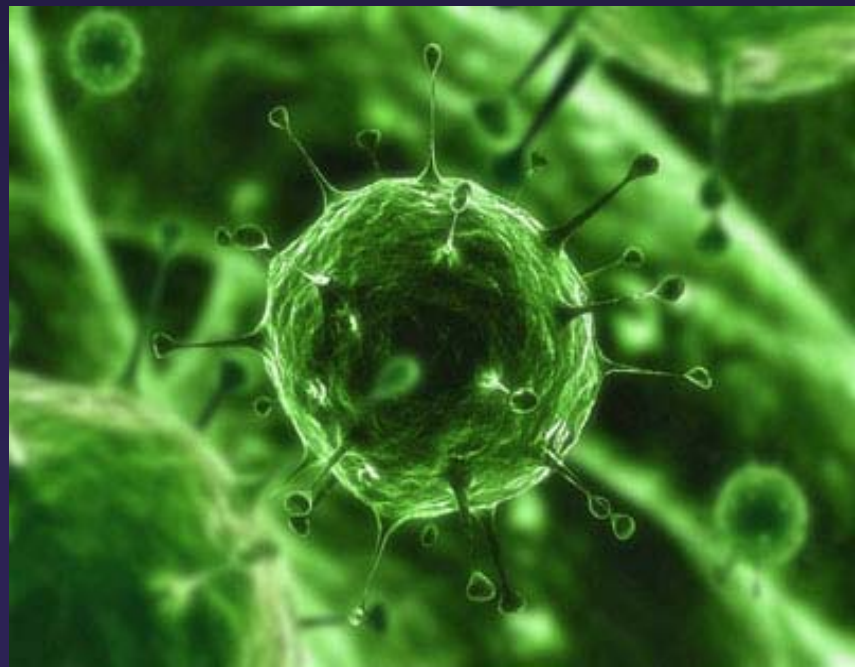
Ο ιός της καταθλιψης: Η γρίπη του καρδιολογικού ασθενούς

Δημήτρης Φαρμάκης
Καρδιολόγος
ΠΓΝ «Αττικόν», Αθήνα



Depression in Heart Disease:
Issues to be addressed

1- Is it another “pandemic flu”?
2- Is it that bad?
3- The chicken or the egg came first?
4- To screen or not to screen?
5- To treat or not to treat?

Issue #1
Depression in Heart Disease: Another pandemic flu?

A swine-flu victim

Depression: Epidemiology

- Life-time risk: 5-10%

Am. Psych. Assoc. 1998

- Chronic medical illness: 10-25%

DSM-IV edition 2000
Egede, Gen Hosp Psychiatry 2007

Depression and Heart Disease

- The relationship between depression and heart disease has been demonstrated since 1930s.

Fuller, Psychiatr Qt 1935

Malzberg, Am J Psychiatry 1937

Depression in CHF

- Overall: ≈30%

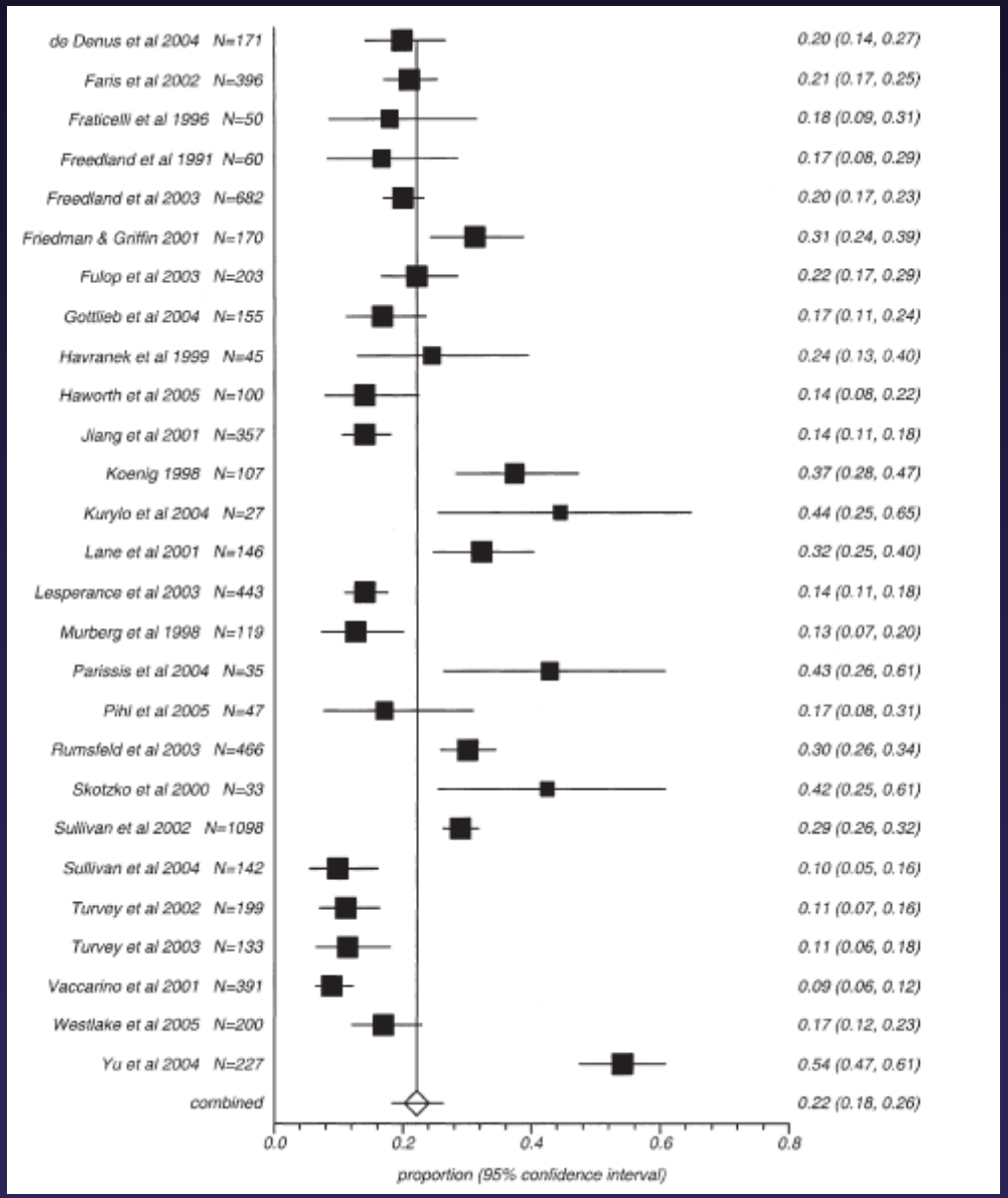
Havranek et al, JACC 2004

- Inpatients: 14-78%
- Outpatients: 13-42%

- Major depression: 14-26%
- Depressive symptoms: 24-85%

Norra et al. IJC 2007

Depression in CHF: prevalence



Overall prevalence: 21.5% (27 studies)

Rutledge et al, JACC 2006

Depression in CAD

- Inpatients: 30% some degree of depression

- Major depression: 15-20% of MI pts
- Depressive symptoms: 10-47% of MI pts

Lichtman et al. Circulation 2008

Thombs et al. Gen Intern Med 2006

Lesperance & Frasure-Smith, J Psychosom Res 2000

Issue #2
Depression in Heart Disease: Is it that bad?

Depression in CHF

- ✓ **risk factor for CHF**

Abramson J et al. Arch Inern Med 2001
Williams SA et al. Psychosom Med 2002

- ✓ **worse prognosis**
  - higher 1 or 2-year mortality and rehospitalization rates (MOS-D or BDI)

Rumsfeld JS et al. EPHESUS sub-analysis. *AHJ 2005*
Jiang W et al. Circ 2004
Jiang W et al. AHJ 2007

