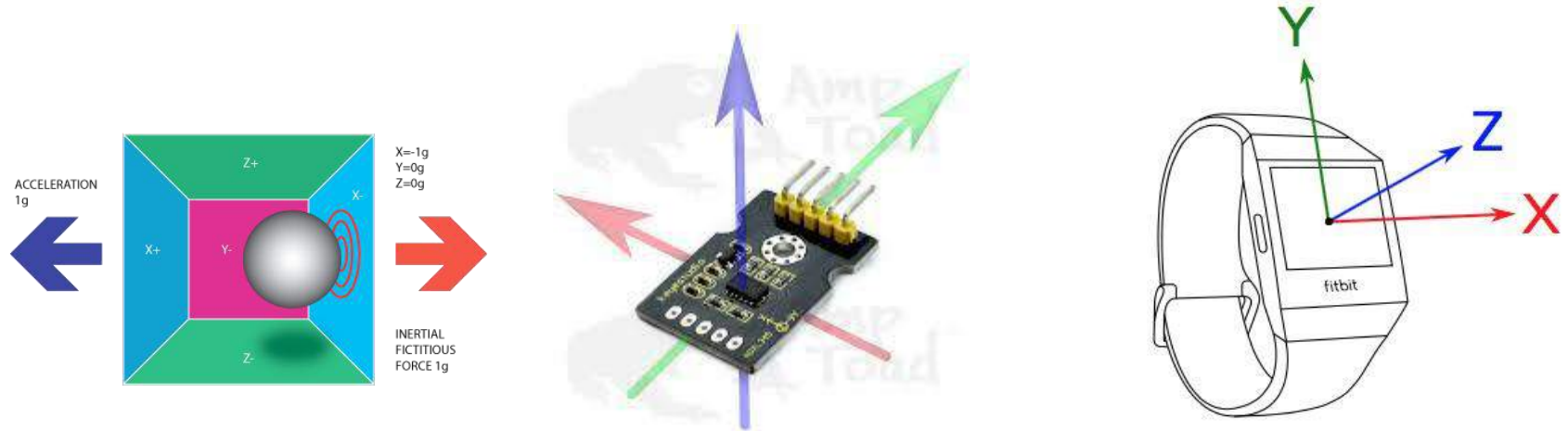


# Fragmentation: overview and applications

Vadim Zipunnikov, PhD

Department of Biostatistics

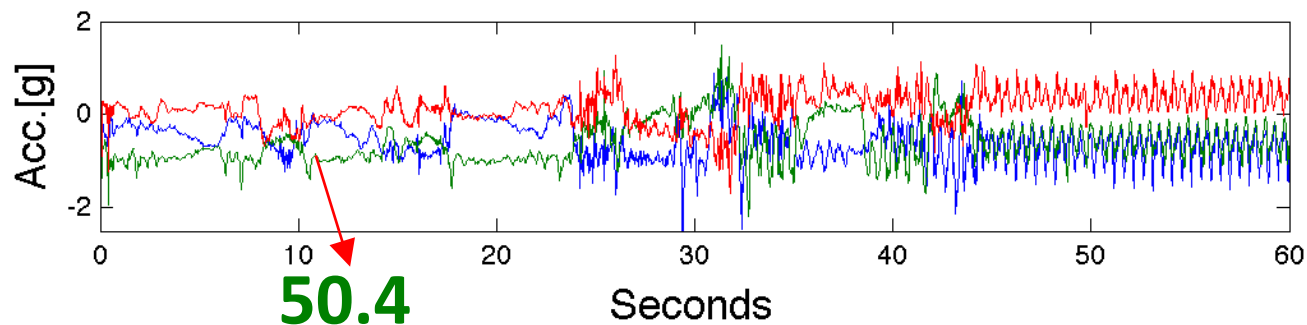
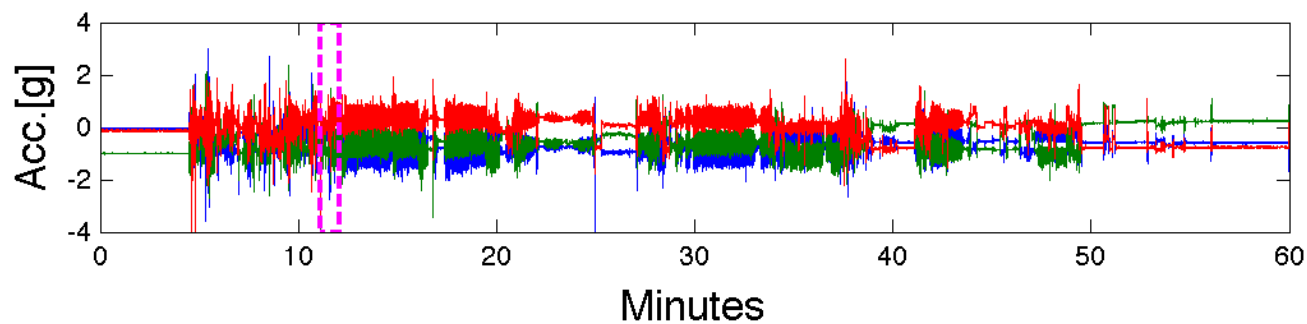
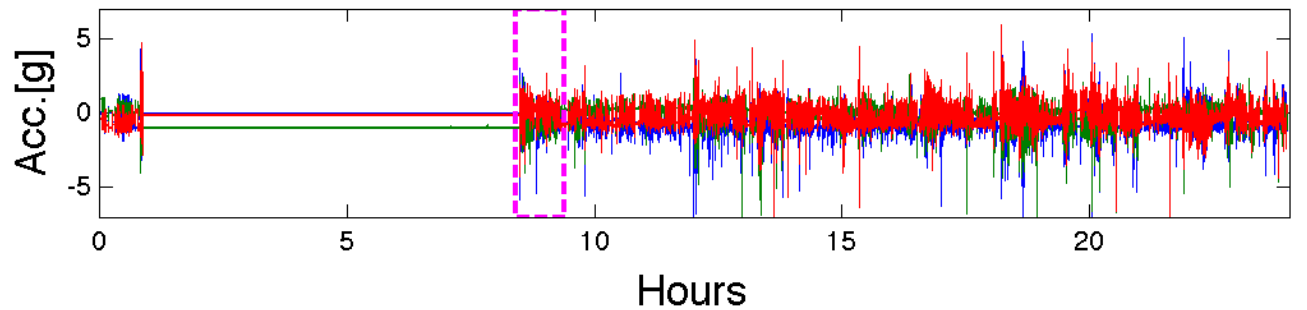
# Accelerometers



