Understanding the Patient with Chronic Comorbid Medical and Psychiatric Conditions

Regional Conference

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American College of Physicians
Leading Internal Medicine, Improving Lives
Session 2: Understanding the Patient with Chronic Comorbid Medical and Psychiatric Conditions

Learning Objectives
1. Identify the most common psychiatric disorders occurring in patients with medical conditions.
2. Understand key issues in managing psychiatric disorders in patients with medical conditions.
3. Know how to treat patients who have pain or other physical symptoms with comorbid psychiatric disorders.
4. Consider tools and practice enhancements that improve outcomes in medical patients with psychiatric disorders.

Faculty

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Indiana University School of Medicine
Research Scientist
VA HSR&D Center for Implementing Evidence-Based Practice and Regenstrief Institute
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Kurt Kroenke, MD, is a professor of medicine at Indiana University, and a research scientist in the Regenstrief Institute and the VA Center of Excellence for Implementing Evidence-Based Practice. Dr Kroenke is a past president of the Society of General Internal Medicine and a past president of the Association for Clinical Research Training. His research focuses on physical and psychological symptoms in medical patients, including pain, depression, anxiety, and somatization. He has published more than 300 peer-reviewed publications. He is co-developer of the Patient Health Questionnaire (including the PHQ-9), which is a widely used measure for the detection and monitoring of common mental disorders.

Faculty Financial Disclosure Statement
The presenting faculty reports the following:

Kurt Kroenke, MD, receives a consulting fee from Eli Lilly and Company.
SESSION 4
1:30–2:30pm

Understanding the Patient with Chronic Comorbid Medical and Psychiatric Conditions

SPEAKER
Kurt Kroenke, MD

Learning Objectives

• Recognize how to detect the most common psychiatric disorders occurring in patients with medical conditions
• Understand key issues in managing psychiatric disorders in patients with medical conditions
• Know how to treat patients who have pain or other physical symptoms with comorbid psychiatric disorders
• Consider tools and practice enhancements that improve outcomes in medical patients with psychiatric disorders

What Do the Poets Say?

Two millennia ago (Ovid)
"I am no better in mind than in body; both alike are sick and I suffer double hurt."

Two centuries ago (Leigh Hunt)
"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."

Overlap of Medical and Psychiatric Disorders

Years Lived with Disability (YLD) in US

<table>
<thead>
<tr>
<th>Rank</th>
<th>Disease</th>
<th>YLD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Low back pain</td>
<td>3.2 million</td>
</tr>
<tr>
<td>2</td>
<td>Major depressive disorder</td>
<td>3.0 million</td>
</tr>
<tr>
<td>3</td>
<td>Other musculoskeletal</td>
<td>2.6 million</td>
</tr>
<tr>
<td>4</td>
<td>Neck pain</td>
<td>2.1 million</td>
</tr>
<tr>
<td>5</td>
<td>Anxiety disorders</td>
<td>1.9 million</td>
</tr>
<tr>
<td>6</td>
<td>Chronic pulmonary disease</td>
<td>1.7 million</td>
</tr>
<tr>
<td>7</td>
<td>Drug use disorders</td>
<td>1.3 million</td>
</tr>
<tr>
<td>8</td>
<td>Diabetes</td>
<td>1.1 million</td>
</tr>
<tr>
<td>9</td>
<td>Osteoarthritis</td>
<td>1.0 million</td>
</tr>
</tbody>
</table>


Depression Increases Mortality

| Disease            | Design      | N     | Risk  \\
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Post MI</td>
<td>Meta analysis</td>
<td>6,367</td>
<td>2.4-2.6</td>
</tr>
<tr>
<td>CAD</td>
<td>Meta analysis</td>
<td>11,018</td>
<td>1.8-2.3</td>
</tr>
<tr>
<td>Cancer</td>
<td>Meta analysis</td>
<td>9,417</td>
<td>1.3-1.4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Cohort study</td>
<td>4,154</td>
<td>1.7-2.3</td>
</tr>
<tr>
<td>Stroke</td>
<td>Cohort study</td>
<td>51,119</td>
<td>1.2</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>Cohort study</td>
<td>1,290</td>
<td>2.2</td>
</tr>
<tr>
<td>Community (overall)</td>
<td>Meta analysis</td>
<td>106,628</td>
<td>1.8</td>
</tr>
</tbody>
</table>


Depression & Anxiety are Similar to Diabetes, Asthma, CHF, & Other Chronic Medical Conditions

