

Epidemiology and Treatment of Depression in Patients with Chronic Medical Illness

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Outline

I Epidemiology

- a) Prevalence of major depression in patients with chronic medical illness
- b) Effect of depression on medical symptom burden
- c) Adverse effect of depression on functional impairment and quality of life
- d) Depression: Association with high risk health behaviors i.e. smoking, obesity, sedentary lifestyle
- e) Association of depression with poor adherence to medical regimens
- f) Association of depression with complications of medical illness and mortality
- g) Association of depression with medical costs

II Treatment studies

- a) Evidence that depression can be effectively treated in patients with medical illness
- b) Cost offset effect of improving quality of depression care in patients with diabetes

III. Antidepressants in female patients and patients with hepatic and renal failure

Pre-Lecture Exam

Question 1

1. Physiologic effects of depression can include:
(Choose the single best answer)
 - A. Reduced immune function
 - B. Memory/concentration impairment
 - C. Glucose intolerance
 - D. Increase autonomic arousal
 - E. Amplification of pain

Question 2

- 2. True or False:** Treatment for depression in patients who are medically ill has been shown to reduce mortality.

Question 3

3. Choose the single best answer:

In individuals with at least 50% stenosis of one or more coronary arteries, functional status at one year follow-up correlated most closely with

- A. Degree of occlusion of coronary arteries**
- B. Glucose regulation**
- C. Reduction of cholesterol levels**
- D. Anxiety and depression severity**
- E. Participation in a cardiac rehabilitation program**

Question 4

- 4. Choose the single best answer: The increase in the risk of non-cardiac death in depressed individuals is:**
- A. Not different**
 - B. 100-200%**
 - C. 300-400%**
 - D. 800%**

Question 5

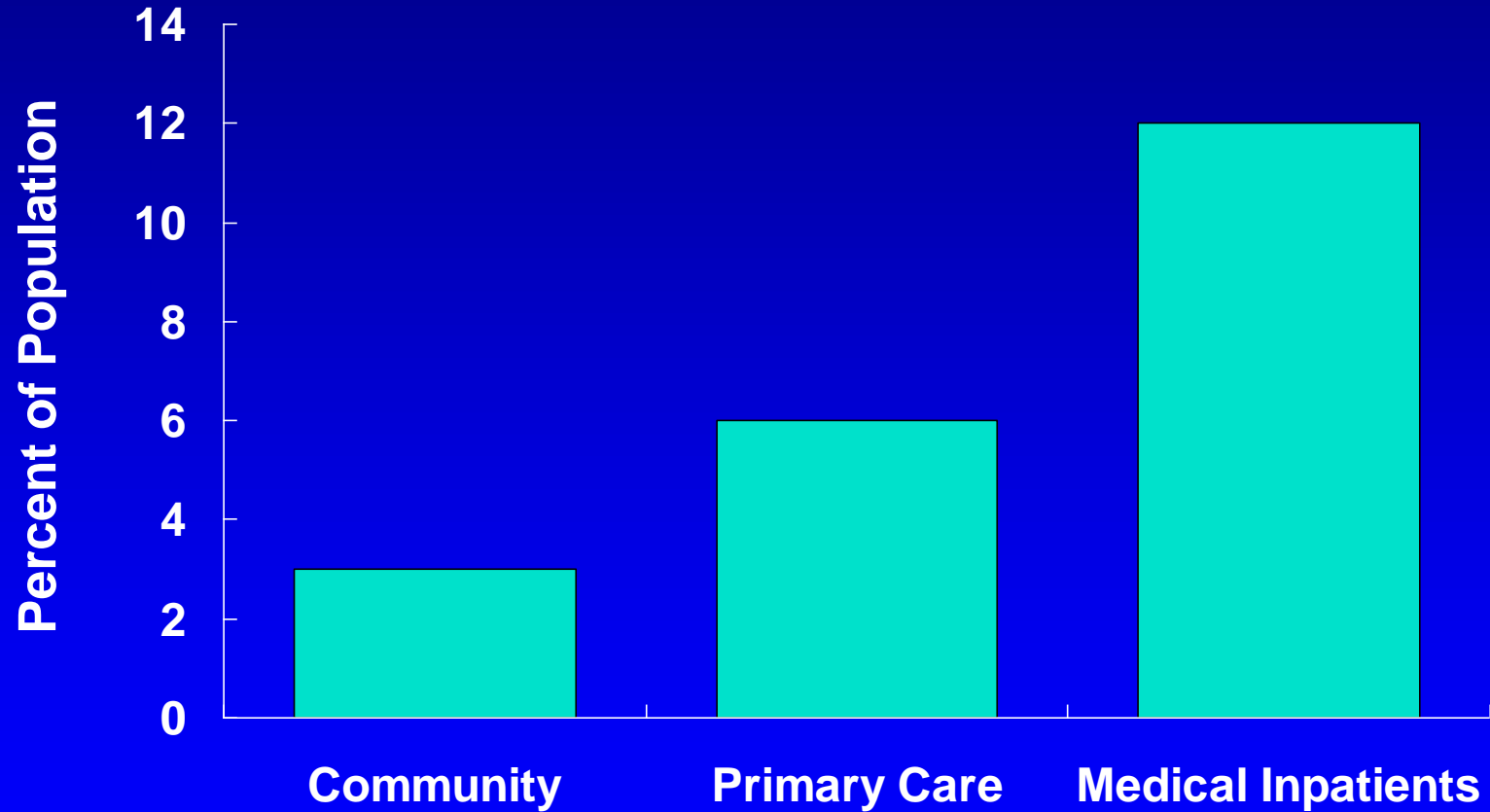
5. True or False: Antidepressant medication does not reduce pain in non-depressed individuals.

Depression and Chronic Medical Illness

Major Teaching Points

- Increased prevalence of major depression in the medically ill
- Depression amplifies physical symptoms associated with medical illness
- Comorbidity increases impairment in functioning
- Depression decreases adherence to prescribed regimens
- Depression is associated with adverse health behaviors (diet, exercise, smoking)
- Depression increases complications of disease and mortality

Prevalence Of Major Depression



Major Depression Prevalence: Chronic Medical Illness

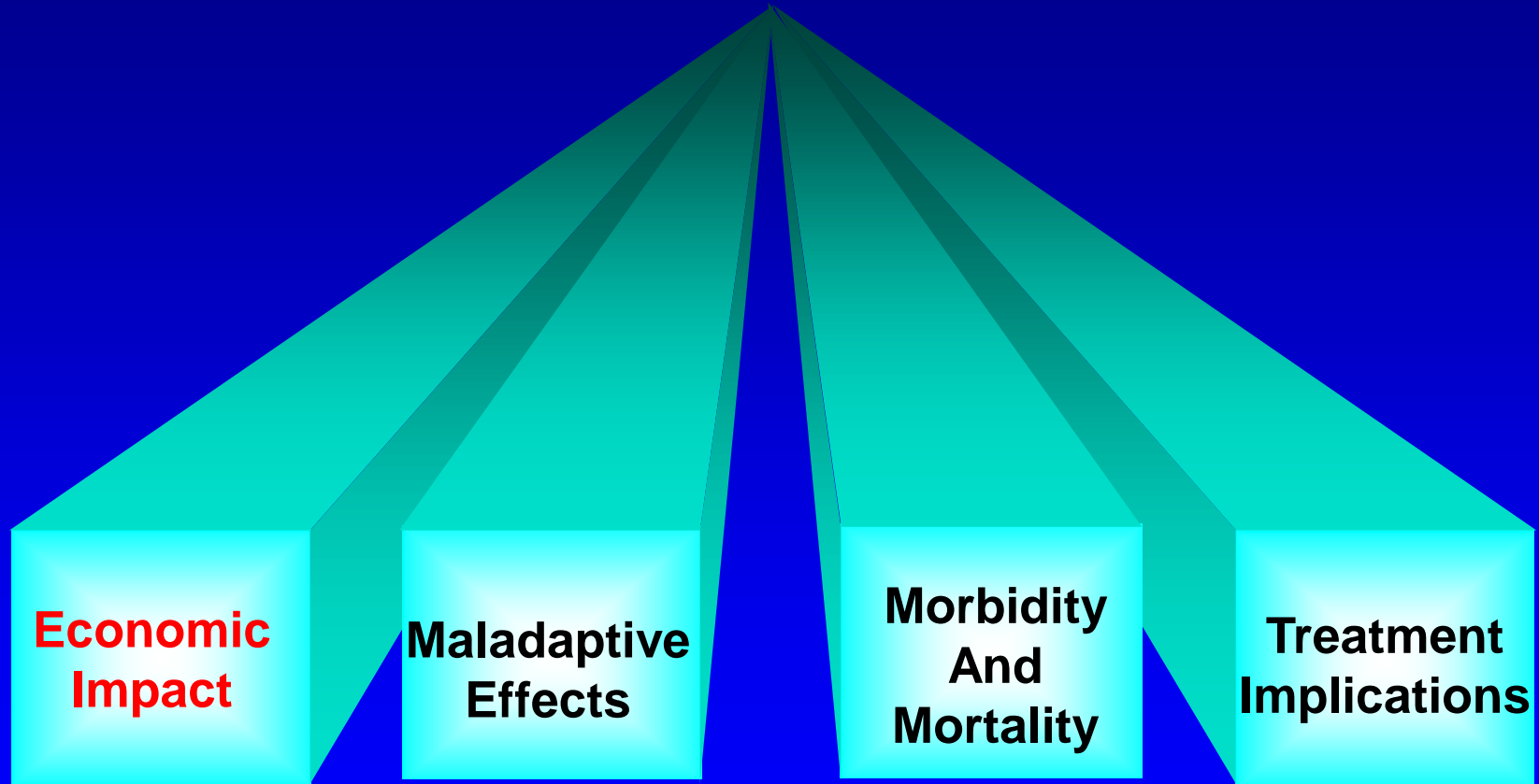
- Heart disease 15 to 23%
- Diabetes 11 to 12%
- Chronic obstructive pulmonary disease (COPD) 10 to 20%

Depression Prevalence Is Especially High in Neurological Illness

Lifetime prevalence

- Parkinson's disease: 40-50% lifetime prevalence
- Huntington's disease: 40% lifetime prevalence. Depression may antedate chorea by years
- Multiple sclerosis: 10-50% lifetime prevalence
- Alzheimer's disease: 15-55% prevalence
- CVAs: 30-50% lifetime prevalence

Impact Of Depression In Chronic Medical Illness



Economic Impact Of Mental Disorders

High Utilizers Of General Medical Care



**The Top 10% Of
Healthcare Utilizers
Account For:**

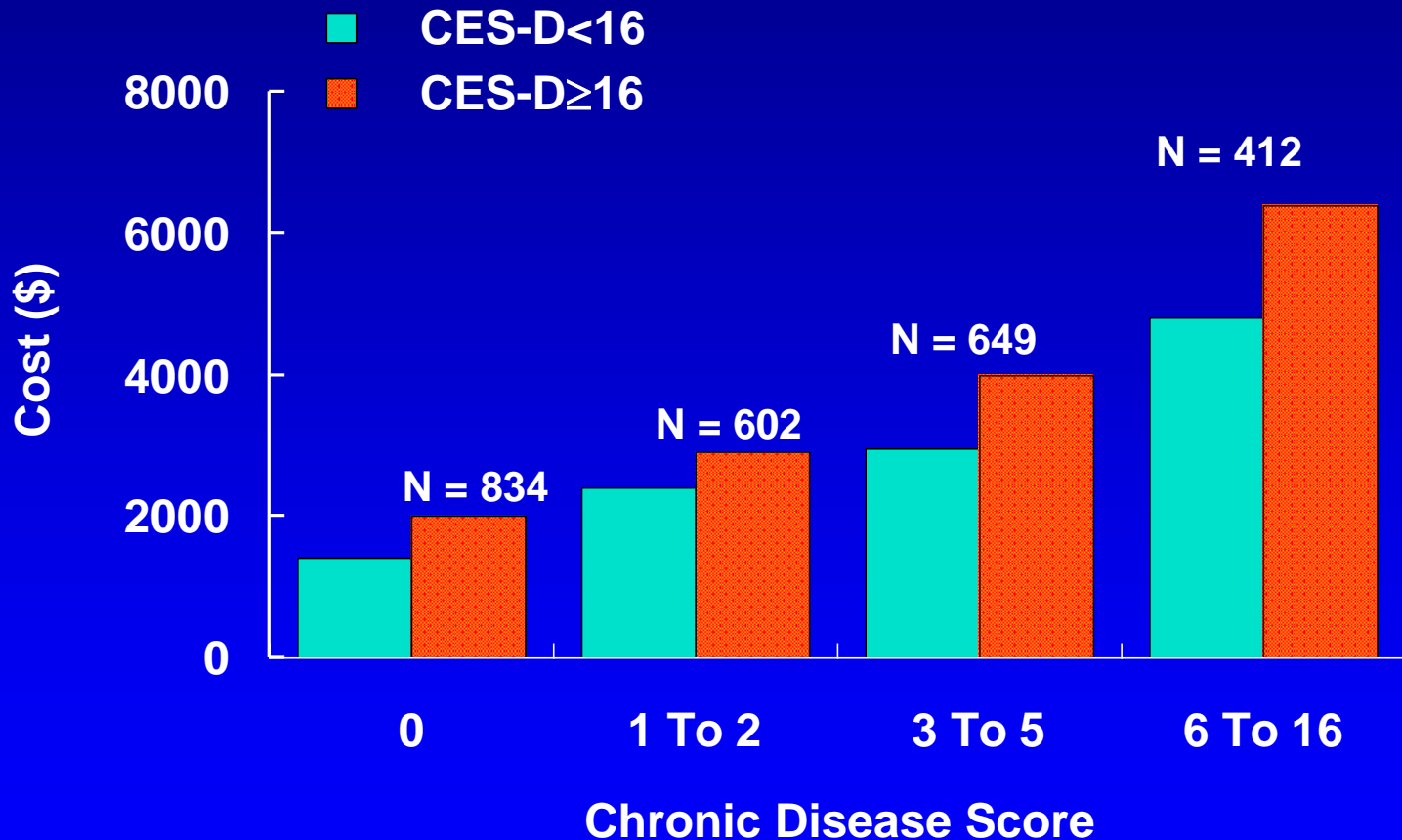
- 29% of primary care visits
- 52% of specialty visits
- 40% of in-hospital days
- 26% of prescriptions
- >Two-thirds have 1 or more chronic medical illnesses

