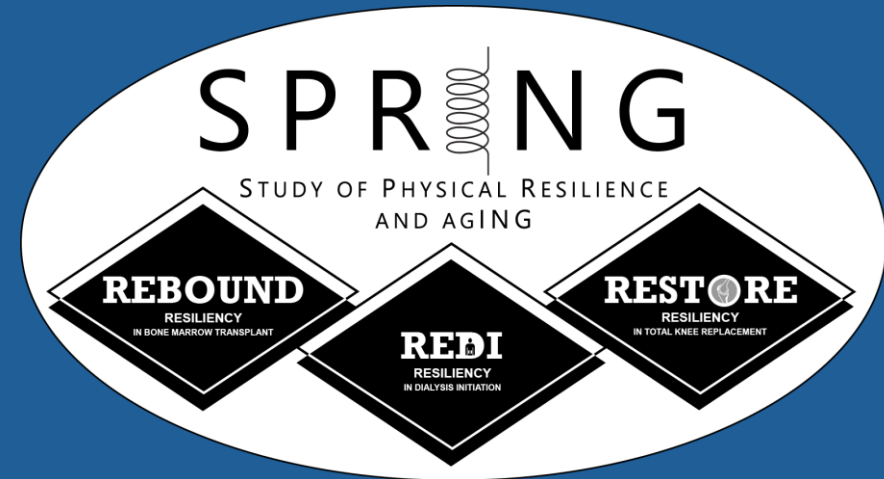


Bioinformatics and science-informed modeling approaches in resilience research

AGS/NIA R13 Bench-to-Bedside
Conference Series

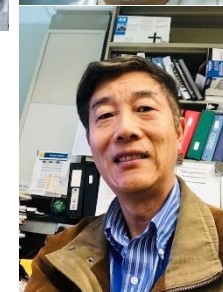
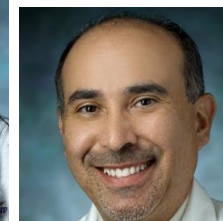
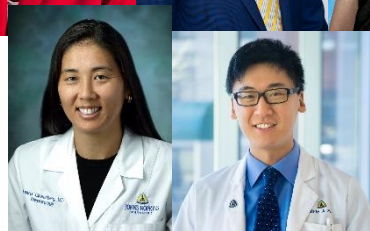
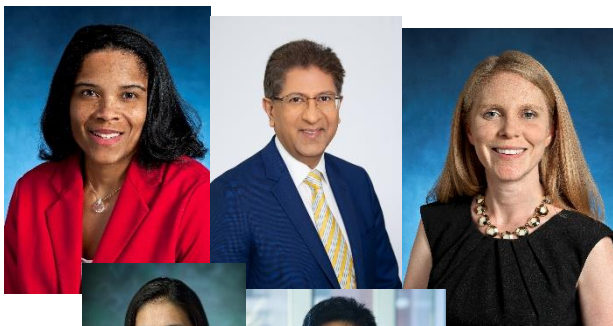
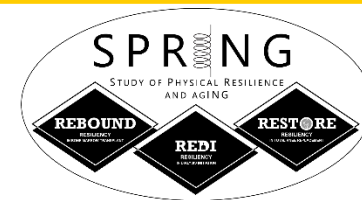
Overview of the Resilience World –
State of Science

October 13, 2022



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

SPRING Team



What is Resilience?

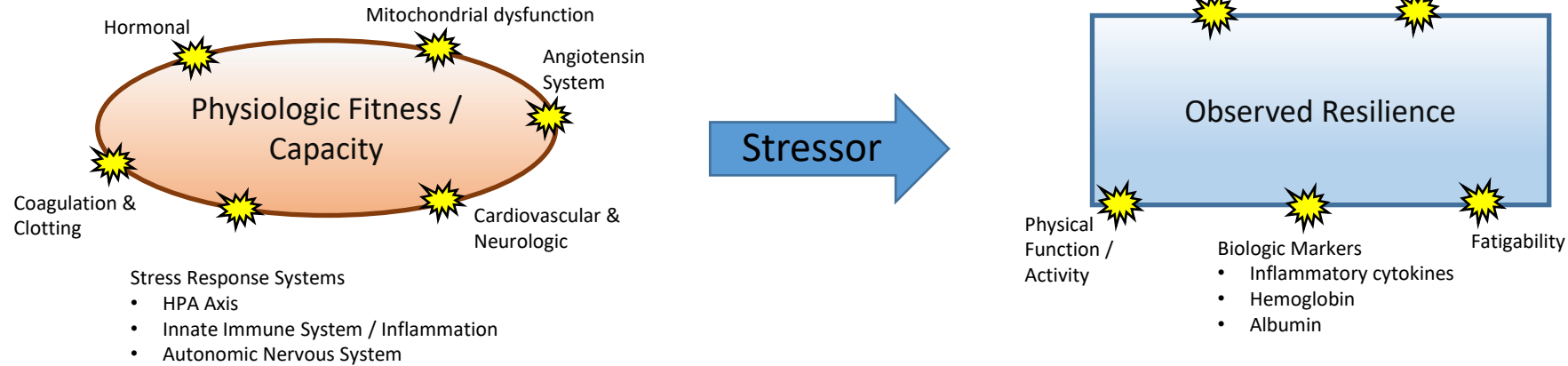
- Materials: Elasticity (Tredgold, 1818)
- Ecosystems: **Capacity** to absorb / manage disturbance to retain ~ the same identity & functioning (Walker et al., 2004)
- Psychological: **Ability** to **bounce back** following adversity (Wagnild & Collins 2011)
- NIA: **Ability** to **resist/recover** from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

