

Depression and Chronic Illness

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Outline

- Depression IS a “medical” illness
- Diagnosing depression in patients with medical illness
- Comorbid illness – 3 categories
- Measuring and monitoring depression
- Depression’s impact (and amelioration)

WHO GLOBAL BURDEN OF DISEASE: Disability-Adjusted Life-Years (DALYs)

1990	2020
1 Lower respiratory infection	1 Ischemic heart disease
2 HIV	2 Unipolar major depression
3 Conditions arising during the perinatal period	3 Road traffic accidents
4 Diarrheal diseases	4 Cerebrovascular disease
5 Unipolar major depression	5 Chronic obstructive pulmonary disease
6 Ischemic heart disease	6 Lower respiratory infections
7 Vaccine-preventable disease	

Murray & Lopez, WHO: Global Burden of Disease, 1996; Michaud, JAMA, 2001

How Depression is like Diabetes, Asthma CHF, and other Chronic Medical Disorders

- Biological underpinning
- Prevalent in primary care
- Chronic course, but can wax and wane
- Varying degrees of severity
- Monitoring and treatment adjustment essential
- Behavioral interventions as well as drugs
- Combined treatment often necessary

Five Myths of Depression Management

1. Screening/diagnosis is sufficient
2. Medications (i.e., antidepressants) are sufficient
3. Monotherapy is sufficient (and one dose fits all)
4. Most patients should achieve remission (nondepressed)
5. Site of care is primary care vs. specialty (mental health)

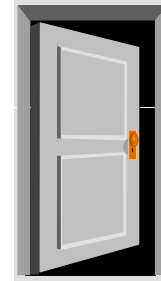
Realities of Depression Management

1. Screening/diagnosis is sufficient
 - Need systems in place to assist in optimal care
2. Medications (i.e., antidepressants) are sufficient
 - Need education, self-management, psychotherapy options
3. Monotherapy is sufficient (and one dose fits all)
 - Many patients will need dose adjustments, and a number of patients will need combined therapy
4. Most patients should achieve remission (nondepressed)
 - Patients will experience a wide range of improvement
5. Site of care is primary care vs. specialty (mental health)
 - Level of care should be integrated and tailored to response

Realities of Diabetes Management

1. Screening/diagnosis is sufficient
 - Need systems in place to assist in optimal care
2. Medications (i.e., insulin/oral agents) are sufficient
 - Need education, self-management, diet, exercise
3. Monotherapy is sufficient (and one dose fits all)
 - Many patients will need dose adjustments, and a number of patients will need combined therapy
4. Most patients should achieve remission (normal HgbA1C)
 - Patients will experience a wide range of HgbA1C levels
5. Site of care is primary care vs. specialty (endocrinology)
 - Level of care should be integrated and tailored to response

Colin Powell's Wife



4 Ways to Destigmatize Depression

1. Medicalize – neurotransmitter imbalance; analogy with hypertension; “chicken-egg”
2. Celebritize – famous people disclose
3. Publicize – media, schools, public health
4. Optimize – emphasis on treatability

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Case 1

- 70 y/o man with severe CHF
- Depressed mood, orthopnea, edema, dyspnea on walking 1 block, trouble sleeping, fatigue, irritable, decline in appetite, 12 lb weight loss, worries about a lot of things
- Wife diagnosed with breast cancer; he feels guilty he can’t help more.

Does he have major depression?

“SPACE DIGS” [9 DSM-IV Symptoms]

- | | |
|--------------------------------|---------------------|
| • S leep | • D epressed |
| • P sycho M otor | • I nterest |
| • A ppetite | • G uilt |
| • C oncentration | • S uicidal |
| • E nergy | |

more depression-specific

“SPACE DIGS” [9 DSM-IV Symptoms]

- ☆ • **S**leep
- ☆ • **D**epressed
- **P**sychomotor
- **I**nterest
- ☆ • **A**ppetite
- ☆ • **G**uilt
- **C**oncentration
- **S**uicidal
- ☆ • **E**nergy

more depression-specific

Support for inclusive approach

- Compared 2 groups of pts starting depression therapy
 - 235 with diabetes, CAD, or COPD
 - 204 pts without these diseases
- Of the 4 “somatic” symptoms (fatigue, weight/appetite changes, sleep disturbance, and psychomotor agitation/retardation), only fatigue a bit more common in medical pts (54% vs. 45%)
- All 4 somatic symptoms showed robust improvement with depression treatment and this improvement was similar in pts with and without medical comorbidity.

