

What Do We REALLY Know About Depression and CVD?

Questions

Does depression increase CVD risk?

Does depression increase post-MI morbidity and mortality?

What is the prevalence of depression post-MI?

If so, what are the characteristics of depression that affect CVD risk?

If so, what are the mechanisms?

What are the moderators (age, length, gender, typical versus atypical?) for depression and CVD morbidity and mortality?

Does reducing depression reduce risk?

How and when should post-MI depression be identified?

How should post-MI depression be treated?

Does depression increase CVD risk?

In a meta-analysis of longitudinal and case control studies, (11 met authors inclusion criteria of being “high quality”), depressed mood increase risk across a range of CVDS; the combined risk for depression for the onset of MI was OR = 1.60 m 95% CI 1.3-1.9)

Van der Kooy et al *Int J Geriatr Psychiatry*, 2007;22:613.
Wulsin & Singal. *Psychosom Med*, 2003;65:201

Depression may increase risk for type II diabetes, metabolic syndrome

Vaccarino et al. *Psychosom Med* 2008; 70:40.

What is the Prevalence of Depression post MI?

60 prospective studies
100 narrative reviews
Many meta-analyses

3 times more common after an MI

Prevalence rates of 10-20%

Similar rates with angina, CHF, angioplasty

More common in women

Lichtman et al. Depression and Coronary Heart Disease: Recommendations for Screening, Referral, and Treatment AHA Advisory Committee, Circ, under review.

Does depression increase CVD risk post MI?

>2 fold increase in events post-MI

Worse prognosis (even after adjusting for CVD severity, although some negative studies)

Dose response-relationship?

Uncertain:

Role of preexisting depression
Relationship to fatigue

Is Depression More Common in Outpatients with CVD?

Less known

NHIS survey of 30,801 adults

9.3% 12 month prevalence with CVD

4.8% with no comorbid illness

7-19% with no chronic illness

What are the characteristics of depression that affect CVD risk?

Typical versus atypical?

Long-standing?

Hx of PTSD or Adverse Childhood events?

In 17,337 adult health plan members:
CVD risk >1.3- to 1.7 ACEs vs no ACEs

Filitti et al Am J Prev Med. 1998;14;245.

More severe?

Depression and Comorbidity

Depression is highly co-morbid with other psychiatric problems

High rates of anxiety/anxiety disorder

Anxiety (at least phobic avoidance may increase mortality)

What is the interaction of depression/comorbidity and risk?

How Does Depression Effect CVD Morbidity/Mortality--biological mechanisms?

**Sympathetic and/or reduced vagal activity
Reduced heart rate variability**

HPA dysfunction

Increase platelet activation

Impaired vascular function

**Increase CRP , Il-6, ICAM-1 and fibrinogen
(increased inflammatory response)**

Increased metabolic syndrome risk

How Does Depression Effect CVD Morbidity/Mortality?

Life Style:

Reduced activity?

Decreased medication adherence (X3 increased Risk in one study)

Increased tobacco use

Social isolation

Chronic life stress

May reduce the success of risk factor medication

Does reducing depression reduce risk?

ENRICHD:

2481 post MI patients (1084 men, 1397 women)

Randomized to cognitive behavior therapy
or usual care

Followed for up to 3 years post AMI

Main results:

Early treatment effect for CBT on reducing
depression; both groups similar
(and improved!) by 29 months

No overall difference in morbidity and mortality
(Event free survival =76% in both groups)

Berkman et al *Jama*. 2003;289:3106-16.

Does reducing depression reduce risk- -cont?

Subanalyses:

Non-randomized post-hoc analysis found patients treated with SSRI had about 42% reduction in death or recurrent MI

Taylor et al. Arch Gen Psychiatry. 2005;62:792-8.

CBT benefit for white males on secondary endpoint (cardiac mortality or recurrent MI, HR, 0.63; 95% CI, 0.46-0.87)

Schneiderman et al. Psychosom Med 2004, 66:475.

Trend for negative effects in women and minorities? (HRs both about 1.2; 95% CI, .90-1.55)

Berkman et al JAMA, 2003;289:3106.

Does reducing depression reduce risk?

Inconsistent findings with SSRIs

SADHARDT found significant effects for treating depression at least in recurrent, severe depression; SSRIs were safe

Glassman et al Jama. 2002;288:701-9.

CREATE found that citalopram was also safe

Lesperance et al. Jama. 2007;297:367-79.

