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# Depressive Symptom Dimensions and Cardiovascular Prognosis among Women with Suspected Myocardial Ischemia: A Report from the NHLBI-Sponsored WISE Study

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## Abstract

**Context:** Symptoms of depression and cardiovascular disease overlap substantially. Differentiating between dimensions of depressive symptoms may improve our understanding of the relationship between depression and physical health.

**Objective:** To compare symptom dimensions of depression as predictors of cardiovascular-related death and events among women with suspected myocardial ischemia.

**Design:** Cohort study of women with suspected myocardial ischemia who were evaluated at baseline for history of cardiovascular-related problems, depressive symptoms using the Beck Depression Inventory (BDI), and coronary artery disease severity via coronary angiogram. Principal components

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The first author takes full responsibility for the accuracy of the statistical results. All authors had access to the WISE data.

All authors have contributed to the development of this manuscript in important ways, including study design, data collection, participation in multiple internal drafts for editorial purposes, group discussion of findings, and data analyses. The paper has received approval for publication by the participating authors as well as the WISE P&P committee.

analyses (PCA) of the BDI items were conducted to examine differential cardiovascular prognosis according to symptom dimensions of depression.

**Setting:** The Women's Ischemia Syndrome Evaluation (WISE), a National Heart, Lung, and Blood Institute (NHLBI)–sponsored multi-center study assessing cardiovascular function using state-of-the-art techniques in women referred for coronary angiography to evaluate chest pain or suspected myocardial ischemia.

**Participants:** 550 women (mean age = 58.4 [11.2] years) enrolled in WISE and followed for a median of 5.8 years.

**Main Outcome Measures:** Cardiovascular-related mortality and events (stroke, myocardial infarction, and congestive heart failure).

**Results:** Using a three-factor structure from PCA, somatic/affective (hazards ratio [HR]=1.35, 95% confidence interval [CI]=1.04-1.74) and appetitive (HR=1.42, 95%CI=1.21-1.68) but not cognitive/affective (HR=.89, 95%CI=.70-1.14) symptoms predicted cardiovascular prognosis in adjusted multivariate Cox regression analysis. Using a two-factor structure from PCA, adjusted results indicated that somatic (HR=1.63, 95% CI=1.28-2.08) but not cognitive/affective (HR=.87, 95% CI=.68-1.11) symptoms predicted worse prognosis.

**Conclusions:** In a sample of women with suspected myocardial ischemia, somatic but not cognitive/affective depressive symptoms were associated with an increased risk of cardiovascular-related mortality and events. These results support the need to research dimensions of depression in CVD populations and have implications for understanding the connection between depression and CVD.

**Unstructured Abstract—**Differentiating between dimensions of depressive symptoms may improve our understanding of the relationship between depression and cardiovascular disease (CVD). This study examined depressive symptom dimensions as predictors of cardiovascular-related death and events among women undergoing coronary angiography to evaluate suspected myocardial ischemia (n=550; mean age=58.4 [11.2] years). Baseline evaluation included depressive symptom assessment using the Beck Depression Inventory (BDI) and coronary artery disease severity testing via coronary angiogram. Incidence of the women's cardiovascular-related mortality and events (stroke, myocardial infarction, and congestive heart failure) was tracked for a median of 5.8 years. Principal components analyses (PCA) of the 21 BDI items were conducted to derive depression symptom dimensions. Using a three-factor structure, somatic/affective (HR=1.35, 95% CI=1.04-1.74) and appetitive (HR=1.42, 95%CI=1.21-1.68) but not cognitive/affective (HR=.89, 95%CI=.70-1.14) symptoms predicted cardiovascular prognosis in adjusted multivariate Cox regression analysis. Using a two-factor structure, adjusted results indicated that somatic (HR=1.63, 95% CI=1.28-2.08) but not cognitive/affective (HR=.87, 95% CI=.68-1.11) symptoms predicted prognosis. Thus, in a sample of women with suspected myocardial ischemia, somatic but not cognitive/affective depressive symptoms were associated with worse cardiovascular prognosis. These results support the need to research depressive symptom dimensions in CVD populations and have implications for understanding the connection between depression and CVD.

