Published in final edited form as:
*Psychosom Med*. 2012 January ; 74(1): 33–38. doi:10.1097/PSY.0b013e3182405ac4.

# Are Somatic Symptoms of Depression Better Predictors of Cardiac Events than Cognitive Symptoms in Coronary Heart Disease?

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## Abstract

Several recent studies have found that somatic symptoms of depression predict cardiac events in patients with established CHD, but cognitive symptoms of depression do not. However, other studies have not supported this finding, and the research in this area is complicated by methodological differences and inconsistencies in the classification of “cognitive” and “somatic” symptoms. In addition, somatic symptoms are more common than cognitive symptoms in cardiac patients, and are often associated with more severe depression. These factors may confound the relationship between somatic symptoms and cardiac outcomes. Some reasons why somatic symptoms may be more common than cognitive symptoms in cardiac patients are considered, as well as whether somatic symptoms are likely to be symptoms of depression or of medical illness. Finally, some directions for future research are proposed.

### Keywords

Behavioral symptoms; depression; depressive disorder; myocardial ischemia; myocardial revascularization; prognosis

Several recent studies have reported that somatic symptoms of depression predict cardiac events in patients with coronary heart disease (CHD) or heart failure, but cognitive symptoms do not (1–8). For example, de Jonge and his colleagues (1) found that somatic/affective but not cognitive/affective depression symptoms predicted cardiac events following acute myocardial infarction, even after adjusting for left ventricular ejection fraction and other major prognostic medical variables. Similar findings have been reported in women undergoing angiography for suspected myocardial ischemia (4), in patients with documented, medically stable CHD (3), and in patients with chronic heart failure (7). Even in studies of individuals initially free of clinically significant CHD, somatic but not cognitive symptoms of depression predict subclinical atherosclerotic progression (9).

Does this mean, as some of these reports suggest, that “depression” may not be the same disorder in cardiac patients as it is in psychiatric patients? That when “depression” questionnaires are administered to cardiac patients, their responses are driven not only by depression but also by the symptoms of heart disease? Or that depressed cardiac patients need treatments that selectively target the somatic symptoms of depression? We acknowledge that studies of specific symptoms in relation to cardiac outcomes may help to clarify the relationship between depression and cardiac mortality. However, this body of research requires careful scrutiny before meaningful conclusions can be drawn from it.

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Although it is possible that somatic symptoms of depression are more predictive of cardiac events than are cognitive symptoms, it is important to be aware that some studies have not found this to be the case (10–17). In one of the earliest studies comparing somatic and cognitive symptoms of depression, Barefoot et al. (10) found that only negative affect independently predicted survival in patients with angiographically diagnosed coronary artery disease when included in a model with somatic and other depression symptoms. On the other hand, some studies have found that both cognitive and somatic symptoms predict cardiac outcomes (12, 13), whereas others have found that cognitive but not somatic symptoms are predictive (11, 16, 17). Thus, some findings do not support the dominance of somatic over cognitive and affective symptoms as predictors of cardiac outcomes. Table 1 presents a representative sample of the studies that have compared the predictive values of various depression symptom subsets in post-ACSI, revascularization, and stable CHD patient populations.

## Inconsistencies in Methodology

Evaluation of this research is complicated by numerous inconsistencies among studies as to whether particular symptoms are classified as “cognitive” or “somatic”. First, two different approaches have been used to classify symptoms. Some investigators have depended on the “face validity” of the items. Others have utilized factor analysis or principal component analysis of depression questionnaires to produce factor or component scores. These statistical approaches complicate this area of research in a number of ways. First, different analyses of the same questionnaire can, and often do, produce different factor structures, because of differences in the samples, analytic procedures, and/or decision rules. For example, one investigator might choose to include an item on a “somatic” factor only if it loads highly on that factor but not on any other factor, but another investigator might count the same item on multiple factors if it loads highly on multiple factors. The latter decision rule makes it possible for a single item to be counted both as a “somatic” symptom and as a “cognitive” symptom within the same study.