Economic Impact Of Mental Disorders

High Utilizers Of General Medical Care

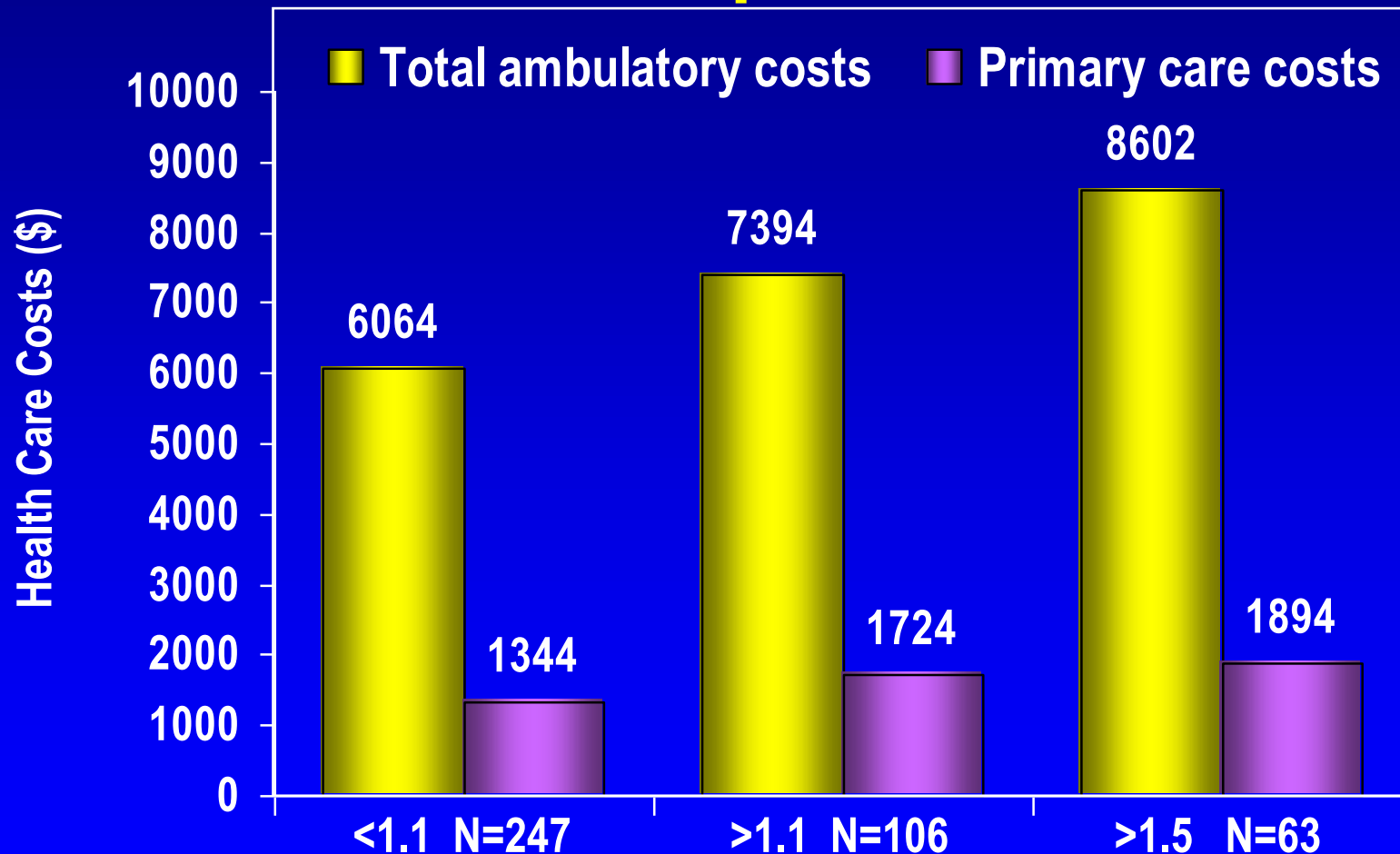
- **50% of high utilizers are psychologically distressed**
- **1-month prevalence of psychiatric disorders in high utilizers**
 - **depressive disorders 40.3%**
 - **generalized anxiety disorder 21.8%**
 - **somatization disorder 20.2%**
 - **panic disorder 11.8%**
 - **alcohol abuse 5.0%**

Depressive Symptoms And Mean Annual Costs At Different Levels Of Chronic Disease Score



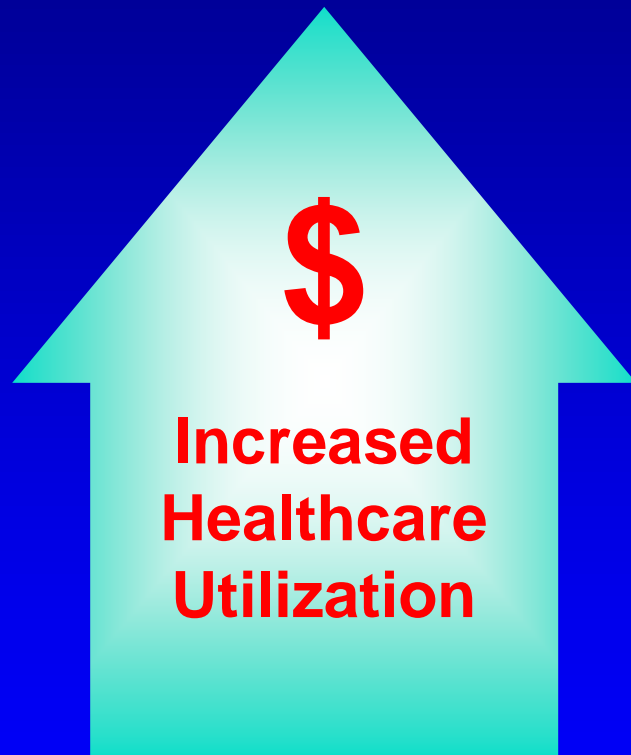
CES-D = center for epidemiologic studies-depression scale
Unutzer. JAMA. 1997.

Health Care Costs Are Higher in Patients With Diabetes and Depression



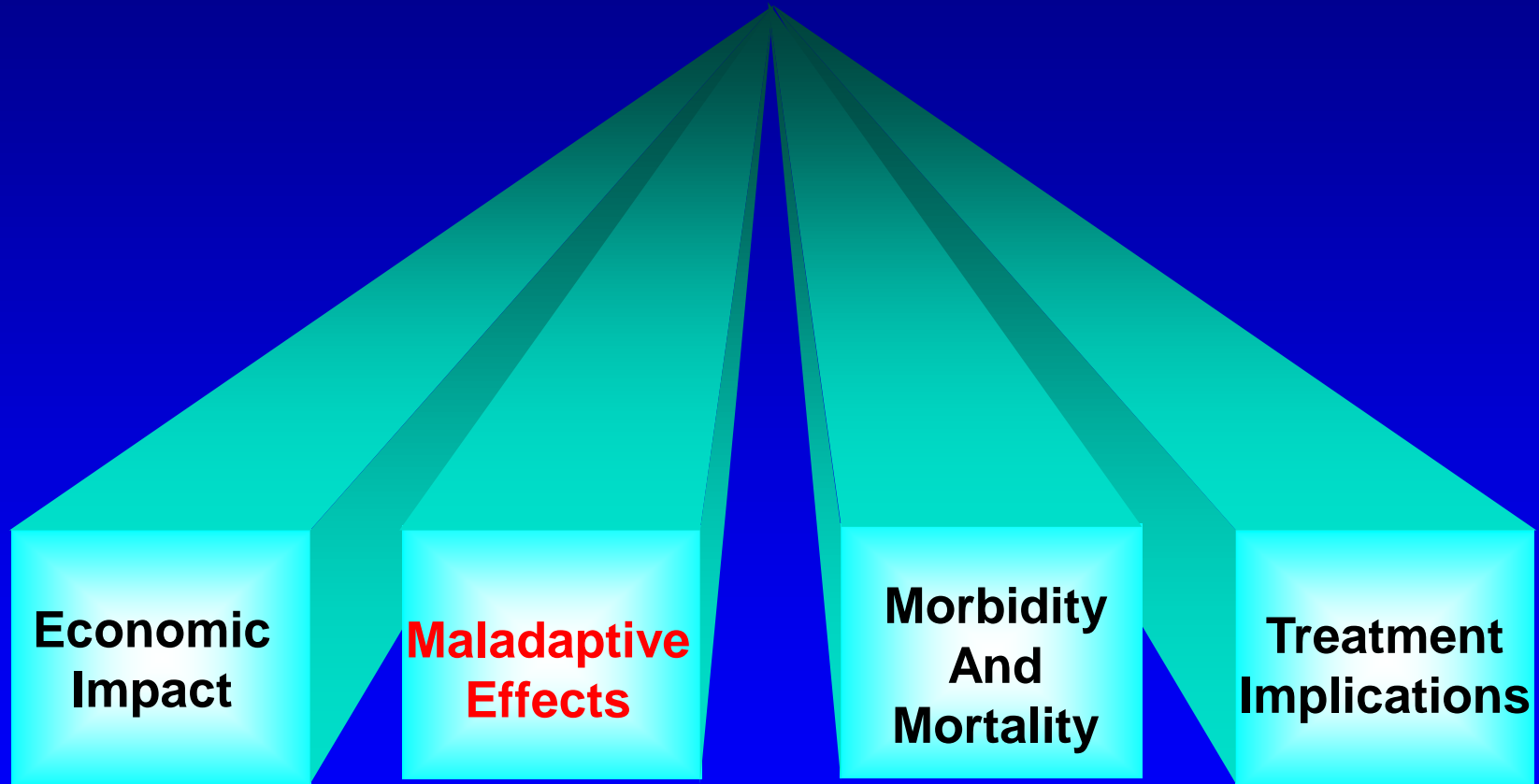
Economic Impact Of Mental Disorders

Medical Inpatients With Psychiatric Comorbidity



- Length of stay
- Use of medical services
- Medical costs
- ER costs
- Rehospitalization rates for at least 4 years after discharge

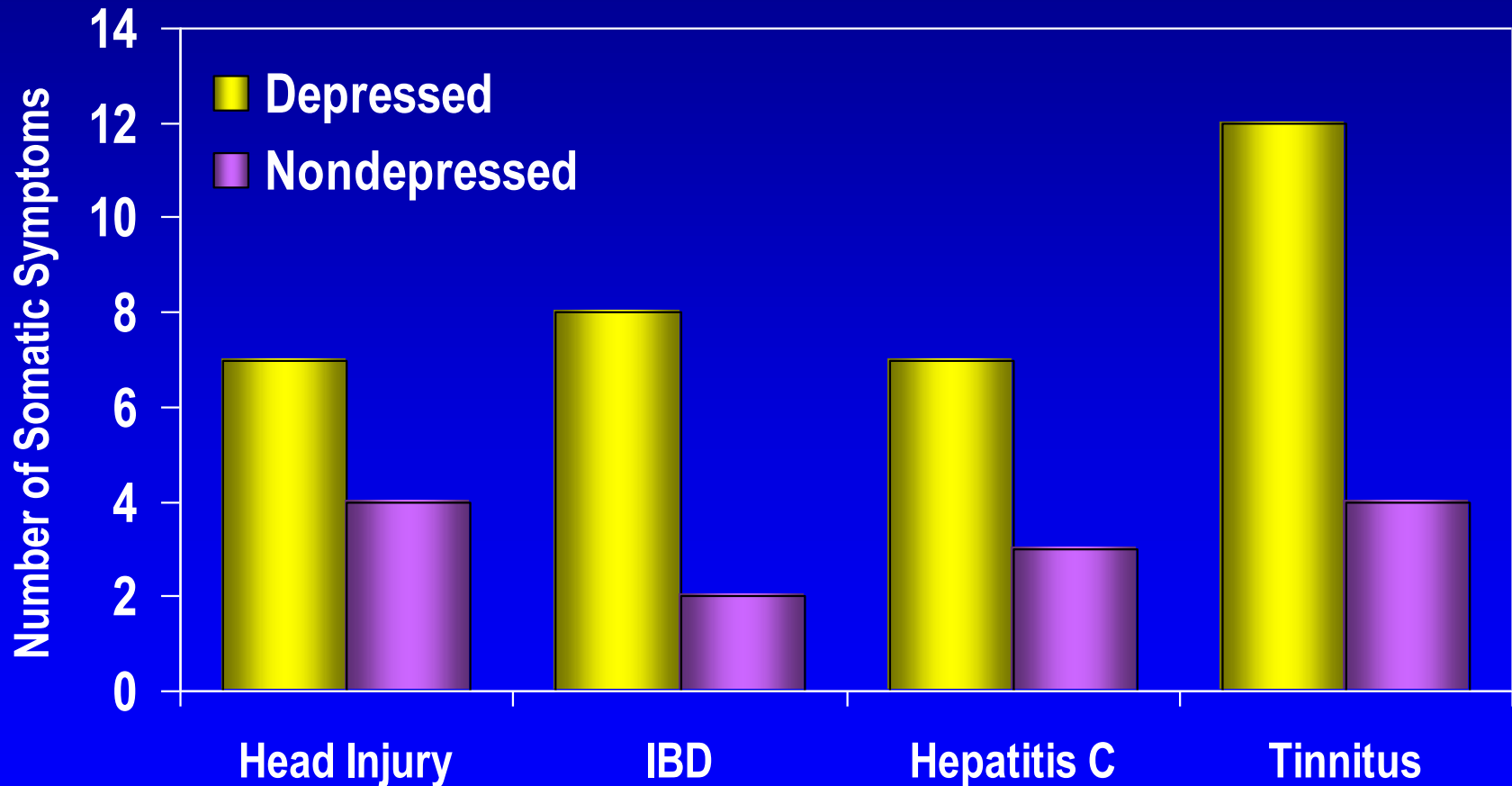
Impact Of Depression In Chronic Medical Illness