Simon and Von Korff, Psychol Med 2005;35:1-10

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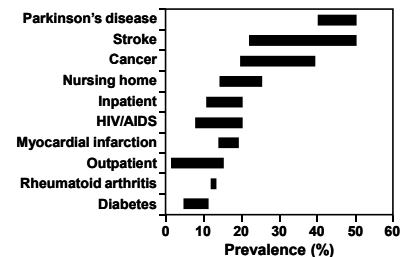
Comorbidity

- **Medical comorbidity**
 - Cardiovascular disease
 - CNS disease (stroke, dementia, ...)
 - Cancer
 - Other (HIV, diabetes, arthritis, ...)
- **Psychiatric – e.g., anxiety**
- **Physical symptoms – e.g., pain**

Medical Comorbidity

Depression can be treated safely and effectively

Prevalence of Depression in the Medically Ill and Elderly



Cohen-Cole et al. In: *Psychiatric care of the medical patient*. NY: Oxford University Press; 1993:53
Evans et al. *J Clin Psychiatry*. 1999;60(suppl 4):40

Medical Comorbidity

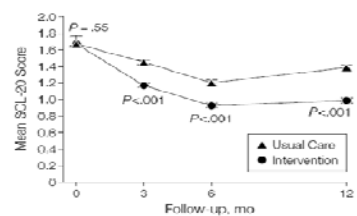
many diseases at least double depression risk

- **Cardiovascular disease**
 - MI, CHF, post-procedures, ...
- **CNS disease**
 - stroke, dementia, Parkinson's, ...
- **Cancer**
- **Other**
 - HIV, diabetes, arthritis, COPD, renal, ...)

Depression is Treatable in CAD

Trial	N	Treatment	Duration
SADHART	364	Sertraline	6 mo.
ENRICHD	2481	Cognitive-behavioral therapy	6 mo.
CREATE	284	Citalopram <i>and/or</i> Interpersonal psychotherapy	3 mo.
Bypassing the Blues	302	Telephone-based collaborative care	8 mo.

Figure 2. Mean SCL-20 Depression Score



IMPACT Trial

1801 Primary Care Patients with Late-Life (>60) Depression

Randomized to Care Management or Usual Care

Care Management
• Antidepressants, or
• Problem-Solving Therapy (PST)

Unutzer et al, JAMA 2002

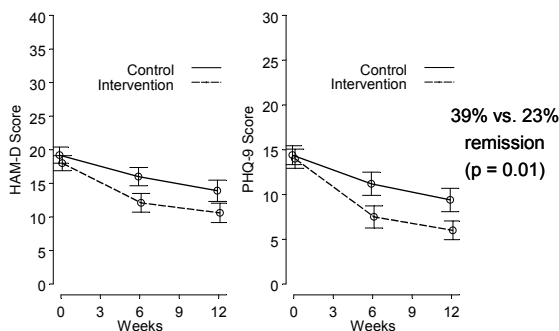
Scores on the 20 depression items from the Symptom Checklist-90 (SCL-20) ranged from 0 to 4. Error bars indicate SEs.

AIM Poststroke Depression Trial

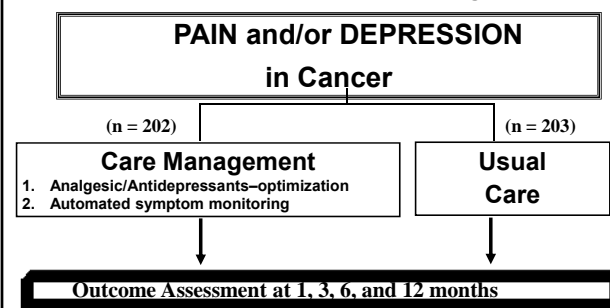
- 189 patients with at least moderately severe depression (mean HAM-D = 18.5) 4 weeks following a stroke
- Randomized to either depression care management or attention-placebo group
- Every other week care manager phone calls for 12 weeks, optimizing antidepressants in intervention group