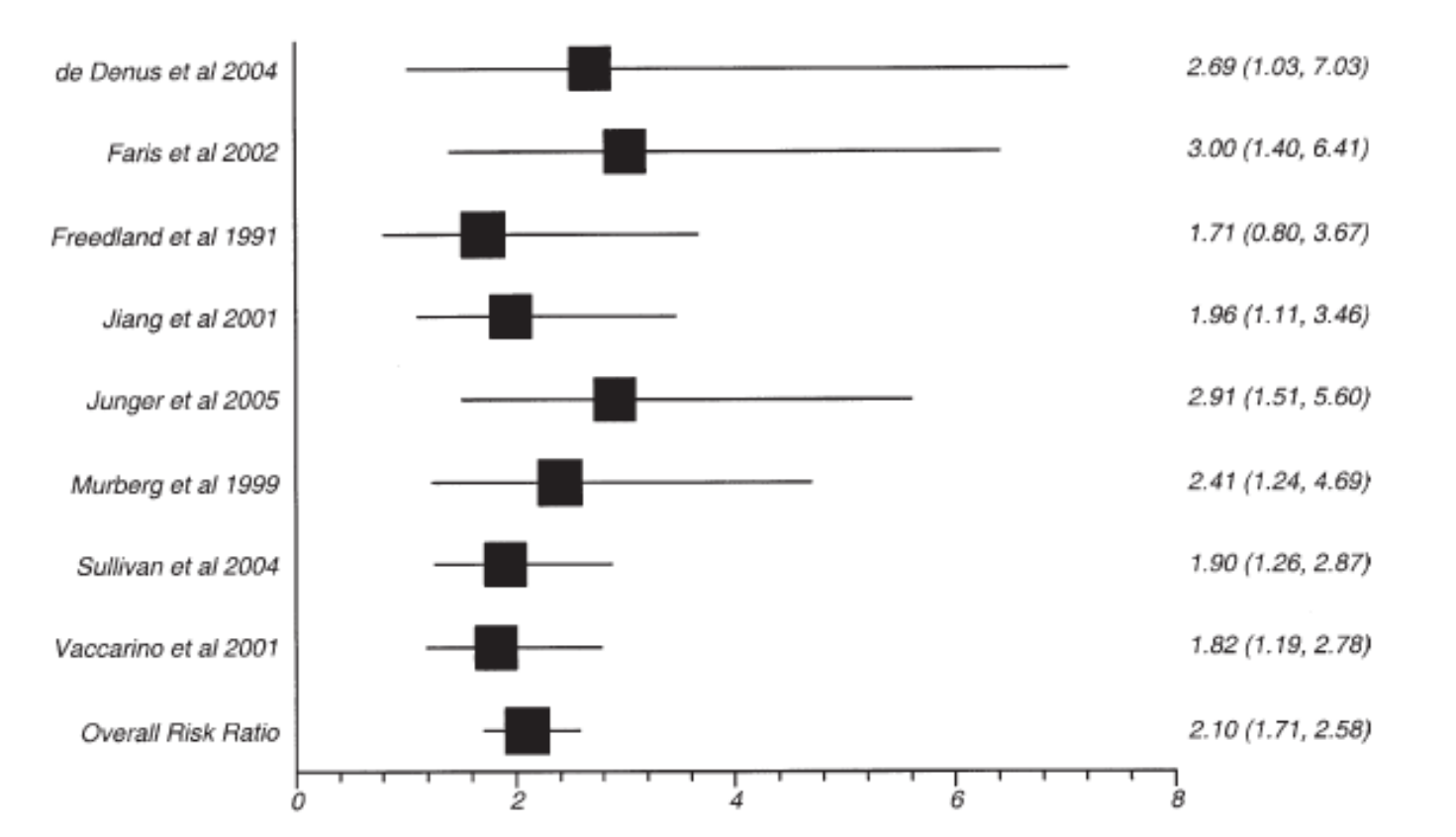
- ✓ **reduced exercise capacity**

Ingle L et al. Eur J Heart Fail 2005
Skotzko CE et al. J Cardiac Fail 2000

- ✓ **impaired QoL**

Rumsfeld JS et al. JACC 2003

Depression in CHF: prognosis



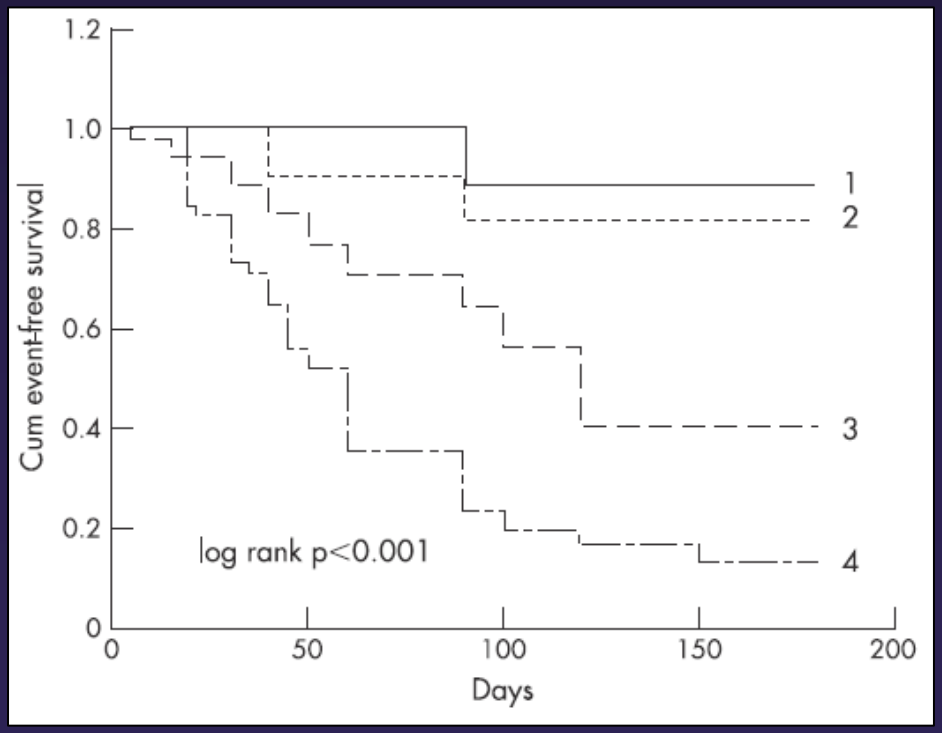
Overall relative risk for death and associated cardiac events: 2.1 (8 studies)

Rutledge et al, JACC 2006

BNP and Depression in CHF

Clinical and prognostic implications of self-rating depression scales and plasma B-type natriuretic peptide in hospitalised patients with chronic heart failure

J T Parissis, M Nikolaou, D Farmakis, V Bistola, I A Paraskevaidis, S Adamopoulos, G Filippatos, D T Kremastinos

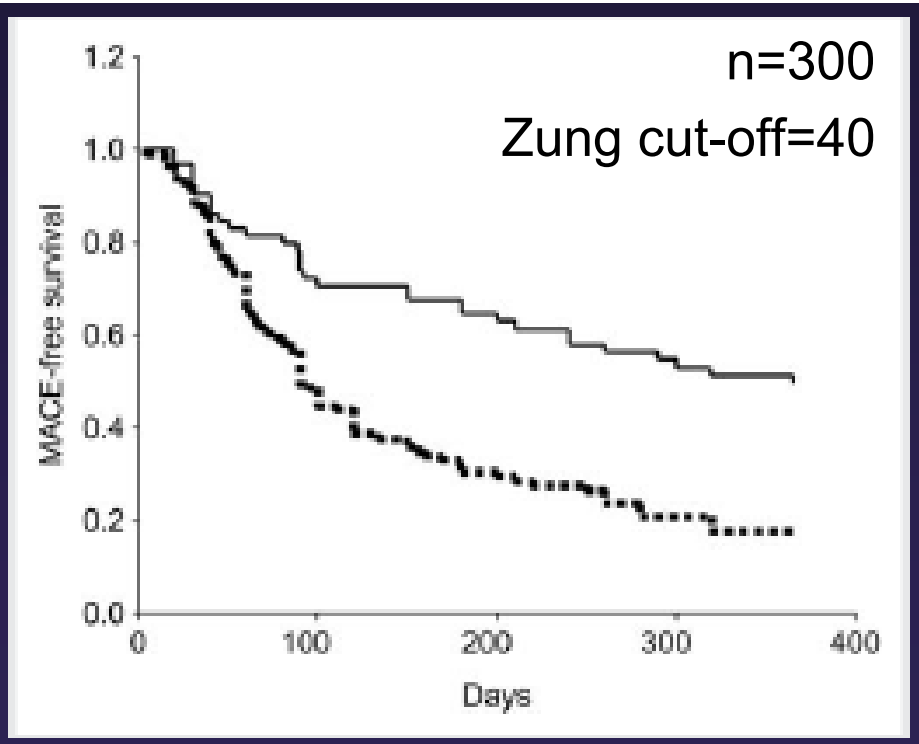


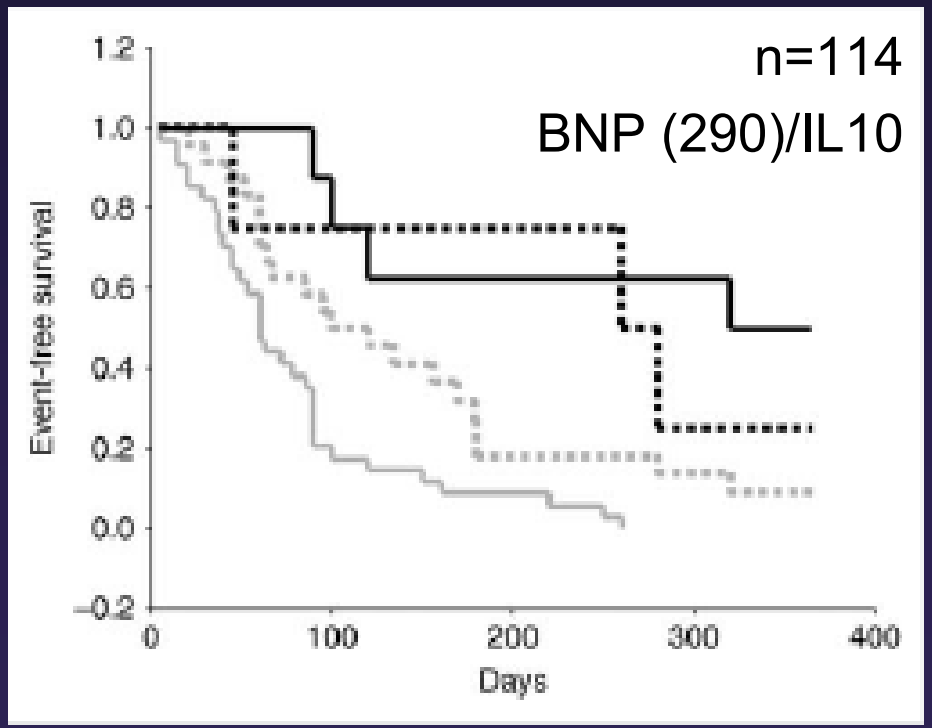
- Event-free survival for depressive status (Zung SDS, cut-off value of 40) and BNP (cut-off value of 290 pg/ml, $p<0.001$, log rank test).

