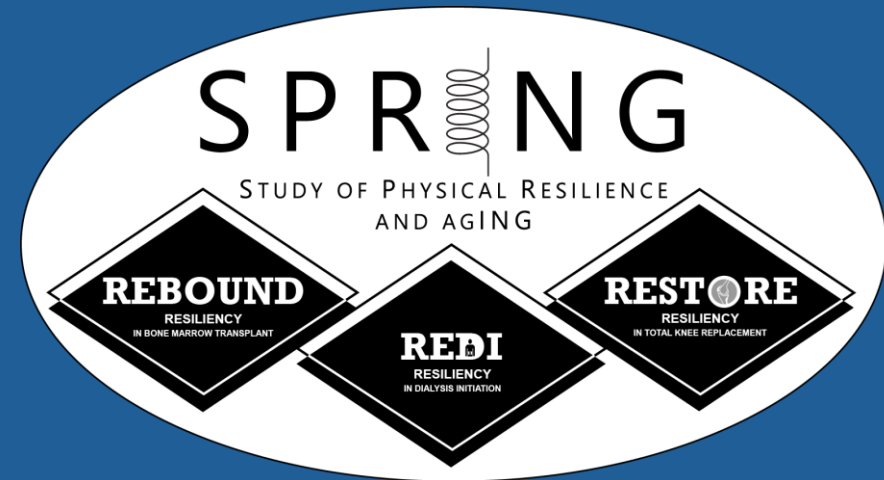


# Bioinformatics and science-informed modeling approaches in resilience research

AGS/NIA R13 Bench-to-Bedside  
Conference Series

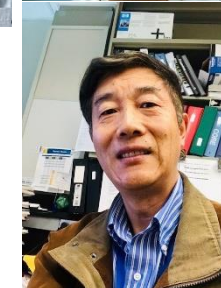
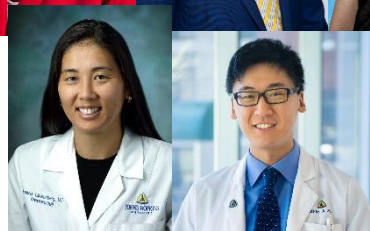
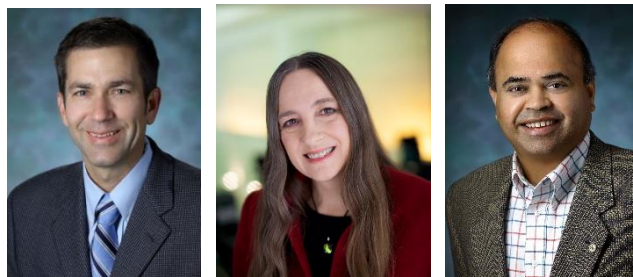
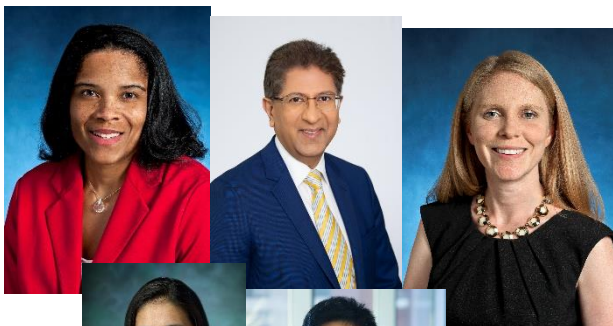
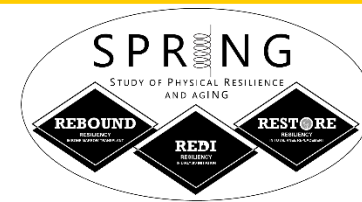
Overview of the Resilience World –  
State of Science

October 13, 2022



Karen Bandeen-Roche PhD, Johns Hopkins Bloomberg School of Public Health

# SPRING Team



# What is Resilience?

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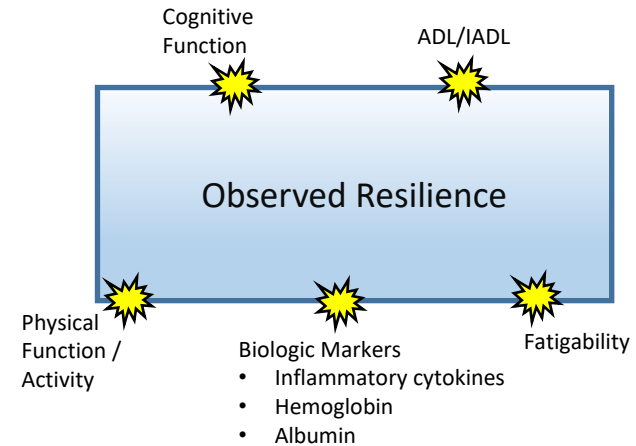
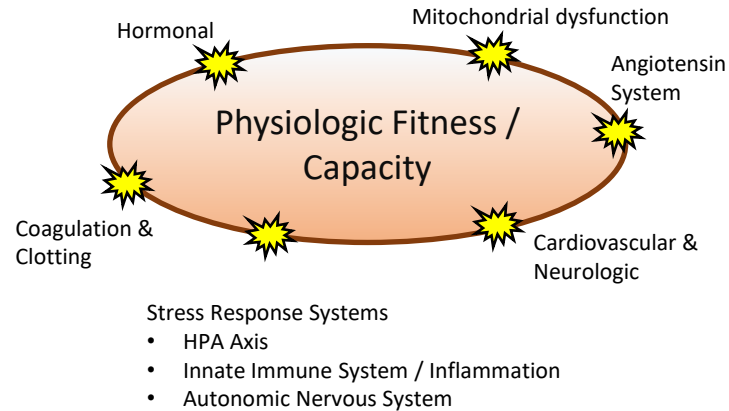
- Materials: Elasticity (Tredgold, 1818)
- Ecosystems: **Capacity** to absorb / manage disturbance to retain ~ the same identity & functioning (Walker et al., 2004)
- Psychological: **Ability** to **bounce back** following adversity (Wagnild & Collins 2011)
- NIA: **Ability** to **resist/recover** from adverse effects of a stressor (Hadley et al., 2017)

