Depression, HRV, and CAD Pilot Study

METRIC Research-in-Progress

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Overview

Aims

1. Quantify how depression affects ANS function
2. Examine how ANS dysfunction can predict obstructive (versus microvascular) CAD

Background I

This is a pilot study examining the relationship between depression and CAD. 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.

Background II

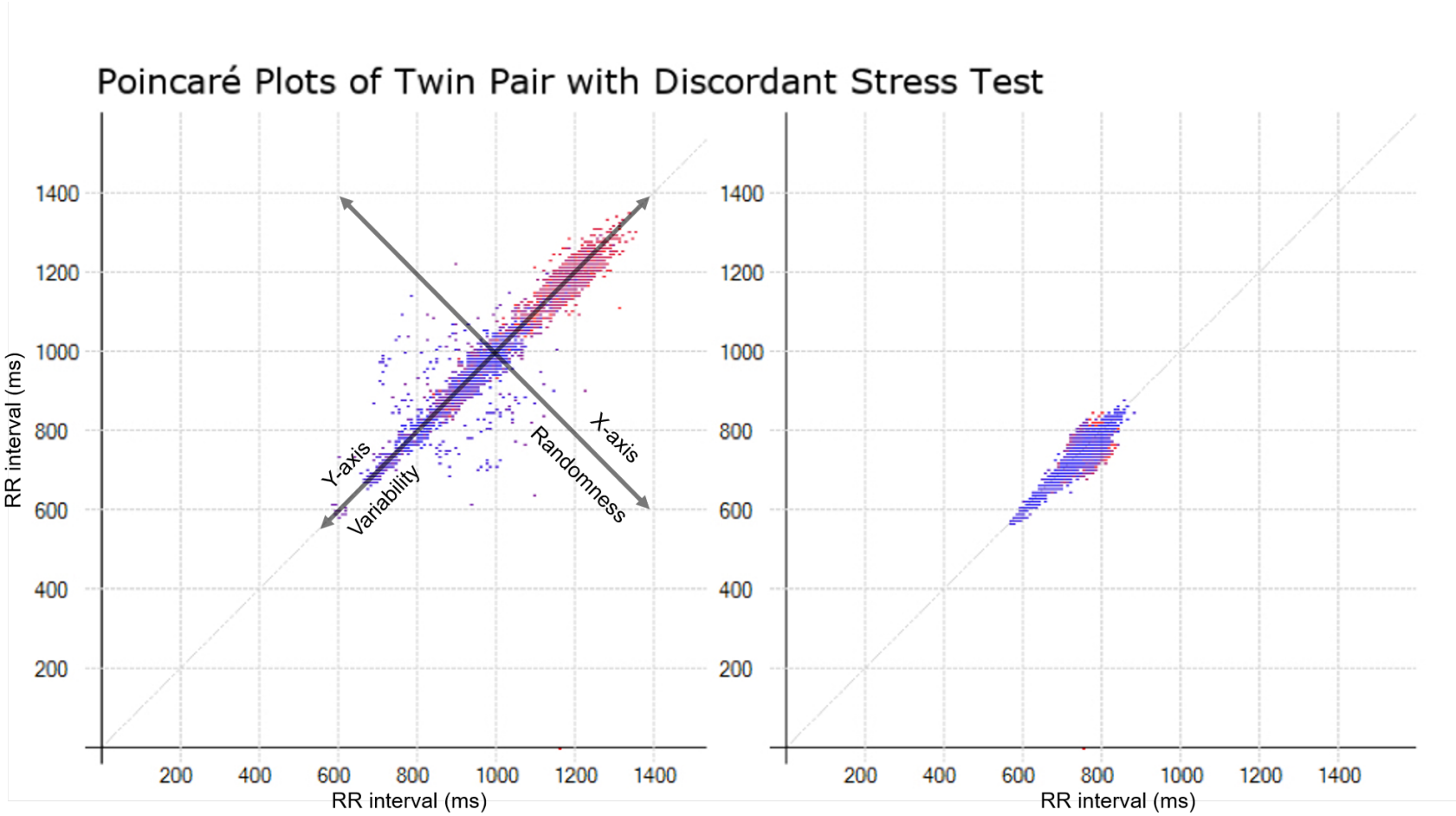


Figure 1: Poincare plot

Emory Cardiovascular Biobank

- Ongoing prospective cohort of patients undergoing cardiac catherization
- Includes clinical history and biomarkers
- Includes psychological questionnaires (including depression by PHQ9)
- Over 7000 patients enrolled overall
- Have enrolled 36 patients thus far