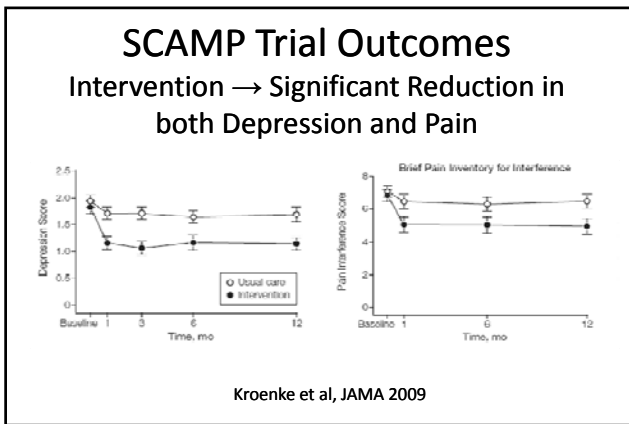
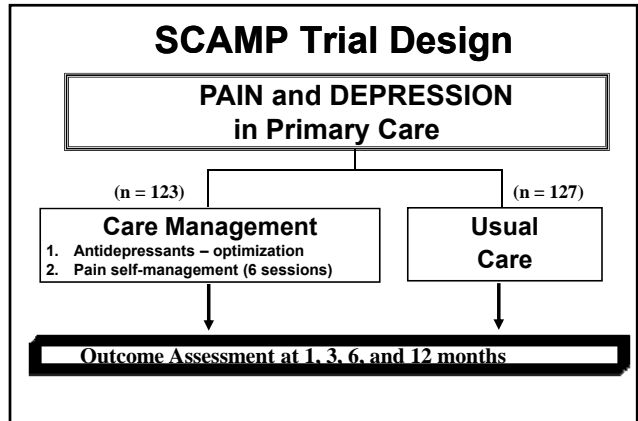
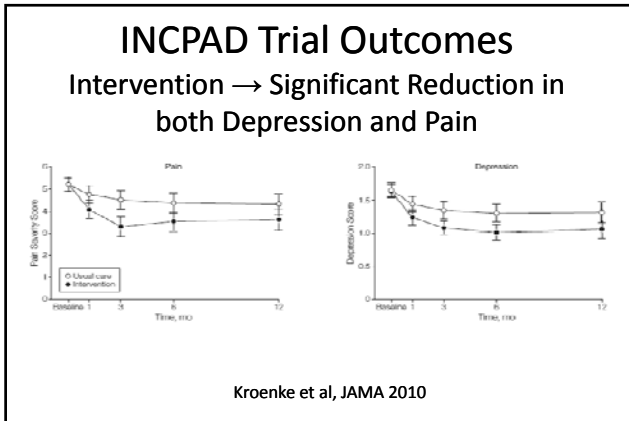
Williams, Kroenke, et al; Stroke 2007

AIM Poststroke Depression Trial Outcomes



INCPAD Trial Design





- ### Treating Depression in Arthritis
- 1801 depressed primary care older adults treated in IMPACT trial
 - 1001 (56%) had co-existing arthritis
 - Depression intervention also led to ↓pain severity and pain interference
 - Improvement for pain < depression (effect size of 0.3 vs. 0.6)
- Lin et al, JAMA 2003

TEAMCare Trial: Treating Depression and Medical Disease Simultaneously

- Collaborative care: 214 primary care pts with depression *plus* diabetes and/or CAD
- Nurse care manager/physician team co-managed depression, diabetes and CAD.
- Intervention significantly improved all 4 outcomes: depression, HgbA1C, LDL cholesterol, and blood pressure.

Katon et al, N Engl J Med 2010

Collaborative/enhanced care in medical settings improves depression in ...

Medical condition	1 st author	Year	†
Coronary artery disease	Rollman	2009	
Geriatric patients	Unutzer	2002	✓
Stroke	Williams	2007	✓
Cancer	Kroenke	2010	✓
Chronic pain	Kroenke	2009	✓
Arthritis	Lin	2003	✓
Diabetes and CAD	Katon	2010	

† Our site either led or participated in the trial

Impact of Comorbidity in Depression

- Decreases recognition
- Complicates treatment
- Aggravates time management (short visits with competing demands)
- Influences patient-MD communication (are symptoms medical or psychiatric?)
- Increases need for co-management (PCP, medical specialists, psychiatry)

Psychiatric Comorbidity

Comorbidity can be hidden and make depression more difficult to treat

Anxiety and Depression

Similarities

- Prevalent: 10-15% of primary care pts
- Comorbid: 30-50% overlap one another
- Common treatments
 - Antidepressants
 - Cognitive-behavioral therapy

Differences

- Anxiety – more diagnostic splitting
- Does anxiety have less
 - Disability?
 - Stigma?
 - Suicide risk?
- Anxiety – more differential treatments?

Common Anxiety Disorders (965 primary care patients)

Disorder	Prevalence	Disability Days (3 mo)
Posttraumatic stress	8.6%	12.5
Generalized anxiety	7.6%	18.1
Panic	6.8%	17.7
Social anxiety	6.2%	15.9