The co-existence of depression and cardiovascular disease (CVD) has been well-established [1]. Although knowledge about the etiology, biology, and treatment of depression and CVD has increased in the past two decades [2], the exact mechanisms linking these two illnesses have yet to be established. Research has demonstrated that depression and CVD may each precede the other, that they may develop concurrently, and that early signs of CVD may be mistaken for depressive symptoms [2]. Even in the absence of clearly delineated mechanisms for their relationship, the co-existence of depression and CVD is associated with worse CVD prognosis [2, 3]. Disappointingly, treatment of depression in CVD patients has not been demonstrated to reduce subsequent clinical events (e.g., ENRICHD [4], SADHART [5], and MIND-IT [6] trials). However, since the treatments in these trials only partially alleviated depressive symptoms,

the conclusion cannot be definitively made that depression treatments do not improve CVD prognosis. Nevertheless, these unsuccessful studies underscore our incomplete understanding of the link between depression and CVD [7].

The Beck Depression Inventory (BDI, 8) is a 21-item self-report measure of depressive symptoms that is frequently used within CVD populations [9]. The BDI assesses both cognitive/affective and somatic depressive symptoms [10]. The BDI's somatic items (e.g., difficulty sleeping, fatigue), frequently overlap with symptoms experienced by individuals with a variety of medical illnesses, making depression severity difficult to assess with this measure in medical populations [11]. Nevertheless, the majority of researchers conducting depression studies on cardiovascular patients utilize the BDI rather than other self-report measures that contain primarily or exclusively cognitive/affective symptoms, such as the Hospital Anxiety and Depression Scale (HADS; 12).

Beck and colleagues recognized the potential for misdiagnoses among patients with certain medical conditions and designed a modified version of their original scale to assess depressive symptoms within medical populations: the BDI for Primary Care [13]. This modified version includes only the cognitive/affective items from the original scale, thus circumventing the potential problem of overlapping depressive and CVD symptoms and reducing the potential for misdiagnoses of depression. However, only one identified study [14] has used this modified scale (referred to as the BDI-Fast Scale) to examine the relationship between depressive symptoms and subsequent cardiovascular events in patients with CVD.

On the other hand, Simon and von Korff [15] concluded in a meta-analysis that somatic depression symptoms do not constitute a significantly greater proportion of overall depressive symptoms among medically ill patients than among generally physically healthy individuals – a finding that argues against the necessity of using depression measures that de-emphasize somatic symptoms when assessing CVD populations. Taken together, the literature on this topic remains inconclusive, and whether or not measures such as the BDI are biased by somatic symptom overlap remains unclear since this possibility has not been tested empirically.

Recently, de Jonge and colleagues [16] used factor analysis to examine the differential abilities of cognitive/affective and somatic depressive symptoms as assessed by the BDI to predict CVD prognosis within a mixed-gender post-myocardial infarction (post-MI) population. Their analysis revealed three factors, which they labeled cognitive/affective, somatic/affective, and appetitive, based on a combination of the labels used by Beck and Steer [10] in the BDI manual and Morley et al. [17] in a factor analysis of the BDI items in a chronic pain population. Neither of the factor structures from the two prior reports [10, 17] aligned precisely with those discovered in the two post-MI samples (which were subjected to cross-validation through multi-sample structural equation modeling) examined by de Jonge and colleagues (13). Results revealed a significant bivariate association between the somatic/affective symptom scale score and CVD prognosis, such that somatic/affective symptoms predicted a higher risk of events. The relationship between cognitive/affective symptoms and CVD prognosis was not statistically significant. Neither of the two factors remained significant in multivariate analyses with combined cardiovascular-related events and mortality as the endpoint. However, the somatic/affective factor's hazard score was only slightly reduced after covariate adjustment (from 1.39 to 1.30), and it continued to predict cardiovascular-related mortality. Appetitive symptoms, a factor comprised of only two BDI items (loss of appetite and weight loss) did not significantly predict CVD prognosis in any of the models. Moreover, at baseline, four indicators of poor physical health were significantly correlated with somatic/affective and appetitive symptoms, while only one was related to cognitive/affective symptoms [16]. Notably, the reporting of these analyses [16] have been called into question [18], particularly with regard to de Jonge et al.'s failure

to address issues that may impact the results' interpretability, such as multicollinearity and high inter-factor correlations.

