

Depression In Patients With Chronic Medical Illness

Pharmacokinetics in the Severely Medically Ill

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Pre-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**
- 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%**

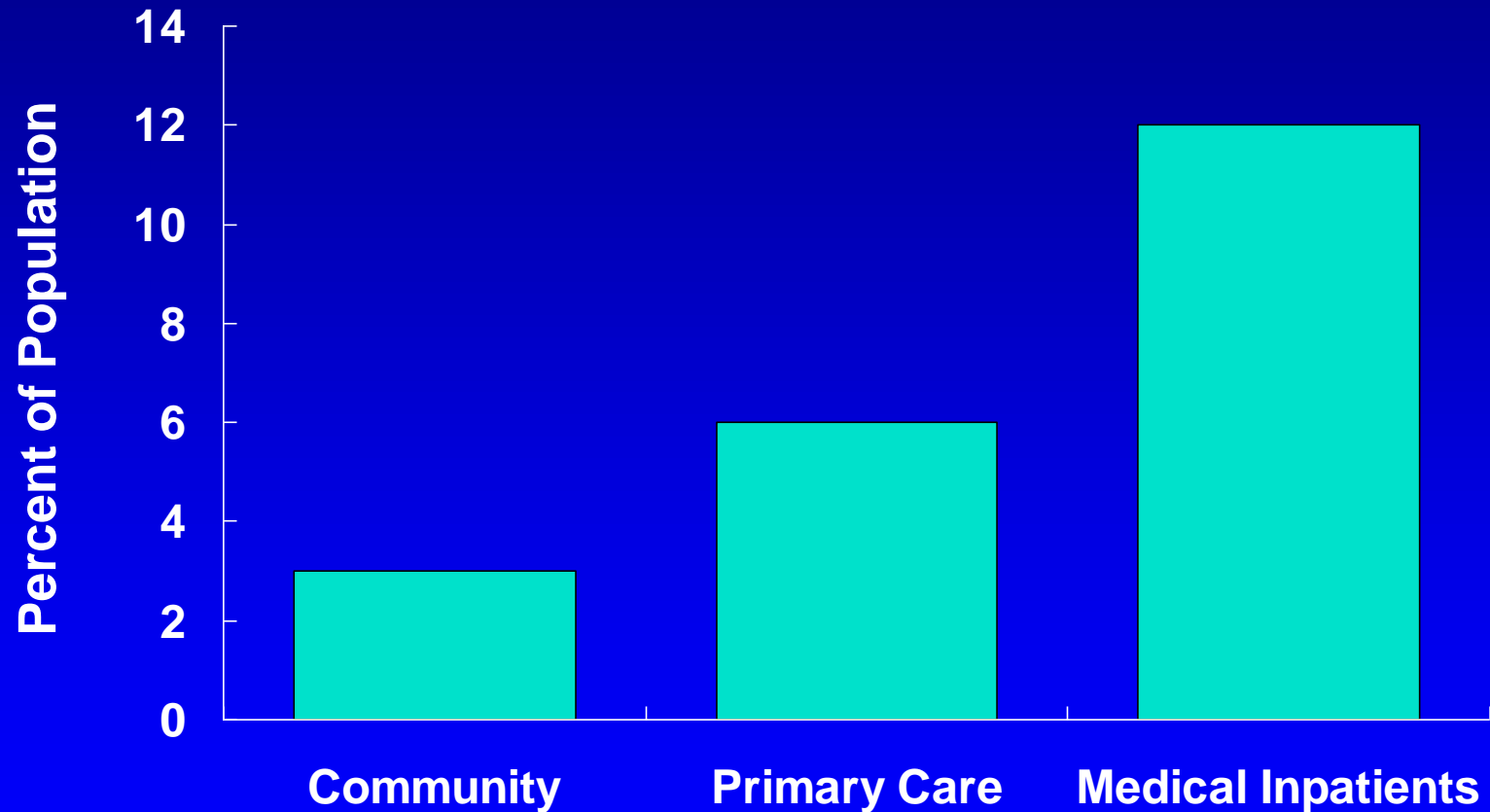
Question 5

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

Depression And Chronic Medical Illness

- **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 and self management (diet, exercise)**
- **Depression increases mortality**

Prevalence Of Major Depression



Prevalence Of Depression In Medical Illness

Setting Or Disease	Prevalence Rate (%)
Outpatient	2 - 15
Inpatient	12
Cancer	18 - 39
Myocardial infarction	15 - 19
Rheumatoid arthritis	13
Parkinson's disease	10 - 37
Stroke	22 - 50
Diabetes	10 - 14