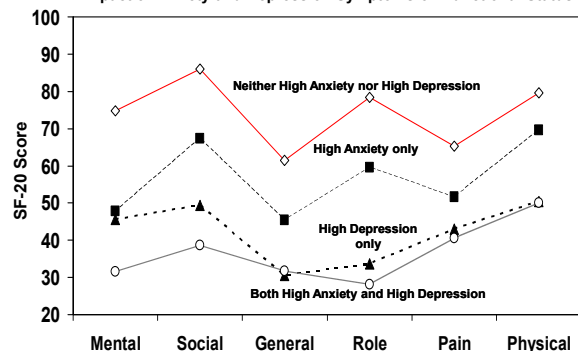
Kroenke et al, Ann Intern Med 2007

Importance of Measuring both Anxiety and Depression

- Survey of 2740 primary care patients
- Defining high anxiety as GAD-7 \geq 15, & high depression as PHQ-8 \geq 15
 - 3.2% had high depression only
 - 3.3% had high anxiety & high depression
 - 4.7% had high anxiety only – *which would be missed if screened for depression only*
- Anxiety and depression had additive & adverse effects on quality of life and disability

Kroenke, Ann Intern Med 2007; Kroenke, Psychosomatics 2009

Impact of Anxiety and Depression Symptoms on Functional Status



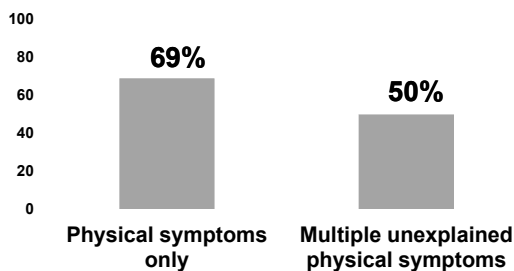
Alcohol and Depression

- Alcohol disorders are associated with a higher risk of depression, and vice-versa.
- Although it used to be thought depression could not be effectively treated in the presence of an alcohol disorder, simultaneous rather than sequential treatment is now recommended.
- Alcoholism increases the risk of treatment-resistant depression as well as suicide

Physical Symptom Comorbidity

Physical symptoms are the most common way depression presents

How do depressed patients present in primary care? (1146 cases of major depression, 14 countries)



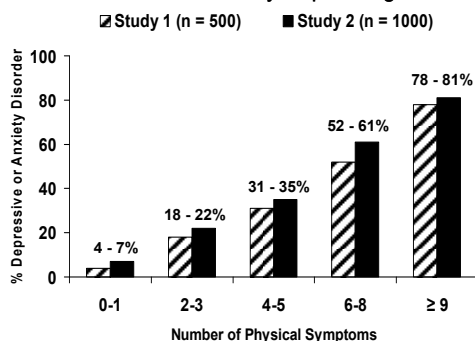
Simon, N Engl J Med, 1999

Unexplained Somatic Symptoms

	<u>Depression</u>	<u>Anxiety</u>
Abdominal pain	63%	53%
Chest pain	66%	49%
Dizziness	58%	52%
Short of breath	63%	46%
Headache	53%	46%
Back pain	54%	46%

Kroenke et al, Arch Fam Med, 1994

Symptom Count is an ESR for Psychopathologic Inflammation

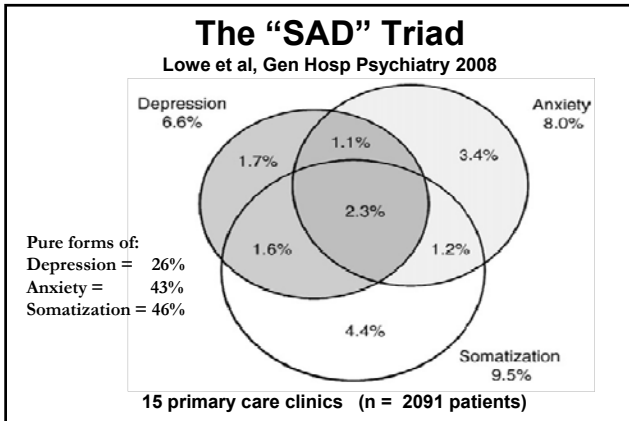


Kroenke & Resnicus, Med Clin North Am, 2006

Depression and Likelihood of Diagnosing a Physical Disorder

Clinic	N	Depression	Odds of physical disorder
Gastroenterol.	116	29%	0.28
Rheumatology	185	25%	0.24
Neurology	433	32%	0.29