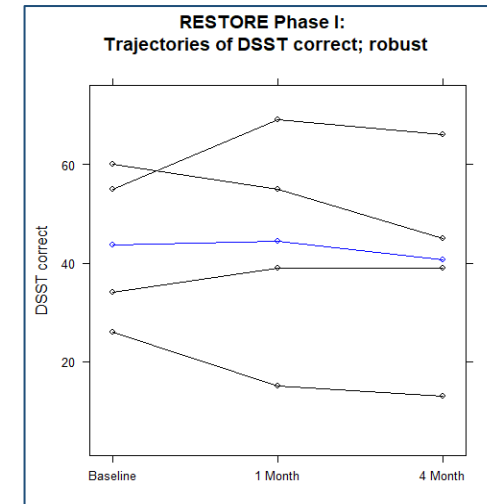
Physical resilience: Before and After the Fact



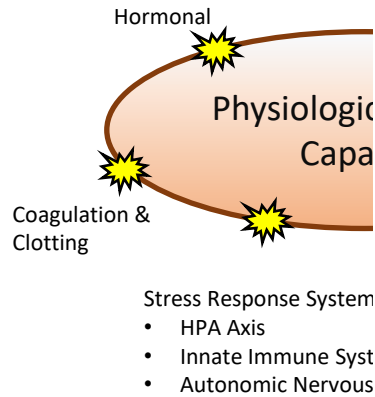
Csete, M. E. & Doyle, J. C. Reverse engineering of biological complexity. *Science*. **295**, 1664–1669 (2002).

Resilience capacity = function of health of all of the above

Gold standard testing mechanism: Dynamic stimulation



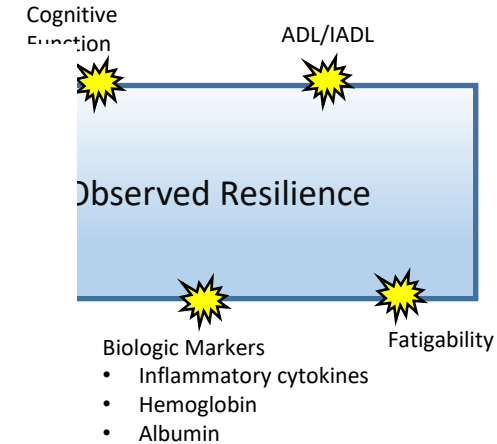
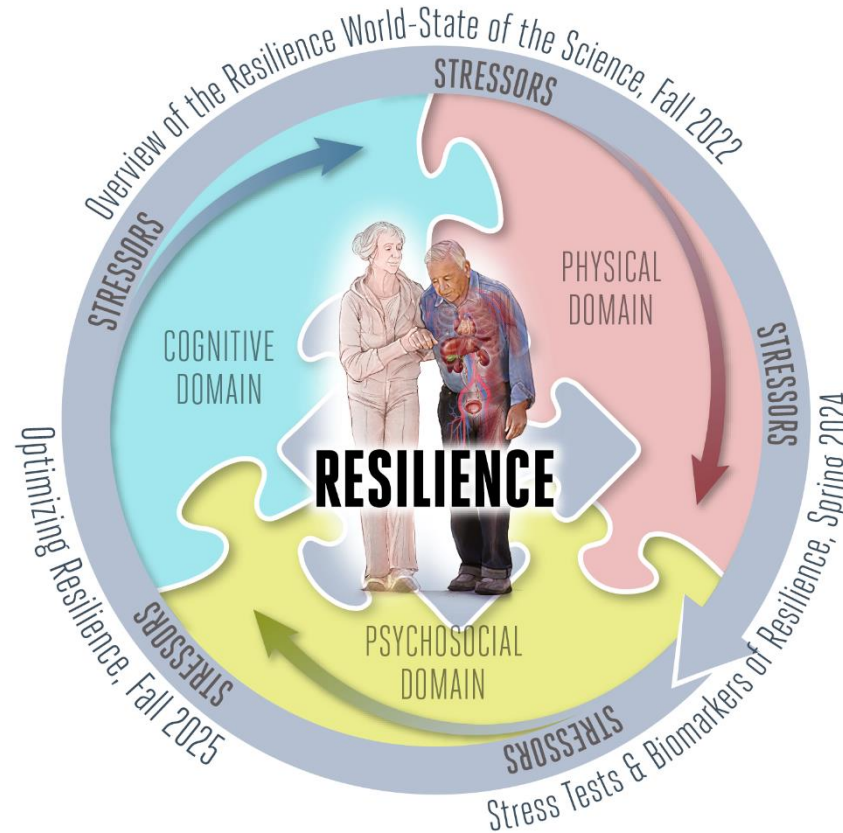
Physical resilience: Before and After the Fact



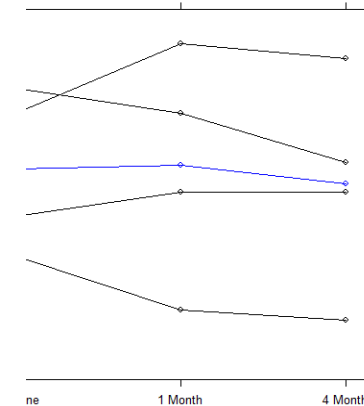
Csete, M. E. & Doyle, J. K. (2019). Engineering of biological systems. *Science*. **295**, 1664-1669.