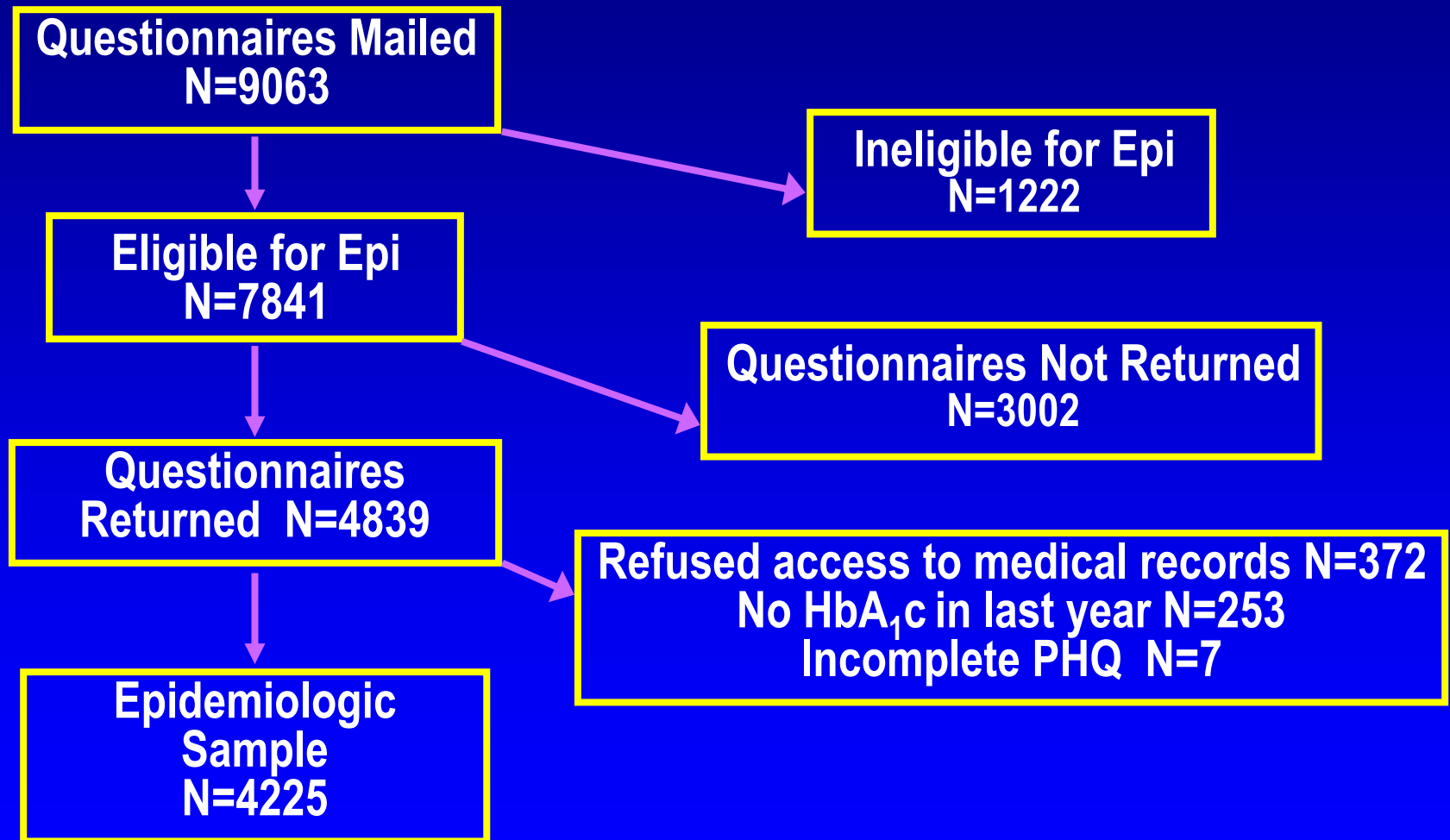
4 Maladaptive Effects of Affective Illness on Chronic Medical Illness

- Amplification of somatic symptoms (especially pain) and functional disability
- Increased adverse health behaviors (obesity, smoking, sedentary lifestyle)
- Decreased self-care and adherence to medical regimens
- Direct maladaptive physiologic effects
 - Modulated by autonomic nervous system, hypothalamus, and immunologic effects

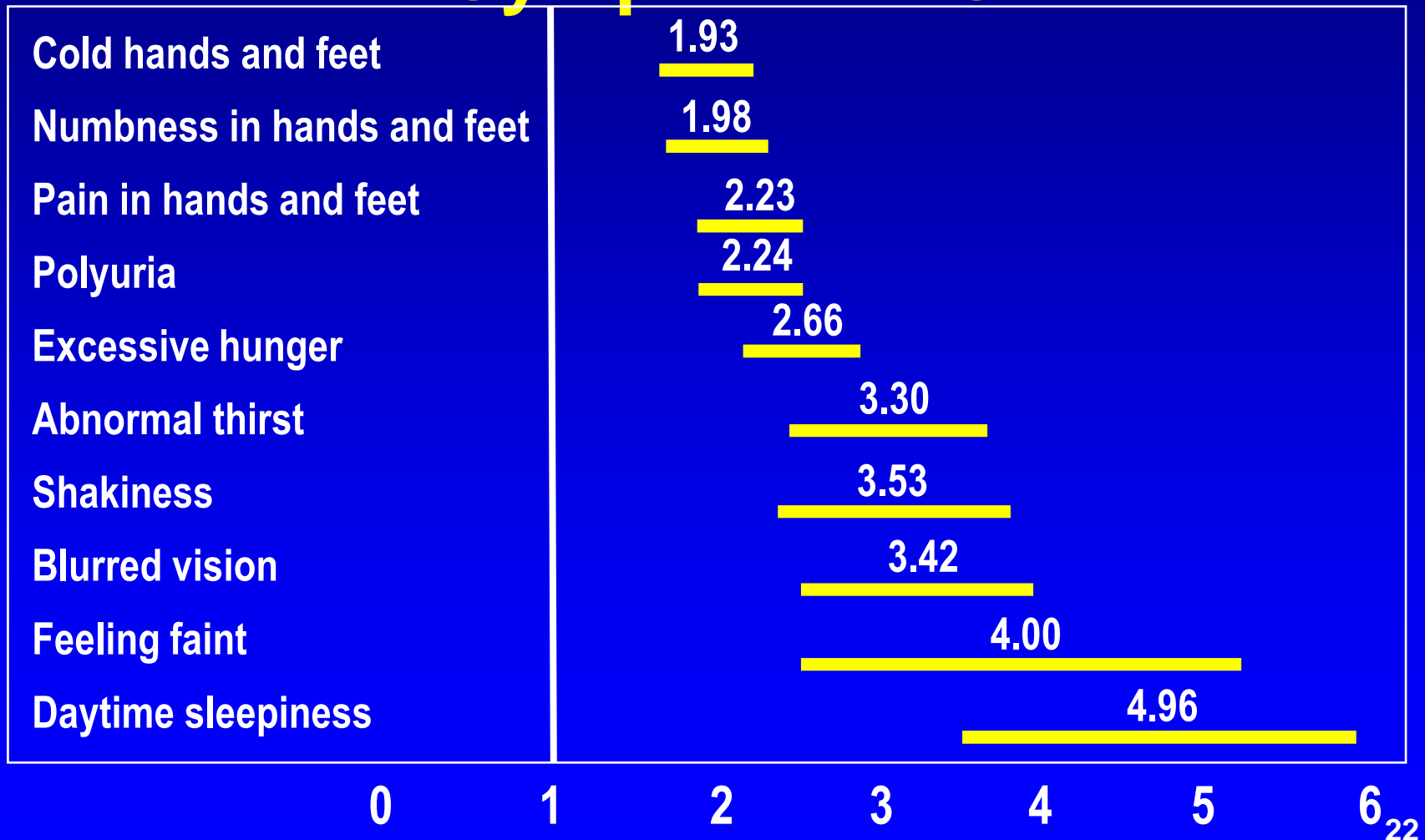
Depression Comorbidity Amplifies Number of Somatic Symptoms



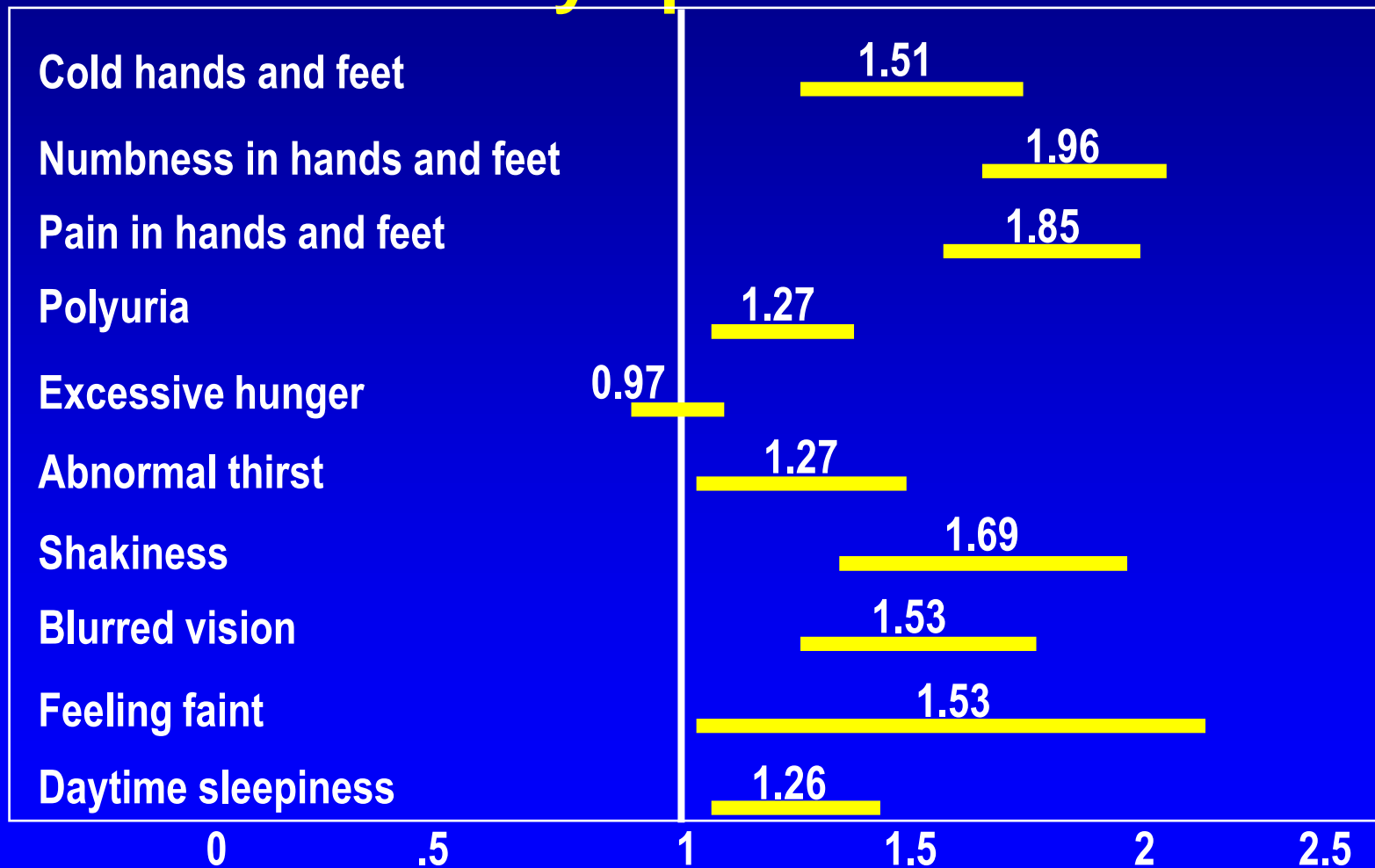
Recruitment for Pathways Epidemiological Study