Description

Population

Demographic description

Table 1: Population

	[ALL] N=31	N
gend: Male	28 (93.3%)	30
race:		30
African American Black	5 (16.7%)	
Asian	2 (6.67%)	
Caucasian White	23 (76.7%)	
blbmi	30.4 (6.96)	30
setting:		31
Inpatient	11 (35.5%)	
Outpatient	20 (64.5%)	
age	62.4 (13.2)	30

Depression

Depression scoring

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

Depression table

Table 2: Depression scoring

	Low Depression N=21	High Depression N=7
gend: Male	20 (95.2%)	6 (100%)
race:		
African American Black	2 (9.52%)	2 (33.3%)
Asian	2 (9.52%)	0 (0.00%)
Caucasian White	17 (81.0%)	4 (66.7%)
adm_reason:		
Heart Failure	1 (5.00%)	0 (0.00%)
Heart Transplant	2 (10.0%)	1 (14.3%)
Non-ST Elevation Myocardial	2 (10.0%)	0 (0.00%)
Non-ST Elevation Myocardial,Unstable Angina	2 (10.0%)	1 (14.3%)
Other	1 (5.00%)	1 (14.3%)
Positive Stress Test	4 (20.0%)	1 (14.3%)
Positive Stress Test,Unstable Angina	3 (15.0%)	2 (28.6%)
PreOp Cardiac Clearance	4 (20.0%)	0 (0.00%)
Unstable Angina	1 (5.00%)	1 (14.3%)

Coronary artery disease

Cardiac catherization

- Every patient presents for cardiac catherization 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

CAD Severity

Table 3: CAD Severity Scores

	[ALL] N=27	N
cass50	1.15 (1.06)	27
cass70	1.00 (1.00)	27
gensini	52.6 (52.6)	27
stenosis:		27
0	7 (25.9%)	
1	20 (74.1%)	

