

tilda

Staidéar Fadaimseartha na
hÉireann um Dhul in Aois

The Irish Longitudinal
Study on Ageing



Trinity College Dublin

Coláiste na Tríonóide, Baile Átha Cliath

The University of Dublin



WHO Collaborating Centre
for Longitudinal Studies
on Ageing and the Life Course



Developing novel physiological biomarkers of autonomic dysregulation contributing to mortality risk

Prof Cathal McCrory presenting on behalf of Dr. Belinda Hernandez

Global cardiovascular disease burden

Cardiovascular disease is the leading cause of mortality worldwide and contributes to functional loss and excess healthcare system costs

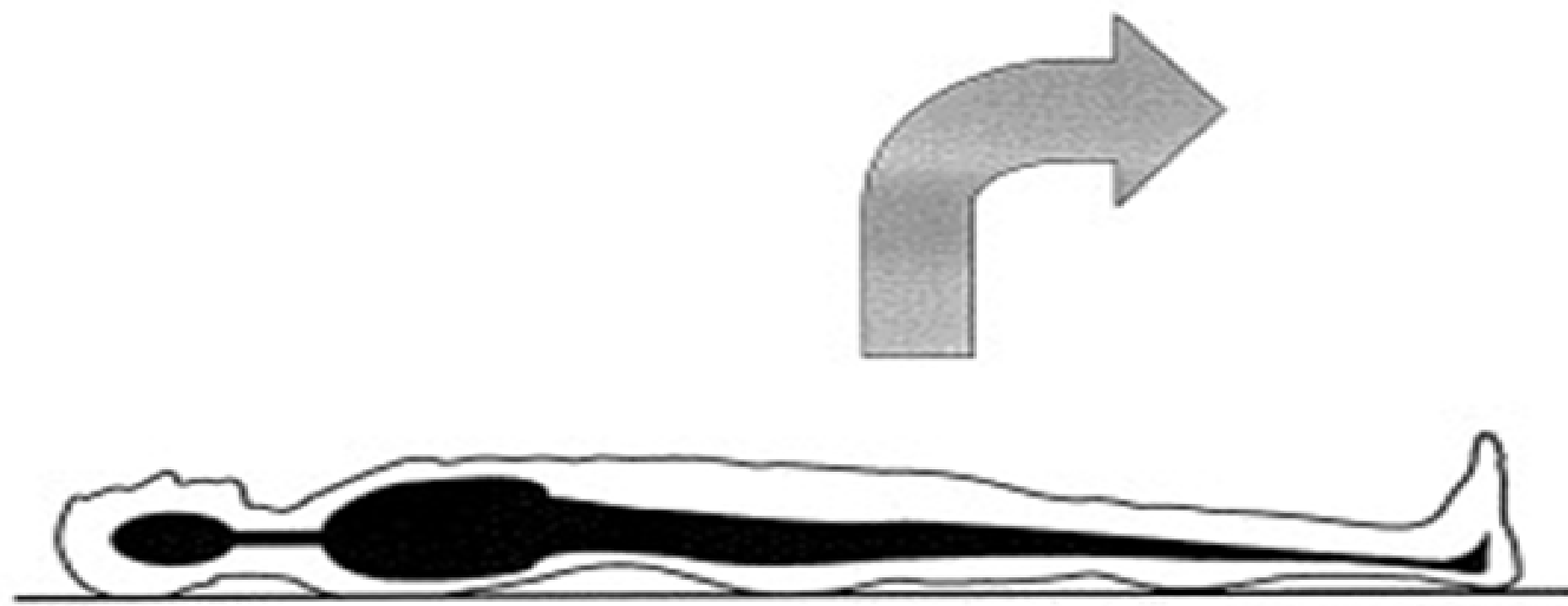
- Worldwide cost of CVD = 1,044 billion out to 2030 ([World Heart Federation](#))
- European cost of CVD = E282 billion in 2021 ([European Heart Journal, 2023](#))
 - 46% healthcare costs, 28% for informal care, 9% for social care, 17% productivity losses
- US cost of CVD = \$252.2 billion 2019-2020, ([Centers for Disease Control](#))

Modifiable risk factors include:

- Hypertension, Dietary risks, High LDL cholesterol, Smoking, Alcohol, High blood sugar levels, BMI, Kidney dysfunction, Pollution (PM, lead)