- Detects acceleration in three orthogonal planes
- <https://www.youtube.com/watch?v=irjG9Y4NGnE>



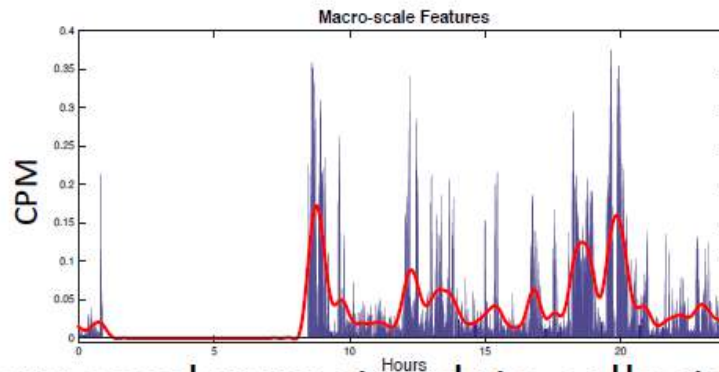
Data



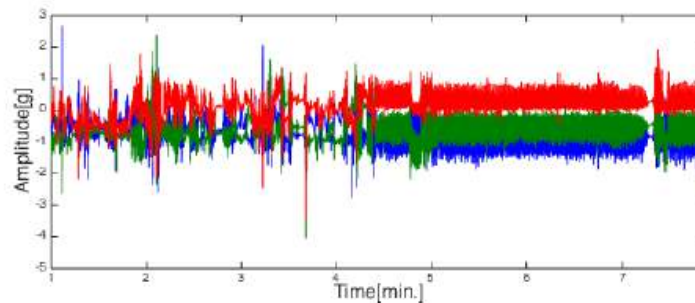
50.4  
Activity Count

# Macro- and Micro-scale

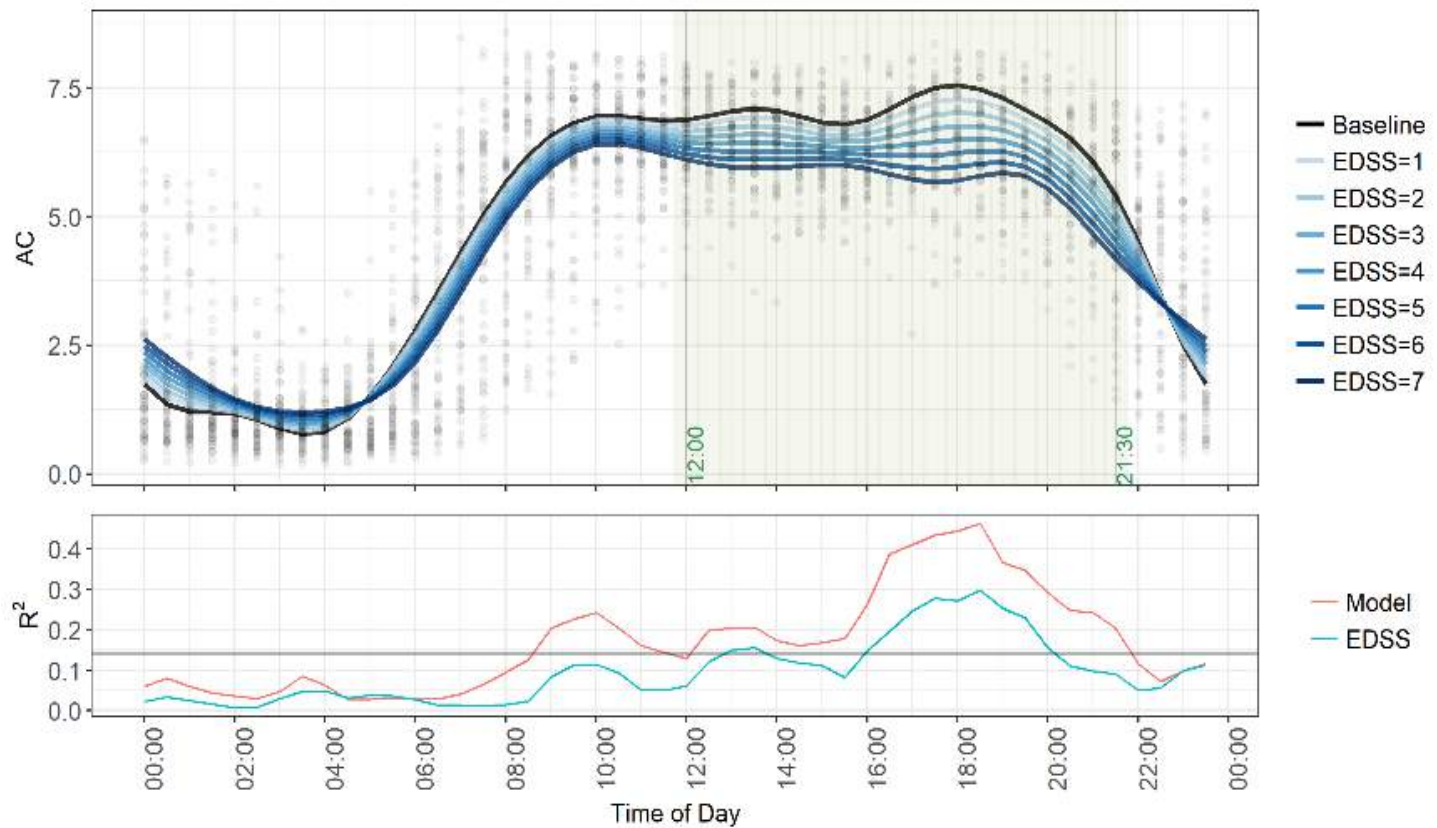
- **Macro-scale** – summarized data (1 minute intervals)



