Behavioral Cardiology Symposium:
Clinical Overview and Treatment Strategies Related to Depression and Anxiety in Heart Disease

Quad City Health Initiative / QC Hearts and Mind Team
Robert Young Center
Trinity Regional Health System
Genesis Health System
Davenport, IA  June 12, 2012

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Cleveland Clinic
Behavioral Cardiology Symposium: Clinical Overview and Treatment Strategies Related to Depression and Anxiety in Heart Disease

Disclosure: Leopoldo Pozuelo, MD, FACP, FAPM

With respect to the following presentation, there has been no relevant (direct or indirect) financial relationship between the party listed above (and/or spouse/partner) and any for-profit company in the past 12 months which could be considered a conflict of interest.
Outline of Presentation

• Depression impact on heart disease
• Mechanistic Pathways
• Current Treatment Strategies
• Future Delivery of Care
• Break
• Case Discussions
WHO Global Burden of Disease Study (GBD)

- Projected 2020 Top 5 cause of disability using disability adjusted life years (DALY)

1. Ischemic Heart Disease
2. Unipolar Major Depression
3. Road Traffic Accidents
4. Cerebrovascular Disease
5. COPD

Prevalence of Major Depression

- MI 16%
- Unstable Angina 15%
- CHF 14%
- Catheterization 17%
- CABG 20%

—Jiang et al. Am Heart Journal July 2005
Prospective Depression Studies:

In HEALTHY individuals + depression
Develop CAD morbidity

In CARDIOVASCULAR individuals + depression
Worsening CAD morbidity
Prospective Depression Studies

In HEALTHY individuals
+ depression
Develop CAD morbidity
INTERHEART study

- Attributable risk factors (prevalence of risk factor, and size of the increase in risk) to MI in 52 countries
- 15,000 case controlled studies
  - Lifetime smoking (37.5%)
  - Psychosocial factors (depression, stress, low generalized locus of control) (32.5%)
  - Hypertension and Obesity (< 30 %)

*Lancet* 2004
Prospective Depression Studies

In CARDIOVASCULAR individuals + depression → Worsening CAD morbidity
Frasure-Smith Land Mark Study

Frasure-Smith N et al. *JAMA*. 1993

- **Depressed (n = 35)**
- **Nondepressed (n = 187)**

Mortality (%) over Months After Heart Attack
Depression and long term mortality risk in CAD patients


N = 1250
Background: AHA Recommendation 2008

AHA Science Advisory

Depression and Coronary Heart Disease
Recommendations for Screening, Referral, and Treatment
A Science Advisory From the American Heart Association Prevention Committee of the Council on Cardiovascular Nursing, Council on Clinical Cardiology, Council on Epidemiology and Prevention, and Interdisciplinary Council on Quality of Care and Outcomes Research
Endorsed by the American Psychiatric Association
Judith H. Lichman, PhD, MPH, Co-Chair; J. Thomas Bigger, Jr, MD; James A. Blumenthal, PhD, ABPP; Nancy Brauner-Smith, PhD; Peter G. Kuhlmann, PhD; François Lespérance, MD; Daniel B. Mark, MD, MPH; David S. Sheps, MD, MSPH; C. Barr Taylor, MD; Erika Sivarajan Froelicher, RN, MA, MPH, PhD, Co-Chair

Abstract—Depression is commonly present in patients with coronary heart disease (CHD) and is independently associated with increased cardiovascular morbidity and mortality. Screening tests for depressive symptoms should be applied to identify patients who may require further assessment and treatment. This multispecialty consensus document reviews the evidence linking depression with CHD and provides recommendations for healthcare providers for the assessment, referral, and treatment of depression. (Circulation, 2008;118:1768-1775.)

Key Words: AHA Scientific Statement • depression • coronary disease • psychosocial factors • assessment, patient outcomes

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Cleveland Clinic

4th Annual QC Hearts and Mind Symposium | June 12, 2012 | 12
Does the same hold for Anxiety in Heart Disease?

In HEALTHY individuals + Anxiety Does the same hold for Anxiety in Heart Disease?

In CARDIOVASCULAR individuals + Anxiety Does the same hold for Anxiety in Heart Disease?

Develop Heart Disease?

Worsening Heart Disease?
Anxiety and Risk of Incident Coronary Heart Disease
A Meta-Analysis

Annelieke M. Roest, MSc,* Elisabeth J. Martens, PhD,* Peter de Jonge, PhD,*† Johan Denollet, PhD*
Tilburg and Groningen, the Netherlands

Objectives The purpose of this study was to assess the association between anxiety and risk of coronary heart disease (CHD).

Background Less research has focused on the association of anxiety with incident CHD in contrast to other negative emotions, such as depression.

Methods A meta-analysis of references derived from PubMed, EMBASE, and PsycINFO (1980 to May 2009) was performed without language restrictions. End points were cardiac death, myocardial infarction (MI), and cardiac events. The authors selected prospective studies of (nonpsychiatric) cohorts of initially healthy persons in which anxiety was assessed at baseline.