- n=155 CHF pts

Plasma B-type natriuretic peptide and anti-inflammatory cytokine interleukin-10 levels predict adverse clinical outcome in chronic heart failure patients with depressive symptoms: a 1-year follow-up study

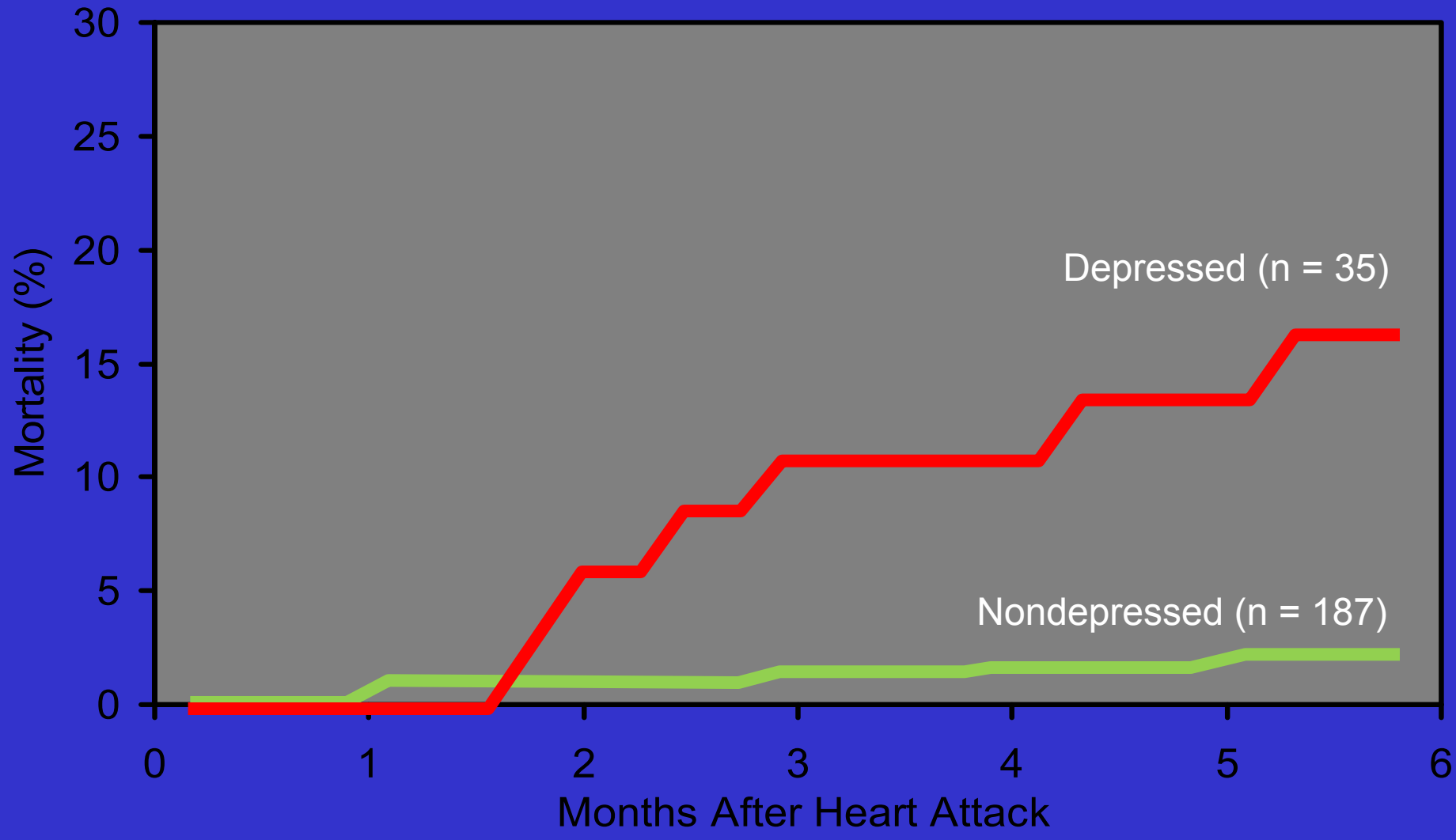
John T. Parissis*, Dimitrios Farmakis, Maria Nikolaou, Dionysia Birmpa, Vassiliki Bistola, Ioannis Paraskevaidis, Ignatios Ikonomidis, Stavroula Gaitani, Koula Venetsanou, Gerasimos Filippatos, and Dimitrios Th. Kremastinos





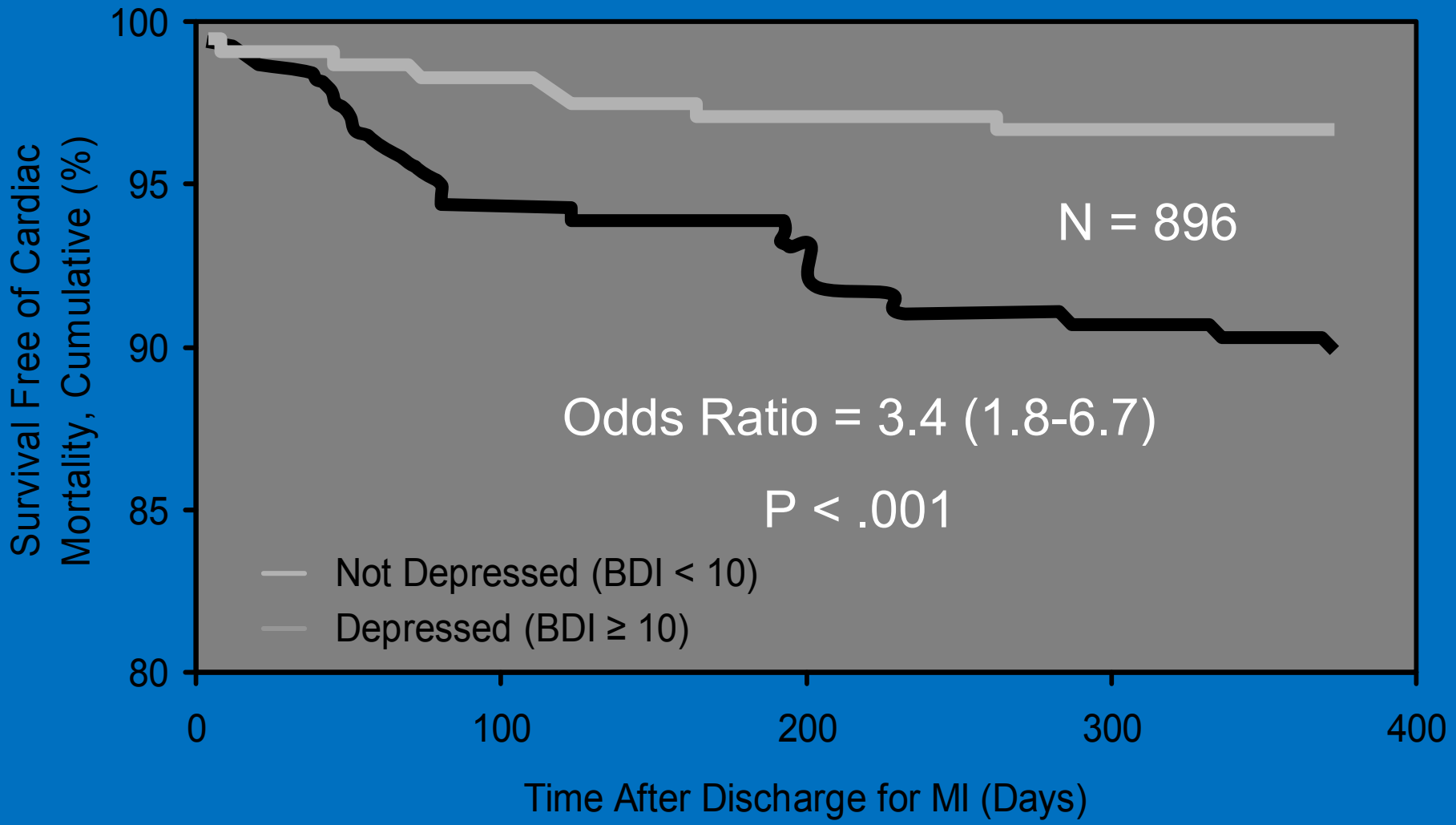
European Journal of Heart Failure (2009) **11**, 967–972