Second, the items that are called “somatic” or “somatic/affective” based on factor analyses often differ from the items that are classified as somatic in studies that are based on face validity. In the de Jonge et al. (1), and Martens et al. (5) studies, for example, “dissatisfaction” (item 4) on the BDI loaded higher on the “somatic/affective” factor (0.69 and 0.72 respectively) than on the “cognitive” factor (.49 and .38), yet dissatisfaction is generally considered to be a cognitive item based on its face validity. Similarly, “indecisiveness” was the item with the second highest loading on the “somatic/affective” factor in the de Jonge et al. study, yet it would ordinarily be classified as a cognitive symptom. Interestingly, none of the “face valid” somatic symptoms (BDI items 15–21) except for “work difficulty” loaded as highly on the somatic/affective factor in either study as did “dissatisfaction”. On the other hand, none of the traditional somatic symptoms loaded on the “cognitive” factor, and the cognitive symptoms of guilt, punishment, self-dislike, and self-accusation loaded only on the cognitive factor. Nevertheless, these factors clearly represent something other than either purely cognitive or purely somatic depressive symptoms.

Third, both the somatic and the cognitive/affective items on well-validated depression questionnaires are indicators of a single, underlying depression factor. For example, by applying an advanced technique known as hierarchical factor analysis to data obtained from a sample of primary care patients, Arnau et al. found that the first-order “cognitive” and “somatic” factors on the BDI-II reflected a single, underlying, second-order “depression” factor (18). Thus, both the cognitive and somatic items on the BDI-II are indicators of depression, even in medical patients, and “cognitive depression” and “somatic depression”

are forms of “generic depression”, not two distinct constructs. Furthermore, when these two highly correlated factors are pitted against each other in the same statistical model, multicollinearity may be present, and this may be responsible for some of the contradictory findings in this area (19).

## Frequency and Severity of Cognitive and Somatic Depression Symptoms

If somatic symptoms turn out to better predictors of cardiac events than cognitive symptoms, a possible reason is that somatic symptoms are more common in relatively severe depression than they are in milder cases (20). Thus, the dominance of somatic symptoms in some predictive models may simply be an artifact of a more fundamental relationship between the severity of depression and the risk of cardiac events (21). For example, Smolderen et al. (8) used the upper quartiles of scores on cognitive and somatic subscales of the Patient Health Questionnnaire (PHQ-9) (22) to define “cognitive” and “somatic” patient subgroups. This method ensured that the cognitive and somatic subgroups were approximately the same size. However, the somatic group scored an average of 2 points higher on the PHQ-9 total score than did the cognitive group.

In addition to reflecting more severe depression, somatic symptoms may be more prevalent than cognitive/affective symptoms in patients with CHD (23). In the Hoen et al. study (3), for example, cognitive/affective symptoms predicted cardiovascular events in age-adjusted analyses ($p=0.006$), but the effect was no longer significant after adjustment for additional covariates ($p=0.09$). Somatic symptoms remained significant even after covariate adjustment ($p=0.002$). However, fewer patients reported cognitive than somatic symptoms. Also, the confidence intervals around the hazard ratios overlapped considerably. Depressed mood, for example, was reported by 114 participants and was associated with a 32% increased risk of CV events that was not statistically significant. Fatigue was associated with an almost identical risk (34%), but 267 patients reported this symptom, yielding a narrower confidence interval and a significant effect. In women with suspected myocardial ischemia, Linke et al. (4) found that somatic symptoms predicted mortality whereas cognitive symptoms did not. However, somatic symptoms accounted for about three-fourths of the BDI total scores in a three factor solution, and two thirds of the BDI total scores in a two factor solution. Unfortunately, few reports have provided enough information to determine whether differential symptom frequency or severity may have contributed to the findings. These data should be reported in future studies and evaluated as potential explanations for the findings.

## Reporting Bias or Actual Frequency?

Why do depressed CHD patients tend to report more somatic than cognitive symptoms? One possibility is that many depressed patients believe that cognitive and affective symptoms are less socially acceptable, more stigmatizing, or riskier to report than somatic symptoms (24). Men with heart disease often report fewer symptoms of depression than are observed by a spouse or friend (25, 26), and depressed cardiac patients more readily admit to irritability than to depressed mood (27). It is probably easier for many medical patients to admit to sleep or appetite disturbances than to thoughts of hopelessness or suicide, even when these cognitive symptoms are present. This sort of reporting bias would result in lower total scores from patients who selectively report somatic symptoms than in those who are willing to report a broader range of symptoms. Consequently, it may seem as though the former are less severely depressed than some of them actually are. This problem could complicate efforts to investigate whether differences in the overall severity of depression explain the differential predictive value of somatic symptoms.

