

## Mental Health Symposium Depression and Chronic Heart Disease

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### Depression and Heart Disease Introduction

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- Which Diseases?  
CAD; MI, CHF; Diabetes.
- What Is The Data?
- Is The Relationship Cause and Effect?
- Is There A Plausible Biologic Connection?
- Does Treatment Of Depression Make A Difference?

## Depression and Heart Disease

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- Premise 1. There is an association of depression with certain forms of heart disease.
- Premise 2. There is a worse outcome in heart disease associated with depression.
- Premise 3. In depression there is a predilection for heart disease.
- Premise 4. Treatment of depression improves any predilection for adverse outcomes from heart disease.

## Behavior Links to Cardiac Function

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- HF-HRV: high frequency heart rate variability is an indicator of parasympathetic cardiac autonomic function .
- Latent constructs of depression anxiety and anger were measured in 653 volunteers, ages 30-54 yrs.
- Depression and anxiety related inversely to HF HRV, anger related directly.
- Negative affect as a common pathway to impairment in cardiac autonomic function

Bleil, Psychosomatic Medicine 2008

## Biologic Link of CAD and Depression

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- 306 patients with angiographic CAD and controls with no CAD.
- Screened for depression using Hospital Anxiety and Depression scale; all Gemeine Depressions Skala-L questionnaires.
- No relationships among depression, CAD or blood coagulations and fibrinolysis, fibrinogen, prothrombin fragment FI & 2, Factor XIII, A subunit, Factor XIII B subunit, TPA, PAI, fibrinolysis inhibitor and D-dimer.

European Journal. of CV Prevention and Rehab  
14:782-7 2007

## Anxiety and Depression in Chronic CAD

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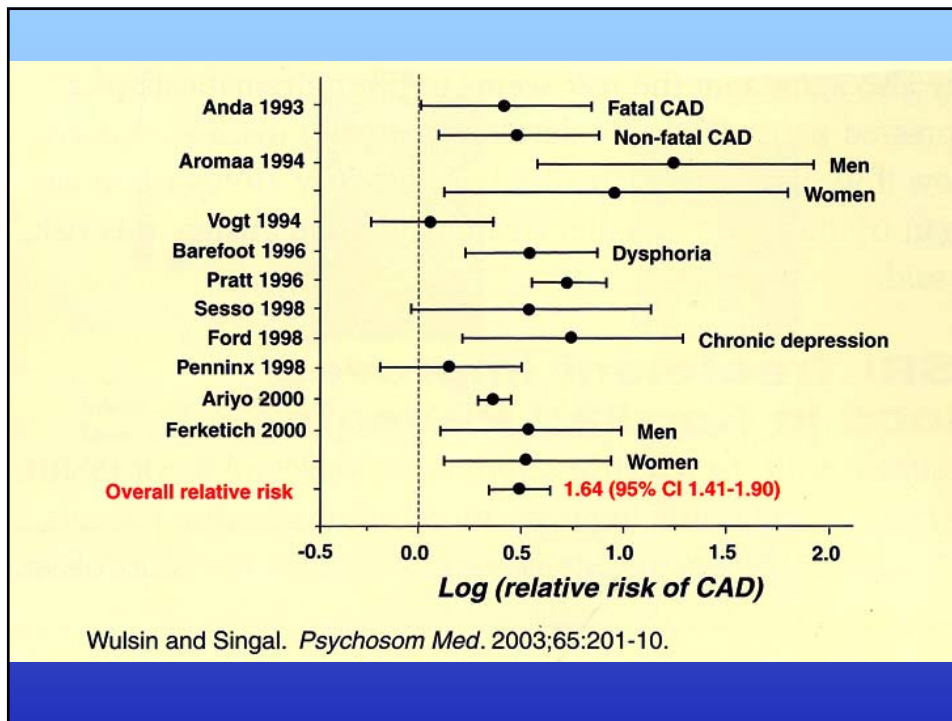
- Prospective, cohort study 1052 CAD patients in cardiac rehab. Evaluated with hospital anxiety and depression.
- 16% had borderline, 8.3% had manifest anxiety scale scores.
- 11.8% had borderline, 5.9% had manifest depression scores.
- After adjusting for covariates manifest anxiety had a hazard ratio of 2.32 for CVD events during 3 yr follow-up.
- Those with depressive symptoms had a hazard ratio of 1.47 for CVD events

