

# Stress and Cardiovascular Disease

Maddury Jyotsna  
Prof. of Cardiology  
Nizam's Institute of Medical Sciences

“ For every affection of the mind that is attended with either pain or pleasure, hope or fear, is the cause of an agitation whose influence extends to the heart, and there induces change from the natural constitution, in the temperature, the pulse and the rest”

- Dr William Harvey, 1628

## Case 1

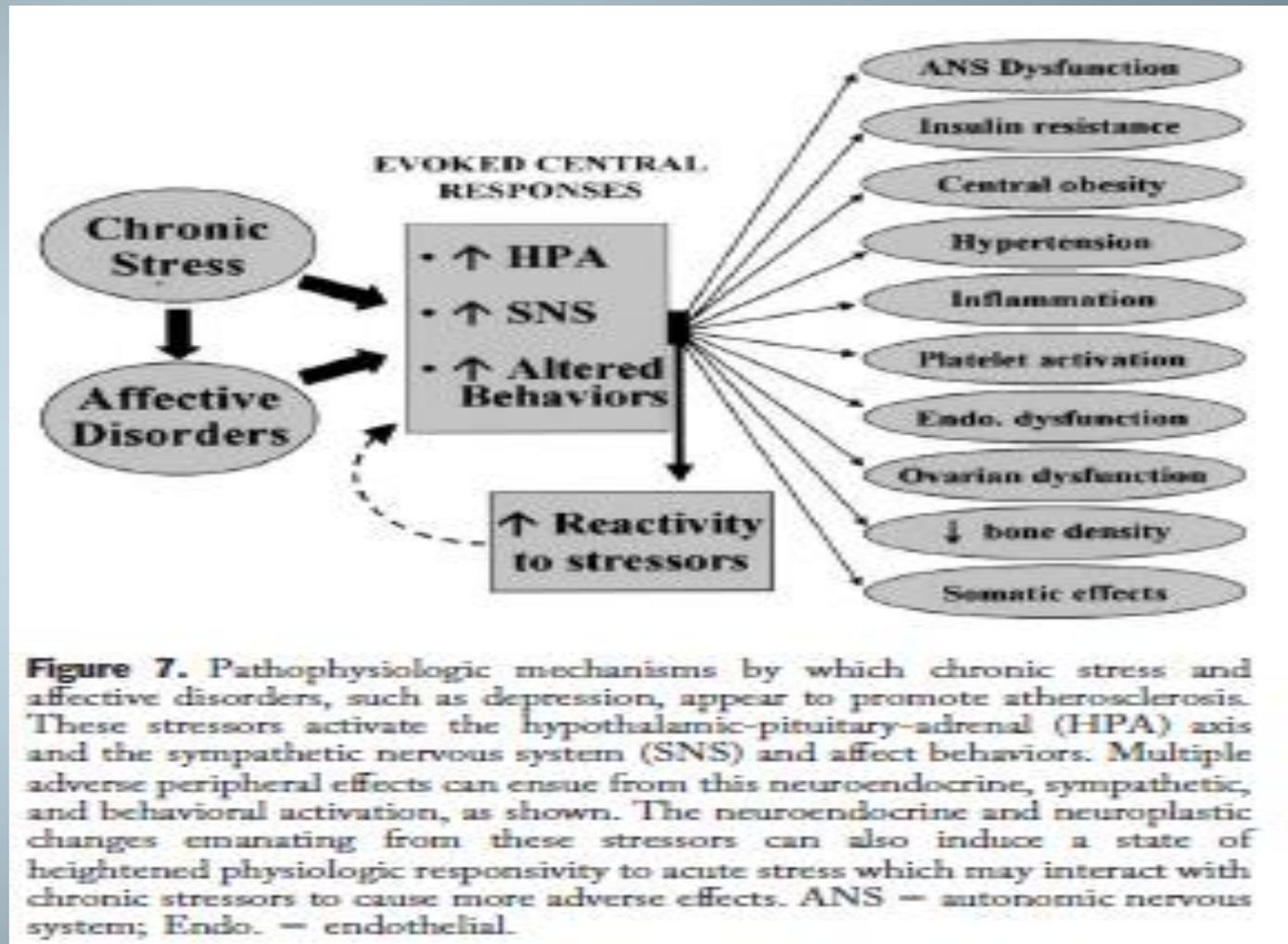
- 55 year old diabetic, hypertensive patient was shouting at a person who was responsible for huge economic loss to him, suddenly developed sub-sternal chest pain with sweating.
- Rushed to EMD – ECG showed AMI.
- Treated with primary angioplasty.

## **Associations of four emotional triggers and occurrence of acute myocardial infarction**

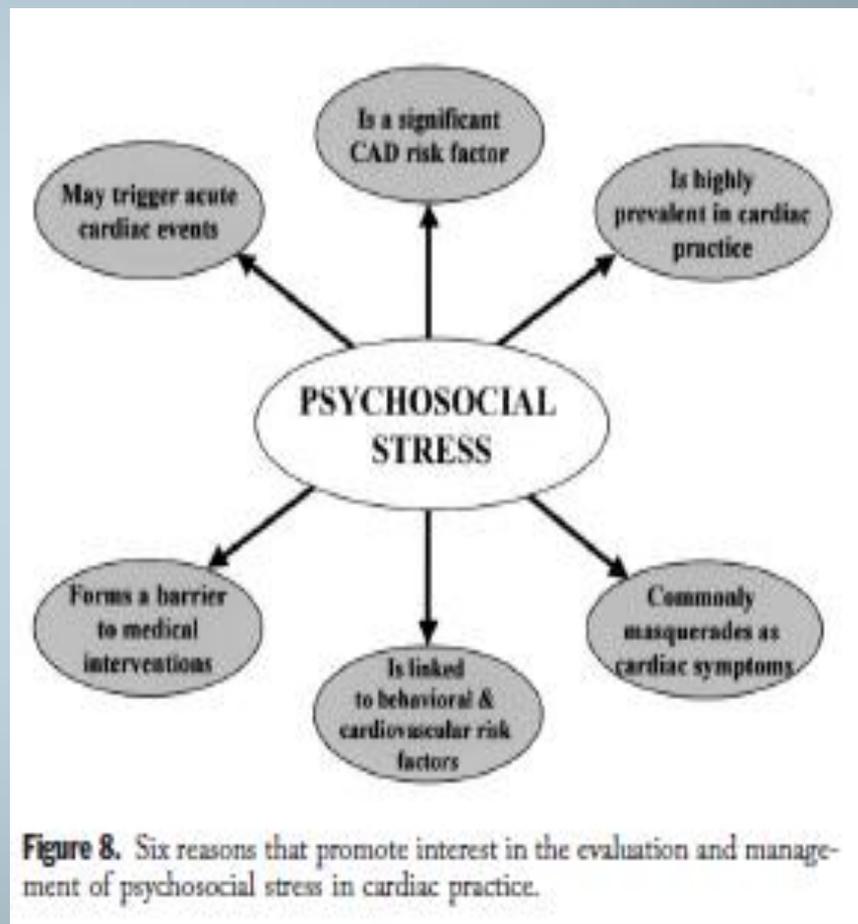
- p value
- Anger (4 studies) 0.00
- Anxiety 0.01
- Bereavement 0.00
- Depressed mood 0.04