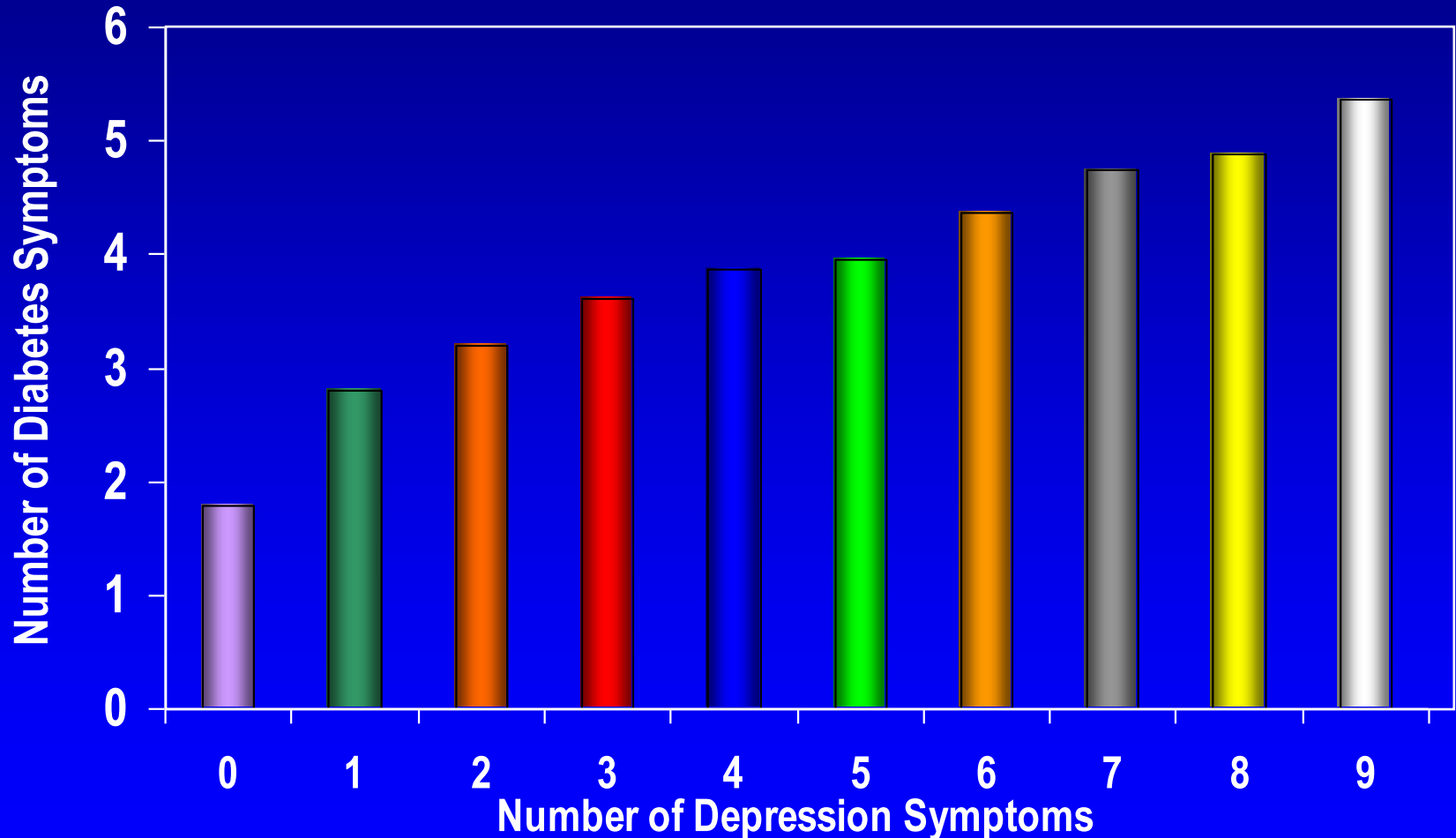
Relationship of Major Depression to Diabetes Symptoms – Odds Ratios

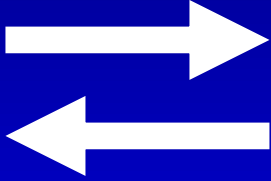


Number of Diabetes Complications (≥ 2) also Increases Number of Diabetes Symptoms



Number of Diabetes Symptoms and Depression Symptoms Highly Correlated

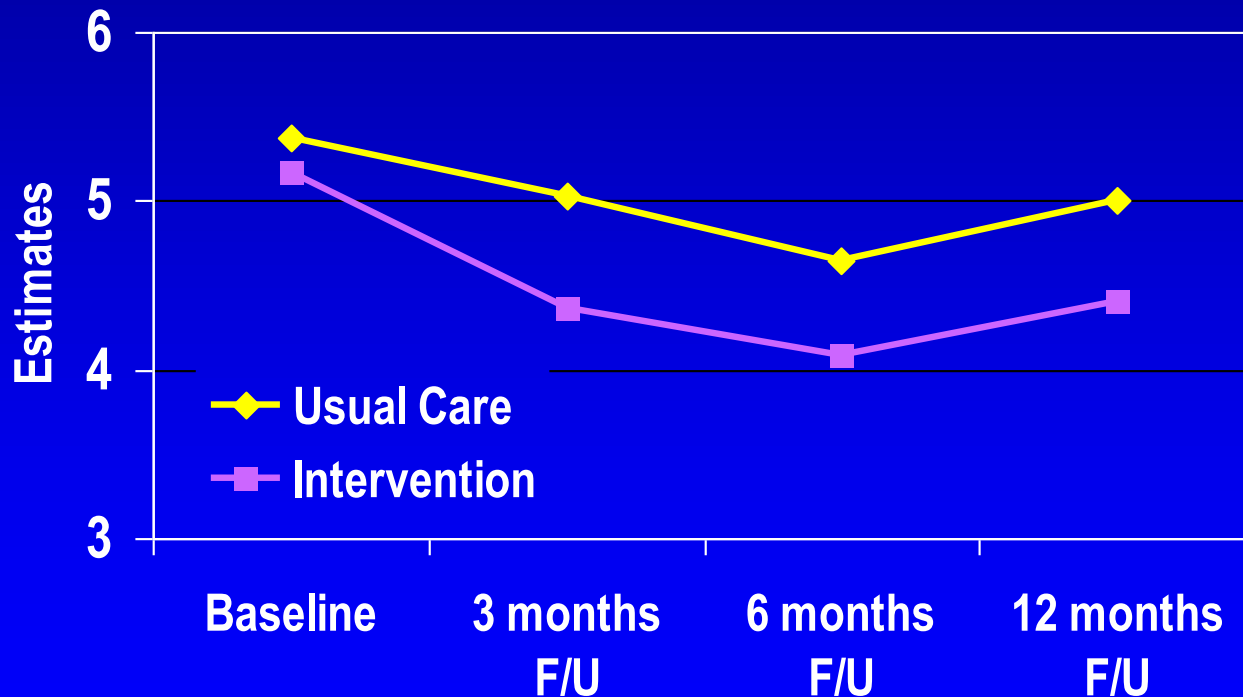


Pain  **Depression**

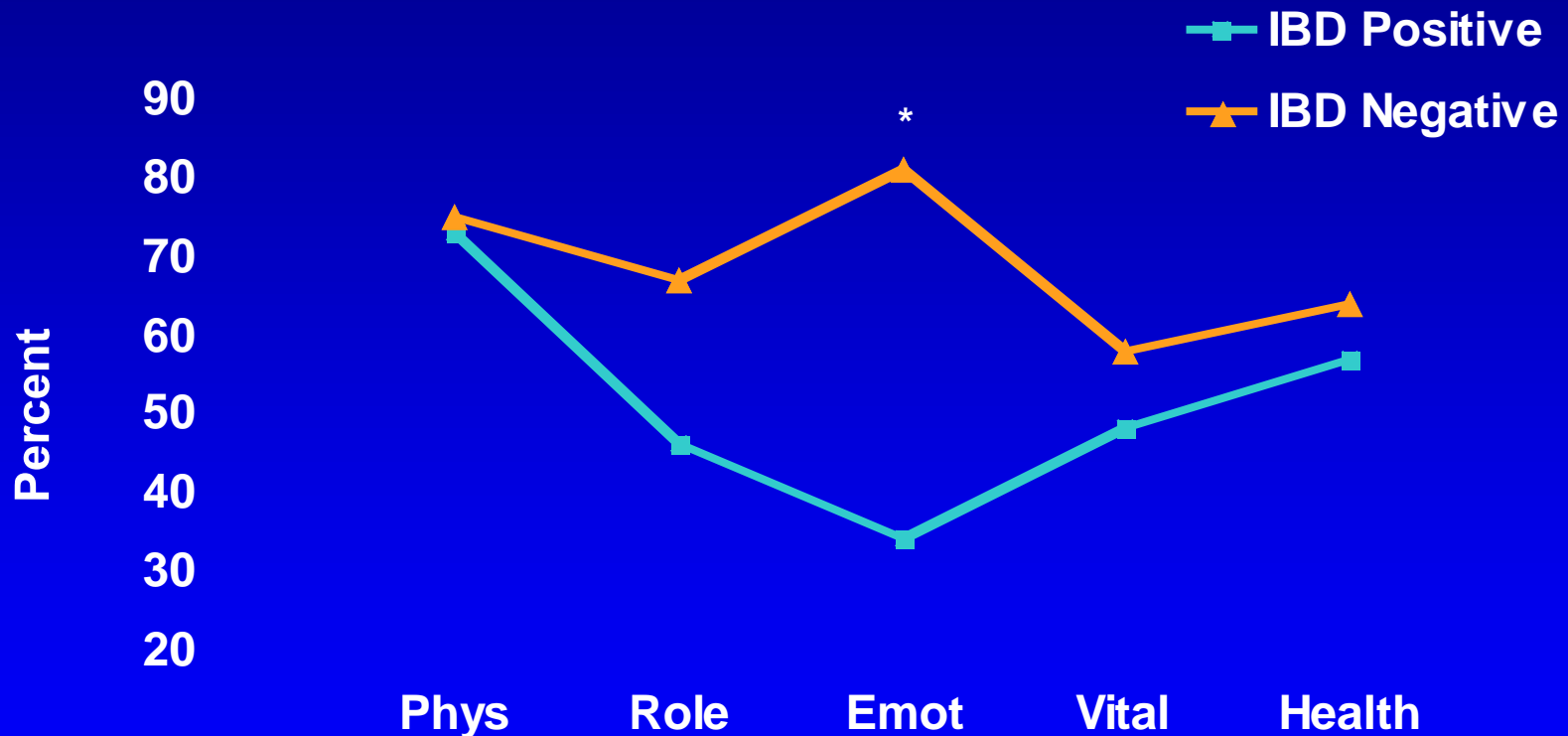
Bidirectional Relationship

Treatment of Depression Improves Pain Outcomes in Patients With Arthritis and Depression

Arthritis Interference With Daily Activities (0-10)



SF-36 Disability Ratings In IBD Patients With And Without Psychiatric Illness



* $P < .001$ IBS vs comparators.

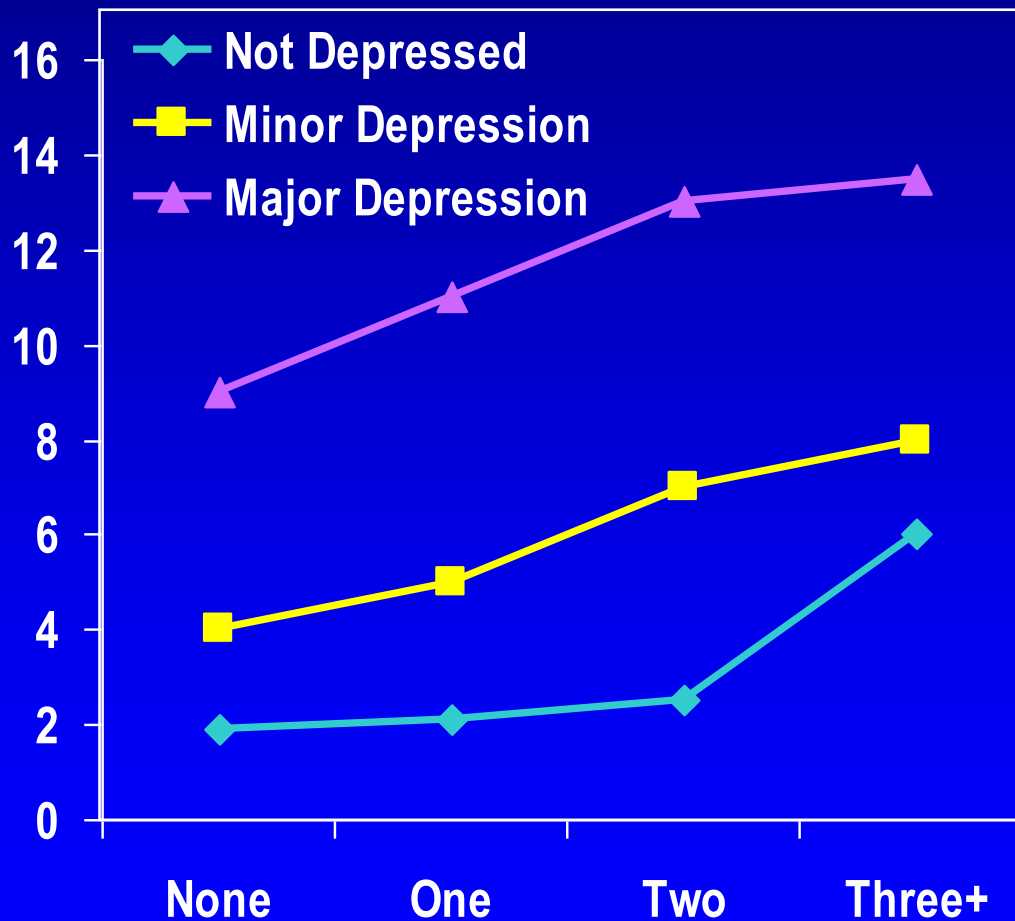
IBD = inflammatory bowel disease.