European J. of CV Preventions & Rehab 2007  
14:547-54

## High Frequency of Anxiety and Angina Pectoris in Depressed Women with CAD

- 121 Swedish women with CAD in Cardiac Rehab Trial; 23.1% had scores consistent with depression.
- Scores of  $\geq 19$  were strongly linked to angina pectoris and higher rates of anxiety.

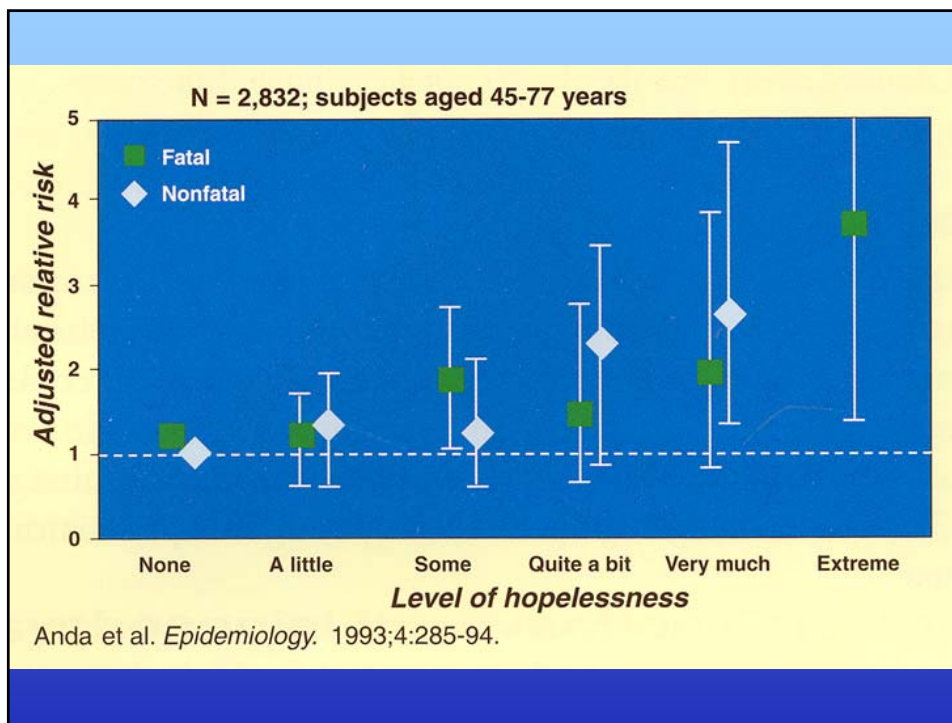
Gender Medicine  
4:146-151 2007



## Depression as a Predictor of Hospitalization for CHD

- Family coronary heart disease database at the Karolinska Institute identified all people, age 25 to 64 at onset of depression and all age 25 to 79 at onset of non-fatal CHD in Sweden.
- Standardized ratios (SIR's) of CHD of those with and without depression were compared.
- 1767 cases of CHD among those with depression the SIR was 2.17 strongest for those  $\leq 40$  yrs.
- Depression is a clinically important risk factor for CHD in those 25-50 yrs.

Sundquist, AM J Preventive Medicine 2005



## Association of Post MI Depression with Somatic Health

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- 1205 Post MI patients assessed with composite international diagnostic Interview during 1<sup>st</sup> year after MI and type – D personality with the DS -14 at one year
- Prevalence rates were 17.1% for post MI depression and 18.7% for type –D
- Post MI depression was associated with LVEF (odds ratio 3.17), greater comorbidity (OR 1.46) whereas type –D was not.

