

# Depressive Symptom Dimensions and Cardiovascular Prognosis among Women with Suspected Myocardial Ischemia

A Report from the NHLBI-  
Sponsored Women's Ischemia  
Syndrome Evaluation (WISE)

Society of Behavioral Medicine, 30<sup>th</sup> Annual Meeting  
April 23, 2009  
Montreal, Quebec • Canada

Sarah E. Linke<sup>1</sup>, MS, Thomas Rutledge<sup>2,3</sup>, PhD,  
B. Delia Johnson<sup>4</sup>, PhD, Viola Vaccarino<sup>5</sup>,  
MD, PhD, Vera Bittner<sup>6</sup>, MD, MSPH, Carol E.  
Cornell<sup>7</sup>, PhD, Wafia Eteiba<sup>4</sup>, MD, David S.  
Sheps<sup>8,9</sup>, MD, David S. Krantz<sup>10</sup>, PhD,  
Susmita Parashar<sup>5</sup>, MD, MPH, MS, C. Noel  
Bailey Merz<sup>11</sup>, MD

<sup>1</sup>San Diego State University/University of California San Diego  
Joint Doctoral Program in Clinical Psychology, <sup>2</sup>University of  
California, San Diego, <sup>3</sup>VA San Diego Healthcare System,  
<sup>4</sup>University of Pittsburgh, PA, <sup>5</sup>Emory University, Atlanta, GA,  
<sup>6</sup>University of Alabama at Birmingham, AL, <sup>7</sup>University of  
Arkansas for Medical Sciences, Little Rock, AR <sup>8</sup>University of  
Florida, Gainesville, FL, <sup>9</sup>North Florida/South Georgia VA  
Healthcare System, <sup>10</sup>Uniformed Services University of the  
Health Sciences, <sup>11</sup>Cedars-Sinai Medical Center, Los Angeles, CA

This work was supported by contracts from the National Heart, Lung and Blood Institutes, nos. N01-HV-68161, N01-HV-68162, N01-HV-68163, N01-HV-68164, grants U0164829, U01 HL649141, U01 HL649241, a GCRC grant MO1-RR00425 from the National Center for Research Resources, and grants from the Gustavus and Louis Pfeiffer Research Foundation, Denville, New Jersey, The Women's Guild of Cedars-Sinai Medical Center, Los Angeles, California, The Ladies Hospital Aid Society of Western Pennsylvania, Pittsburgh, Pennsylvania, and The Edythe Broad Endowment for Women's Heart Research, Los Angeles, California.

# Introduction

- The co-existence of depression and cardiovascular disease (CVD) has been well-established.
  - Associated with worse CVD prognosis
- The exact mechanisms linking depression & CVD have yet to be established.
  - May each precede the other
  - May develop concurrently
  - Early signs of CVD may be mistaken for depressive symptoms, especially in women

# Introduction

- Beck Depression Inventory (BDI)
  - 21-item self-report measure of depressive symptoms
  - Frequently used within CVD populations
  - Assesses both cognitive/affective and somatic types of depressive symptoms
  - Somatic items (e.g., difficulty sleeping, fatigue) frequently overlap with symptoms of other medical illnesses
    - Depression severity can be difficult to assess with the BDI in medical populations

# Introduction

- de Jonge and colleagues' BDI study (2006)
- Factor analysis revealed three factors:
  - cognitive/affective
  - somatic/affective
  - appetitive
- Relationships with cardiovascular prognosis
  - Significant association between somatic/affective symptom scale score in unadjusted models
  - Only CV death related to somatic sx's in adjusted models
  - No significant associations with other two factors

# Introduction

- de Jonge et al's study (2006) was unique & compelling but had certain limitations that should be addressed in other studies
  - Post-MI, mixed-gender population
  - Factor analysis results different from others
  - Somatic/affective vs. cognitive/affective
    - Are these truly different constructs?
  - Statistical problems (e.g., multicollinearity & high inter-factor correlations)

# Purpose

The purpose of this study was two-fold:

- 3) To create composite factors (e.g., somatic, cognitive/affective) from the 21 BDI items via data reduction techniques
- 4) To subsequently examine and compare the differential associations of these identified depressive symptom types with cardiovascular-related events, including congestive heart failure (CHF), myocardial infarction (MI), stroke, and cardiovascular-related death

# Methods

- The Women's Ischemia Syndrome Evaluation (WISE) study was designed to improve the understanding and diagnosis of ischemic heart disease in women.
- Women undergoing angiography for suspected myocardial ischemia at one of four sites were enrolled in the WISE study.
  - 936 women enrolled in WISE
  - 550 participants included in this analysis