MIND-IT: No effect of mirtazapine with 91 pts post MI using LOCF on Ham-D, significant on BDI and using models. Safe?

Honig et al Psychosom Med 2007; 69:606.

How and when should post-MI depression be identified?

1. **Validity**
Agreement amongst common scales > .60
2. **Sensitivity and specificity**

Measure	Sensitivity	Specificity
BDI >10	81%	68%
BDI > 8	88%	72%
HADS-D >8	65%	90%
HADS-D >4	75%	78%
SCL-90-D >23 or 28	75%	81%

Thombs et al *Psychosomatics* 2007;48:185

How and when should post-MI depression be identified?

Sensitivity and specificity--cont

Any depressive disorder 3 months after "cardiac hospitalization"
MINI used as criterion;28% depression rate

Measure	Sensitivity	Specificity
HADS ≥ 5	78%	81%
HADS ≥ 8	39%	94%
PHQ ≥ 5	82%	81%
PHQ,categorical	37%	94%

Stafford,et al. Gen Hosp Psych 2007;29,415

Subjects

- *48 depressed subjects
 - Randomized to CBT or WLC (5-6 months)
- *20 non-depressed subjects
- *At “high” risk for CVD
- *All depressed subjects met criteria for major and or minor depressive disorder.
- *Exclusions: Subjects with evidence of cognitive dysfunction, alcohol or substance abuse, or taking medications potentially affecting psychophysiology that could not be stopped

Measures

Self-report: At baseline assessment, Beck Depression Inventory (BDI), Hamilton, perceived stress, quality of life. Before and after each task: Positive and Negative Affect Scale (PANAS).

Medical: History and PE, lipids, weight/height, c-reactive protein (CRP), asymmetric dimethylarginine, flow and nitro-mediated vasodilation

Cortisols: two days waking, waking plus 30, noon, 5, 9; and after each task. (DHEA also on waking)

Psychophysiology: Continuous heart rate (Finapres), SBP and DBP two minutes into each task (Dinamap), presystolic ejection period (PEP) with impedance cardiography, RSA adjusted for lung volume (RSA_{TF}), heart rate spectra, baroreflex control, respiration, affect

Ambulatory: negative and positive affect, heart rate, respiration, activity

Trier Stress Test

Baseline: five minutes of baseline

Anticipation: five minutes before stressors

Speech: five minutes speech in front of panel

Math: five minutes of mental arithmetic in front of
panel

Recovery: 5 and 10 minutes after stressors

Data Analysis--Baseline

Measure	Depressed (n = 48)	Non-Depressed (n = 20)	Cohen's D
SBP (mmHG)	132.8 (25.6)	144.3 (26.6)	0.44
DBP (mmHG)	73.7 (19.)	81.1 (16.9)	0.41
HR (bpm)	75.7 (13.6)	69.2 (11.6)	0.51
Total Cholesterol (mg/dL)	216.8 (51.8)	192.8 (34.6)	0.54
LDL (mg/dL)	134.3 (42.7)	128.7 (31.6)	0.15
HDL (mg/dL)	59.9 (25.3)	50.5 (12.8)	0.47
LDL/HDL	3.9 (1.2)	4.0 (0.19)	0.03
Triglycerides (mg/dL)	146.8 (76.0)	133.7 (69.6)	0.18
BMI (kg/m ²)	29.5 (6.2)	27.8 (3.8)	0.34
Waking cortisol (ug/dl)	0.81 (1.3)	0.55 (0.18)	0.29
Wake +30 min cortisol rise (ug/dl)	0.15 (0.55)	0.39 (0.54)	0.44
Log cortisol slope	-0.16 (0.05)	-0.15 (0.5)	0.26
C-reactive protein (mg/l)	2.8 (2.9)	1.0 (0.9)*	0.88
FMVD (% change)	3.1 (6.3)	4.8 (5.3)	0.29
NitroVD (% change)	16.8 (8.3)	16.4 (10.1)	0.06
ADMA (micromol/l)	0.56 (0.17)	0.58 (0.16)	0.13