Journal of Psychosomatic Research 2007  
63: 471-82 2007

## Influence of Gender on Depression in Acute Coronary Syndrome (ACS)

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- 944 ACS patients surveyed (716 were using zung self assessment tool 228 women).
- 35% of men, 45% of woman were depressed. ( $p \leq .005$ )
- Predictors of depression (odds ratio) were

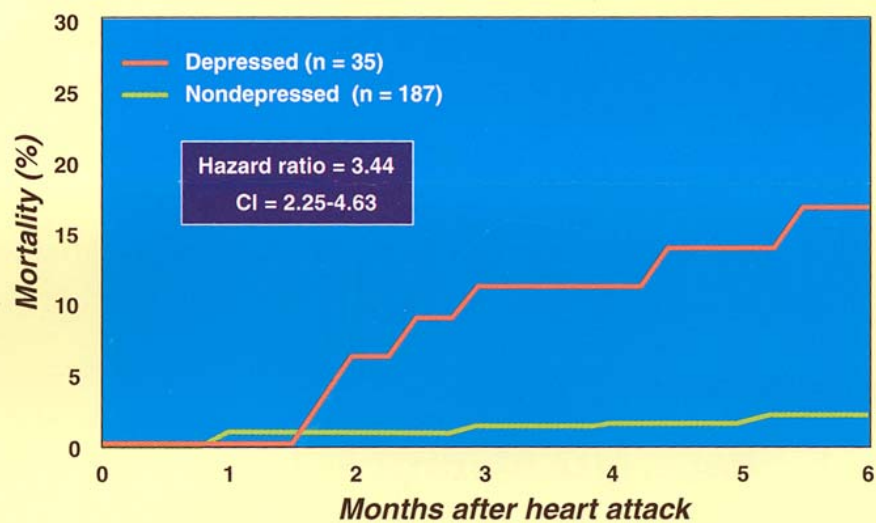
Female gender	1.64
Diabetes	1.42
Prior MI	1.56
Smoking	1.41

Naqvi, Gender Medicine 2007

## Depression and Outcome after MI

- Registry of 1873 MI patients were surveyed for depression at hospitalization or at 1 month and followed to 6 months.
- Compared to non-depressed patients, all categories (transient, new or persistent) were associated with re-hospitalization, mortality, angina or physical limitation.

Parashar, Arch IM, 2006



Frasure-Smith et al. *JAMA*. 1993;270:1819-25.

## Beta Blockers and Depression after MI

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- 127 non-beta-blocker users and 254 beta-blocker users post MI were assessed for depression at 3,6,12 months using Beck DI.
- No differences in presence of depression at any of the time intervals was found.
- Longer term of higher dosage effects could not be ruled out.

JACC 48: 2215-7 2006

## Effect of Depression on Late Mortality after MI

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- Prospective study of 284 patients hospitalized for MI.
- Major depression, dysthymia or Beck score  $\geq 10$  present in 26.8%.
- Predicted death at 4 months but not at 8yrs.

Parakh, JACC 2008

## Depression is a Risk Factor for Mortality after MI

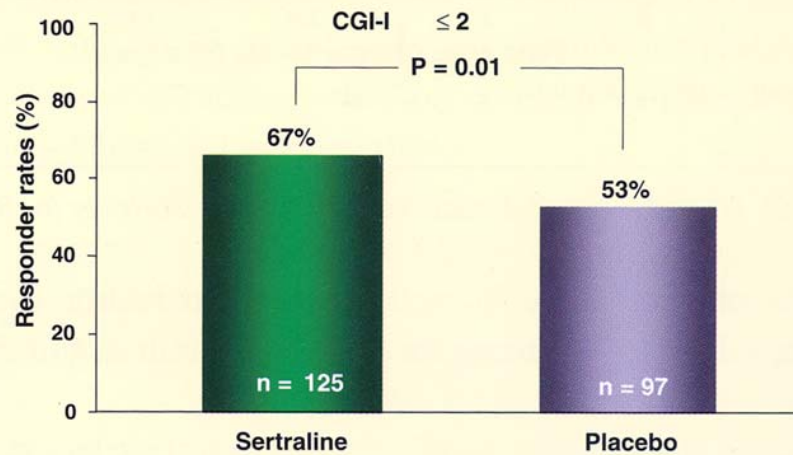
Fact or Artifact?