[Eur Heart J. 2013 Jan 21; 34\(4\): 300–306.](#)

# Proposed Mechanisms Relating Chronic Stress to Atherosclerosis

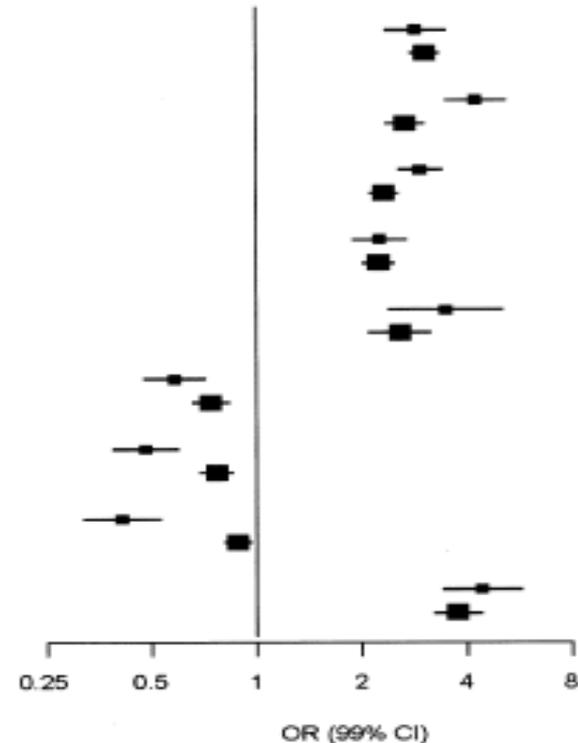


# Six Reasons that Promote Interest in Evaluation and Management of Psychosocial Stress in Heart Disease



# INTERHEART Study: Psychosocial Index and Risk of Acute MI

Risk Factor	Gender	Cont %	Case %	OR (99%CI)	PAR (99%CI)
Curr Smok	female	9.3	20.1	2.86 (2.36,3.48)	15.8 (12.9, 19.3)
	male	33.0	53.1	3.05 (2.78,3.33)	44.0 (40.9, 47.2)
Diabetes	female	7.9	25.5	4.26 (3.51,5.18)	19.1 (16.8, 21.7)
	male	7.4	16.2	2.67 (2.36,3.02)	10.1 ( 8.9, 11.4)
Hypertension	female	28.3	53.0	2.95 (2.57,3.39)	35.8 (32.1, 39.6)
	male	19.7	34.6	2.32 (2.12,2.53)	18.6 (17.7, 21.5)
Abd Obesity	female	33.3	45.6	2.26 (1.90,2.68)	35.9 (28.9, 43.6)
	male	33.3	46.5	2.24 (2.03,2.47)	32.1 (28.0, 36.5)
PS Index	female	-	-	3.49 (2.41,5.04)	40.0 (28.6, 52.6)
	male	-	-	2.58 (2.11,3.14)	25.3 (18.2, 34.0)
Fruits/Veg	female	50.3	39.4	0.56 (0.48,0.71)	17.8 (12.9, 24.1)
	male	39.6	34.7	0.74 (0.66,0.83)	10.3 ( 8.9, 15.2)
Exercise	female	16.5	9.3	0.48 (0.39,0.59)	37.3 (26.1, 50.0)
	male	20.3	15.8	0.77 (0.69,0.85)	22.9 (16.9, 30.2)
Alcohol	female	11.2	6.3	0.41 (0.32,0.53)	46.9 (34.3, 60.0)
	male	29.1	29.6	0.86 (0.81,0.96)	10.5 (6.1, 17.5)
ApoB/ApoA-1 Ratio	female	14.1	27.0	4.42 (3.43,5.70)	52.1 (44.0, 60.2)
	male	21.9	35.5	3.76 (3.23,4.38)	53.8 (48.3, 59.2)



**Figure 5.** Risk of acute myocardial infarction for men and women for each of nine coronary artery disease (CAD) risk factors evaluated in the international INTERHEART case-control study. Results are adjusted for age, gender, and geographic location. The prevalence of each CAD risk factor is presented for controls and cases in the third and fourth columns; prevalence rates are not calculated for the psychosocial (PS) index as it is derived from a statistical model. Reprinted with permission from Yusuf et al. *Lancet* 2004;364:937-52 (43). Abd = abdominal; CI = confidence interval; Curr = current; OR = odds ratio; PAR = population-attributable risk; Smok = smoking; Veg = vegetables.

Psychosocial index based on individual items of depression, locus of control, work or home stress, financial stress, and adverse life events.