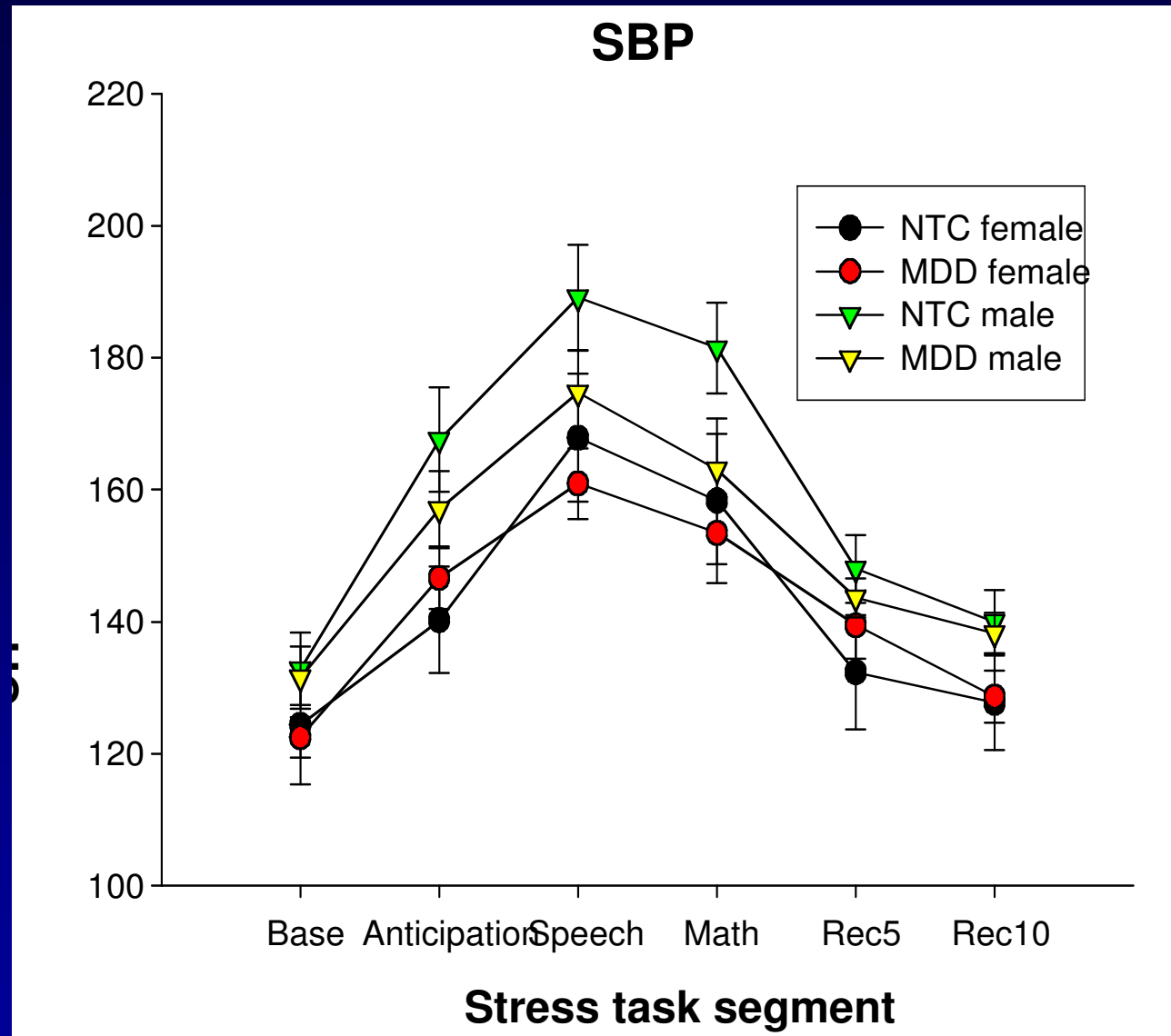