Heart rate variability

Overview of HRV

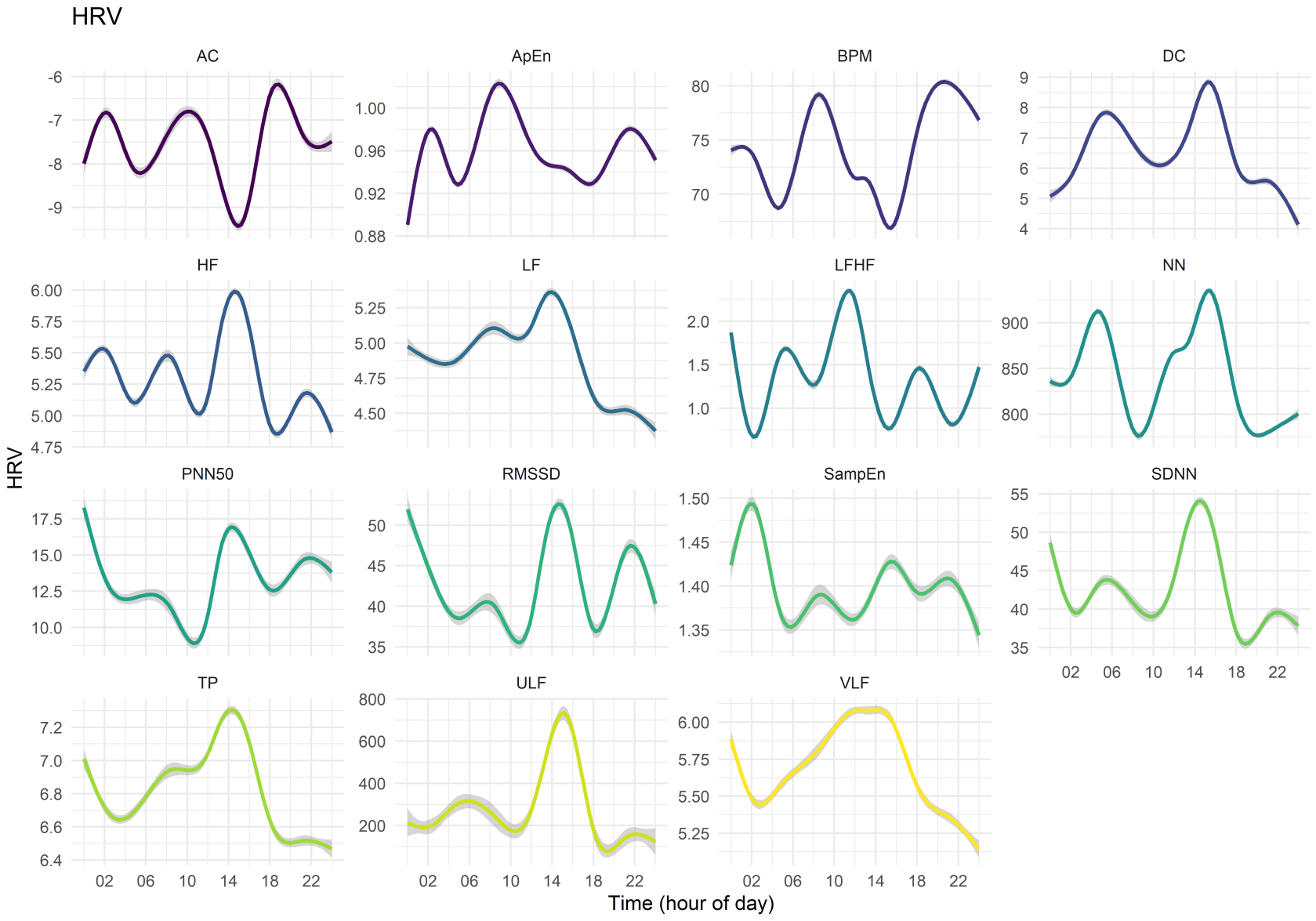
- ECG data was collected using the VivaLNK patch
- this records data for up to 72 hours
- ECG was started the AM of LHC, and continued for several hours after event
- HRV is generated through the Emory HRV Toolbox
- Frequency domain was log-transformed
- HRV was blocked into averaged 1-hour segments for analysis
- Approximately 25% of the HRV data was considered unusuable and discarded