- **Micro-scale** – raw accelerometry data collected (10Hz+)



# Disability in Multiple Sclerosis



# Fragmentation: overview

Junrui Di, PhD

Pfizer, Digital Medicine





## Patterns of sedentary and active time accumulation are associated with mortality in US adults: The NHANES study

Junrui Di, Andrew Leroux, Jacek Urbanek, Ravi Varadhan, Adam P. Spira, Jennifer Schrack, Vadim Zipunnikov  
DOI: <https://doi.org/10.1101/182337>

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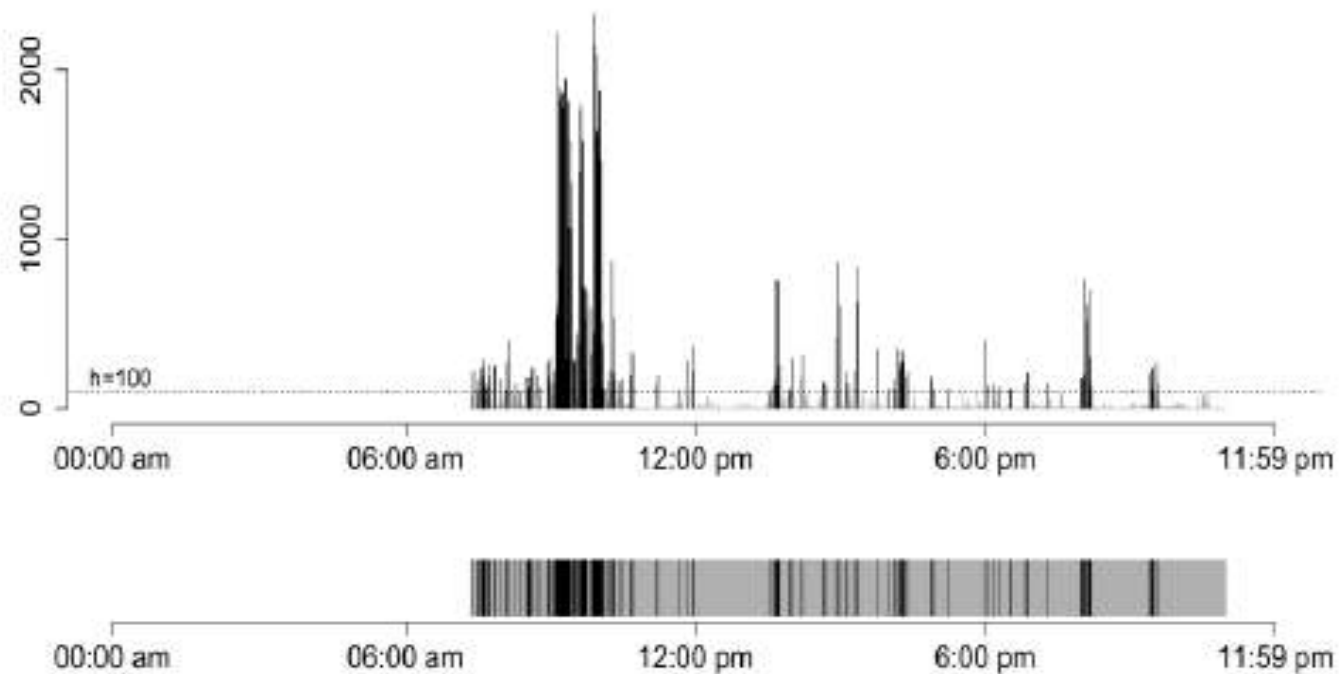
# Fragmentation: overview

Junrui Di, PhD

Pfizer, Digital Medicine



## Fragmentation





# Motivation: Sedentary Behavior

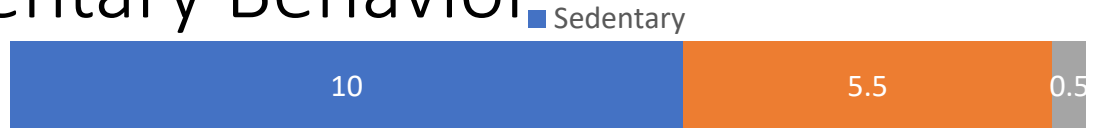
- Time spent in a day

- Sedentary E.g. sitting, driving, reading
- Active = LIPA + MVPA
  - light physical activity (LIPA) e.g. walking
  - moderate to vigorous activity (MVPA) e.g. exercise



- Sedentary behavior is a risk factor for a wide range of diseases and comorbidities.

- Quantified as absolute duration or proportion of waking hours spent in sedentary state.