Bias against reporting cognitive or affective symptoms may be especially problematic in studies of depressed cardiac patients who are not seeking treatment for depression. Martens

and colleagues (23) found that cognitive symptoms are more frequently reported in depressed psychiatric patients than in depressed cardiac patients. The psychiatric patients in their study were being treated for depression at a psychiatric clinic. The cardiac patients, in contrast, were participants in an observational study of post-MI depression, not treatment-seeking depressed patients. Patients seeking treatment for depression are probably more likely to acknowledge that they are depressed, and they may be more willing to endorse statements such as "I am worthless," or "I don't deserved to be loved", two items on the Cognition Checklist that were used to measure cognitive symptoms in the Martens et al. study (23).

Another explanation for why depressed cardiac patients may report fewer cognitive symptoms is that they may actually *have* fewer cognitive symptoms. Cognitive symptoms are often present in individuals who are "depressed about being depressed" (28). That is, depressed mood and other symptoms of depression may be viewed by depressed patients as evidence of their personal inadequacy. This may initiate a vicious cycle of guilt, hopelessness, self-criticism, and even suicidal ideation in some cases. In contrast, many cardiac patients may attribute their depressive symptoms to their heart disease or believe depression to be a "natural" and understandable reaction to a life-threatening cardiac event (29, 30). Consequently, these patients may be less vulnerable to becoming depressed about their depression, and this could minimize the cognitive and affective symptoms while making the somatic symptoms more salient.

One implication of the observation that patients are more likely to experience or report somatic than cognitive symptoms of depression is that some depression screening tools, including ones recommended by the American Heart Association (31) and a National Heart, Lung, and Blood Institute advisory panel (32), may not be optimal for identifying these patients. For example, the PHQ-2 asks only about dysphoric mood and anhedonia, and therefore may fail to identify cardiac patients with predominantly somatic symptoms of depression. The full PHQ-9 or other screening tools that sample a wider range of symptoms should be considered when screening for depression in cardiac patients.

## Symptoms of Depression, Heart Disease, or Something Else?

It has also been suggested that somatic symptoms predict cardiac outcomes because the BDI and similar depression questionnaires assess symptoms of heart disease in addition to depression. The primary somatic symptoms of depression include pervasive fatigue, sleep disturbances, and appetite disturbances. Of these, only fatigue is generally considered to be a symptom of heart disease, especially in heart failure patients with poor cardiac output, or in patients with a recent major cardiac event. Interestingly, in a recent study comparing depressed patients with heart failure and depressed psychiatric patients, those with heart failure reported less depressed mood and fewer feelings of worthlessness and guilt compared to the psychiatric patients, but the groups did not differ on any of the somatic depression symptoms, including fatigue (33).

Furthermore, most prognostic studies of the effects of depression in cardiac patients have adjusted for standard indices of cardiac disease severity and other risk factors for mortality. It is possible that some unmeasured or unknown component of heart disease that happens to produce the same somatic symptoms as depression may account for the effects of somatic symptoms on cardiac outcomes, or that the measures of illness severity and cardiac risk that have been used as covariates are inadequate. However, this concern applies to studies of other cardiac risk factors as well. Residual confounding is always a possible alternative explanation for any putative risk factor.

When considering explanations other than depression for the presence of somatic depression symptoms, it must be pointed out that these symptoms overlap with those of "vital exhaustion" and "sickness behavior" (34). Whether these constructs describe the same underlying disorder or have distinct etiologies and underlying biological processes has been subject of much discussion and debate in the literature (e.g. 34, 35, 36, 37, 38).

## Covariate Adjustment

What about the observation that the cardiovascular risks that have been attributed to depression often diminish after covariate adjustment? Depression is often associated with other cardiac risk factors such as diabetes, obesity, smoking, and poor aerobic capacity (39). Consequently, the risk for cardiac events associated with depression often decreases when these factors are included as covariates in a covariate-adjusted model. However, that does not mean that depression is not the principal contributor to elevated depression scores in cardiac patients, or that depression itself is not a risk factor. Depression may be part of a broader network of cardiac risk factors, such as the metabolic syndrome (40, 41), and it may increase the risk for cardiac events by adding to the burden of the proinflammatory and procoagulant processes and the cardiovascular autonomic dysregulation that are associated with both depression and with other cardiac risk factors (39). Adjusting for the effects of other cardiac risk factors may mask important interactions. Zeigelstein and his colleagues, for example, found an interaction between a BDI score >10 and Killip class >1 in patients with a recent MI (42). The one year mortality rate in patients with both depression and Killip class >1 was significantly higher (17%) than in those with neither (4.6%), Killip class >1 alone (5.2%), or BDI > 10 alone (5.2%). It is also likely that behavioral patterns associated with depression, such as physical inactivity, poor adherence to medical treatment regimens, and disturbed sleep, worsen the effects of other cardiac risk factors