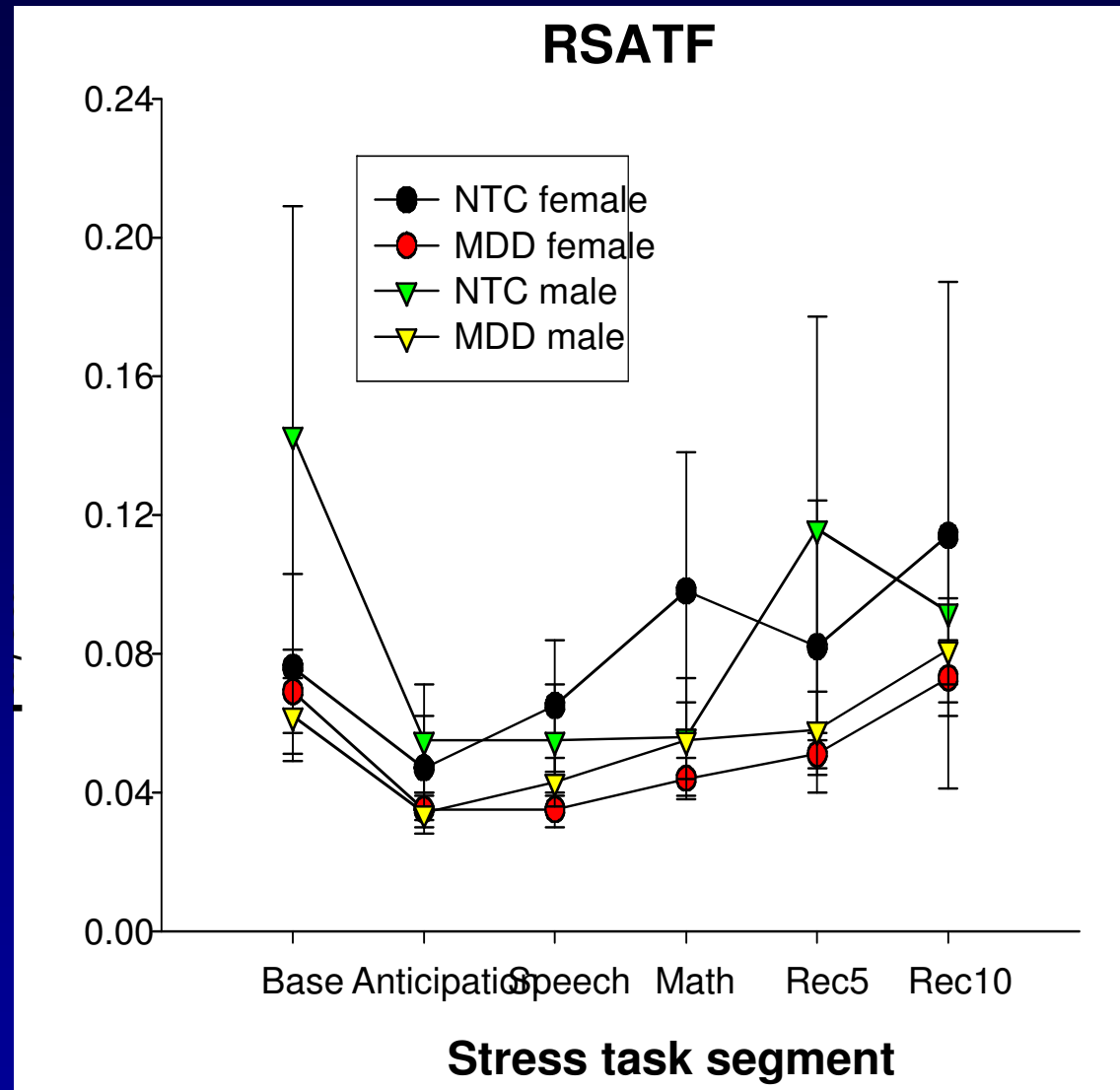