Results Twenty studies reporting on incident CHD comprised 249,846 persons with a mean follow-up period of 11.2 years. Anxious persons were at risk of CHD (hazard ratio [HR] random: 1.26; 95% confidence interval [CI]: 1.15 to 1.38; p < 0.0001) and cardiac death (HR: 1.48; 95% CI: 1.14 to 1.92; p = 0.003), Independent of demographic variables, biological risk factors, and health behaviors. There was a nonsignificant trend for an association between anxiety and nonfatal MI (HR: 1.43; 95% CI: 0.85 to 2.40; p = 0.180). Subgroup analyses did not show any significant differences regarding study characteristics, with significant associations for different types of anxiety, short- and long-term follow-up, and both men and women.

Conclusions Anxiety seemed to be an independent risk factor for incident CHD and cardiac mortality. Future research should examine the association between anxiety and CHD with valid and reliable anxiety measures and focus on the mechanisms through which anxiety might affect CHD.

(J Am Coll Cardiol 2010;56:38–46) © 2010 by the American College of Cardiology Foundation
Scared to Death? Generalized Anxiety Disorder and Cardiovascular Events in Patients With Stable Coronary Heart Disease

The Heart and Soul Study

Elisabeth J. Martens, PhD; Peter de Jonge, PhD; Becya Na, MPH; Beth E. Cohen, MD, MAS; Heather Lett, PhD; Mary A. Whooley, MD

Context: Anxiety is common in patients with coronary heart disease (CHD), but studies examining the effect of anxiety on cardiovascular prognosis and the role of potential mediators have yielded inconsistent results.

Objectives: To evaluate the effect of generalized anxiety disorder (GAD) on subsequent cardiovascular events and the extent to which this association is explained by cardiac disease severity and potential behavioral or biological mediators.

Design: Prospective cohort study (Heart and Soul Study).

Setting: Participants were recruited between September 11, 2000, and December 20, 2002, from 12 outpatient clinics in the San Francisco Bay Area and were followed up until March 18, 2009.

Participants: One thousand fifteen outpatients with stable CHD followed up for a mean (SD) of 5.6 (1.8) years.

Main Outcome Measures: We determined the presence of GAD using the Diagnostic Interview Schedule. Proportional hazards models were used to evaluate the association of GAD with subsequent cardiovascular events and the extent to which this association was explained by potential confounders and mediators.

Results: A total of 371 cardiovascular events occurred during 5711 person-years of follow-up. The age-adjusted annual rate of cardiovascular events was 9.6% in the 106 participants with GAD and 6.6% in the 900 participants without GAD (P = .03). After adjustment for demographic characteristics, comorbid conditions (including major depressive disorder), cardiac disease severity, and medication use, GAD remained associated with a 62% higher rate of cardiovascular events (hazard ratio, 1.62; 95% confidence interval, 1.11-2.37; P = .01). Additional adjustment for a variety of potential behavioral and biological mediators had little effect on this association (hazard ratio, 1.74; 95% confidence interval, 1.13-2.67; P = .01).

Conclusions: In outpatients with CHD, a robust association between GAD and cardiovascular events was found that could not be explained by disease severity, health behaviors, or biological mediators. How GAD leads to poor cardiovascular outcomes deserves further study.

Arch Gen Psychiatry. 2010;67(7):750-758
Anxiety and Cardiovascular Events / Arrhythmia

**Abstract**

**Background:** The Fédération Internationale de Football Association (FIFA) World Cup, held in Germany from June 9 to July 9, 2006, provided an opportunity to examine the relation between emotional stress and the incidence of cardiovascular events.

**Methods:** Cardiovascular events occurring in patients in the greater Munich area were prospectively assessed by emergency physicians during the World Cup. We compared these events with events that occurred during the control period: May 1 to June 8 and July 30 to July 31, 2006, and Aug 1 to July 31 in 2005 and 2007.

**Results:** Acute cardiovascular events were assessed in 4797 patients. On days of conflict involving the German team, the incidence of cardiovascular events was 2.66 times that during the control period (95% confidence interval [CI], 1.23 to 5.38; 0.04 to 8.88); for men, the incidence was 2.26 times that during the control period (95% CI, 1.32 to 3.84; 0.04 to 8.88), and for women, it was 3.26 times that during the control period (95% CI, 1.48 to 6.85; P = 0.000). Among patients with coronary events on days when the German team played, the proportion with known coronary heart disease was 45.7%, as compared with 30.8% of patients with events during the control period. On those days, the highest incidence of events was observed during the first 2 hours after the beginning of each match. A similar pattern of serious events during that period, as compared with the control period, showed no increase in the incidence of myocardial infarction with 95% confidence interval without statistically significant or consistent increase by a factor of 2.45 (95% CI, 1.47 to 4.12) of myocardial infarction without 95% confidence interval or consistent increase by a factor of 3.07 (95% CI, 2.32 to 3.86) of coronary artery disease among major symptoms by a factor of 3.07 (95% CI, 2.32 to 3.86) of coronary artery disease among major symptoms by a factor of 3.07 (95% CI, 2.32 to 3.86).

**Conclusions:** Vehement soccer matches more than double the risk of an acute cardiovascular event. In view of this increased risk, particularly in men with known coronary heart disease, preventive measures are urgently needed.

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**Figure 1.** Daily Cardiovascular Events during the Study Population from May 1 to July 31 in 2003, 2005, and 2006.