## Statistical Framework

### Nonparametric

Metrics	Interpretation	Definition	Estimation
AAC ( $\mu$ )	average duration	$Ed_i$	$\frac{T}{n}$
nAAC ( $^*\mu$ )	normalized average	$\frac{Ed_i}{^*d}$	$\frac{T}{^*dn}$
Gini ( $g$ )	normalized variability	$\frac{E d_i-d_j }{2\mu}$	$\frac{\sum_{ij}  d_i-d_j }{2n \sum_t d_t}$
AH ( $\bar{h}$ )	average hazard	$h(t) = \frac{F'(t)}{1-F(t)} \bar{h} = \frac{1}{m} \sum_{t \in \mathcal{D}} \hat{h}(t)$	
Systematic Derivation		$l_\psi(\hat{F}) = \int_0^{*d} \psi(\hat{F}(t))dt$	
AAC	$\hat{\mu} = \int_0^{*d} (1 - \hat{F}(t))dt$		
nAAC	$^*\hat{\mu} = \frac{1}{^*d} \int_0^{*d} (1 - \hat{F}(t))dt$		
Gini	$\hat{g} = \frac{1}{\hat{\mu}} \int_0^{*d} \hat{F}(t)(1 - \hat{F}(t))dt$		
AH	$\bar{h} = \frac{1}{^*d} \int_0^{*d} \frac{\hat{F}(t)-\hat{F}(t-1)}{1-\hat{F}(t-1)}dt$		

# Between-State Transition Probabilities

- Assumption: two state system (sedentary (S) and active (A))

$P_S = \Pr(x_t = 0)$ : proportion of time spent sedentary

$P_A = \Pr(x_t = 1)$ : proportion of time spent active

0, 1 for sedentary and active bout respectively,  $x_t$  is the type of bout

- Between-state transition probabilities

$ASTP = \Pr(x_{t+1} = 0 | x_t = 1)$

$SATP = \Pr(x_{t+1} = 1 | x_t = 0)$

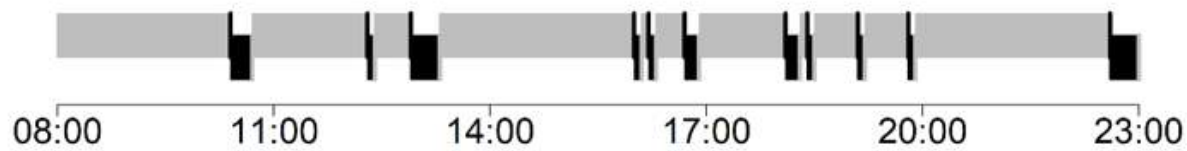
- Estimation

$$\widehat{ASTP} = \frac{n_A}{T_A} = 1/\text{average active bout}$$

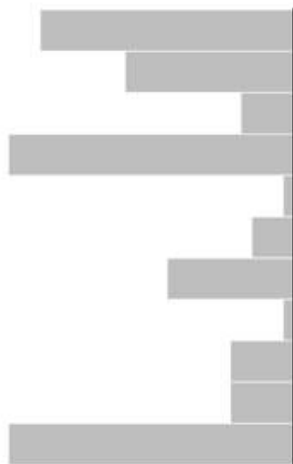
$$\widehat{SATP} = \frac{n_S}{T_S} = 1/\text{average sedentary bout}$$