Resilience capacity = function of resilience capacity

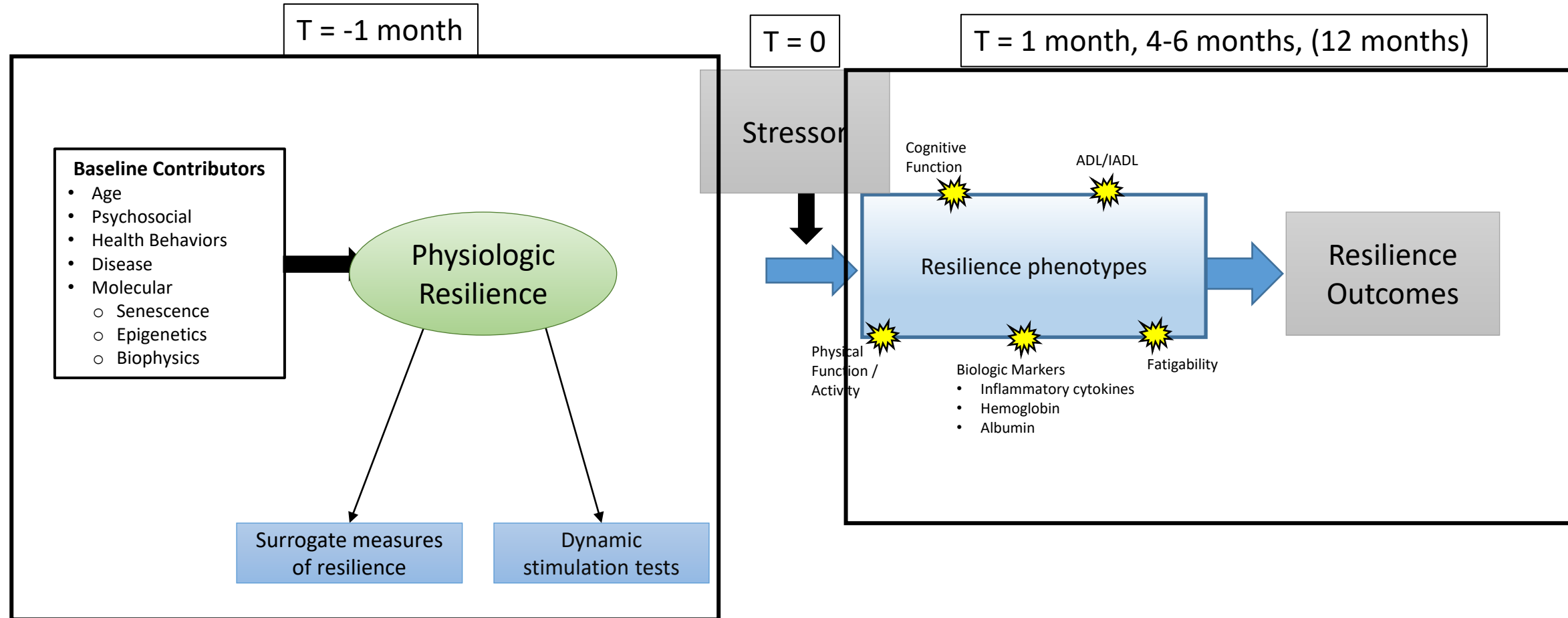
Gold standard testing mechanism



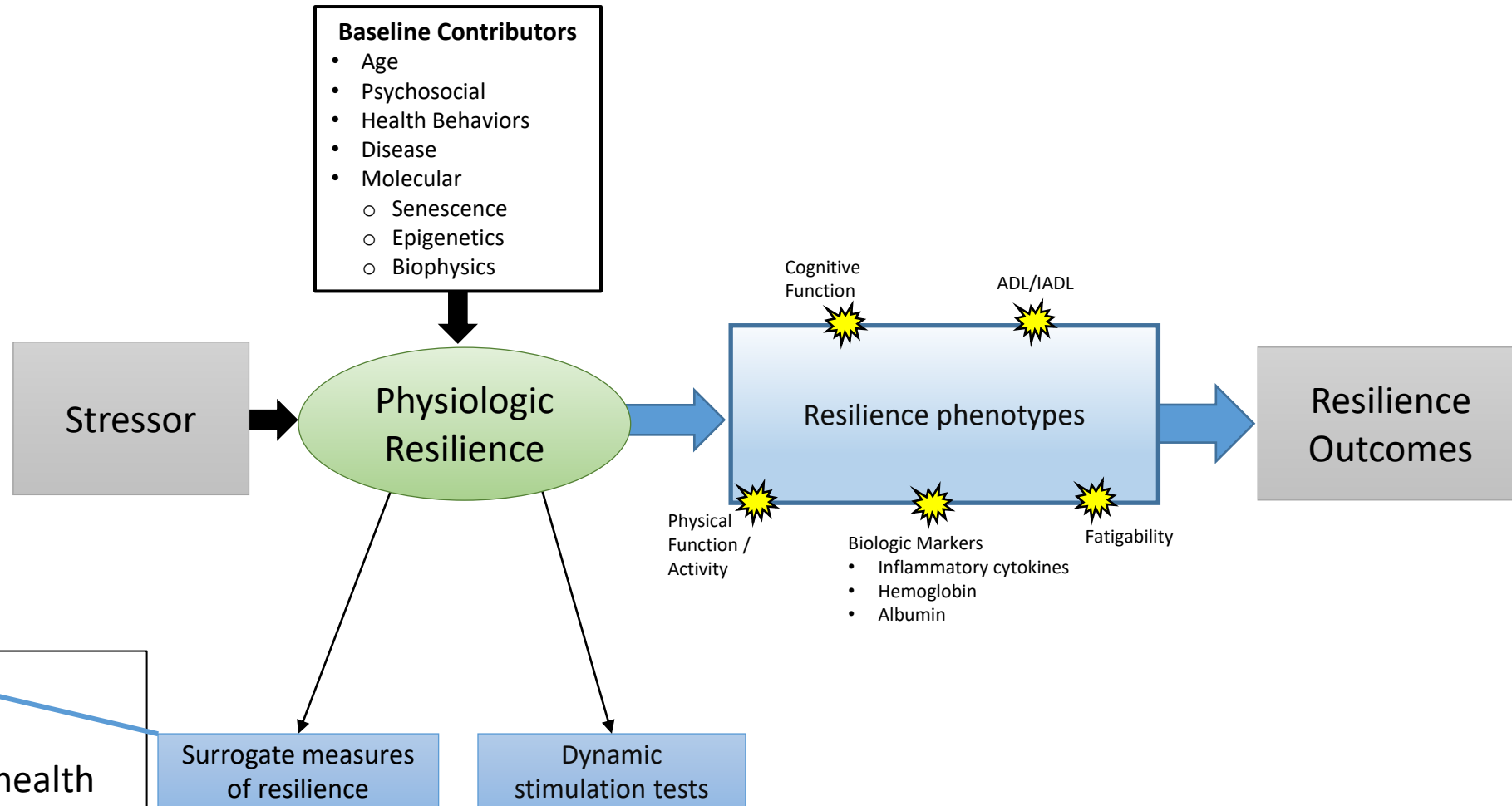
RESTORE Phase I: trajectories of DSST correct; robust