Credit: Whitson et al., 2016

# What is Physical Resilience?

- Physical:
  - **Capacity** to bounce back from a physical challenge (Resnick et al., 2011)
  - Whole-person characteristic that determines **ability** to **resist** functional decline / **recover** physical health after a stressor (Whitson et al., 2016)
  - **Ability** of a physiologic system to **recover** from a stressor which is **powerful enough** that the **system** is pushed into a state far from its original equilibrium state, ultimately retaining essential identity and function (Varadhan et al., 2019)

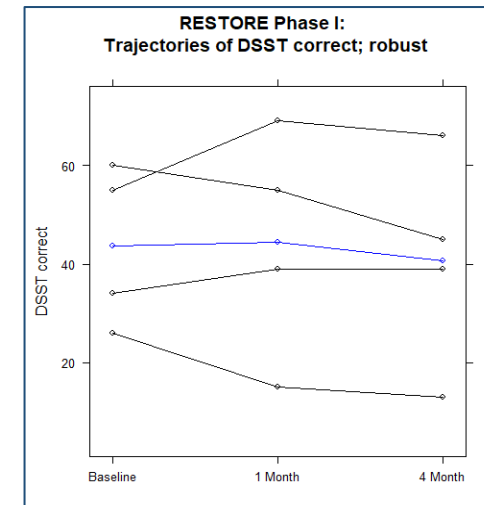
# Physical resilience: Before and After the Fact



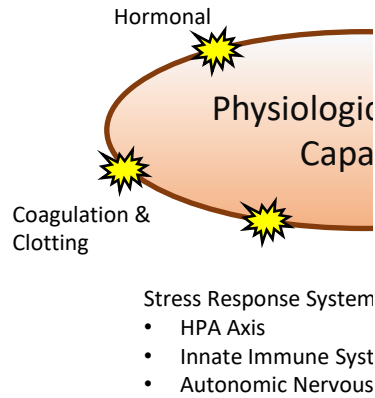
Csete, M. E. & Doyle, J. C. Reverse engineering of biological complexity. *Science*. **295**, 1664–1669 (2002).

**Resilience capacity = function of health of all of the above**

**Gold standard testing mechanism: Dynamic stimulation**



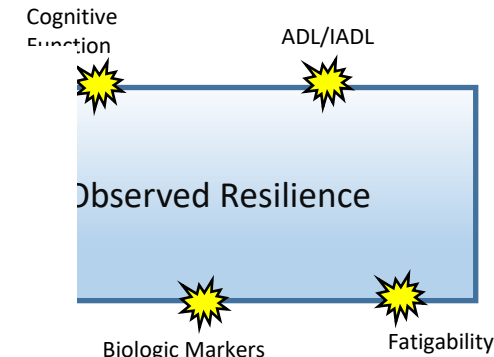
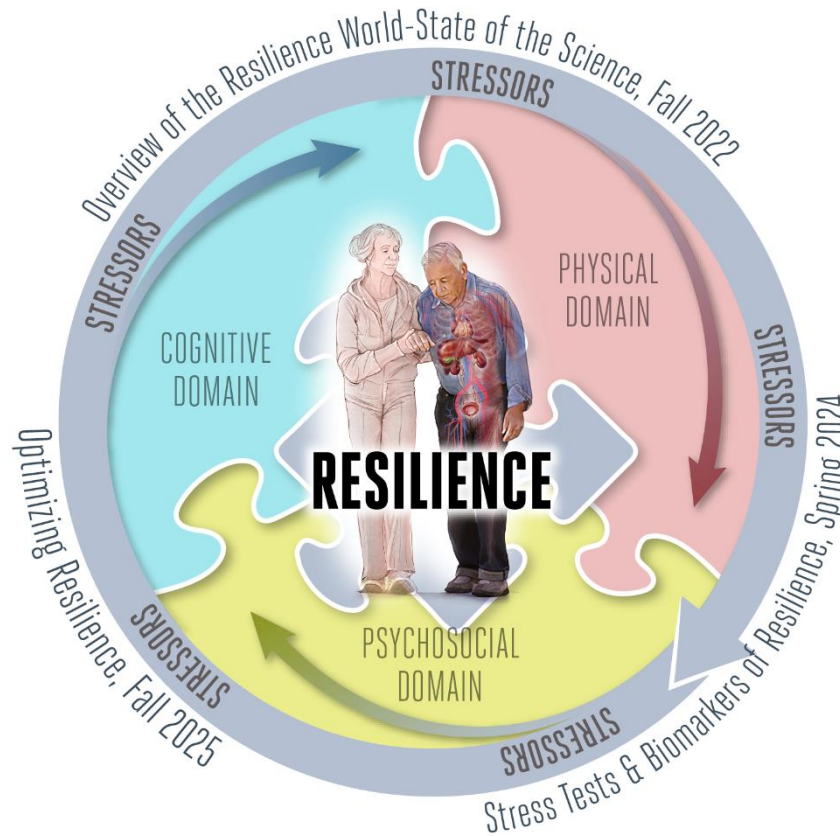
# Physical resilience: Before and After the Fact



Csete, M. E. & Doyle, J. K. *Engineering of biological systems*. *Science*. **295**, 1664-1669 (2002)

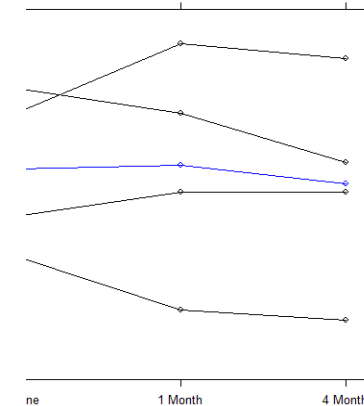
Resilience capacity = function of resilience capacity

