

# Depression, HRV, and CAD Pilot Study

METRIC Research-in-Progress

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## Introduction

# Background I

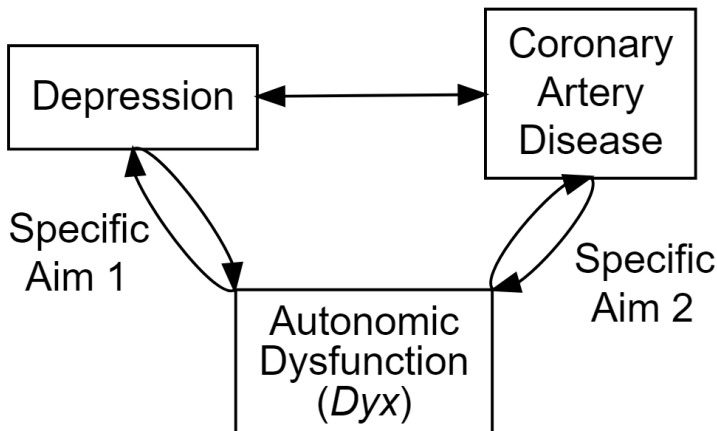


Figure 1: DAG

# Background II

- ▶ Up to 20% of patients with CAD have depression, and cardiovascular mortality is 3 times higher in patients with comorbid CAD and depression. No current interventions exist that decrease this risk.
- ▶ We have shown using the non-linear HRV metric, Dyx, is a powerful predictor of CAD, and can also be a useful marker for Depression. This is a pilot study examining the relationship between depression and CAD using HRV metrics

# Hypothesis

1. We hypothesize that elevated PHQ-9 scores will associate with abnormal HRV
2. We hypothesize that abnormal HRV will associate with obstructive CAD (stenosis  $> 70\%$ ), and that abnormal HRV will associate with a greater number of obstructed vessels in a dose-response manner

## Methods

# Methods

- ▶ Using the Emory Cardiovascular Biobank, we have an ongoing recruitment of a prospective cohort undergoing cardiac catheterization
- ▶ Clinical history and biomarkers are generated (including blood samples)
- ▶ Psychological questionnaires are performed, including depression by PHQ9
- ▶ ECG data is collected using the VivaLNK patch (6-24 hours of data per patient)

# Depression scoring

- ▶ Each patient is given a questionnaire, the PHQ9
- ▶ The scores are validated and suggest severity/category of depression
- ▶ Scores  $\geq 10$  are considered moderate to severe depression, and accepted cut-off



# Cardiac catheterization

- ▶ Every patient presents for cardiac catheterization to be enrolled
- ▶ Are either inpatient or outpatient
- ▶ Etiology: pre-op, heart transplant, UA, NSTEMI, STEMI, positive stress test
- ▶ Scored by angiographic severity indices - CASS and Gensini scores

# Heart rate variability collection I

- ▶ ECG data was collected using the VivaLNK patch
- ▶ this records data for up to 72 hours
- ▶ ECG was started the AM of LHC, and continued for several hours after event
- ▶ HRV was generated through signal processing in Matlab (PhysioNet Cardiovascular Signal Toolbox)
- ▶ Frequency domain was log-transformed
- ▶ HRV was blocked into averaged 1-hour segments for analysis
- ▶ *Dyx* was also generated, which summarizes a Poincare plot by the ratio of the kurtoses of the y-axis and x-axis