Watkins et al. [19] examined cognitive and somatic symptoms of depression as assessed by the BDI in relation to medical comorbidities following acute MI among patients enrolled in the ENRICHD trial. The researchers separated the items according to their face content, creating a cognitive and a somatic factor. Results revealed that although both factors were positively and statistically significantly correlated with medical comorbidity, the relationship was stronger for somatic (r=.24) than for cognitive (r=.06) symptoms [19].

The purpose of the current study is two-fold: 1) to create composite factors (e.g., somatic, cognitive/affective) from the 21 BDI items via data reduction techniques in a sample comprised of women with suspected myocardial ischemia; and 2) 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, over a median of 5.8 years. In light of the previously summarized research conducted on this topic in similar cardiac populations, we hypothesized that somatic but not cognitive depressive symptoms would predict cardiovascular-related events in this sample.

## Methods

### Study Design

Women undergoing angiography for suspected myocardial ischemia at one of four sites (University of Alabama at Birmingham; University of Florida, Gainesville; University of Pittsburgh, Pittsburgh, PA; and Allegheny General Hospital, Pittsburgh, PA) were enrolled in the Women's Ischemia Syndrome Evaluation (WISE) study. The WISE study was designed to improve the understanding and diagnosis of ischemic heart disease in women. Exclusion criteria included current pregnancy, cardiomyopathy, recent myocardial infarction or revascularization procedure (percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG]), a history of congenital heart disease, language barrier preventing questionnaire completion, and an inability to provide consent, among others. The complete design and methodology of the WISE study are described elsewhere [20]. In short, each woman's demographic characteristics, cardiovascular risk profile, and history of other known risk factors were gathered in an extensive baseline evaluation. Race was determined via participants' self-reported selection from a list of options created by the research team, including an “other” option, in order to assess whether cardiovascular-related health differences exist among women from various racial backgrounds. To enable the assessment of psychosocial characteristics that may be related to cardiovascular outcomes, the women completed a battery of psychosocial questionnaires, including the BDI [8] to assess depressive symptoms. All participants were queried about their history of certain cardiovascular-related events and conditions, including CHF, PCI, CABG, MI, cerebrovascular disease (e.g., stroke, transient ischemic attack), peripheral vascular disease (e.g., claudication, peripheral vascular surgery), as well as cardiovascular risk factors (e.g., diabetes, hypertension, dyslipidemia). The WISE Angiographic Core Laboratory, which was blinded to all other subject data, analyzed coronary angiograms using a quantitative method described in detail elsewhere [21]. The angiogram results were used to assign each participant a continuous coronary artery disease severity score based on a modified Gensini index [22].

All participants provided written informed consent that was approved by the institutional review board (IRB) at their local WISE clinical site. Although 936 women were enrolled in WISE, this study examined a sub-sample of 550 women for whom data were available on all variables included in the analyses. Most of the missing data points (269[29%]) were due to the

fact that psychosocial questionnaires, including the BDI, were not added to the WISE protocol until the study's second year. The remaining missing data points (117[12.5%]) were due to missing follow-up or covariate data and/or incomplete BDI scores (i.e., skipping BDI items).

## Clinical event tracking

Women were contacted via telephone and/or mail six weeks post-baseline and annually thereafter for a median of 5.8 years to track their subsequent adverse cardiovascular events (HF, stroke, and MI) and mortality, together referred to as clinical events or cardiovascular prognosis. The names of treating physicians, clinical centers, and hospitals were collected and subsequently contacted for relevant documentation and test results of reported clinical events. Death certificates were obtained in order to confirm deaths reported by significant others and were reviewed by an independent study physician blinded to the patient's CVD status or other study data. For purposes of the current study, deaths were counted as clinical events if they were classified as definitely or probably due to cardiovascular reasons.