Prevalence Of Mental Disorders In Chronic Physical Illness

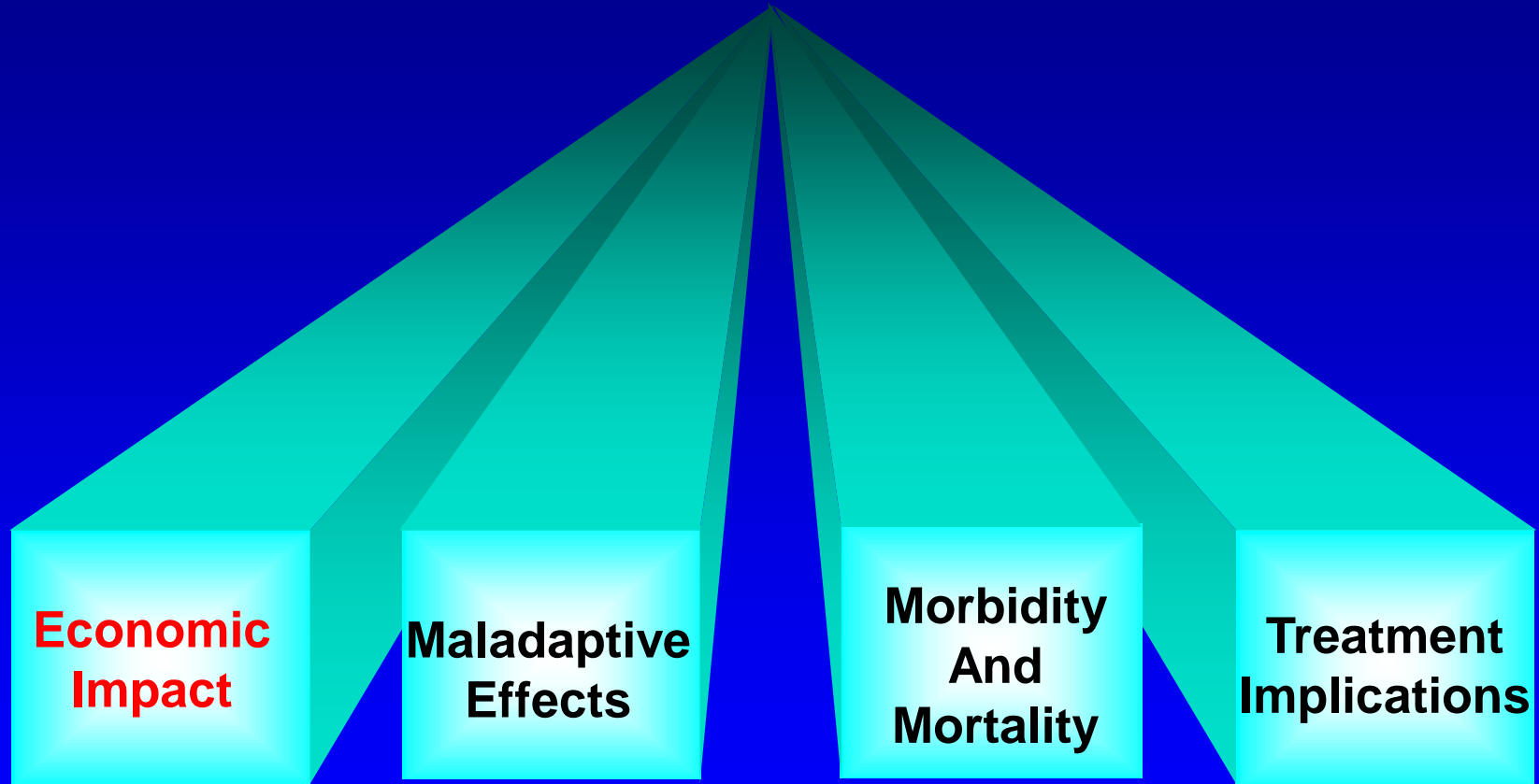
Condition	Prevalence (%)
Neurological disorder	37.5
Heart disease	34.6
Chronic lung disorder	30.9
Cancer	30.3
Arthritis	25.3
Diabetes	22.7
Hypertension	22.4

Social Origins Of Depression In Old Age

Murphy's Study

- **Significantly more severe life events**
 - physical illness
 - life-threatening illness in someone close
 - separations/deaths
- **Vulnerability factors**
 - chronic personal health difficulty
 - poor health of loved one
 - inadequate housing
 - marital/ family relationship problems