The FIFA World Cup 2006 in Germany started on June 9, 2006, and ended on July 9, 2006. The 2006 World Cup matches with German participation are indicated by numbers 1 through 2: match 1, Germany versus Costa Rica; match 2, Germany versus Poland; match 3, Germany versus Ecuador; match 4, Germany versus Sweden; match 5, Germany versus Argentina; match 6, Germany versus Italy; and match 7, Germany versus Portugal (for third-place standing). Match 8 was the final match, Italy versus France.
• Effects of Emotional Stress

ABSTRACT

BACKGROUND
Reversible left ventricular dysfunction precipitated by emotional stress has been reported, but the mechanism remains unknown.

METHODS
We evaluated 19 patients who presented with left ventricular dysfunction after a sudden emotional stress. All patients underwent coronary angiography and serial echocardiography. Five underwent endomyocardial biopsy. Plasma catecholamine levels in 13 patients with stress-induced myocardial dysfunction were compared with those in 7 patients with idiopathic dilated cardiomyopathy.

RESULTS
The mean age of patients with stress-induced cardiomyopathy was 63 years, and 95 percent were women. Clinical presentations included chest pain, pulmonary edema, and cardiogenic shock. Diffuse T-wave inversion and a prolonged QT interval occurred in most patients. Seventeen patients had mildly elevated serum troponin I levels, but only 1 of 19 had an angiographic evidence of clinically significant coronary disease. Severe left ventricular dysfunction was present at admission (median ejection fraction, 0.20; interquartile range, 0.15 to 0.30) and rapidly resolved in all patients (ejection fraction at two to four weeks, 0.60 [interquartile range, 0.55 to 0.65]; P<0.001). Endomyocardial biopsy showed mononuclear infiltrates and contraction band necrosis. Plasma catecholamine levels at presentation were markedly raised among patients with stress-induced cardiomyopathy than among those with idiopathic dilated cardiomyopathy. (normal range, 34 to 376 pg per milliliter [interquartile range, 47 to 275]; norepinephrine level, 224 pg per milliliter [interquartile range, 270 to 290]; 1129 pg per milliliter [interquartile range, 106 to 304]; and dopamine level, 301 pg per milliliter [interquartile range, 106 to 134]; 0.05 for all comparisons).

CONCLUSIONS
Emotional stress can precipitate severe, reversible left ventricular dysfunction in patients without coronary disease. Exaggerated sympathetic stimulation is probably central to the cause of this syndrome.
“Takotsubo”

Fishing pot

narrow neck with wide base to hold octopus

Figure 3. Ventriculographic Assessment of Cardiac Function and MRI Assessment of Myocardial Viability at Admission in a Patient with Stress Cardiomyopathy.

Contrast-enhanced ventriculography during diastole, in Panel A, and systole, in Panel B, demonstrates apical and mid-ventricular akinesis, with relative sparing of the base of the heart (arrow). In Panel C, MRI in the long-axis view reveals that the akinetic regions seen on ventriculography are dark and hypoenhanced, consistent with the presence of viable myocardium. Panel D, which is presented for purposes of comparison, shows hyperenhancement (arrow), indicative of necrosis and decreased viability, after an acute anterior myocardial infarction.
Epidemiology and Prevention

Risk of Acute Myocardial Infarction After the Death of a Significant Person in One’s Life
The Determinants of Myocardial Infarction Onset Study

Elizabeth Mostofsky, MPH, ScD; Malcolm Maclure, ScD; Jane B. Sherwood, RN; Geoffrey H. Tofler, MD; James E. Muller, MD; Murray A. Mittleman, MD, DrPH

Background—Acute psychological stress is associated with an abrupt increase in the risk of cardiovascular events. Intense grief in the days after the death of a significant person may trigger the onset of acute myocardial infarction (MI), but this relationship has not been systematically studied.

Methods and Results—We conducted a case-crossover analysis of 1985 participants from the multicenter Determinants of Myocardial Infarction Onset Study interviewed during index hospitalization for an acute MI between 1989 and 1994. We compared the observed number of deaths in the days preceding MI symptom onset with its expected frequency based on each patient’s control information, defined as the occurrence of deaths in the period from 1 to 6 months before infarction. Among the 1985 subjects, 270 (13.6%) experienced the loss of a significant person in the prior 6 months, including 19 within 1 day of their MI. The incidence rate of acute MI onset was elevated 21.1-fold (95% confidence interval, 13.1–34.1) within 24 hours of the death of a significant person and declined steadily on each subsequent day. The absolute risk of MI within 1 week of the death of a significant person is 1 excess MI per 1394 exposed individuals at low (5%) 10-year MI risk and 1 per 320 among individuals at high (20%) 10-year risk.

Conclusions—Grief over the death of a significant person was associated with an acutely increased risk of MI in the subsequent days. The impact may be greatest among individuals at high cardiovascular risk. (Circulation. 2012;125:491-496.)