Continued need for monitoring and early risk identification

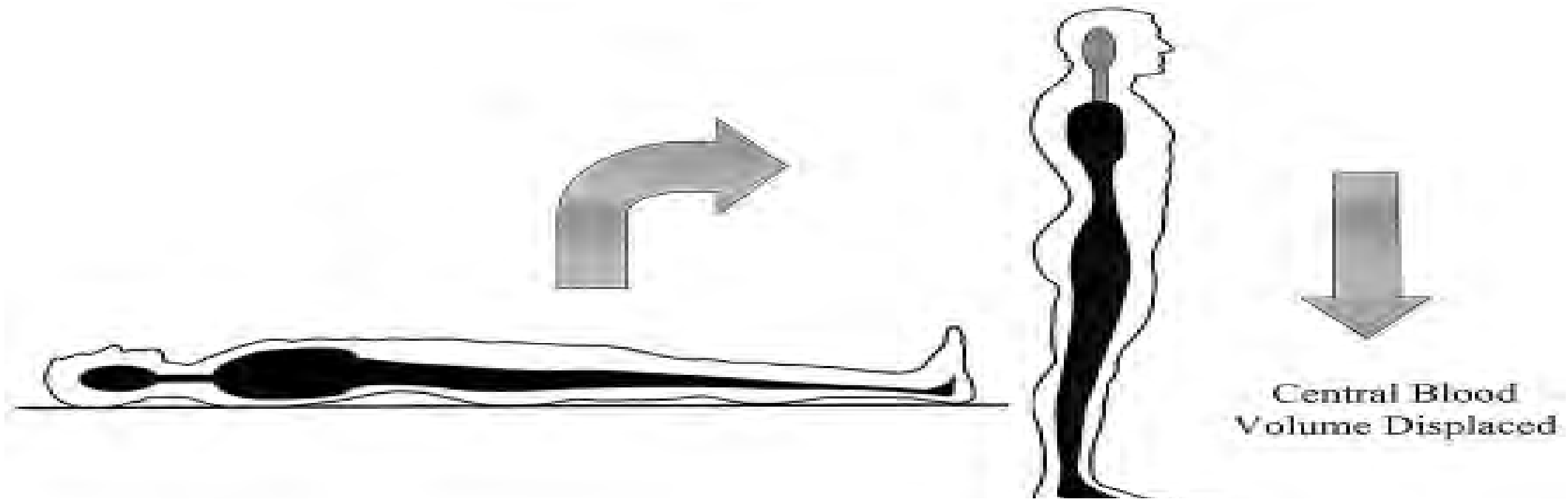
The active stand



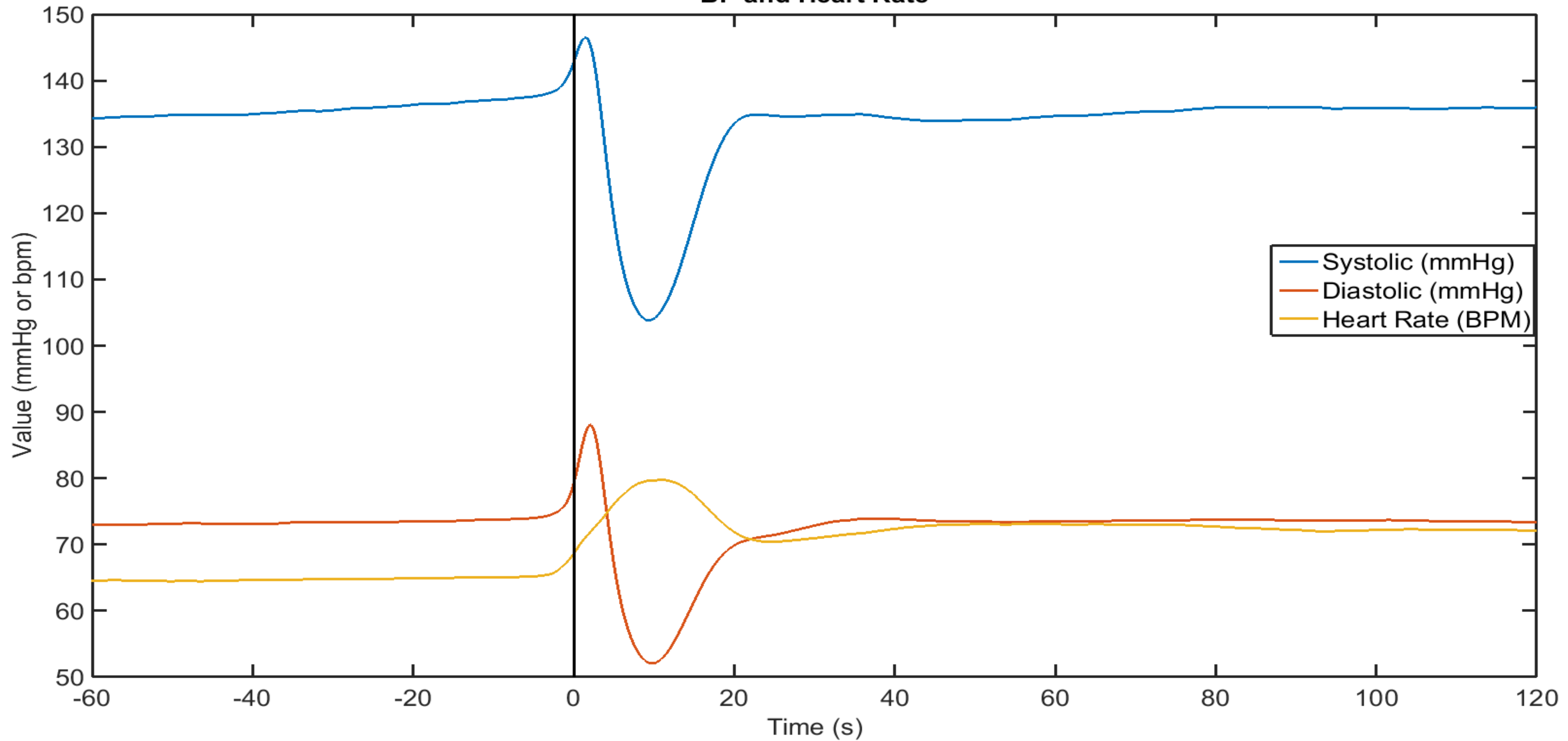
Venous and arterial reservoirs are at the same height

