Complex Cases: Medical diagnoses complicated by mental health symptoms

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Disclosure Statement:
Relevant financial relationships in the past 12 months

- Consultant/Speaker: None
Disclosure Statement:
Relevant financial relationships in the past 12 months

- Financial: I do not have any competing financial interests. In fact, I have nothing really to invest due to three primary factors:
Disclosure Statement:
Relevant financial relationships in the past 12 months

- Bipolar Disorder
- Depression and Somatic Symptom Disorders
What does a “Med-Psych” Doc do anyways?
## 2006 Internal Medicine Clinic Schedule

<table>
<thead>
<tr>
<th>Time</th>
<th>Pat.</th>
<th>Demographic</th>
<th>Reason for Visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00</td>
<td>JT</td>
<td>35 yo M</td>
<td>f/u lipids, depression</td>
</tr>
<tr>
<td>8:20</td>
<td>LN</td>
<td>59 yo M</td>
<td>f/u BP, depakote level (anger s/p traumatic brain injury)</td>
</tr>
<tr>
<td>8:40</td>
<td>MS</td>
<td>74 yo M</td>
<td>f/u CML treatment, insomnia</td>
</tr>
<tr>
<td>9:00</td>
<td>CF</td>
<td>66 yo W</td>
<td>Establish care: leg pain, anxiety</td>
</tr>
<tr>
<td>9:40</td>
<td>KA</td>
<td>41 yo W</td>
<td>Urgent: Upper respiratory symptoms (diabetic)</td>
</tr>
<tr>
<td>10:00</td>
<td>GW</td>
<td>50 yo M</td>
<td>Establish care: f/u from ER for non-cardiac CP</td>
</tr>
<tr>
<td>10:20</td>
<td>TM</td>
<td>25 yo W</td>
<td>f/u obesity, irritable bowel, borderline PD</td>
</tr>
</tbody>
</table>
Why Is This Talk Important?  
A Case of “Nanotechnology”

- Mr. H is a 56 year-old WM with a Master’s degree in political science who has a 20+ year history of episodic psychosis. Mr. H while “in preparation” for his evaluation issues the following chief complaint:

- “I have had recent anal probing and there are all kinds of things on earth being done through nanotechnology. It has caused me to think about suicide. I need a magnet to get rid of it.”
A Case of “Nanotechnology”
What would you do first?

• A. Offer him an oral antipsychotic
• B. Check a urine drug screen
• C. Initiate a monitoring plan to ensure safety
• D. Rectal Exam
Impact of a Pilot Educational Program to Improve Care the Med-Psych Way

- Internal medicine residents taught to evaluate and treat patients with psychiatric disorders
- 11-item test administered before the clinic experience and then at year’s end (evaluating retention of information)
Impact of a Pilot Educational Program to Improve Care the Med-Psych Way

Secondary Result:
General medicine faculty who were less than 10 years removed from medical school scored much lower on the 11-item test than faculty who had graduated from medical school more than 10 years ago (p = 0.04). This led to speculation that perhaps more experienced internists have a better psychiatric fund of knowledge.

Impact of a Pilot Educational Program to Improve Care the Med-Psych Way

Yours Truly

Older = Wiser?
State of Mental Health in America

Overall Ranking

States that rank in the top ten are in the Northeast and Midwest, while most states that rank in the bottom ten are in the South and the West.

Overall Ranking

<table>
<thead>
<tr>
<th>Rank</th>
<th>State</th>
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<th>Rank</th>
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<tr>
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<td>Minnesota</td>
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<td>New Mexico</td>
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<td>Connecticut</td>
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<td>Nebraska</td>
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<td>4</td>
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<td>Wyoming</td>
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<td>Alabama</td>
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<td>Rhode Island</td>
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<td>Michigan</td>
<td>49</td>
<td>Nevada</td>
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<td>16</td>
<td>Delaware</td>
<td>33</td>
<td>Texas</td>
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<td>Arizona</td>
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<td>17</td>
<td>Maine</td>
<td>34</td>
<td>Montana</td>
<td>51</td>
<td>Oregon</td>
</tr>
</tbody>
</table>
AM Northwest Interview: Highlighting the Mental Health Crisis in Oregon

NPR: Adventist Hospital Opens New Portland Psychiatric Center
by Kristian Foden-Vencil
Follow OPB | June 6, 2017 9:45 a.m. | Portland
The Emotional Wellness Center
Finalist, AABH Program of the Year 2018

Monday-Friday 8:30-5pm
Officially Opened: June 12, 2017
Officially Closing: June 7, 2019

“We want it to be inviting and warm and not as, maybe … psychiatric, if I can put it that way,” said Raj. “Sometimes psychiatric, we think cold, Spartan, let’s not do damage to anything. Here, patients say, ‘I can function normally. I do belong in an office, not in a place with a bed and four walls.’”