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

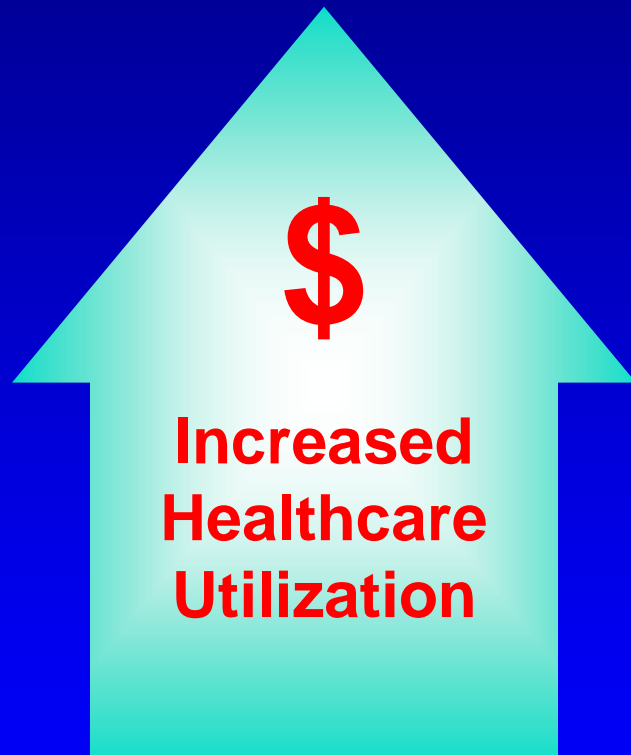
Economic Impact Of Mental Disorders

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%**

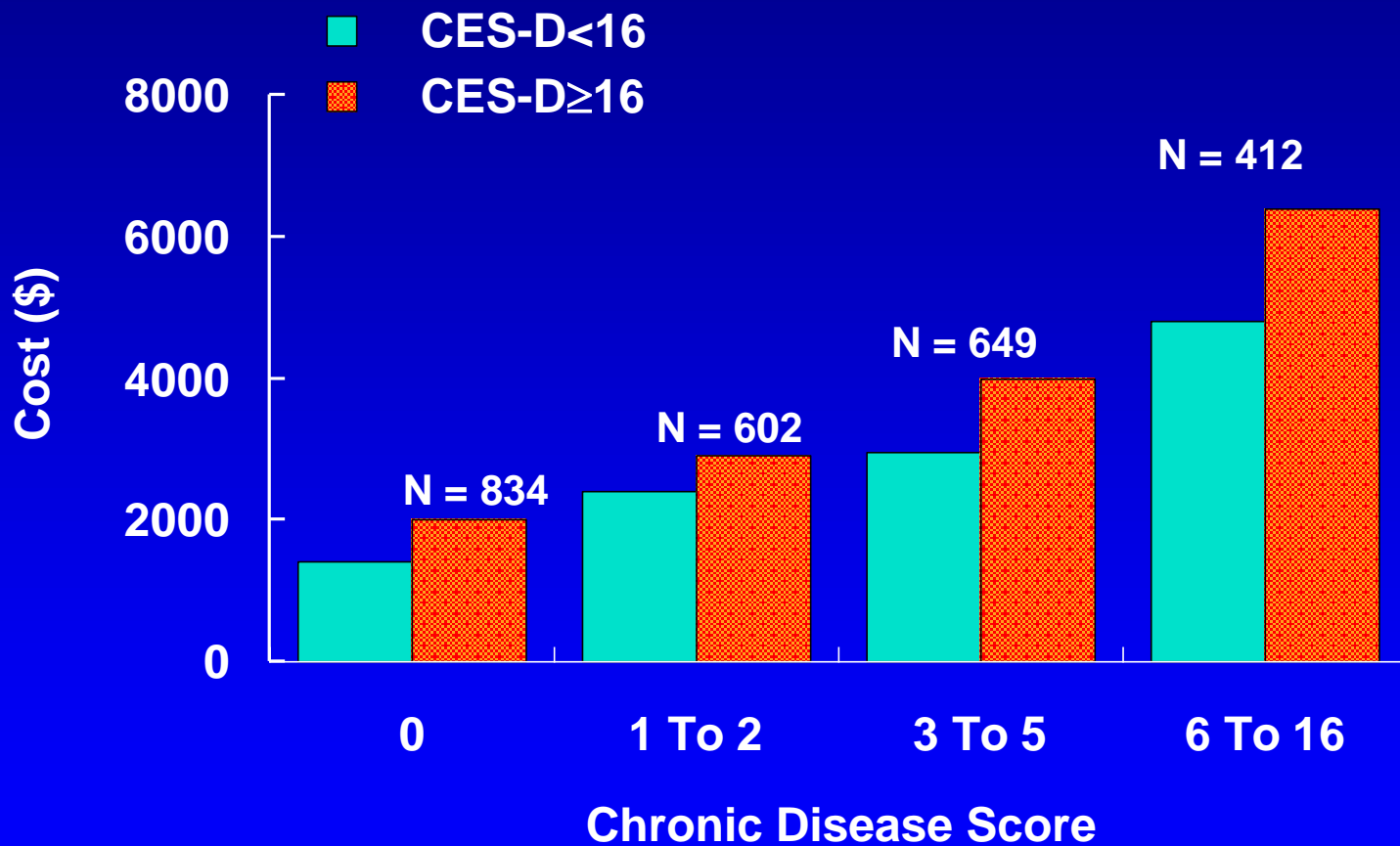
Economic Impact Of Mental Disorders

Medical Inpatients With Psychiatric Comorbidity



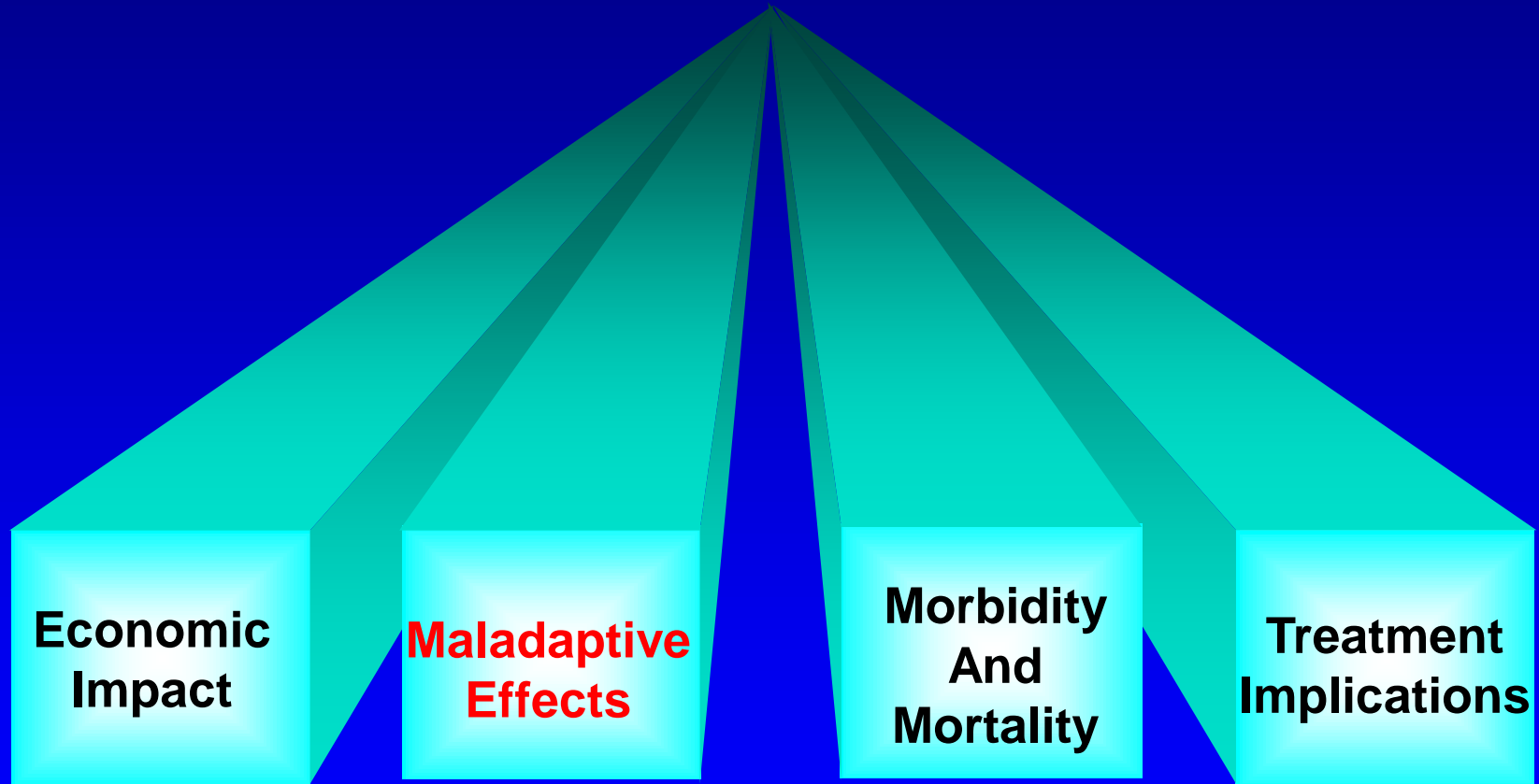
- Length of stay
- Use of medical services
- Medical costs
- ER costs
- Rehospitalization rates for at least 4 years after discharge