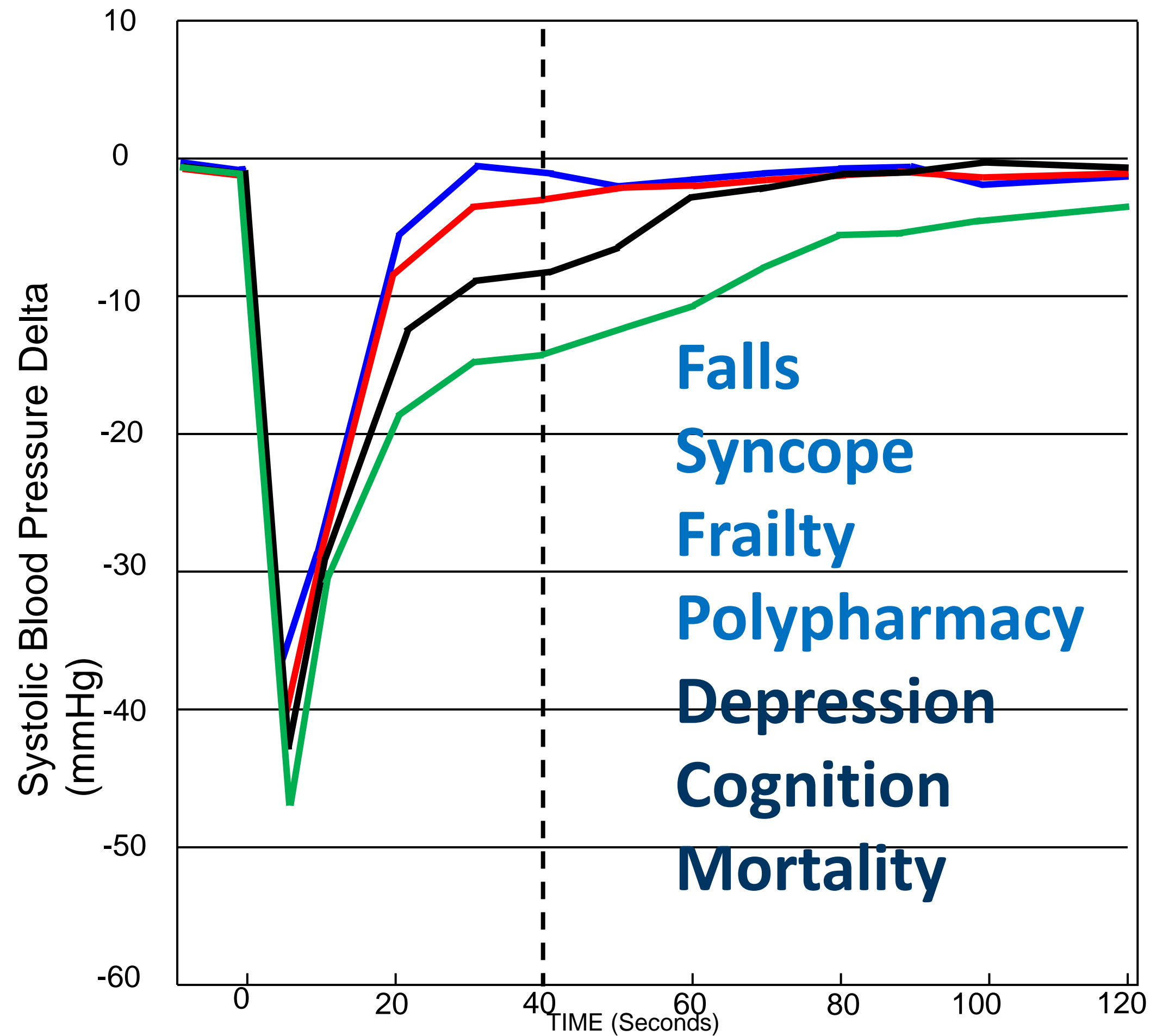
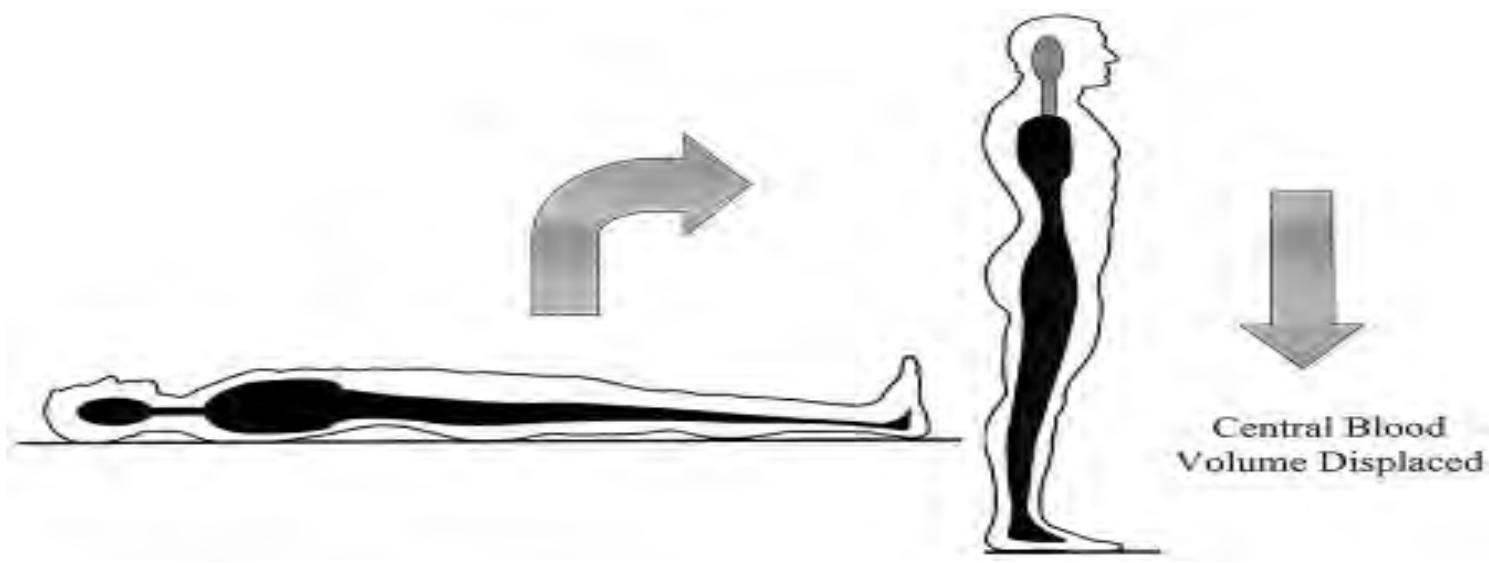
“The active stand is one of two physical stressors that demand the full capabilities of the reflexes that govern cardiovascular function”