Depression in CAD: Increased Mortality Post-MI



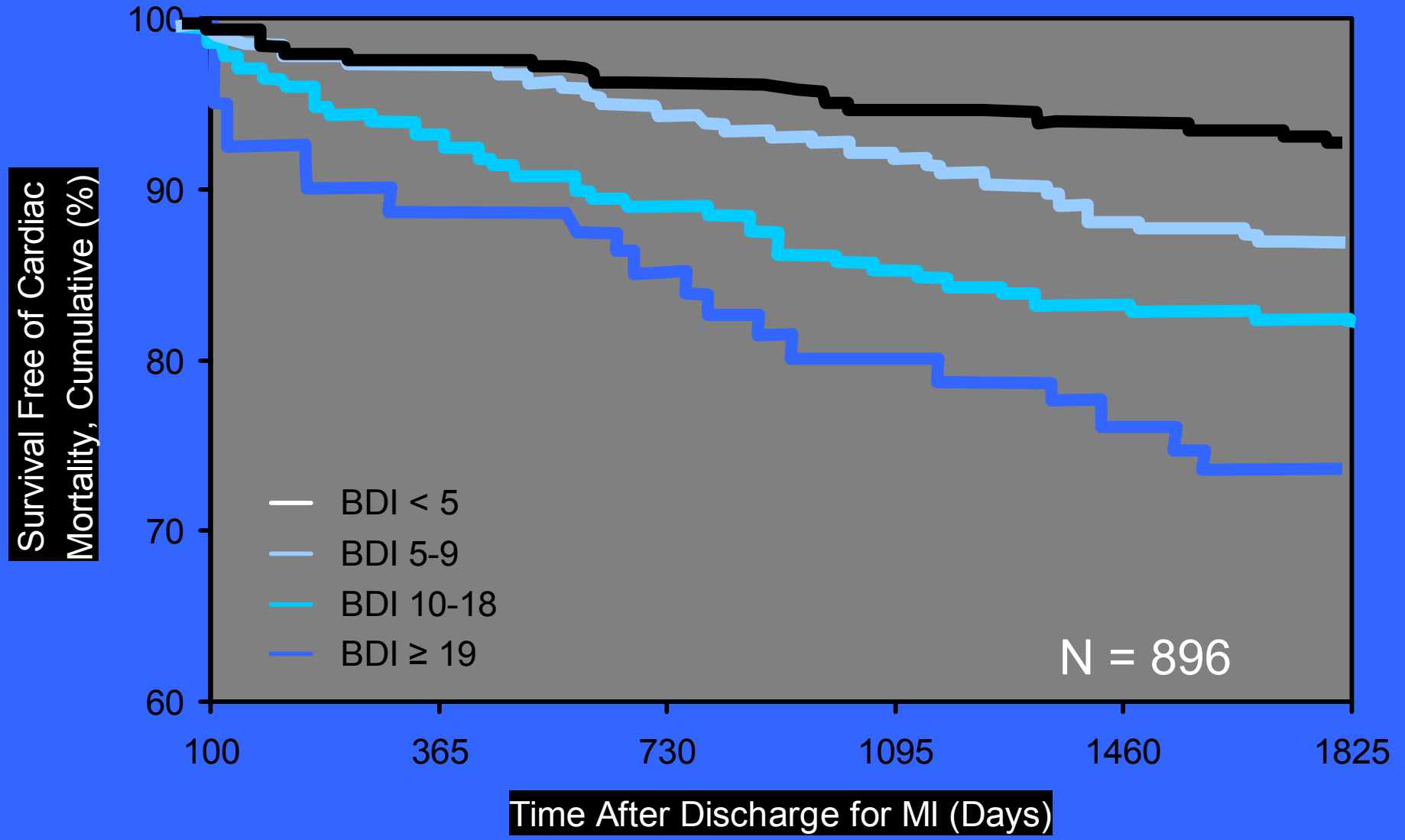
Frasure-Smith N et al. JAMA 1993

Depression and 1-Year Post-Myocardial Infarction (MI) Cardiac Mortality



Frasure-Smith N et al. *Psychosom Med.* 1999

Long-Term Survival Impact of Increasing Levels of Post-MI Depression



Lespérance,2000.

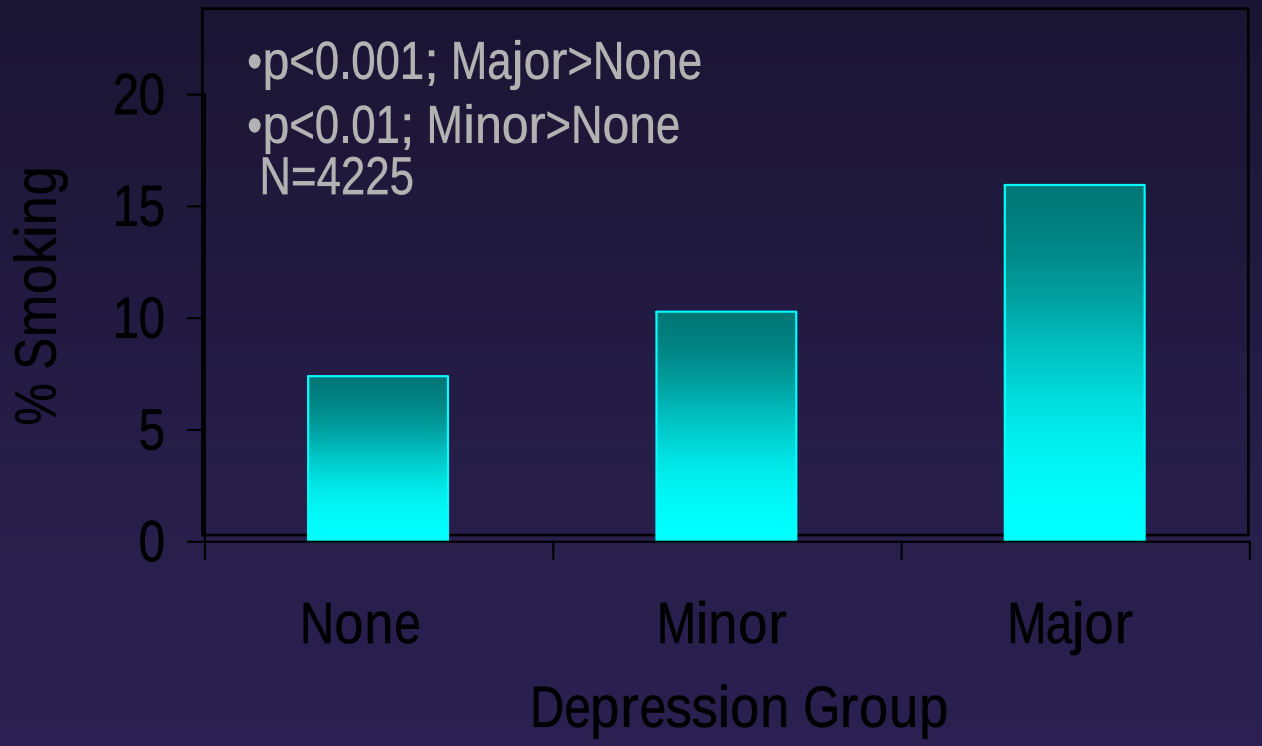
Meta-Analysis of the Adverse Effect of Depression on Patient Adherence

- The relationship between depression and noncompliance with medical regimen recommended by a nonpsychiatrist physician was significant with an

  OR= 3.03 (95% CI, 1.96-4.89).

DiMatteo MR, et al. Arch Intern Med. 2000

Depression Is Associated with ↑% Smoking



Adjusted for demographics, medical comorbidity, DM type and duration, treatment type, HbA1c and clinic.

Katon et al, Diabetes Care, 2004

Issue #3
Depression in Heart Disease: The chicken or the egg came first?

"... 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"