The principal mediators and moderators of depression as a cardiac risk factor have not been firmly established, and deserve further attention. Longitudinal studies that recognize the changing nature of these factors over time are especially needed

## Depression Without Cognitive Symptoms?

Can somatic symptoms actually be symptoms of depression in the absence of any cognitive or affective symptoms? Dysphoric mood and anhedonia are the cardinal symptoms of major and minor depression. Unless at least one of these symptoms is present, a patient cannot meet the DSM-IV criteria for a major or minor depressive episode (43). However, individuals who do not meet the diagnostic criteria for major depression but who have somatic symptoms of depression also tend to have family and personal histories of mood disorders, shortened REM latency, and an increased proportion of sleep time spent in REM, all of which are factors associated with major depressive disorder (44). Somatic symptoms of depression, especially disturbed sleep, often herald major depressive episodes and are better predictors of episodes than are cognitive or affective symptoms (45–48). In patients whose depression is in partial remission, residual somatic symptoms are more common than cognitive or affective symptoms, and they are risk factors for recurrent or chronic depression (49–51). Thus, isolated somatic symptoms of depression may reflect an inter-episode phase of major depressive disorder, they may eventually evolve into a recurrent episode of major depression, or they may reflect a chronic, subthreshold mood disorder. Patients with a recent acute coronary syndrome who have residual depression symptoms following treatment are at higher risk for mortality (52), so perhaps the goal of treatment should not be to target somatic symptoms per se, but rather to treat each patient to complete remission.

## Summary and Conclusions

Although some studies have reported that somatic symptoms of depression are better predictors of cardiac events than are cognitive symptoms, this question is far from settled. Future studies should address the potentially confounding effects of differences in the frequency and severity of the different types of symptoms, as well as those of the overall burden of depression. Furthermore, factor analytic techniques should be carefully evaluated, especially when a decision is made to include symptoms in more than one factor, or when traditionally cognitive or affective symptoms are included in a “somatic” factor or vice versa. Researchers should consider reporting both factor analytic and face valid methods in the same study to facilitate comparisons among studies and to evaluate the sensitivity of the findings to differences in methodology. It would also be helpful to move away from reliance on unreplicated exploratory factor analyses and to depend instead on more rigorous methods of confirmatory factor analysis (CFA) (53).

Finally, it seems remarkable that after determining an ejection fraction, establishing the severity of coronary artery stenosis, and documenting a history of acute coronary events, heart failure, diabetes, renal function, etc. from medical records or by direct evaluation of patients, it is possible to identify an additional two fold or greater risk of death in post-MI patients merely by asking about symptoms of general fatigue, disturbed sleep, increased or decreased appetite, and perhaps dysphoric mood and irritability (e.g. 54). Researchers who suspect that these symptoms do not represent depression, but instead some aspect of heart disease or medical comorbidity that is being overlooked in routine cardiovascular evaluations, should be working to discover their true cause. In the meantime, *depression* remains the most plausible explanation for the increased risk of mortality in patients who report symptoms of depression.

## Acknowledgments

This manuscript was supported in part by Grant No. RO1 HL08933601A2 from the National Heart, Lung, and Blood Institute, and by the Lewis and Jean Sachs Charitable Lead Trust.

## Abbreviations

| | |
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| **ACS** | Acute coronary syndrome |
| **BDI** | Beck Depression Inventory |
| **CHD** | coronary heart disease |
| **MI** | myocardial infarction |
| **PHQ-9** | Patient Health Questionnnaire |