Key Words: bereavement ■ crossover studies ■ epidemiology ■ myocardial infarction
Outline of Presentation

• Depression impact on heart disease
• Mechanistic Pathways
• Current Treatment Strategies
• Future Delivery of Care
• Break
• Case Discussions
Proposed Mechanistic Pathways
Measurement of Autonomic Tone

Table 1. Practical Clinical Indicators of Abnormal Cardiac Autonomic Function

<table>
<thead>
<tr>
<th>Indicator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resting heart rate greater than 90 beats/min</td>
</tr>
<tr>
<td>Inability to achieve 85% of predicted maximal heart rate on treadmill testing</td>
</tr>
<tr>
<td>Abnormal heart rate recovery (failure to decrease heart rate &gt;12 beats/min during the first minute after peak exercise)</td>
</tr>
<tr>
<td>Abnormal heart rate variability (failure to change heart rate, R-R interval, by ≥10 beats/min during 1 minute of slow deep breaths)</td>
</tr>
</tbody>
</table>

*Mayo Proceedings, 2002*
Heart Rate Recovery (HRR) as Prognostic Factor

Watanabe, Lauer. Circulation 2001;104:1911-1917
Depression and decreased HRR

- Stress test
- Heart Rate Recovery over 2 min
- Beck Depression Inventory

Vagal Tone implications

PTSD

Depression

Psychiatric Medications / Disorders

↓ Cardiac Function
↑ Heart Failure & Death

↓ Vagal Tone

↓ Heart Rate Variability
↓ Heart Rate Recovery

↑ Systemic Inflammation

↑ Plaque Rupture & Acute Coronary Syndrome

↑ Arterial Inflammation
Parasympathetic Tone and Inflammation

Outline of Presentation

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• Current Treatment Strategies
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• Case Discussions
### Screening Instruments for Depression

#### PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use “0” to indicate your answer)

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by any of the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or eating less</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

**Total Score:**

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

<table>
<thead>
<tr>
<th>Not difficult at all</th>
<th>Somewhat difficult</th>
<th>Very difficult</th>
<th>Extremely difficult</th>
</tr>
</thead>
</table>
# Screening Instruments for Anxiety

## GAD-7

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by the following problems? (Use &quot;✓&quot; to indicate your answer)</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Feeling nervous, anxious or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Worrying too much about different things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Trouble relaxing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Being so restless that it is hard to sit still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Becoming easily annoyed or irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Feeling afraid as if something awful might happen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

*(For office coding: Total Score T = ___ + ___ + ___)*

[www.phqscreeners.com](http://www.phqscreeners.com)
Screening Anxiety and Depression

<table>
<thead>
<tr>
<th>PHQ-4</th>
<th>Over the last 2 weeks, how often have you been bothered by the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Feeling nervous, anxious or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2.</td>
<td>Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3.</td>
<td>Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
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<td>4.</td>
<td>Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

*(For office coding: Total Score $T = ___ + ___ + ___)*

[www.phqscreeners.com](http://www.phqscreeners.com)
How to Build a Clinic

Site Matters: Winning the Hearts and Mind of Patients in a Cardiology Clinic

Phase I referral to psychiatry clinic

Phase II seen in cardiology clinic

PHQ were 6.38 / 6.80
Consultation Clinics

• **CBHC** (Cardiovascular Behavioral Health Clinic)
  - 2005, Located in the Cardiac Rehab offices
  - All Cardiac Rehab and Preventive Cardiology adm SF-36
  - Low MCS (mental composite score) trip a flag in the EMR to refer to the CHBC..
  - One psychiatrist, two half days a week

• **ABHC** (Arrhythmia Behavioral Health Clinic)
  - 2008, Located in the Device Clinic
  - Referrals from Device and EP clinicians
  - No prescreening or pop up in the EMR
  - One psychiatrists, two psychologists, one half day a week
Cardiovascular Behavioral Health Clinics at Cleveland Clinic

![Bar chart showing new consults and follow-ups from 2005 to 2011.](image-url)
SSRI

• Fluoxetine 20 – 40 mg (long half life)
• Sertraline ** 50 – 150 mg
• Paroxetine 20 – 40 mg
• Citalopram ** 30 – 40 mg
• Escitalopram ** 10- 20 mg

** Use on consult service due to less drug-drug interactions
Celexa (citalopram hydrobromide): Drug Safety Communication - Abnormal Heart Rhythms Associated With High Doses

[Posted 08/24/2011]

AUDIENCE: Psychiatry, Cardiology

ISSUE: FDA notified healthcare professionals and patients that the antidepressant Celexa (citalopram hydrobromide) should no longer be used at doses greater than 40 mg per day because it can cause abnormal changes in the electrical activity of the heart. Changes in the electrical activity of the heart (prolongation of the QT interval of the electrocardiogram [ECG]) can lead to an abnormal heart rhythm (including Torsade de Pointes), which can be fatal. Patients at particular risk for developing prolongation of the QT interval include those with underlying heart conditions and those who are predisposed to low levels of potassium and magnesium in the blood.

Studies did not show a benefit in the treatment of depression at doses higher than 40 mg per day. Previously, the citalopram drug label stated that certain patients may require a dose of 60 mg per day. The citalopram drug label has been revised to include the new drug dosage and usage recommendations, as well as information about the potential for QT interval prolongation and Torsade de Pointes. See the FDA Drug Safety Communication Data Summary for additional information.

BACKGROUND: Celexa (citalopram hydrobromide) is in a class of antidepressants called selective serotonin reuptake inhibitors (SSRIs).