Gold standard testing mechanism

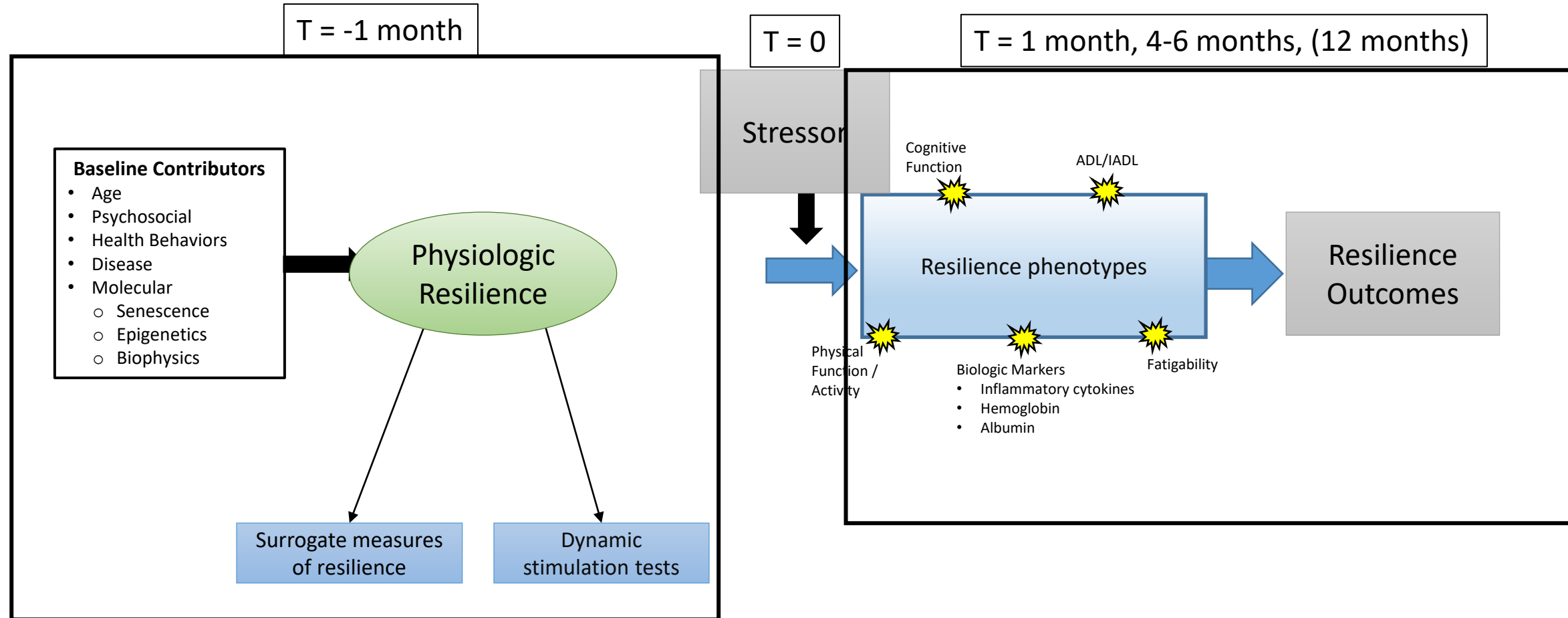


- Biologic Markers
- Inflammatory cytokines
  - Hemoglobin
  - Albumin
- Fatigability

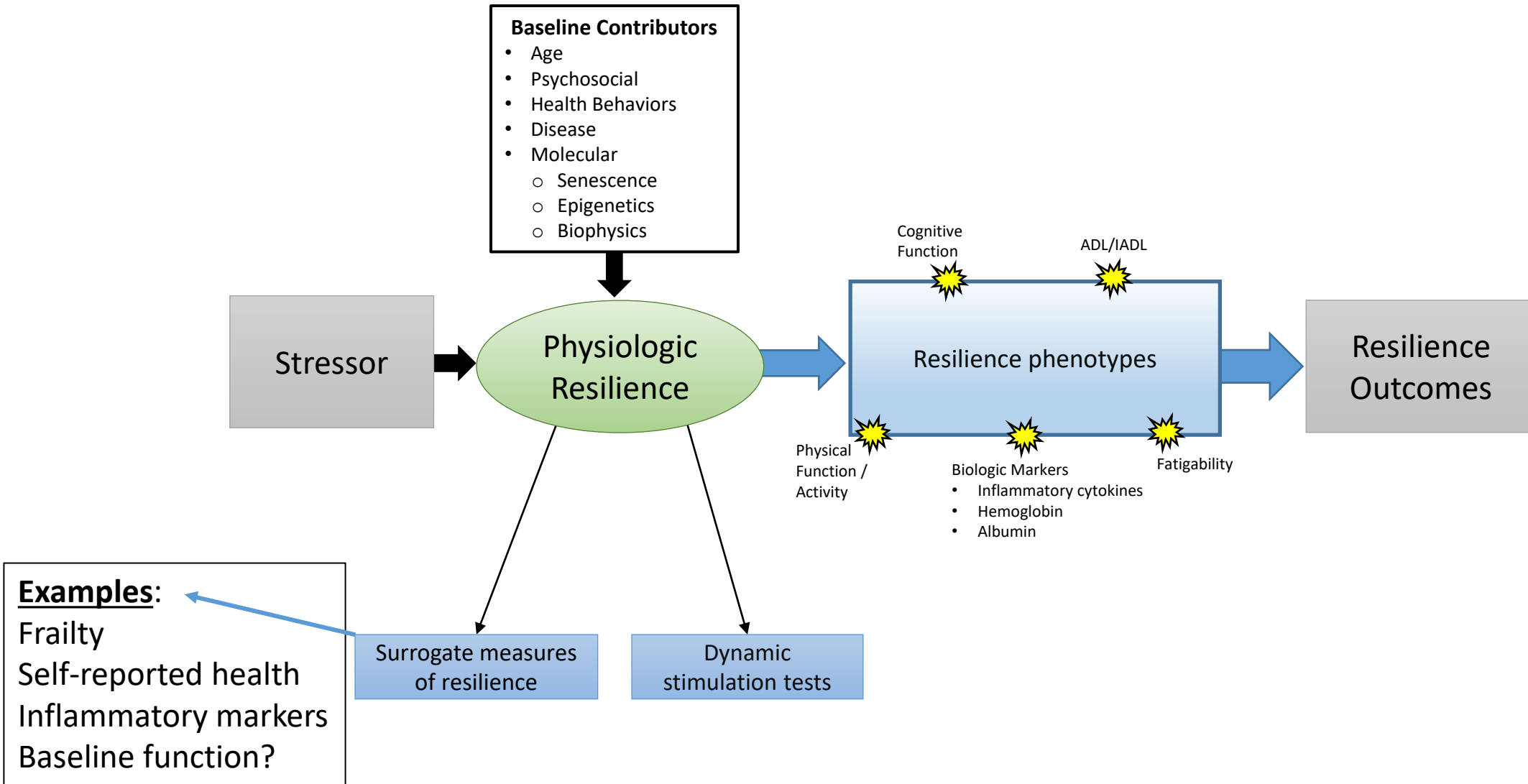
RESTORE Phase I: trajectories of DSST correct; robust