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



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

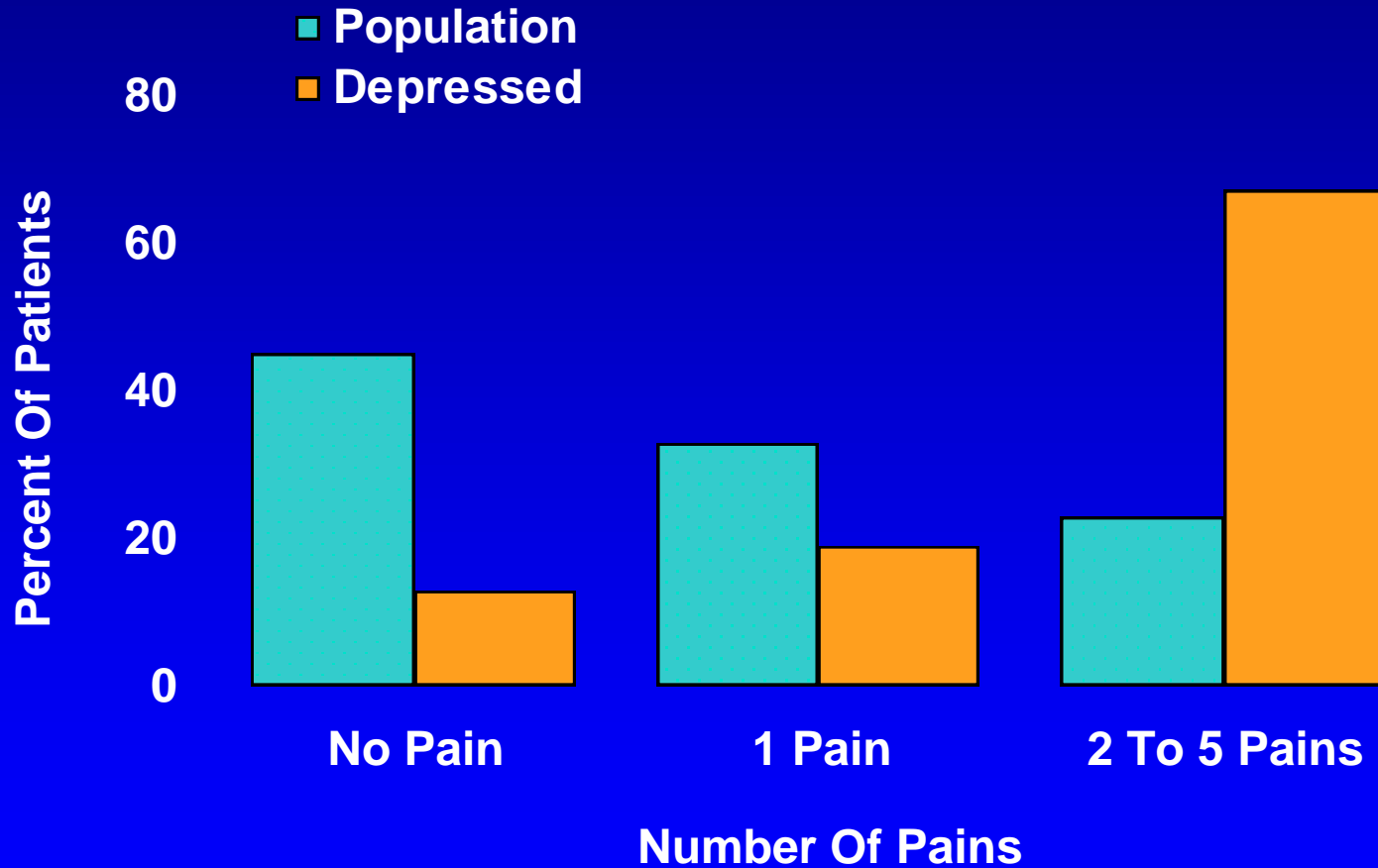
Impact Of Depression In Chronic Medical Illness



Three Maladaptive Effects Of Affective Illness On Chronic Medical Illness

- **Amplification of somatic symptoms (especially pain) and functional disability**
- **Decreased self-care and adherence to medical regimens**
- **Direct maladaptive physiologic effects**
 - **modulated by autonomic nervous system, hypothalamus, and immunologic effects**

Pain Status: General Healthcare Population vs Depressed Patients*



*N=164 patients receiving antidepressants.
Katon et al. Unpublished data.

Physical Symptoms And Association With Psychiatric Disorders

Number Of Symptoms	Number Of Patients	With Psychiatric Disorder N (%)		
		Anxiety	Mood	Any
Physical (N=1000)				
0-1	215	2 (1)	5 (2)	16 (7)
2-3	225	17 (7)	27 (12)	50 (22)
4-5	191	25 (13)	44 (23)	67 (35)
6-8	230	68 (30)	100 (44)	140 (61)
≥9	130	68 (48)	84 (80)	113 (81)
Somatoform (N=900)				
0	654	68 (10)	107 (16)	102 (25)
1-2	143	42 (29)	60 (42)	74 (52)
3-5	87	35 (40)	40 (46)	77 (89)
≥6	49	27 (55)	34 (68)	45 (94)

Pain  **Depression**

Bidirectional Relationship

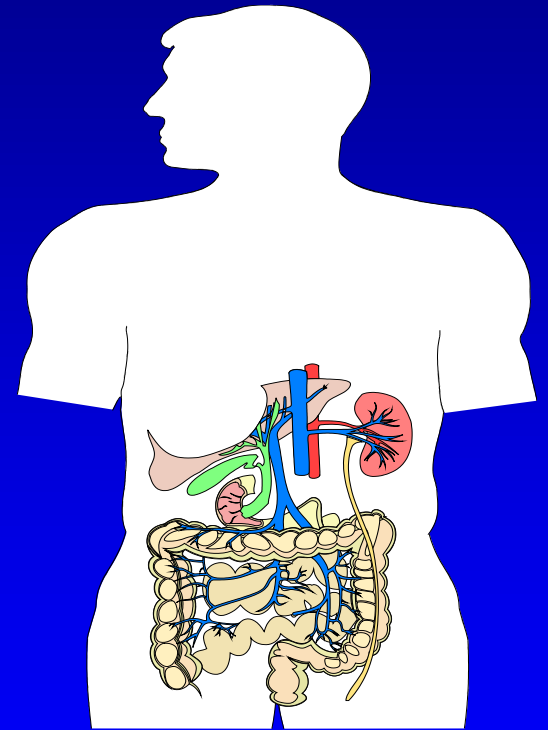
Psychiatric Illness And Symptoms Of Poor Glucose Control

- 71% of diabetic patients had lifetime history of ≥ 1 psychiatric illness
- Recent psychiatric illness significantly associated with symptoms of poor glucose control

Conclusion

- **Diabetes symptoms may be unreliable indicators of poor metabolic control when features suggestive of anxiety or depression are present**
- **Poor metabolic control (as measured by Hb A_{1c}) not related to increased symptom reporting**

**The Effect Of DSM-IV
Depressive And Anxiety
Disorders On GI Symptom
Reporting in Patients With
Inflammatory Bowel Disease
(IBD)**