$n_A, n_S$ : total number of active and sedentary bouts

$T_A, T_S$ : total number of active and sedentary time



Sedentary Bouts



S  $\rightarrow$  A Transitions

$$SP = \frac{T_S}{T_S + T_A}$$

$$SATP = \frac{n_S}{T_S}$$

Active Bouts



A  $\rightarrow$  S Transitions

$$AP = \frac{T_A}{T_S + T_A}$$

$$ASTP = \frac{n_A}{T_A}$$

# Properties and Intuitions for ASTP and SATP

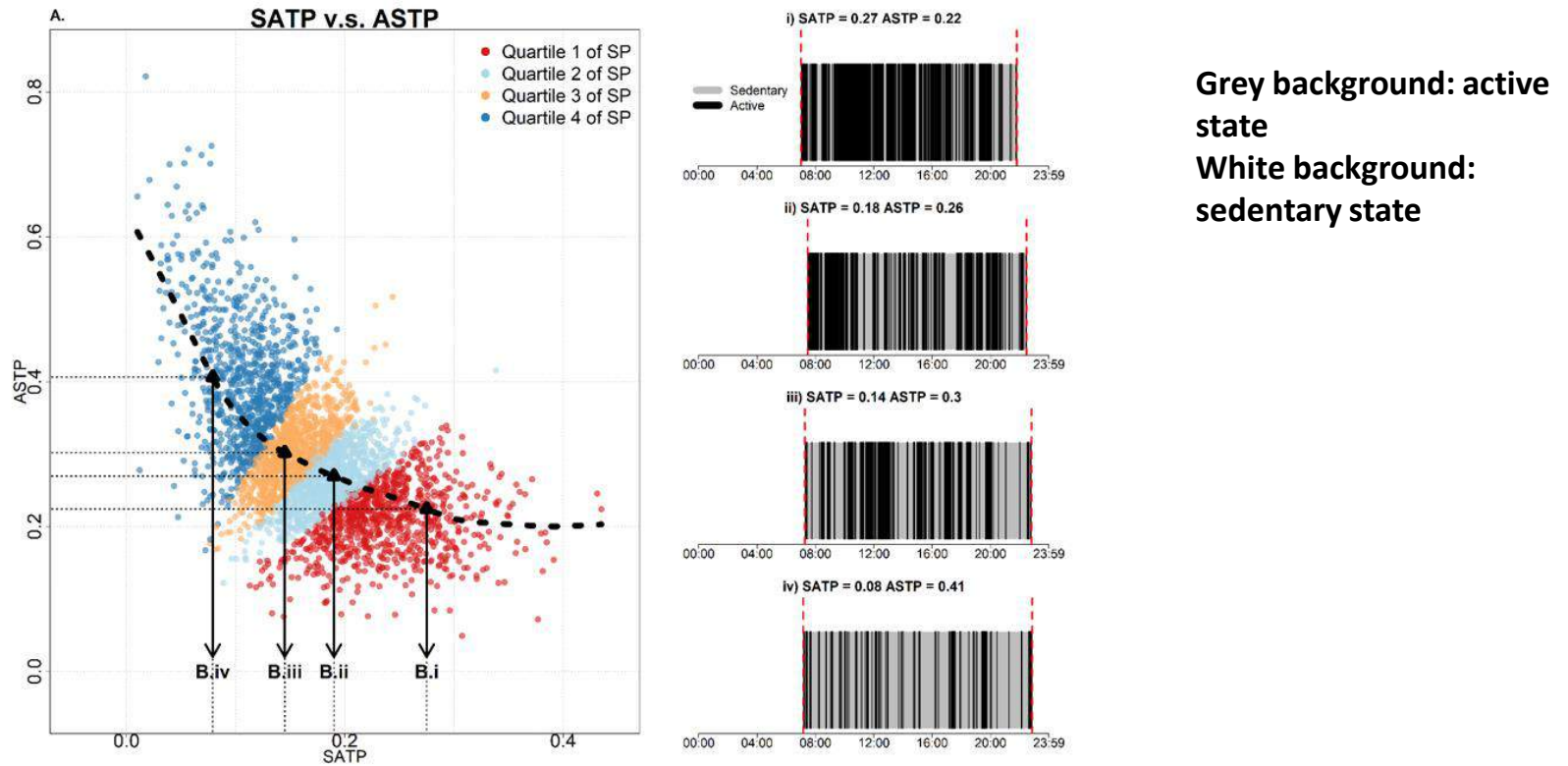


Figure 2. ASTP and SATP stratified by quartiles of total daily sedentary proportions ( $P_S$ ).

# Results of Survival Models for ASTP and SATP

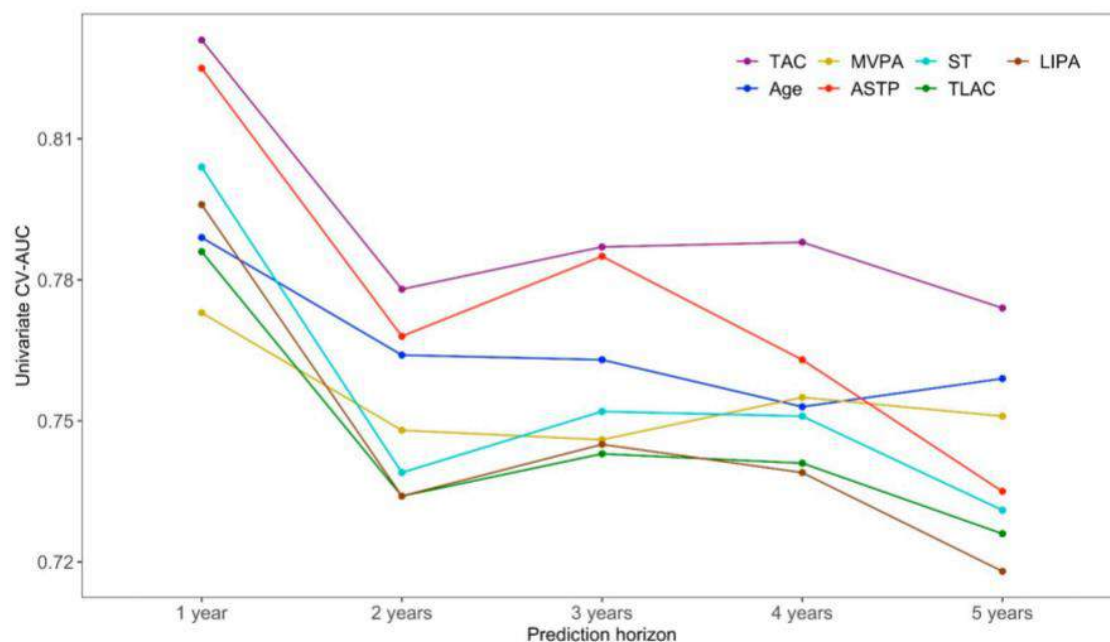
Final	HR	Beta	P value
ASTP	1.33 (1.18, 1.50)	0.29 (0.17, 0.41)	<0.0001
SATP	0.47 (0.27, 0.80)	-0.76 (-1.30, -0.23)	0.005
Low P <sub>s</sub>	0.21 (0.10, 0.45)	-1.56 (-2.30, -0.81)	<0.0001
High P <sub>s</sub>	ref	ref	
SATP   Low P <sub>s</sub>	2.71 (1.53, 4.81)	1.00 (0.43, 1.57)	0.0006

- Two behavioral strategies of reducing sedentary time: **prolonging active bouts** and **breaking sedentary bouts**.
- Benefits of prolonging active bouts exist regardless of overall sedentary time.
- Only for those who are extremely sedentary, there is an benefit of reducing their total sedentary time via more frequent breaking their sedentary bouts.





# Quantifying the Varying Predictive Value of Physical Activity Measures Obtained from Wearable Accelerometers on All-Cause Mortality over Short to Medium Time Horizons in NHANES 2003–2006