# Conceptual Framework for Physical Resilience: Data collection timeline

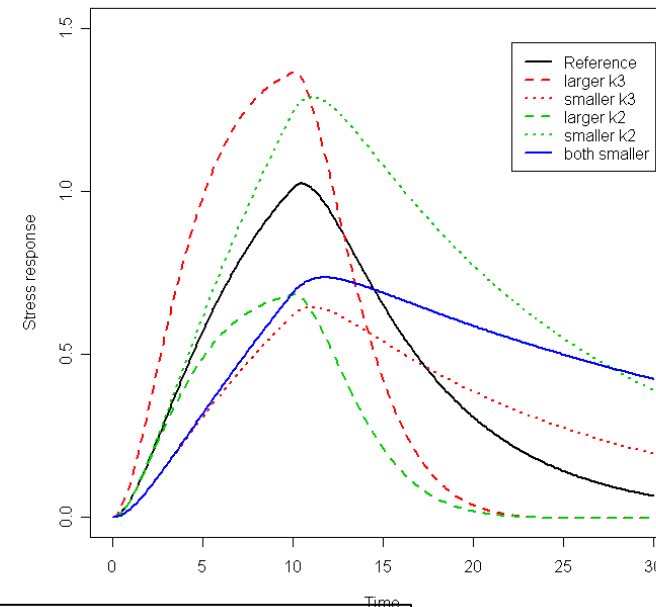
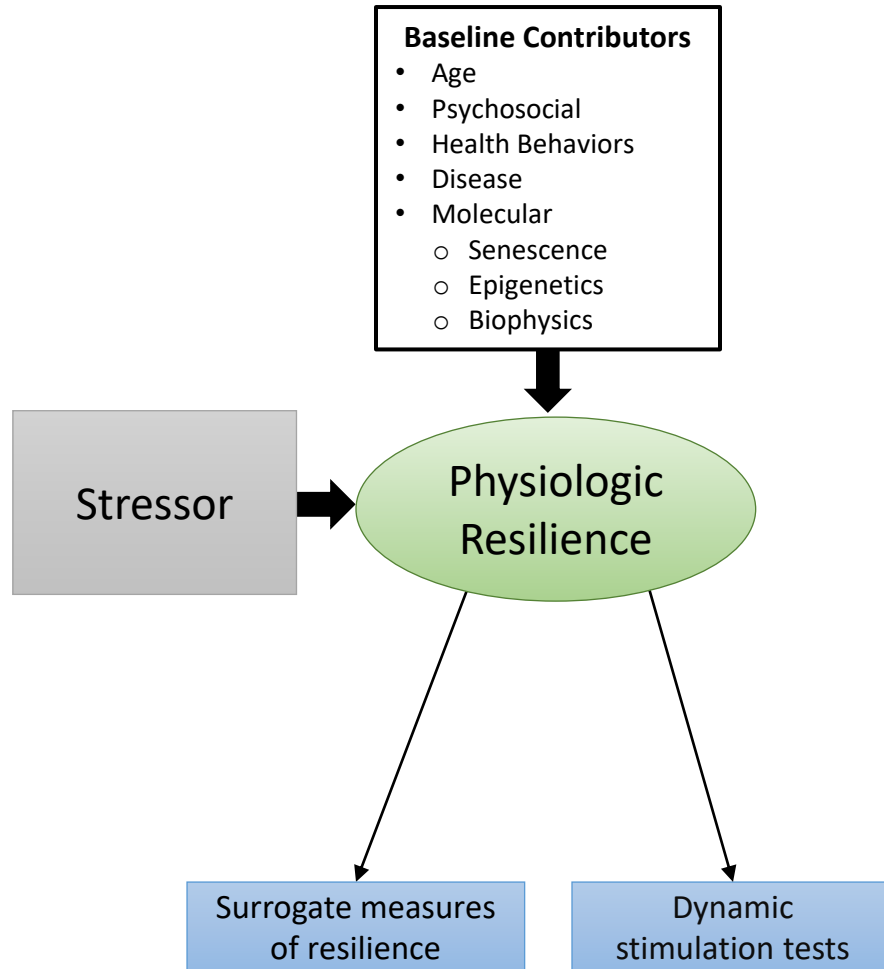