- 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

Case 1
David: A 68-year-old man
- Retired police sergeant, lives with his wife who is currently undergoing treatment for breast cancer
- Last three months
  - Increasing fatigue, trouble sleeping, forgetfulness, low mood
  - Worried about his wife’s health, medical bills
  - Thinking a lot more about death

David (cont)
- PMH: CHF controlled with meds, OA, BPH, recent DM diagnosis
- Meds:
  - lisinopril
  - metformin
  - carvedilol
  - tamsulosin
  - furosemide
  - low dose aspirin
  - codeine/APAP PRN
- Physical exam: normal vital signs and cardiopulmonary exam
- Labs notable for HbA1C = 8.2

“SPACE DIGS”
[9 DSM Symptoms for Major Depression]

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

more depression specific

Support for Inclusive Approach to Criteria

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

Depression Rates in Patients with Chronic Medical Conditions

<table>
<thead>
<tr>
<th>Medical Illness</th>
<th>Depression (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>22-29</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>17-27</td>
</tr>
<tr>
<td>Cerebrovascular</td>
<td>14-19</td>
</tr>
<tr>
<td>Alzheimer’s</td>
<td>30-50</td>
</tr>
<tr>
<td>Parkinson’s</td>
<td>4-75</td>
</tr>
<tr>
<td>Epilepsy</td>
<td></td>
</tr>
<tr>
<td>-- Uncontrolled</td>
<td>20-65</td>
</tr>
<tr>
<td>-- Controlled</td>
<td>3-9</td>
</tr>
<tr>
<td>Diabetes</td>
<td></td>
</tr>
<tr>
<td>(self reported)</td>
<td>9-26</td>
</tr>
<tr>
<td>(dx interview)</td>
<td>9</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>5-20</td>
</tr>
<tr>
<td>Pain</td>
<td>30-54</td>
</tr>
<tr>
<td>Obesity</td>
<td>20-30</td>
</tr>
<tr>
<td>General population</td>
<td>10-11</td>
</tr>
</tbody>
</table>


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)


David

His PHQ-9 score is 16, and you make a diagnosis of major depression, which he reluctantly accepts.

P4 Suicidality Screener

"Have you had thoughts of actually hurting (harming) yourself in some way?"

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


Suicidal Assessment Outcomes

- Most (~90%) who endorse 9th item of PHQ9 have passive thoughts (ie, “being better off dead”) rather than active thoughts of self-harm
- Most respond “No” to the first three P’s of P4, that is:
  - No plan for self harm
  - No past history of suicidal attempt
  - Probability of acting is “not at all likely”
- Even if “on fence,” four F’s often prevent action:
  - Family, Faith, Fear of failing, and Future hope


Medical Disease May Not Fully Explain Symptoms in Patients with Psychiatric Comorbidity

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

“Medical Depression” is Uncommon

- Most depression due to medical causes (cancer, CNS disease, etc) will have other signs and symptoms
- Depression preceding or comorbid with dementia is more common, whereas depression masquerading as dementia (ie, “pseudodementia”) is not common
- Lab testing has a low yield, although recent CBC, TSH, comprehensive chemistry profile, may be advisable
- Only a few medications (eg, steroids, interferon) are clearly linked to depression
- Temporal relationship to medication initiation is key

Depression is Treatable in Coronary Artery Disease

<table>
<thead>
<tr>
<th>Trial</th>
<th>N</th>
<th>Treatment</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>SADHART</td>
<td>364</td>
<td>Sertraline</td>
<td>6 mos</td>
</tr>
<tr>
<td>ENRICHED</td>
<td>2481</td>
<td>Cognitive-behavioral therapy</td>
<td>6 mos</td>
</tr>
<tr>
<td>CREATE</td>
<td>284</td>
<td>Citalopram and/or Interpersonal psychotherapy</td>
<td>3 mos</td>
</tr>
<tr>
<td>Bypassing the Blues</td>
<td>302</td>
<td>Telephone based collaborative care</td>
<td>8 mos</td>
</tr>
</tbody>
</table>

Antidepressant Drug Interactions

Cytochrome P450 Inhibition

- Most important enzymes are 2D6 and 3A4
- Rank ordered from “cleanest” to “dirtiest” antidepressant
  1. Escitalopram → the least interactions
  2. Most other antidepressants → intermediate
  3. Fluoxetine, paroxetine → the most potential interactions
- Drugs affected = psychotropics; cardiovascular; opiates; antiretrovirals; anticancer; etc
- Clinical significance not certain in many cases