Quality of HRV data

Table 4: 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 measures I



Aim 1: Relationship between Depression and ANS Dysfunction

Differences in population

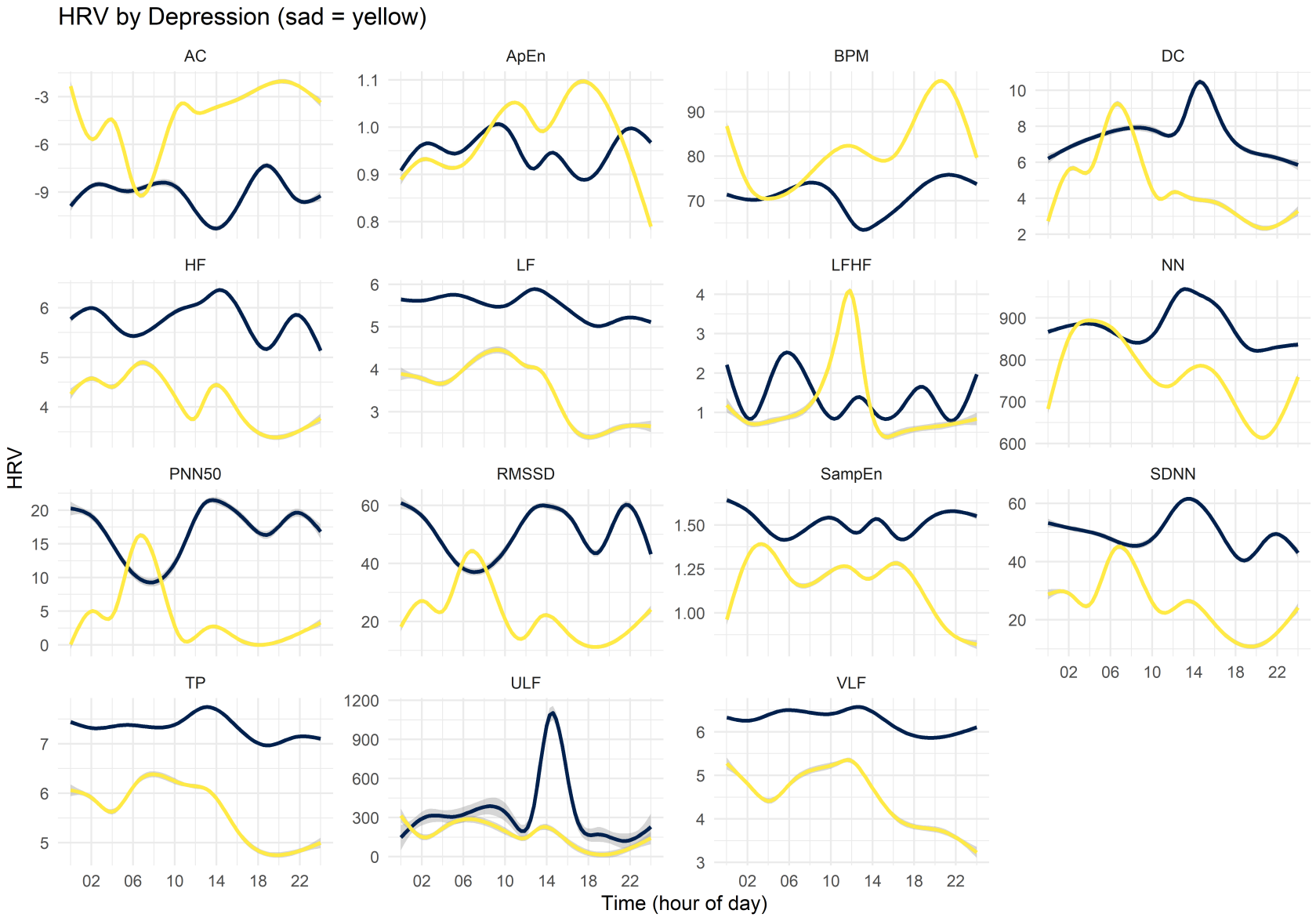
Table 5: HRV by Depressive Sx Burden

	0 N=17	1 N=6	p.overall
HF	6.09 (1.41)	4.44 (1.11)	0.014
LF	6.13 (1.24)	4.47 (1.49)	0.041
VLF	6.63 (0.99)	5.47 (1.35)	0.093
AC	-10.86 (8.20)	-4.17 (2.11)	0.006
DC	9.34 (5.35)	4.74 (2.16)	0.008
DYX	2.55 (0.75)	2.16 (0.83)	0.344
NN	926 (171)	794 (149)	0.103