# Conceptual Framework for Physical Resilience: Data collection



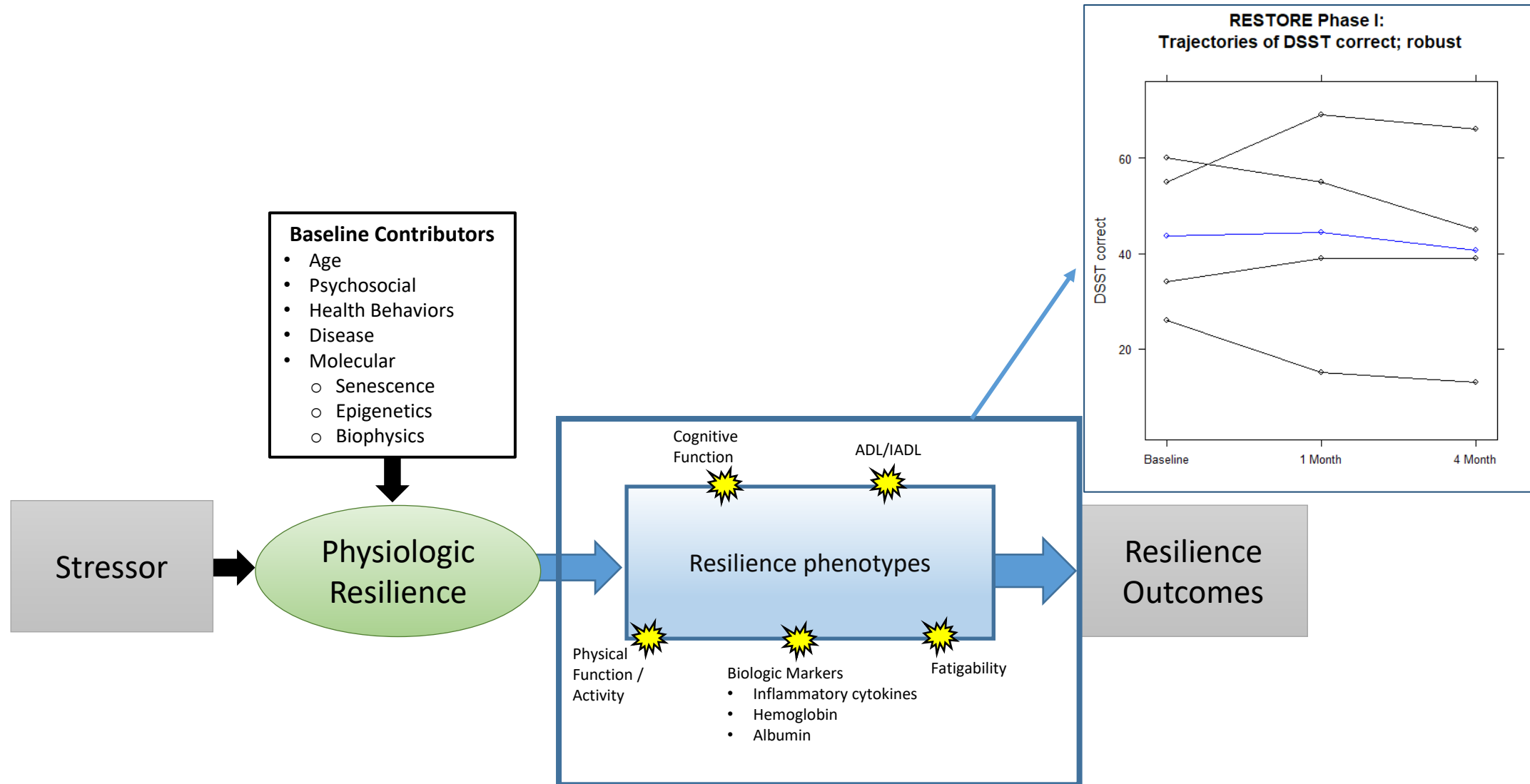


# Conceptual Framework for Physical Resilience: Data collection