- The Lund Report
The Emotional Wellness Center – Part Deux
Finalist, AABH Program of the Year 2018

Monday-Friday 8:30-5pm

10101 SE Main St, Suite 3001
Portland, OR 97216

Officially Re-Opening for Medication Management Consultation and Transcranial Magnetic Stimulation Treatment.

Coming soon: esketamine delivery
Outline

- Cognitive Impairment/Changes
- Key Endocrinopathies
- Cardiovascular Disease
- Obesity?
- Medication issues
- Most importantly, your questions
How complex can “confusion” be?
Memory problems: How best to assess and address

The Journal of Family Practice • 915 views • 3 years ago

Y. Pritham Raj, MD discusses assessing your patients' cognitive function, and interventions to recommend for impaired memory.

EVIDENCE-BASED REVIEWS

Clearing up confusion


By Y. Pritham Raj, MD

Author and Disclosure Information
The Cache County Memory Study: 12 years and moving forward

The Cache County Study on Memory, Health, and Aging is internationally recognized as one of the world’s premier studies on healthy aging, memory and Alzheimer’s disease. Participants and family members can take great pride in the contributions they are making. The study was founded in 1995 by the Dean of the College of Family Life at Utah State University, Bonita Wyse. Dean Wyse recognized that Cache County had the greatest life expectancy of all U.S. Counties in the 1990’s and that...
Mr. D is a 65 year-old with heart disease (he had a stent placed 6 months ago) who has been complaining of vague chest pain and “stress” over the past two weeks. His vital signs have been fine, but...he looks really depressed and “not sharp.” You both conclude that it is probably depression that is driving his symptoms. You call my office asking about treatment for his symptoms...what should we do next?
Select the BEST option

1. Give him an antidepressant
2. Check him for bipolar disorder
3. Schedule another heart test right away
4. Screen him for memory impairment

Answer: Perhaps all of the above – which highlights how complicated these situations can be. But I am definitely interested in screening him for cognitive changes.
Select the BEST option

1. Give him an antidepressant
2. Check him for bipolar disorder
3. Schedule another heart test right away
4. Screen him for memory impairment
Screening for Cognition

• Mini-Cog: 3 item recall + clockface

• Six-item Screener (4 = impaired)
  – What year is this?
  – What month is this?
  – What day of the week is this?
  – Three item recall (1 minute)

  – Higher sensitivity (94%) than Mini-Cog (75%)

  » Wilber ST et al. Acad Emerg Med Volume 12, Issue7 612-616
Attention! A good bedside test for delirium?

Niamh A O’Regan,1 Daniel J Ryan,1 Eve Boland,2 Warren Connolly,2 Ciara McGlade,1 Maeve Leonard,3 Josie Clare,4 Joseph A Eustace,5 David Meagher,6,7 Suzanne Timmons1

ABSTRACT

Background Routine delirium screening could improve delirium detection, but it remains unclear as to which screening tool is most suitable. We tested the diagnostic accuracy of the following screening methods (either individually or in combination) in the detection of delirium: MOTYB (months of the year backwards); SSF (Spatial Span Forwards); evidence of subjective or objective ‘confusion’.

Methods We performed a cross-sectional study of general hospital adult inpatients in a large tertiary referral hospital. Screening tests were performed by junior medical trainees. Subsequently, two independent formal delirium assessments were performed: first, the Confusion Assessment Method (CAM) followed by the Delirium Rating Scale-Revised 98 (DRS-R98). DSM-IV (Diagnostic and Statistical Manual of Mental Disorders, fourth edition) criteria were used to assign delirium diagnosis. Sensitivity and specificity ratios with 95% CIs were calculated for each screening method.

Results 265 patients were included. The most precise screening method overall was achieved by simultaneously performing MOTYB and assessing for subjective/objective confusion (sensitivity 93.8%, 95% CI 82.8 to 98.6; specificity 84.7%, 95% CI 79.2 to 89.2). In older patients, MOTYB alone was most accurate, whereas in younger patients, a simultaneous combination of SSF (cut-off 4) with either MOTYB or assessment of subjective/objective confusion was best. In every case, addition of the CAM as a second-line screening step to improve specificity resulted in considerable loss in sensitivity.

Conclusions Our results suggest that simple attention tests may be useful in delirium screening. MOTYB used alone was the most accurate screening test in older people.
Cognitive Evaluation Importance
A Look at the Numbers

- 2009: 39.6 million people 65 and older (12.9% of the US population)
- 2030 projections: 72.1 million (19% of the population)
  » US Administration on Aging

- Alzheimer’s Stats:
  - 5.1 million have AD at present
  - National Institute on Aging data: prevalence of AD doubles every five years beyond age 65.
  » Alzheimer’s Foundation of America
Types of Dementia

- Alzheimer's disease.
- Vascular dementia.
- Dementia with Lewy bodies (DLB)
- Mixed dementia.
- Parkinson's disease.
- Frontotemporal dementia.
- Creutzfeldt-Jakob disease.
- Normal pressure hydrocephalus.

https://www.alz.org/alzheimers-dementia/what-is-dementia/types-of-dementia
Plaques and Tangles of: Alzheimer’s Disease