## Statistics

Principal components analysis (PCA) was conducted using the WISE sample (n = 550) in order to reduce the 21 individual BDI items into fewer factors/components while retaining original item information. PCA was selected rather than factor analysis for two primary reasons: 1) its ultimate goal is to reduce data into components useful for other purposes (in this case to predict cardiovascular prognosis according to aggregate types of depressive symptoms rather than individual depressive symptoms), as opposed to the primary goal of factor analysis, which is to reveal underlying variables that cause manifest variables to covary [23]; and 2) its superior ability to remedy multicollinearity among factors, should they exist [23, 24].

Promax rotation was selected since it is an oblique method, which allows factors to correlate with each other (as BDI factors are expected to do), as opposed to an orthogonal method, which artificially forces factors to be uncorrelated [23, 25]. Factor scores were calculated on the basis of unstandardized item factor loadings and transformed into standardized z-scores (using the Anderson-Rubin method) to increase their interpretability.

PCA was first conducted to examine a solution with all factors with eigenvalues > 1. A scree plot of eigenvalues and the number of complex items were used as additional criteria for selecting the best overall solution [26]. Although three factors emerged in this initial analysis, a combination of the aforementioned criteria indicated that either two or three factors may form the optimal solution of the analysis. Subsequently, a PCA specified to extract only two factors was completed for two purposes: 1) to permit a comparison between two data-driven solutions, since the original PCA's results were inconclusive in terms of whether a two- or three-factor solution was optimal; and 2) to examine a solution comparable to the traditional two-factor structure of the BDI (i.e., cognitive vs. somatic symptoms).

Bivariate correlations between all pairs of factors in each solution were conducted to assess inter-factor correlations. Three diagnostic tests for multicollinearity – variance inflation factor (VIF), tolerance, and condition number or index (κ) – [24] were examined within linear regression analyses in which raw factor scores predicted time to first event after baseline. Subsequently, multivariate hazard ratios and 95 percent confidence intervals (CI) were computed using Cox regression in order to examine differences in time to first event among the women according to standardized factor scores. Angiographic severity scores were included as a covariate in adjusted multivariate models in order to control for baseline CAD severity. An additional covariate included in the adjusted multivariate models, history of prior CVD, was determined by adding the total number of cardiovascular-related events or conditions (PCI, CABG, CHF, MI, cerebrovascular disease, peripheral vascular disease) each

woman had reportedly previously experienced. Four additional covariates (education, race, history of diabetes, history of smoking) were included in ancillary adjusted multivariate models that were conducted to further scrutinize the relationship between depression symptom types and cardiovascular outcomes. These four covariates were selected from a larger pool of CVD risk factors based on their sustained individual prediction of cardiovascular outcomes after depression dimension factor scores, angiographic severity scores, and history of prior CVD were included in the model. Analyses were conducted using SPSS Version 11.5, and the significance criterion was set at $p < .05$.

## Results

Baseline characteristics of the women are listed in Table 1. Notably, 39% of the women reported a history of at least one cardiovascular-related event or condition before baseline evaluation, including approximately 17% who had previously experienced multiple events or conditions. Coronary angiography severity scores were positively skewed, indicating a low amount of coronary obstruction within this population. Approximately half of the women reported that they were current or former smokers. A large majority of the women (83.6%) identified themselves as white, and 41% reported that they had obtained at least some higher education after achieving a high school diploma or equivalent.

### Principal Components Analysis

KMO (.931) and Bartlett's test of sphericity ($p<.001$) indicated that the factor matrix was adequate for data reduction. Both models contained some items that loaded >.32 on more than one factor (i.e., crossloading), making the classification of these items uncertain [23]. Similarly, the irritability item did not attain this minimum >.32 loading on any factor in either model, indicating that it may not contribute to and/or belong with any of the identified factors [23].