Walker et al. *Gen Hosp Psychiatry*. 1996;18:220.

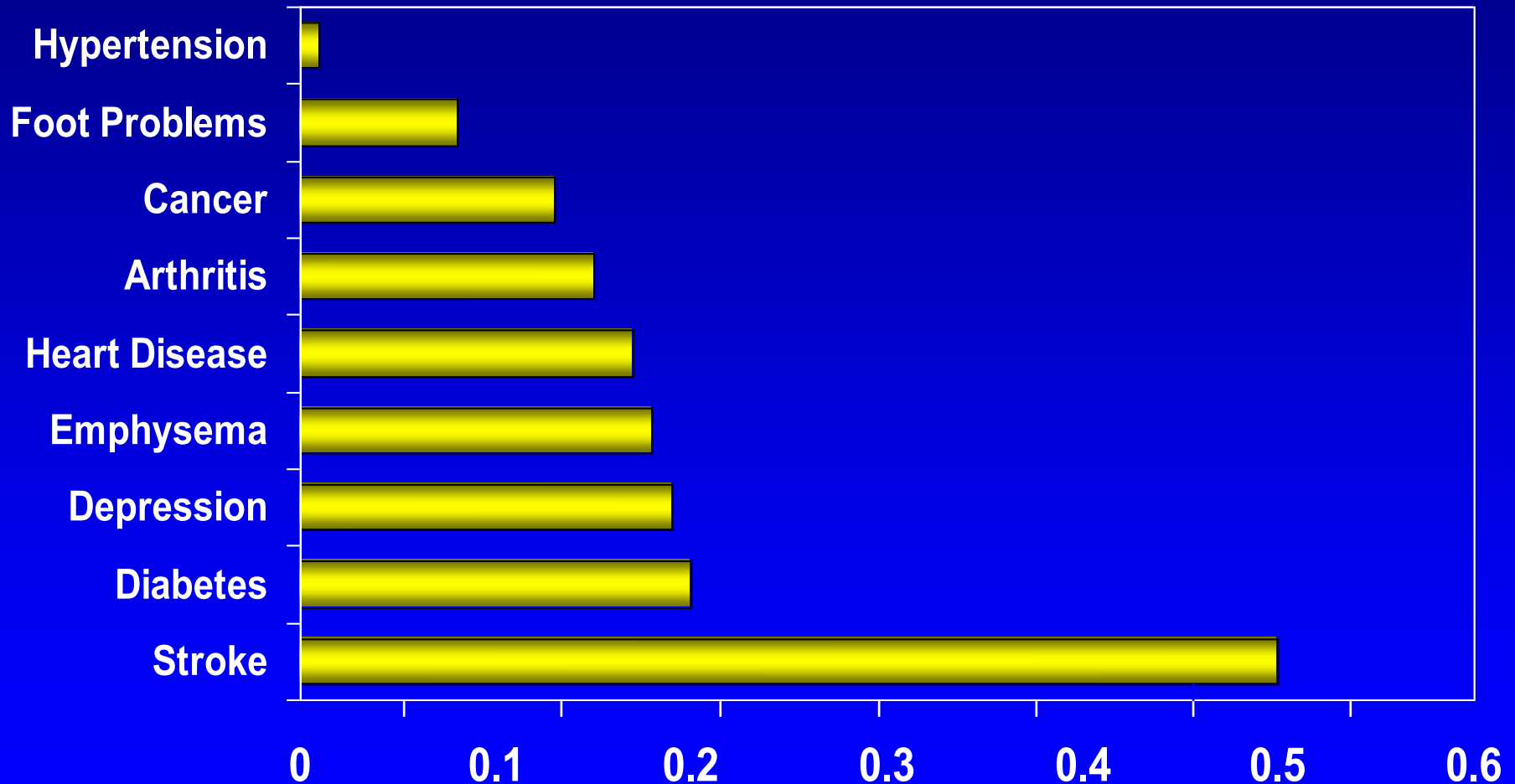
Depression/Anxiety: Impact On Quality Of Life In Patients With CAD

Baseline depression/anxiety is a better predictor than the number of coronary vessels with $\geq 50\%$ occlusion of decreased quality of life over a 1-year period

Depression Has Larger Impact on Days Reduced Household Work Than Diabetes Complications



Depression Decreases in Quality Adjusted Life Years (QALYs) Over 4 Years



Sample of 2558 primary care patients age >65 in a staff model HMO.
Unutzer J, et al. *Int Psychogeriatr.* 2000;12(1):15-33.

Depression Decreases Adherence to Medical Regimens

- Depression may affect adherence by
 - Adversely influencing expectations and benefits about efficacy of treatment
 - Increasing withdrawal and social isolation
 - Reducing cognitive functioning and memory
 - Influencing dietary choices and reducing energy to exercise and follow self-management regimens (ie, checking blood glucose)

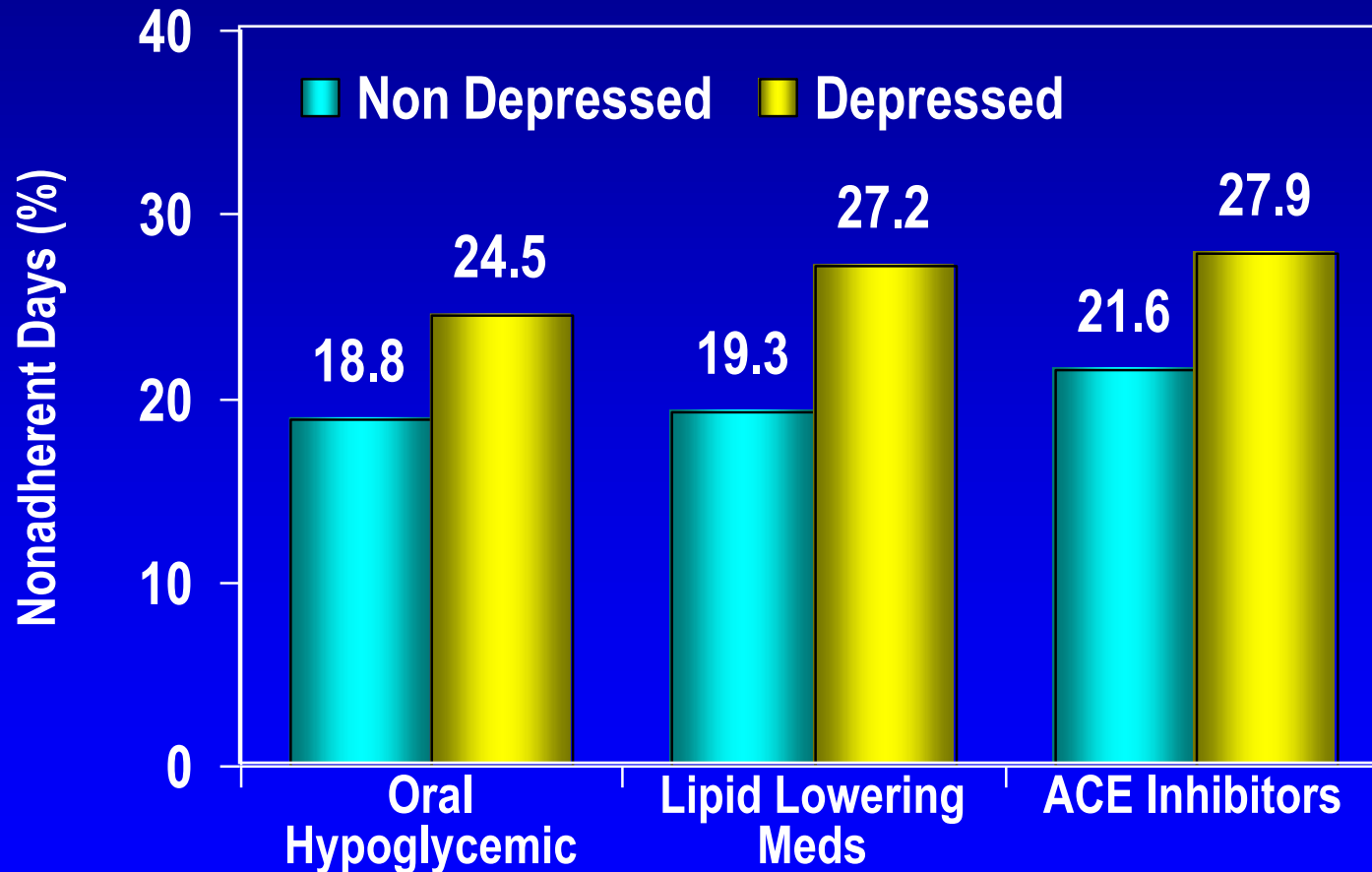
Meta-Analysis of the Adverse Effect of Depression on Patient Adherence

- Compared to nondepressed patients, the odds are 3 times greater that depressed patients would be nonadherent with medical treatment recommendations

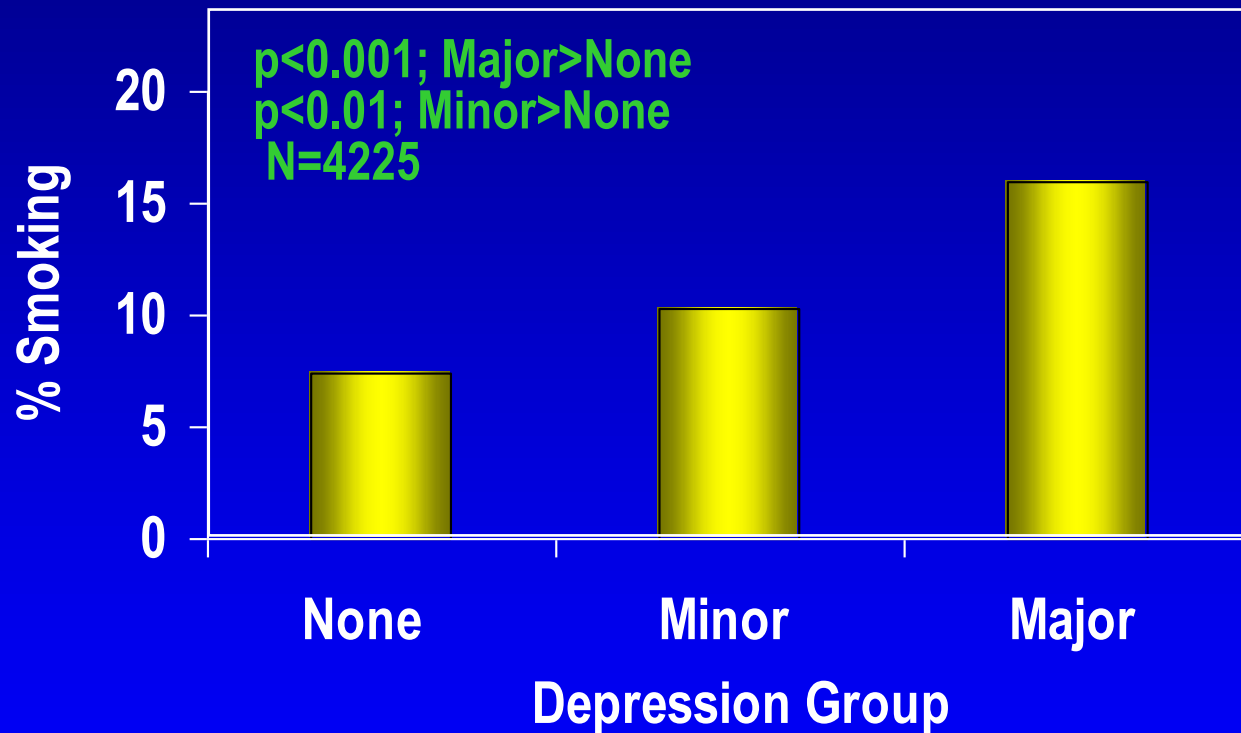
Depression Adversely Impacts Self-Management of Chronic Medical Illness

- Depressed patients with MI are more likely to drop out of exercise programs¹
- Smokers with history of depression are 40% less likely to succeed in quitting smoking over a 9-year period compared to nondepressed smokers²
- Patients with major depression and coronary artery disease are less likely to adhere to low-dose aspirin therapy than nondepressed controls³
- Patients with history of depression compared to nondepressed are more likely to develop depression with smoking cessation⁴