Beta amyloid “plaques”

Atrophy

Neurofibrillary Tangles ($p$-Tau protein)
Dementia By the Numbers

Two Medication Classes FDA Approved to Treat Dementia:

Cholinesterase Inhibitors – such as donepezil (Aricept), galantamine (Reminyl), and rivastigmine (Exelon)

Memantine (Namenda)

Zero Medications FDA approved to control behavior or agitation
What about Genetic Testing for AD

- Apolipoprotein E (APOE) ε4 allele genotype is a robust predictor of a person’s lifetime risk of developing AD
- Newer data suggests that knowing your genotype (patients age 52–89) affects verbal memory tests and subjective reports of memory – due to low “self-efficacy” (belief in one’s own abilities)
  - Informed ε4+ had worse test performance and recall than ε4+ uninformed group (p = .001)
  - Uninformed ε4+ rated memory better than uninformed ε4- on capacity scale (p = .03)

Vascular Dementia

- Vascular dementia is a general term describing problems with reasoning, planning, judgment, memory and other thought processes caused by brain damage from impaired blood flow to the brain.
- Happens typically in “step-wise” fashion.
- Can develop vascular dementia after a stroke but strokes don't always cause vascular dementia.
- Statistics vary widely as to the prevalence, but it is estimated that it affects between 1 percent and 4 percent of people over 65. That percentage doubles every five to 10 years after age 65.
Lewy Body Dementia/Disease

- Lewy body dementia causes a progressive decline in mental abilities. People with Lewy body dementia may experience visual hallucinations, and changes in alertness and attention.
- Other effects include Parkinson's disease-like symptoms such as rigid muscles, slow movement and tremors.
- Abnormal protein – alpha-synuclein
Case 1 continued…

- Mr D scored much lower than you expected on the memory tests for a college-educated man. He looks depressed but admits to issues with memory loss over time. He notes a remote history of smoking and used to drink heavily while filming Diff’rent Strokes – but that was years ago.
- So now the plot thickens. What is our next move?
Alcohol

- Third leading cause of preventable death in the United States (after smoking and obesity). Annually, 85,000 deaths are attributable at a cost of $185 billion.
Fig 1  White matter hyperintensities on magnetic resonance imaging (axial fluid attenuated inversion recovery sequence) in two 80 year old patients: (left) minor white matter hyperintensities; (right) extensive white matter hyperintensities predominating in
T2 White Matter Hyperintensities

- Predict an increased risk of stroke, dementia, and death. Therefore white matter hyperintensities indicate an increased risk of cerebrovascular events when identified as part of diagnostic investigations, and support their use as an intermediate marker in a research setting. Their discovery should prompt detailed evaluation for risk factors of stroke and dementia.

» Debette S. BMJ 2010;341:c3666
Case 1 Provisional Diagnosis: Cognitive Impairment, Not Dementia (CIND) or DSM-5 mild NCD

- According to the American Association of Geriatric Psychiatry (AAGP): CIND is a clinical syndrome consisting of measurable or evident decline in memory or other cognitive abilities with little effect on day-to-day functioning that does not meet criteria for dementia listed by the DSM.

- Neuropsychiatric symptoms (NPS) are nearly universal in dementia through the course of illness. As a result, and because NPS are associated with a worse prognosis in dementia, the occurrence of NPS in MCI/CIND is also of interest.

Wow, that was complex!
Got another one?
The Endocrine System – A Snapshot
A Complex Case of Schizophrenia?

- Over a 6 year period, a 45 year-old woman developed persecutory ideas, social withdrawal, self-neglect and a thought disorder.
A Complex Case of Schizophrenia?

- Over a 6 year period, a 45 year-old woman developed persecutory ideas, social withdrawal, self-neglect and a thought disorder. Some months before her admission to a psychiatric hospital, a psychiatrist noticed obesity and bruises on her forearms.
A Complex Case of Schizophrenia??
Cushing’s Syndrome

• NIH definition: Hormonal disorder caused by prolonged exposure of the body's tissues to high levels of the hormone cortisol. Sometimes called "hypercortisolism," it is relatively rare and most commonly affects adults aged 20 to 50.

• Causes:
  – pituitary adenoma (known as Cushing's disease)
  – adrenal hyperplasia or neoplasia
  – ectopic ACTH production (e.g. small cell lung cancer)
  – iatrogenic (steroid use)
Cushing’s Syndrome

Magnetic resonance image (GE-sequence, Gd-DTPA 0.1 mmol/kg)
Transverse T1-weighted slice through the upper pole of the left kidney shows a well-defined, lobulated mass in the left adrenal gland with attenuated contrast enhancement.
A Case of Low Energy

• 67 year-old woman with multiple sclerosis (MS) and chronic back pain – on both muscle relaxants and opiates – presents for low energy.

• She relates a remote history of taking thyroid replacement but stopped it either because of financial constraints or laboratory improvement (she’s not sure)

• Her neurologist had checked her TSH: 8.1 uIU/ml
What Would You Do Next?