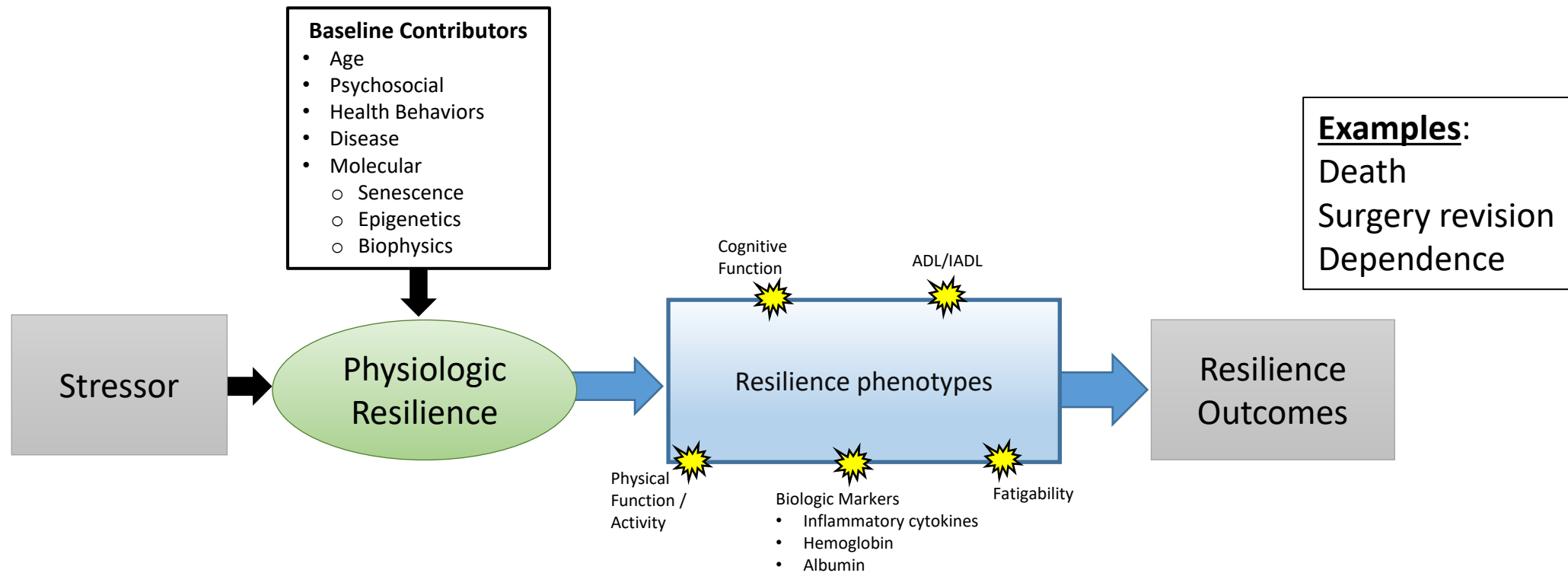


**Example:**  
Oral glucose tolerance test

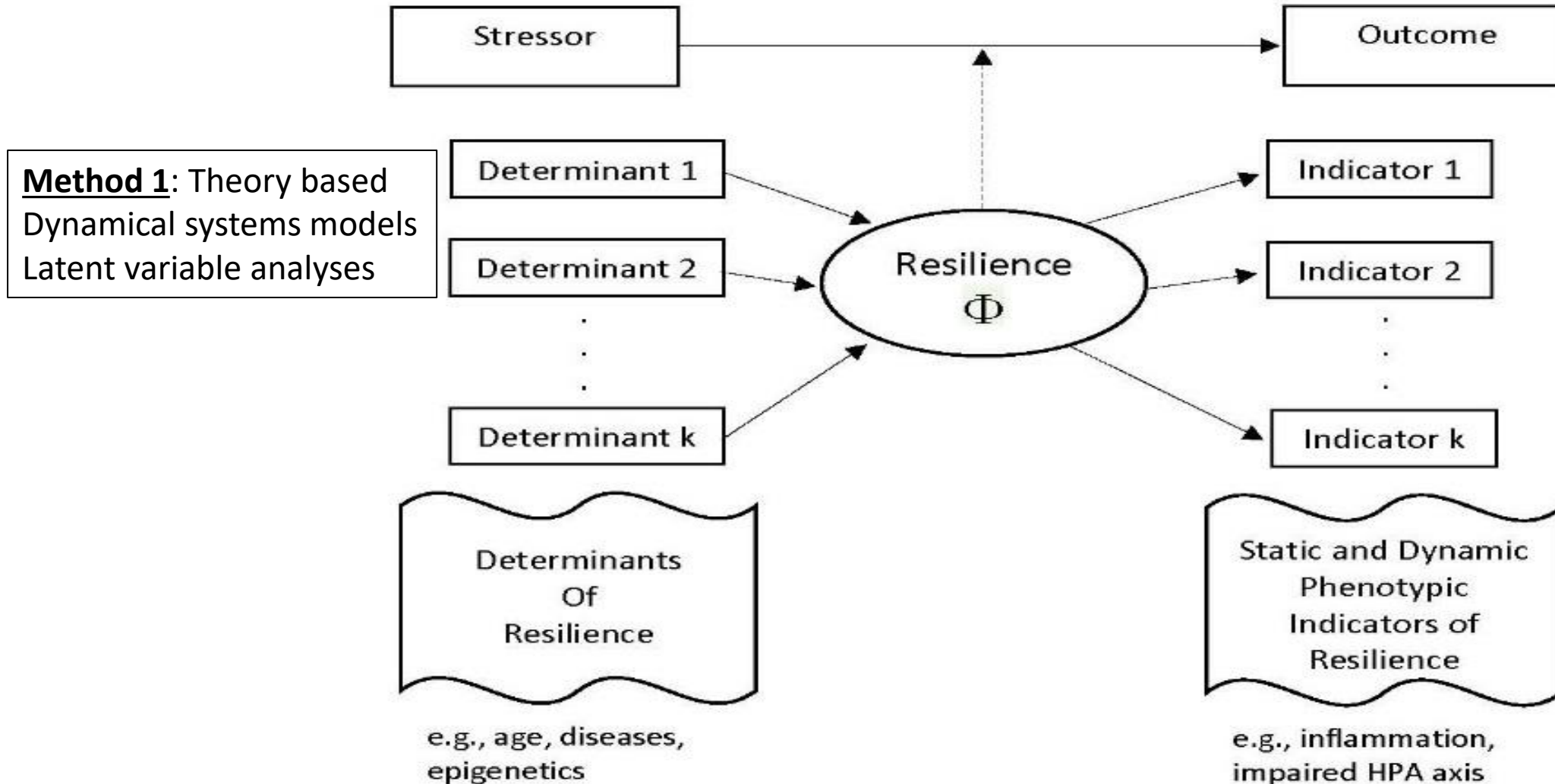
# Conceptual Framework for Physical Resilience: Data collection