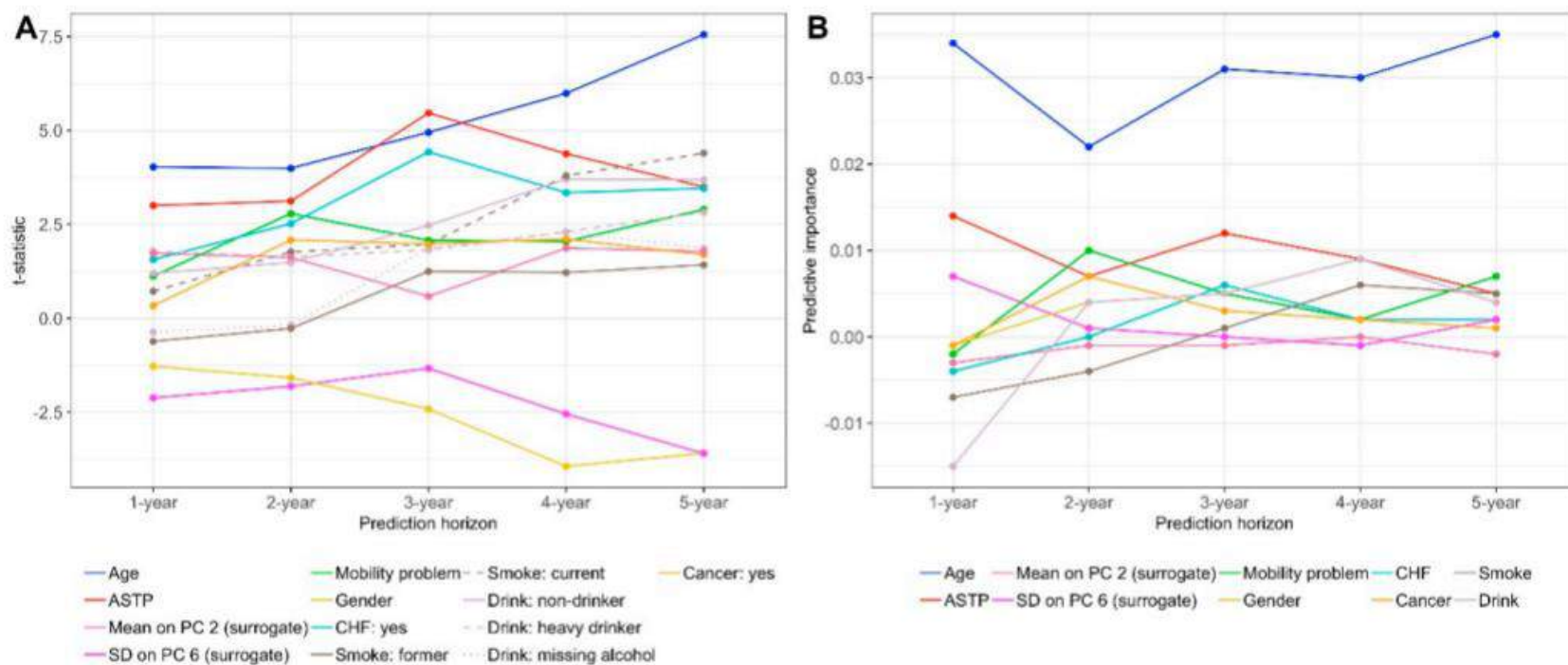
Lucia Tabacu<sup>1,\*</sup>, Mark Ledbetter<sup>2</sup>, Andrew Leroux<sup>3</sup>, Ciprian Crainiceanu<sup>4</sup> and Ekaterina Smirnova<sup>5</sup>



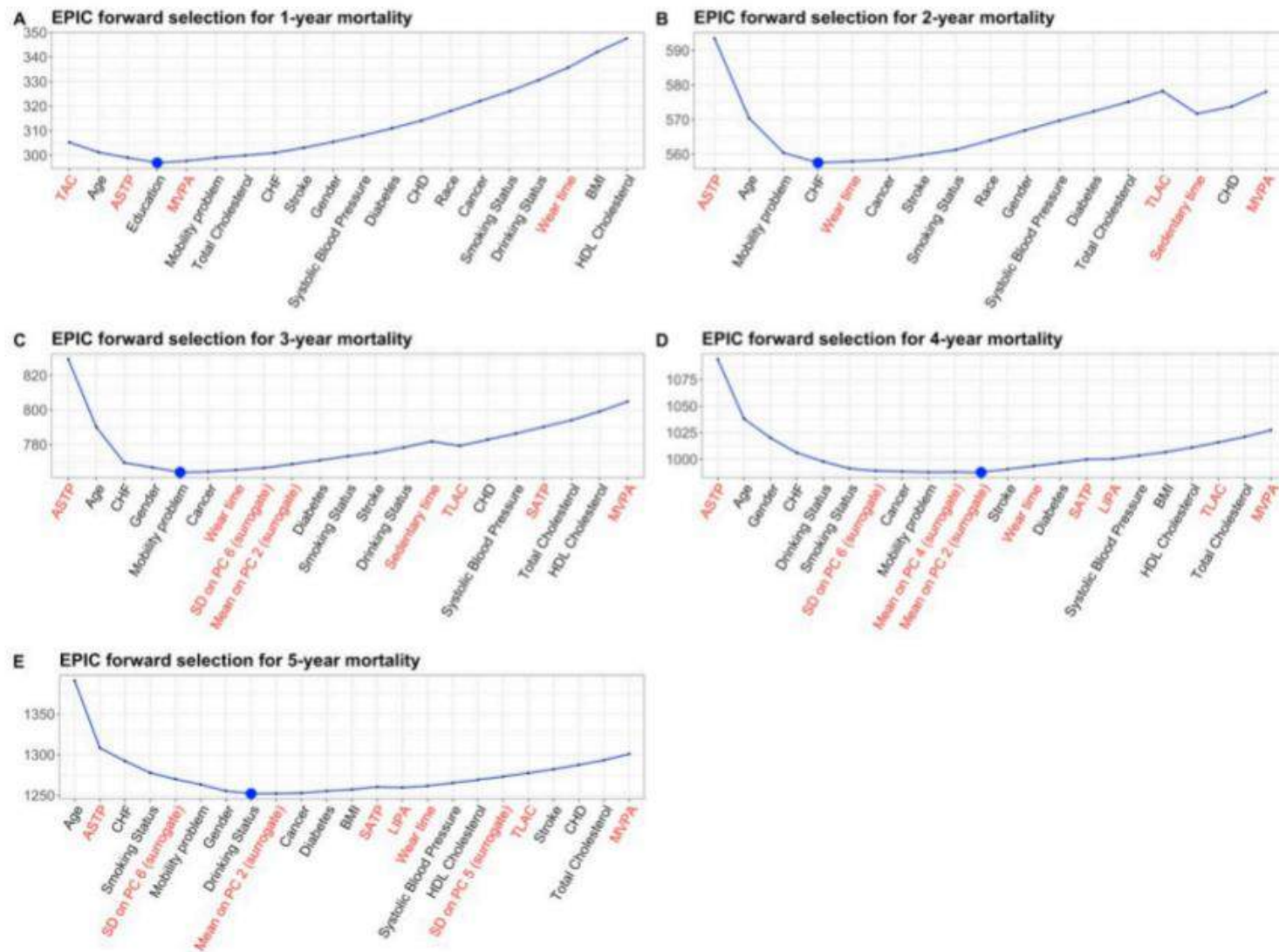
**Figure 1.** The cross-validated area under the curve (CV-AUC) values for the top seven predictors in the univariate five-year all-cause mortality logistic regression models across one- to five-year mortality prediction horizons. The x-axis corresponds to the prediction horizon and the y-axis is the CV-AUC (higher indicates better prediction performance).