• A. Start levothyroxine at 1.6 mcg/kg
• B. Ask instead, “what would Brown-Séquard do?”
• C. Repeat the TSH in a few weeks
• D. Start levothyroxine at 25 mcg/day and go up from there, adjusting every 6 weeks or so
• E. None of the Above
Subclinical Hypothyroidism

- Usual definition:
  - free T4 = normal
  - TSH elevated in the 4.5-10 uIU/ml range
  - Severe when TSH is 10-20 uIU/ml

- Key drugs associated: amiodarone, lithium, interferon
Our Low Energy Case Continued

- She’s now in your office after you chose to repeat the labs:

<table>
<thead>
<tr>
<th>Component Results</th>
<th>Value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>4.64</td>
<td>0.34 – 5.60 uIU/ml</td>
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</table>

<table>
<thead>
<tr>
<th>Component Results</th>
<th>Value</th>
<th>Range</th>
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</thead>
<tbody>
<tr>
<td>FREE T4</td>
<td>0.7</td>
<td>0.6 – 1.2 ng/dL</td>
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</table>
USPSTF: Routine thyroid screening?

Thyroid Dysfunction: Screening
Release Date: March 2015

Recommendation Summary

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<th>Population</th>
<th>Recommendation</th>
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<tr>
<td>Nonpregnant, asymptomatic adults</td>
<td>The USPSTF concludes that the current data are insufficient to assess the balance of benefits and harms of screening for thyroid dysfunction in nonpregnant, asymptomatic adults. The American Thyroid Association recommends thyroid dysfunction screening after age 35, with a recheck every 5 years.</td>
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Depression and Hypothyroidism

<table>
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<tr>
<th>Hypothyroidism symptoms that indicate treatment</th>
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<tr>
<td><strong>With psychiatric overlap</strong></td>
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<tr>
<td>Fatigue</td>
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<tr>
<td>Hypersomnolence</td>
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<tr>
<td>Cognitive impairment (forgetfulness)</td>
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<tr>
<td>Difficulty concentrating/learning</td>
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<tr>
<td>Weight gain/fluid retention</td>
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<tr>
<td><strong>Somatic symptoms</strong></td>
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<tr>
<td>Dry, itchy skin</td>
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<tr>
<td>Brittle nails and hair</td>
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<tr>
<td>Constipation</td>
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<tr>
<td>Myalgias</td>
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<tr>
<td>Heavy and/or irregular menses</td>
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<tr>
<td>Increased miscarriage risk</td>
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<tr>
<td>Cold sensitivity</td>
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</tbody>
</table>
Depression and Subclinical Hypothyroidism

• Subclinical hypothyroidism found to carry 3x higher lifetime depression prevalence in young and middle-aged women


• Subclinical hypothyroidism can contribute to treatment-resistant depression

For which co-morbid medical condition would you have the lowest threshold to start thyroid replacement?

- A. Systemic lupus erythematosus (SLE)
- B. Congestive heart failure (CHF)
- C. Restless leg syndrome (RLS)
- D. Irritable bowel syndrome (IBS)
- E. All of the Above
Figure 1. Thyroid function and HF progression: the vicious pathophysiological circle.

Anthony Martin Gerdes, and Giorgio Iervasi Circulation. 2010;122:385-393

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So it sounds like: not only should we SCREEN, but we should TREAT subclinical hypothyroidism?
Subclinical hypothyroidism: Merely monitor or time to treat?


**Discussant:** Y Pritham Raj, MD

Thyroid dysfunction enters the differential diagnosis for most mood, anxiety, thought, and cognitive disorders. Because more than one-half of the estimated 27 million Americans with hyperthyroidism or hypothyroidism are undiagnosed, the American Thyroid Association recommends universal screening for thyroid dysfunction after age 35, with a recheck every 5 years. Although some clinicians feel this recommendation is excessive, strategic screening with a thyroid-stimulating hormone (TSH) test is important for patients with psychiatric illnesses.

Valproic acid may have little difficulty initiating levothyroxine replacement (typically 1.6 mcg/kg/day) for patients with overt hypothyroidism. Treating hyperthyroidism (low TSH and high T4) can be more complex and generally is left to an internist or endocrinologist. But how should you treat subclinical thyroid dysfunction?

**Treat or wait?**

Subclinical hypothyroidism (SH)—in which T4 is normal—usually is a laboratory diagnosis defined in a spectrum:

- TSH of 4.5 to 10 mU/L is mild SH (80% of cases)
- TSH of 10 to 20 mU/L is more severe SH
Subclinical Hypothyroidism

• Actually, perhaps NOT.
• Observation may be the best strategy especially in the elderly because although easy to treat, other data demonstrated no correlation between mood and SH. And although statistically significant associations were seen among anxiety, cognition, and elevated TSH, the magnitude of the associations lacked clinical relevance.