GI Symptoms In Patients With Inflammatory Bowel Disease (IBD)

Symptoms Consistent With IBD

<u>Symptom</u>	<u>N (%)</u>
Constipation	6 (15.0)
Anorectal pain	12 (30.0)
Incontinence	12 (30.0)
Bloating	7 (17.5)
Diarrhea	6 (15.0)
Abdominal pain	1 (2.5)

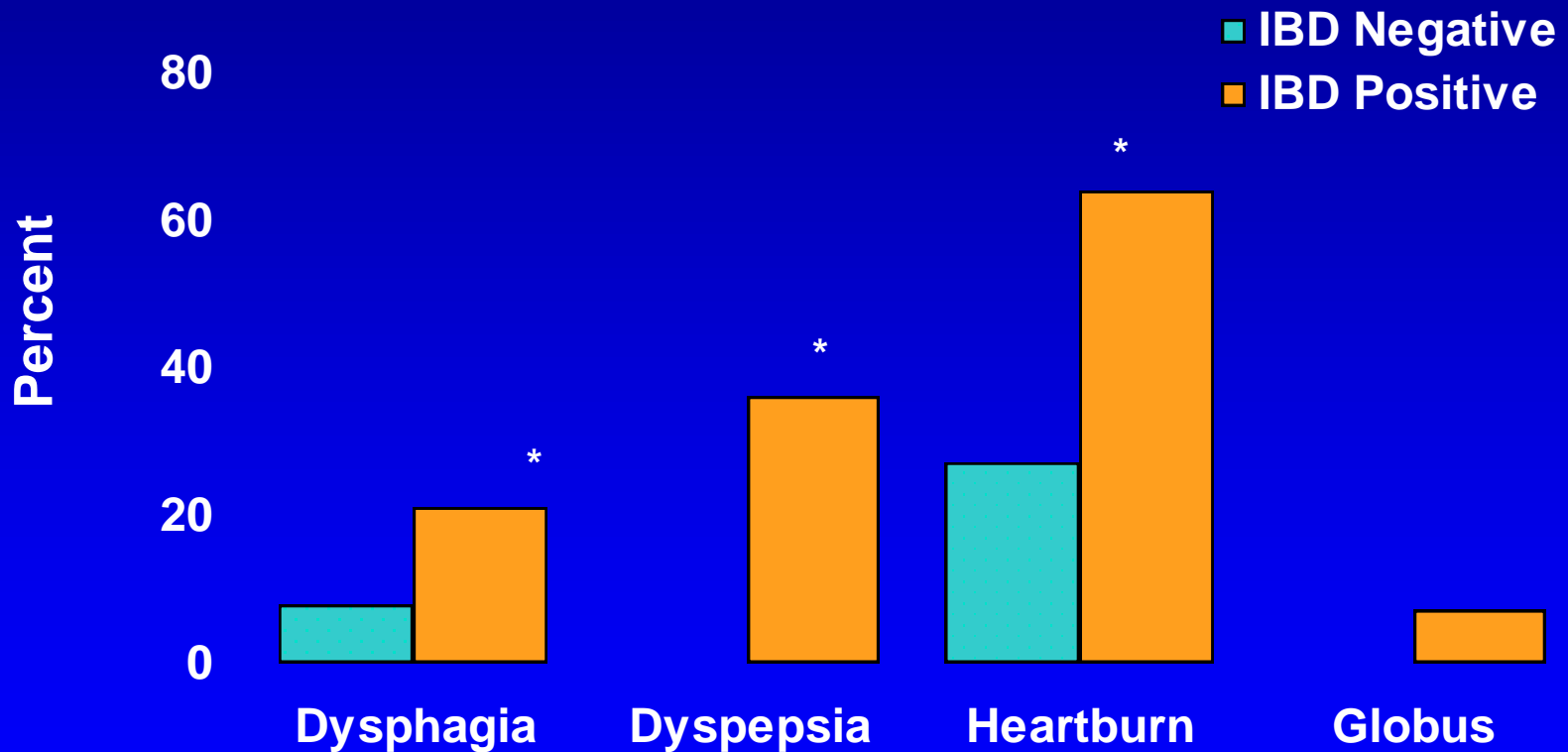
GI Symptoms In Patients With Inflammatory Bowel Disease (IBD)

Symptoms Not Consistent With IBD

Symptom	N (%)
Globus	1 (2.5)
Rumination	2 (5.0)
Dysphagia	5 (12.5)
Chest pain	9 (22.5)
Heartburn	16 (40.0)
Dyschezia	13 (32.2)