# **The term “Psychosocial” broadly categorizes factors which are:**

- Psychologic – e.g, anxiety, depression
- Psychosocial – e.g., work stress, discrimination, emotional support
- Social-structural – e.g., socioeconomic status, social integration, neighborhood effects

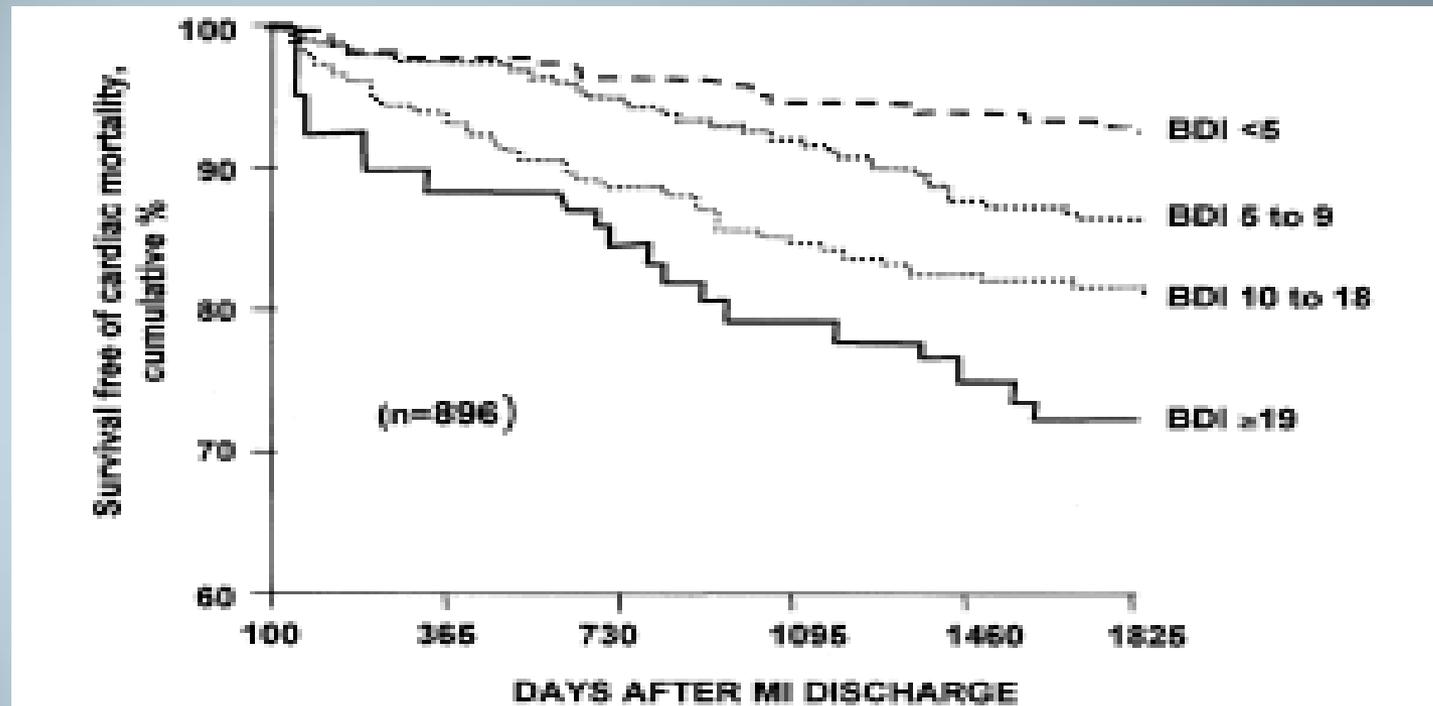
# Depression

- Estimated prevalence of major depression in India is 14%, but up to 30% in cardiac patients
- Characterized by a depressed mood and combination of other symptoms such as weight change, sleep disturbance, insomnia, fatigue, feelings of guilt, worthlessness, and/or hopelessness.
- Of all psychosocial factors, evidence of association with CVD is strongest for depression.

## Depression and CVD (cont)

- Frasure-Smith et al (JAMA 1993) reported a 4-fold increase in mortality during 6 months following acute MI from depression in cardiac patients.
- Meta-analysis examining depression as a factor in development of CHD in healthy individuals showed a risk factor-adjusted RR=2.69 for CHD incidence ( Rugulies, Am J Prev Med 2002).

# Depressive Symptoms and Cardiac Free Survival in Post-MI Patients



**Figure 1.** Post-myocardial infarction (MI) patients were recruited and assigned to one of four categories based on the Beck Depression Inventory (BDI), ranging from no depressive symptoms (BDI <5) to moderate to severe depressive symptoms (BDI  $\geq 19$ ). During the five-year follow-up period, a gradient relationship was observed between the magnitude of depressive symptoms and the frequency of deaths, with increased events occurring even in patients with mild depressive symptoms (BDI 5 to 9) (2).

## **CASE # 2**

- An 68-year-old female presented to the EMD with chest pain of ten hours duration, which began while watching television.
- The pain was 9/10, substernal and non-radiating, pressure-like, without other associated symptoms.

- Vital signs were: BP of 185/88 mm Hg, pulse of 71 beats/min, respirations of 20 breaths/min, O<sub>2</sub> sat of 98% on room air, and temperature of 35.7°C.
- She reported medical history of hypertension, hypothyroidism, gout, and a hysterectomy.

- Cardiac risks included age, hypertension, and family history of coronary disease.
- Her daughter stated that her mother had been under extreme stress due to sudden accidental death of her son two weeks ago.
- Her physical exam was unremarkable.

- Initial ECG revealed a NSR with ST elevation in V2 and V3, ST depression in V4 and V5, and T wave inversions in inferior and precordial leads.
- Chest radiograph revealed no acute disease.
- Lab studies showed
  - Troponin I of 3.23 ng/ml
  - White blood cell count 12,000/mm<sup>3</sup>.