O'Malley et al, J Psychosom Res, 1998; Arch Intern Med, 1998; Ekstrand, 2002



Medically Explained May not Explain

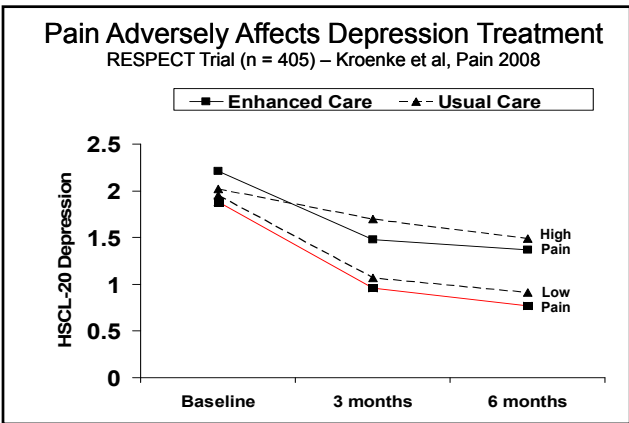
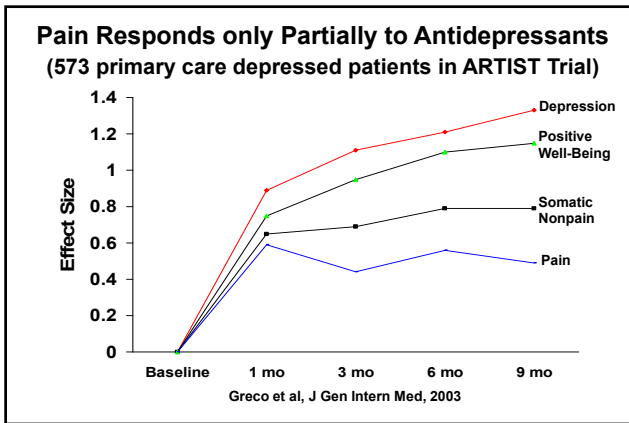
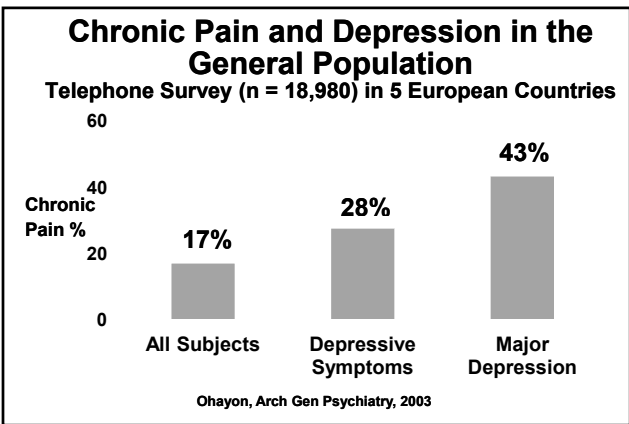
- Medline Search (1966-2006)
- 30 studies (N ~17,000)
- Relationship between disease-specific somatic symptoms and depression / anxiety in 4 diseases
 - Cardiac disease (CHF and CAD) n = 9
 - Pulmonary disease (Asthma & COPD) n = 9
 - Diabetes n = 7
 - Arthritis (Osteo- and Rheumatoid) n = 5
- Depression (anxiety) explained as much of the variance in disease-specific somatic symptoms as did physiological measures of disease severity

Katon, Lin, Kroenke, Gen Hosp Psychiatry 2007

The Problem of Pain

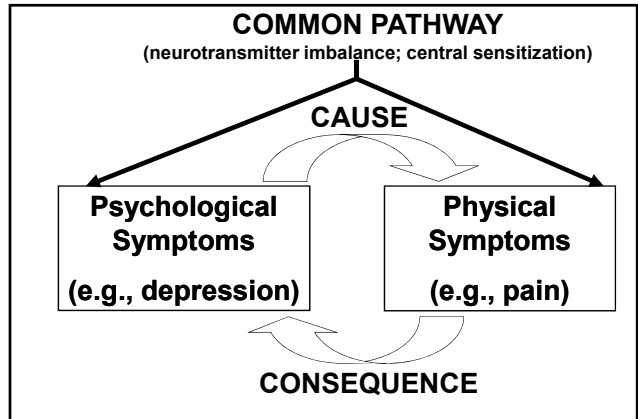
- 5th vital sign campaign
- Analgesics 2nd most prescribed drug class
- Opiate predicament
- Work disability – #1 cause
- CAM use – #1 reason
- Pain clinics – ? role

Time cover February 26, 2005.



Treatment Options for Pain in Patients with Depression

- Ask about pain when starting treatment for depression (or if treatment-resistant)
- Antidepressant selection (e.g., TCAs, SNRIs)
- Co-management of pain
 - Optimize analgesics
 - Multidisciplinary pain clinic referral
- Behavioral (psychological) therapies
 - Cognitive-behavioral therapy (CBT)
 - Pain self-efficacy programs



There is no conclusive evidence that any antidepressant is more effective (or faster-acting) than any other antidepressant

Therefore, antidepressant selection can be based upon costs, secondary conditions, and/or side effects

Comorbid Conditions That Might Favor a Particular Antidepressant

SSRI	Anxiety; CAD (sertraline; citalopram)
SNRI	Anxiety; Pain
Bupropion	Obesity; Sexual dysfunction; Smoking cessation
Mirtazapine	Anorexia; Insomnia

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Case 2

- A 72 y/o man reports 3 months of fatigue, trouble sleeping, no interest in family life or hobbies, irritability, and low mood.
- You diagnose major depression and start citalopram 20 mg qd
- He returns for follow-up in 2 weeks.
How would you determine, in your own practice, if he is getting better?