Comorbid Conditions That Might Favor a Particular Antidepressant

<table>
<thead>
<tr>
<th>Antidepressant</th>
<th>Comorbid Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSRI</td>
<td>Anxiety, Coronary artery disease</td>
</tr>
<tr>
<td>SNRI</td>
<td>Anxiety, Pain</td>
</tr>
<tr>
<td>Buproprion</td>
<td>Obesity, Sexual dysfunction, Smoking cessation</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Underweight, Insomnia</td>
</tr>
</tbody>
</table>

Barriers to Depression Treatment

(Internet survey of 78,753 depressed persons)

<table>
<thead>
<tr>
<th>Barrier</th>
<th>% Respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Don’t want employer to know</td>
<td>64%</td>
</tr>
<tr>
<td>Embarrassed if friends knew</td>
<td>44%</td>
</tr>
<tr>
<td>Family would be disappointed</td>
<td>28%</td>
</tr>
<tr>
<td>Antidepressants are addicting</td>
<td>27%</td>
</tr>
<tr>
<td>Counseling raises bad memories</td>
<td>43%</td>
</tr>
</tbody>
</table>

Four 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
David: Take Home Points

- Same criteria are used for diagnosing depression in medical patients, but a particular emphasis on “Digs”
- The two “S” words (suicidality & stigma) should be addressed prior to starting treatment
- Escitalopram has the fewest drug drug interactions, while paroxetine and fluoxetine have the most
- Medications are not a common cause of depression

Case 2
Beth: A 38-year-old woman with pain

- Administrative assistant, single, lives alone
- Pain in neck, back, and legs that has been especially bothersome the past year
- Sleeps poorly, feels exhausted, and says, “my nerves are shot”
- Has had to take more sick days the last six months
- No pain relief from NSAIDs, gabapentin, cyclobenzaprine
- She tried one of her friend’s hydrocodone pills which helped her pain and she is requesting a prescription
- PE: Wgt =102 lb (BMI = 19), BP=96/60, pulse=92

Beth

- Labs normal including TSH
- Rheumatologist referral: fibromyalgia diagnosis, prescribed pregabalin

She is referred back to primary care for a three-month follow up
- Still complains of fatigue, insomnia, and irritability
- PHQ-9 depression score = 14 (normal < 10)
- GAD=7 anxiety score = 16 (normal < 10)
- AUDIT-C alcohol screen = 7 (normal < 4)
- She also is worried about not being able to lose weight

Depression Reduces Likelihood of a Physical Diagnosis in Referrals to Specialists

<table>
<thead>
<tr>
<th>Clinic</th>
<th>N</th>
<th>% Depressed</th>
<th>Odds of a Physical Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastroenterology</td>
<td>116</td>
<td>29</td>
<td>0.28</td>
</tr>
<tr>
<td>Rheumatology</td>
<td>185</td>
<td>25</td>
<td>0.24</td>
</tr>
<tr>
<td>Neurology</td>
<td>433</td>
<td>32</td>
<td>0.29</td>
</tr>
</tbody>
</table>


Association of Functional Somatic Syndromes with Depression and Anxiety

- Meta analysis of 244 studies:
  - Irritable bowel syndrome — Fibromyalgia
  - Nonulcer dyspepsia — Chronic fatigue
- Syndromes had greater association with depression and anxiety than healthy controls or patients with related, organic syndromes
- Effect size was modest (0.68) — thus, depression and anxiety do not entirely explain functional syndromes

Symptoms Must be Measured & Monitored Like Any Other Disease

- Sphygmomanometer
- Glucometer
- Peak Flow Meter

**PHQ-9, GAD-7, and PHQ-15 for Depression, Anxiety and Somatization**

- 5, 10, and 15 = mild, moderate, severe symptom thresholds on all 3 scales
- PHQ-2, GAD-2, and SSS-8 are ultra brief versions
- 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
- Download (with translations) at www.phqscreeners.com

**Antidepressants and Cognitive Behavioral Therapy for Functional Somatic Syndromes**

<table>
<thead>
<tr>
<th>Somatic Syndrome</th>
<th>TCA</th>
<th>SSRI</th>
<th>SNRI</th>
<th>CBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irritable bowel syndrome</td>
<td>++</td>
<td>+</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Back pain</td>
<td>+</td>
<td>–</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>Headache</td>
<td>++</td>
<td>–</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>++</td>
<td>±</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Neuropathic pain</td>
<td>++</td>
<td>–</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Chronic fatigue syndrome</td>
<td>–</td>
<td>–</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Tinnitus</td>
<td>±</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Menopausal syndrome</td>
<td>++</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other pain syndromes</td>
<td>+</td>
<td>–</td>
<td>±</td>
<td></td>
</tr>
</tbody>
</table>