Depression Decreases Medication Adherence in Patients With Diabetes



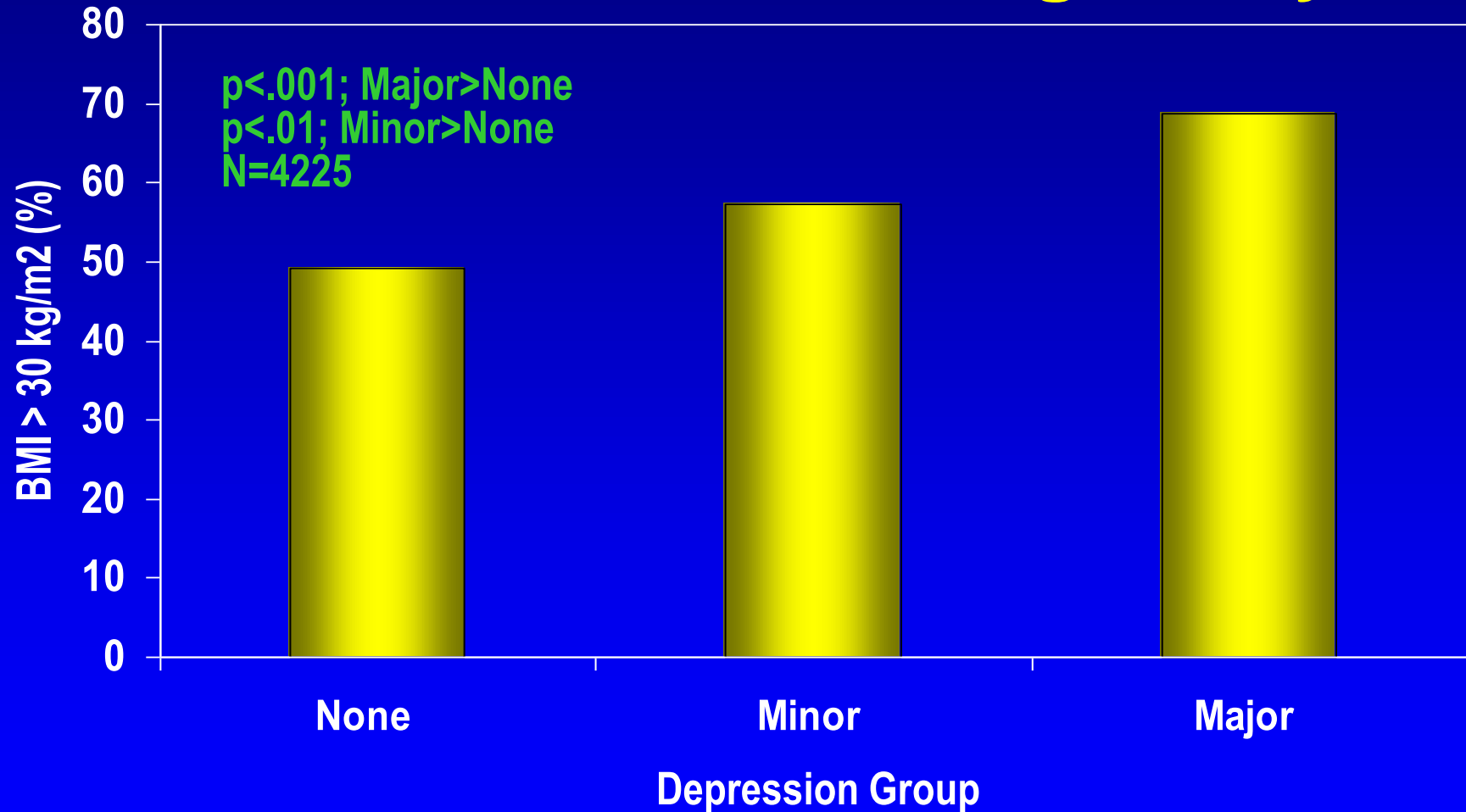
Depression Is Associated With an Increased Percent of Smoking



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

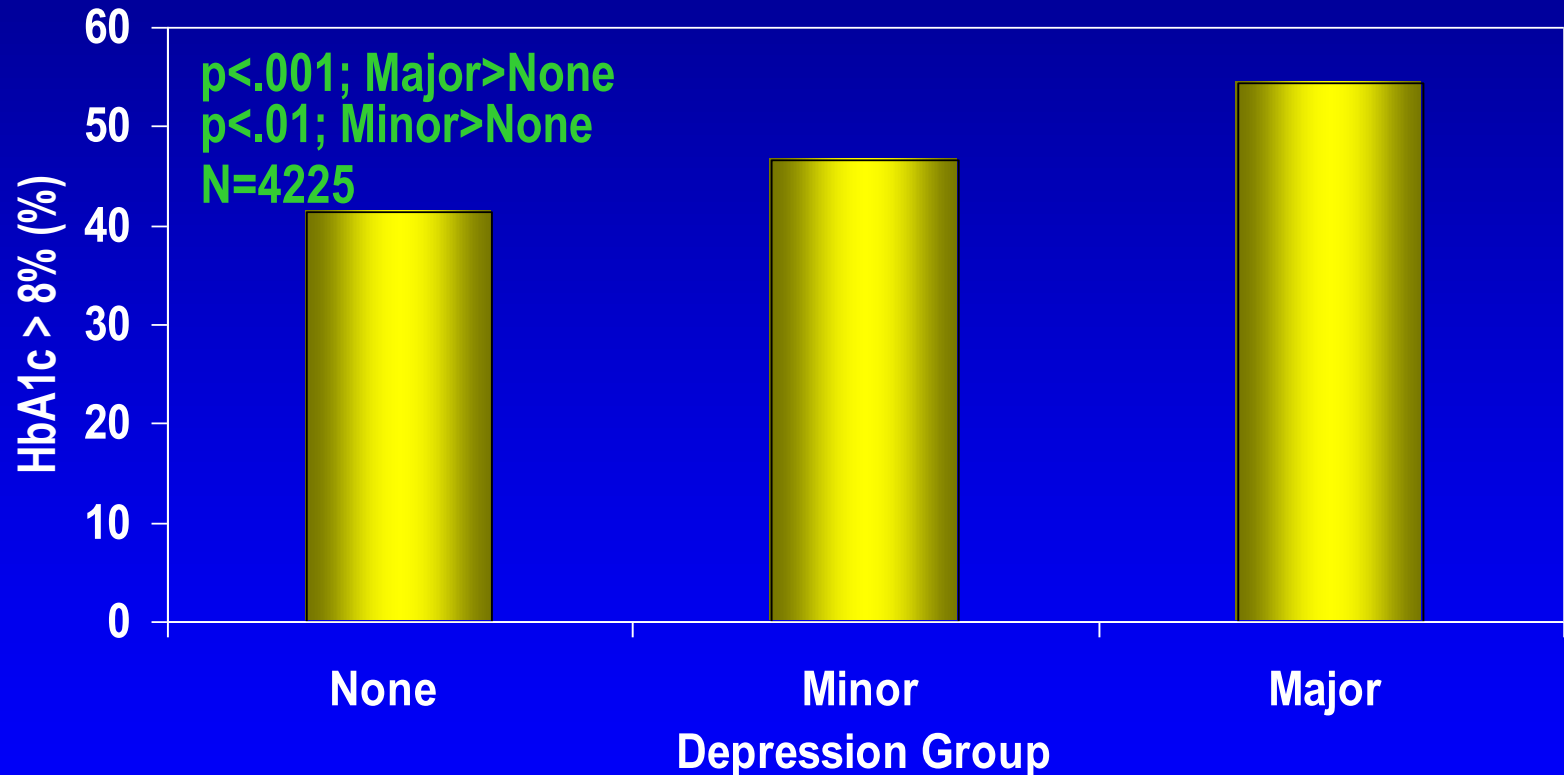
Katon et al, Diabetes Care, 2004

Depression is Associated with an increased BMI >30 kg/m² by



Adjusted for demographics, medical comorbidity, diabetes severity, diabetes type and duration, treatment type, HbA1c and clinic
Katon et al, *Diabetes Care*, 2004

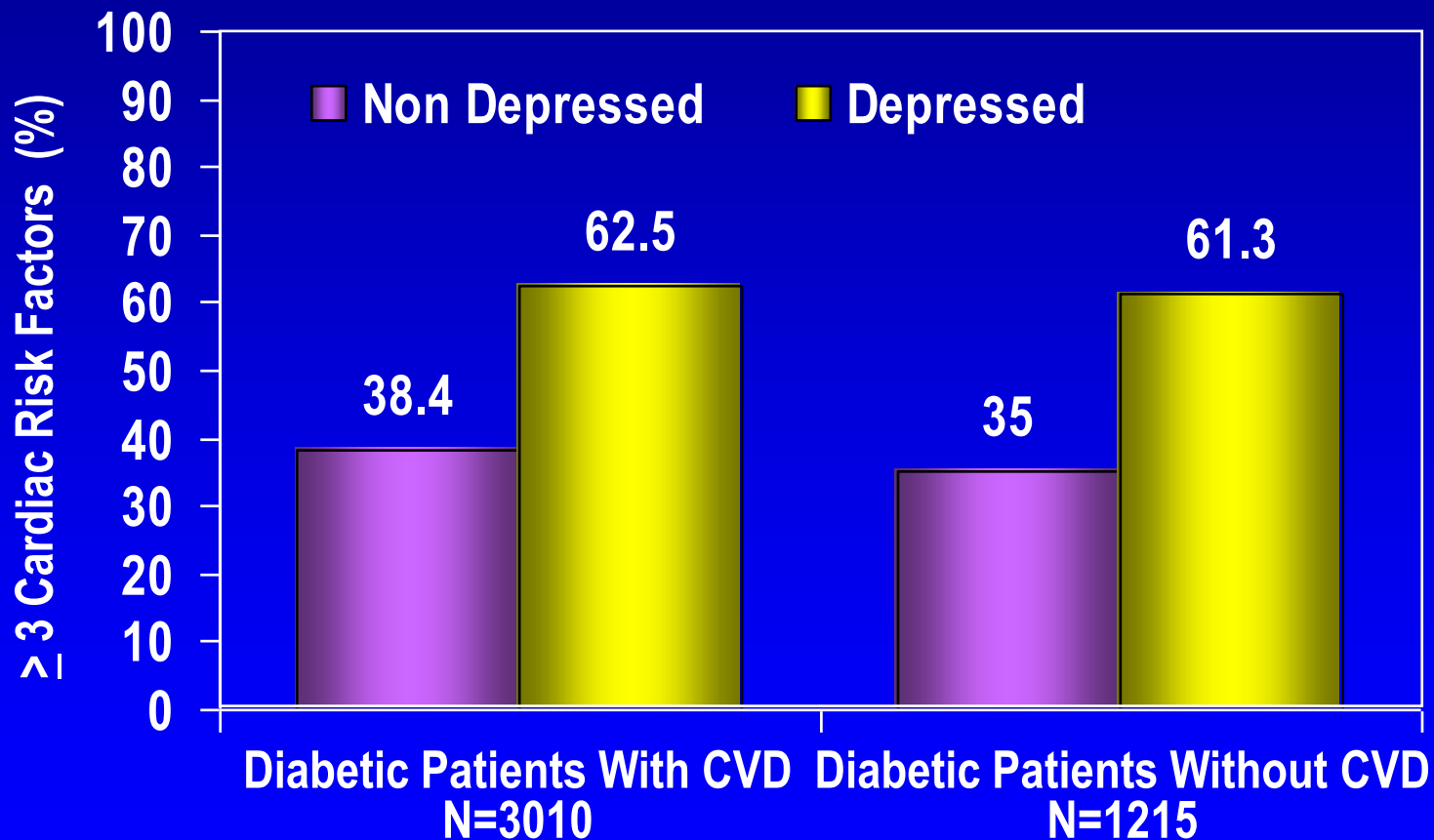
Depression Is Associated With Higher Percentage with HbA1c > 8%



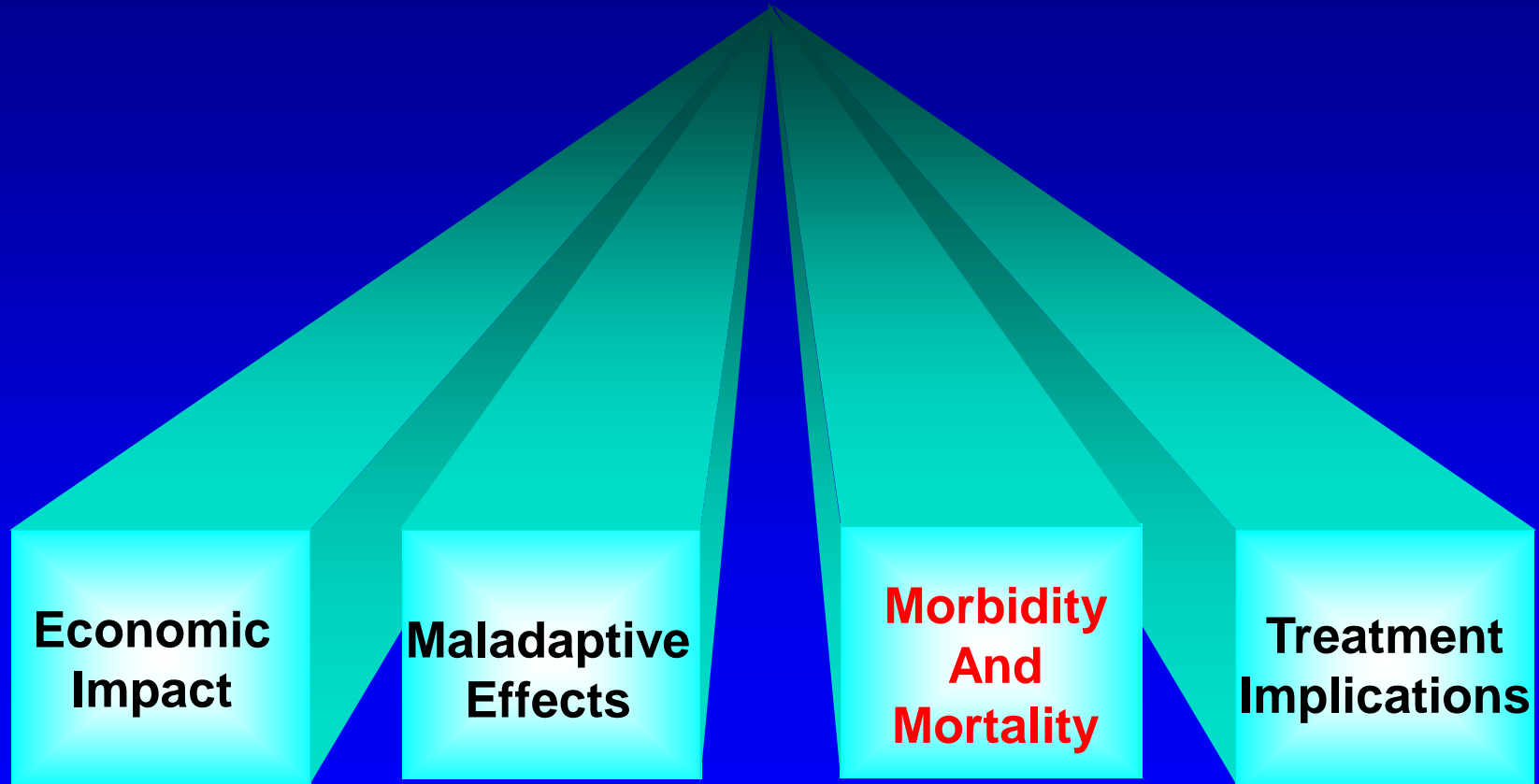
Adjusted for demographics, medical comorbidity, diabetes severity, diabetes type and duration, treatment type and clinic.