(Rowell, 1993)



BP and Heart Rate

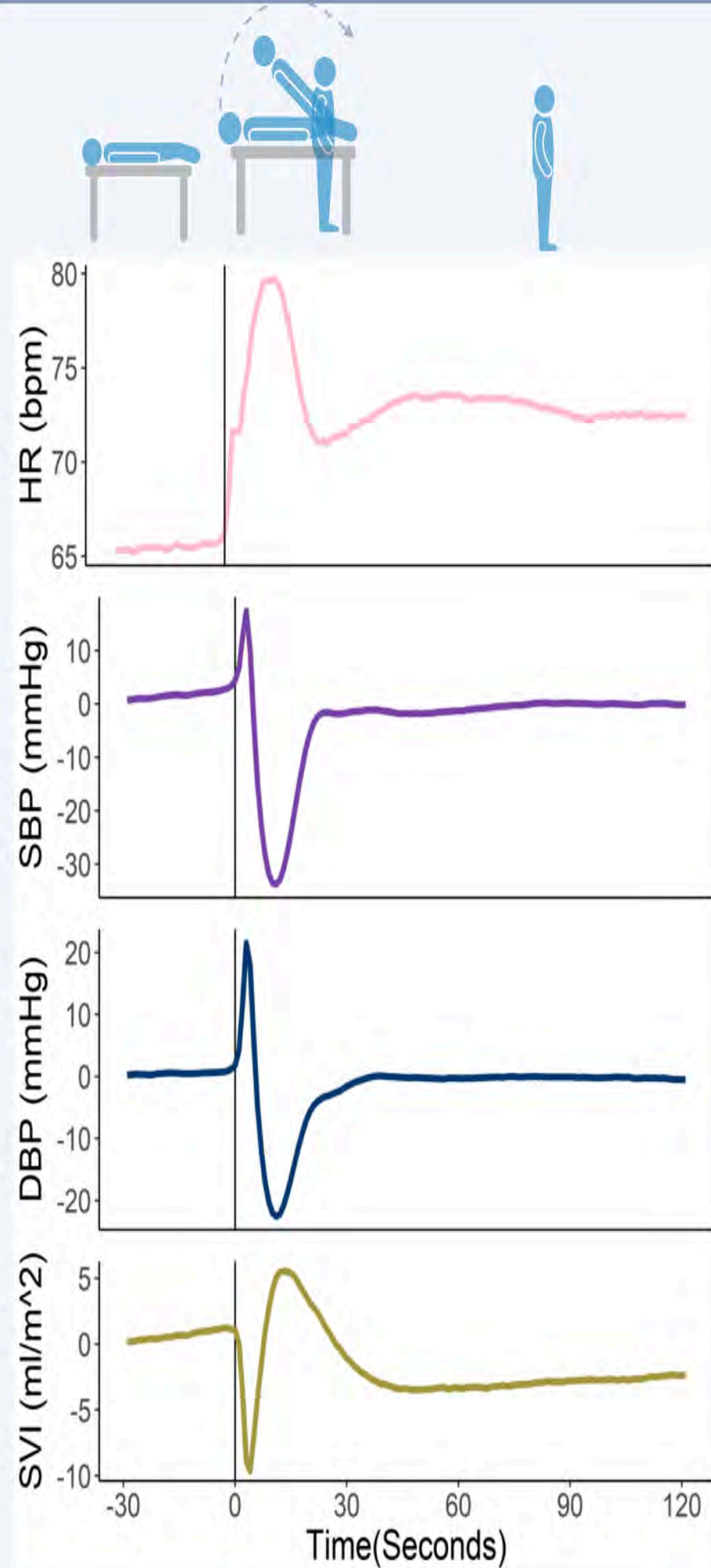




- Age 50-59
- Age 60-69
- Age 70-79
- Age 80+

Hypertension 2018
Circ Research 2016
Circulation 2014
JAGS 2014; 2016
Age & Aging 2014, 2016; 2017;
 2018
Am J Psych 2019

Aims and objectives