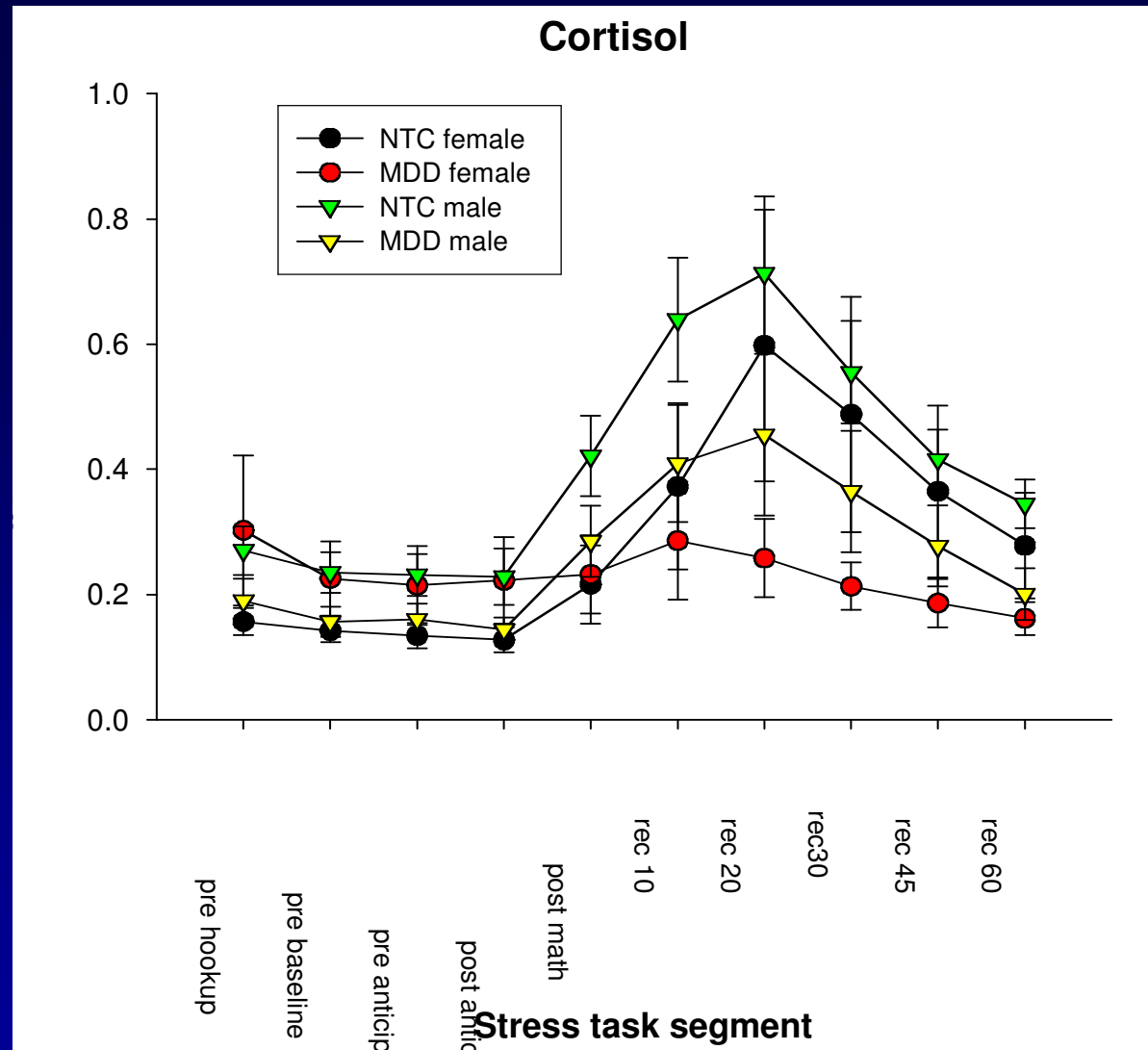