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**Table 1**

Studies of Somatic vs. Cognitive/Affective Depression Symptoms and Cardiac Events

| Source | Sample Size | Depression Measure | Symptom Classification Method | Follow-up Duration | Outcome | Results | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | Symptom Subset | Risk Statistic | p |
| **Acute Coronary Syndrome** | | | | | | | | |
| Martens et al., 2010 | 437 | BDI-1 | Factor analysis | 2.8 years | Cardiac death or recurrent MI | Somatic | 1.31‡ | 0.04 |
| | | | | | | Cognitive/Affective | Not reported‡ | NS |
| Roest et al., 2010 | 913 | BDI-1 | Principal components analysis | 1 year | All-cause mortality | Somatic | 1.92† | 0.001 |
| | | | | | | Cognitive/Affective | 1.07† | 0.73 |
| Smolderen et al., 2009 | 2,347 | PHQ-9 | Item face validity | 4 years | Hospitalizations | Somatic | 1.16‡ | 0.01 |
| | | | | | | Cognitive/Affective | Not reported‡ | NS |
| de Jonge et al., 2006 | 494 | BDI-1 | Factor analysis | 2.5 years | All-cause mortality | Somatic | 1.07‡ | 0.30 |
| | | | | | Readmission | Somatic | 1.30‡ | <0.10 |
| | | | | | | Cognitive/Affective | 1.05‡ | <0.74 |
| | | | | | | Appetitive | 1.09‡ | <0.43 |
| | | | | | Cardiac mortality | Somatic | 3.91‡ | <0.001 |
| | | | | | | Cognitive | 0.40‡ | <0.04 |
| | | | | | | Appetitive | 0.94‡ | <0.83 |
| Frasure-Smith & Lespérance, 2003 | 896 | BDI-1 | Principal components analysis | 5 years | Cardiac mortality | Somatic | 1.51‡ | <0.001 |
| | | | | | | Cognitive | 1.34‡ | 0.002 |
| Irvine et al., 1999 | 671 | BDI-1 | Item face validity | 2 years | Sudden cardiac death | Somatic[1] | 1.00†† | 0.95 |
| | | | | | | Cognitive[1] | 1.09†† | 0.06 |
| Lespérance et al., 1996 | 222 | DIS | DSM-III | 1.5 years | Cardiac mortality | MDD[2] | 3.96† | 0.008 |
| | | | | | | MDD[3] | 4.76† | 0.003 |
| **Revascularization** | | | | | | | | |
| Tully et al., 2011 | 226 | BDI-II | Factor analysis | 4.9 years | Cardiovascular events | Somatic | 1.18‡ | 0.38 |
| | | | | | | Cognitive | 1.36‡ | 0.04 |

| Source | Sample Size | Depression Measure | Symptom Classification Method | Follow-up Duration | Outcome | Results | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | **Symptom Subset** | **Risk Statistic** | **p** |
| Connerey et al., 2007 | 309 | BDI-1 | Item face validity | 9.3 years | Cardiac mortality | Affective | 0.79‡ | 0.09 |
| | | | | | | Somatic | 1.07‡ | 0.12 |
| | | | | | | Cognitive | 1.10‡ | 0.007 |
| Pedersen et al., 2007 | 534 | Maastricht Questionnaire (MQ) | Principal components/item analysis | 2 years | All-cause mortality and nonfatal MI | Fatigue | 1.35‡ | 0.42 |
| | | | | | | Depression[4] | 2.69‡ | 0.007 |
| | | | | | | Hopelessness | 1.9‡ | 0.001 |
| **Known or Suspected Stable Coronary Heart Disease** | | | | | | | | |
| Hoen et al., 2010 | 1,019 | PHQ-9 | Item face validity | 6.1 years | Cardiovascular morbidity/mortality | Somatic | 1.14‡ | 0.002 |
| | | | | | | Cognitive | 1.08‡ | 0.09 |
| Linke et al., 2009 | 550 | BDI-I | Principal components analysis | 5.0 years | Cardiovascular morbidity/mortality | Somatic | 1.39‡ | 0.01 |
| | | | | | | Cognitive | 0.81‡ | 0.09 |
| Barefoot et al., 2000 | 1,250 | Zung Depression Scale | Factor analysis | 15.2 years | Cardiac deaths | Somatic | 1.31†† | 0.003 |
| | | | | | | Well Being | 1.26†† | 0.001 |
| | | | | | | Negative Affective[5] | 1.42†† | 0.001 |
| | | | | | | Hopelessness | 1.50†† | 0.015 |

†Adjusted Odds Ratio (OR)

‡Adjusted Hazard Ratio (HR)

††Adjusted Relative Risk (RR)

[1]Placebo group only

[2]MDD with sleep/appetite disturbance

[3]MDD without sleep/appetite disturbance

[4]6 of 7 symptoms are cognitive

[5]Only negative affect remained in the model with all symptom groups