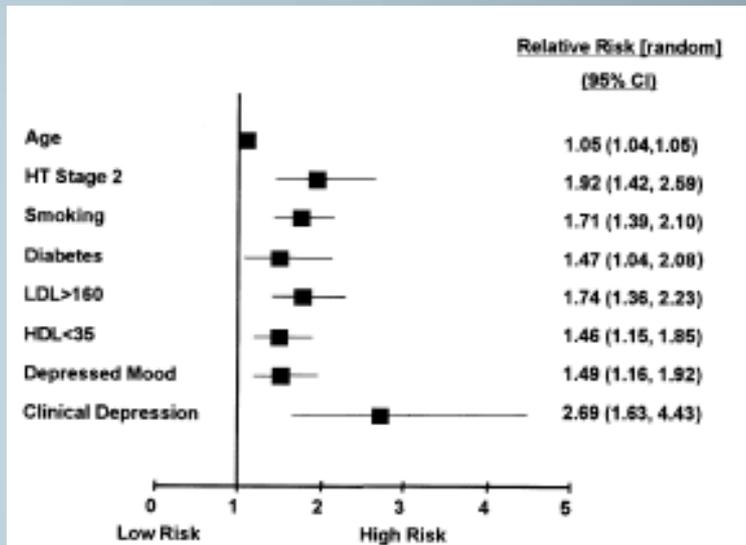
- Serum electrolytes were normal.
- She had cardiac catheterization with left ventriculography, which showed mid-anterior and apical akinesia with preserved anterobasal and posterobasal function, with an EF of 30%.

- Coronary arteries were unremarkable
- Echocardiogram showed apical akinesis with reduced LV function with EF of 34%.
- The mid septum showed marked hypertrophy with a thinned apex.

**DIAGNOSIS???**

# **TAKOTSUBO CARDIOMYOPATHY**

# Depression and CHD



**Figure 4.** The risk ratios for traditional risk factors reported for men in the Framingham study (28). The risk ratios for depressive symptoms and clinical depression are from a recent meta-analysis by Rugulies et al. (3). The risk ratios for traditional risk factors are for death due to cardiac disease, myocardial infarction, coronary artery insufficiency, and development of angina. For depressive symptoms and clinical depression, the risk ratios are for death due to cardiac disease and myocardial infarction. CI = confidence interval; HT = hypertension; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

# Anxiety and CHD

- Anxiety is characterized by heightened levels of perceived fear and nervousness— may include panic disorder, social phobia, obsessive-compulsive disorder, acute stress disorder, posttraumatic stress disorder.
- Clear relation to sudden cardiac death in a dose-dependent fashion
- 32-year follow-up of men in the Normative Aging Study who reported two or more phobic anxiety symptoms had a 3.2-fold increased risk of fatal CHD and 5.7-fold increased risk of sudden death.
- Ventricular arrhythmia may be the underlying mechanism since no relation seen between anxiety and MI. Anxious individuals also have reduced heart rate variability.

# Personality Constructs: Type A Behavior Pattern

- Began with classic work by Friedman and Rosenman on the Type A Behavior Pattern (TABP), the most widely known psychosocial risk factor, shown to be related to both CAD risk and recurrent MI; however subsequent studies showed no relationship, so this has been of diminished interest.
- The Recurrent Coronary Prevention Project did show intervention from counselling on Type A behavior to reduce recurrent MI rates and cardiac deaths (Friedman et al., Am Heart J 1986)

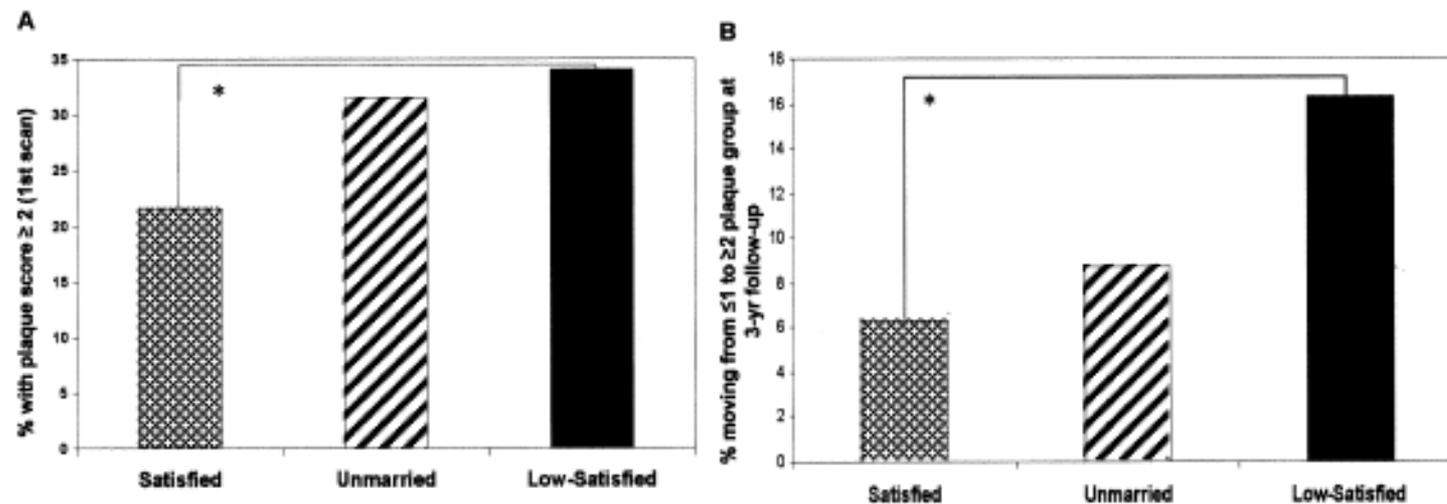
# Hostility

- Reflects emotional (anger, contempt), behavioral (verbal and physical aggression), and cognitive (cynicism, mistrust) factors.
- Predicts incident CHD in healthy individuals, even after risk factor adjustment (Niaura et al.. Health Psychol 2002).
- Hostility is associated with heightened cardiovascular reactivity and higher blood pressure.
- Higher prevalence in those with lower SES; has been suggested as a mechanism linking low SES with CVD outcomes.
- May be a stronger indicator of incident CHD than of recurrent CHD or its progression.