# Quantifying the Varying Predictive Value of Physical Activity Measures Obtained from Wearable Accelerometers on All-Cause Mortality over Short to Medium Time Horizons in NHANES 2003–2006

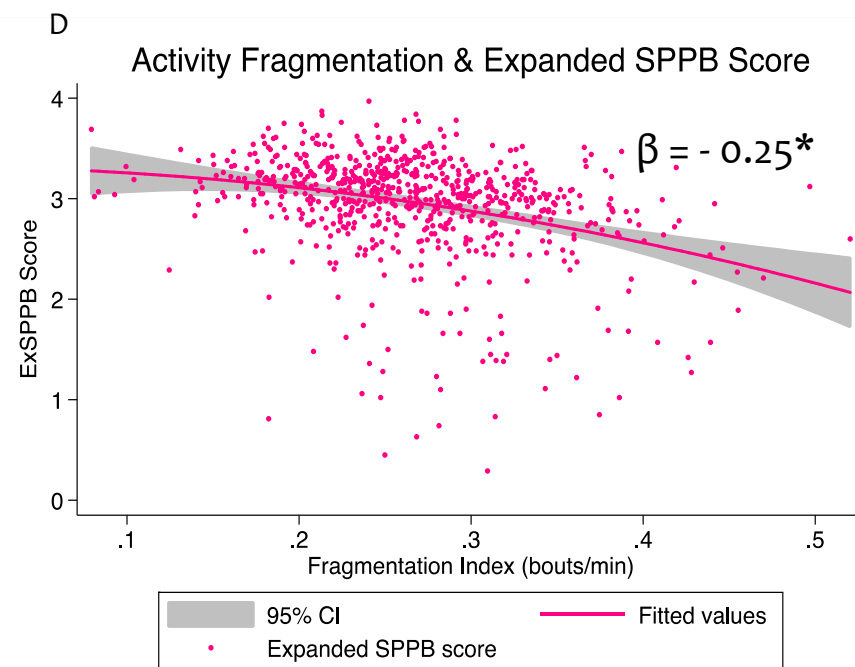
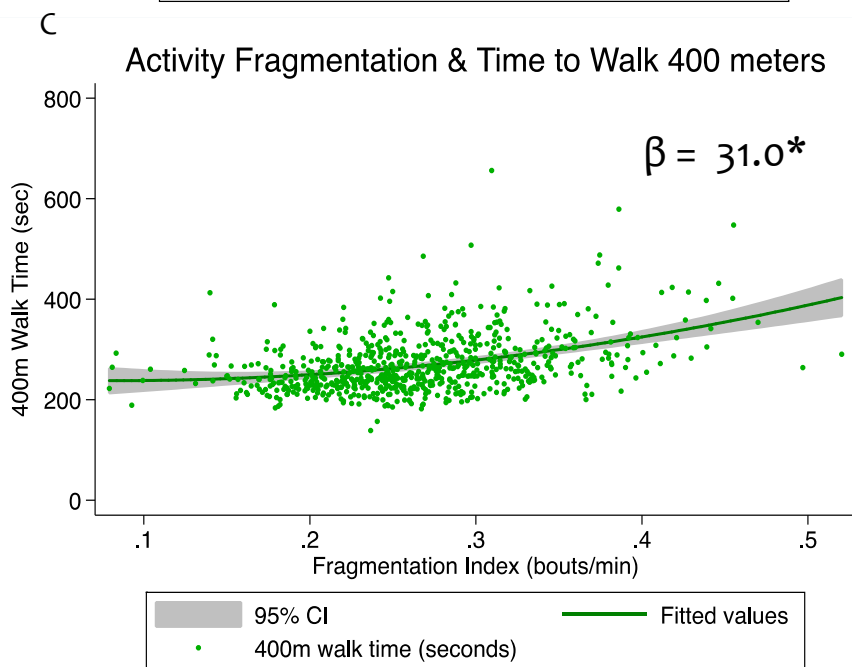
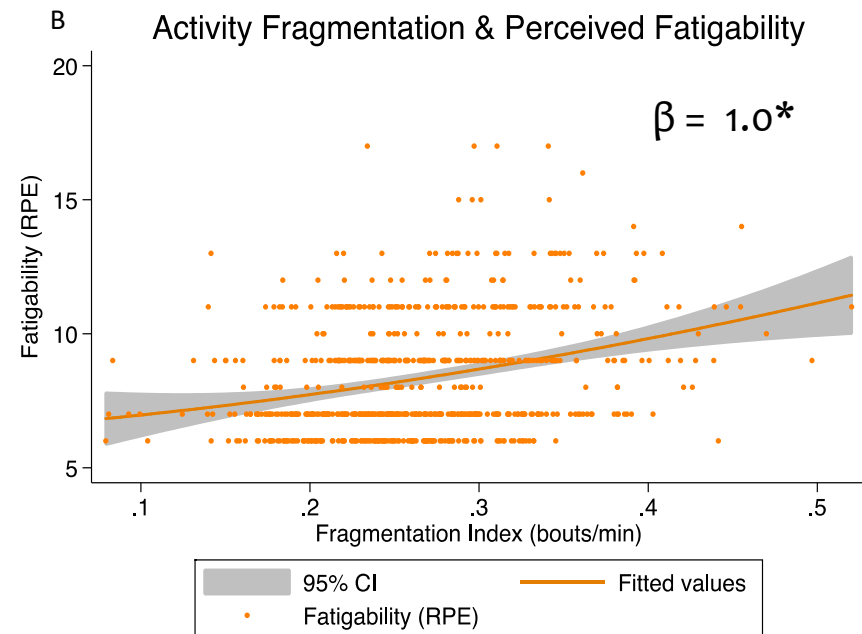
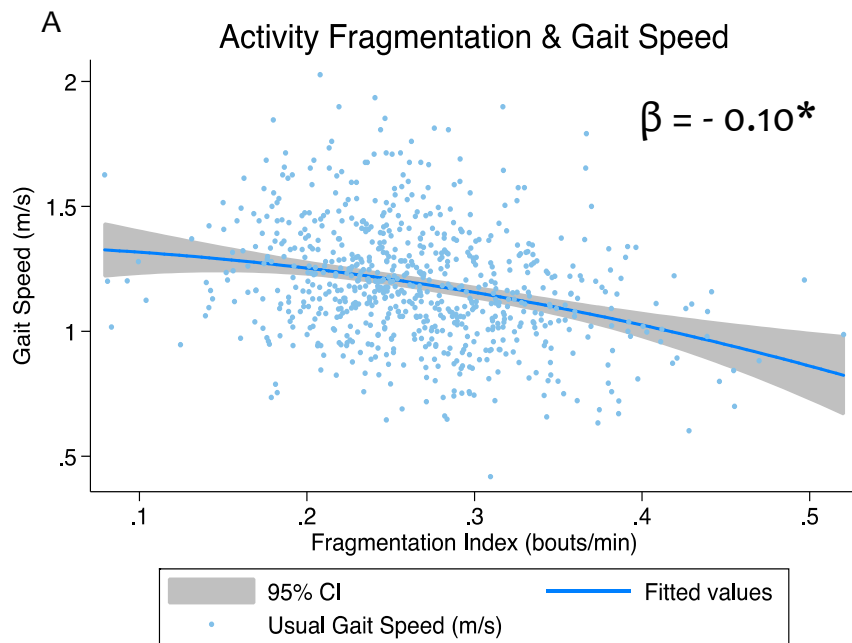
Lucia Tabacu<sup>1,\*</sup>, Mark Ledbetter<sup>2</sup> , Andrew Leroux<sup>3</sup>, Ciprian Crainiceanu<sup>4</sup> and Ekaterina Smirnova<sup>5</sup> 