The Active Stand Experiment is a test of short-term neuro and cardiovascular functioning in response to standing.

Participants rest for 10 minutes and are asked to stand as quickly as possible. They remain standing for 2 minutes.

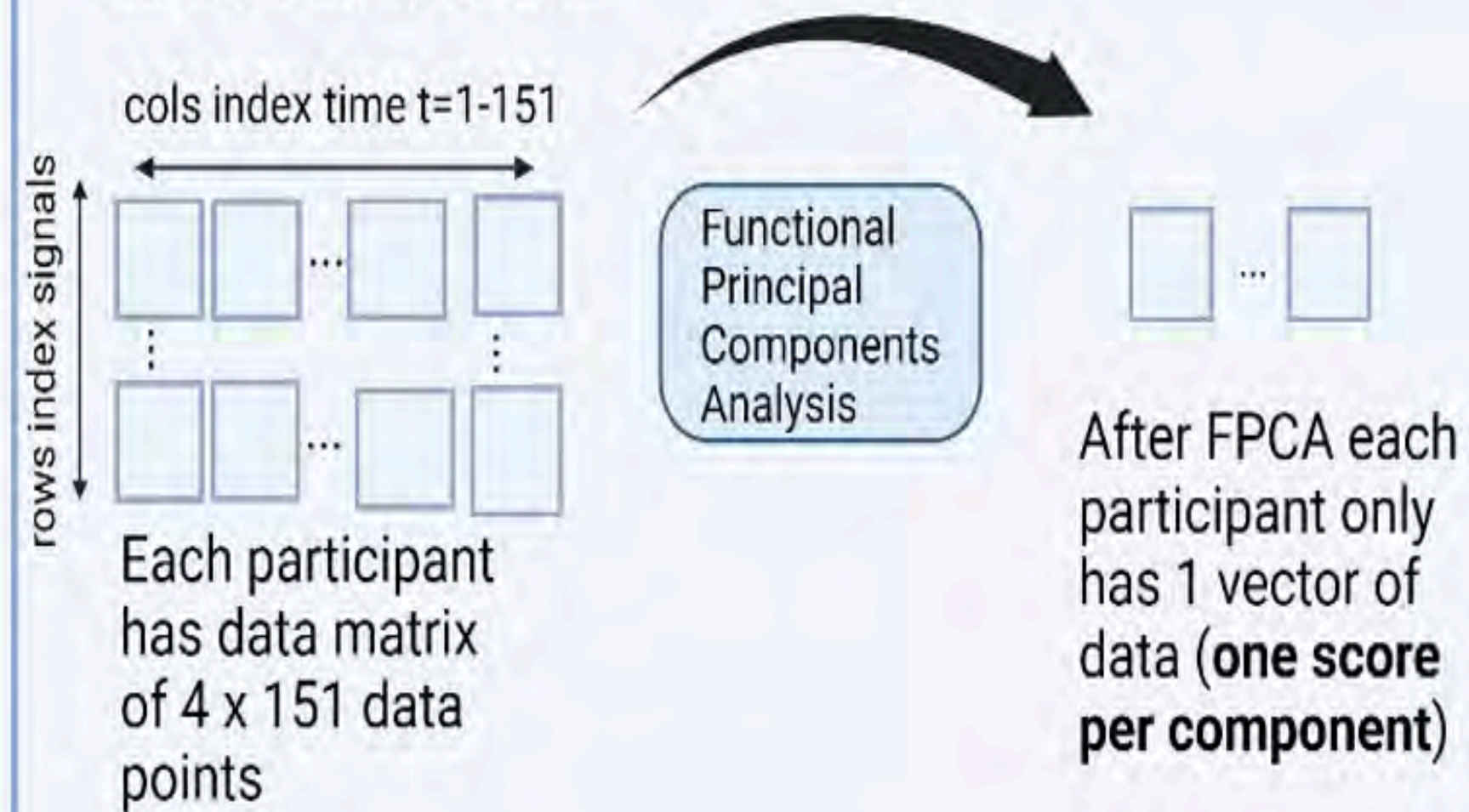
Beat-to-beat cardiovascular responses are captured at 1Hz / once per second.