## **Social Relations**

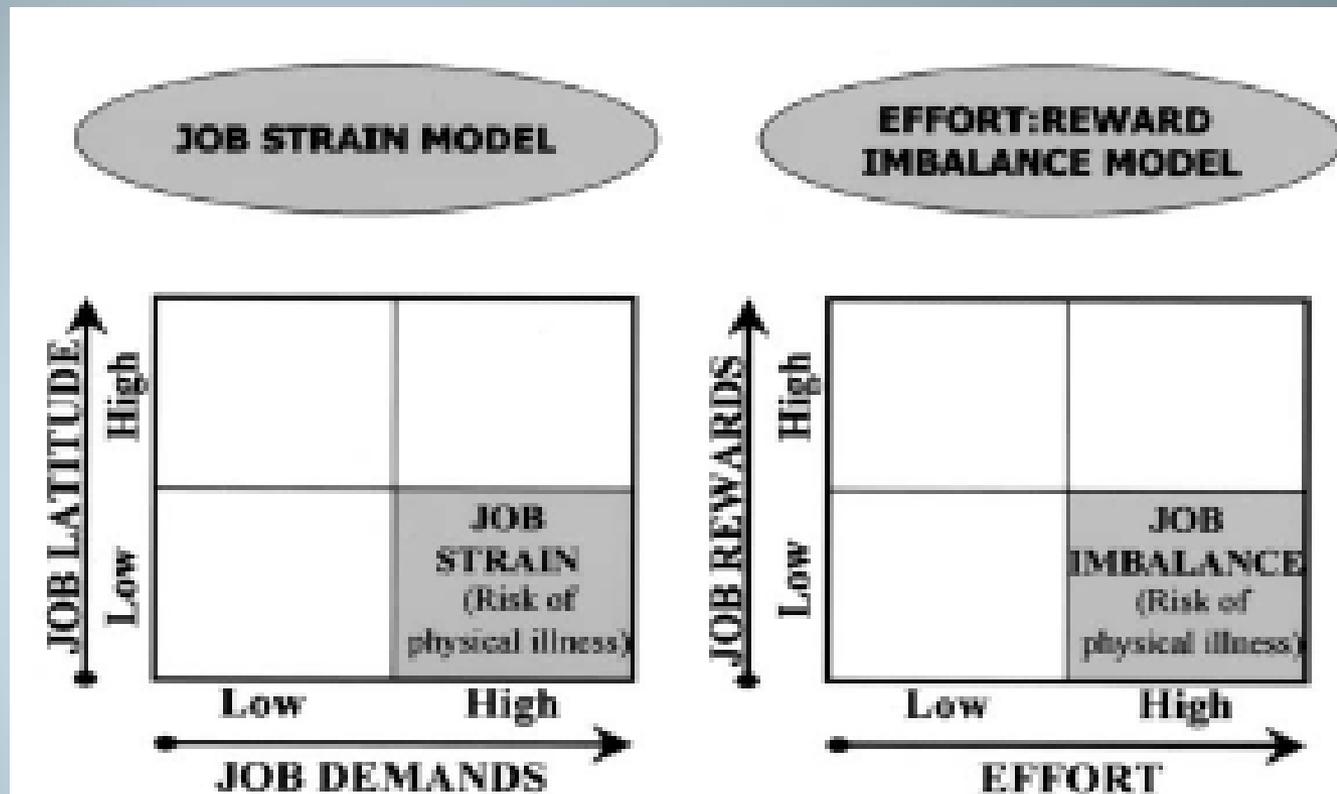
- Vast literature on social networks, social support, and CVD
- Alameda County Study showed those who lacked ties to others (index of contacts with friends and relative, marital status, and church membership) were 1.9-3.1 times more likely to die over 9 years, including from ischemic heart disease and other causes.
- A large study in Tecumseh, Michigan found a strong positive association in men, but not women between social support and mortality,. Even after adjustment for other risk factors.
- US Physicians Study showed socially isolated men had a 1.8-fold significantly greater risk of fatal CHD in multivariable analysis.

# Marriage Satisfaction and Carotid Plaque Presence and Progression



**Figure 3.** Postmenopausal females ( $n = 390$ ) were divided into those in satisfying marriages (left of each panel), unmarried (middle of each panel), and in low-satisfying marriages (right of each panel). After 11 years of follow-up, the women in satisfied marriages had the lowest and the women in unsatisfying marriages had the highest percentage of significant plaque (left panel). Serial carotid ultrasonography was performed after three years in a subgroup of this patient population ( $n = 206$ ) and revealed that women in low-satisfying marriages also had the greatest progression of plaque during follow-up (right panel). Reprinted with permission from Gallo et al. *Psychosom Med* 2003;65:952–62 (34). \*Groups differ significantly at  $p < 0.05$ .

# Conceptual Models of Work Stress



**Figure 2.** Two leading conceptual models of work stress. In the job strain model (left), the amount of job demand and decision latitude determines the degree of job strain. High demand but low decision latitude characterizes job strain. In the effort-reward imbalance model (right), increased job effort may result from either extrinsic demands or personal overcommitment, and "reward" may occur in the form of money, recognition, prestige, security, or career opportunities. High effort with low reward characterizes job imbalance.

# Job Strain and CHD

- Falk et al (Am J Pub Health 1992) showed job strain to be associated with a 2-fold increase in mortality; this was amplified when accompanied with poor social networks.
- Other studies have shown a higher prevalence of MI in those with increased job strain, and higher job control to be associated with a lower prevalence of hypertension.
- Some studies have shown no relation of job demands or strain with hypertension or elevated blood pressure.

# **Effort-Reward Imbalance (ERI)**

- This construct argues that risk is increased when workplace effort is not commensurate with tangible—eg salary or intangible—support rewards.
- Prospective studies show ERI predicts CVD incidence, even after adjustment for other risk factors.

# CASE#3

- AN EXAMPLE FROM CORPORATE WORLD

- Ranjan, just 42 years of age, was the CEO of SAP-Indian Subcontinent, the youngest CEO of an MNC in India.
- He was very active in sports, was a fitness freak and a marathon runner.
- Just after Diwali, on 21st Oct, he returned home from his gym after a workout, collapsed with a massive heart attack and died.

- It was certainly a wake-up call for corporate India.
- Ranjan was an avid marathoner ( in Feb 09, he ran Chennai Marathon), the question came as to why an exceptionally active, athletic person succumb to heart attack at 42 years of age.