# Conceptual Framework for Physical Resilience: Data collection

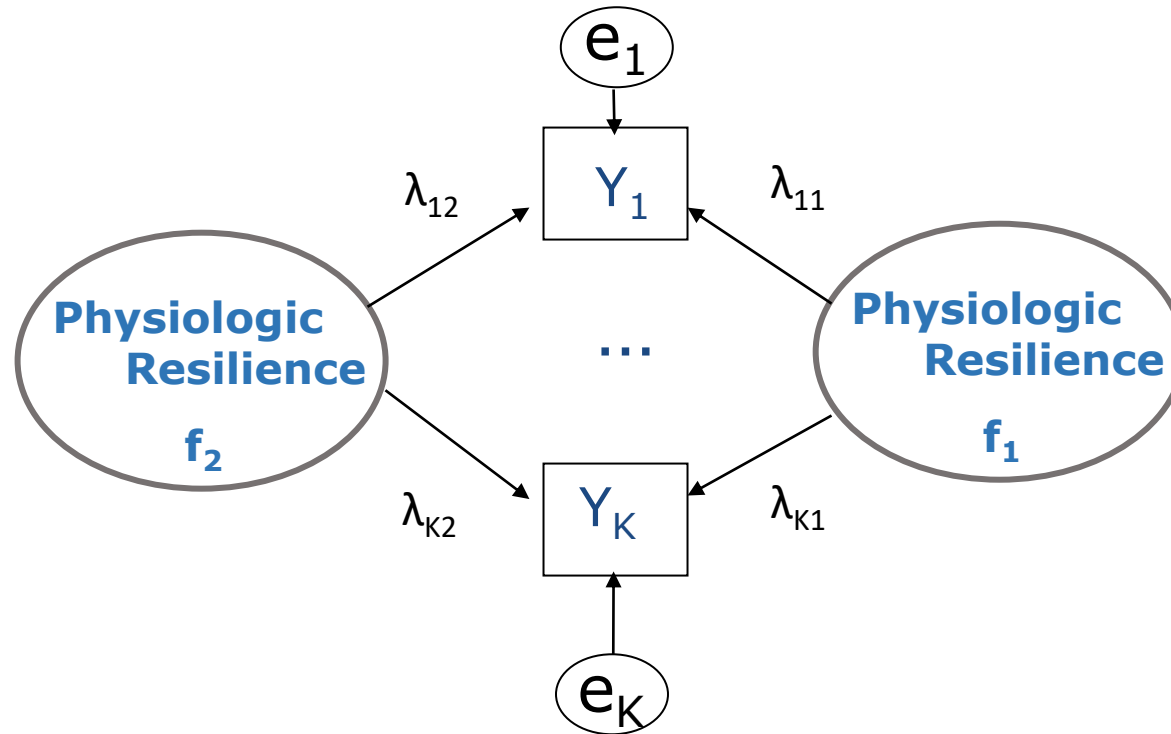


# Approach to Analyzing Physiologic Resilience



# Approach to Analyzing Physiologic Resilience - Example

- Indicator  $k$ , person  $i = \lambda_{k1} f_{i1} + \lambda_{k2} f_{i2} + \dots + \epsilon_{ki}$




- $\lambda$ s scientifically informed (ex/ differential equations)

# SPRING EXAMPLE: HRV, ACTH-STIM, Salivary Cortisol

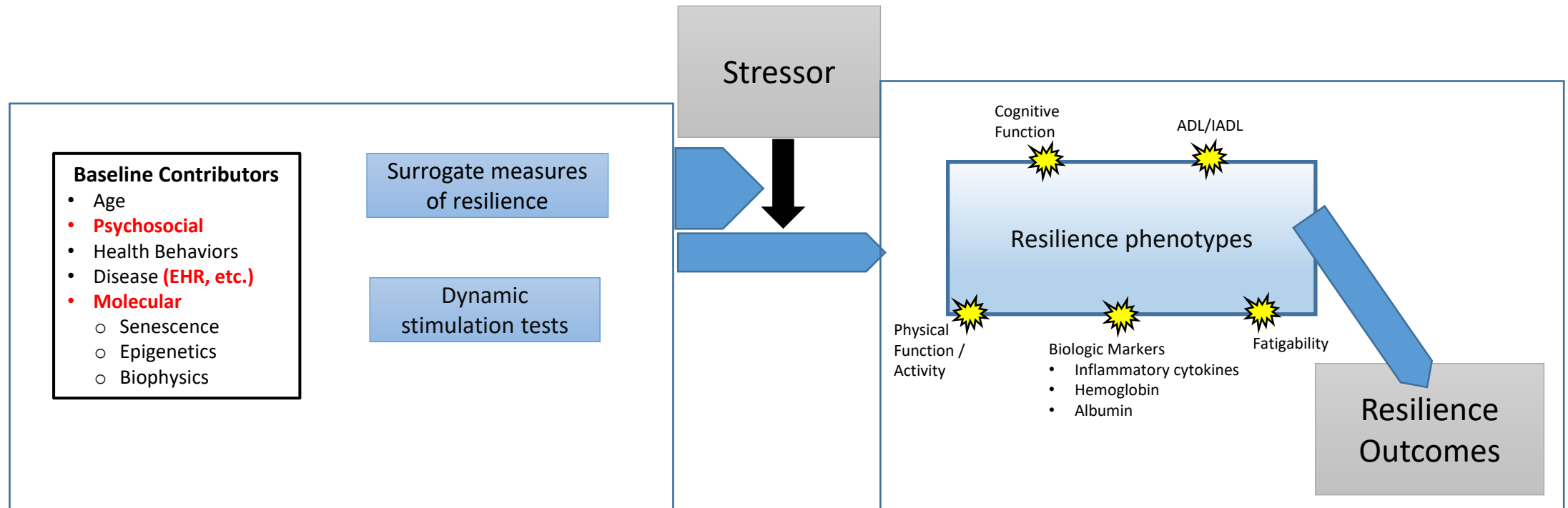
Pilot data: n=79; PCA approximation

Theory: Steady state, adaptation mechanisms

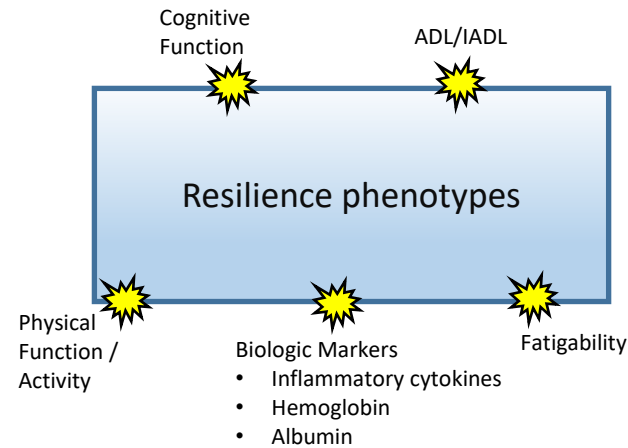
Indicator	f1	f2
HRV - Steady		
HRV - Adapt		
ACTH - Steady		
ACTH - Adapt		
Saliv Cort-Steady		
Saliv Cort-Adapt		