Functional Bowel Comorbidity

In Patients With IBD

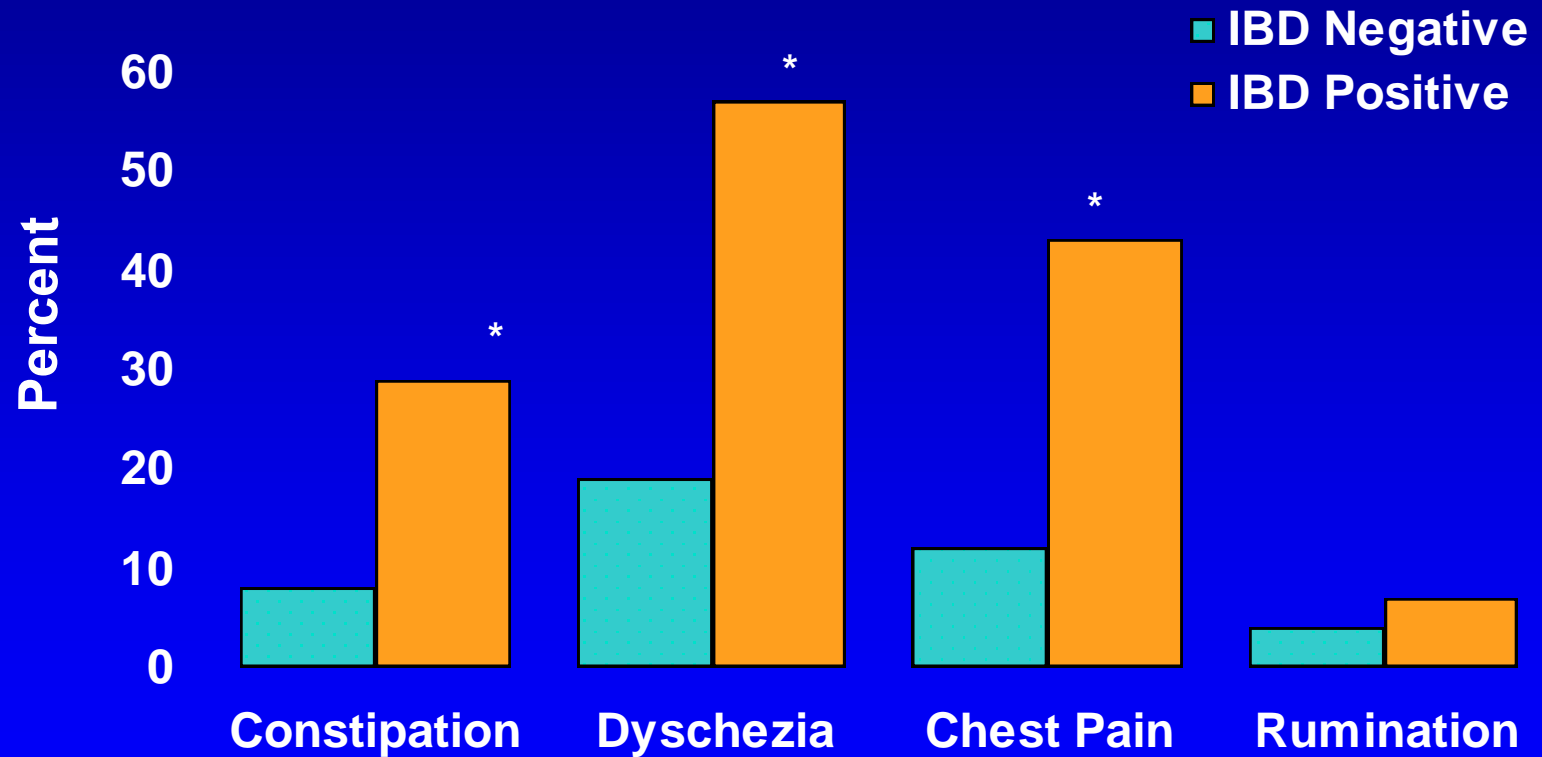


* $P < .05$

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

Functional Bowel Comorbidity

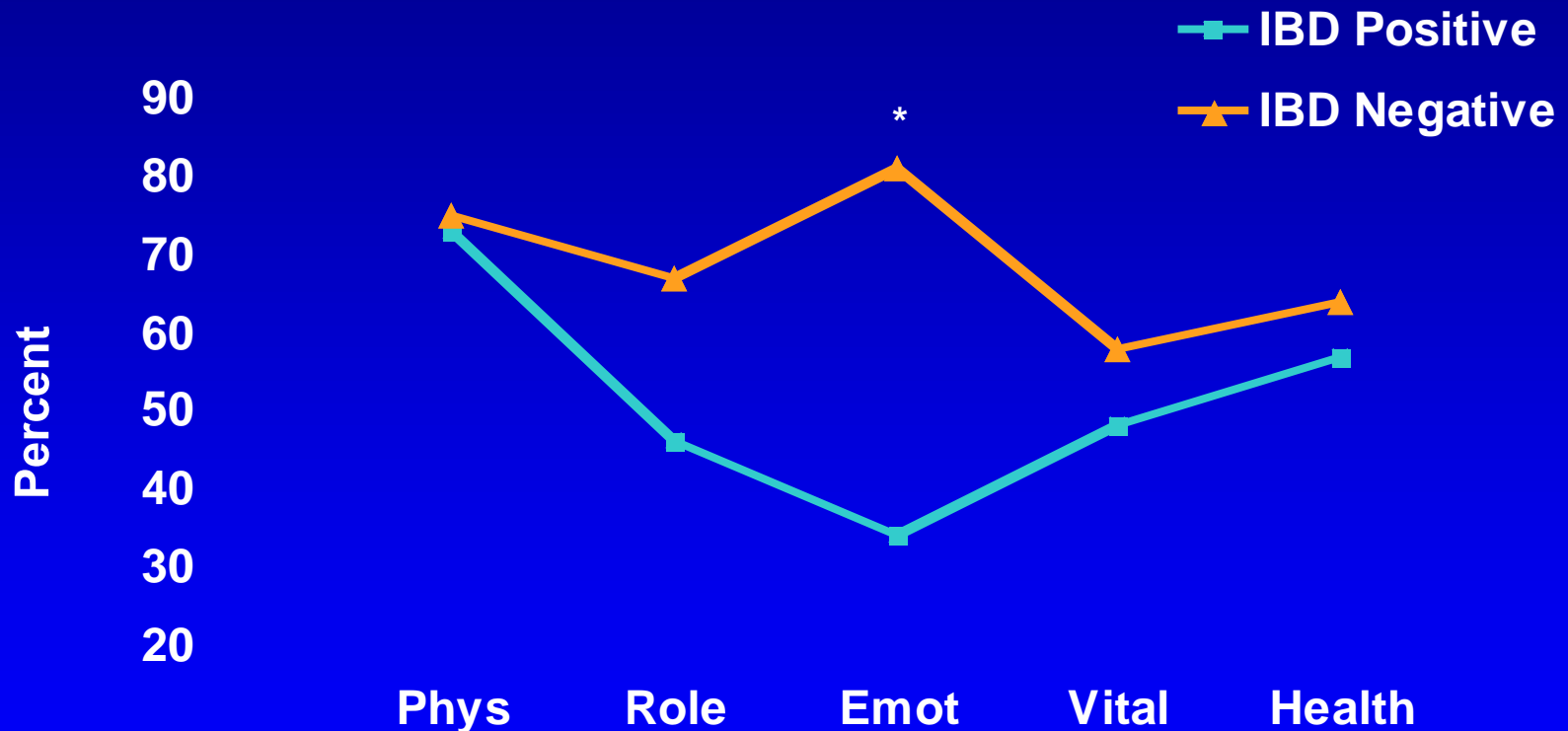
In Patients With IBD



* $P < .05$

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

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

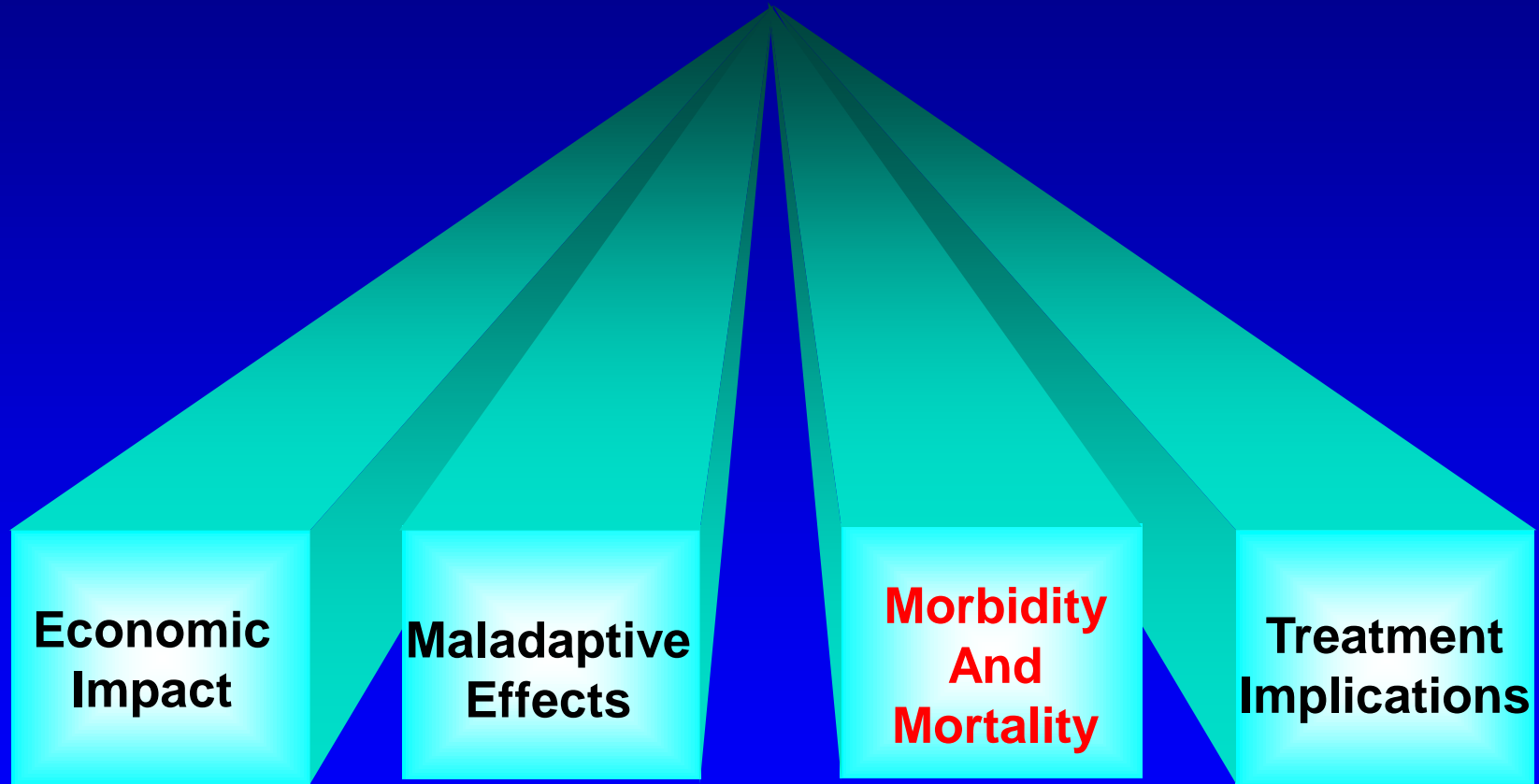


* $P < .001$ IBS vs comparators.

IBD = inflammatory bowel disease.

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

Impact Of Depression In Chronic Medical Illness



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

Impact On Self-Management Of Chronic Medical Illness

- Depressed post-MI patients more likely to drop out of exercise programs
- Depressed smokers 40% less likely to quit smoking over a 9-year period
- Depressed CAD patients less likely to adhere to low-dose aspirin therapy

Blumenthal et al. Psychosom Med. 1982;44:519.

Anda et al. JAMA. 1990;264:1541.

Carney et al. Health Psychol. 1995;14:88.

Depression And Death

Long-Term Follow-Up

- 4.3 times more death in depressed patients
- No deaths from suicide
- Increased risk same for physically healthy and not healthy
- None were treated for depression
- Cause of death:
 - cardiovascular 63%
 - cancer 22%
 - other (mostly pulmonary) 15%

Increased Risk Of Death In Depressed Nursing Home Patients

- 12.6% of 454 new admissions to 8 nursing homes suffered from major depression
- Major depression increased the likelihood of death by 59% in the first year after diagnosis