**REASON????**

- Ranjan had mentioned that he faced a lot of stress, that is a common element in most of our lives.
- We used to think that by being fit, one can conquer the bad effects of stress.

- Ranjan used to make do with 4-5 hours of sleep.
- Said in an earlier interview of Ranjan on NDTV in the program 'Boss' Day Out': Boss' Day Out: Ranjan Das of SAP India

- Short sleep duration ( <5 or 5-6 hours ) increased risk for high BP by 350% to 500% compared to those who slept longer than 6 hours per night.
- Young people ( 25-49 years of age ) are twice as likely to get high BP if they sleep less.

- Individuals who slept less than 5 hours a night had a 3-fold increased risk of heart attacks.
- Complete and partial lack of sleep increased the blood concentrations of High sensitivity C-Reactive Protein (hs-cRP), the strongest predictor of heart attacks. Even after getting adequate sleep later, the levels stayed high!!

- Just one night of sleep loss increases very toxic substances in body such as Interleukin-6 (IL-6), Tumour Necrosis Factor-Alpha (TNF-alpha) and C-reactive protein (cRP).
- They increase risks of many medical conditions, including cancer, arthritis and heart disease

- Sleeping for  $\leq 5$  hours per night leads to 39% increase in heart disease. Sleeping for  $\leq 6$  hours per night leads to 8% increase in heart disease.

**Table 14-1. Selected Clinical Trials Involving Psychosocial and/or Behavioral Interventions to Reduce Cardiovascular Disease Risk**

<u>Program</u>	<u>Sample</u>	<u>Intervention</u>	<u>Major Outcome(s)</u>	<u>Secondary Outcome(s)</u>
<b>Recurrent Coronary Prevention Project</b>	<b>Post-MI cardiac patients (n=862)</b>	<b>Type A counseling (Ix) vs cardiac counseling (4.5 year program)</b>	<b>Lower recurrence of nonfatal MI at 3, 4.5 years. During final 3.5 years of Ix, fewer cardiac deaths.</b>	<b>During program: - reduced type A behavior, hostility, anger, impatience, and depression.</b>
<b>ENRICH</b>	<b>Post-MI cardiac patients (n=2481)</b>	<b>CBT-based individual and group therapy with SSRIs for severely depressed (Ix) vs usual care</b>	<b>No Ix effect on event-free survival.</b>	<b>Reduced depression and higher social support.</b>
<b>Ischemic Heart Disease Life Stress Monitoring Program</b>	<b>Post-MI cardiac patients (n=461)</b>	<b>Monthly stress monitoring and home-based nurse visits for highly distressed (Ix) vs usual care</b>	<b>2-fold higher cardiac mortality among controls. At 7 years, fewer MI recurrences.</b>	<b>No effect of Ix on general, cardiac, or elective bypass surgery readmissions during program or at follow-up.</b>
<b>Montreal Heart Attack Readjustment Trial</b>	<b>Post-MI cardiac patients (n=1376)</b>	<b>Monthly stress monitoring and home-based nurse visits vs usual care</b>	<b>No Ix effect on survival.</b>	<b>No effect of Ix on psychological factors</b>

Abbreviation: IX= intervention, LV= left ventricular, Ss = subjects CBT= cognitive behavioral therapy SSRI= selective serotonin reuptake inhibitor; from Bennett and Berkman, Preventive Cardiology 2005

## **Intervening on Depression: ENRICHD Trial (Berkman LF et al., JAMA 2003)**

- Enhancing Recovery in Coronary Heart Disease (ENRICHD) study was a multicenter randomized clinical trial of 2,481 post-MI patients
- Subjects met criteria DSM-IV criteria for major depression, minor depression with hx of major depression, or met certain criteria on a social support instrument.
- Primary endpoint of cardiovascular mortality and non-fatal recurrent MI
- Intervention involved 6 group sessions over 6 months, followed by open group membership
- Intervention did not increase event-free survival after 29 months (75.8% vs/ 75.9%). Also no differences in mortality or infarction in any of the subgroups (e.g. those isolated and depressed).
- There were, however, significant improvements in depression and social support effected by the intervention.

# Intervention Trials on Stress

- Based on the Ischemic Heart Disease Life Stress Monitoring Program, involving 461 male pts recovering from MI randomized to a stress monitoring intervention vs. usual care. Intervention involved home nursing interventions, individually tailored involving education, support, collaborative problem solving, and referral.
- After 1 year, risk of death due to cardiac causes was reduced in half, and after 7 years differences still persisted (Fraser-Smith et al, Psychosom Med 1985 and 1989).
- Montreal Heart Attack Readjustment Trial involved treatment of life stress in a larger cohort of 1376 men and women post-MI, but showed no benefit, and in fact a significant increase in cardiac and all-cause mortality among women in the intervention group (Fraser-Smith et al., The Lancet 1997).
- Those responding to the support intervention within two home visits had improved outcomes, compared to those who continued to display high levels of distress.