William Harvey, 1628

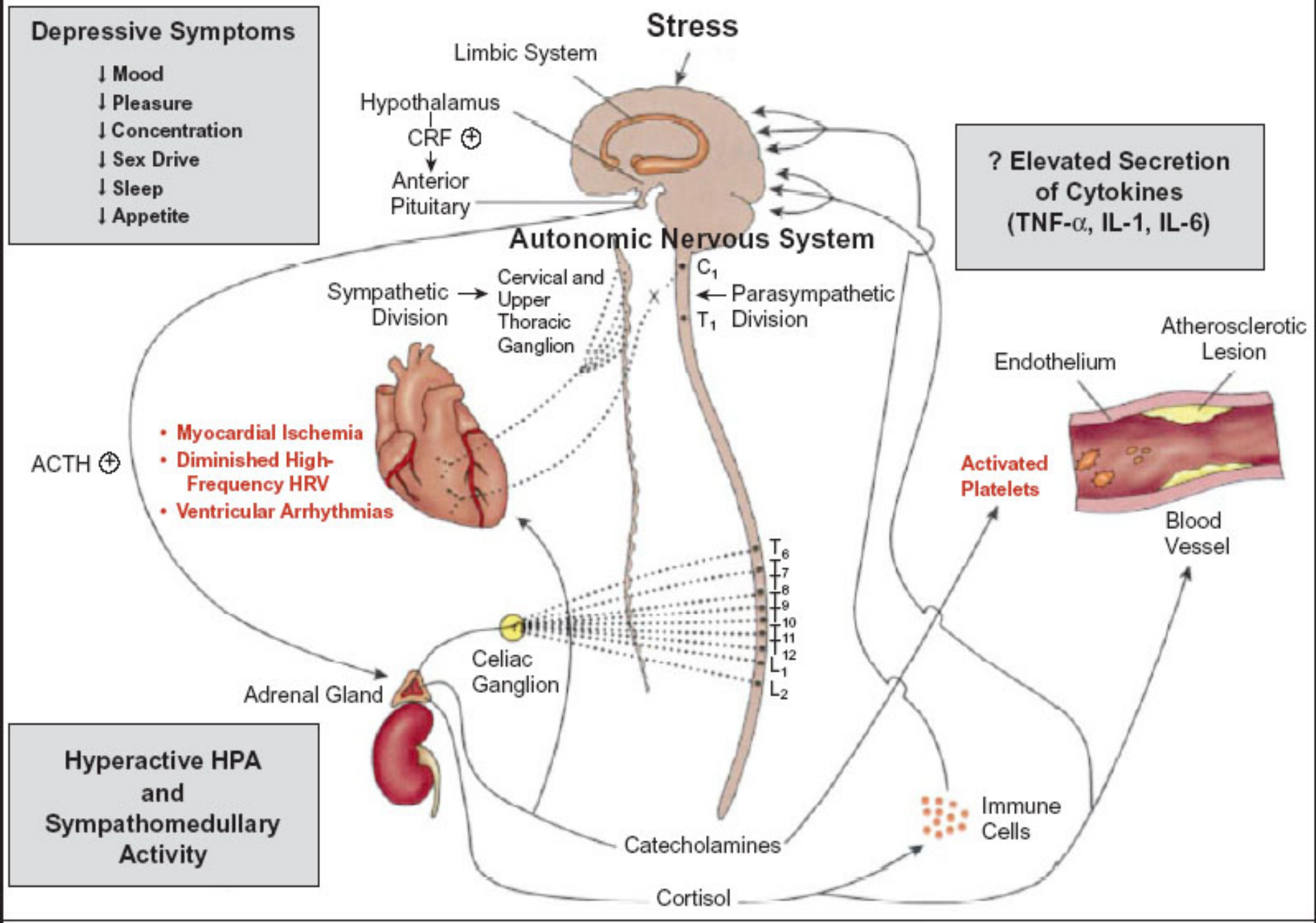
Pathophysiology

Bidirectional pathway

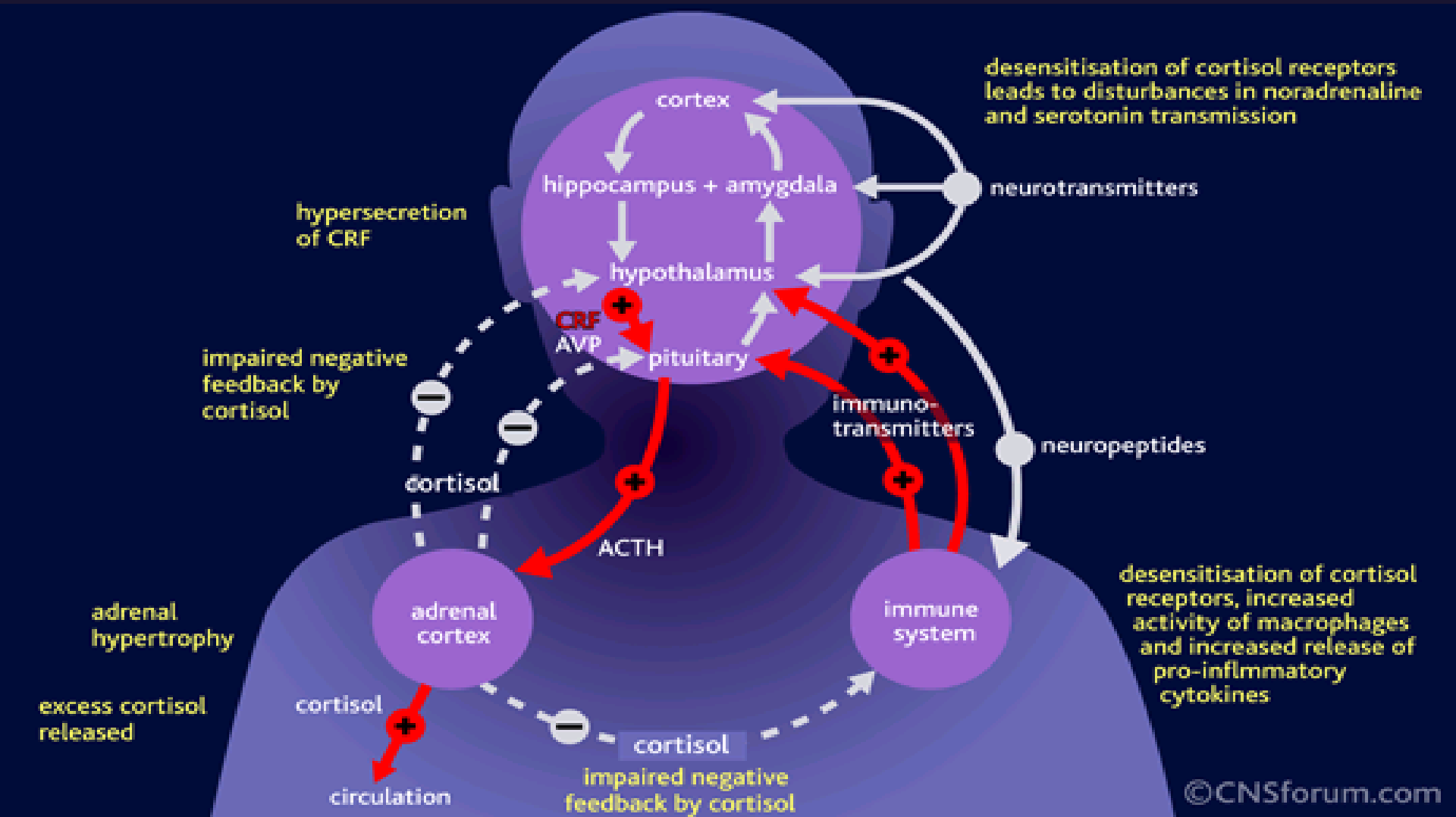
- Neurohormonal activation – SNS – HPA
- Inflammatory activation
- Hypercoagulability
- Sleep-related breathing disorders
- Genetic predisposition
- Poor compliance with therapy/diet
- Refusal to exercise
- Poor social support
- Poor QoL due to cardiac therapies
- Psychotropic drug effects

Joynt et al, JCF 2004
Norra et al, IJC 2007
Dimos et al, HJC 2009

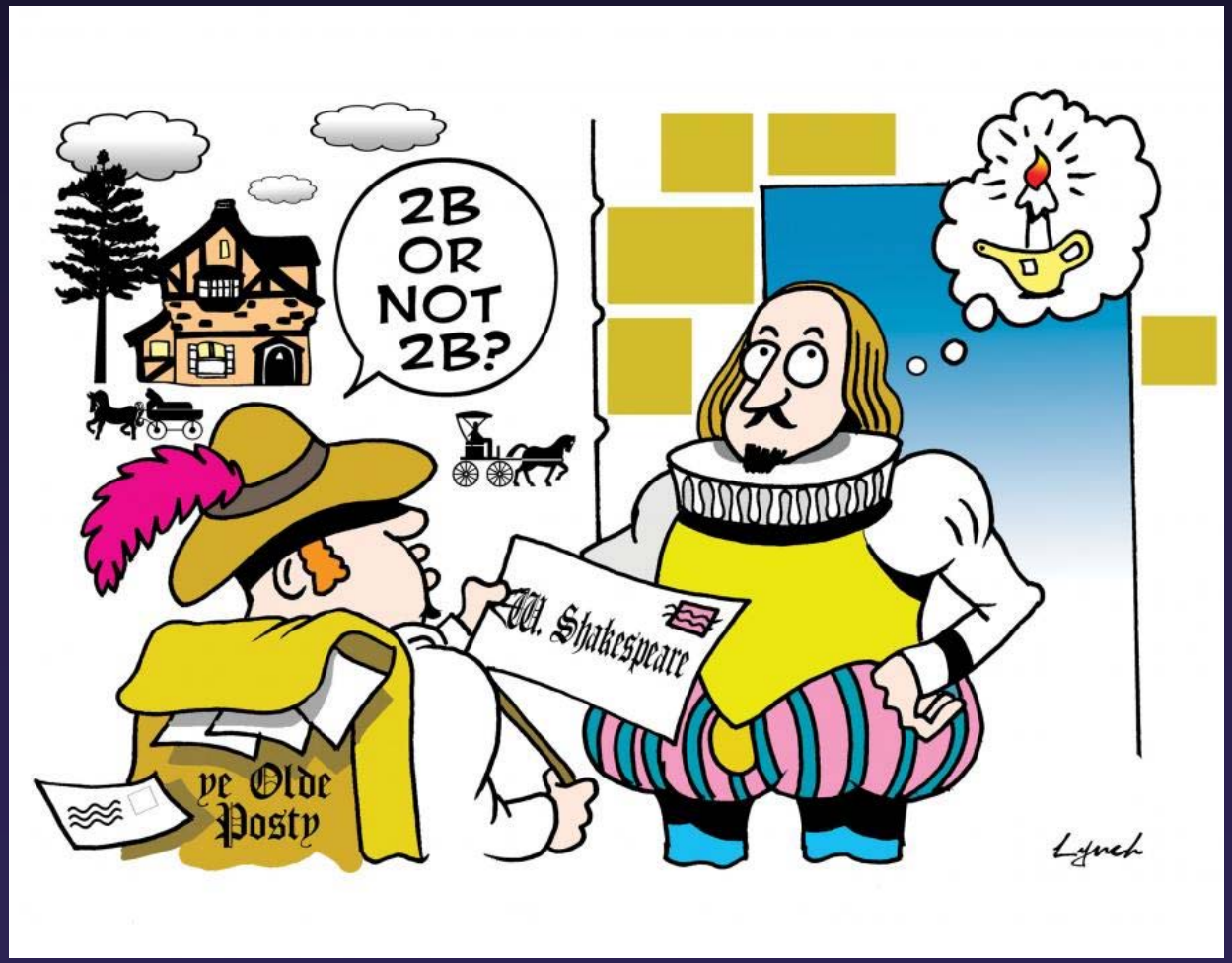
The Relationship Between Major Depression and Cardiovascular Disease



Hypothalamic-Pituitary-Adrenal (HPA) axis in depression



Issue #4
Depression in Heart Disease: To screen or not to screen?



For screening

- Depression scores are fairly accurate
- Depression deserves treatment regardless of its cardiovascular effects
- Screening plus collaborative care is cost effective in primary care settings

Whooley, JACC 2009

Against screening

- Most pts who screen positive do not have major depression

- Depression treatment leads only to a small change in depression scores

- No evidence that screening improves cardiac outcomes

Ziegelstein et al, JACC 2009

JAMA®

Depression Screening and Patient Outcomes in Cardiovascular Care: A Systematic Review

Brett D. Thombs; Peter de Jonge; James C. Coyne; et al.

- Depression screening instruments with predefined cutoffs (11 trials):
  - sensitivity 84% (39% - 100%)
  - specificity 79% (58% - 94%)

- No trials have assessed whether screening for depression improves depressive symptoms or cardiac outcomes in patients with cardiovascular disease.