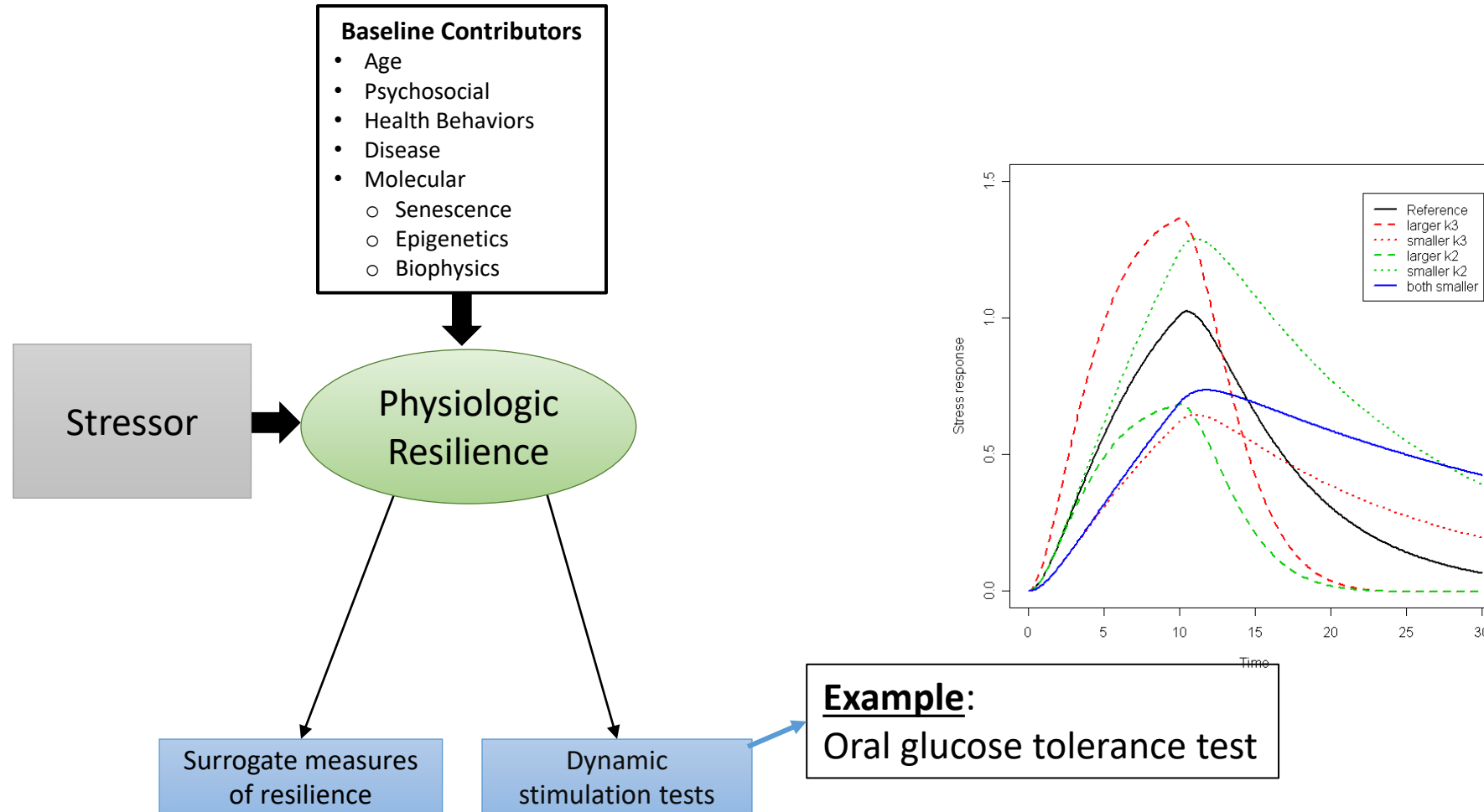
Conceptual Framework for Physical Resilience: Data collection timeline