Mean signals throughout the stages of the experiment are shown to the left.

Methodological approach

Functional Principal Component Analysis: A Brief Overview

Dimensionality Reduction:



Functional Principal Component Analysis (FPCA) is a dimensionality reduction method which can transform high dimensional time-series data down to a small number of single scores without much loss of information.

Each participant is given a score for each component. These scores can be used as a covariate in standard regression models.

Analytical approach

EXTRACTED

- 2 components for HR
- 5 components for SBP
- 6 components for DBP
- 4 for SVI

Components entered simultaneously using elastic net predicting all-cause and cause specific mortality

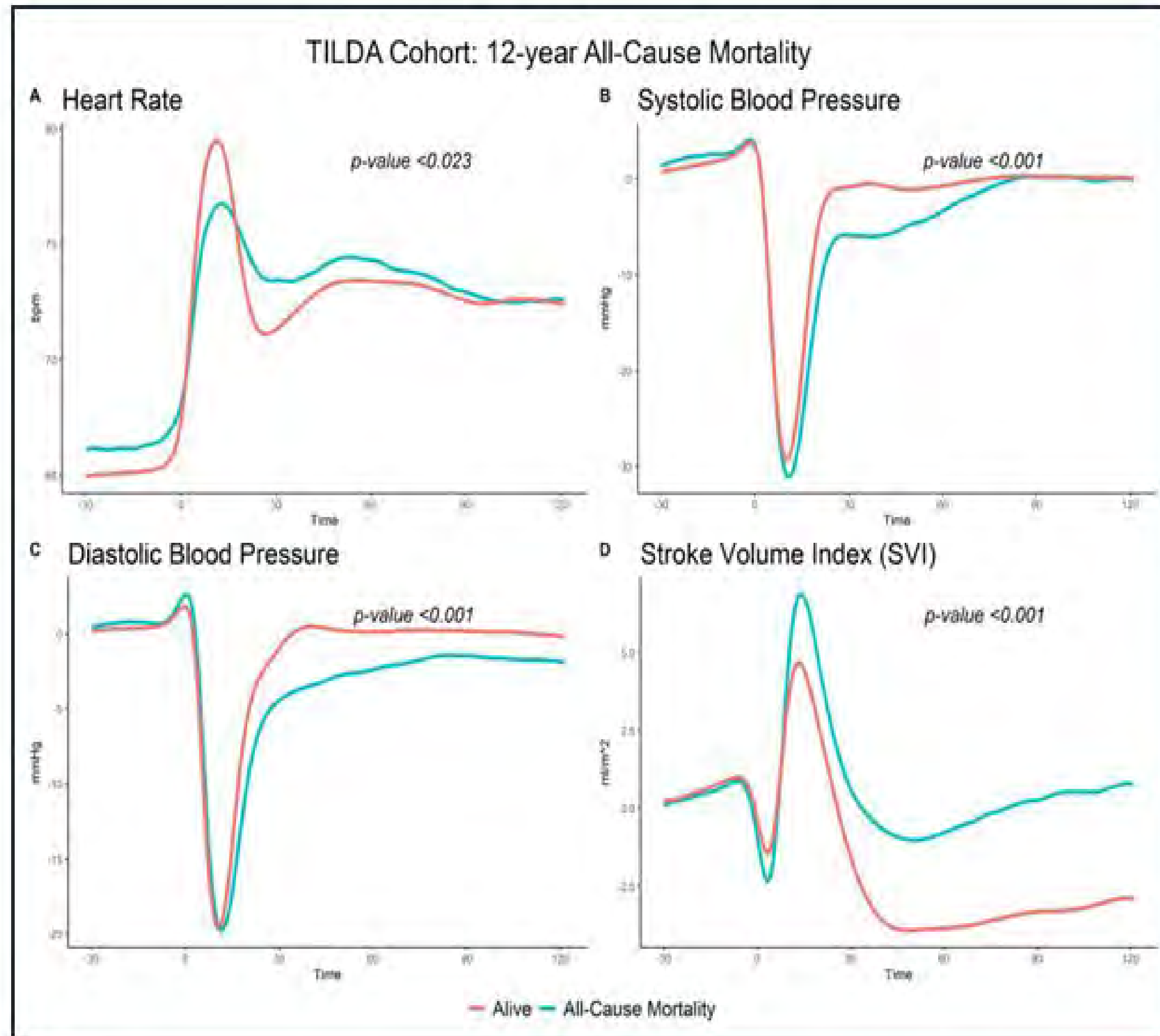
while adjusting for: age, sex, education, smoking history, BMI, hypertension, high cholesterol, depression, anxiety, psychosis and frailty.