- 588 subjects followed for 8 yrs. after MI.
- Depression was assessed immediately before and 12 months after MI using standardized questionnaire.

- Multivariate predictors of cardiac death

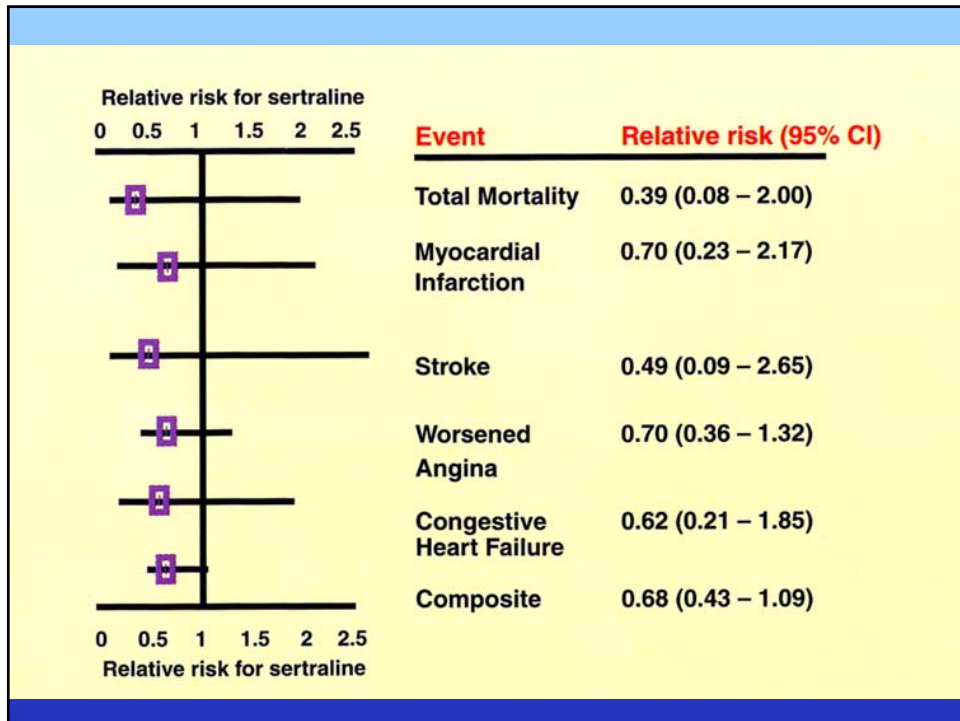
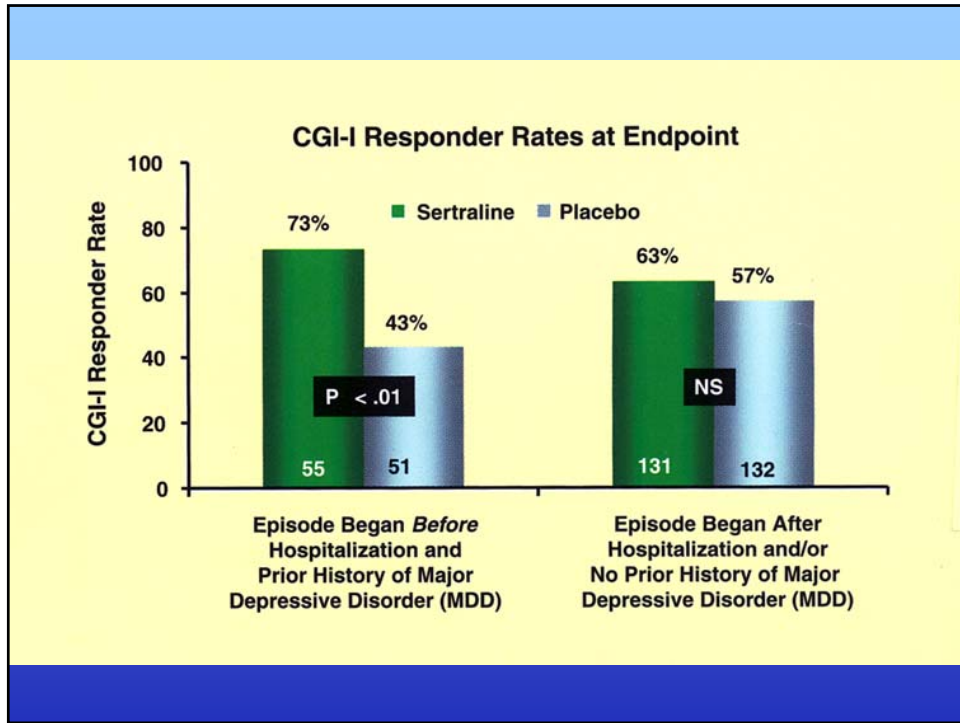
	HR
Older Age	1.04
Previous Angina	1.8
Prior MI	1.6
Beta Blocker Use	0.5
ACE Inhibitor	0.6
Depression before or after not associated with cardiac death.	