# Methods

- Extensive baseline evaluations included:
  - Demographic characteristics
  - Cardiovascular risk profiles
  - History of other known risk factors
  - Psychosocial measures (including the BDI)
  - Coronary angiography
- Clinical event tracking
  - Information gathered for median of 5.8 years through patient/family interviews & records

# Statistics

- Principal components analysis (PCA)
  - Promax rotation (an oblique method)
  - Factor scores calculated on the basis of unstandardized item factor loadings and transformed into standardized z-scores
  - Eigenvalues  $> 1$ , scree plot, # of complex items
- Cox regression
  - Multivariate hazard ratios
  - Time to first event (HF, MI, stroke, CV death)

Table 1. Baseline characteristics of the WISE subsample included in this analysis

<b>Baseline Characteristic</b>	<b>No. (%) of Total (N = 550)</b>
Age, mean (SD), y	58.4 (11.2)
CAD severity score, mean (SD)	13.3 (12.7)
≤ High school education	325 (59.1)
White	460 (83.6)
Cigarette smoking, current or former	288 (52.4)
Medical history	
Diabetes mellitus	119 (21.6)
Hypertension (n = 549)	314 (57.2)
Dyslipidemia (n = 519)	269 (51.8)

# Table 1. Baseline characteristics of the WISE subsample included in this analysis

Cardiovascular-related events or conditions	No. (%) of Total (N = 550)
No. of events or conditions	
Any	216 (39.3)
1	121 (22.0)
2	70 (12.7)
3	15 (2.7)
4 or 5	10 (1.8)
Types of events or conditions	
Congestive heart failure	44 (8.0)
Myocardial infarction	103 (18.7)
Coronary artery bypass graft surgery	26 (4.7)
Percutaneous coronary intervention	81 (14.7)
Cerebrovascular disease	50 (9.1)
Peripheral vascular disease	44 (8.0)

# Results

- Principal Components Analysis
  - KMO (.931) and Bartlett's test of sphericity ( $p < .001$ ) indicated adequate factor matrix for data reduction
  - Depending on criteria used, 2 or 3 factors emerged to form the optimal solution
  - Both models contained some items that loaded  $> .32$  on more than one factor (i.e., crossloading), making classification uncertain
  - Irritability item did not attain  $> .32$  loading on any factor in either model

	Factor from 3-Factor Principal Components Analysis (PCA)			Factor from 2-Factor PCA		Corresponding dimensions in previous studies' constructs	
	Cognitive/affective	Somatic/affective	Appetitive	Cognitive/affective	Somatic	de Jonge et al.	Beck & Steer
Sadness	.568			.579		Somatic/affective	Cognitive
Pessimism	.621			.644		Cognitive/affective	Cognitive
Sense of failure	.865			.851		Cognitive/affective	Cognitive
Dissatisfaction	.369	.480		.449	.391	Somatic/affective	Cognitive
Guilt	.764			.762		Cognitive/affective	Cognitive
Punishment	.769			.761		Cognitive/affective	Cognitive
Self-dislike	.744			.816		Cognitive/affective	Cognitive
Self-accusations	.813			.845		Cognitive/affective	Cognitive
Suicidal thoughts	.456			.511		Cognitive/affective	Cognitive
Crying	.453			.440		Somatic/affective	Cognitive
Irritability		.299			.313	Somatic/affective	Cognitive

	Factor from 3-Factor Principal Components Analysis (PCA)			Factor from 2-Factor PCA		Corresponding dimensions in previous studies' constructs	
	Cognitive/affective	Somatic/affective	Appetitive	Cognitive/affective	Somatic	de Jonge et al.	Beck & Steer
Social withdrawal	.413	.343		.474		Cognitive/affective	Cognitive
Indecisiveness	.360	.428		.448	.305	Somatic/affective	Cognitive
Negative body image		.519		.309	.301	Cognitive/affective	Somatic
Work difficulty		.808			.740	Somatic/affective	Somatic
Insomnia		.661			.687	Somatic/affective	Somatic
Fatigability		.883			.803	Somatic/affective	Somatic
Loss of appetite			.647		.466	Appetitive	Somatic
Weight loss			.764		.413	Appetitive	Somatic
Somatic preoccupation		.487			.389	Somatic/affective	Somatic
Decreased libido		.414			.499	Somatic/affective	Somatic

# Results

- Individual BDI items and sub-scale scores
  - Correlations between sub-scale scores (i.e., inter-factor correlations) were significant, as expected
    - Somatic/affective & cognitive/affective ( $r=.66$ )
    - Appetitive & somatic/affective symptoms ( $r=.26$ )
    - Appetitive & cognitive/affective symptoms ( $r=.23$ )
    - Somatic & cognitive/affective ( $r=.61$ )
  - Multicollinearity did not appear to pose a problem
    - VIF: 1.079-1.816
    - Tolerance: .551-.927
    - $\kappa$ : 2.243-5.305)

Table 4. Cox regression analyses demonstrating the relationships among depressive symptom types from the 3-factor and 2-factor models and cardiovascular prognosis.