Source; Setting[a]	Instrument; Cutoff Score
Frasure-Smith et al[33,50] 1995, 1998; Canada	BDI ≥ 10[b]
Freedland et al,[34] 2003; United States	BDI ≥ 10[b]
Dickens et al,[36] 2004; Great Britain	HADS ≥ 17[e]
Huffman et al,[46] 2006; United States	2-items from BDI[e]
Gutierrez,[45] 1999; Canada	BDI ≥ 13[b]
Strik et al,[29] 2001; the Netherlands[f]	BDI ≥ 10[e] HADS ≥ 13[e] HADS-D ≥ 4[e] SCL-90-D ≥ 25[e]
McManus et al,[35] 2005; United States	CES-D-10 ≥ 10[b] PHQ-9 ≥ 10[b] PHQ-2 ≥ 3[b] 2-item yes/no[b]
Denollet et al,[37] 2006; the Netherlands	SAD4 ≥ 3[g]
Low and Hubley,[48] 2007; Canada	BDI-II ≥ 14[b] GDS ≥ 11[b]
Stafford et al,[47] 2007; Australia[h]	HADS-D ≥ 6[e] PHQ-9 ≥ 6[e]
Frasure-Smith et al,[49] 2008; Canada	BDI-II ≥ 14[b] HADS-A ≥ 8[b]

JAMA. 2008;300(18):2161-2171

Diagnosis

- **Underdiagnosed in 30-50% of CHF pts**

  Ormel et al, Arch Gen Psychiatry 1991

  - **Common symptoms with CHF**
  - **Mistaken as “normal” reaction to somatic illness**

Diagnosis

- **Underdiagnosed in 30-50% of CHF pts**

  Ormel et al, Arch Gen Psychiatry 1991

  - **Common symptoms with CHF**
  - **Mistaken as “normal” reaction to somatic illness**

- **Diagnostic tools:**
  - **Symptoms – DSM-IV (2000) or ICD-10 criteria (WHO 1991)**
  - **Scales**

DSM-IV (2000)

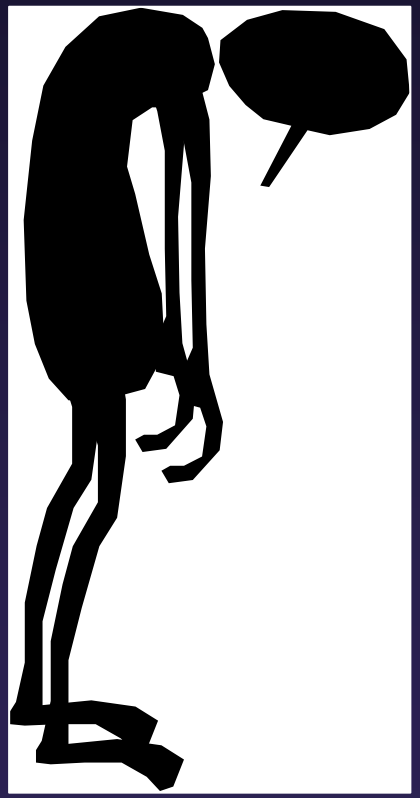
- ≥ 5 symptoms (≥ 1 main)

Main

- Depressed mood
- Loss of interest or pleasure

Additional

- Fatigue or loss of energy
- Inability to think, concentrate or indecisiveness
- Insomnia or hypersomnia
- Feelings of worthlessness or inappropriate guilt
- Recurrent thought of death or suicidal ideation
- Psychomotor agitation or retardation
- Significant weight loss or gain (>5% /month)



Difficulties in Diagnosis

- Atypical symptoms, esp. in elderly:
  - Irritability
  - Anxiety
  - Hypochondriac problems
  - Insomnia
  - Fatigue
- Hallmarks:
  - Persistance of somatic symptoms despite CHF treatment optimization
  - Poor compliance with therapy

Norra et al, IJC 2007

Scale

Common psychometric rating instruments for depression

	Scale	Format	Time	Items	Advantages	Disadvantages	Scoring
Self-rated	Beck Depression Inventory (BDI) [87]	Multiple choice	10–15 min	21	Widely used, easily administered. Norms available. Good with somatic symptoms	High rate of false positives. Somatic items may not be due to depression.	5–9 normal, 10–18 mild to moderate, 19–29 moderate to severe, 30–63 severe depression
	Zung Self-Rating Depression Scale (SDS) [92]	Likert scale	5–7 min	20	Short, easily administered		Depression: 50–80
	Geriatric Depression Scale (GDS) [93]	Yes/no	10 min	15/30	Short, easy to use with elderly, cognitively impaired and patients with visual or physical problems or low motivation.	High false negative rates in minor depression, bad sensitivity for symptoms of fear or negativism	0–9 normal, 10–19 mild, 20–30 severe depression
	Center for Epidemiologic Studies-Depression Scale (CES-D) [94]	Likert scale	5–7 min	20	Short, easily administered to a broad spectrum of patients		Depression: 23–60
	General Health Questionnaire (GHS) [95]	Likert scale	5–7 min	12	Short, easily administered to a broad spectrum of patients	Not very sensitive to depression	11–14 normal, 15–19 distress, 20–36 severe problems, psychological distress
Observer-rated	Hamilton Rating Scale for Depression (HAM-D) [96]	Multiple choice	<30 min	22	Frequently used, well accepted by patients, evaluation of severity of sickness widely established	Psychometrical qualities not optimal, not DSM-IV-compatible	10–13 mild, 14–17 mild to moderate,>17 moderate to severe depression
	Montgomery and Asberg Depression Rating Scale (MADRS) [97]	Multiple choice	10–15 min	10	Good reliability and validity, high correlation with HAM-D	No somatic symptoms	<8 normal, 8–17 mild, 18–35 moderate, 36–60 severe depression
	Bech–Rafaelsen Melancholia Rating Scale (BRMES) [91]	Multiple choice	15–20 min	11	Good reliability and validity		15–25 moderate, 16–44 severe depression

Norra et al, IJC 2007

European Heart Journal (2008) **29**, 2388–2442
doi:10.1093/eurheartj/ehn309

ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008‡

Depression and mood disorders

The prevalence of clinically significant depression has been found to be as high as 20% in HF patients and may be much higher in patients screened with more sensitive instruments or in patients with more advanced HF. Depression is associated with increased morbidity and mortality.[94]

- There is limited evidence regarding screening and assessment tools as well as of the efficacy of psychological and pharmacological interventions in patients with HF. However, screening for depression and initiating appropriate treatment should be considered in patients with suggestive symptoms.

Class of recommendation IIa, level of evidence C

AHA Science Advisory

Depression and Coronary Heart Disease
Recommendations for Screening, Referral, and Treatment

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.

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.

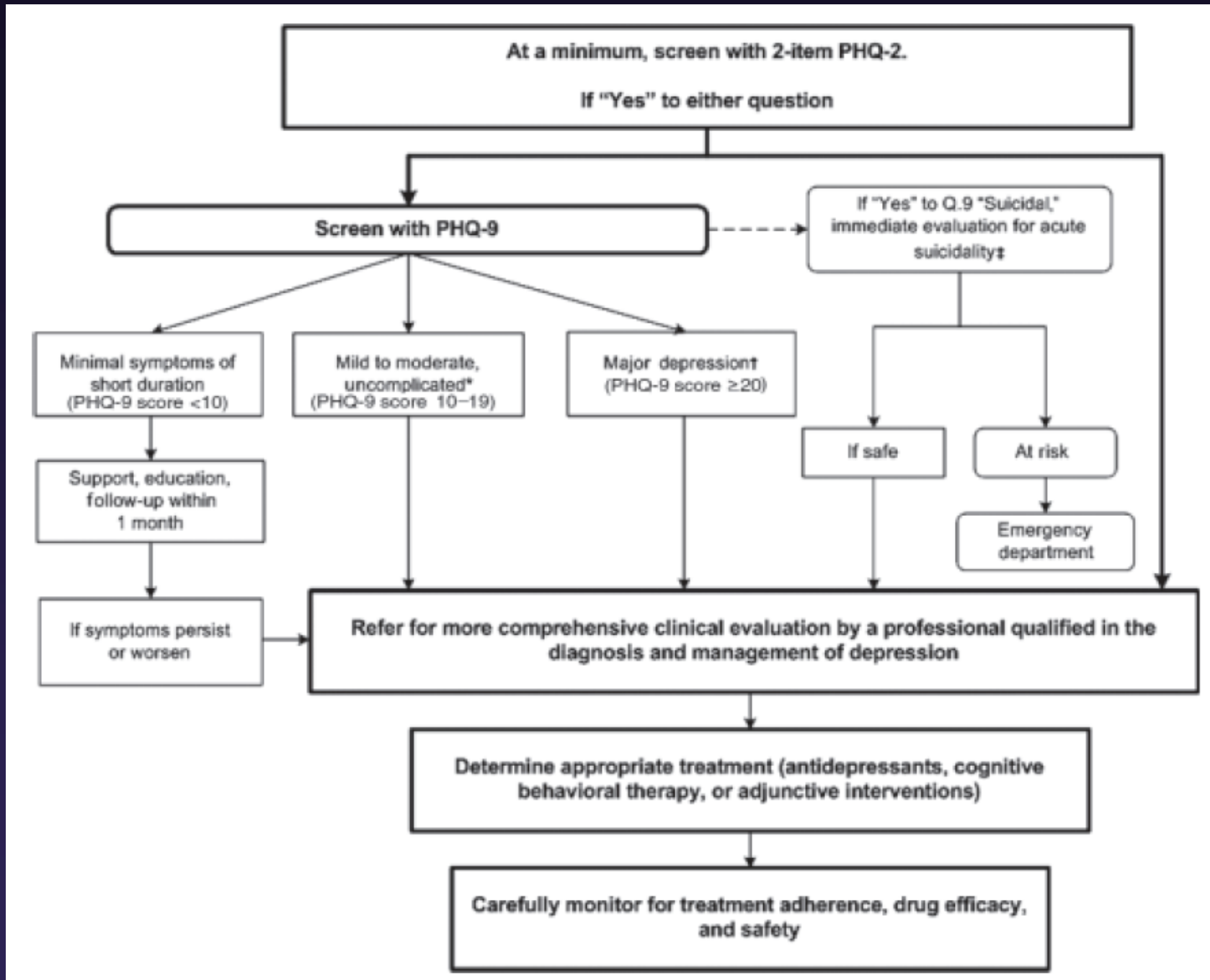
(6) Feeling bad about yourself, feeling that you are a failure, or feeling that you have let yourself or your family down.