Figure shows that subjects showed significant reactivity to stress tasks.



RSA_{TF} was significantly lower during TSST in depressed, compared to non-depressed subjects: $F = 5.59$; $p = .02$



Cortisol was significantly lower during TSST in depressed, compared to non-depressed subjects: $F = 4.83$, $p = .03$.

Summary of Baseline Findings

Depressed, compared to non-depressed:

- *Flatter cortisol response to acute psychological stress
(as cortisol suppresses proinflammatory cytokines
may suggest mechanism for CVD)
- *Higher c-reactive protein (inflammation?)
- *Lower RSA_{tf} (restricted response to
cardiovascular change?)
- *Otherwise not different (e.g.: flow mediated vasodilation,
CVD risk-factors, AMDA)

*Taylor et al *Psycho Med*: 68, 538, 2006

Intervention Effects

48 depressed subjects randomized to
16 session CBT or WLC

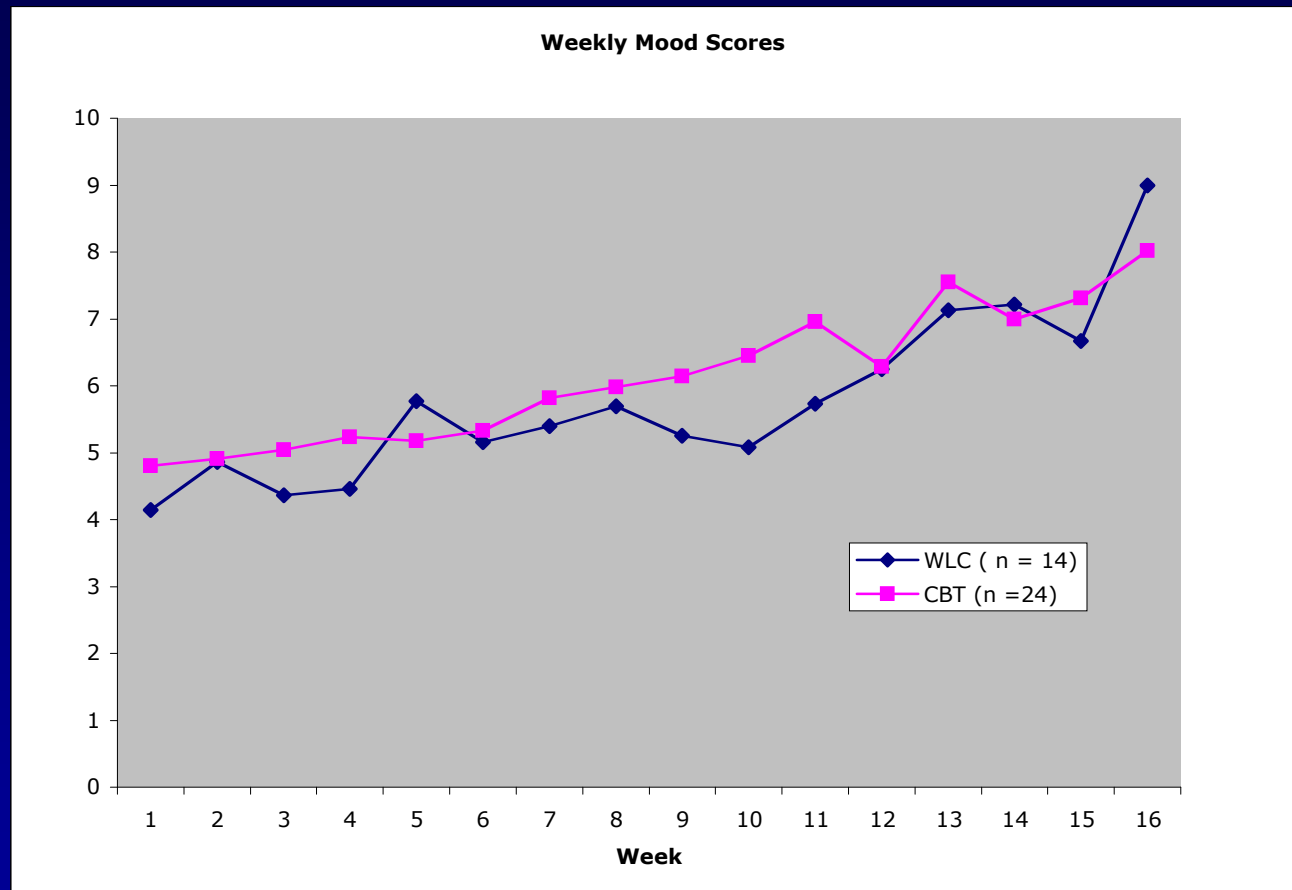
Intervention:

ENRICHD* CBT plus:

- *Phone calls for missed sessions
- *Workbook
- *Behavioral activation
- *Highly directed intervention
- *Stress management

*ENRICHD investigators. JAMA, 289, 3106, 2003

Weekly Mood Score



Change in depressed mood over 16 sessions for the initial CBT group and then the WLC group which was started about six months later.