# Suggested open ended questions to screen for psychosocial Risk Factors

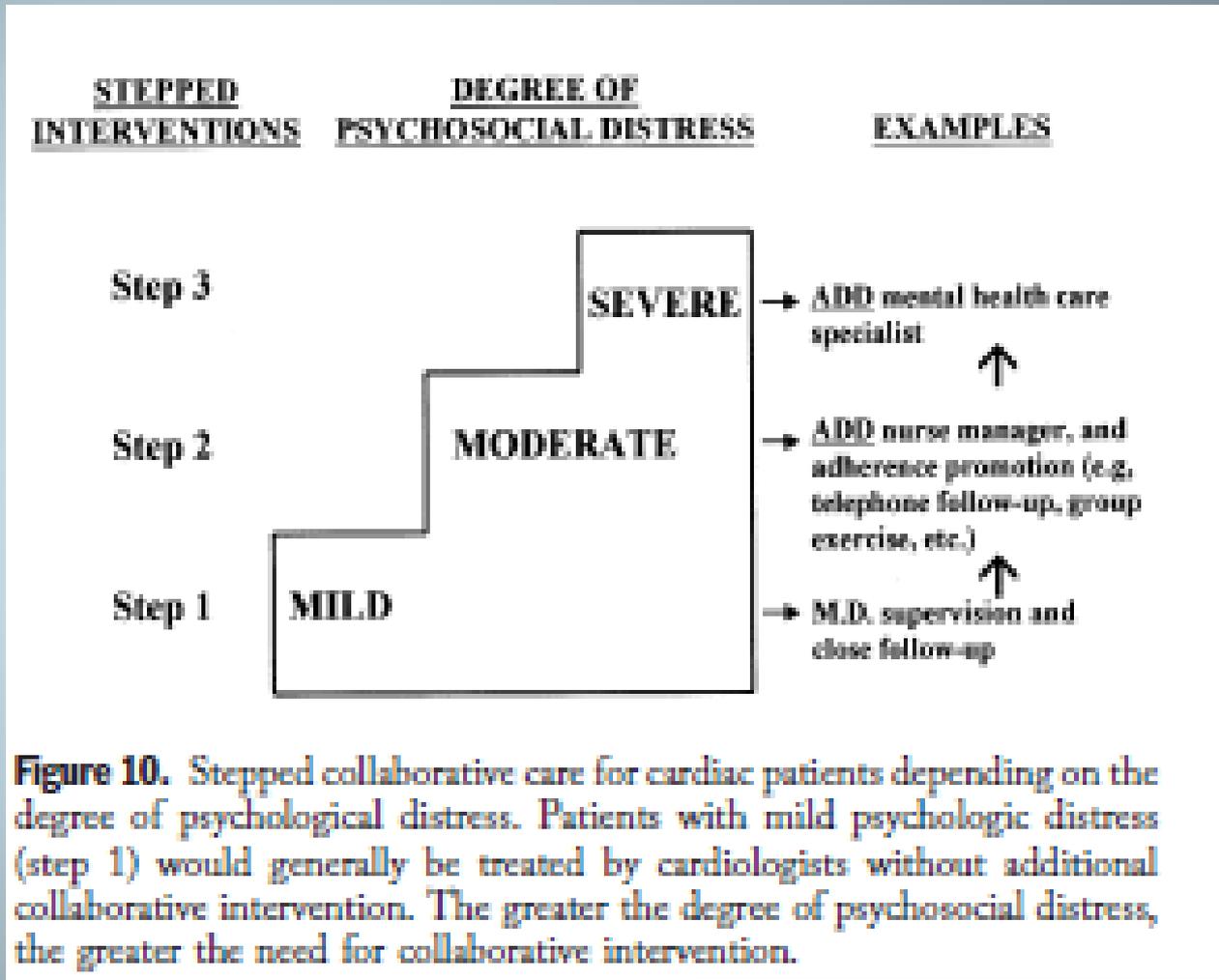
- How would you describe your energy level?
- How you being sleeping?
- How has your mood been recently?
- What kind of pressure have you been under at work or at home?
- What do you do to unwind after work or at the end of the day? Do you have difficulty unwinding?
- Who do you turn to for support?
- Are there any personal issues that we have not covered that you would like to share with me?

**Table 2.** Behavioral and Medical Interventions for Psychosocial Risk Factors

Type of Intervention	Targeted Condition	Intensity of Intervention	
		Less Intense <sup>a</sup>	More Intense
Exercise training	Psychologic distress	Exercise prescription plus general guidelines	Supervised exercise
Nutritional counseling	Management of stress by overeating	Provide nutritional advice	Supervised dietary instruction, weight management, and behavior modification
Relaxation training	General stress and stress caused by specific situations	Advise patient to initiate relaxation training; provide audiotapes, videotapes, or instructional scripts	Teach muscle relaxation, imagery, autogenic training, diaphragmatic breathing, or biofeedback.
Stress management	General stress and stress caused by specific situations	Recommend vacations, hobbies, yoga, relaxing music, pets, or pleasurable activities	Teach behavioral strategies (e.g., problem-solving, self-monitoring, appropriate goal-setting, relapse-prevention techniques)
Social support	Poor structural or functional support	Provide specific social suggestions (e.g., join walking groups or engage in socially altruistic activities)	Use staff as a support base, enroll patient in support group, or facilitate family involvement
Health information	Specific stress situations (e.g., at work or home) or low health literacy	Provide situation-specific information in form of book, articles, pamphlet, audiotapes, videotapes, or Web sites	Discuss and answer patient questions regarding materials related to health and treatment recommendations

<sup>a</sup>Most amenable to direct cardiologist management.

# Stepped Collaborative Approach for Managing Psychosocial Stress



**Figure 10.** Stepped collaborative care for cardiac patients depending on the degree of psychological distress. Patients with mild psychologic distress (step 1) would generally be treated by cardiologists without additional collaborative intervention. The greater the degree of psychosocial distress, the greater the need for collaborative intervention.

## **AHA Science Advisory on Depression (Lichtman J et al. Circulation 2008)**

- The recommendations, which are endorsed by the American Psychiatric Association, include:
  - early and repeated screening for depression in heart patients;
  - the use of two questions to screen patients – if depression is suspected the remaining questions are asked (9 questions total);
  - coordinated follow-up for both heart disease and depressive symptoms in patients who have both.

## Table 1. Patient Health Questionnaire: 2 Items\*

---

Over the past 2 weeks, how often have you been bothered by any of the following problems?

- (1) Little interest or pleasure in doing things.
  - (2) Feeling down, depressed, or hopeless.
- 

\*If the answer is “yes” to either question, then refer for more comprehensive clinical evaluation by a professional qualified in the diagnosis and management of depression or screen with PHQ-9.