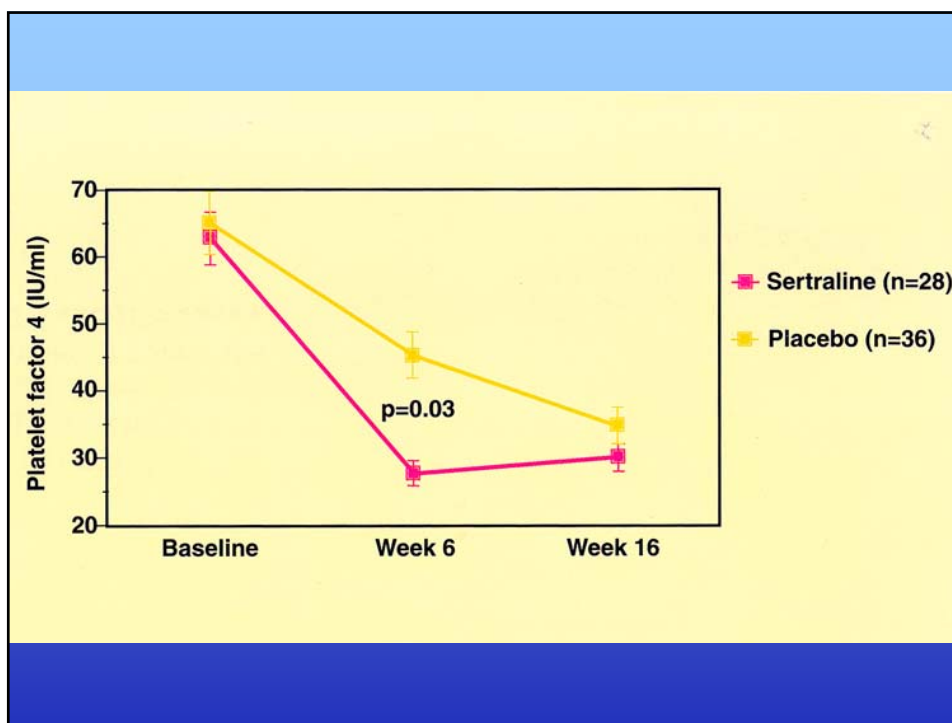
JACC 50:1519-20, 2007



Inferences regarding efficacy extend to Week 24

Mean dose: sertraline 68.8 mg/day; placebo 70.5 mg/day equivalent  
Glassman et al. *JAMA* . 2002;208:701-9.





## Depression in MI and CAD

- Is Common, especially in younger women.
- Confers higher likelihood of death or recurrent angina, although not in all studies.
- The duration of adverse effects may or may not last for 8 years.

## Depression in MI and CAD (continued)

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- Has behavioral linkages such as medication adherence, activity levels, eating habits or delays in seeking treatment for cardiac symptoms.
- May have biologic linkage due to cytokines, endothelial dysfunction, autonomic dysfunction or thrombotic factors .
- Treatment with SSRI's appears to be safe and effective for depression improvement but may not improve cardiac risk.