The three-factor solution's aptness was questionable due to the third factor's inclusion of only two items, which may render it unstable and weak, as at least three items are generally advised to comprise each factor [23]. The item loadings for these three factors are presented in Table 2. Based on the face content of the items that loaded on each of them, the three factors were conceptualized as 1) cognitive/affective, 2) somatic/affective, and 3) appetitive.

The second PCA, constrained to two factors, appeared to produce an adequate solution. Both factors had eigenvalues > 1, the scree plot supported a two-factor solution, and both factors were comprised of multiple, strongly-loading items. Based on the face content of the items that loaded on these factors, they were conceptualized as 1) cognitive/affective and 2) somatic. All of the affective items that had higher loading values on the somatic/affective component of the three-factor solution loaded more strongly on the cognitive/affective component of the two-factor solution, except for the irritability item, which loaded weakly (.313) on the somatic factor. In addition, the two appetitive items (loss of appetite and weight loss) from the three-factor solution loaded on the somatic component of the two-factor solution.

### Analysis of Individual BDI Items and Sub-scale Scores

Means of the total BDI score and sub-scale scores for each of the factor structures are listed in Table 3. Also listed in Table 3 are the percentages of the total BDI score attributable to each factor, as well as the mean score on each item (possible range: 0-3) within each factor. Somatic/affective symptoms comprised nearly three-fourths of the total BDI score in the three-factor structure, and somatic symptoms comprised more than two-thirds of the total score in the two-factor structure. All items were positively skewed, with all but two item means < 1.

As expected, correlations among sub-scale scores (i.e., inter-factor correlations) were large and significant. The strong correlation between the somatic/affective and cognitive/affective sub-scale scores in the three-factor solution (r=.66) was reduced in the two-factor solution (r=.61) but remained large nonetheless. The correlations between appetitive and somatic/affective symptoms (r=.26) and between appetitive and cognitive/affective symptoms (r=.23) in the three-factor solution were much lower but still statistically significant. Despite these large inter-factor correlations, multicollinearity did not appear to pose a problem, as the diagnostic test values were all well within acceptable limits [24] (VIF: 1.079-1.816; tolerance: .551-.927; κ: 2.243-5.305).

### Relationship between Factor Structure and Cardiovascular Prognosis

Altogether, 91 (16.5%) of the women experienced at least one adverse cardiovascular-related outcome during the mean 5.8-year follow-up period, for a total of 107 independent events, including those experienced by women who had multiple events. Among these events were 31 cases of CHF, 19 cases of MI, 28 cases of stroke, and 29 cardiovascular-related deaths. An additional 19 women died from causes not determined to be cardiovascular-related. Results from unadjusted and adjusted multivariate Cox regression analyses in which the three factors from the initial PCA or two from the second PCA were included as the independent variables predicting cardiovascular events are presented in Tables 4 and 5, respectively. None of the cognitive/affective factors was significant in any of the models. However, the somatic/affective and appetitive components of the three-factor model were significant predictors of events in the unadjusted and adjusted multivariate analyses. Similarly, the somatic factor of the two-factor structure remained significant in both the unadjusted and adjusted multivariate models. In identical models with only 1) cardiovascular-related death or 2) non-cardiovascular-related death as the outcome of interest, none of the factor components remained significant after adjustments.

### Ancillary Analyses

Results from the ancillary adjusted multivariate Cox regression analyses in which four additional variables were included as covariates are also presented in Tables 4 and 5. The previously significant relationship between the somatic/affective component of the three-factor model and cardiovascular prognosis failed to remain statistically significant after controlling for the four additional covariates. None of the predictive values of the other factors from either of the models decreased appreciably in these ancillary analyses.

## Discussion

In a sample of 550 women with suspected myocardial ischemia, symptom dimensions of depression measured by the BDI and determined through PCA were examined in relation to cardiovascular prognosis over 5.8 years of follow-up. Results indicated that somatic/affective and appetitive but not cognitive/affective symptoms of depression significantly predicted cardiovascular events in a three-factor model. Similarly, somatic but not cognitive/affective symptoms significantly predicted cardiovascular events in a two-factor model. These findings persisted in models adjusted for history of CVD events and conditions as well as CAD severity at baseline. Thus, the predictive ability of somatic symptoms was not entirely attributable to increased somatic symptomotology due to more severe physical disease at baseline, although an overlap of somatic symptoms between depression and physical illness cannot be dismissed.