# Heart rate variability collection II

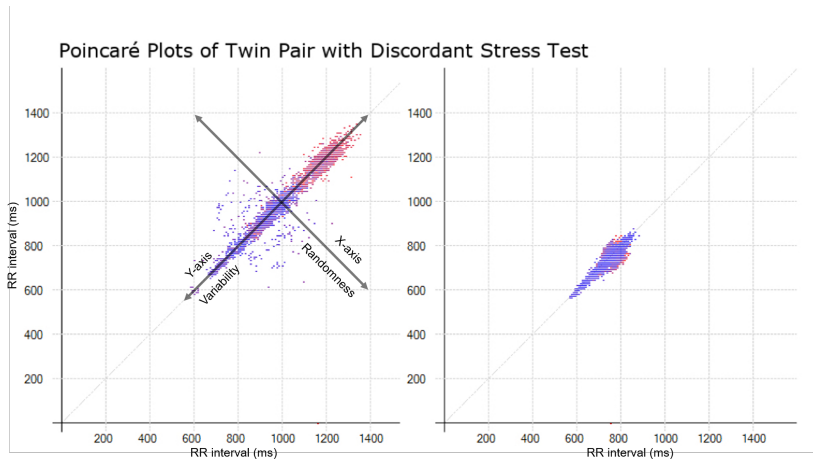


Figure 2: Poincare plot

## Results

# Demographic description

Table 1: Population

	[ALL] N=31	N
age	62.4 (13.2)	30
Gender: Male	28 (93.3%)	30
race:		30
African American Black	5 (16.7%)	
Asian	2 (6.67%)	
Caucasian White	23 (76.7%)	
Body Mass Index	30.4 (6.96)	30
setting:		31
Inpatient	11 (35.5%)	
Outpatient	20 (64.5%)	
PHQ > 9:		28
0	21 (75.0%)	
1	7 (25.0%)	
CASS-70 >= 1:		27
0	10 (37.0%)	
1	17 (63.0%)	

## Heart Rate Variability

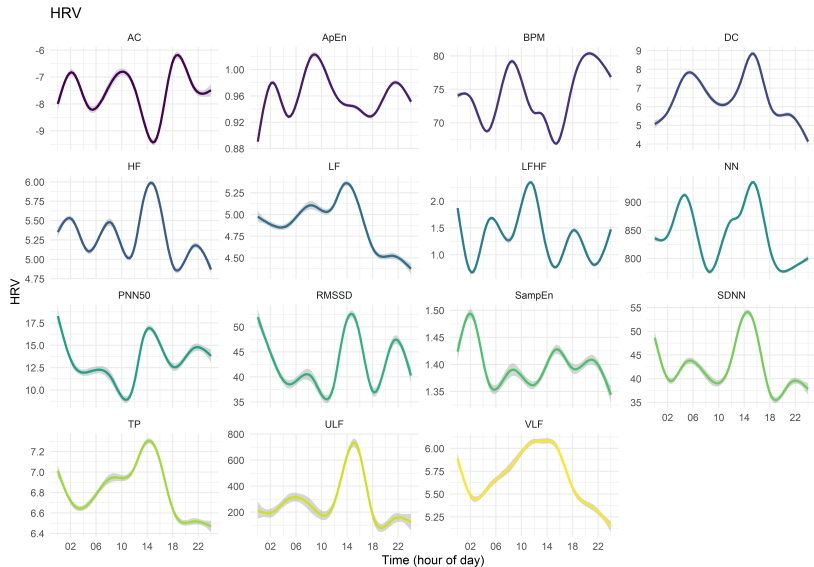
# Quality of HRV data

- ▶ Arrhythmia, artifact were excluded from analysis
- ▶ Approximately 25% of the HRV data was considered unusable and discarded

Table 2: HRV quality

	[ALL] N=28	N
Duration	12.9 (9.35)	28
PercentNotAnalyzed	26.8 (31.2)	28
PercentLowQualityWind	26.8 (31.2)	28

