decline?
  - Depression / anxiety?
- Improvement re existing pieces?
  - Exhaustion; weight loss?
  - Different cutoffs or scaling?
- Physiotype rather than phenotype?
- Value of aggregate over components?
- A beta version, or a proof of principle?

Frailty phenotype
Where we stand: Prediction

- …i.e. utility for screening, diagnosing & targeting adverse geriatric outcomes

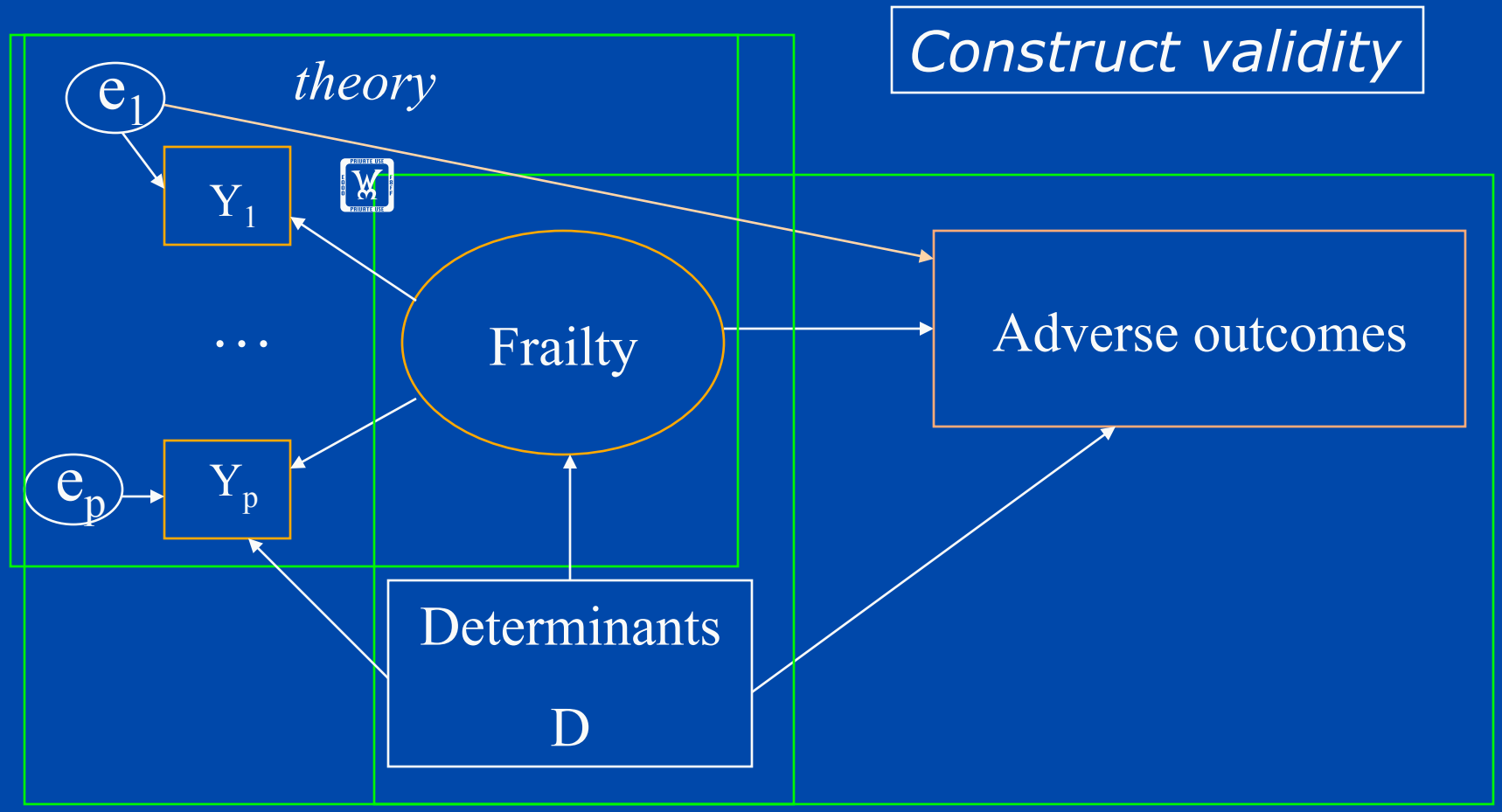
- Needed
  - Rigorous delineation of predictive accuracy
  - Comparison to competitors
  - Threshold relationships?

- Is this the primary goal?
  - If so: Why genetic, physiological discovery?

Frailty phenotype
Where we stand: Construct validity

- Discriminant: What is frailty not?
- External
  - Multisystemic dysregulation
  - Specificity re vulnerability to stressors
    - WHAS II challenge study
- Refinement of the construct?
  - "Vulnerable" vs. "already broken" (Ferrucci)
  - Placement in pathology-to-disability path?

Identifying Frailty
Latent Variable Paradigm



Data on Content Validity
More than Component Parts

- WHAS: Disease-adjusted analysis, mobility disability vs. components
  - Slowness=strongest predictor

    OR=17, 95% CI [7.8, 38] vs.

    6.6, 95% CI [2.2, 20] for weakness
  - All but weight loss predict (multiply)

- InCHIANTI: "Frailty" specifically associated with generalized inflammatory dysregulation, as opposed to components

Discriminant Validity Data
More than disease (WHAS)

- Frail, # diseases associated, not redundant
  - "Frail" rare if no (2%) or 1 (5%) disease
  - "Intermediate" not rare these cases (>29%)
  - Many with comorbid diseases robust (>28%)

- Frailty strongly predicts mobility disability, independently of age, # diseases
  - OR for severe disability = 29 (95% CI [9.3,88])
  - Little interaction w disease: not severity marker

Discriminant Validity Data
More than disease (WHAS)

- Mortality analysis with propensity scoring

ADJUSTMENT	FRAILTY OR (CI)
None	2.42 (1.81,3.24)
Disease count, age	1.81 (1.33,2.45)
Cluster-based C/D/S vars.	1.74 (1.28,2.36)
Elements of score	1.69 (1.23,2.30)
Propensity score	1.67 (1.22,2.28)
P. Score: Mid-90	1.51 (1.07,2.13)

Frailty: Aims & Status

- Sensitivity and specificity: A measure tied explicitly to systemic dysregulation
- Validate theory that frailty is:
  - More than a marker of disease
  - More than severe disability
  - A ***syndrome***: more than component parts
  - A result of vulnerability to stressors & loss of reserve
- Product: A target for interventions
  - Deliverable: A refined summary variable
  - Either: A causal intermediary or measured surrogate
- Much accomplished; much worthwhile to do

Acknowledgments

- Hopkins Colleagues

  Linda Fried, Paulo Chaves, Yi Huang, Jeremy Walston, Qian-Li Xue, Scott Zeger

- Colleagues outside of Hopkins

  Luigi Ferrucci, Jack Guralnik

- Funding / Institutional Support

  Johns Hopkins Older Americans Independence Center, National Institute on Aging, Brookdale National Foundation