RECOMMENDATION: Citalopram causes dose-dependent QT interval prolongation. Citalopram should no longer be prescribed at doses greater than 40 mg per day. Citalopram should not be used in patients with congenital long QT syndrome. Patients with congestive heart failure, bradycardia, or abnormal heart rhythms.
Older Antidepressants

- **Tricyclic Antidepressants (TCA)**
  - First Generation Tricyclics
    - Amirtiptyline, Doxepin
    - Highly anticholinergic, hypotensive, sedating
  - Second Generation Tricyclics
    - Desipramine, Nortiptyline
    - Less anticholinergic, hypotensive, sedating
## Classification of Antidepressants

- **(∗) Good for both depression AND anxiety**

<table>
<thead>
<tr>
<th>Serotonergic</th>
<th>Dual Acting</th>
<th>Dopamine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>TCAs (amitriptyline)</td>
<td>Bupropion</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Venlafaxine</td>
<td></td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Duloxetine</td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>Desvenlafaxine</td>
<td></td>
</tr>
<tr>
<td>Escitalopram</td>
<td>Mirtazapine</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(serotonin and NE)</td>
<td>(some NE kick)</td>
</tr>
</tbody>
</table>
**Antidepressants to use in Cardiac Patients**

(* Good for both depression AND anxiety *)

<table>
<thead>
<tr>
<th>Serotonergic</th>
<th>Dual Acting (serotonin and NE)</th>
<th>Dopamine (some NE kick)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sertraline</td>
<td>Duloxetine + Mirtazapine ++</td>
<td>Bupropion</td>
</tr>
<tr>
<td>Citalopram*</td>
<td>*</td>
<td></td>
</tr>
<tr>
<td>Escitalopram</td>
<td>+ (mild interaction BB) + +</td>
<td></td>
</tr>
<tr>
<td>* (&lt; / = 40mg)</td>
<td>+ (weight gain)</td>
<td></td>
</tr>
</tbody>
</table>
Length of Treatment

Severity

Symptoms

“Normalcy”

Syndrome

Response

Progression to disorder

Treatment Phases

Acute (6-12 weeks)

Continuation (4-5 months)

Maintenance (≥1 year)

Time

Remission

Recovery

Relapse

Recurrence

**Rx Pearls**

- **PRN use of Benzodiazepine**
  - Acute, vs Chronic, Benefit Risk
  - Prescriber Comfort

- **Anxious Patient**
  - Titrate up slowly antidepressant to decrease activation
  - Wellbutrin only one not front line
  - May add short term benzodiazepine in first couple weeks
    - **Lorazepam** 0.5-1.0 mg bid, **Clonazepam** 0.5 mg bid
    - **Alprazolam**, 0.25 tid,
  - Buspirone not effective for acute panic attacks
Benzodiazepine oral equivalencies

- Librium  10 mg
- Valium    5 mg *
- Ativan    1 mg *
- Klonopin  0.5 mg
- Xanax     0.25 mg

* remember , IV twice as powerful as po

0.5mg IV Ativan = 1mg po Ativan
"Normalcy"

Symptoms

Response

Remission

Recovery

Relapse

Recurrence

Severity

Syndrome

Treatment Phases

Acute (6-12 weeks)

Continuation (4-5 months)

Maintenance (≥1 year)

Time


Cleveland Clinic
Psychotherapy

Cognitive Behavioral Therapy (CBT)

- Identify and alter negative thinking patterns
- Promote healthier behaviors
- Coaching Technique
- Validated
CBT techniques

• **Decrease** the *anticipatory* catastrophic thinking
• **Improve** the *avoidant behaviors* and helplessness
• Use relaxation techniques
• Short course, focusing on the here and now
Exercise

• Physical Health Effects
• Emotional Health Effects
• Restores HRV balance
• Other unforeseen benefits
Cleveland Clinic Cardiac Rehabilitation Data (N = 4601)
Depressive Symptoms, Health Behaviors, and Risk of Cardiovascular Events in Patients With Coronary Heart Disease

Mary A. Whooley, MD
Peter de Jonge, PhD
Eric Wittinghoff, PhD
Christian Otto, MD
Rudolf Moos, PhD
Robert M. Carney, PhD
Sadia Ali, MD, MPH
Sumania Dowray, MPH
Becya Na, MPH
Mitchell D. Feldman, MD, MPH
Nelson B. Schiller, MD
Warren S. Browner, MD, MPH

Depression has long been recognized as a risk factor for the development of cardiovascular disease in healthy patients, for recurrent events in patients with established cardiovascular disease, and for adverse outcomes after coronary bypass graft surgery. Depression is also a risk factor for the development of heart failure and for adverse outcomes in patients with existing heart failure.1-4 In a recent survey of 245,404 adults from 60 countries, patients with comorbid depression reported worse overall health than those with asthma, diabetes, arthritis, or cardiovascular disease alone.5 Based on the results of this study, the World Health Organization highlighted the detrimental effects of depression on medical illnesses as one of its 10 most important global public health statistics for 2007.6

Despite the substantial body of evidence demonstrating a strong link between depression and cardiovascular disease, the explanation for this association remains unclear. Several candidate mechanisms have been suggested as potential mediators, including smoking, lack of exercise, medication nonadherence,13 worse underlying cardiac disease severity,14 lower heart rate variability,17 antidepressant toxicity,18 enhanced activity of the hypothalamic-pituitary axis,19 greater catecholamine levels,20 dietary factors, low omega-3 fatty acid levels,21 increased serotonin and platelet activation,22 and inflammatory

Context: Depressive symptoms predict adverse cardiovascular outcomes in patients with coronary heart disease, but the mechanisms responsible for this association are unknown.