Katon et al, Diabetes Care, 2004

Depression Is Associated With a Higher Number of Cardiac Risk Factors



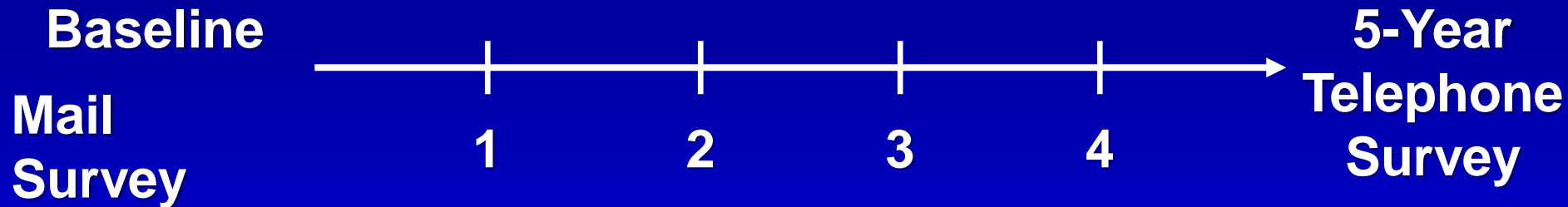
Impact Of Depression In Chronic Medical Illness



Depression Is Associated With Increased Diabetes Complications

- Meta-analysis of 27 studies showed a significant association between depression and a range of diabetes complications with effect sizes in the small to moderate range (95% CI 0.17 to 0.32)

Pathways Epidemiology Study



Disease control (HbA1c, LDLs, blood pressure)

Pharmacy refills (adherence)

ICD-9 diagnosis

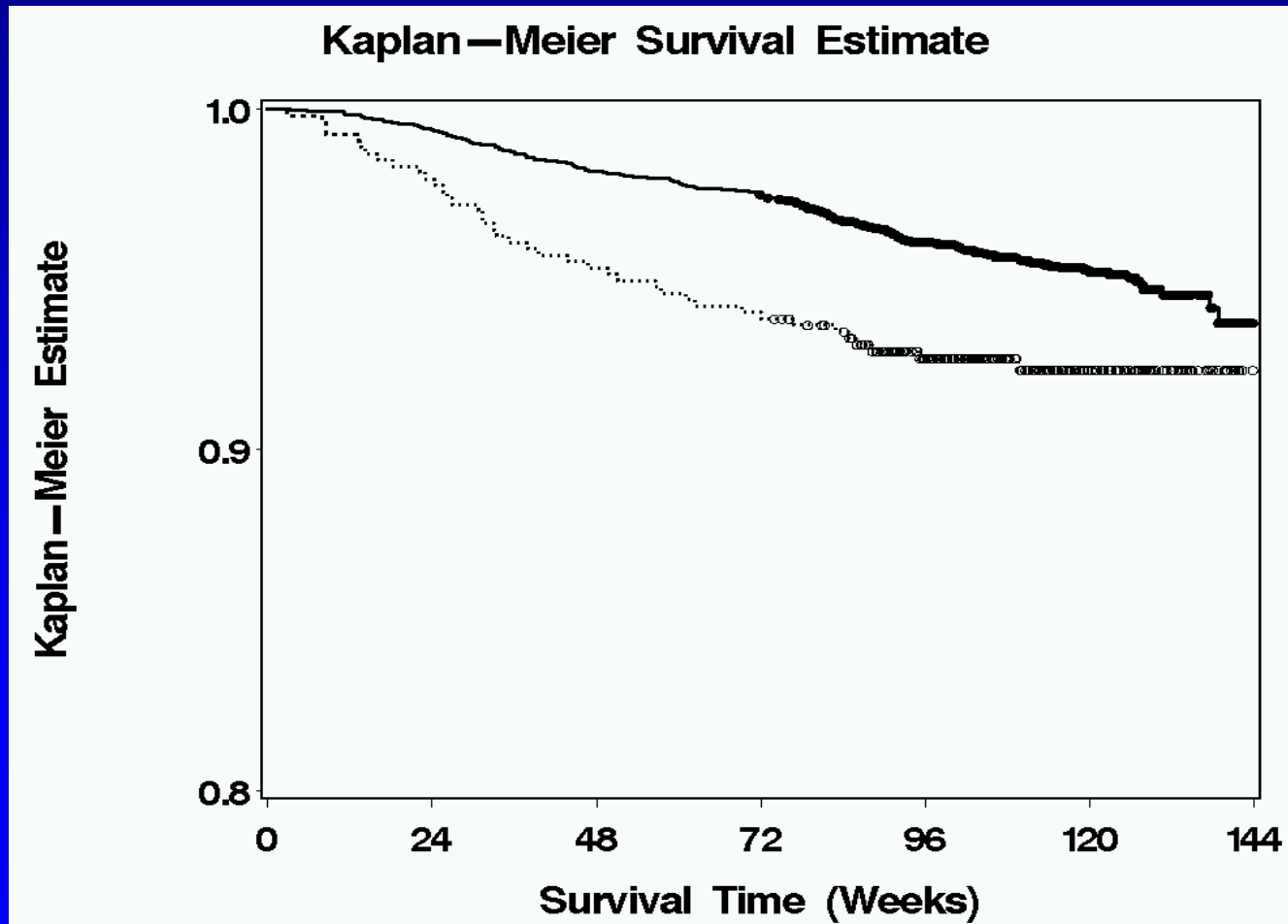
**Macrovascular/microvascular complications
(chart review)**

Mortality (Washington State mortality data)

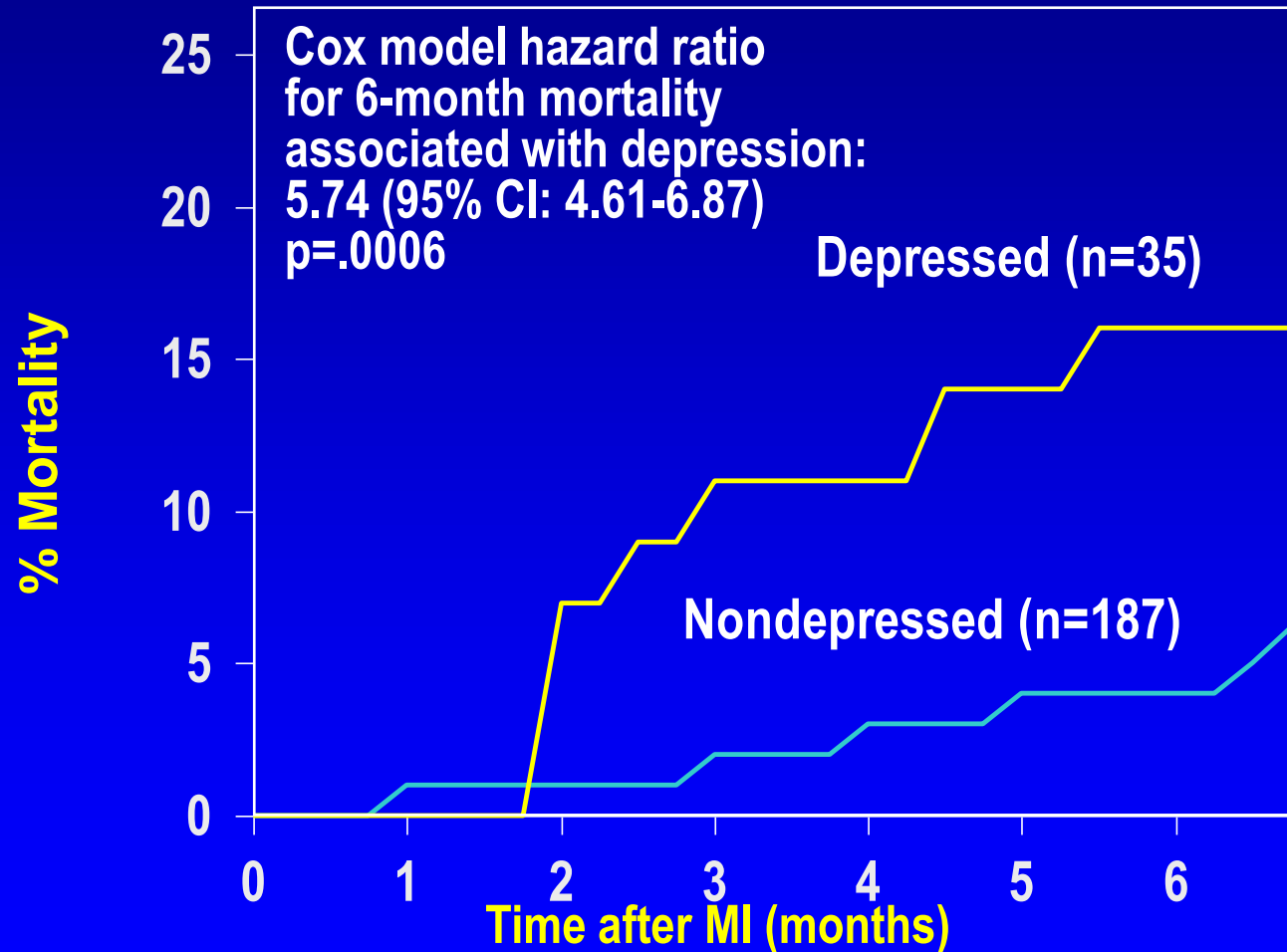
Depression: Association with Complications and Mortality

	Minor Depression	Major Depression
Microvascular Complications	1.05 (0.83, 1.33)	1.33 (1.08, 1.65)
Macrovascular Complications	1.32 (0.99, 1.75)	1.38 (1.08, 1.78)
Mortality (All cause)	1.23 (0.94, 1.61)	1.53 (1.19, 1.96)
Foot Ulcers	1.32 (0.74, 2.35)	1.99 (1.22, 3.24)
Dementia	_____	2.69 (1.77, 4.07)

Depression Increases Mortality Rate in Patients With Diabetes by 2-Fold



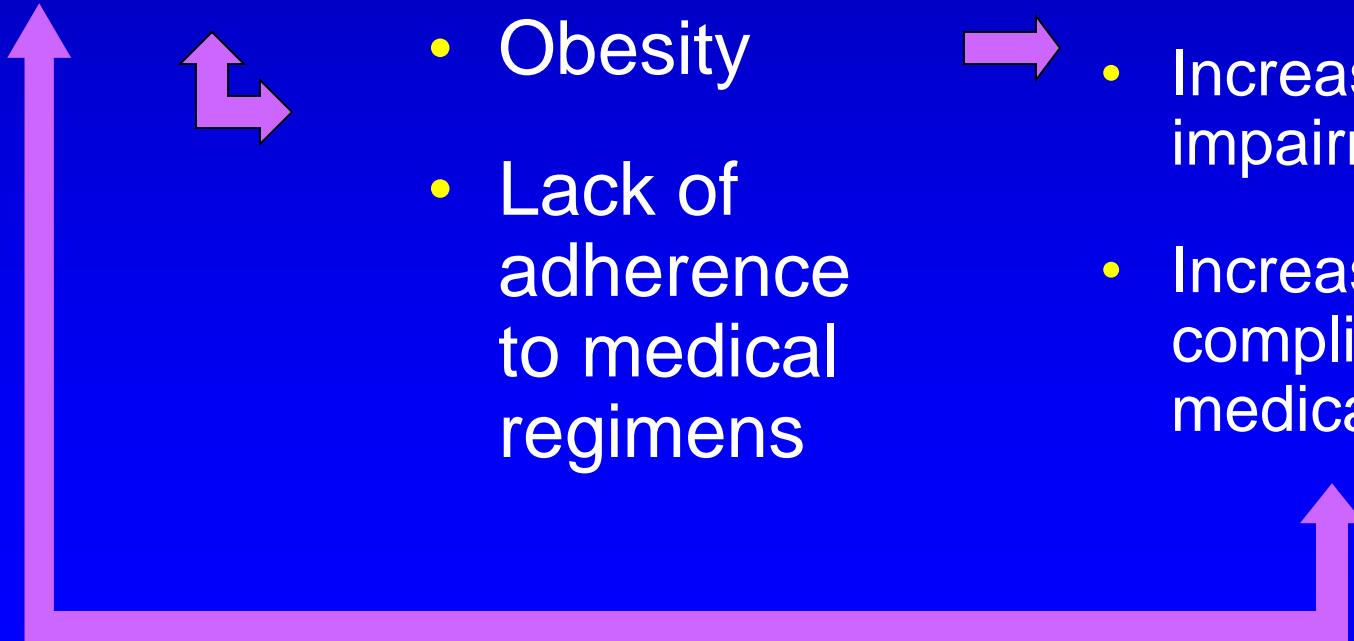
Depression Associated With Increased Mortality Post-Myocardial Infarction