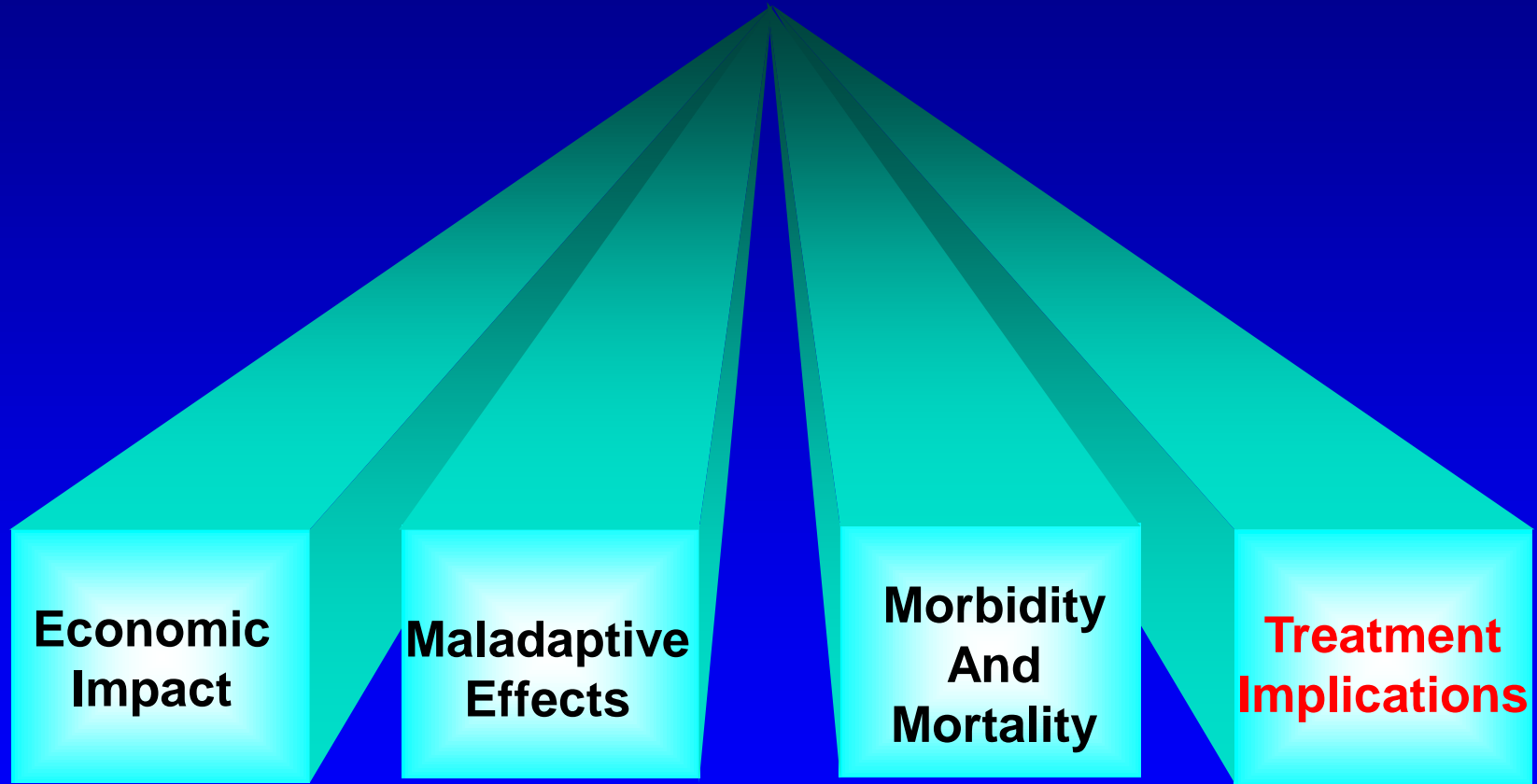
6-Month Mortality Post-MI

- Depressed post-MI patients have a three- to four-fold increased risk of death over the next 6 months when controlling for other risk factors
- Impact of depression on mortality is at least as significant as left ventricular dysfunction and history of previous MI

Depression: Association With Acute Myocardial Infarction

- Depressed patients are 4 times as likely to have an MI
- Depressed patients have a relative risk of 1.71 ($P=.005$) for MI and 1.59 ($P<.001$) for death from all causes

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:

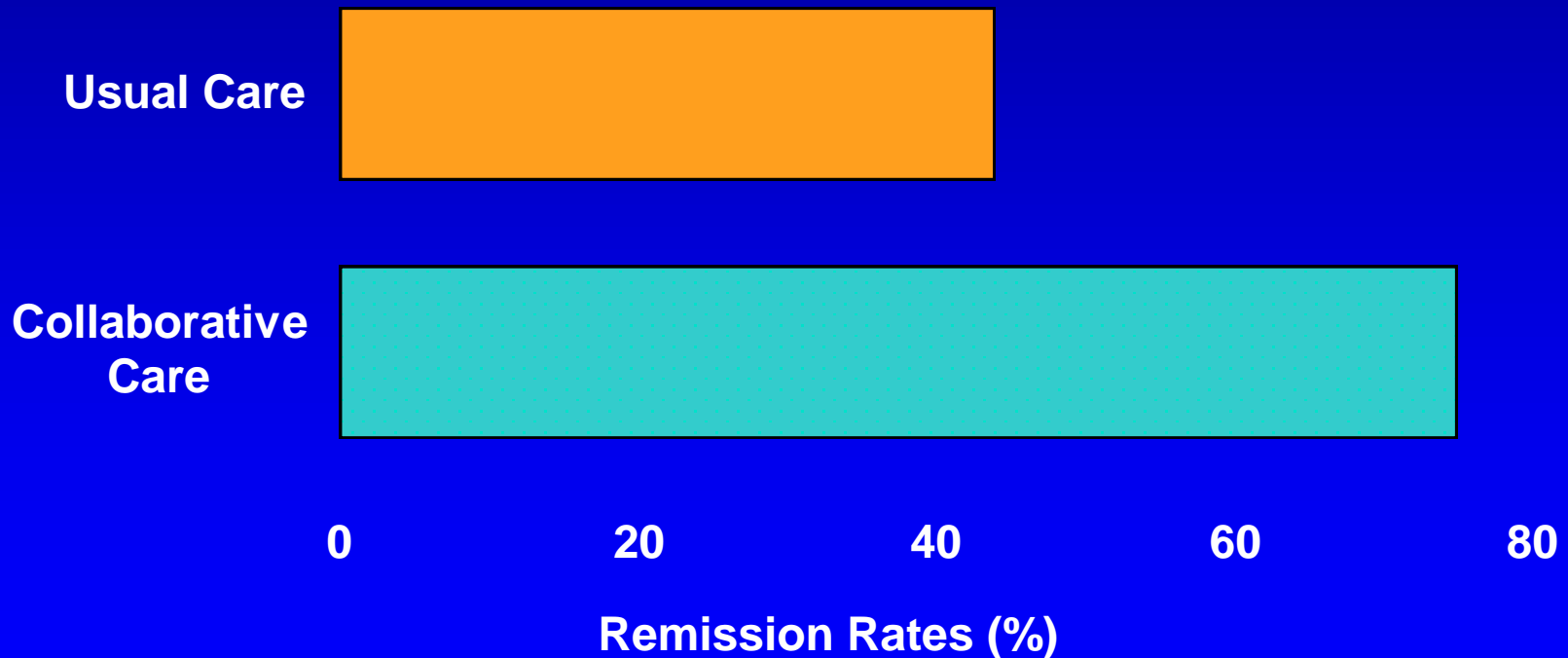
- More effective than placebo
- A median of 58% of patients reported at least 50% pain reduction
- Response is greater when a specific pain diagnosis is made
- Greater response for pain in the head region
- Response not dependent on presence of depression
- Doses similar to those used for depression

SSRIs In Chronic Pain

- **Tricyclics > heterocyclics**
- **Mixed drugs 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**

Adding Value To Healthcare

The Psychiatrist In The Medical System Collaborative Care Of Depression



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

- **TCAs**
 - Use levels
 - Rarely affected
- **SSRIs**
 - No adjustments
 - Possible exception paroxetine, which may accumulate
- **MAOIs**
 - 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
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 - D. Increase autonomic arousal
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Question 2

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 - B. 200%**
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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