### Mechanisms

Results from this study have implications for the mechanisms by which depression may affect cardiovascular prognosis. Individuals reporting depressive symptoms at baseline, when their CVD symptoms were acute, may have subsequently engaged in negative health behaviors often

associated with both depressed mood and the progression of CVD, such as smoking and physical inactivity. Alternatively, perhaps certain physiological correlates of depression (e.g., inflammation, ANS activity) contributed to the worse prognosis [27]. Likewise, somatic symptoms may be more closely related to the physiological alterations associated with depression; indeed, somatic symptoms are reminiscent of the vital exhaustion concept [28]. These hypotheses differ from the idea that somatic depressive symptoms may simply be physical manifestations of more severe CVD but do not negate the somatic-CVD link. Indeed, the relationship between somatic/affective depressive symptoms and cardiovascular prognosis remained after controlling for CAD severity score and history of CVD. However, since many factors play prognostic roles in CVD outcomes, our ability to characterize baseline disease severity was limited. Moreover, the greater prevalence of somatic than cognitive/affective symptoms in this population should also be noted, as somatic symptoms had greater potential for statistical relationships with cardiovascular prognosis.

### Treatment implications

Differentiating between cognitive and somatic symptoms of depression may also have important treatment implications. A question that has been posed many times but continues to emerge is whether treating depression within the context of CVD can improve future physical health outcomes in addition to allaying depressive symptoms. Although treatment trials have been largely discouraging [4-6], hope still remains that treating depression will increase event-free survival. Indeed, a secondary analysis of patients in the ENRICHD trial who were treated with anti-depressants in addition to CBT indicated that this combination treatment was associated with increased event-free survival, despite a lack of relatively greater improvement in BDI scores over time [29]. Similarly, results from the SADHART trial [30] showed a trend toward increased event-free survival among depressed post-MI patients treated with sertraline. Moreover, non-responders to mirtazapine in MIND-IT experienced worse prognosis compared to treatment responders and untreated controls [31]. However, the fact that these three studies' primary results showed no effect of depression treatment on cardiovascular prognosis [4-6] must be emphasized.

The precise mechanisms underlying the effectiveness of anti-depressants are unknown. As suggested by the ENRICHD writing group [4], these results may indicate that anti-depressants improve CVD prognosis through mechanisms not mediated by decreased depressive symptoms. Previous observational research also demonstrated a reduced risk for MI associated with antidepressants, particularly SSRIs [32]. These results may reflect the inhibitory effects of SSRIs on platelets [33] or combinations of other effects. Perhaps other types of depression treatments should be more thoroughly examined in this context. For example, recent evidence demonstrates that exercise is as efficacious at alleviating depressive symptoms as antidepressants [34] and also improves clinical outcomes in CHD patients [35].

One potential criticism on this topic is that the small effects of minimal reductions in depressive symptoms seen in treatment studies (1-4% of variance) could not realistically be expected to translate into end results related to cardiovascular prognosis. However, minimal to modest improvements in other risk factors for worse cardiovascular prognosis (e.g., overweight/obesity, inactivity, hyperlipidemia, hypertension) are often associated with improved prognosis [36, 37]. The null primary findings of studies on the effect of depression treatment on cardiovascular prognosis [4-6] underscore our currently incomplete understanding of the depression/CVD link.

### Comparison with previous research

We attempted to closely duplicate the methods employed by de Jonge and colleagues [16] in order to facilitate an accurate comparison of the two studies' results. Our ability to generally

support the previous findings strengthens the literature on this topic. However, in the process of reproducing their methodology, we sacrificed a certain degree of quality control, particularly with regards to omitting certain covariates in the primary multivariate models. Therefore, we conducted ancillary adjusted multivariate analyses, controlling for four additional variables that appeared to statistically influence the relationship between depression dimensions and cardiovascular outcomes. The inclusion of these covariates resulted in a diminished relationship between somatic/affective symptoms of depression (from the three-factor model) and cardiovascular risk that was no longer statistically significant. However, the relationships between cardiovascular risk and both appetitive (from the three-factor model) and somatic (from the two-factor model) symptoms of depression remained significant after adjusting for these four additional covariates.