Objective: To determine why depressive symptoms are associated with an increased risk of cardiovascular events.

Design and Participants: The Heart and Soul Study is a prospective cohort study of 1017 outpatients with stable coronary heart disease followed up for a mean (SD) of 4.8 (1.4) years.

Setting: Participants were recruited between September 11, 2000, and December 20, 2002, from 12 outpatient clinics in the San Francisco Bay Area and were followed up to January 12, 2008.

Main Outcome Measures: Baseline depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-2). We used proportional hazards models to evaluate the extent to which the association of depressive symptoms with subsequent cardiovascular events (heart failure, myocardial infarction, stroke, transient ischemic attack, or death) was explained by baseline disease severity and potential biological or behavioral mediators.

Results: A total of 341 cardiovascular events occurred during 4876 person-years of follow-up. The age-adjusted annual rate of cardiovascular events was 10.0% among the 199 participants with depressive symptoms (PHQ score \( \geq 10 \)) and 6.7% among the 818 participants without depressive symptoms (hazard ratio [HR], 1.50; 95% confidence interval, [CI], 1.16-1.95; \( P = .002 \)). After adjustment for comorbid conditions and disease severity, depressive symptoms were associated with a 31% higher rate of cardiovascular events (HR, 1.31; 95% CI, 1.00-1.71; \( P = .04 \)). Additional adjustment for potential biological mediators attenuated this association (HR, 1.24; 95% CI, 0.94-1.63; \( P = .12 \)). After further adjustment for potential behavioral mediators, including physical inactivity, there was no significant association (HR, 1.05; 95% CI, 0.79-1.40; \( P = .75 \)).

Conclusion: In this sample of outpatients with coronary heart disease, the association between depressive symptoms and adverse cardiovascular outcomes was largely explained by behavioral factors, particularly physical inactivity.

www.jama.com

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Heart and Soul Study JAMA Nov 26, 2008

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% Confidence Interval)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depressive symptoms&lt;sup&gt;a&lt;/sup&gt;</td>
<td>1.05 (0.79-1.40)</td>
<td>.75</td>
</tr>
<tr>
<td>Age per 10-y increase</td>
<td>1.72 (1.52-1.94)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Medical history</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.06 (0.83-1.34)</td>
<td>.64</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.76 (1.38-2.25)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.31 (0.98-1.75)</td>
<td>.07</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1.27 (0.96-1.67)</td>
<td>.09</td>
</tr>
<tr>
<td>Left ventricular ejection fraction per 10% decrease</td>
<td>1.40 (1.26-1.56)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Log C-reactive protein per SD increase</td>
<td>1.27 (1.13-1.43)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Current smoking</td>
<td>1.39 (1.17-1.66)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Medication nonadherence</td>
<td>1.90 (1.31-2.76)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Physical inactivity&lt;sup&gt;b&lt;/sup&gt;</td>
<td>1.44 (1.14-1.82)</td>
<td>.002</td>
</tr>
</tbody>
</table>

<sup>a</sup>A score of 10 or higher on the Patient Health Questionnaire.

<sup>b</sup>Not at all or a little vs fairly, quite, very, or extremely active.
Heart and Soul Study JAMA Nov 26, 2008

- Depressive symptoms predict adverse cardiovascular events (ACE) in CAD pt, but mechanism unknown
- Depressive symptoms were associated with a 31% higher rate of ACE
  - Adjust for potential BIOLOGICAL mediators, the risk is 24%
  - Adjust for potential BEHAVIORAL mediators, the risk is 5%
- The association depression and ACE was largely explained by behavioral factors, particularly physical inactivity
Outline of Presentation

• Depression impact on heart disease
• Mechanistic Pathways
• Current Treatment Strategies
  • Future Delivery of Care
• Break
• Case Discussions
Successful Projects Lead to Community Impact

Relationship to QCHI: QCHI Project

Project Description: To help Quad Citizens live healthy from the inside out.

Target Audience: All residents of the Quad Cities.

Start Date/Current Status: The project team assembled in June 2008 and has created a collaborative plan for action. Team Workgroups will implement the plan for the benefit of all the residents of the Quad Cities.

Project Goals and Objectives:

1. Increase the community’s understanding of mental health/mental illness and thus reduce the stigma associated with mental health care
2. Preserve and increase access to care for persons with mental illness
3. Promote mental health as integral to our overall health and well-being

Project Performance/ Accomplishments:

Through joint planning exercises the group has selected four issues for development: Public Awareness & Community Education, Service Trailblazers, Youth, and Medical Integration.
Collaborative Care for Patients with Depression and Chronic Illnesses

Wayne J. Katon, M.D., Elizabeth H.B. Lin, M.D., M.P.H., Michael Von Korff, Sc.D., Paul Ciechanowski, M.D., M.P.H., Evette J. Ludman, Ph.D., Bessie Young, M.D., M.P.H., Do Peterson, M.S., Carolyn M. Rutter, Ph.D., Mary McGregor, M.S.N., and David McCulloch, M.D.
The Bypassing the Blues trial: Collaborative care for post-CABG depression and implications for future research