Case 2 – Answer Options

How would you treat this patient?

1. Ask him if he is feeling better, with a global question or two.
2. See how many of the 9 DSM-IV depressive symptoms he still has
3. Use a brief depression rating scale

Measurement Helps Disease Monitoring

Sphygmomanometer



Peak Flow Meter



Glucometer

I don't care what depression measure you use

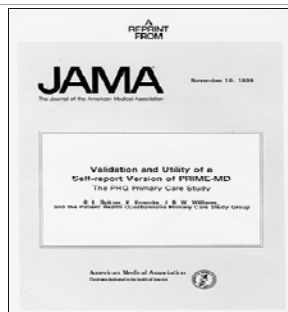
- Review of 16 scales (2-28 items)
 - 38 studies, 32,000 patients
 - Time to complete: 2-6 minutes
- Sensitivity = 85 %
Specificity = 74 %
+ Likelihood Ratio = 3

Williams et al, Gen Hosp Psychiatry, 2002

Ideal Symptom Measure

- Ultra-brief
- All-purpose
- Self-administered
- Free

The Patient Health Questionnaire (PHQ) Primary Care Study



PHQ Main Papers

Spitzer RL, Williams JBW, Kroenke K, et al

-- Validation in nearly 10,000 patients

- PRIME-MD study (n = 1000)
 - JAMA 1994; 272:1749-1756
- PHQ Primary Care study (n = 3000)
 - JAMA 1999; 282:1737-1744
- PHQ Ob-Gyn study (n = 3000)
 - Am J Ob Gyn 2000; 183:759-769
- PHQ GAD-7 study (n = 2740)
 - Arch Intern Med 2006; 166:1092-1097

PHQ - 9

1. Over the **last 2 weeks**, how often have you been bothered by the following problems?

	Not at all 0	Several days 1	More than half the days 2	Nearly every day 3
a. Little interest or pleasure in doing things	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
b. Feeling down, depressed, or hopeless	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
c. Trouble falling or staying asleep, or sleeping too much	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
d. Feeling tired or having little energy	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
e. Poor appetite or overeating	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
f. Feeling bad about yourself, or that you are a failure . . .	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>
g. Trouble concentrating on things, such as reading . . .	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>
h. Moving or speaking so slowly . . .	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
i. Thoughts that you would be better off dead . . .	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Subtotals:	3	4	9	
TOTAL = 16				

PHQ-9 as Severity Measure

- **Cutpoints** proposed on PHQ-9 for depression severity are:
 - ≥ 5 = mild
 - ≥ 10 = moderate
 - ≥ 15 = moderately severe
 - ≥ 20 = severe
- **Response to therapy** = 5 point ↓
- **Remission** = score < 5

PHQ-9 Observer Version (OV) for patients with advanced cognitive impairment

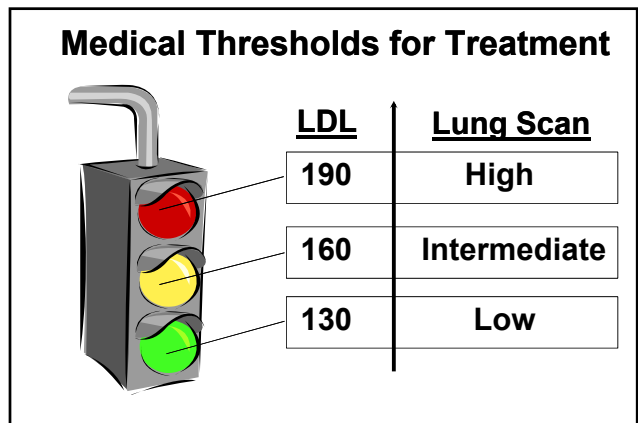
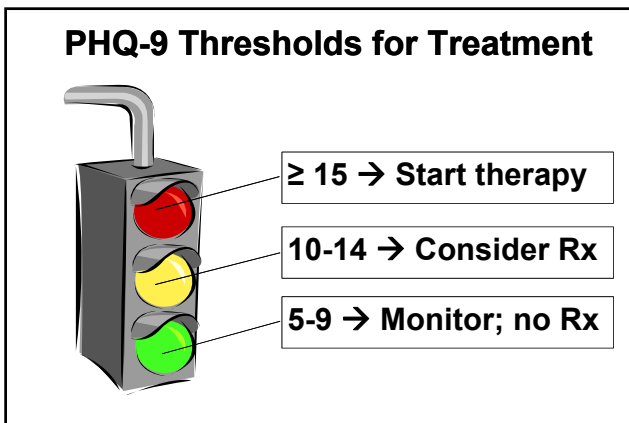
-- Has 10th item ("being short-tempered, easily annoyed")
-- First 4 items are shown below