(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.

Circulation. 2008;118:1768-1775.



Circulation. 2008;118:1768-1775.

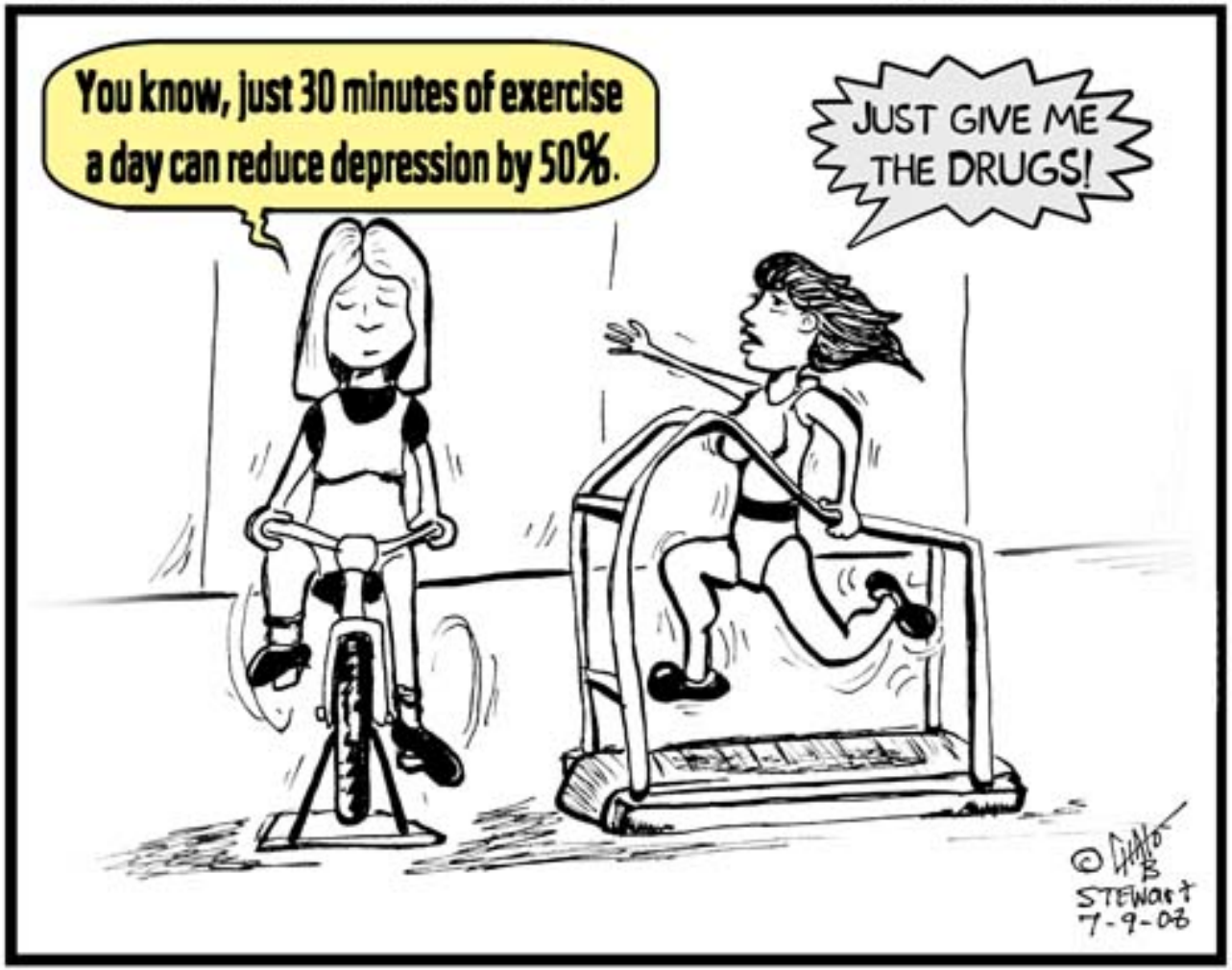
Issue #5
Depression in Heart Disease: To treat or not to treat?

Depression-specific therapy

- Limited and empirical data
- SSRIs (sertraline and citalopram): safe and effective, esp. in moderate/severe or recurrent depression
- Tricyclic antidepressants / MAO Inhibitors: maybe cardiotoxic / contraindicated
- Cognitive-behavioral therapy: maybe effective / alternative to drugs
- Exercise: beneficial but often pts are not compliant…

MentalHealthHumor.com

By: Chato B. Stewart



Reduce Depression

www.MentalHealthHumor.Today.com

JAMA®

Sertraline Treatment of Major Depression in Patients With Acute MI or Unstable Angina *JAMA. 2002;288:701-709*

Alexander H. Glassman; Christopher M. O'Connor; Robert M. Califf; et al
for the Sertraline Antidepressant Heart Attack Randomized Trial (SADHART) Group

- Sertraline was (i) safe; (ii) effective in recurrent depression

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JAMA®

Online article and related content current as of February 15, 2010.

Effects of Citalopram and Interpersonal Psychotherapy on Depression in Patients With Coronary Artery Disease: The Canadian Cardiac Randomized Evaluation of Antidepressant and Psychotherapy Efficacy (CREATE) Trial *JAMA. 2007;297:367-379*

François Lespérance; Nancy Frasure-Smith; Diana Koszycki; et al.

- Citalopram was effective and safe; Psychotherapy had no added value

JAMA®

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JAMA®

Online article and related content current as of February 15, 2010.

Effects of Treating Depression and Low Perceived Social Support on Clinical Events After Myocardial Infarction: The Enhancing Recovery in Coronary Heart Disease Patients (ENRICHD) Randomized Trial

Writing Committee for the ENRICHD Investigators *JAMA. 2003;289:3106-3116*

• Cognitive behavior therapy had no effect on event-free survival and slight improvement in depression and social isolation

JAMA®

Depression Screening and Patient Outcomes in Cardiovascular Care: A Systematic Review

Brett D. Thombs; Peter de Jonge; James C. Coyne; et al.

- Depression treatment (medication or cognitive behavioral therapy) in CVD pts (6 trials):

- modest improvement in depressive symptoms

- no improvement in cardiac outcomes

Source	No. Randomized[b]
Efficacy	
Strik et al,[59] 2000	Fluoxetine 27 Placebo 27
Glassman et al,[60] 2002[g]	Sertraline 186 Placebo 183
Honig et al,[30] 2007	Mirtazapine 47 Placebo 44
Lespérance et al,[61] 2007[i]	Citalopram 142 Placebo 142 Interpersonal psychotherapy and clinical management 142 Clinical management only 142
Effectiveness	
van Melle et al,[32] 2007[j]	Active treatment 209 Usual care 122[k]
Cardiovascular outcomes	
Berkman et al,[31] 2003[l]	Cognitive behavioral therapy 925 Usual care 909

JAMA. 2008;300(18):2161-2171

HF-specific or alternative therapy

Effects of Levosimendan on Quality of Life and Emotional Stress in Advanced Heart Failure Patients

John T. Parissis · Constantinos Papadopoulos · Maria Nikolaou · Vassiliki Bistola · Dimitrios Farmakis · Ioannis Paraskevaidis · Gerasimos Filippatos · Dimitrios Kremastinos

Cardiovasc Drugs Ther (2007) 21:263–268

- 63 pts with ADCHF
- Levosimendan improved Zung SDS and BDI
- Zung SDS and BDI improvement was correlated with BNP reduction

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Cardiovasc Drugs Ther (2007) 21:263–268

- 63 pts with ADCHF
- Levosimendan improved Zung SDS and BDI
- Zung SDS and BDI improvement was correlated with BNP reduction

Effects of darbepoetin-alpha on quality of life and emotional stress in anemic patients with chronic heart failure

Kallirrhoe Kourea, John T. Parissis, Dimitrios Farmakis, Ioannis Paraskevaidis, Fotios Panou, Gerasimos Filippatos and Dimitrios Th. Kremastinos

Eur J Cardiovasc Prev Rehabil 15:365–369 © 2008

- 41 CHF pts with anemia
- Darbepoetin improved Zung SDS and BDI
- Zung SDS improvement was correlated with 6-min walk test increase

Effects of functional electrical stimulation on quality of life and emotional stress in patients with chronic heart failure secondary to ischaemic or idiopathic dilated cardiomyopathy: A randomised, placebo-controlled trial

Apostolos Karavidas [a], John Parissis [b,*], Sophia Arapi [a], Dimitrios Farmakis [b], Dimitrios Korres [a], Maria Nikolaou [b], John Fotiadis [a], Nikolaos Potamitis [a], Xenia Driva [a], Ioannis Paraskevaidis [b], Evaggelos Matsakas [a], Gerasimos Filippatos [b], Dimitrios T. Kremastinos [b]

Exercise capacity, emotional status and quality of life measurements at baseline and after treatment in the two study groups

Variable	FES		Placebo		*F*	*p*
	Before	After	Before	After		
6MWT	455.8±93.7	498.1±97.3	451.9±75.7	454.4±78.8	19.413	<0.001
BNP	563.5±136.2	529.5±137.3	521.7±90.5	523.6±89.6	4.252	0.053
KCCQ functional	0.52±0.14	0.67±0.10	0.51±0.15	0.52±0.13	76.666	<0.001
KCCQ summary	0.43±0.16	0.59±0.13	0.39±0.14	0.41±0.14	41.508	<0.001
Zung SDS	45.8±13.6	38.3±11.8	51.0±13.2	51.3±13.5	27.098	<0.001
BDI	11.75±9.2	7.45±7.2	16.3±9.9	16.6±9.8	17.768	<0.001

- 30 pts, stable CHF
- FES, 30 min/day, 5 days/week, 6 weeks
- FES improved Zung SDS and BDI
- Zung SDS and BDI improvement correlated with 6-min WT and KCCQ improvement

European Journal of Heart Failure 10 (2008) 709–713

Conclusions

Issue #1
Depression in Heart Disease: Another pandemic flu?