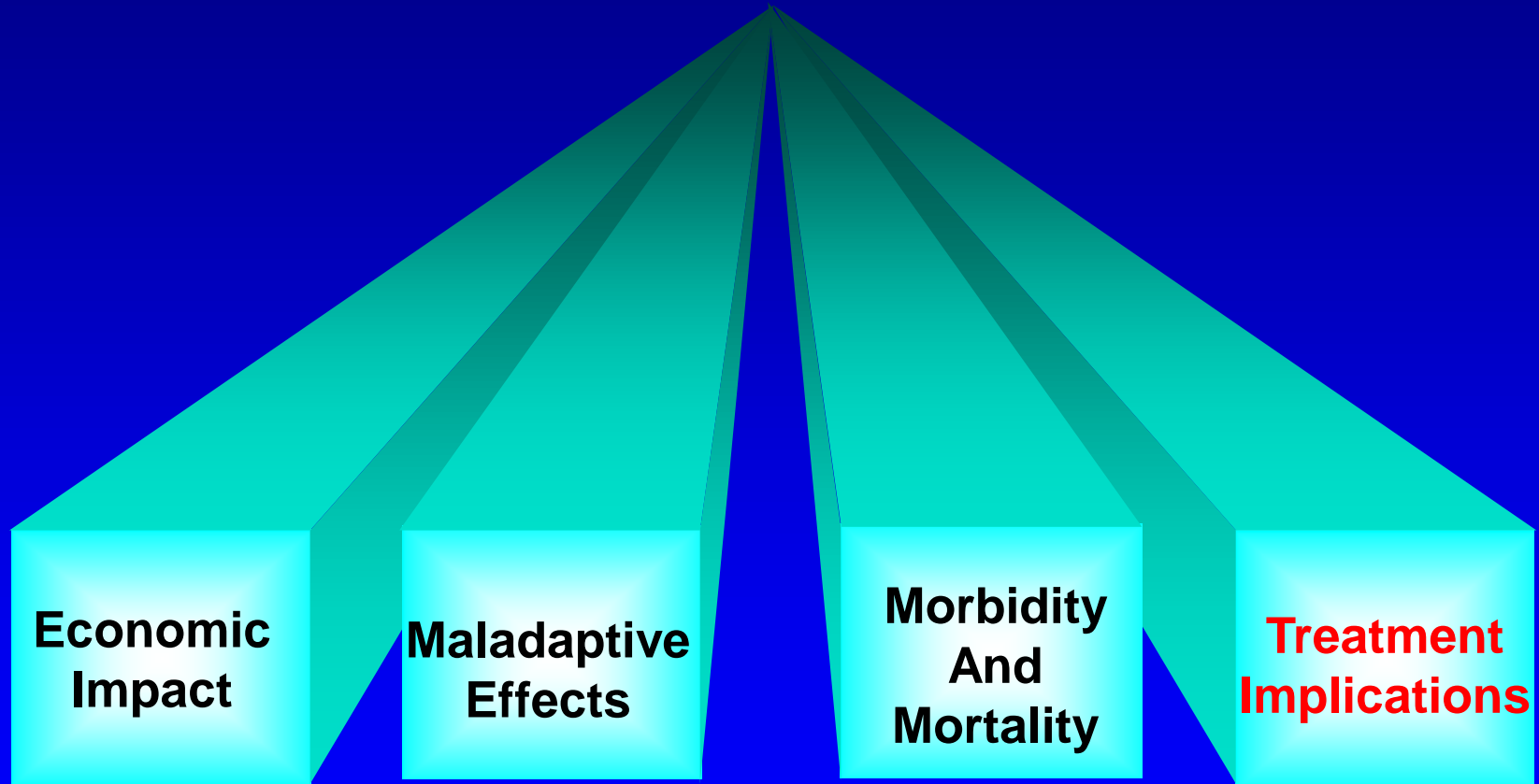
Adverse Bidirectional Interaction

Major
Depression

- Smoking
 - Sedentary lifestyle
 - Obesity
 - Lack of adherence to medical regimens
-
- Medical illness at earlier age
 - Poor symptom control
 - Increased functional impairment
 - Increased complications of medical illness



Impact Of Depression In Chronic Medical Illness



Antidepressant Treatment Trials In Patients With Chronic Medical Illness

Major depression is responsive to antidepressant treatment in patients with:

- Cancer
- Chronic tinnitus
- COPD
- Diabetes
- Inpatient rehabilitation needs
- Ischemic heart disease
- Parkinson's disease
- Rheumatoid arthritis
- Stroke
- HIV+

Antidepressant Analgesia In Chronic, Nonmalignant Pain

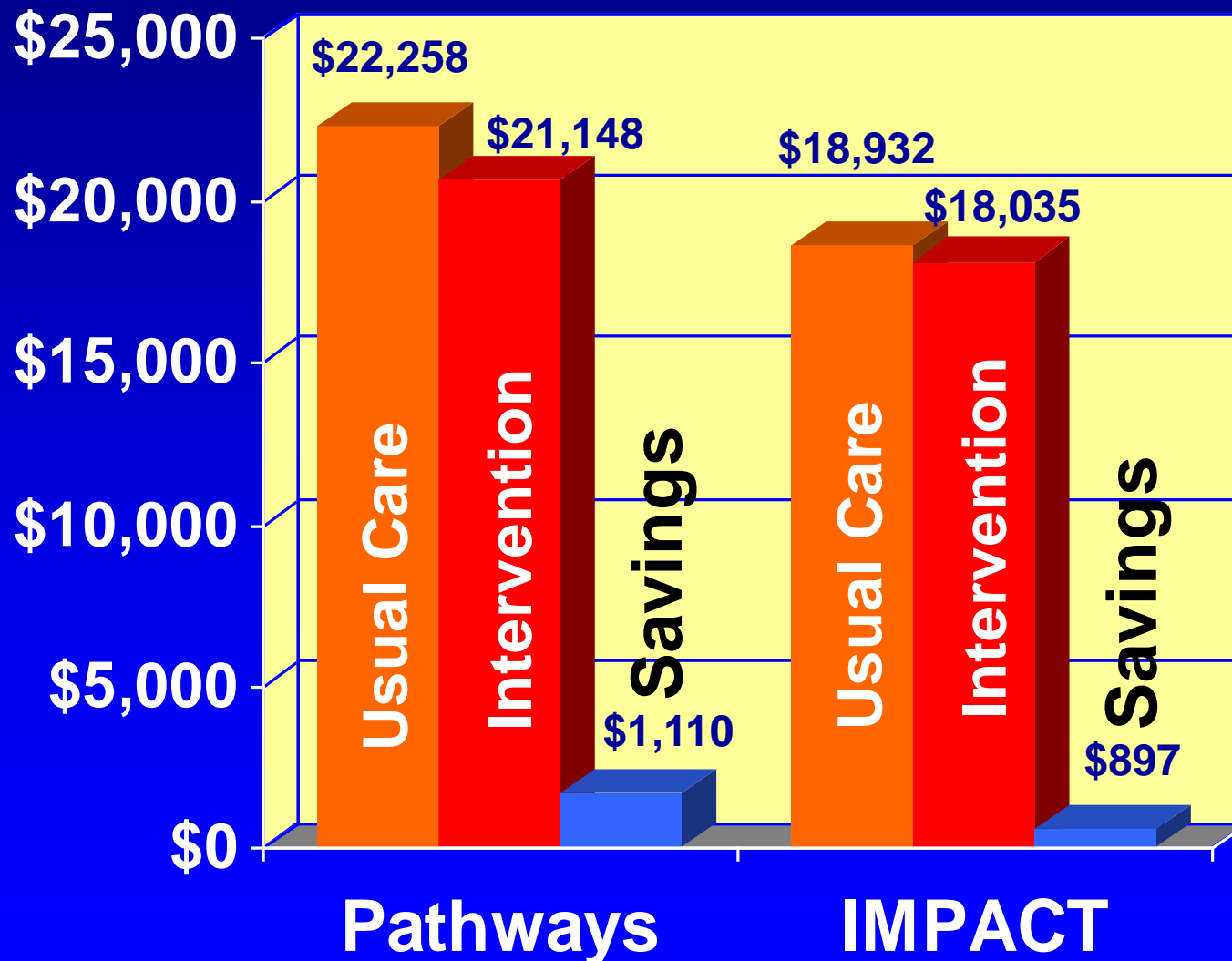
Summary of 28 studies:

- More effective than placebo
- A median of 58% of patients reported at least 50% pain reduction
- Response is greater when a specific pain diagnosis is made
- Greater response for pain in the head region
- Response not dependent on presence of depression
- Doses similar to those used for depression

Antidepressants in Chronic Pain

- **Tricyclics > heterocyclics**
- **Mixed drugs (SNRIs) are more effective than selective drugs - further study warranted**
- **Both pure serotonergic and pure noradrenergic drugs may have less effect size than drugs with mixed effects**

Two Collaborative Care Trials Demonstrate Improved Depression Care in Diabetes Lowers Total Health Care Costs Over 2 Years



Antidepressants With Short Elimination Half-Life

Implications For Therapy In Female Patients

- **Faster time to steady state and washout**
- **Less drug accumulation**
- **Better control of adverse effects**
- **Ability to switch to alternate agent without washout**
- **Limited fetal exposure in event of conception**

PSYCHOPHARMACOLOGY IN THE MEDICALLY ILL PATIENT

Hepatic Disease

- **Factors**
 - **Metabolic capacity (MC)**
 - **Free fraction of drug (FF)**
 - **Hepatic blood flow (HBF)**

PSYCHOPHARMACOLOGY IN THE MEDICALLY ILL PATIENT

Hepatic Disease

	MC	FF	HBF
Moderate-severe cirrhosis	↓	↑	↓
Acute viral hepatitis	↓/-	↓	↑/-

PSYCHOPHARMACOLOGY IN THE MEDICALLY ILL PATIENT

Severe Hepatic Illness

- Reduce Dose by 25-50%
- For TCAs — Use Levels
- Gabapentin and Lithium — Renal Excretion

PSYCHOPHARMACOLOGY IN THE MEDICALLY ILL PATIENT

Severe Hepatic Illness

Suggested Modifications Clinical Conditions

None

Mild hepatic illness
Enzyme limited

Reduce by 25%

Hepatic excretion $\leq 40\%$
Normal renal function
Agent flow/enzyme limited

Reduce by 25-50%

Enzyme limited
Protein binding altered
Chronic rx

PSYCHOPHARMACOLOGY IN THE MEDICALLY ILL PATIENT

Hepatic Illness

- **Flow Limited**
 - Significant first-pass metabolism
 - Reduced flow due to architectural hepatic damage
- **Enzyme Limited**
 - Damage to hepatocytes
 - Sensitive to altered protein binding

SEVERE HEPATIC ILLNESS

Rule of Thumb*

- **Most psychotropics are highly protein-bound, administered chronically, and enzyme-sensitive**
- **Reduce by 25-50%**

*** Lithium and gabapentin — exclusively renal excretion — are exceptions**

RENAL ILLNESS

- **Rate of Drug Excretion**
 - **Glomerular filtration**
 - **Tubular secretion**
- **May Decline at Different Rates**
- **Altered by Protein Binding Changes**

RENAL ILLNESS

- **For Most Psychotropic Drugs**
 - Hepatic metabolism
 - Renal excretion of metabolites
 - Metabolites may increase and cause toxicity or displace parent drug from protein
- **Use Creatinine Clearance to Adjust Dosage**

RENAL ILLNESS

- **TCA**s
 - Use levels
 - Rarely affected
- **SSRI**s
 - No adjustments
 - Possible exception paroxetine, which may accumulate
- **MAOI**s
 - Avoid unless no alternative
 - No adjustment

RENAL ILLNESS

- **Venlafaxine**
 - If creatinine clearance is <30 ml/min, adjust dose
 - T_{1/2} increase
 - by 50% in moderate to severe
 - by 180% in dialysis

RENAL ILLNESS

Rule of Thumb

- **Creatinine Clearance**
 - **>30 ml/min — no adjustment**
 - **>10 ml/min — reduce by 50%**

Post Lecture Exam

Question 1

1. Physiologic effects of depression can include:
(K-type question)
 - A. Reduced immune function
 - B. Memory/concentration impairment
 - C. Glucose intolerance
 - D. Increase autonomic arousal
 - E. Amplification of pain

Question 2

- 2. True or False:** Treatment for depression in patients who are medically ill has been shown to reduce mortality.

Question 3

3. Choose the single best answer:

In individuals with at least 50% stenosis of one or more coronary arteries, functional status at one year follow-up correlated most closely with

- A. Degree of occlusion of coronary arteries**
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- C. Reduction of cholesterol levels**
- D. Anxiety and depression severity**
- E. Participation in a cardiac rehabilitation program**

Question 4

- 4. Choose the single best answer: The increase in the risk of non-cardiac death in depressed individuals is:**
- A. Not different**
 - B. 200%**
 - C. 400%**
 - D. 800%**

Question 5

5. True or False: Antidepressant medication does not reduce pain in non-depressed individuals.

Answers to Pre & Post Competency Exams

1. All of the above
2. False
3. D
4. C
5. False