Subclinical Hypothyroidism

- Persons 85-89 years of age in the Leiden 85-Plus study with higher TSH levels and lower free thyroxine levels had a survival benefit.

- HR for mortality per SD increase of 0.21 ng/dL (2.67 pmol/L) of free thyroxine increased 1.16-fold (95% CI, 1.04-1.30; \( P = .009 \)).

Subclinical Hypothyroidism

• In a prospective observational study the TSH of >37% of patients with SH returned to normal with observation alone.

• In fact, <27% of patients with SH went on to develop overt hypothyroidism during the study period, on average within 31.7 months.

Subclinical Hypothyroidism

Bottom Line

Practice Points

- Subclinical thyroid dysfunction is largely a laboratory diagnosis that merits observation but not necessarily treatment.

- Watchful waiting is preferable in patients age ≥65 with mild subclinical hypothyroidism (TSH <10 mU/L) unless they have prominent mood, cognitive, or medical conditions—such as congestive heart failure or hyperlipidemia—that could benefit from early thyroid replacement.

- In adults age <65, consider TSH 4.5 to 10 mU/L as a threshold for initiating thyroid replacement, particularly if anti-TPO antibodies are present (although prevailing recommendations still favor the watchful waiting approach).⁶

Surks MI, Ortiz E, Daniels GH, et al. Subclinical thyroid disease scientific review and guidelines for diagnosis and management. JAMA. 2004;291(2):228-238.
Hyperthyroidism (low TSH, High Free T4) For treating, think B-blockers

<table>
<thead>
<tr>
<th>Hyperthyroidism symptoms</th>
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<tbody>
<tr>
<td>Psychiatric overlap</td>
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<tr>
<td>Decrease or increase in appetite</td>
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<tr>
<td>Insomnia</td>
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<tr>
<td>Fatigue</td>
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<tr>
<td>Mood instability</td>
</tr>
<tr>
<td>Irritability</td>
</tr>
<tr>
<td>Anxiety, nervousness</td>
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<tr>
<td>Somatic signs and symptoms</td>
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<tr>
<td>Frequent bowel movement, e.g., diarrhea</td>
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<tr>
<td>Heart palpitations</td>
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<tr>
<td>Heat intolerance</td>
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<tr>
<td>Increased sweating</td>
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<tr>
<td>Light or missed menstrual periods, fertility problems</td>
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<tr>
<td>Muscle weakness</td>
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<tr>
<td>Shortness of breath</td>
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<tr>
<td>Sudden paralysis</td>
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<tr>
<td>Tremor, shakiness, dizziness</td>
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<tr>
<td>Vision changes</td>
</tr>
<tr>
<td>Weight loss or gain</td>
</tr>
<tr>
<td>Thinning of hair</td>
</tr>
<tr>
<td>Itching and hives</td>
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<tr>
<td>Possible increase in blood sugar</td>
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</tbody>
</table>

Hyperthyroidism:
I was taught that b-blockers actually cause depression, isn’t that true?

• According to one large meta-analysis (35K patients on b-blockers), fatigue and sexual dysfunction, yes. But depression, NO.
  » Ko DT et al. JAMA 2002;288:351-357

• Another prospective multicenter trial (254 pts on b-blocker and 127 comparison) showed no difference on Beck Depression Inventory at 3, 6, and 12 months.
The causal association between b-blockers and depression would be:
Which Augmentation Strategy for Major or Treatment-resistant Depression are you most FEARFUL of?

A. 2nd Antidepressant (such as bupropion)
B. Lithium
C. Atypical antipsychotics
D. Lamotrigine
E. Thyroid hormone

F. Transcranial Magnetic Stimulation
G. Intranasal esketamine
STAR*D
4041 Patients
Citalopram

30% Remission
Higher dose – 41.8mg
Longer duration – 47 days

565 Non-Remitters Augmented for 12 weeks with:

Bupropion SR
DA + NE reuptake inh.
Max: 400mg
39% Remission

Buspirone
5HT-1A partial agonist
Max: 60mg
32.9% Remission

Cognitive Therapy

STAR*D
Non-remitters with Citalopram and a 2\textsuperscript{nd} Agent

142 patients enrolled in 3\textsuperscript{rd} stage 14 week trial with:

- **Lithium**
  - Max: 900mg
  - 15.9\% Remission

- **Triiodothyronine (T(3))**
  - Max: 50ug
  - 24.7\% Remission

*AJP. 2006 Sep;163(9):1519-30*
TMS (transcranial magnetic stimulation) – 18 minute outpatient procedure typically done daily for 4-6 weeks approved by the FDA in October ‘08 for Treatment-resistant depression
Mr. B is a 55 yo man with single vessel CAD and stage I HTN who presents complaining of vague chest pain and “stress” over the past two weeks. His vital signs, exam and ECG are normal. He looks depressed so you astutely give him a PHQ-9 screening questionnaire. His score returns 20/27 and you both conclude that it is probably depression that is driving much of his symptom complex. He would like pharmacotherapy for his major depression…
Cardiovascular Disease (CVD) Drives 25-Year Loss in Life Expectancy Among the Mentally Ill

- 50% to 80% of patients with diagnosable mental illness are smokers, as compared with approximately 25% of the US population as a whole
- The mentally ill are less likely to undergo revascularization procedures and are more likely to die following an MI
- People with severe mental illness are up to two times more likely to have diabetes, dyslipidemia, hypertension, obesity, and/or metabolic syndrome

SADHART

- Successful treatment of depression can lead to a significant improvement in quality of life for patients with heart disease.