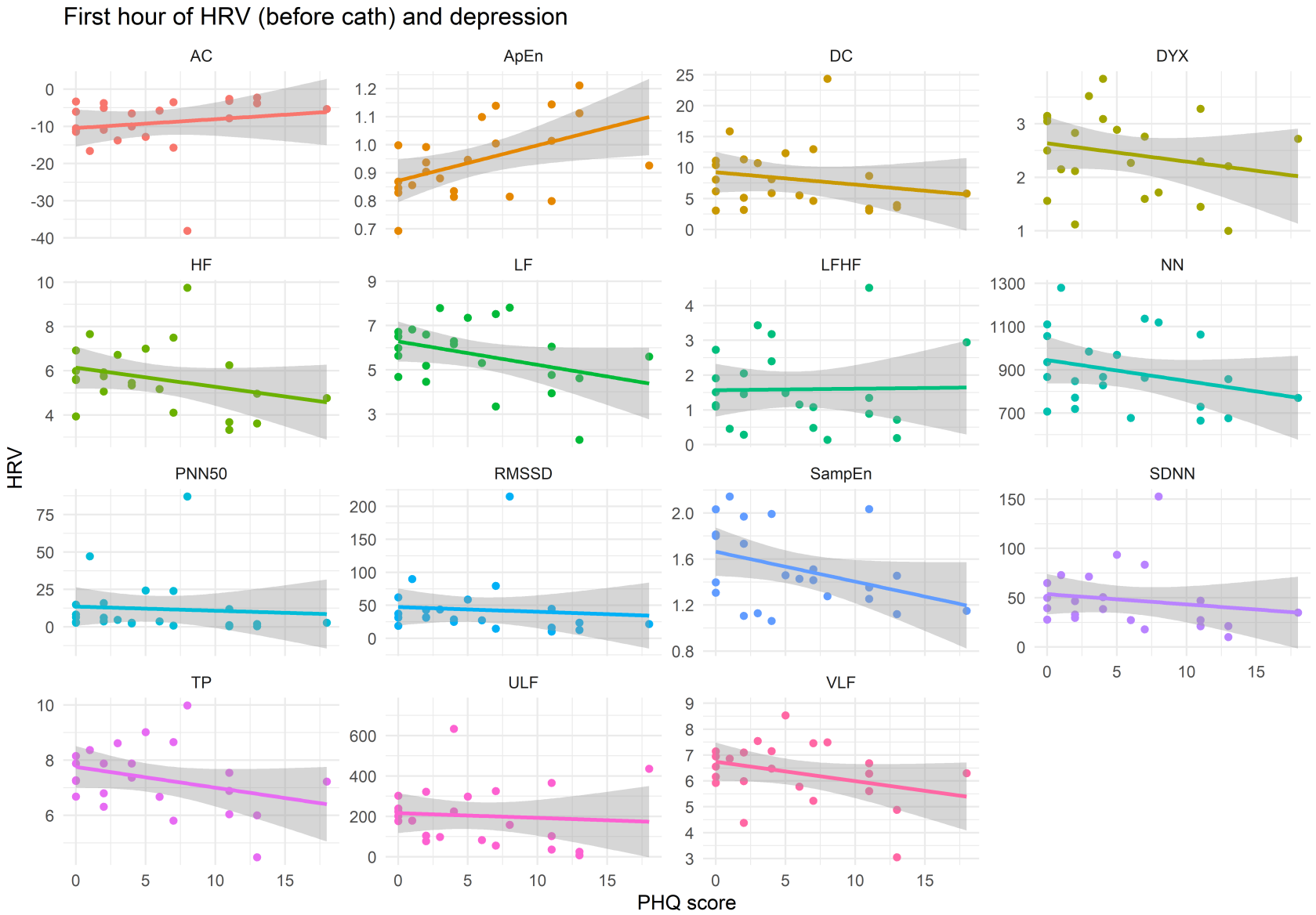
Hourly differences

- We expect to study the circadian differences in depression and HRV
- awaiting more complete data sets to perform cosinor analysis

Visualizing Differences in HRV by Depression



Measures of association I



Measures of association II

Table 6: First hour of HRV and depression

	Dependent variable:			
	sad			
	(1)	(2)	(3)	(4)
HF	−1.960**			
	(−3.780, −0.139)			
LF		−1.070*		
		(−2.260, 0.124)		
VLF			−1.100*	
			(−2.360, 0.157)	
SampEn				−3.840
				(−9.370, 1.690)
gend	10.900	13.500	13.900	15.000
	(−7,743.000, 7,765.000)	(−7,740.000, 7,767.000)	(−7,740.000, 7,768.000)	(−7,739.000, 7,769.000)
age	−0.021	−0.027	−0.053	−0.051
	(−0.129, 0.088)	(−0.128, 0.074)	(−0.150, 0.045)	(−0.153, 0.052)
Constant	−1.350	−7.530	−5.470	−8.030
	(−7,755.000, 7,753.000)	(−7,762.000, 7,746.000)	(−7,759.000, 7,749.000)	(−7,762.000, 7,746.000)
Observations	22	22	22	22
Log Likelihood	−6.250	−7.910	−8.290	−9.140
Akaike Inf. Crit.	20.500	23.800	24.600	26.300