**Special Issues in Women**

- Premenstrual/syndrome mood disorder
  - SSRIs and CBT effective for both PMS and PMMD; continuous better than intermittent/cyclic use
- Pregnancy
  - Antidepressants (AD) produce small increased risk of prematurity and low birth weight
  - AD & psychotherapy effective for postpartum depression
- Perimenopausal depression
  - SSRIs effective for both depression and hot flashes
- Intimate partner violence → 10 to 20% of depression

**Alcohol and Eating Disorders**

- Alcohol and eating disorders are associated with a much higher risk of depression
- For both, psychological treatments may be particularly important rather than antidepressants alone
- 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

**Beth: Take Home Points**

- Physical symptoms (both pain and nonpain) are a common presentation of depression and anxiety; particular if multiple, poorly explained, or persistent
- Monitoring and adjusting treatment by using brief patient reported measures can improve outcomes
- Cognitive behavioral therapy is the most evidenced based nonpharmacological treatment for psychological and physical symptoms

**Case 3**

**John: A 42-year-old accountant**

- Having trouble during tax season focusing on work
- Several episodes of palpitations, chest tightness, diaphoresis, dizziness; one spell waking him from sleep
  - BP taken at pharmacy: BP =170/96, P=102
- Daytime fatigue, feeling down, irritable
- Tried sertraline but stopped after two weeks because he didn’t like how it made him feel
- Uses marijuana and alcohol recreationally
- Thinks he might have adult ADHD and a prescription might help his concentration and performance
Distinguishing Anxiety from Depression

• **Similarities**
  – Each has prevalence of 10% to 15% in primary care
  – Commonly co-occur (30% to 50% of patients have both)
  – Both respond to antidepressants and CBT

• **Differences**
  – Anxiety has more subtypes (“diagnostic splitting”)
    – GAD, Panic, Social Anxiety, PTSD, OCD
  – Psychotherapy may be especially important for certain types of anxiety
  – Anxiety may have somewhat less disability, stigma, and suicide risk


Suspecting Bipolar Disorder

• **Family history** of bipolar disorder
• **Poor response** to antidepressants
• **Course:** onset at young age (< 20) or postpartum; rapid cycling
• **DIGFAST**
  – Distractability – Activity ↑ (hyber)
  – Insomnia – Speech pressured
  – Grandiosity – Thoughtlessness
  – Flight of ideas – Risky behaviors

Suspecting ADHD in Adults

• 2% to 4% of adults are estimated to have ADHD, but the prevalence is 10% if other psychiatric disorders are present
• Inattention > hyperactivity in adults
• By adulthood, 15% children who had ADHD still have full ADHD, 50% have partial ADHD, 35% resolved

**Common “clues”**
  – Still not “settled down” after age 30
  – Changes in jobs and relationships
  – Underachiever
  – Increased rates of accidents (MVA; other)
  – Unhealthy life style


Brief Screeners for Common Psychiatric Disorders

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Screener(s)</th>
<th>Items</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>PHQ-9( PHQ-2)</td>
<td>9 (2)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>GAD-7 (GAD-2)</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Somatization</td>
<td>PHQ-15 (SSS-8)</td>
<td>15 (8)</td>
</tr>
<tr>
<td>Alcohol</td>
<td>PHQ, AUDIT-C</td>
<td>8, 3</td>
</tr>
<tr>
<td>Eating</td>
<td>PHQ, SCOFF</td>
<td>6, 5</td>
</tr>
<tr>
<td>Bipolar</td>
<td>MDQ, PDI-4</td>
<td>13, 4</td>
</tr>
<tr>
<td>ADHD</td>
<td>ASRS, PDI-4</td>
<td>6, 4</td>
</tr>
<tr>
<td>Suicidality</td>
<td>P4</td>
<td>4</td>
</tr>
</tbody>
</table>


John (cont)

• Lab tests normal including electrolytes, creatinine, TSH, and ECG
• Diagnosed with mixed anxiety and depressive disorder (with features of GAD and some panic attacks)
• Started on low dose sertraline and alprazolam. Latter tapered off after eight weeks as sertraline dose optimized
• Symptoms partially improve, but stresses at work and interpersonal difficulties prompt a mental health referral for adjunctive psychotherapy

Multifactorial Interventions for Treating Psychiatric Disorders in Primary Care

• More than 40 randomized trials
• Most trials had care manager who provided patient education, communicated with physicians, and monitored treatment adherence and response
• Some trials also provided psychological treatments and/or direct linkages to a psychiatrist
• Tracking clinical response with a depression measure and adjusting therapy was an essential feature
• Many of the clinical contacts were telephone-based
• Improvement rates averaged 20% higher than usual care