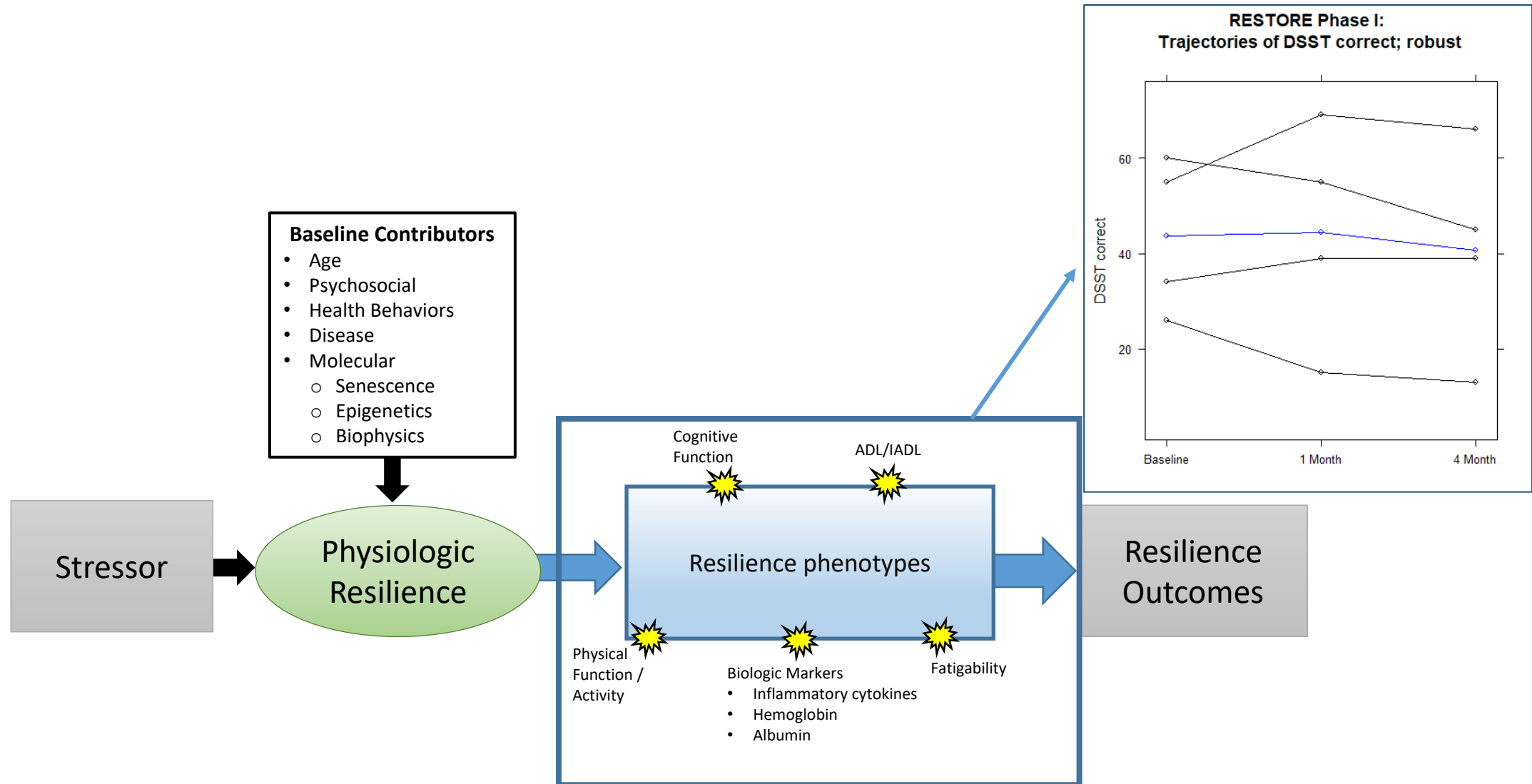
Conceptual Framework for Physical Resilience: Data collection



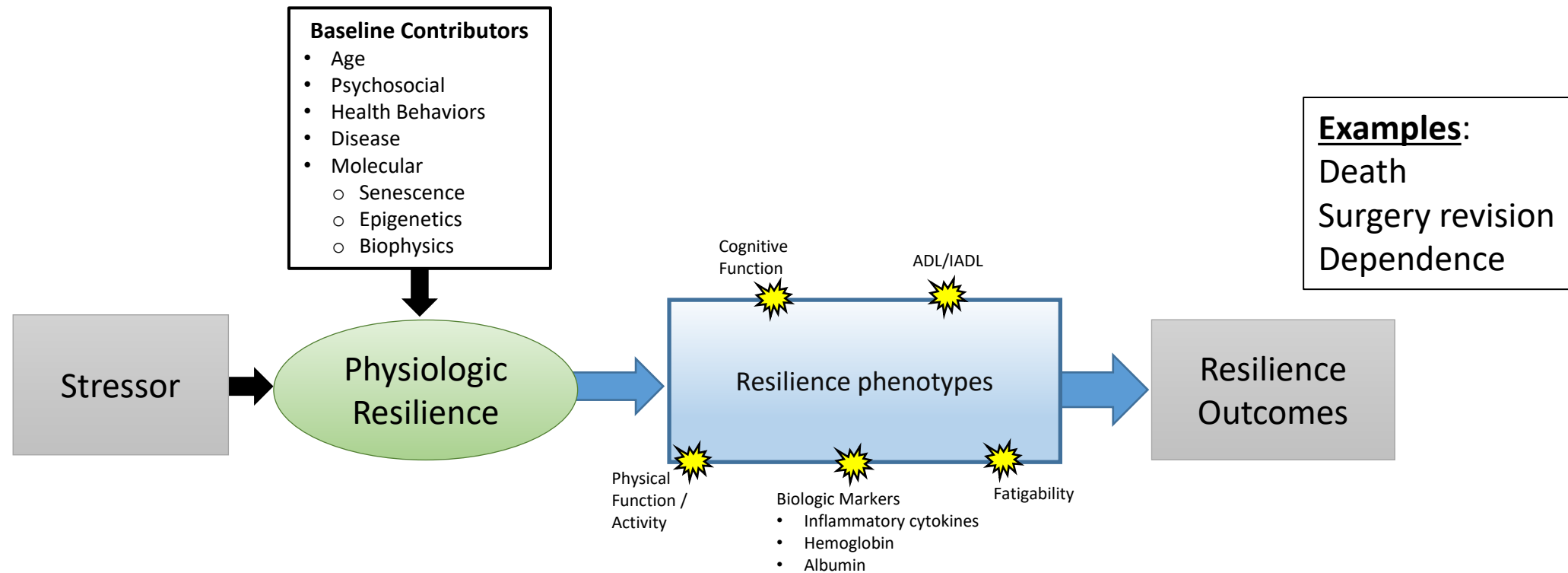
Conceptual Framework for Physical Resilience: Data collection