Note: $^{*}p<0.1$; $^{**}p<0.05$; $^{***}p<0.01$

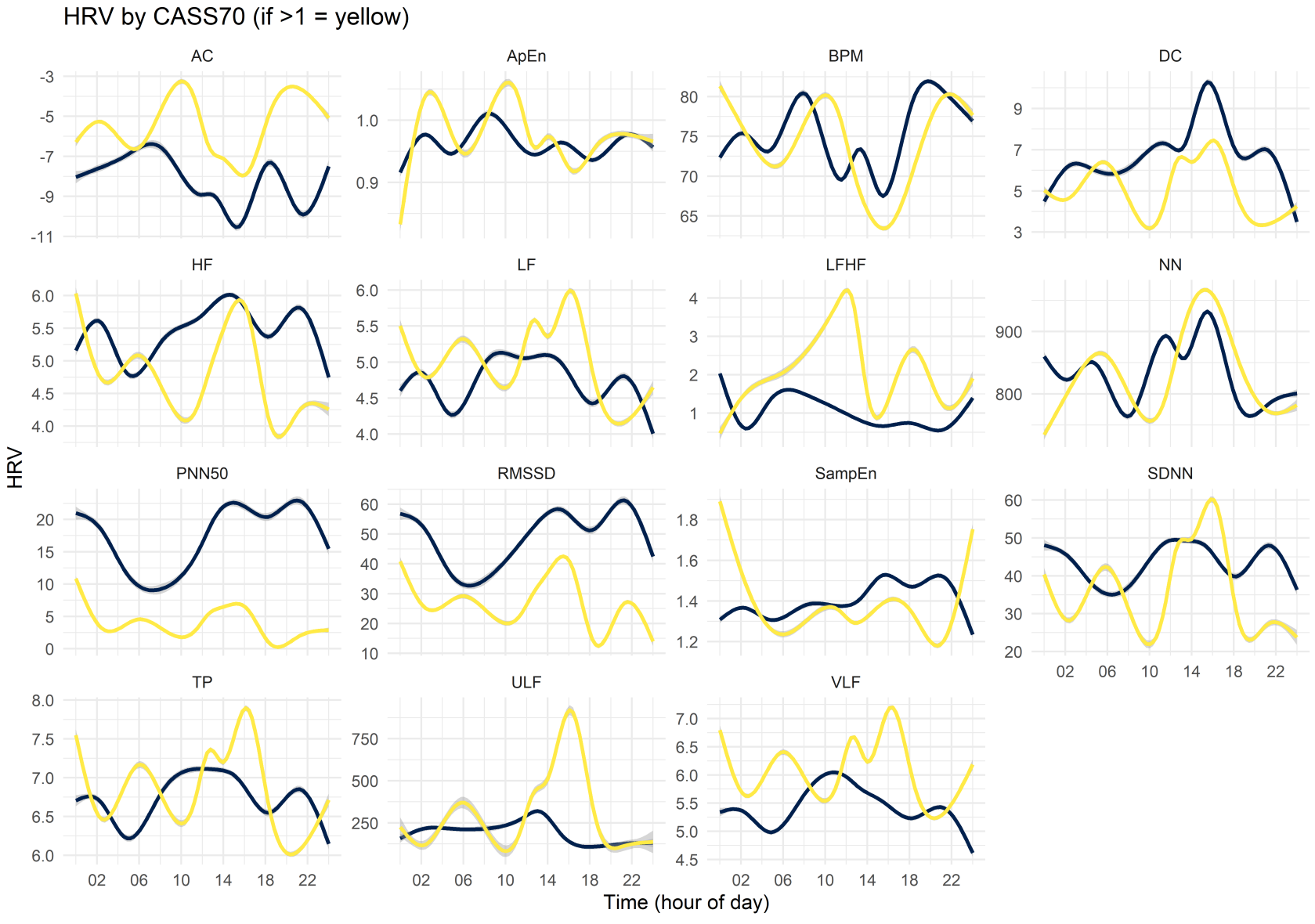
Aim 2: Relationship between CAD and ANS Dysfunction

Differences in population

Table 7: HRV by Obstructive CAD

	0 N=8	1 N=16	p.overall
LFHF	1.32 (1.25)	1.61 (1.13)	0.582
NN	808 (143)	942 (176)	0.062
SDNN	51.3 (45.2)	54.1 (30.2)	0.878
RMSSD	55.7 (69.3)	46.9 (26.7)	0.738
PNN50	17.2 (30.3)	12.9 (13.2)	0.715
AC	-10.48 (11.6)	-9.04 (4.93)	0.744
DC	8.36 (6.85)	8.44 (4.49)	0.975
SampEn	1.28 (0.24)	1.51 (0.34)	0.070
ApEn	0.96 (0.13)	0.95 (0.12)	0.783
DYX	2.31 (0.88)	2.53 (0.75)	0.550