**Figure 2. (A)** The t-statistic values of the combined model coefficients in each prediction horizon. Each line corresponds to a t-statistic coefficient value (y-axis) as a function of the horizon prediction model (x-axis). **(B)** Predictive importance of each variable in the combined model measured by the difference between the CV-AUC of the full combined model and the combined model without that variable across prediction horizons.



**Figure A1.** Multivariate models for one- to five-year all-cause mortality plotted as a function of the forward selection procedure. Accelerometry predictors are shown in red on the horizontal axis. NHANES Pooled Cohorts Study, United States, 2003–2006.





# Association of Total Daily Physical Activity and Fragmented Physical Activity With Mortality in Older Adults

Amal A. Wanigatunga, PhD, MPH; Junrui Di, PhD; Vadim Zipunnikov, PhD; Jacek K. Urbanek, PhD; Pei-Lun Kuo, MD, MPH; Eleanor M. Simonsick, PhD; Luigi Ferrucci, MD, PhD; Jennifer A. Schrack, PhD

Table 3. Hazard Ratios for Total Activity, Activity Fragmentation, and Time Spent in Various Bout Lengths<sup>a</sup>

Variable	Hazard Ratio (95% CI)		
	Model 1 <sup>b</sup>	Model 2 <sup>c</sup>	Model 3 <sup>d</sup>
Total physical activity, h/d	0.88 (0.74-1.03)	0.86 (0.72-1.03)	0.87 (0.73-1.03)
Activity fragmentation <sup>e</sup>	1.60 (1.13-2.26)	1.74 (1.19-2.54)	1.49 (1.02-2.19)
Activity spent in bouts, % <sup>f</sup>			
<5 min	1.35 (1.09-1.66)	1.40 (1.12-1.76)	1.28 (1.01-1.61)
5-10 min	0.89 (0.54-1.49)	0.88 (0.51-1.49)	0.99 (0.58-1.69)
≥10 min	0.78 (0.64-0.96)	0.76 (0.61-0.985)	0.81 (0.65-1.01)



Junrui Di  
junruidi

Pinned

cdHOTS

Construct and decompose higher order tensorian statistics

R 2

actigraphy-profiles

A visualization tool for displaying minute-level actigraphy profiles

R

ActFrag

Activity Fragmentation Metrics Extracted From Minute Level Activity Data

R 2

ActCR

Extract Circadian Rhythms Metrics from Actigraphy Data

R 3



# Joint work with

- Jennifer Schrack, JHU
- Jacek Urbanek, JHU
- Amal Wanigatunga, JHU
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- Jiawei Bai, JHU
- Ciprian Crainiceanu, JHU
- Ellen Mowry, MD
- Kate Fitzgerald, MD
- Kathy Zackowski, PhD OT
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- Fan Tian, MS
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- Junrui Di, Pfizer
- Lei Huang, Google
- Daisy Zhu, Johns Hopkins University
- Yu Du, Eli Lilly
- Ximin Li, Johns Hopkins University
- Kathleen Merikangas, NIMH
- Haochang Shou, University of Pennsylvania
- Rahul Ghosal, JHU
- Vijay Varma, NIA
- Luigi Ferrucci, NIA
- Paul Rosenberg, Psychiatry
- Amber Watts, University of Kansas