a. Little interest or pleasure in doing things	ii. Symptom frequency			
	1-2 Days "Often"	3-5 Days "Some days"	6-10 Days "More than half the days"	11-14 Days "Nearly every day"
<input type="checkbox"/> 0: No <input type="checkbox"/> 1: Yes	0	1	2	3
<input type="checkbox"/> 0: No <input type="checkbox"/> 1: Yes	0	1	2	3
<input type="checkbox"/> 0: No <input type="checkbox"/> 1: Yes	0	1	2	3
<input type="checkbox"/> 0: No <input type="checkbox"/> 1: Yes	0	1	2	3

PHQ-9 Uptake

- Hundreds of publications
- > 60 different languages
- Guidelines (AMA, AHA, MacArthur, NICE in United Kingdom, VA, ...),
- Large healthcare systems (e.g., Kaiser, VA, Magellan, NYC, UK, ...)
- Surveys (MEPS, NHANES, BRFSS, ...)
- Medicare (all 16,000 nursing homes)

Kroenke, Spitzer, Williams, Lowe, Gen Hosp Psychiatry 2010



GAD-7

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all (0)	Several days (1)	More than half the days (2)	Nearly every day (3)
Feeling nervous, anxious, or on edge				
Not being able to stop or control worrying				
Worrying too much about different things				
Trouble relaxing				
Being so restless that it is hard to sit still				
Becoming easily annoyed or irritable				
Feeling afraid as if something awful might happen				

PHQ-4

Over the last 2 weeks, how often have you been bothered by the following problems?	Not at all (0)	Several days (1)	More than half the days (2)	Nearly every day (3)
Feeling nervous, anxious, or on edge				
Not being able to stop or control worrying				
Little interest or pleasure in doing things				
Feeling down, depressed, or hopeless				

PHQ Depression and Anxiety Scales

- 5, 10, and 15 = mild, moderate, and severe symptoms on both PHQ-9 and GAD-7
- For both depression and anxiety scales
 - Cutpoint of ≥ 10 on full scale has sensitivity of 88% and specificity of 82%
 - Cutpoint of ≥ 3 on short scale (2 core items) has similar operating characteristics
- PHQ-4 is a useful “ultra-short” screener

Kroenke et al, Gen Hosp Psychiatry 2010

Facts about Depression Scores

1. Scores typically do not substitute for talking with patients but facilitate it.
2. Scores “objectify” (validate) depression for patients
3. Scores are useful not only in primary care but all clinical settings including psychiatry
4. Scores can standardize communication & care among clinicians by using a common metric
5. Scores are more useful for treatment decisions than for diagnostic decisions.

www.phqscreeners.com

- Website with all scales in PHQ family
- All scales can be downloaded for free
- All currently available translations into other languages are also on website
- Up-dated bibliography and a few key articles can also be downloaded

A Brief Algorithm for Assessing Suicidality

The P4 Screener: Evaluation of a Brief Measure for Assessing Potential Suicide Risk in 2 Randomized Effectiveness Trials of Primary Care and Oncology Patients

Priyanka Dube; Kurt Kroenke, MD; Matthew J. Bair, MD, MSc; Dale Theobald, MD, PhD; and Linda S. Williams, MD

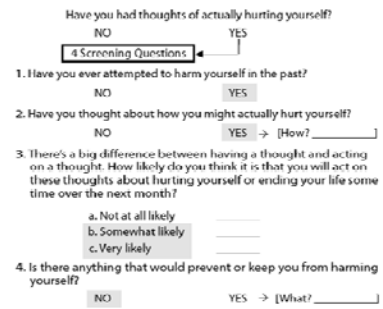
Primary Care Companion J Clinical Psychiatry
2010;12:e1-e8

9th item of the PHQ-9

How often have you been bothered by ...

- Thoughts that you would be better off dead or of hurting yourself in some way

Figure 1. Screener for Assessing Suicide Risk^{a,b}
P4 Screener^{a,b}



Dube P, et al. Primary Care Companion J Clinical Psychiatry 2010;12:e1-e8

P4 Suicidality Screener

- “Have you had thoughts of actually hurting (harming) yourself in some way?”