Compared sensitivity of FPCA to using established cut-points



Dr. Belinda Hernandez
Biostatistician

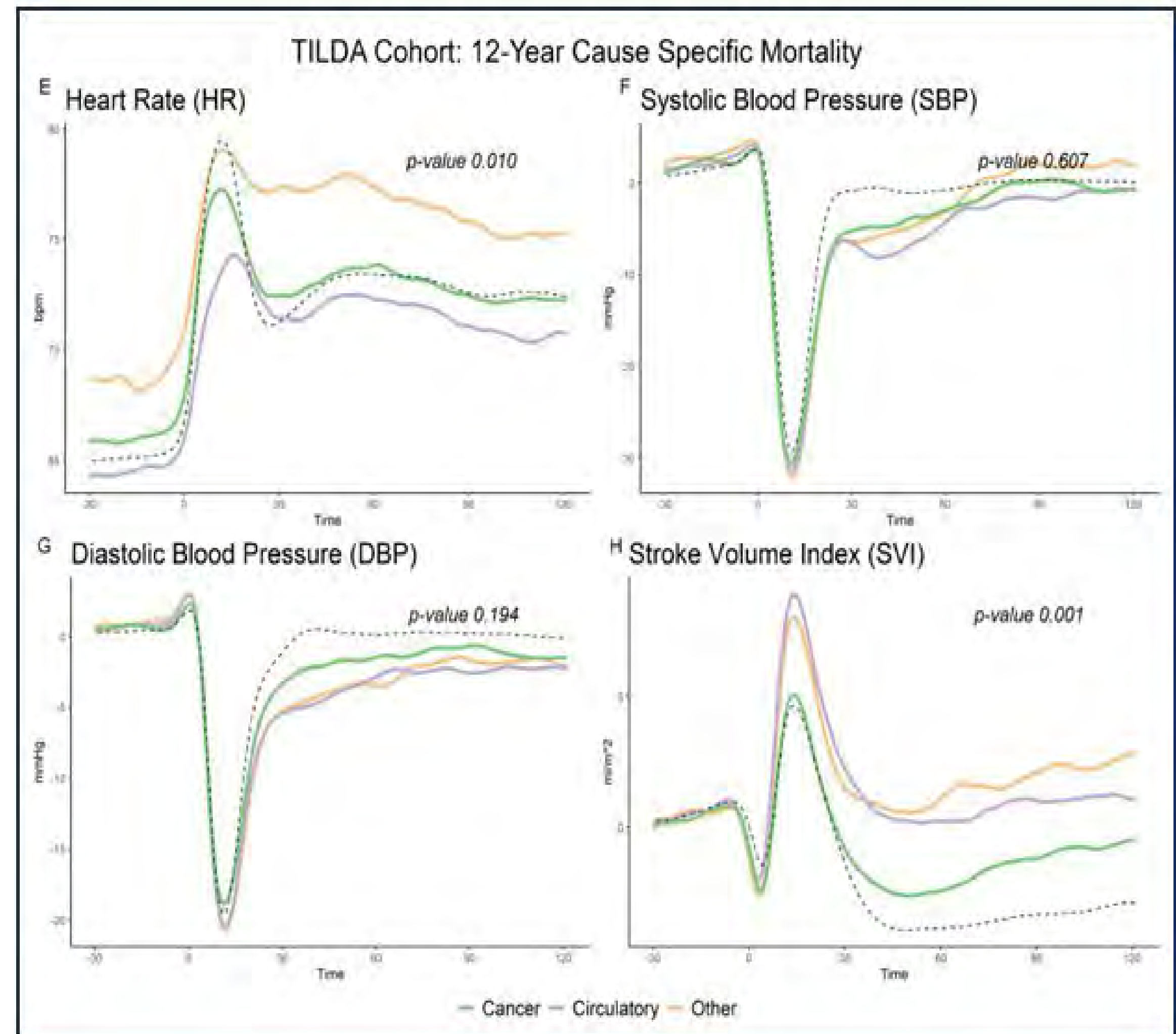
Results - 12-year mortality



Mean haemodynamic signals according to survival status for all-cause mortality.