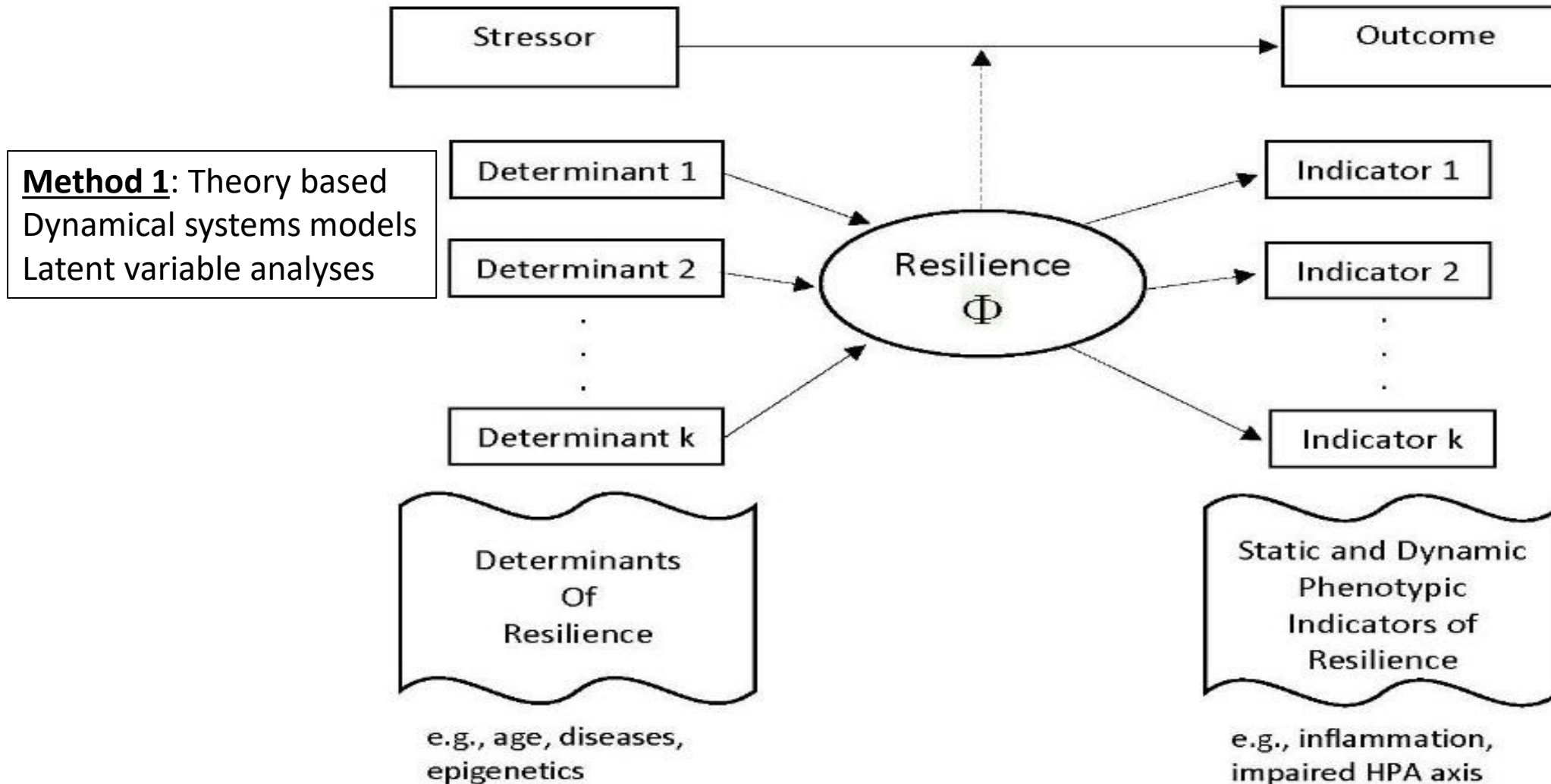
Conceptual Framework for Physical Resilience: Data collection