- Specifically, showed the safety of treating acute-MI or unstable-angina patients with sertraline. The 24 week randomized trial of 369 patients found that sertraline was both safe and effective.

Various SADHART Trial publications including:
- Circulation 2003;108:939-44
Power of Prayer?
Monitoring and Actualization of Noetic TRAinings

- Noetic interventions are defined as "a healing influence performed without the use of a drug, device or surgical procedure." 4 noetic therapies—stress relaxation, imagery, touch therapy, and prayer—were piloted with heart patients undergoing acute coronary interventions.
- Patients who received noetic therapies were shown to have a 25 to 30 percent reduction in adverse outcomes (such as death, heart failure, post-procedural ischemia, repeat angioplasty or heart attack) than those without such therapies. Of the individual noetic arms, the absolute incidence of adverse outcomes during the index hospitalization was lowest overall in patients assigned to off-site prayer.
Integrative noetic therapies as adjuncts to percutaneous intervention during unstable coronary syndromes: Monitoring and Actualization of Noetic Training (MANTRA) feasibility pilot
Mitchell W. Krucoff, MD et al. Durham, NC

Table I. Off-site prayer group methods

<table>
<thead>
<tr>
<th>Affiliation</th>
<th>Location</th>
<th>No. praying</th>
<th>Prayer, frequency and duration</th>
<th>Information provided</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unity School of Christianity Buddhist</td>
<td>Unity Village, Mo</td>
<td>NA</td>
<td>24-h vigil, 30 d in lighted chapel Medicine Buddha mantra; evenings, 1 h</td>
<td>Patient name, ailment</td>
</tr>
<tr>
<td>Buddhist</td>
<td>Nalanda Monastery, France</td>
<td>18</td>
<td>Medicine Buddha mantra, mantra of the deity that wears a leaf robe</td>
<td>Patient name, ailment</td>
</tr>
<tr>
<td>Buddhist</td>
<td>Kopan Monastery, Nepal</td>
<td>150 monks</td>
<td>Medicine Buddha mantra, mantra of the deity that wears a leaf robe</td>
<td>Patient name, ailment</td>
</tr>
<tr>
<td>Catholic Jewish</td>
<td>Carmelite Monastery, Towson, Md</td>
<td>17</td>
<td>Daily mindfulness and vespers Printed prayer placed in Western Wall</td>
<td>Patient name, ailment</td>
</tr>
<tr>
<td>Catholic</td>
<td>Virtual Jerusalem, Israel</td>
<td>NA</td>
<td>Daily prayers and motivation by Holy Spirit</td>
<td>Patient name, ailment</td>
</tr>
<tr>
<td>Fundamentalist Christian</td>
<td>Abundant Life Christian Center, Sanford, NC</td>
<td>Congregation</td>
<td>Daily prayers and motivation by Holy Spirit</td>
<td>Patient name, ailment</td>
</tr>
<tr>
<td>Baptist Moravian</td>
<td>Elkin, NC</td>
<td>3 congregations</td>
<td>Daily prayers and alter prayer Daily prayer service</td>
<td>Patient name, ailment</td>
</tr>
<tr>
<td></td>
<td>Raleigh, NC</td>
<td>8</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

NA, Not available.
Heart and Soul Study
Can you be scared to death?

- Patients with stable coronary heart disease (CHD) plus generalized anxiety disorder (GAD) have a 74% higher risk of experiencing cardiovascular events such as stroke, myocardial infarction, and death than patients with CHD only. Even after adjusting for depression, the risk was 62% higher.

Anxiety and Stroke

• In 6019 patients in the First National Health and Nutrition Examination Survey followed for 16.29±4.75 years, a total of 419 incident stroke cases were identified from hospital/nursing home discharge reports and death certificates.

• Reporting more anxiety symptoms at baseline was associated with increased risk of incident stroke after adjusting for other cardiovascular risk factors. Findings persisted when additionally controlling for depression.