↓ IF YES

- “Do you have any specific plan of how you might hurt yourself?”
- “Have you ever tried to hurt or harm yourself in the past?”
- “How likely is it you will act on these thoughts?” (probability)
- “Is there anything preventing you from harming yourself

Suicidal Assessment Outcomes

- Most who endorse 9th item of PHQ-9 have passive thoughts (“life not worth living”) rather than active thoughts of self-harm
- Most respond “no” to the first 3 P’s
 - Plan for self-harm
 - Past history of suicidal attempt
 - Probability > low (“not at all likely”)
- Even if “on fence”, 3 F’s prevent action:
 - Family, Faith, and Fear of failing

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Depression Increases Mortality

Disease	Design	N	Risk ↑
Post-MI	Meta-analysis	6,367	2.4-2.6
CAD	Meta-analysis	11,018	1.8-2.3
Cancer	Meta-analysis	9,417	1.3-1.4
Diabetes	Cohort study	4,154	1.7-2.3
Stroke	Cohort study	51,119	1.2
RA	Cohort study	1,290	2.2
Community	Meta-analysis	106,628	1.8

van Melle, Psychosom Med 2004; Barth, Psychosom Med 2004; Satin, Cancer 2009; Katon, Diabetes Care 2005; Williams, Am J Psych 2004; Ang, J Rheum 2005; Cuijpers, J Aff Dis 2002

Adverse Impact of Depression on other Outcomes

- Increased noncompliance with medical treatment regimens (meta-analysis of 12 studies)
- Increased health care use and disability (population survey of 30,801 individuals)
- Poorer control of medical condition, worse prognosis, greater morbidity in patients with a variety of medical disorders (multiple studies).

DiMatteo, Arch Intern Med 2000; Egede, Gen Hosp Psychiatry 2007;

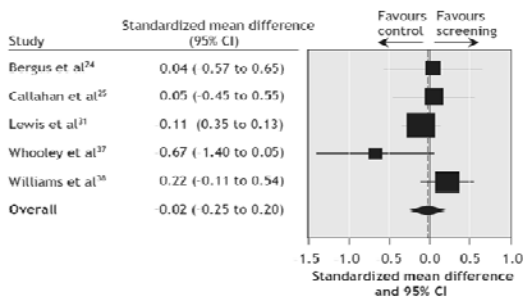
US Preventive Services Task Force Depression Screening Recommendation

The USPSTF recommends screening adults for depression when staff-assisted depression care supports are in place to assure accurate diagnosis, effective treatment, and follow-up. (Grade B recommendation)

“Staff-assisted depression care supports” refers to clinical staff that assist the primary care clinician by providing some direct depression care, such as care support or coordination, case management, or mental health treatment.

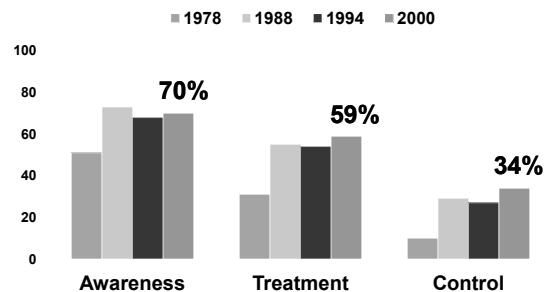
USPSTF, Ann Intern Med, 2009

Depression Screening Alone May Not Affect Patient Outcomes



Gilbody et al, CMAJ, 2008

Trends in Hypertension Awareness, Treatment & Control



Adherence to Depression Guidelines

- 1131 depressed primary care patients from 45 practices in 3 effectiveness trials
- Less than half completed minimal treatment
 - ≥ 2 months of antidepressant therapy
 - ≥ 4 sessions of psychotherapy
- Only 26% of elderly (≥ 65 y/o) completed minimal treatment.

Hepner, Ann Intern Med 2007

Adherence to Depression Guidelines (< 50% adherence to following areas – “SAD ME”)

- **S**uicidal assessment (ask; refer if +)
- **A**lcohol (& anxiety) screen if refractory
- **D**epression critical information
 - Past history of depression, including treatment
 - Severity of current depression (e.g., scale)
 - Bipolar
- **M**onitor response (adjust treatment)
- **E**lderly

Hepner, Ann Intern Med 2007

Barriers to Integrating Medical and Mental Health Care

- Payment constraints
- Privacy concerns
- Patient reluctance
- Psychiatric workforce

The mind may undoubtedly affect the body;
but the body also affects the mind.
There is a re-action between them;
and by lessening it on either side, you diminish the pain on both.

Leigh Hunt, an 18th century poet