# Overview of HRV I





## Depression and HRV

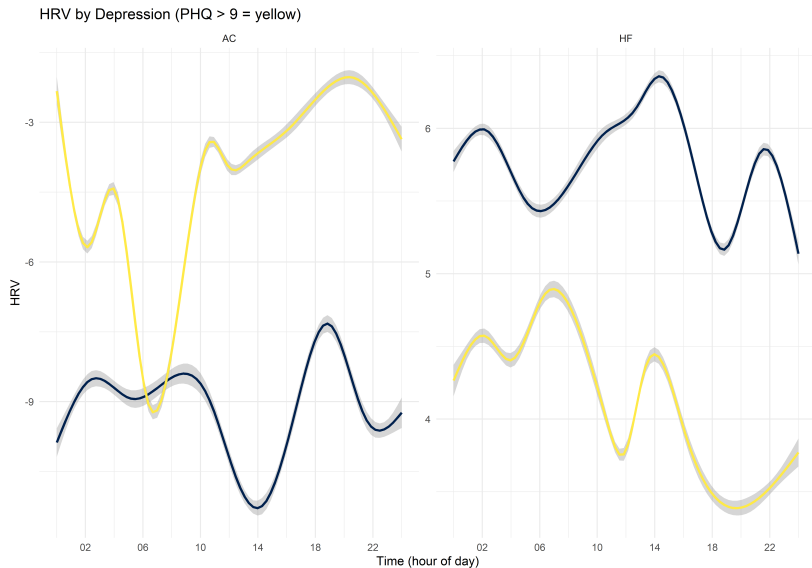
# HRV by Depressive Sx Burden Status

Table 3: HRV by Depressive Sx Burden

	PHQ $\leq$ 9 N=17	PHQ $>$ 9 N=6	p.overall
Mean HF (SD)	6.09 (1.41)	4.44 (1.11)	0.014
Mean LF (SD)	6.13 (1.24)	4.47 (1.49)	0.041
Mean VLF (SD)	6.63 (0.99)	5.47 (1.35)	0.093
Mean SDNN (SD)	55.3 (33.0)	27.0 (12.9)	0.008
Mean RMSSD (SD)	51.2 (46.9)	21.7 (12.4)	0.027
Mean PNN50 (SD)	15.2 (22.0)	3.12 (4.44)	0.045
Mean AC (SD)	-10.86 (8.20)	-4.17 (2.11)	0.006
Mean DC (SD)	9.34 (5.35)	4.74 (2.16)	0.008
Mean SampEn (SD)	1.56 (0.35)	1.39 (0.34)	0.323
Mean ApEn (SD)	0.91 (0.11)	1.03 (0.15)	0.109
Mean DYX (SD)	2.55 (0.75)	2.16 (0.83)	0.344

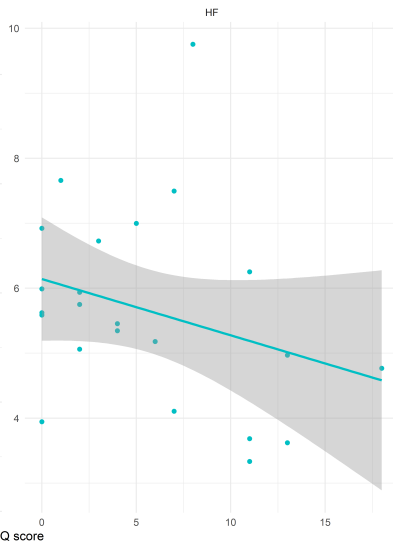
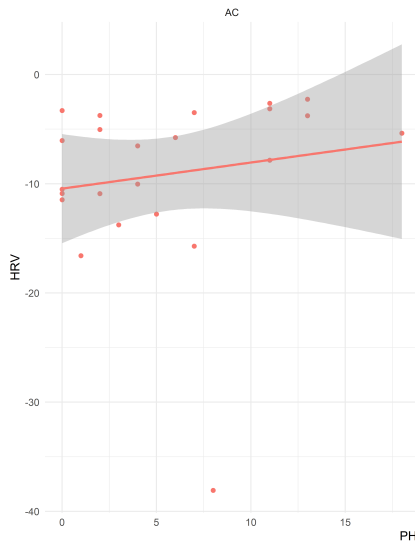
- First hour of recorded HRV was used (prior to catheterization)

# Visualizing Differences in HRV by Depression I



# Visualizing Differences in HRV by Depression II

First hour of HRV (before cath) and depression



# Regression Models of HRV and Depression

Table 4: First hour of HRV and depression

	<i>Dependent variable:</i>		
	PHQ > 9		
HF	−1.96** (−3.78, −0.14)		
LF		−1.07* (−2.26, 0.12)	
AC			0.91 (−0.18, 2.00)
Observations	22	22	22
Log Likelihood	−6.25	−7.91	−6.22
Akaike Inf. Crit.	20.50	23.80	20.40