ABSTRACT

Depressive symptoms are reported by up to one-half of patients following coronary artery bypass graft (CABG) surgery, and are associated with numerous adverse outcomes, including poorer health-related quality of life, worse functional status, and delayed recovery. Strategies to detect and then manage depression in CABG patients and in cardiac populations are of great interest given the potential for depressive treatment to reduce cardiovascular morbidity. Yet, many tested interventions have had little or no effect on mood symptoms in cardiac patients. "Collaborative care" is a safe and proven-effective strategy for treating depression is conceptually consistent with patients' primary care physicians, however, has not been tested previously in patients with cardiac disease. This article presents the design and main outcome findings from the National Institutes of Health-funded Bypassing the Blues study, the first trial to examine the impact of a collaborative care strategy for treating depression among patients with cardiac disease, and our efforts to improve upon and expand the model for treating other cardiac conditions.

Coronary artery bypass graft (CABG) surgery is one of the most common and costly medical procedures performed in the United States. However, up to one-half of post-CABG patients report significant increases in mood symptoms following surgery, and these individuals are more likely to report poorer health-related quality of life (HRQOL) and worse functional status.1-4 To experience either improved QOL and discharge from the hospital or to experience either reduced depression and improved QOL, despite satisfactory surgical results. Strategies to detect and then manage depression in CABG patients and in cardiac populations are of great interest given the potential for depressive treatment to reduce cardiovascular morbidity. Yet, the Advisory Council on Mental Health Care has advocated regular screening and treatment of cardiac patients for depression.5,6 For patients with heart disease, there is an increased risk of suicide and depression.7-11 The present study is the first to examine the impact of a collaborative care strategy for treating depression among patients with cardiac disease, and our efforts to improve upon and expand the model for treating other cardiac conditions.

In recognition of the prevalence and serious burden associated with this condition, a recent American Heart Association (AHA) Science Advisory has advocated regular screening and treatment of cardiac patients for depression.6 For patients with cardiac disease, there is an increased risk of suicide and depression.7-11 The present study is the first to examine the impact of a collaborative care strategy for treating depression among patients with cardiac disease, and our efforts to improve upon and expand the model for treating other cardiac conditions.

- Study with Telephone Directed Care
- Clinical Trial based on previous intervention studies
- Delivered Collaborative Care Model
- Primary Outcome was decreased depression
- Cost Efficacy Data
- Cost Saving Data?
Future Trials

Rationale and design of WEBCARE: A randomized, controlled, web-based behavioral intervention trial in cardioverter-defibrillator patients to reduce anxiety and device concerns and enhance quality of life

Susanne S Pedersen*1,2, Viola Spek1, Dominic AMJ Theuns2, Marco Alings3, Pepijn van der Voort4, Luc Jordaens2, Pim Cuijpers5, Johan Denollet1 and Krista C van den Broek1

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Email: Susanne S Pedersen* - s.s.pedersen@uvt.nl, Viola Spek - v.r.m.spek@uvt.nl; Dominic AMJ Theuns - d.theuns@erasmusmc.nl; Marco Alings - marco@alings.org; Pepijn van der Voort - pepijn.vd.voort@catharina-ziekenhuis.nl; Luc Jordaens - l.jordaens@erasmusmc.nl; Pim Cuijpers - P.Cuijpers@psy.vu.nl; Johan Denollet - denollet@uvt.nl; Krista C van den Broek - C.C.L.T.vandenBroek@uvt.nl

* Corresponding author
Future Delivery of Behavioral Medicine

• Collaborative Care Models
  – Nurse specialist, psychologist, SW, psychiatrist
  – Patient Preference Psychotherapy Antidepressant
  – Problem Solving Therapy
  – Stepped Care Approach with Outcome Measurements

• Web Based Delivery of Therapy
  – Self Assessment, Therapy, Outcomes
  – Expansion in Behavioral Cardiology

• Tailored Approach to Men and Women
  – Different response to mental health issues and treatments
Outline of Presentation

• Depression impact on heart disease
• Mechanistic Pathways
• Current Treatment Strategies
• Future Delivery of Care
• Break
• Case Discussions
Break Time!

pozuell@ccf.org
Outline of Presentation

• Depression impact on heart disease
• Mechanistic Pathways
• Current Treatment Strategies
• Future Delivery of Care
• Break
• **Case Discussions**
## Screening Instruments for Depression

### PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use “x” to indicate your answer)</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Little interest or pleasure in doing things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Feeling down, depressed, or hopeless</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Trouble falling or staying asleep, or sleeping too much</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Feeling tired or having little energy</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Poor appetite or overeating</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Trouble concentrating on things, such as reading the newspaper or watching television</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>9. Thoughts that you would be better off dead or of hurting yourself in some way</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

For office coding: ______ + ______ + ______ + ______ = Total Score: ______

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

<table>
<thead>
<tr>
<th>Not difficult at all</th>
<th>Somewhat difficult</th>
<th>Very difficult</th>
<th>Extremely difficult</th>
</tr>
</thead>
</table>
## Screening Instruments for Anxiety