Depression is at least 2-3 times more frequent in pts with HD

Issue #2
Depression in Heart Disease: Is it that bad?

Depression is associated with:

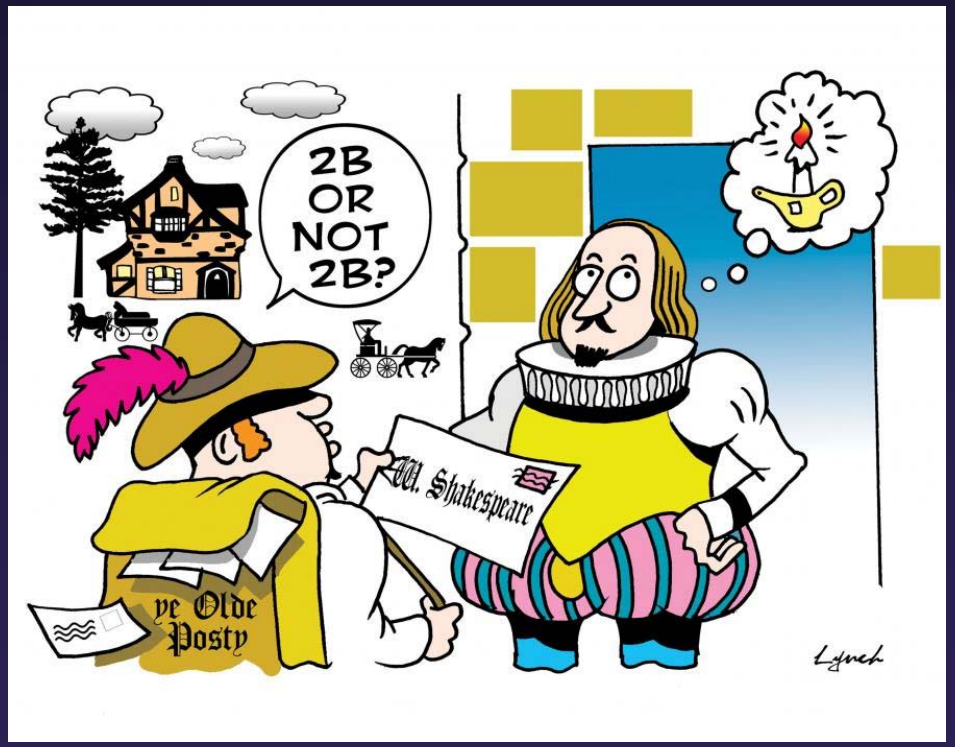
- increased cardiac risk
- worse cardiac outcome

Issue #3
Depression in Heart Disease: The chicken or the egg came first?

Common and bidirectional pathogenetic mechanisms

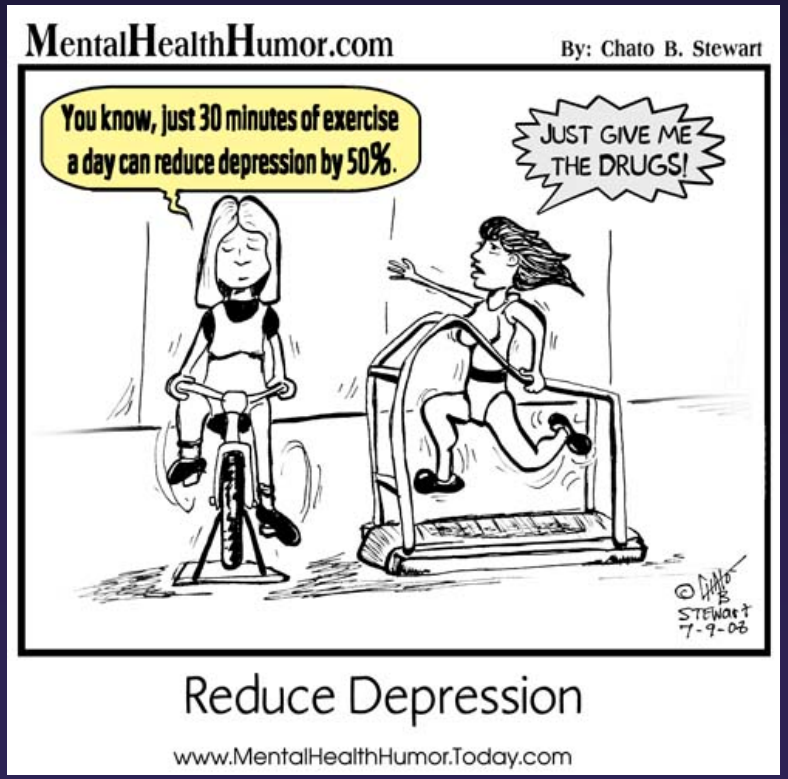
Issue #4
Depression in Heart Disease: To screen or not to screen?

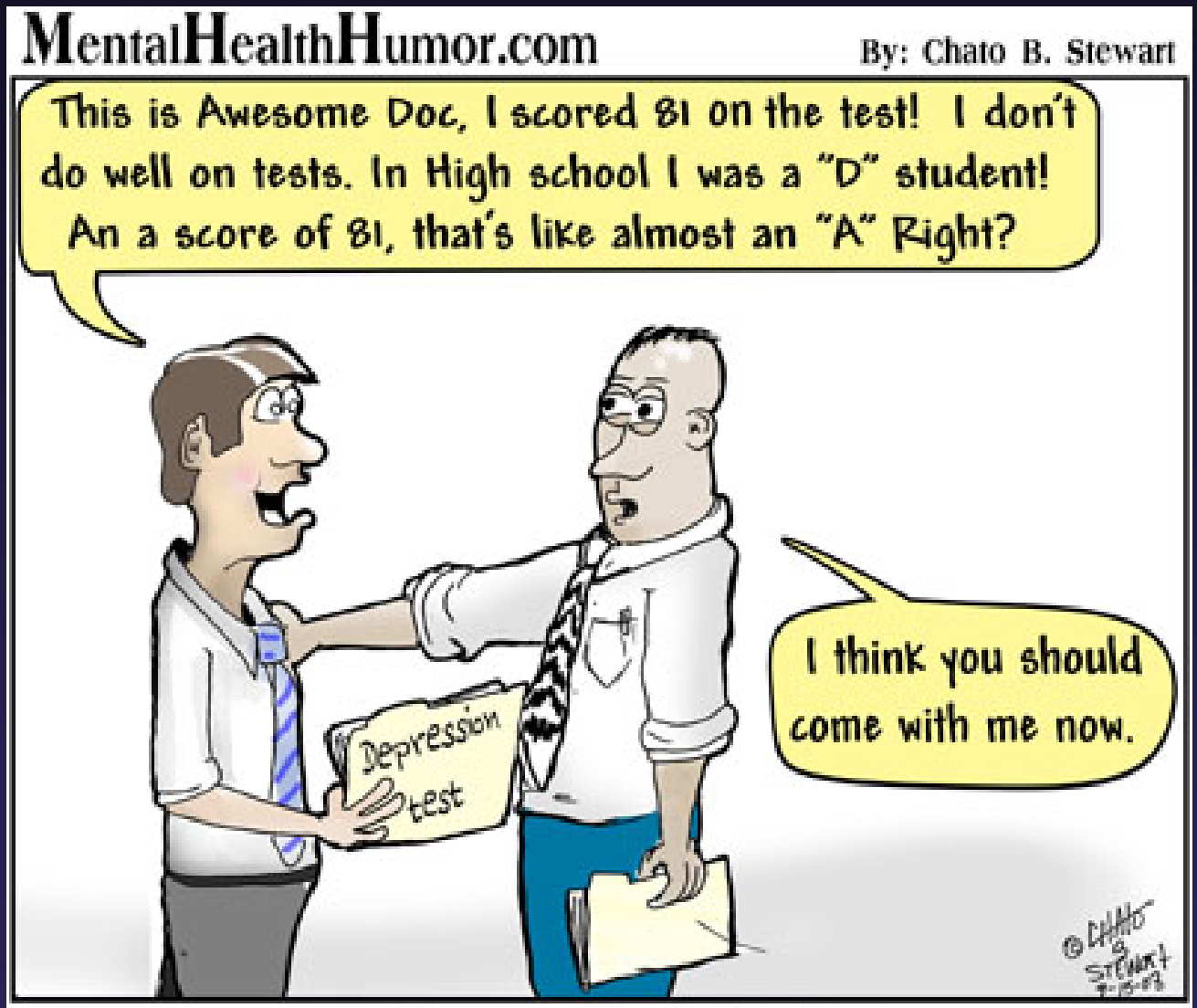
Fairly accurate and cost-effective but with no obvious clinical benefit



Issue #5
Depression in Heart Disease: To treat or not to treat?

- SSRIs are safe and may improve mood but not cardiac outcomes
- Exercise and other measures may be of value





Depression Test