Effects of CBT

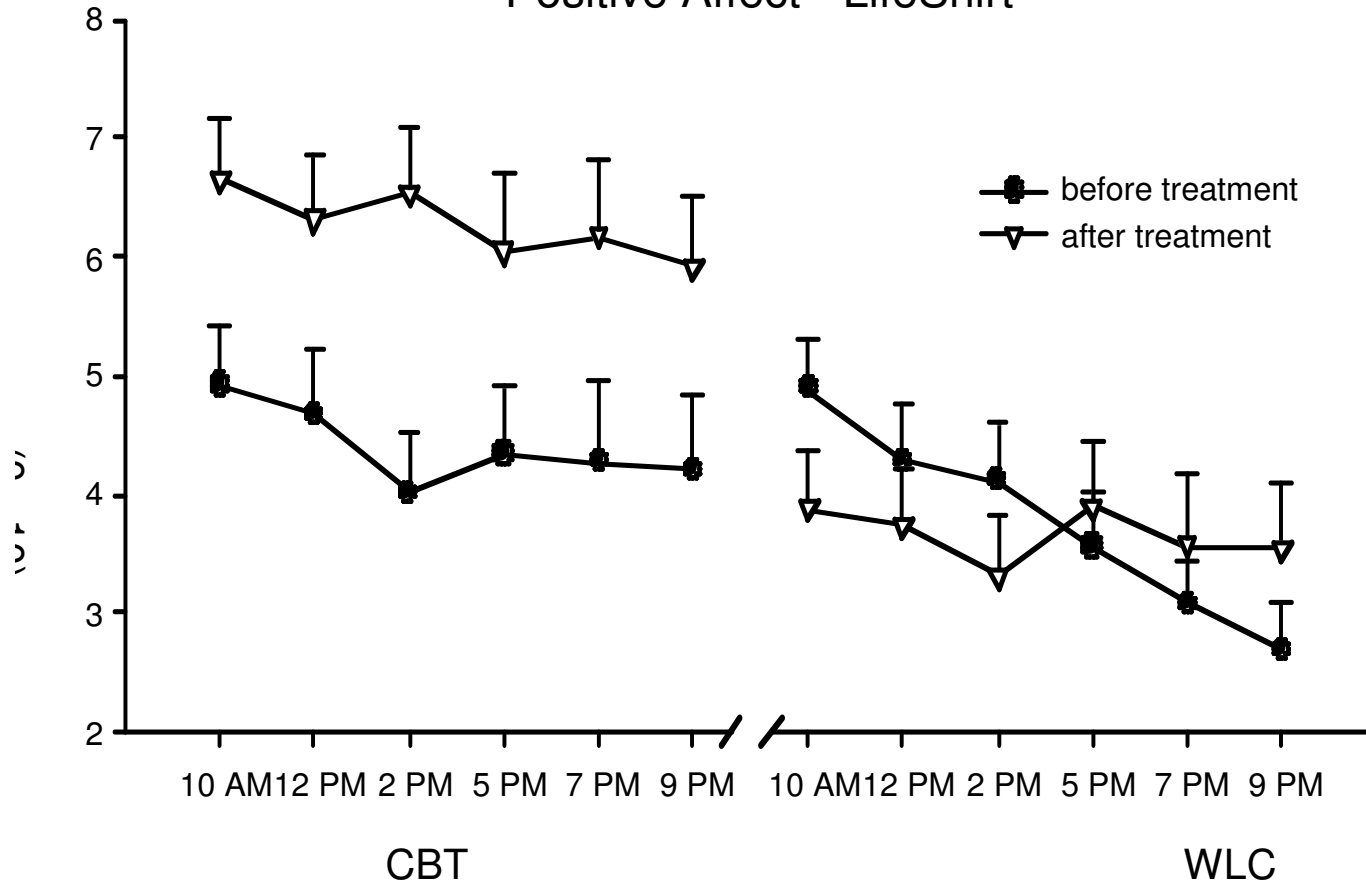
***improved mood, psychological functioning: 57% of CBT pts were not depressed at 6 months compared to 4% of WLC**