### GAD-7

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by the following problems?</th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Use <em>✓</em> to indicate your answer)</td>
<td></td>
<td>--------------</td>
<td>-------------------------</td>
<td>------------------</td>
</tr>
<tr>
<td>1. Feeling nervous, anxious or on edge</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>2. Not being able to stop or control worrying</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>3. Worrying too much about different things</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>4. Trouble relaxing</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>5. Being so restless that it is hard to sit still</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>6. Becoming easily annoyed or irritable</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>7. Feeling afraid as if something awful might happen</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

(For office coding: Total Score $T = ____ + ____ + ____)$
Screening Anxiety and Depression

<table>
<thead>
<tr>
<th>PHQ-4</th>
<th></th>
<th>Not at all</th>
<th>Several days</th>
<th>More than half the days</th>
<th>Nearly every day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over the last 2 weeks, how often have you been bothered by the following problems? (Use &quot;✓&quot; to indicate your answer)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>3. Little interest or pleasure in doing things</td>
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<td></td>
</tr>
</tbody>
</table>

(For office coding: Total Score $T = \_ + \_ + \_ + \_ )$

www.phqscreeners.com
CASE # 1

- 52 y/o female
- Onset of A Fib age 50 (when spouse bought motorcycle)
- Htx of 2 ablations, recurrence
- “can stress affect a fib?“
- “I know when I am in it“
- Worrier at baseline, PCP Rx Valium “he tells me not taking enough of it“
- PHQ GAD
Benzodiazepine oral equivalencies

- Librium 10 mg
- Valium 5 mg *
- Ativan 1 mg *
- Klonopin 0.5 mg
- Xanax 0.25 mg

* remember, IV twice as powerful as po

0.5mg IV Ativan = 1mg po Ativan
Length of Treatment

Time

Severity

Syndrome

Response

Remission

Recovery

Relapse

Recurrence

Acute
(6-12 weeks)

Continuation
(4-5 months)

Maintenance
(≥1 year)

“Normalcy”

Symptoms

Progression to disorder


CASE # 2

• 69 retired male, avid sailor
• Afib / Flutter since age 60
• “it comes and goes”
• One month prior told had to get rid of boat, father in law died, worse “skipped beats”
• Methodical, checks pulse # times a day, unpredictability of this, set off by activity?
• Wife is sick of me, fed up, tired of me
• “By the way, can you do an EKG to make sure ok? “
Psychotherapy

Cognitive Behavioral Therapy (CBT)

- Identify and alter negative thinking patterns
- Promote healthier behaviors
- Coaching Technique
- Validated
CBT techniques

• **Decrease** the *anticipatory* catastrophic thinking
• **Improve** the *avoidant behaviors* and helplessness
• Use relaxation techniques
• Short course, focusing on the here and now
CASE # 3

• 68 Female CHF
• Always a worrier, about good and bad things
• Previous history of depression
• With heart “acting up” can’t do her chores
• Comorbid DM and renal disease
• Loss of sense of humor, harder to put up a good face
• What to do?
SSRI

- **Fluoxetine** 20 – 40 mg (long half life)
- **Sertraline** 50 – 150 mg
- **Paroxetine** 20 – 40 mg
- **Citalopram** 30 – 40 mg
- **Escitalopram** 10- 20 mg

** Use on consult service due to less drug- drug interactions
Length of Treatment

- **“Normalcy”**
- **Symptoms**
- **Response**
- **Progression to disorder**

**Treatment Phases**
- **Acute** (6-12 weeks)
- **Continuation** (4-5 months)
- **Maintenance** (≥1 year)

**Severity**

**Symptoms**

**Time**

**Severity**

- **Remission**
- **Recovery**
- **Relapse**
- **Recurrence**

# Antidepressants to use in Cardiac Patients

(* Good for both depression AND anxiety *)

<table>
<thead>
<tr>
<th>Serotonergic</th>
<th>Dual Acting (serotonin and NE)</th>
<th>Dopamine (some NE kick)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sertraline</td>
<td>Duloxetine + Mirtazapine ++</td>
<td>Bupropion</td>
</tr>
<tr>
<td>Citalopram*</td>
<td>(mild interaction BB)</td>
<td></td>
</tr>
<tr>
<td>Escitalopram</td>
<td>+ (weight gain)</td>
<td></td>
</tr>
<tr>
<td>* (&lt; / = 40mg)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
CASE # 4

• 45 Male, admitted with ventricular arrhythmia
• History of HOCM, brother who died of SCD
• “mood is good for most of the day, but I get down thinking when is my time coming”
• Endorsed low mood, loss of concentration at work
• Scheduled to get an ICD device (primary prevention)
• What to do?
Screening Anxiety and Depression

### PHQ-4

<table>
<thead>
<tr>
<th>Over the last 2 weeks, how often have you been bothered by the following problems? (Use “✓” to indicate your answer)</th>
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<td>3. Little interest or pleasure in doing things</td>
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<td>3</td>
</tr>
</tbody>
</table>

*(For office coding: Total Score T = ____ + ____ + ____)*

[www.phqscreeners.com](http://www.phqscreeners.com)
Q and A

Cases from the Audience!

- Depression / Anxiety / Stress Management
- Barriers to Diagnosis and Treatment
- Cardiac Rehabilitation and Exercise
- Outcome Measurements
- Collaborative Care Models
Thank You

pozuell@ccf.org