Measure of Cardiovascular Prognosis	Symptom Dimension					
	Cognitive/Affective		Somatic/Affective		Appetitive	
	HR (95% CI)	P-Value	HR (95% CI)	P-Value	HR (95% CI)	P-Value
3-Factor Model						
Unadjusted multivariate analysis	.84 (.66-1.08)	.177	1.36 (1.06-1.74)	.015	1.47 (1.25-1.74)	<.001
Adjusted multivariate analysis	.89 (.70-1.14)	.359	1.35 (1.04-1.74)	.022	1.42 (1.21-1.68)	<.001
Ancillary adjusted multivariate analysis	.85 (.66-1.09)	.205	1.19 (.91-1.55)	.207	1.30 (1.10-1.55)	.003
2-Factor Model						
Unadjusted multivariate analysis	.79 (.62-1.02)	.068	1.71 (1.36-2.14)	<.001	-----	-----
Adjusted multivariate analysis	.87 (.68-1.11)	.258	1.63 (1.28-2.08)	<.001	-----	-----
Ancillary adjusted multivariate analysis	.81 (.64-1.03)	.089	1.39 (1.08-1.79)	.011	-----	-----

# Discussion

- Significant somatic and appetitive results persisted as predictors of clinical events in models adjusted for history of CVD events and conditions as well as CAD severity at baseline.
  - The predictive ability of somatic symptoms was not entirely attributable to increased somatic symptomatology due to more severe physical disease at baseline.
  - However, an overlap of somatic symptoms between depression and physical illness cannot be dismissed.

# Discussion

- Mechanisms by which depression may affect cardiovascular prognosis
  - Women reporting depressive symptoms at baseline may have subsequently engaged in negative health behaviors often associated with both depressed mood and the progression of CVD.
  - Alternatively, perhaps certain physiological correlates of depression (e.g., inflammation, ANS activity) contributed to the worse prognosis.
  - Somatic symptoms may be more closely related to physiological alterations associated with depression.
    - Somatic symptoms similar to vital exhaustion?

# Discussion

- Comparison with previous research (de Jonge et al, 2006)
  - Three of the BDI items that loaded on either the somatic/affective or cognitive/affective component in one sample loaded on the opposite component in the other sample
    - Unique population characteristics
    - Different disease type/severity
    - Gender differences

# Limitations

- Results may not extrapolate to other populations
- This sub-sample of subjects (550/936) may not have been representative of the entire WISE sample
- Self-reported cardiovascular-related events and conditions that occurred prior to baseline were not verified by medical records
- Depressive symptom severity only assessed at baseline
- Some may have altered their lifestyles or modified their risk factor profiles via medications and/or psychotherapy during follow-up
- Mechanisms underlying the differential association between cognitive/affective vs. somatic depressive symptoms not explored
- PCA is influenced by sample specific characteristics, making the stability of its factors rather precarious



Thank you!

Questions?

# Table 3. Beck Depression Inventory (BDI) total score and factor components

Variable	Total Scale Mean (SD)	Mean response to all items on scale (SD)	Mean (SD) % of Total BDI
Total BDI Score	10.4 (8.0)	.50 (.38)	100%
Cognitive/affective symptoms*	3.0 (4.1)	.30 (.41)	19.7 (20)
Somatic/affective symptoms*	6.7 (4.3)	.75 (.48)	72.5 (22)
Appetitive symptoms*	0.74 (1.2)	.37 (.59)	7.8 (14)
Cognitive/affective symptoms§	4.5 (5.4)	.35 (.41)	32.3 (24)
Somatic/affective symptoms§	5.9 (3.6)	.74 (.45)	67.7 (24)

\*Factors obtained from the three-factor principal components analysis (PCA)

§Factors obtained from the two-factor principal components analysis (PCA)

# Discussion

- Treatment implications: can treating depression decrease CVD risk?
  - Treatment trials have been largely discouraging (e.g., ENRICHD, SADHART, MIND-IT), but...
    - ENRICHD patients treated with CBT + anti-depressants had increased event-free survival
    - SADHART trend toward increased event-free survival among depressed post-MI patients treated with sertraline
    - Non-responders to mirtazapine in MIND-IT experienced worse prognosis compared to treatment responders and untreated controls