Many items loaded strongly or even nearly equally well on more than one dimension in this study and the de Jonge study [16], suggesting that some symptoms measure more than one construct in cardiovascular populations. A few key differences between de Jonge's study and the current one should be noted, however. Although both samples initially produced a three-factor structure, 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 (Table 1). No obvious explanations for these specific items' variability are apparent. However, the populations from which the samples were drawn are different in some noteworthy respects. For instance, the WISE population consists solely of women who presented with signs and symptoms of myocardial ischemia at baseline, while the two populations from which de Jonge's samples were drawn included both genders, and all had recently experienced an MI – a major event that may have impacted responses to the BDI in a much different way than symptoms of myocardial ischemia would have. The varying degrees of disease severity among the samples may also help to explain the differential results.

Barefoot and colleagues [38] reached quite different conclusions in their examination of the relationship between depressive symptoms and prognosis. This group reported that negative affective symptoms of depression (including sadness, crying, suicidal ideas, irritability, and restlessness), but not well-being, somatic, or appetitive symptoms, predicted mortality in CAD patients. Although Barefoot et al. [38] also used factor analytic techniques in their study, depressive symptoms were assessed using the Zung Self-Rating Depression Scale (SDS39) rather than the BDI, so differences between their results and ours should be interpreted with caution. Nevertheless, since these two particular scales contain relatively equal representations of cognitive/affective and somatic symptoms of depression, other potential explanations for the differing study results may be more plausible.

Another noteworthy point to consider is that all of the aforementioned studies that have used factor analysis to examine the differential effects of cognitive/affective and somatic symptoms of depression on CVD prognosis have included both genders in their CVD patient populations, unlike the WISE population. Although no significant differences have been found between genders on cognitive symptoms of depression, women tend to report more somatic depression symptoms than men [40]. Perhaps the somewhat differing results obtained between this study and those of the similar studies can be attributed to the greater elevation and representation of somatic symptoms within this exclusively female sample.

Although relatively few factor analytic studies of depressive symptoms have been conducted within CVD populations, many other populations, including those with various medical diseases or complications, have been examined using similar analyses [41, 42]. Results have varied widely across specific types of populations, suggesting that they can probably not be accurately extrapolated to other populations or even to other samples that vary on secondary characteristics, as is evident by the results presented above.

### Limitations

As noted above, the results of this study cannot necessarily be extrapolated to populations other than women with symptoms of myocardial ischemia. Also, the sub-sample of subjects included in these analyses (550/936) may not have been completely representative of the entire WISE sample, and power was lowered by the missing data. Self-reported cardiovascular-related events and conditions that occurred prior to baseline were not verified by medical records and hence may not have been entirely accurate. Furthermore, depressive symptom severity was assessed at baseline, when some of the depressive symptoms women were experiencing may have been temporary, attributable to their acute cardiovascular concerns. Hence, their baseline depressive symptom levels were likely transitory – either increasing or decreasing in response to their subsequent health status. Similarly, some women may have altered their lifestyles or modified their risk factor profiles via medications and/or psychotherapy during follow-up, thus increasing or decreasing their risk of events over time. Future studies would serve the literature if they incorporated repeated assessments of depressive symptoms and other risk factors, gathered at various points during follow-up. Future studies investigating the mechanisms underlying the differential association between cognitive/affective versus somatic depressive symptoms and subsequent event rates are also warranted.

A few statistics-related limitations are noteworthy. PCA is influenced by sample specific characteristics, making the stability of its factors rather precarious. We elected to use PCA (an exploratory method) rather than confirmatory factor analysis, despite its deviation from standard best-practice methods for replication attempts, due to inconsistencies in the results obtained across previous samples exploring the BDI's factor structure. Finally, PCA was conducted using the standard matrix of Pearson correlations rather than that of polychoric inter-item correlations, as is recommended by some researchers when analyzing ordinal variables [43].