***reduced triglyceride/HDL**

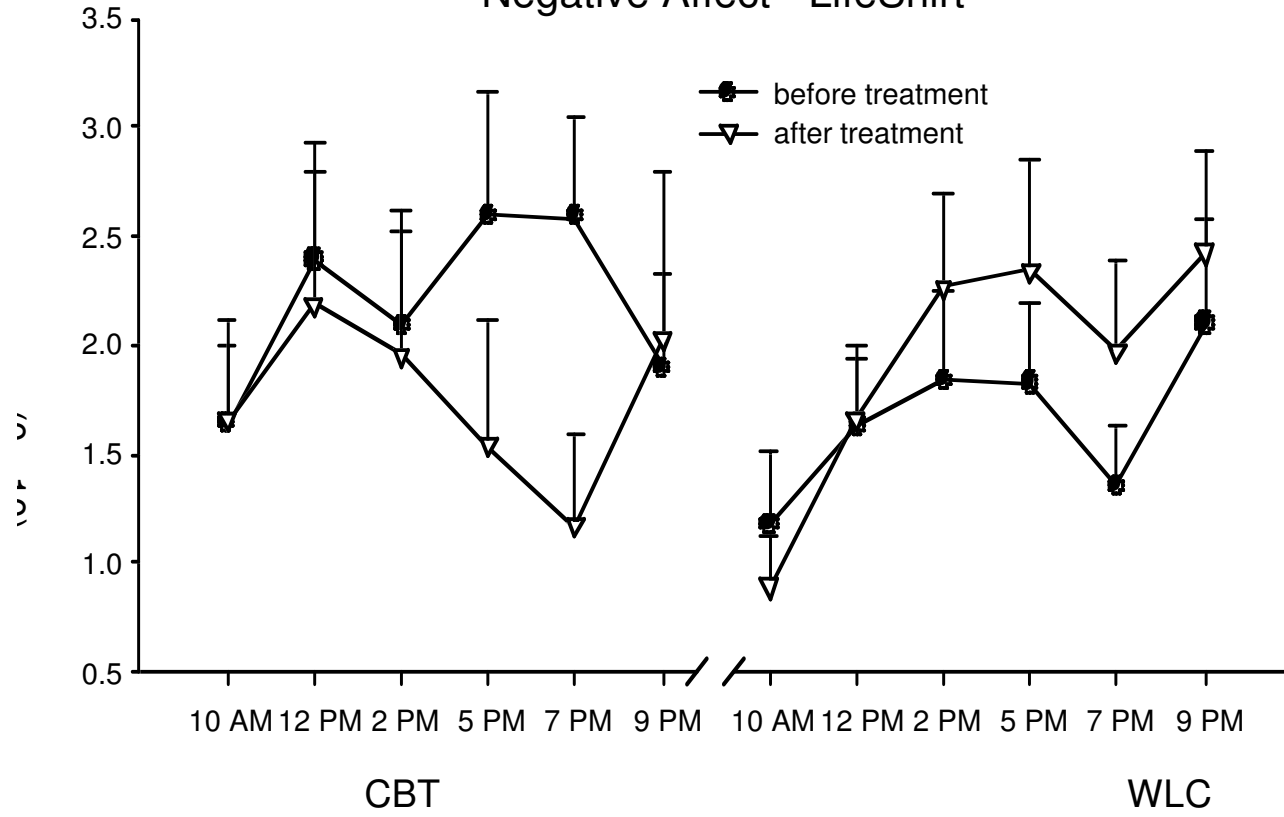
***reduced heart rate**

***no effect on other variables**

Positive Affect - LifeShirt



Negative Affect - LifeShirt



Summary of study findings

Depressed patients have abnormalities in HPA function (reduced response to acute stress), higher levels of inflammation (c-reactive protein), and impaired ANS activity (RSA_{tf}).

HPA hyporeactivity might impair suppression of stress-related inflammatory response

CBT improves depression

Improved depression does not affect HPA function, ? ANS activity; may affect metabolic syndrome indices

HPA, ANS activity are stable

Why Treat Depression?

Depression Affects Quality of Life
Reduces participation in cardiac rehabilitation
programs
Increases health care costs and utilization
Greatly reduces quality of life

“Thus, whether depression impacts cardiac outcomes directly or indirectly, the need to screen and treat depression is imperative”

---AHA Advisory Group

How to Treat Depression?

Long-standing, recurrent, co-morbid condition

Patient preference needs to be considered

Monitor progress/adherence

Co-ordinate care

Treat to remission?

Prevent relapse once remission has occurred

Sustain remission

How to Treat Depression?

Pharmacologic and psychotherapy outcomes appear similar in CVD and non-CVD patients

Sertraline and citalopram are first line antidepressants

Follow Star*D guidelines?

CBT

In ENRICHD 12-16 sessions over 12 weeks were recommended

Exercise may help

Combined therapy

So, What Do We Really Know?

Does depression increase CVD risk?--Maybe

Does depression increase post-MI morbidity and mortality?--Yes

If so, what are the characteristics of depression that affect CVD risk?--Don't know

**What is the prevalence of depression post-MI?
--Increased**

If so, what are the mechanisms?--Not sure

What are the moderators (age, length, gender, typical versus atypical?) for depression and CVD morbidity and mortality?--Don't know

So, What Do We Really Know?

Does reducing depression reduce risk?

--Possibly

How and when should post-MI depression be identified?

**--Screening instruments known;
perform differently in CVD populations**

How should post-MI depression be treated?

**--Follow clinical guidelines with
sertraline or citalopram as first choice
for antidepressants; personally, I prefer
CBT and exercise**