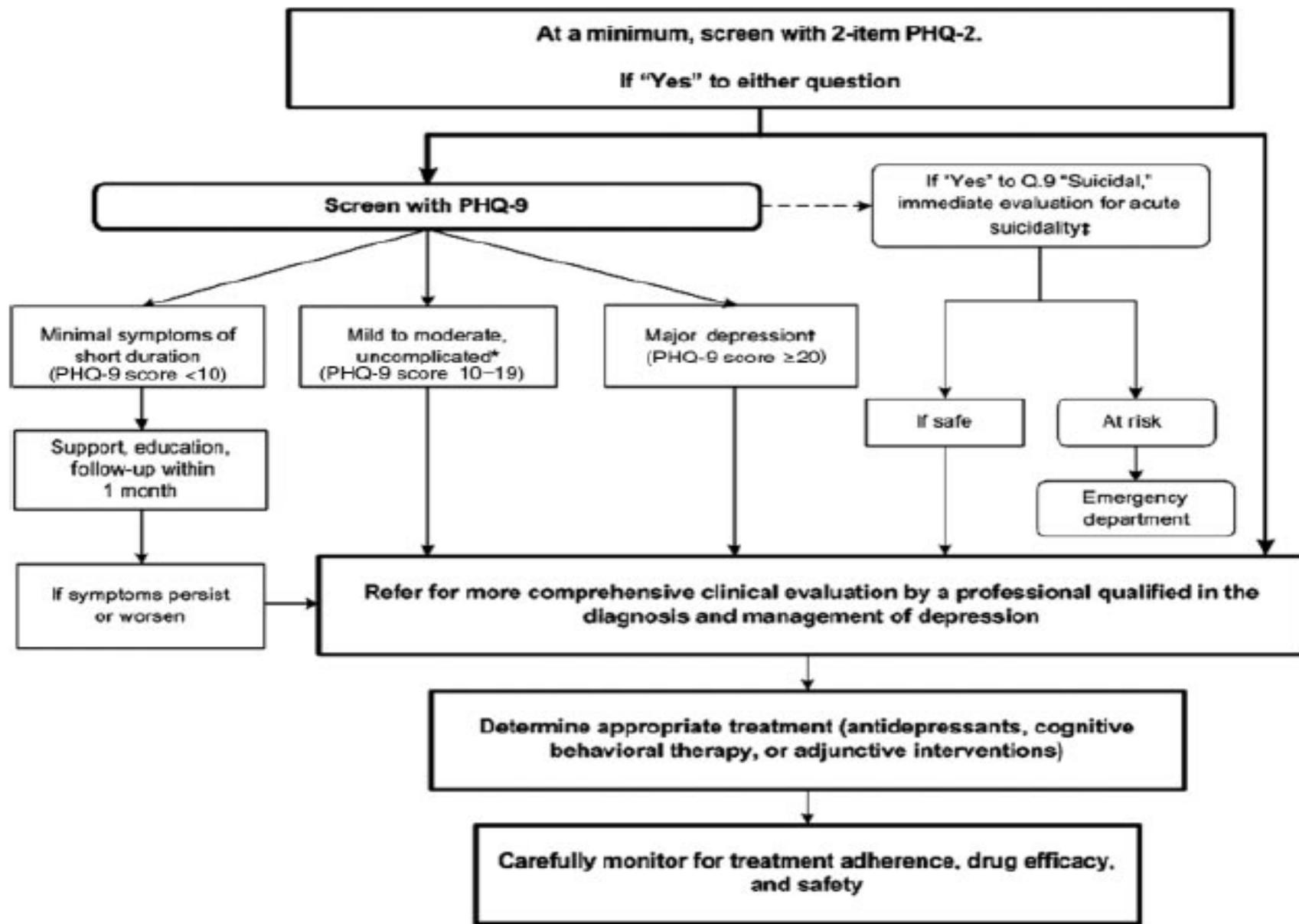
## **Table 2. Patient Health Questionnaire-9 (PHQ-9)\* Depression Screening Scales**

---

Over the past 2 weeks, how often have you been bothered by any of the following problems?

- (1) Little interest or pleasure in doing things.
  - (2) Feeling down, depressed, or hopeless.
  - (3) Trouble falling asleep, staying asleep, or sleeping too much.
  - (4) Feeling tired or having little energy.
  - (5) Poor appetite or overeating.
  - (6) Feeling bad about yourself, feeling that you are a failure, or feeling that you have let yourself or your family down.
  - (7) Trouble concentrating on things such as reading the newspaper or watching television.
  - (8) Moving or speaking so slowly that other people could have noticed. Or being so fidgety or restless that you have been moving around a lot more than usual.
  - (9) Thinking that you would be better off dead or that you want to hurt yourself in some way.
- 

\*Questions are scored: not at all=0; several days=1; more than half the days=2; and nearly every day=3. Add together the item scores to get a total score for depression severity.



# **AHA Science Advisory on Depression: Other Recommendations**

- Patients who have depressive symptoms should be evaluated by a professional qualified in diagnosing and managing depression, and should be screened for other psychiatric disorders, such as anxiety.
- Treatment options include cognitive behavioral therapy, physical activity, cardiac rehabilitation, antidepressant drugs or combinations of those treatments.
- Selective serotonin reuptake inhibitor (SSRI) treatment soon after a heart attack is considered safe, relatively inexpensive and may be effective for treating depression.
- Routine screening for depression in coronary heart disease patients should be done in multiple settings, including the hospital, physician's office, clinic and cardiac rehabilitation center, to avoid missing the opportunity to effectively treat depression in cardiac patients and improve physical health outcomes.
- Coordination of care between health providers is essential for patients with combined medical and psychiatric diagnoses.

# Summary

- Ample empirical evidence of associations between a number of psychosocial factors (including depression, anxiety, hostility, social networks and support, and occupational stress) and cardiovascular disease (CVD) morbidity and mortality.
- Adverse psychosocial characteristics tend to cluster with traditional biological and behavioral risk factors; the highest levels of psychosocial risk are generally found among the socially disadvantaged.
- Results of large-scale clinical trials of psychosocial interventions have been mixed with respect to their impact on CVD outcomes.
- Greater innovation in the consideration of psychosocial influences on cardiovascular outcomes, behavioral risk factors, and intermediary biological processes may enhance clinical efforts to improve both primary and secondary prevention outcomes.

From Bennett and Berkman, Preventive Cardiology 2005

**THANK YOU**