### Summary

In conclusion, in a sample of women with suspected myocardial ischemia, somatic but not cognitive/affective depressive symptoms were associated with an increased risk of cardiovascular-related mortality and events. These results support the need to research dimensions of depression in CVD populations and have implications for understanding the connection between depression and CVD.

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**Table 1**

Baseline characteristics of the WISE sub-sample included in this study

| Baseline Characteristic (N=550) | n | % of total |
|---|---|---|
| Age | 58.4* | 11.2** |
| Coronary artery disease (CAD) severity score | 13.3* | 12.7** |
| High school education or less | 325 | 59.1 |
| White race | 460 | 83.6 |
| History of diabetes | 119 | 21.6 |
| History of hypertension (n=549) | 314 | 57.2 |
| History of dyslipidemia (n=519) | 269 | 48.9 |
| History of cigarette smoking (current or former) | 288 | 52.4 |
| History of any cardiovascular-related event or condition | 216 | 39.3 |
| History of heart failure | 44 | 8.0 |
| History of myocardial infarction | 103 | 18.7 |
| History of coronary artery bypass graft surgery | 26 | 4.7 |
| History of percutaneous coronary intervention | 81 | 14.7 |
| History of cerebrovascular disease | 50 | 9.1 |
| History of peripheral vascular disease | 44 | 8.0 |
| History of one event or condition | 121 | 22.0 |
| History of two events or conditions | 70 | 12.7 |
| History of three events or conditions | 15 | 2.7 |
| History of four or five events or conditions | 10 | 1.9 |

*Mean

**Standard deviation

**Table 2**

Individual Item Factor Loadings of Beck Depression Inventory (BDI) Depressive Symptom Dimensions and Relationships with Previous Dimensional Constructs.

| | Factor from Two-Factor Principal Components Analysis (PCA) | | | Factor from Three-Factor PCA | | Corresponding dimensions in previous studies' constructs | |
|---|---|---|---|---|---|---|---|
| | Cognitive/ affective | Somatic/ affective | Appetitive | Cognitive/ affective | Somatic/ affective | de Jonge et al. [16] | Beck & Steer [10] |
| 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 |
| 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 |

* Factor loadings < .30 are not reported (except for irritability on the three-factor solution) for easier readability. Italics indicate loadings greater than .30 but lower than those of the same item on another factor in the same analysis.

**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)

**Table 4**

Results from Cox Regression Analyses Demonstrating the Relationships Among Depressive Symptom Dimensions from the Three-Factor Model and Cardiovascular Prognosis.

| Measure | Symptom Dimension from Three-Factor Model | | | | | |
|---|---|---|---|---|---|---|
| | Cognitive/Affective | | Somatic/Affective | | Appetitive | |
| **Cardiovascular prognosis** | **HR (95% CI)** | **p** | **HR (95% CI)** | **p** | **HR (95% CI)** | **p** |
| 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 |

HR (95% CI) = Hazard Ratio (95% Confidence Interval)

* Adjusted for coronary artery disease (CAD) severity scores and self-reported history of cardiovascular-related events and conditions.

** Additional adjustments for education, race, history of diabetes, and history of smoking.

## Table 5

Results from Cox Regression Analyses Demonstrating the Relationships Among Depressive Symptom Dimensions from the Two-Factor Model and Cardiovascular Prognosis.

| Measure | Symptom Dimension from Two-Factor Model | | | |
|---|---|---|---|---|
| | Cognitive/Affective | | Somatic/Affective | |
| **Cardiovascular prognosis** | **HR (95% CI)** | **p** | **HR (95% CI)** | **p** |
| 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 |

HR (95% CI) = Hazard Ratio (95% Confidence Interval)

* Adjusted for coronary artery disease (CAD) severity scores and self-reported history of cardiovascular-related events and conditions.

** Additional adjustments for education, race, history of diabetes, and history of smoking.