» Lambiase MJ et al. Stroke. Published online before print December 19, 2013, doi: 10.1161/STROKEAHA.113.003741
Long-term Benzodiazepines for Anxiety
A Few Words About The Benzos

- Best if used for a SHORT period of time
- Multiple risk factors for dependence
  - Alcoholics
  - Use of benzos with short half lives/rapid onset of action (xanax, valium, halcion, tranxene)*
  - Use of higher potency benzos (klonopin, xanax, ativan, valium)*
- Associated with Falls in the elderly**
- Suppress REM sleep and stage 3 and 4 sleep

* Brand names used for purposes of easy identification

**
Complex Metabolic Case

• Mrs. C is a 60 year-old woman with a history of diabetes mellitus type 2 who has not been adhering well to her insulin and is beginning to have issues with peripheral neuropathy. When asked why she often skips her insulin she answers: “What’s the point? Every time I use insulin, I seem to gain weight – I hate it!”
Obesity Trends* Among U.S. Adults
BRFSS, 1985
(*BMI ≥30, or ~ 30 lbs. overweight for 5’ 4” person)

Source: Behavioral Risk Factor Surveillance System, CDC.
Obesity Pandemic over the Decades

[Images showing maps of the United States indicating obesity rates across different decades (1990, 1999, 2009). The maps use color coding to represent different percentage ranges of obesity.]
Obesity Pandemic - 2017
US Prevalence

Prevalence\(^\text{†}\) of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2017

\(^\text{†}\)Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.
Research Disclaimer:
I was the site primary investigator for Orexigen at Duke in ‘04-’06 during the phase III trial of what has become known as Contrave® which was approved for marketing in the United States in 2014.
Key CDC Statistics

- **COSTS**: More than one-third (34.9% or 78.6 million) of U.S. adults are obese. The estimated annual medical cost of obesity in the U.S. was $147 billion in 2008 U.S. dollars; the medical costs for people who are obese were $1,429 higher than those of normal weight.

- **DEMOGRAPHICS**: Non-Hispanic blacks have the highest age-adjusted rates of obesity (47.8%) followed by Hispanics (42.5%), non-Hispanic whites (32.6%), and non-Hispanic Asians (10.8%).

- **SOCIOECONOMICS**: There is no significant relationship between obesity and education among men. Among women, however, there is a trend—those with college degrees are less likely to have obesity compared with less educated women.
1 in 6.7 Americans receive Food Stamps
Any Correlation to Obesity?
Increased Weight and Dementia

• A study of 8,534 Swedish twins, suggests just being overweight is a risk factor for dementia.
• About one out of every 20 people above the age of the 65 has dementia. The Alzheimer's Society reports a healthy lifestyle could reduce the risk.
• Those with a body mass index (BMI) greater than 30 were 288% more likely to develop dementia than those with a BMI between 20 and 25.

Current NIH/WHO Definitions:

- **Overweight**: BMI 25–29.9 kg/m²
- **Class 1 obesity**: BMI 30–34.9 kg/m²
- **Class 2 obesity**: BMI 35–39.9 kg/m²
- **Class 3 obesity**: BMI ≥40.0 kg/m²

BMI correlates with total adiposity, morbidity & mortality
Weight-associated Mortality

Relative Mortality

Moderate

Very Low

Low

Moderate

High

Very High

Men, age < 65

Women, age < 65

Men, age > 65

Body Mass Index (kg/m²)
BMI Correlates with Pain

- Survey of over 1 million Americans
- BMI 25-29  20% more pain
- BMI 30-34  68% more pain
- BMI 35-39  136% more pain
- BMI >40  254% more pain

Stone et al.
Cancer and Obesity

• Review by the International Agency for Research on Cancer (IARC) found that those who avoid gaining weight can decrease their risk for developing 5 types of cancer: cancer of the colon, esophagus, kidney, breast, and uterus. The new research links excess weight with cancers of the stomach, liver, gallbladder, pancreas, ovary, thyroid and even includes meningioma and multiple myeloma.

• "The review certainly concluded crystal clear, as you say, that obesity causes cancer," said Graham Colditz, MD, who chaired the IARC review.

BMI or Waist-Hip Ratio
Apples to Apples or Apples to Pears?
BMI may not be “gold standard”
Think Waist-Hip Ratio

• NHANES III with 15,184 adults (52.3% women) aged 18 to 90 years.

• Results: Persons with normal-weight central obesity had the worst long-term survival. For example, a man with a normal BMI (22 kg/m²) and central obesity had greater total mortality risk than one with similar BMI but no central obesity (hazard ratio [HR], 1.87 [95% CI, 1.53 to 2.29]), and this man had twice the mortality risk of participants who were overweight or obese according to BMI only (HR, 2.24 [CI, 1.52 to 3.32] and 2.42 [CI, 1.30 to 4.53], respectively). Women had similar findings.

Stress/Burnout – Linked to Obesity?