Conceptual Framework for Physical Resilience: Data collection

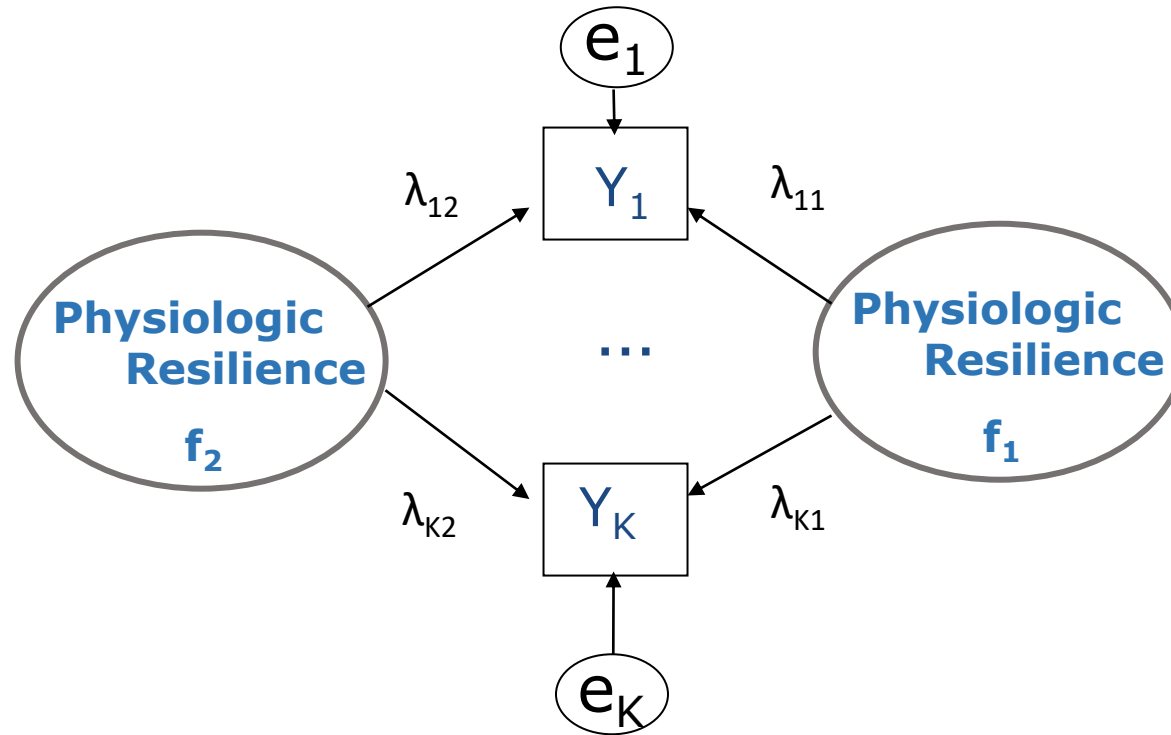


Approach to Analyzing Physiologic Resilience



Approach to Analyzing Physiologic Resilience - Example

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




- λ s scientifically informed (ex/ differential equations)