Results - 12-year mortality

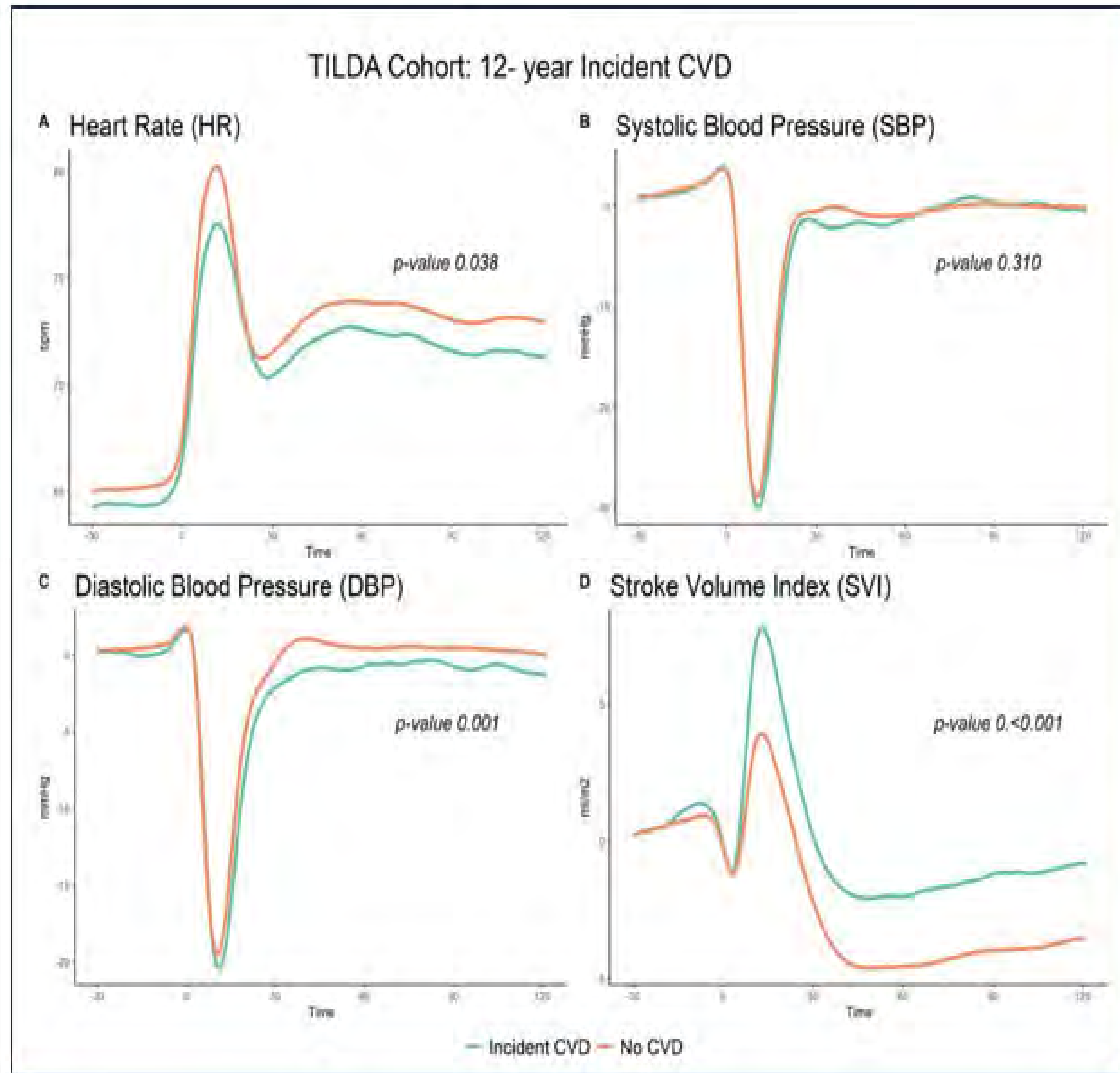
Mean trace of haemodynamic signals according to Cause-Specific Mortality status. Dashed black line indicates the mean curve for participants who were alive at the last day of follow up 31st January 2022 for reference



Multivariable models

- Components associated with **higher HR, higher baseline and poorer SBP recovery** 30-90 seconds after stand were associated with **all-cause mortality** after adjustment for medication usage, frailty status, behavioural and demographic risk factors.
- **Deaths of the circulatory system** were associated with components that differentiate **blunted HR peak** and **higher HR in recovery** as well as **higher baseline SBP** and **poorer SBP recovery**
- With the exception of OH40 for all cause mortality, OH 10-60s and baseline SBP were not associated with all cause or cause specific mortality.

12-year incident CVD



CVD multivariable analyses

- The components associated with **incident CVD** were related to **lower HR** and **elevated post stand SVI**
- For the **clinical cohort** components related to **blunted drop in DBP** to the nadir and **impaired blood pressure recovery from 35 seconds onwards** were significantly associated with presence of CVD. **AUC 0.64 95% CI (0.56,0.71)**, sensitivity 0.63, specificity 0.60.

Discussion

- **Functional principal component scores** of haemodynamic responses to standing were independently **associated** with **12 year all-cause and cause specific mortality** and also independently associated with **12-year incident CVD** even after adjustment for health, frailty, behavioural and demographic risk factors.
- **Incorporating such dynamic features** of hemodynamic responses to standing over the entire trace of the curve can **uncover more subtle relationships** with health outcomes
- **These models can be easily incorporated into a clinical setting** and used for prediction of health outcomes by identifying impaired recovery of DBP as a significant factor associated with CVD after covariate adjustment on a clinical validation cohort.

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The
A T L A N T I C
Philanthropies

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