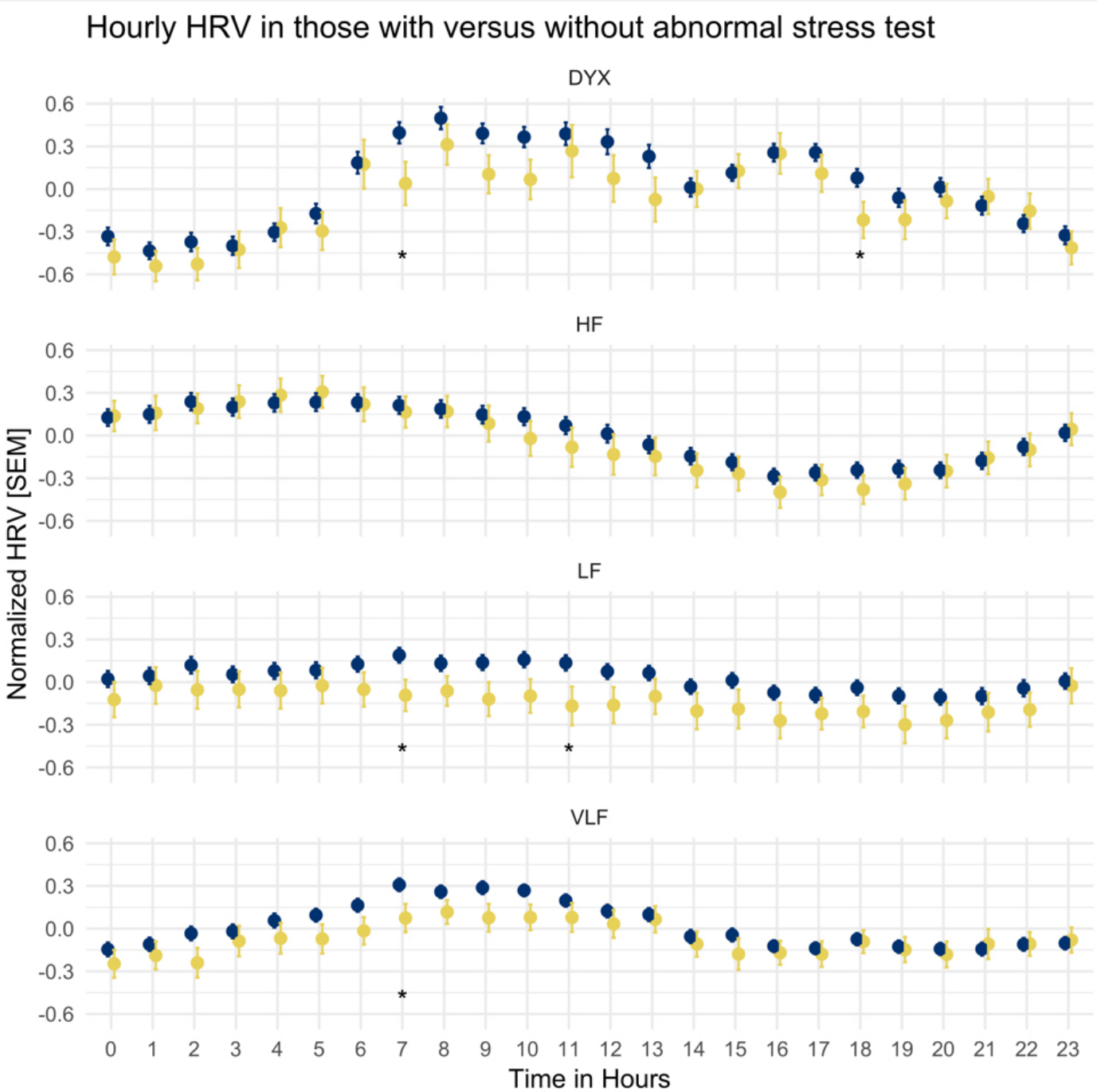
Visualizing Differences in HRV by CAD



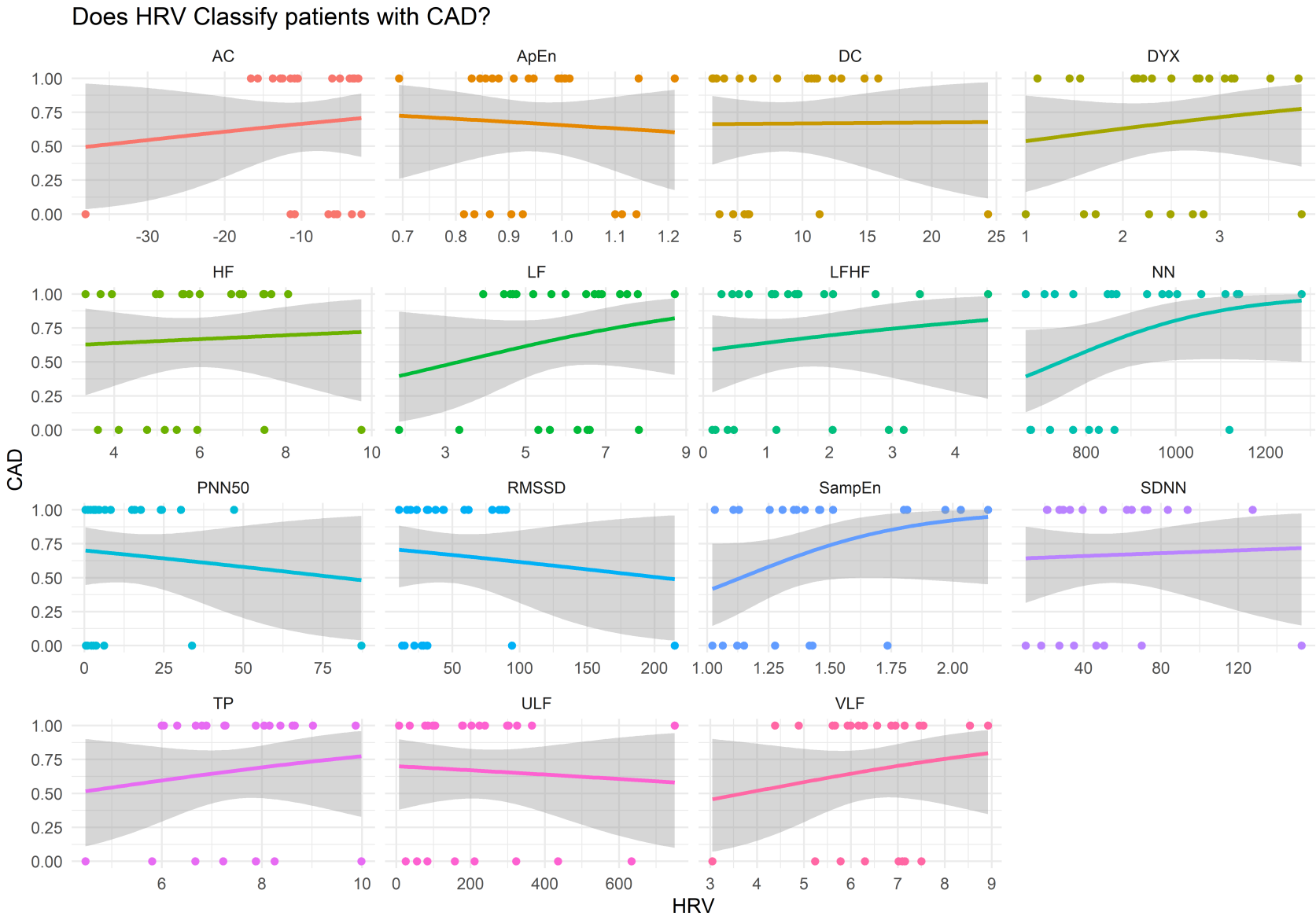
Hourly differences I

- We expect time-of-day to be an important factor based on prior research
- Early morning increase in sympathetic outflow "mimics" that of increased stress to identify at risk patients

Hourly differences II



Measuring association I



DYX exploration

```
##
##  Welch Two Sample t-test
##
## data:  DYX by cad
## t = -2, df = 19, p-value = 0.03
## alternative hypothesis: true difference in means is not equal
## 95 percent confidence interval:
##  -1.732 -0.103
## sample estimates:
## mean in group 0 mean in group 1
##            1.69            2.61
```

Future Directions and Limitations

Future Directions and Limitations

- Larger sample size
- Identify times of catherization 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