SPRING EXAMPLE: HRV, ACTH-STIM, Salivary Cortisol

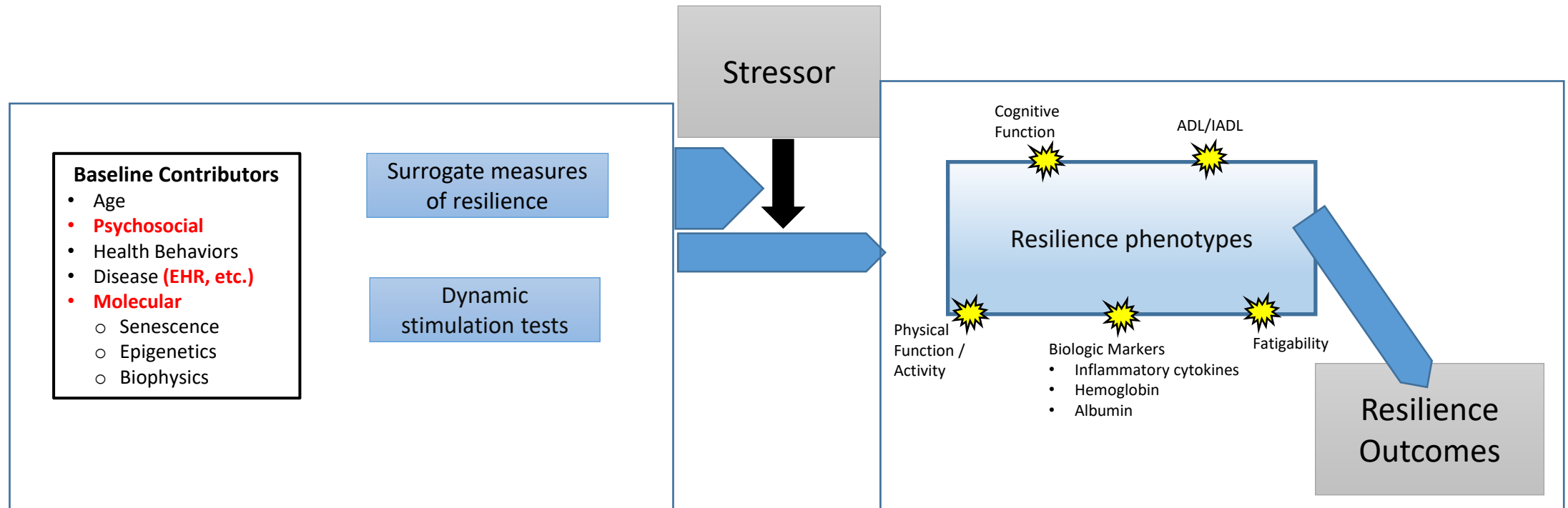
Pilot data: n=79; PCA approximation

Theory: Steady state, adaptation mechanisms

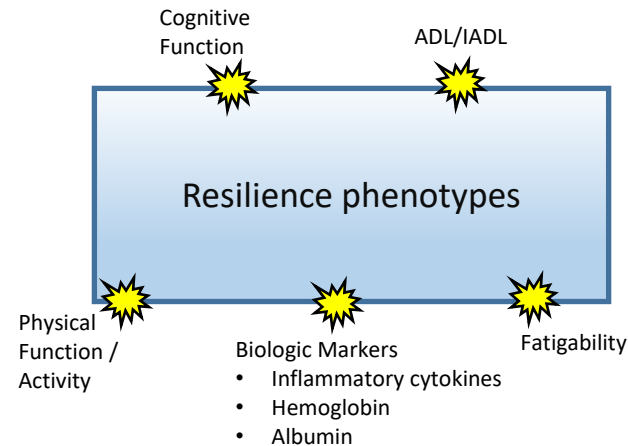
Indicator	f1	f2
HRV - Steady		
HRV - Adapt		
ACTH - Steady		
ACTH - Adapt		
Saliv Cort-Steady		
Saliv Cort-Adapt		

Approach to Analyzing Physiologic Resilience

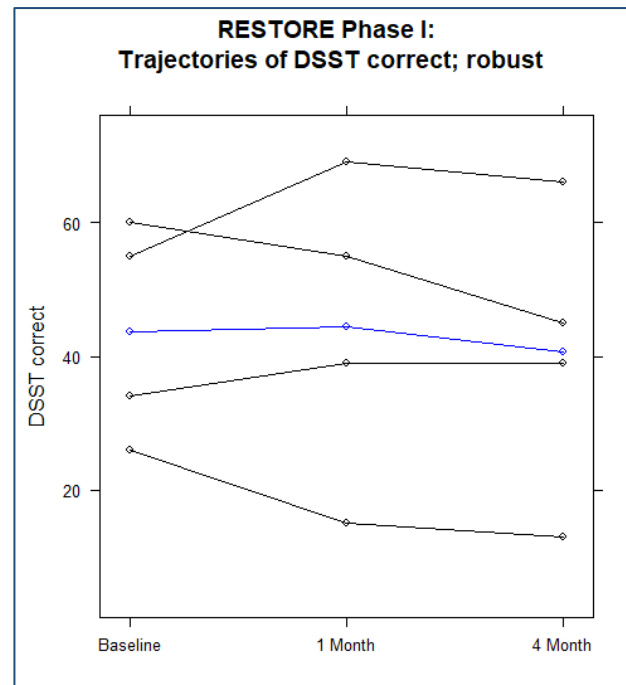
Method 2: Data driven Machine learning



Approach to Analyzing Observed Resilience



Resilience
Outcomes



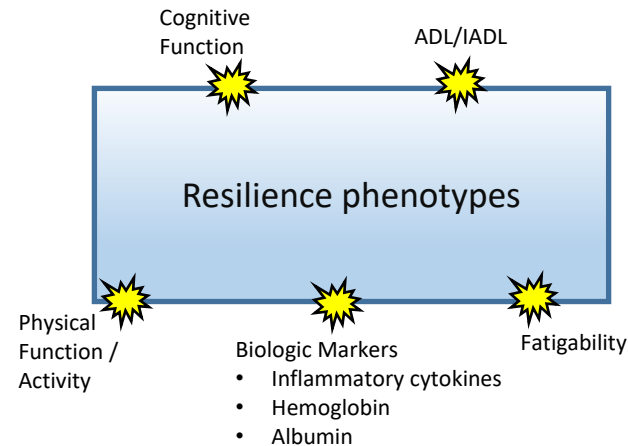
Trajectory analysis
Growth curves
Latent growth curves

Raw versus expected?

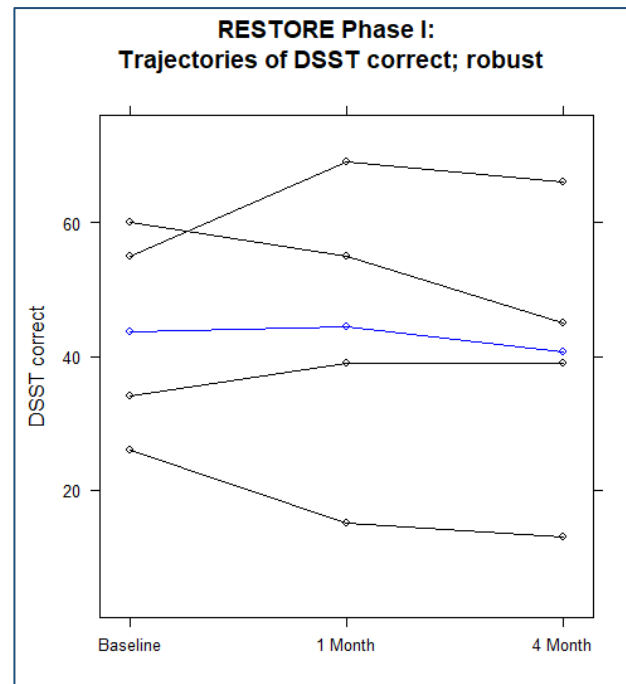
Functional data analysis?

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

- **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**