## Depression in Chronic Heart Failure

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- Of 581 patients in the quality of life sub-study of the Digitalis Investigations Group Trial (DIG), 23% reported they were “much” or “very much” depressed .
- At a 33 month follow-up, mortality was 40% in the depressed group compared to 17% in a matched non-depressed group.
- This association persisted after adjustment for propensity scores and other co-variables.
- There was no association with repeat hospitalization.

Okmuwo, Comprehensive Therapy 2007

## In Heart Failure, TNF Is Associated with Higher Risk of Depression

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- Proinflammatory cytokines may contribute to progression of HF and are implicated in depression.
- TNF alpha, IL-1 and IL-6 measures in 129 ambulatory HF patients.
- Compared to those with TNF alpha in the lowest in the quartile, those were in the highest nearly 5 fold higher.
- After multi-variate adjustment, those with TNF in the highest vs. the lowest quartile were associated with a nearly 5 fold increase in depression.

Moorman, J. Cardiac Failure 2007

## Depression Determines Quality of Life in Heart Failure

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- 167 ambulatory patients were recruited with HF (NYHA II – IV).
- QOL measured with SF-36 and depression assessed with the PHQ-9.
- In multivariate analysis, the PHQ-9 explained QOL variance.
- LVEF, and NT-pro BNP did not correlate with QOL.

Muller-Tasch, J. Card., Failure 2007

## Effect of Depression Treatment in HF

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- Randomized, Guided Trial of Paroxetine for 12 weeks in 25 patients showed significantly more recovery from depression than with placebo.
- Clinically significant depression associated with Hazard ratio (HR) of 1.56 for death or HF hospitalization in 204 patients followed for 3 yrs. But anti depressant medication associated with HR of 1.75.

Sherwood, Arch IM, 2007

## Depression in Heart Failure:

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- Is Common.
- Even more than biologic factors may determine QOL.
- Can be an adverse prognosis for death.
- Can be relieved by medication treatment.
- Treatment of which may or may not be safe.

## Examining a Bi-directional Association Between Depressive Symptom and Diabetes

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- Depressive symptoms defined as CES-D score  $\geq 16$  and use of anti depressive medications.
- Impaired fasting glucose is FBG 100-125mg/dl.
- Type 2 diabetes is FBG  $\geq 126$  or receiving treatment.

Golden, JAMA 2008

## Examining a Bidirectional Association Between Depressive Symptom and Diabetes (Continued)

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### Analysis I

- 5201 participants, without type 2 diabetes at baseline, estimate relative hazard incident diabetes with and without depressive symptoms over 3.1 yrs.
- Results showed incident rate of diabetes was 22.0 and 16.6/1000 person years for those with and without depression but was no longer significant (odds ratio 1.08) after adjustment for lifestyle factors.

## Examining a Bi-directional Association Between Depressive Symptom and Diabetes (Continued)

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### Analysis II

- 4847 people without depressive symptoms at baseline and calculated the odds of developing depression over 3.1 yrs. For those with and without diabetes.
- Results showed the incident rate for depressive symptoms per 1000 person/yr were 36.8 for normal FBS, 27.9 for impaired FBS, 31.2 for untreated diabetes and 61.9 for treated diabetes. There was a strong odds ratio of 1.54 of developing depression with treated diabetes, not with untreated diabetes or glucose intolerance.

Golden, JAMA 2008

## Depression and Heart Disease

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- Depression is common in most forms of HD.
- Depression is also associated with worse cardiac outcome and highly associated with QOL.
- Screening for depression is important.
- Treatment of depression improves mood and QOL but may not change medical outcome.
- Employment, having a life partner and physical exercise all help reduce depression in this setting.

## Depression Associated Biologic Processes

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- Autonomic dysregulation.
- Inflammation.
- Insulin resistance.
- Platelet aggregation.
- Decreased cellular immunity.

## Depression Associated Behavioral Processes

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- Inactivity.
- Eating disorders.
- Compliance with medications and follow-up.
- Interference with teaching and learning about heart disease.
- Misrecognition of early warning cardiac symptoms.