*Note:*

\*  $p < 0.1$ ; \*\*  $p < 0.05$ ; \*\*\*  $p < 0.01$

## Coronary Artery Disease and HRV

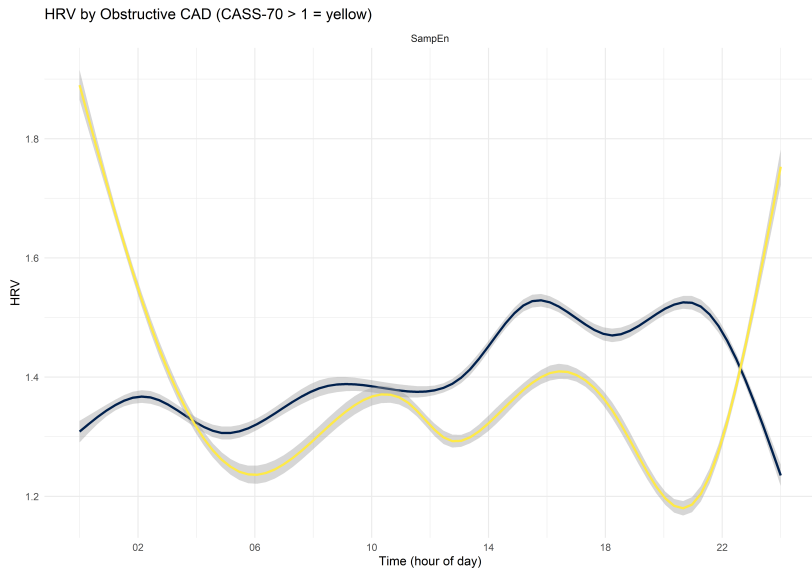
# HRV by Obstructive Coronary Artery Disease

Table 5: HRV by Obstructive CAD by CASS-70

	Nonobstructive N=8	Obstructive > 70% N=16	p.overall
Mean HF (SD)	5.79 (1.99)	5.95 (1.48)	0.840
Mean LF (SD)	5.42 (1.94)	6.10 (1.40)	0.395
Mean VLF (SD)	6.14 (1.47)	6.55 (1.21)	0.504
Mean SDNN (SD)	51.3 (45.2)	54.1 (30.2)	0.878
Mean RMSSD (SD)	55.7 (69.3)	46.9 (26.7)	0.738
Mean PNN50 (SD)	17.2 (30.3)	12.9 (13.2)	0.715
Mean AC (SD)	-10.48 (11.6)	-9.04 (4.93)	0.744
Mean DC (SD)	8.36 (6.85)	8.44 (4.49)	0.975
Mean SampEn (SD)	1.28 (0.24)	1.51 (0.34)	0.070
Mean ApEn (SD)	0.96 (0.13)	0.95 (0.12)	0.783
Mean DYX (SD)	2.31 (0.88)	2.53 (0.75)	0.550

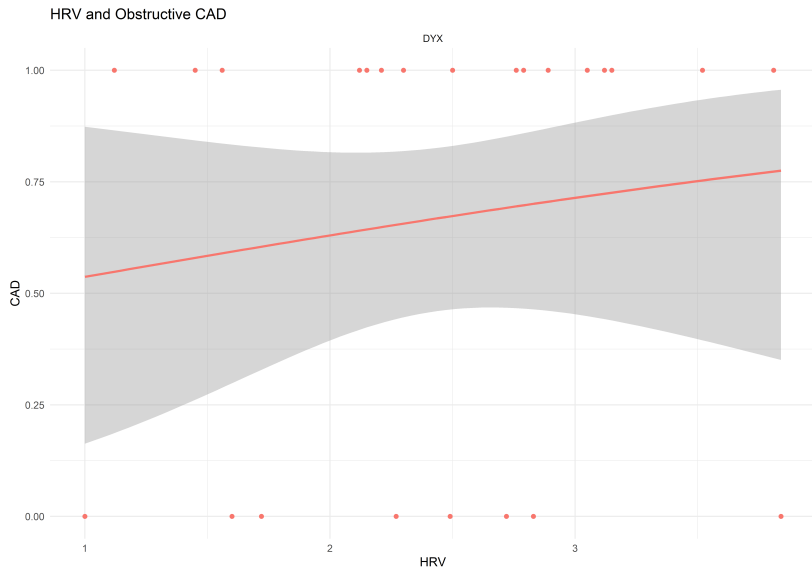
- First hour of recorded HRV was used (prior to catheterization)

# Visualizing Differences in HRV by CAD I





# Visualizing Differences in HRV by CAD II



## Discussion

# Interpretation of Findings

- ▶ Depression is associated with ANS dysfunction, particularly decreases in HF HRV
- ▶ CAD may have associations with ANS dysfunction that can be measured, but may require more complex analyses and adjustments
- ▶ HRV may serve as a marker for ANS dysfunction, and may be the mediating factor in patients with comorbid depression and CAD

# Future Directions and Limitations

- ▶ Larger sample size
- ▶ Identify times of catheterization to control for sedation
- ▶ Consider stratifying effects of medications (e.g. beta blockers)
- ▶ Subset of patients with first-time angina (versus known CAD)
- ▶ Cosinor/complex time series analyses
- ▶ Circadian / time-of-day adjustment
- ▶ Adjustment for risk factors