ABDOMINAL FAT ACCUMULATION

Normal Stress

High Stress
## Medication-Related Weight Gain: antidepressants

<table>
<thead>
<tr>
<th>Drug</th>
<th>Weight Gain</th>
<th>Diabetes</th>
<th>QTc Prolongation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SSRI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>+</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>+</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>+</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>+</td>
<td>N/A</td>
<td>+/-</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>++</td>
<td>N/A</td>
<td>+/-</td>
</tr>
<tr>
<td>Sertraline</td>
<td>+</td>
<td>N/A</td>
<td>+/-</td>
</tr>
<tr>
<td><strong>Atypical Agent</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupropion</td>
<td>N/A</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>++++</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td><strong>SNRI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Desvenlafaxine</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Milnacipran</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>N/A</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td><strong>Serotonin Modulator</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trazodone</td>
<td>+</td>
<td>N/A</td>
<td>+/- (dose dependent)</td>
</tr>
<tr>
<td>Vilazodone</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Nefazodone</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>TCA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>+++</td>
<td>N/A</td>
<td>+++</td>
</tr>
<tr>
<td>Desipramine</td>
<td>+</td>
<td>N/A</td>
<td>+++</td>
</tr>
<tr>
<td>Doxepin</td>
<td>++++</td>
<td>N/A</td>
<td>+++</td>
</tr>
<tr>
<td>Imipramine</td>
<td>++++</td>
<td>N/A</td>
<td>+++</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>+</td>
<td>N/A</td>
<td>+++</td>
</tr>
<tr>
<td>Trimipramine</td>
<td>++++</td>
<td>N/A</td>
<td>+</td>
</tr>
<tr>
<td><strong>MAOI</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Phenelzine</td>
<td>++</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Selegiline</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Tranycypromine</td>
<td>+</td>
<td>N/A</td>
<td>N/A</td>
</tr>
</tbody>
</table>

Special Thanks to Jacob McFarland, PharmD
Medication-Related Weight Gain: second generation antipsychotics

Side effects associated with second generation antipsychotics

<table>
<thead>
<tr>
<th>Drug</th>
<th>Weight Gain</th>
<th>Diabetes</th>
<th>QTc Prolongation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olanzapine</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Clozapine</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
</tr>
<tr>
<td>Paliperidone</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Quetiapine</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Risperdone</td>
<td>+++</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Asenapine</td>
<td>++</td>
<td>+</td>
<td>+/-</td>
</tr>
<tr>
<td>Iloperidone</td>
<td>++</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Aripiprazole</td>
<td>+</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>+/-</td>
<td>+/-</td>
<td>+/-</td>
</tr>
<tr>
<td>Ziprasidone</td>
<td>+/-</td>
<td>+/-</td>
<td>++</td>
</tr>
</tbody>
</table>
Physical Activity

Think Walk, NOT Exercise
Exercise Equivalent to Pharmacotherapy

• SMILE study: 16 weeks of aerobic exercise training was comparable to that of standard medication (Zoloft) and combined exercise/meds for depression

Exercise Equivalent to Pharmacotherapy

- SMILE study: 16 weeks of aerobic exercise training was comparable to that of standard medication (Zoloft) and combined exercise/meds for depression.

- 10 Month Continuation study: Remitted subjects in the exercise group had significantly lower relapse rates than subjects in the medication group.
Pearl: Consensus Recommendation for Physical Activity

- Adults should accumulate at least 30 minutes of moderate-intensity physical activity (not necessarily exercise) each day
- This is equivalent to walking about 1.5 miles at a pace of 3-4 mph
- Doing more exercise and perhaps more strenuous exercise may provide additional health benefits

Statement endorsed by American College of Sports Medicine/Centers for Disease Control and Prevention, American Heart Association, NIH, the Surgeon General, and US Dietary Guidelines 2005
Dietary Approach

Then

Now
Preaching to the Choir: Vegetarianism Anyone?

- The adjusted hazard ratio (HR) for all-cause mortality in all vegetarians combined vs nonvegetarians was **0.88 (95% CI, 0.80-0.97)**.
- Vegans: **0.85 (95% CI, 0.73-1.01)**
- Lacto-ovo-vegetarians: **0.91 (95% CI, 0.82-1.00)**
- Pesco-vegetarians: **0.81 (95% CI, 0.69-0.94)**
- Semi-vegetarians: **0.92 (95% CI, 0.75-1.13)**

Significant associations with vegetarian diets were detected for cardiovascular mortality, noncardiovascular noncancer mortality, renal mortality, and endocrine mortality.
Rates of Major Cardiovascular Events
Mediterranean Style

1. Mediterranean diet supplemented with extra-virgin olive oil: hazard ratio 0.70 (95% confidence interval [CI], 0.54 to 0.92)

2. Mediterranean diet supplemented with mixed nuts: 0.72 (95% CI, 0.54 to 0.96)

3. A control diet = advice to reduce dietary fat

Final Complex Case:
Any Case Involving the “S” Word
Suicide Statistics

• Every day 86 Americans take their own lives and another 1,500 attempt (largest proportion is women).

• Suicide rated as 11th leading cause of death

  » CDC Data

• Receiving a diagnosis of dementia (especially early) increases a person's risk for suicide, particularly if symptoms of depression and anxiety are present. Nursing home admission was ironically associated with lower suicide risk (OR: 0.3)

US Suicide Statistics (2014)

Source: US Centres for Disease Control and Prevention
Near-Suicide
Thank You

*Fortune Favors the Prepared Mind*

- Louis Pasteur