# Approach to Analyzing Physiologic Resilience

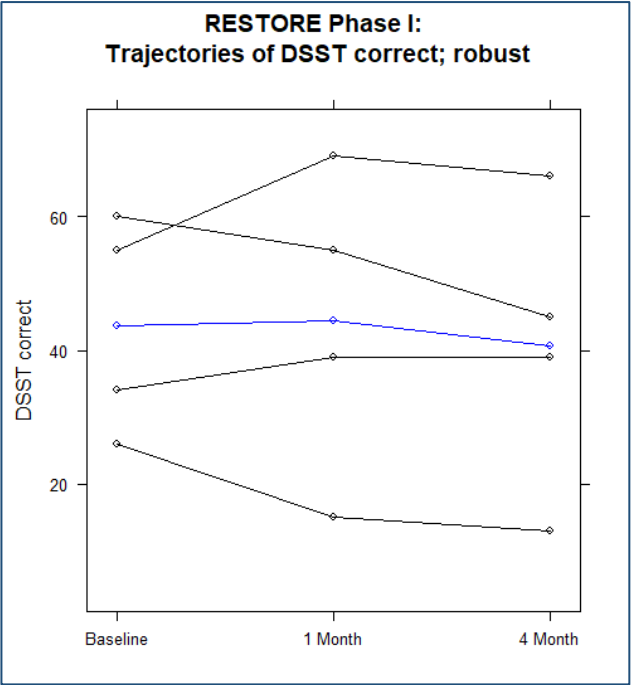
**Method 2:** Data driven  
Machine learning



# Approach to Analyzing Observed Resilience



Resilience Outcomes

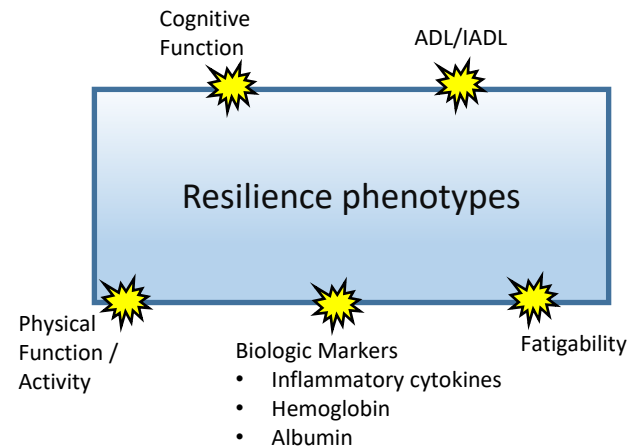


Trajectory analysis  
Growth curves  
Latent growth curves

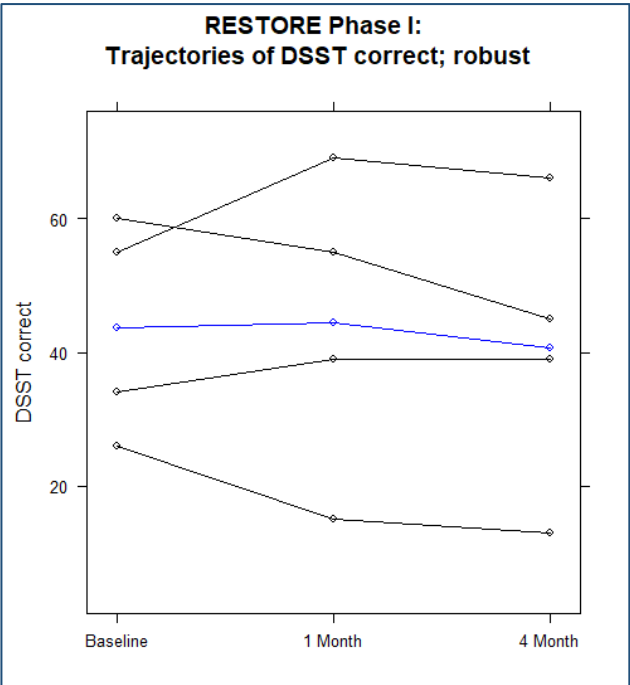
Raw versus expected?  
Functional data analysis?  
Multivariate versions



# Approach to Analyzing Observed Resilience



Resilience Outcomes



Colón-Emeric C et al. **Two Approaches to Classifying and Quantifying Physical Resilience in Longitudinal Data.** J Gerontol A Biol Sci Med Sci. 2020; 75(4):731-738.

Hladek MD et al. **Physical Resilience Phenotype Trajectories in Incident Hemodialysis: Characterization and Mortality Risk Assessment.** Kidney Int Rep. 2022;7(9):2006-2015.

**Many papers in broader resilience lit**

# High priority gaps / scholarship areas

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- **Theory** regarding physiologic (underlying) resilience
  - **Methods** by which to fit to data
- **Specificity, multidimensionality** regarding observed resilience
- Improved **data**
  - Finer grain time scale
  - Larger cohorts
- **Hybrid methods**
  - Leveraging / iterating the best of theory driven, empirical approaches
- **Validation / translation**